Action to Control Cardiovascular Risk in Diabetes (ACCORD) Trial: Design and Methods

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Most patients with type 2 diabetes mellitus develop cardiovascular disease (CVD), with substantial loss of life expectancy. Nonfatal CVD contributes greatly to excess healthcare costs and decreased quality of life in patients with diabetes. The current epidemic of obesity has raised expectations that CVD associated with type 2 diabetes will become an even greater public health challenge. Despite the importance of this health problem, there is a lack of definitive data on the effects of the intensive control of glycemia and other CVD risk factors on CVD event rates in patients with type 2 diabetes. The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial is a randomized, multicenter, double 2 × 2 factorial design study involving 10,251 middle-aged and older participants with type 2 diabetes who are at high risk for CVD events because of existing CVD or additional risk factors. ACCORD is testing the effects of 3 medical treatment strategies to reduce CVD morbidity and mortality. All participants are in the glycemia trial, which is testing the hypothesis that a therapeutic strategy that targets a glycosylated hemoglobin (HbA_{1c}) level of <6.0% will reduce the rate of CVD events more than a strategy that targets an HbA_{1c} level of 7.0%–7.9%. The lipid trial includes 5,518 of the participants, who receive either fenofibrate or placebo in a double-masked fashion to test the hypothesis of whether, in the context of good glycemic control, a therapeutic strategy that uses a fibrate to increase high-density lipoprotein cholesterol and lower triglyceride levels together with a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (statin) to lower low-density lipoprotein cholesterol will reduce the rate of CVD events compared with a strategy that uses a statin plus a placebo. The blood pressure trial includes the remaining 4,733 participants and tests the hypothesis that a therapeutic strategy that targets a systolic blood pressure of <120 mm Hg in the context of good glycemic control will reduce the rate of CVD events compared with a strategy that targets a systolic blood pressure of <140 mm Hg. The primary outcome measure for all 3 research questions is the first occurrence of a major CVD event, specifically nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death. Upon the expected completion of participant follow-up in 2009, the ACCORD trial should document for the first time the benefits and risks of intensive glucose control, intensive blood pressure control, and the combination of fibrate and statin drugs in managing blood lipids in high-risk patients with type 2 diabetes. **(Am J Cardiol 2007;99[suppl]:21i-33i)**

Type 2 diabetes mellitus is a complex disease characterized by hyperglycemia, insulin resistance, and variable degrees of insulin deficiency. Patients with type 2 diabetes have a high rate of cardiovascular disease (CVD) mortality, nonfatal myocardial infarction (MI), and stroke.[1] This CVD risk is related in part to a high prevalence of other CVD risk factors, such as elevated blood pressure and dyslipidemia. Epidemiologic analyses suggest that the risk for CVD in patients with diabetes increases in a graded fashion with increases in glycosylated hemoglobin (HbA_{1c}), blood pressure, low-density lipoprotein (LDL) cholesterol, and triglycerides and with a decrease in high-density lipoprotein (HDL) cholesterol.[2]

The prevalence of diagnosed diabetes in the United States has increased substantially over time, increasing >4-fold over the past 50 years, with a particularly steep increase

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Table 1
Action to Control Cardiovascular Risk in Diabetes (ACCORD): the protocol-specified double 2 × 2 design*

	BP Trial		Lipid Trial†		
Glycemia Trial	SBP <120 mm Hg	SBP <140 mm Hg	Group A	Group B	Total
HbA_{1c} <6.0%	1,050	1,050	1,450	1,450	5,000
HbA_{1c} 7.0%–7.9%	1,050	1,050	1,450	1,450	5,000
	2,100	2,100	2,900	2,900	
Total	4,200		5,800		10,000

BP = blood pressure; HbA_{1c} = glycosylated hemoglobin; SBP = systolic BP.
* All numbers represent planned sample sizes.
† Treatment group assignments are blinded until the end of the trial.

