

# Recruitment Strategies in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) Trial

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The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial is a randomized, multicenter clinical trial using a double 2 × 2 factorial design in 10,251 participants with type 2 diabetes mellitus at high risk for cardiovascular disease (CVD) events. ACCORD is testing 3 complementary medical treatment strategies that may reduce high rates of major CVD morbidity and mortality in patients with type 2 diabetes. The ACCORD vanguard phase, conducted at 59 clinics in the United States and Canada, recruited 1,174 participants in 20 weeks from January through June 1, 2001, with a recruitment efficiency (R-factor) of 0.65. The recruitment strategies used in this vanguard phase were almost exclusively chart and database review within clinical practices and institutions. Recruitment for the main trial began in February 2003, involved 77 clinics, and resulted in an additional 9,077 participants by October 29, 2005 (total, 10,251). The R-factor during main trial recruitment was 0.96. Although new and refined recruitment strategies were formulated from the vanguard experience, the most powerful determinant of improved recruitment efficiency was the immediate start of enrollment by most clinics at the beginning of the main trial. Recruitment in the main trial required only a brief extension of 3 months and facilitated the nearly complete capture of the expected number of person-years of observation. Described herein are vanguard and main trial recruitment activities, including strategy implementation, screening procedures, randomization results, problems encountered, and lessons learned. © 2007 Elsevier Inc. All rights reserved. (Am J Cardiol 2007;99[suppl]:68i–79i)

The timely recruitment of clinical trial participants is important for achieving the required number of person-years to answer the research question. In the past, clinical trials often experienced significant delays in completing recruitment.<sup>1–3</sup> If goals were not obtained within the planned recruitment period, investigators had to increase the number of clinical

sites, enhance centralized recruitment efforts, and/or extend the recruitment period to ensure that the expected person-year goals were met.<sup>1,4</sup> More recently, better planning has led to improved recruitment, and several trials have recruited within their planned time frames with no significant loss of person-years.<sup>5–7</sup>

In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, a vanguard phase was conducted to assess

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the feasibility of key aspects of the trial, such as achieving treatment goals and obtaining valuable information about screening and recruiting for the main trial. The ACCORD trial infrastructure includes clinical sites in each of 7 clinical center networks (CCNs) and the Coordinating Center, which were identified by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH). The 7 CCN offices manage the clinical sites financially and logistically. Each clinic had extensive and well-documented recruitment plans for the trial. Representatives of all CCNs, the NHLBI Project Office, and the Coordinating Center formed the Recruitment and Retention Subcommittee, which provided guidance, support, and communication for recruitment in the vanguard and main trial recruitment periods.

Descriptions of the ACCORD rationale, design and methods, interventions, and substudies are presented elsewhere in this supplement.<sup>8-12</sup> This report describes issues related to vanguard and main trial recruitment, including the implementation of recruitment strategies, screening procedures and visits, staff training, randomization results, problems encountered, and lessons learned.

## Methods

**Recruitment strategies:** Clinical trial recruitment activities included planning, developing, and testing materials, as well as the implementation, review, and refinement of procedures. Preparation for recruitment began well before the start of randomizations. Clinical sites identified their richest recruitment sources on the basis of success in past trials or advice from experienced recruiters within their CCNs. Centralized training for CCN and clinical site staff members regarding recruitment, protocol management, and operational issues was provided in September 2000 for the vanguard phase and again in January 2003 for the main trial. Some CCNs with geographically dispersed clinics held additional regional training sessions before the start of recruitment. CCNs with clinical sites in close geographic proximity held monthly meetings to review recruitment strategies.

The ACCORD vanguard phase had a recruitment goal of 1,000 subjects within 20 weeks. A total of 59 clinical sites, distributed among all 7 CCNs, participated in the vanguard phase. Because of the short recruitment duration, a limited number of strategies could be fully developed and implemented. The focus was placed on potential participants who were readily available (ie, existing clinical site patients), so a practice-based or institution-based strategy was the primary recruitment approach used. Specific strategies, which varied by clinic, included prescreening potential participants through chart reviews, database searches, and, to a lesser extent, bulk mailing to patients on diabetes mellitus registries, as well as Web-based promotion. Secondary strategies included media-based approaches and community outreach.

The vanguard phase recruitment exceeded its goal of 1,000 participants. However, it was apparent that successful recruitment in the main trial phase would require more broadly based strategies. In preparation for main trial recruitment, clinical sites were provided tools to track progress, such as weekly recruitment worksheets, customized by CCNs, which monitored the efficacy of specific approaches, the materials used, and the amount of effort (staff time) involved. Clinical sites were encouraged to maintain  $\geq 3$  active recruitment strategies at all times. Although some strategies were successful at one time or for some clinical sites, it was worthwhile to repeat some strategies even if they were unsuccessful at other times or other sites.

Table 1 lists strategies used in the main trial and whether they originated with the study overall, a CCN office, or a clinical site. Strategies and materials were shared by communication among Recruitment and Retention Subcommittee representatives and with all clinical sites through weekly updates and individual CCN conference calls. An example of a strategy spread throughout the trial was the "refer-a-friend" idea (asking a recruited participant to refer a friend to ACCORD), which many clinical sites found to be an easy and effective approach that also helped bond current participants to the trial.

To facilitate recruitment for the main trial, the Recruitment and Retention Subcommittee developed and compiled a variety of tools into a single reference source, the Recruitment and Adherence Survival Kit. A similar resource was used in the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) for adherence.<sup>13</sup> The resource used materials and approaches from the vanguard phase and organized strategies and procedures to be easily usable by clinic staff members.

Materials designed for use with medical professionals and institutions included PowerPoint software (Microsoft Corporation, Redmond, WA) presentations that could be used for grand rounds or local meetings of physicians, certified diabetes educators, pharmacists, and nurse practitioners; sample newsletters and flyers for hospital staff members; a sample letter to hospital administrators requesting support for the trial; and a sample letter clinics could send to physicians describing the trial and requesting patient referrals. Media promotional tools included sample dialogues for use on radio or television; press releases, which were adapted for local area specifications and referred to those used nationally; suggestions for contacting media and preparing clinics for large volumes of screening calls; and suggestions for site-specific campaigns, such as targeting rural, urban, minority, or closed medical systems. Examples of materials for community recruitment included suggested lists of patient support groups to contact, a colorful and artistic PowerPoint presentation for potential participants with a script for use by clinic staff members, flyers for health fairs, and issues to consider in displaying posters and brochures and while gathering information and talking with

potential participants. Survival kit binders including the tools were sent to each clinical site; most items were also available on the ACCORD Web site to download and customize for individual clinic use. All recruitment materials received review by local institutional review boards (IRBs) for human subjects, as necessary.

At least 3 CCNs used some type of central recruitment strategies. The Minnesota-Iowa (MN-IA) CCN model, presented as an example, was a natural product of clinical site proximity, a desire for efficiency, and past experience at the Berman Center for Outcomes & Clinical Research in Minneapolis, Minnesota (a CCN hub), in recruiting a large study population from within the metropolitan area of Minneapolis-St. Paul for the Women's Health Initiative (WHI).<sup>14</sup> Five clinical sites in the MN-IA CCN are located in that metropolitan area, which can be reached effectively using targeted strategies with multiple media sources. Central recruitment efforts, used in a limited capacity during the vanguard phase, included a press release and newspaper advertisements. During the main trial, central recruitment activities included mailings to insurance plan members; purchased mailing lists on the basis of disease state; and television, radio, and print advertisements, articles, and interviews. The communications manager and the CCN project manager coordinated and monitored efforts.