Table 2
Action to Control Cardiovascular Risk in Diabetes (ACCORD): observed distribution of participants

	BP Trial		Lipid Trial*		
Glycemia Trial	SBP <120 mm Hg	SBP <140 mm Hg	Group A	Group B	Total
HbA_{1c} <6.0%	1,178	1,193	1,383	1,374	5,128
HbA_{1c} 7.0%–7.9%	1,184	1,178	1,370	1,391	5,123
	2,362	2,371	2,753	2,765	
Total	4,733		5,518		10,251

BP = blood pressure; HbA_{1c} = glycosylated hemoglobin; SBP = systolic BP.
* Treatment group assignments are blinded until the end of the trial.

over the past 5–10 years. The Centers for Disease Control and Prevention (CDC) estimates that in 2005, 14.6 million individuals in the United States were diagnosed with diabetes, and an additional 6.2 million went undiagnosed.[3] It is predicted that by 2050 the number of individuals in the United States with diagnoses of diabetes will have climbed to 39 million.[4]

Coupled with the increases in the prevalence and incidence of diabetes is the increasing burden of death and disability associated with diabetes. Patients with diabetes exhibit CVD at 2–4 times the rate of those without diabetes; women with diabetes are disproportionately affected and exhibit a similar age-adjusted risk for CVD to that of men with diabetes.[5] CVD is the most common cause of death and the single biggest driver of healthcare costs in patients with diabetes. The healthcare costs of diabetes are staggering,[6] with direct medical costs in 2002 estimated at $92 billion and an additional $40 billion in indirect costs due to disability, work loss, and premature mortality. This estimated $132 billion price tag is certainly an underestimate, because it omits costs incurred in undiagnosed individuals, the cost of unreimbursed care, and certain healthcare costs such as care by optometrists and dentists.[7] Although control of CVD risk factors has improved in the United States over the past 30 years,[8] estimates suggest that <5% of patients with diabetes in the United States in 2000 achieved all 5 targets included routinely in guidelines aimed at controlling cardiovascular and microvascular risk (control of blood pressure, LDL cholesterol, and glycemia; smoking cessation; and daily aspirin use).[9]

Clinical trials completed to date have shown that CVD risk can be reduced in patients with diabetes. However, in so doing, they highlight the critical gap in knowledge regarding the relative CVD benefits of intensively targeting normal glucose, blood pressure, and lipid status.[10] As a result, since 1997, scientists on 3 different panels sponsored by the National Institutes of Health (NIH) have concluded that a major randomized clinical trial was needed to determine the effects on CVD of intensive glycemic control, as well as strategies for lipid and/or blood pressure treatments in patients with type 2 diabetes. As a consequence, a number of such trials are under way.[11] The purpose of this report is to present the design of one of these, the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. A fuller discussion of the rationale for conducting the ACCORD trial is presented elsewhere in this supplement.[12]

Study Overview

The overall goal of the ACCORD trial is to determine whether CVD event rates can be reduced in patients with type 2 diabetes who are at high risk for CVD events by intensively targeting 3 important CVD risk factors: hyperglycemia, dyslipidemia, and elevated blood pressure. Tables 1 and 2 present the overall design of the ACCORD trial, which is a randomized, double 2 × 2 factorial design conducted at 77 clinical centers across the United States and Canada. Table 1 lists the original planned distribution of 10,000 randomized participants across the 8 treatment groups. Table 2 presents the realized distribution of the

Table 3
Timetable of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial

Phase	No. of Months	Calendar Dates	Trial Activities
1	10	10/99–7/00	Protocol development
2	2	8/00–9/00	Procedure finalization and training
3	3	10/00–12/00	Vanguard startup and screening
4	24	1/01–1/03	Vanguard recruitment, follow-up, review, and protocol revision
5	34	2/03–10/05	Main trial recruitment and follow-up
6	40	11/05–2/09	Follow-up only
7	4	3/09–6/09	Participant close-out
8	9	7/09–4/10	Analysis and reporting

10,251 participants actually randomized. Whereas the final observed number of participants in the blood pressure trial is 13% greater than originally planned, the number of participants in the lipid trial is 5% less. This shortfall was anticipated a year before the end of recruitment, and revised power estimates reviewed by the investigators and the ACCORD Data and Safety Monitoring Board (DSMB) showed that there was still more than sufficient power to address the lipid hypothesis.