**Screening, informed consent, and run-in:** Full consenting included all procedures done as part of screening, run-in, randomization, intervention, and follow-up. These procedures are described elsewhere in this supplement.<sup>9</sup> Screening and consent processes varied by clinical site, but all required review and approval by local IRBs. Consenting for the screening phase alone (if required by the local IRB) allowed a shorter document for screening, reserving the more complete description of the study for those who appeared eligible. Screening and run-in procedures were to be conducted over 1 or 2 screening visits, depending on the IRB-approved recruitment strategy and the amount of prescreening data to be collected. As a result of the vanguard phase experience, many clinical sites and some CCNs developed more effective telephone prescreening protocols for the main trial.

Prescreening for the vanguard phase, which was primarily by chart review or through databases maintained by clinical sites, occurred before the Health Insurance Portability and Accountability Act (HIPAA)<sup>15</sup> went into effect. For the main trial, local HIPAA guidelines dictated how databases and patient charts could be accessed. Databases could be queried to identify patients who met eligibility criteria such as age, glycosylated hemoglobin (HbA<sub>1c</sub>), and creatinine level. Potential participants were introduced to the trial through phone calls, mailings, or other approaches. Chart screening effectively identified some inclusion and exclusion criteria,<sup>9</sup> although additional tests to establish eligibility (eg, cholesterol level, electrocardiographic findings, HbA<sub>1c</sub>, blood pressure, microalbuminuria) were some-

Table 1  
Recruitment strategies by their originating sources

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- Studywide strategies
    - NIH announcement
    - NIH brochures/posters
    - National recruitment toll-free number
    - National recruitment central Web site
    - Recruitment and Adherence Survival Kit
    - Recruitment video
  - Clinical network-level strategies
    - Public service announcements
    - Radio advertisements
    - TV advertisements
    - Bus advertisements
    - Small and large newspaper circulations
    - Media interviews
    - Data queries from databases
    - Mailings from databases/purchased lists
    - NIH brochures sent with letters to primary care providers
    - Established satellite clinical sites in an effort to capture people from all parts of a town
    - Established regional CCN Web sites and toll-free numbers for recruitment
    - Insurance company letter based on member glycosylated hemoglobin level
    - CDA and ADA Web site links
    - E-mail distribution lists
    - Church events and newsletters
    - Bookmark for placement in local bookstores and libraries
    - Air banner over the state fair
  - Clinical site-level strategies
    - Ambassador program or “refer-a-friend” campaigns
    - Local public service announcements
    - Articles and advertisement in local paid and free magazines and community newspapers
    - Radio advertisement
    - Cable TV interviews
    - Health fairs
    - Various local professional or layperson newsletters
    - Review and recruitment from existing clinics/practices
    - Referrals from primary care and specialty clinics
    - VA approvals to recruit nonveterans (2 clinical sites)
    - Group screenings
    - Special in-service for referring physicians and other health professionals
    - Cardiology, nephrology, neurology clinic screenings
    - Medical staff referrals
    - Regional diabetes mellitus fair
    - Talks at grand rounds and other CME meetings
    - Working with local diabetes associations and national affiliates
    - Diabetes expo

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ADA = American Diabetes Association; CDA = Canadian Diabetes Association; CCN = clinical center network; CME = continuing medical education; NIH = National Institutes of Health; VA = US Department of Veterans Affairs.

times necessary. For potential participants well known to clinical center staff members, much of the eligibility data were collected in advance, and few potential participants required >1 screening visit. The recruitment of potential participants outside of clinical sites was more labor intensive. Because of limited medical record information for prescreening, prospective participants often required addi-

tional screening visits to obtain necessary medical record information and test results for eligibility.

Potential candidates scheduled for clinic screening visits were instructed to report in a fasting state, bring their current medications and self-monitoring blood glucose records, and bring support persons to the visits. The details of the protocol were discussed, and screening consent or full-trial informed consent was obtained. Eligibility status for all 3 components of the trial (glycemia, lipids, and blood pressure) was assessed, and related procedures were performed. If a subject was determined to be provisionally eligible, a second screening visit was scheduled to finalize eligibility. If an individual was screened and found to be ineligible, rescreening could occur.

A run-in procedure, although never validated, is commonly used in trials to identify potentially poor adherence.<sup>16</sup> Although these procedures have traditionally focused on the ability to tolerate medical interventions, willingness to regularly test blood glucose was seen as crucial in ACCORD. Candidates were asked to provide evidence that they had regularly monitored their capillary blood glucose levels  $\geq 2$  times per day for  $\geq 2$  weeks before randomization. A glucose meter and testing supplies were provided if necessary. An 80% frequency of blood glucose monitoring was recommended as a guideline for predicting good adherence, with the decision to randomize individuals with lower frequencies of monitoring left to the discretion of the clinical site principal investigators.

For potential participants who had clinic screening visits during the main trial, clinical site staff members collected answers to at least the first 11 questions on the inclusion and exclusion summary form used to determine eligibility; 95% of these data were completed. These questions included information on diabetes diagnosis, age, sex, race or ethnicity, history of clinical cardiovascular disease (CVD) events (including specific categories for myocardial infarction, stroke, angina, and revascularization procedures), and HbA<sub>1c</sub> levels. These data were compared between subjects eventually enrolled in the study and those not enrolled.

**Recruitment efficiency:** The recruitment efficiency (R-factor), a convenient statistic for measuring the efficiency of the recruitment process, is the ratio of the number of person-years actually accrued divided by the number of person-years expected during the planned recruitment period.<sup>1</sup> In ACCORD, as in other trials, the estimated sample size assumes a constant rate of recruitment over the recruitment period, illustrated by a straight line initiating from the origin of the graph (zero participants at time zero) to 100% sample size at the expected date of completion; an R-factor of 1 is 100% efficiency. Calculating the area under the curve of the recruitment line identifies the proportion of expected person-years during recruitment.<sup>17</sup> We used the R-factor to determine the recruitment efficiency for the vanguard and main trial recruitment phases separately.

## Results

The recruitment goal in the vanguard phase was 1,000 participants enrolled in a 20-week period after the first randomization, which occurred on January 11, 2001. Total randomizations exceeded the planned goal and reached 1,174. A 3-week extension was allowed so potential participants who had been successfully screened but not yet randomized were allowed to enroll. The last vanguard participant was randomized on June 1, 2001.

Figure 1 shows the cumulative number of participants randomized during the vanguard phase over time compared with the cumulative goal (left axis). Also shown is the cumulative number of active clinical sites (right axis). Only 10 of the 59 clinics were active in the first month. As more centers became active during the second, third, and fourth months, the slope of the recruitment line increased sharply. The resultant R-factor was 0.65, indicating that one third of the observed person-years anticipated were lost during this recruitment phase. Because the number of participants randomized in the vanguard phase was small relative to the size of the entire ACCORD cohort, and the vanguard recruitment period was short, the impact on overall power is very small.

The recruitment goal for the main trial was the remaining 8,826 participants over a 30-month period beginning February 2003 and including all 77 main trial clinical sites. Vanguard participants are included with main trial participants in the ACCORD follow-up. The study goal of 10,000 participants was exceeded, with a final number of 10,251 participants randomized. The 10,000th participant was randomized on September 30, 2005, which was 2 months after the original planned closing date of recruitment. To allow clinical sites to deal fairly with those already screened and eligible, randomization was extended 1 additional month until October 29, 2005.

Figure 2 illustrates the number of participants randomized compared with the goal and the number of active clinical sites by week during the main trial recruitment period. The number of active clinical sites was nearly at maximum from the beginning. Actual recruitment was nearly superimposed on the goal line until about 90 weeks. The loss in recruitment efficiency is the triangular area bounded by the goal line and the line of actual performance. The calculated R-factor for ACCORD main trial recruitment was 0.96.