Participants will be treated and followed for 4–8 years (approximate mean, 5.6 years). The primary outcome measure for all 3 research questions is the first occurrence of a major cardiovascular event, specifically a composite outcome of nonfatal MI, nonfatal stroke, or cardiovascular death. Secondary outcomes include other cardiovascular outcomes, total mortality, diabetic microvascular disease (retinopathy, nephropathy, and neuropathy), health-related quality of life, and cost-effectiveness.

All participants were randomized to either intensive or standard glycemic goals in the open-label glycemia trial. Participants randomized to the intensive glycemia treatment group have an HbA_{1c} target of $<6.0\%$. Participants randomized to the standard glycemia treatment group have an HbA_{1c} target of 7.0%–7.9%, with an expectation that the median HbA_{1c} level will be approximately 7.5%. Treatment algorithms using metformin, sulfonylureas, meglitinides, thiazolidinediones, α-glucosidase inhibitors, insulin, and insulin analogues, coupled with lifestyle intervention, have been developed for the 2 groups. Exenatide was added to the available formulary in April 2007. Details of the approaches to glycemia therapy are presented elsewhere in this supplement.[13]

Among the 10,251 randomized participants, 5,518 with moderate levels of dyslipidemia were also randomized to either fenofibrate or matching placebo in a double-masked fashion, in addition to open-label background simvastatin therapy administered in accordance with current guidelines (20–40 mg/day, depending on observed LDL cholesterol values and whether the participant has had a clinical CVD event).[14] This is the only masked intervention in ACCORD. Details regarding the evolution of the lipid protocol are also presented elsewhere in this supplement.[14] Briefly, the standard dose of the masked fenofibrate or identical placebo used in ACCORD is 160 mg/day (or the bioequivalent doses of previous formulations). However, if the estimated glomerular filtration rate (GFR), using the observed serum creatinine level and the abbreviated Modification of Diet in Renal Disease (MDRD) equation,[15] is $\geq$30 and $<$50 mL/min per 1.73 m^2, the participant would be given a reduced dose of 54 mg/day (or the bioequivalent dose) of fenofibrate or placebo. If during follow-up the GFR decreases to consistently $<$30 mL/min per 1.73 m^2, the masked medication is discontinued.[14]

Finally, the other 4,733 participants in ACCORD were further randomized to either an intensive or a standard systolic blood pressure target, $<$120 or $<$140 mm Hg, respectively. Most currently available antihypertensive drug classes are available for use in the 2 groups, and they are administered in an open-label fashion. Details regarding the blood pressure treatment strategies are presented elsewhere in this supplement.[16]

As background treatment, all participants receive nutrition and physical activity counseling, as well as a recommendation to use aspirin daily. For participants with histories of MI, congestive heart failure, nephropathy, or $\geq$1 additional risk factor for CVD, treatment with an angiotensin-converting enzyme inhibitor is recommended, independent of blood pressure level or assigned treatment group. Current smokers receive smoking cessation counseling. All participants receive glucose-lowering therapy by protocol, as well as either lipid-modifying therapy or blood pressure–lowering therapy by protocol. Participants with high blood pressure assigned to the lipid study do not have their blood pressure managed through the study; similarly, participants with dyslipidemia assigned to the blood pressure study do not have their lipids managed through the study. However, information on current guidelines for lipids and blood pressure treatment is provided by the study to participants' personal physicians.

Table 3 presents the timeline of the study. Protocol development, external review, and training occurred over an initial 12-month period beginning in October 1999. Randomization into the vanguard phase began in January 2001, with a recruitment goal of 1,000 participants. The purpose of the vanguard phase was to assess the feasibility of recruitment, achievement of glycemia and blood pressure treatment goals, and achievement of an acceptable level of adherence in the masked lipid trial. On the

basis of the outcomes of these measures in the 1,174 recruited vanguard participants, protocol changes were proposed, reviewed, and approved in the winter of 2002. Main trial recruitment started in February 2003. The ACCORD recruitment goal of 10,000 participants was reached on September 30, 2005, with the inclusion of the vanguard and main trial participants. The last patient was randomized on October 29, 2005. The final visit for the last randomized participant is planned for June 30, 2009, with final study reports expected in the spring of 2010.