Prescreening data reveal that for the vanguard phase, participants were obtained from phone contact (10%), chart review (38%), and clinic visits (50%), a pattern consistent with using local clinic populations as the primary recruitment strategy. In the main trial, participants were obtained from phone contact (42%), chart review (36%), and clinic visits (0%), a pattern consistent with using outside recruitment sources as the primary strategy.

The MN-IA CCN central recruitment model described previously had significant randomization yields. Central and

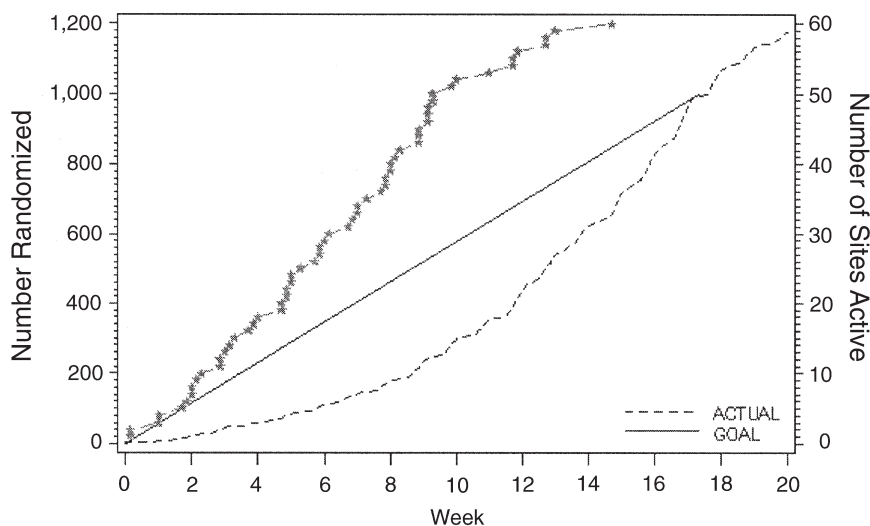


Figure 1. Cumulative number of Action to Control Cardiovascular Risk in Diabetes (ACCORD) vanguard participants randomized (dotted curve; left y-axis), compared with the goal over time (solid curve; x-axis). The cumulative number of clinical sites active is also indicated (starred curve; right y-axis).

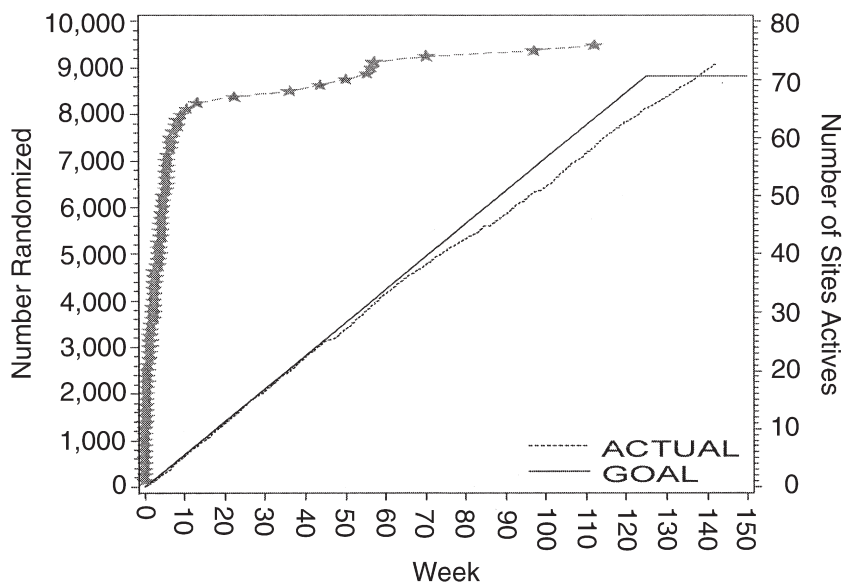


Figure 2. Cumulative number of Action to Control Cardiovascular Risk in Diabetes (ACCORD) main trial participants randomized (dotted curve; left y-axis), compared with the goal over time (solid curve; x-axis). The cumulative number of clinical sites active is also shown (starred curve; right y-axis).

site efforts yielded 144 randomized participants within the 4-month vanguard period. During the main trial, the central CCN recruitment process referred 954 participants to their 5 local clinical sites for further screening, ranging from 89 to 314 potential participants per site. Of the 954, 324 (34%) were randomized. The percentage of randomizations at each site due to MN-IA CCN central efforts ranged from 11% to 59%.

The characteristics of potential participants seen in clinics for screening visits during the main trial but not randomized were similar to those of randomized participants (Table 2). Distributions of race or ethnicity and history of CVD were within 2 percentage points between the groups. Mean and median ages were within 1 year. About 2% of

nonrandomized screenees did not have diabetes diagnoses for >3 months' duration as required, and 6% did not have stable diabetes treatment therapy for  $\geq 3$  months.

Baseline characteristics for the vanguard and main trial participants are listed in Table 3. Study recruitment goals were 50% women, 33% racial or ethnic minority patients, and 40% secondary prevention patients (ie, those with existing CVD). Almost 40% of vanguard participants and 38.4% of main trial participants were women. Secondary prevention participants represented 34.6% of the vanguard participants and 35.3% of the main trial participants. There was a greater proportion of racial or ethnic minorities enrolled in the vanguard phase (42.5%) than the main trial phase (37.0%). Vanguard participants were slightly older,

Table 2  
Main trial recruitment: comparison of randomized and nonrandomized participants

Screening Form Information	Not Randomized (n = 7,514)	Randomized (n = 9,077)
Diagnosis of type 2 diabetes mellitus >3 mo duration (%)	98	100
Stable diabetes treatment therapy >3 mo (%)	94	100
Women (%)	42	38
Race/ethnicity		
White or Caucasian (%)	64	65
Black or African American (%)	21	19
Asian (%)	2	6
French Canadian (%)	1	2
American Indian (%)	2	1
Native Hawaiian or other Pacific Islander (%)	0	0
Other race (%)	5	6
Multiple race (%)	1	0
Spanish, Hispanic, or Latino origin (%)	6	7
Secondary prevention (%)	35	35
Previous myocardial infarction (%)	15	15
Previous stroke (%)	7	6
Previous angina and/or ischemic changes (%)	10	11
Previous CABG procedure (%)	11	11
Previous PTCI/PTCA/atherectomy procedure (%)	11	12
Previous carotid artery revascularization (%)	1	2
Previous peripheral artery revascularization (%)	1	2
Previous AAA repair (%)	0	0
Other previous revascularization procedures (%)	1	1
Age at randomization (yr)		
Mean	63.2	62.1
SD	7.7	6.8
Median	62.4	61.9
25th, 75th percentiles	57.7, 68.3	57.6, 66.9
Qualifying HbA <sub>1c</sub> (%)		
Mean	8.0	8.3
SD	10.9	0.9
Median	7.5	8.1
25th, 75th percentiles	6.7, 8.6	7.8, 9.0

AAA = abdominal aortic aneurysm; CABG = coronary artery bypass graft; HbA<sub>1c</sub> = glycosylated hemoglobin; PTCA = percutaneous transluminal coronary angioplasty; PTCI = percutaneous transluminal coronary intervention.

were more likely not to have graduated from high school, had longer durations of diabetes, and had higher HbA<sub>1c</sub> and low-density lipoprotein levels.