Eligibility and Baseline Characteristics

The ACCORD inclusion and exclusion criteria are presented in Table 4. These criteria were established to identify a trial population with type 2 diabetes and at high risk for CVD events, with expected event rates for sufficient statistical power with the proposed sample size while balancing generalizability and safety.[17] To be eligible, a volunteer needed to fulfill the glycemia eligibility criteria as well as criteria for either the blood pressure or the lipid trial. If a screenee was not eligible for either the blood pressure or the lipid trial, he or she was not eligible for the ACCORD trial at all. If a screenee was eligible for both the blood pressure and the lipid trials, a computerized randomization process assigned the participant to either the lipid or the blood pressure trial. Patients aged >79 years were excluded from the main trial because of increased rates of hypoglycemia in that age group in the vanguard phase. The Protocol Review Committee, appointed by the National Heart, Lung, and Blood Institute (NHLBI), approved the study protocol. Each ACCORD participant has provided written informed consent using procedures reviewed and approved by each clinical site's local institutional review board and based on a template provided by the study group that was approved and subsequently centrally monitored by the Coordinating Center and the NHLBI. The portion of the informed consent document describing the genetics component of ACCORD uses the multilevel approach recommended by the NHLBI.[18]

Specific targets were set to recruit ≥50% women, 33% racial and ethnic minorities, and 50% secondary prevention participants (ie, those with histories of clinical CVD). A full description of the recruitment planning, results, and lessons learned from the vanguard portion of ACCORD is presented elsewhere in this supplement.[17]

Table 5 presents baseline characteristics for the ACCORD trial. As expected, the treatment groups were balanced on these characteristics. Overall, there was an excess of men recruited into ACCORD (61% vs 39%), largely driven by the preponderance of men within US Department of Veterans Affairs (VA) centers. The proportion of participants with clinical CVD at baseline (35.2%) did not reach the 50% target, although sensitivity analyses indicate that this will not substantially affect the overall power of the study.

Hurricane Katrina had a significant impact on the ACCORD clinic in New Orleans, at the Tulane University Health Sciences Center. A total of 193 participants were randomized at this site. Final edits of the baseline data and decisions regarding the handling of any missing participants and data will be made when complete information is available on each of the Tulane participants. Consequently, the data in Table 5 may be modified slightly in the future.

Measurements

A wide range of interview, physical examination, and laboratory data are being collected (Table 6), with the frequency of measurement varying by treatment assignment, but at least at baseline, every 2 years, and at the end of the trial. Blood and urine samples are also stored for future measurements. White blood cells are stored for future DNA extraction for genetic studies in patients who consented to such studies.

Data are collected in 2 substudies of the trial participants to examine visual and cognitive effects of the interventions. In the ACCORD Eye Study (ACCORD-EYE), with 3,537 participants, retinal photographs are obtained and read centrally to determine the effects of the interventions on the incidence and progression of retinopathy. In the ACCORD Memory in Diabetes Study (ACCORD-MIND), with 2,977 participants, cognitive functioning is assessed by a battery of cognitive neuropsychological tests. In a subset of ACCORD-MIND, 630 participants are undergoing serial brain magnetic resonance imaging (MRI) scanning to examine potential intervention effects on cognitive functioning and brain anatomy. These 2 substudies are the subject of other reports in this supplement.[19,20]

Outcomes

The primary end point for ACCORD is the composite of nonfatal MI, nonfatal stroke, or CVD death. Cardiovascular causes of death include fatal MI, congestive heart failure, documented arrhythmia, death after invasive cardiovascular interventions, death after noncardiovascular surgery, fatal stroke, unexpected death presumed to be due to ischemic CVD occurring <24 hours after the onset of symptoms, and death due to other vascular diseases (eg, pulmonary emboli, abdominal aortic aneurysm rupture). The diagnosis of MI is based on the occurrence of a compatible clinical syndrome associated with diagnostic elevation of cardiac enzymes (ie, an increase in troponin T or troponin I to a level indicating myonecrosis and/or an increase in creatine kinase–myocar-