## Conclusion

Strategies for the successful recruitment of participants into clinical trials have been previously reported.<sup>18</sup> The fundamental principles of an overall recruitment plan,<sup>19–21</sup> (including a prompt start,<sup>1</sup> broad entry criteria,<sup>13,22</sup> experienced staff mem-

bers,<sup>23</sup> accessible clinic locations,<sup>3</sup> and extensive planning<sup>24</sup>) are common to clinical trials and cohort studies, both government and industry sponsored. However, each trial presents unique challenges, so investigators and staff members must carefully review the overall plans before trial initiation. Surprisingly few trials have had either pilot or vanguard phases to test eligibility criteria, recruitment methods, and staff performance. In pilot studies, screening and randomization yields<sup>3,25</sup> or information regarding successful recruitment strategies<sup>26,27</sup> that were reported were at times misleading for the subsequent main trials.

Table 3  
Baseline characteristics of the vanguard phase and main trial cohorts

Baseline Characteristic	Vanguard Phase (n = 1,174)	Main Trial (n = 9,077)
Mean age (yr)	63.5	62.1
Women (%)	39.8	38.4
Race/ethnicity		
White (%)	60.2	65.4
Black (%)	22.0	18.9
Hispanic (%)	9.1	7.0
Minority (%)	42.5	37.0
Highest level of education		
Less than high school graduate (%)	19.5	14.2
High school graduate (or GED) (%)	24.9	26.6
Some college (%)	28.0	33.4
College graduate or more (%)	27.6	25.8
Cigarette smoker		
Current (%)	11.4	14.3
Former (%)	44.6	44.0
Never (%)	44.0	41.7
Secondary prevention (%)	34.6	35.3
Mean HbA <sub>1c</sub> (%)	8.7	8.3
Median HbA <sub>1c</sub> (%)	8.5	8.1
Mean fasting plasma glucose, mg/dL (mmol/L)	176.2 (9.8)	175.2 (9.7)
Median duration of diabetes mellitus (yr)	10	9
Mean weight, lb (kg)	201.2 (91.3)	206.8 (93.8)
Mean body mass index	31.7	32.3
Mean waist circumference, in (cm)	41.5 (105.4)	42.1 (106.9)
Mean systolic blood pressure (mm Hg)	140.3	135.9
Mean diastolic blood pressure (mm Hg)	75.5	74.8
Use of antihypertensive medication (%)	82.4	85.8
Use of ACE inhibitor (%)	54.8	52.6
Use of $\beta$ -blocker (%)	22.7	30.0
Mean LDL-C, mg/dL (mmol/L)	114.3 (2.96)	103.7 (2.68)
Mean HDL-C, mg/dL (mmol/L) in women	48.3 (1.25)	46.8 (1.21)
Mean HDL-C, mg/dL (mmol/L) in men	37.8 (0.98)	38.7 (1.00)
Mean total cholesterol, mg/dL (mmol/L)	191.2 (4.94)	182.3 (4.71)
Median triglyceride, mg/dL (mmol/L)	150 (1.68)	156 (1.75)
Use of statins (%)	45.5	61.1
Mean potassium (mmol/L)	4.6	4.5
Mean serum creatinine, mg/dL (mmol/L)	1.0 (88)	0.9 (80)

ACE = angiotensin-converting enzyme; GED = general equivalency diploma; HbA<sub>1c</sub> = glycosylated hemoglobin; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; statin = 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor.

For ACCORD, a vanguard phase was determined to be worthwhile because of numerous uncertainties related to protocol execution and complexity, logistics, and the nature of type 2 diabetes. Our recruitment results show the extreme sensitivity of recruitment to the number of active clinical sites. The vanguard phase, which started recruitment with few active clinical sites, had an R-factor of 0.65, whereas the main trial phase, which started recruitment with almost all clinics active, had an R-factor of 0.96, virtually ensuring no appreciable reduction in statistical power because of delayed participant accrual.

The identification of a summary statistic to capture the efficiency of recruitment into a clinical trial was first suggested in 1987.<sup>1,17</sup> Before that, "recruitment efficiency" had meant any of the following percentages: (1) of those

screened, (2) of potential individuals from a target population, (3) of those consenting to participate, (4) of those retained at preenrollment visits, (5) of those with the disease or condition in the population screened, or (6) of the goal at an individual clinical center.<sup>1</sup> Finally, it might also serve as an estimate of the efficiency of monetary costs for a recruitment effort. Failure to achieve high recruitment efficiency can result in an underpowered trial or the necessity to extend the follow-up period to preserve power and achieve the total number of person-years for the entire trial.

Because the vanguard phase had a small recruitment goal within a short period, the focus was placed on populations that were readily available (ie, existing clinical site patients). Therefore, a practice-based or institution-based

strategy was the primary recruitment approach. It was apparent that successful recruitment of the remaining participants to reach the goal of 10,000 in main trial phase would require more broadly based strategies and earlier clinic activation. Although many of the specific strategies were not used in the vanguard phase, many lessons were learned and subsequently applied to the main trial. Important observations include the following: (1) clinical sites successful at recruiting internally were most likely to be health maintenance organizations; (2) clinical sites without access to large numbers of potential participants internally needed to use community-based recruitment; (3) the successful enrollment of minority and underserved populations was demonstrated, but initial estimates for recruitment from underserved neighborhoods were overly optimistic; (4) the simplification of eligibility criteria before the main trial potentially enhanced recruitment; and (5) the careful interviewing and consenting of potential participants was needed for full understanding of this complex trial (eg, a significant proportion of participants would require insulin treatment, daily multiple blood glucose testing, and frequent follow-up visits to achieve near-normal blood glucose levels). These possibilities required substantial explanation and agreement in the consenting process.

The vanguard phase was completed before HIPAA implementation in April 2003.<sup>15</sup> Knowledge of impending HIPAA requirements allowed the investigators to prepare measures to ensure the maximum protection of participants' health information and confidentiality while minimizing the impact on recruitment. Using the vanguard experience, consent forms for the main trial were revised to include language for obtaining HIPAA authorization. Each clinical site was required to follow NIH as well as local institutional guidelines for HIPAA training.

Many different recruitment strategies were used at the individual clinic level as well as at the CCN level. The success or failure of a strategy was not consistent across all clinical sites or regions or at particular points of time. Clinical sites were therefore encouraged to try different approaches and have  $\geq 3$  strategies in place at all times. Some clinical sites "overrecruit" during some periods to compensate for known periods of difficult recruitment, such as holidays and vacations. Sites associated with health maintenance organizations that screened through their databases had more consistent flows of participants. Clinical sites that depended on sporadic advertising, health fairs, and so on were more likely to have bursts of randomizations. Central recruitment for multiple clinical sites may be useful if they are in close proximity. These "lessons learned" were implemented in the ACCORD main trial recruitment period.

The limitations of our evaluation are as follows. In the recruitment process, data were collected only on screenees who came into clinics. The only prescreening (eg, recruitment source) data collected study wide was a single question asking how the prescreening occurred: at a clinic, by phone contact, or by chart review. Except for data from the

MN-IA CCN central recruitment, other recruitment sources at individual clinical sites were not linked to randomization. Data that were available indicated that the characteristics of vanguard phase and main trial participants demonstrated considerable similarities, and there were important similarities with screenees presenting to clinic.

The substantive reduction in observed person-years in the vanguard phase was clearly related to the number of clinical sites operable at enrollment inception. Although in the vanguard phase, only a limited implementation of recruitment plans was possible, the full implementation of the originally proposed recruitment plans was needed in the main trial. Educational efforts for potential participants in this complex trial protocol were found to be crucial during the vanguard phase and were intensified during main trial recruitment. Our experience in ACCORD indicates that for large clinical trials, the inclusion of a vanguard phase to facilitate recruitment planning, the timely implementation of protocol elements, and site preparedness are critical elements for the achievement of high recruitment efficiency and the preservation of planned study power.

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