Table 4
Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial major inclusion and exclusion criteria

A. Overall inclusion criteria
   1. Type 2 diabetes mellitus defined according to the 1997 ADA criteria for ≥3 mo
   2. An HbA_{1c} level (obtained <3 mo before anticipated date of randomization) of
      a. 7.5%–11%: (i) If on insulin <1 U/kg and on 0 or 1 oral agent or (ii) If not on insulin, and on 0, 1, or 2 oral agents
      b. 7.5%–9%: (i) If on insulin <1 U/kg and on 2 oral agents, (ii) If on insulin >1 U/kg and 0 oral agents, or (iii) If not on insulin and on 3 oral agents
   3. Stable diabetes therapy for >3 mo
   4. Age at randomization
      a. 40–79 yr (inclusive) for anyone with a history of clinical CVD, or
      b. 55–79 yr (inclusive) for anyone without a history of clinical CVD (the age eligibility was modified on the basis of the results of the vanguard phase, so some participants were aged ≥80 yr at randomization)
   5. At high risk for CVD events, defined as
      a. Presence of clinical CVD (prior MI, stroke, arterial revascularization, angina with ischemic changes on ECG at rest, changes on a graded exercise test, or positive cardiac imaging test results,
      b. If no clinical CVD, evidence in the past 2 yr suggesting high likelihood of CVD (1 risk factor: microalbuminuria, ankle-brachial index <0.9, left ventricular hypertrophy by ECG or echocardiography, or >50% stenosis of a coronary, carotid, or lower extremity artery), or
      c. Presence of ≥2 of the following factors that increase CVD risk: LDL-C >130 mg/dL (1 mg/dL = 0.02586 mmol/L) treated with lipid-lowering medication or untreated, low HDL-C (<40 mg/dL for men and <50 mg/dL for women), systolic BP >140 mm Hg or diastolic BP >95 mm Hg treated with BP-lowering medication or untreated, current cigarette smoking, or BMI >32
   6. In addition, all participants must be eligible for either the BP trial or the lipid trial

B. Overall exclusion criteria
   1. History of hypoglycemic coma/seizure within past 12 mo
   2. Hypoglycemia requiring third-party assistance in past 3 mo, with concomitant glucose <60 mg/dL (3.3 mmol/L)
   3. History consistent with type 1 diabetes
   4. Unwilling to do frequent capillary blood glucose self-monitoring or unwilling to inject insulin several times a day
   5. BMI >45
   6. Serum creatinine >1.5 mg/dL (132.6 μmol/L) obtained within the previous 2 mo
   7. Transaminase >2 times the upper limit of normal or active liver disease
   8. Any ongoing medical therapy with known adverse interactions with the glycemic interventions (eg, corticosteroids, protease inhibitors)
   9. Cardiovascular event or procedure (as defined for study entry) or hospitalization for unstable angina within past 3 mo
   10. Current symptomatic heart failure, history of NYHA class III or IV congestive heart failure at any time, or ejection fraction (by any method) <0.25
   11. A medical condition likely to limit survival to <3 yr or a malignancy other than nonmelanoma skin cancer within the past 2 yr
   12. Any factors likely to limit adherence to interventions
   13. Failure to obtain informed consent from participant
   14. Currently participating in another clinical trial
   15. Living in the same household as an already randomized ACCORD participant
   16. Any organ transplantation
   17. Weight loss >10% in past 6 mo
   18. Pregnancy, currently trying to become pregnant, or of child-bearing potential and not practicing birth control
   19. Participants with recurrent requirements for phlebotomy or transfusion of red blood cells

C. Additional lipid trial criteria (for entry into lipid trial)
   1. Inclusion criteria: (a) Lipids measured within the previous 12 mo with (i) Estimated LDL-C off statin therapy of 60–180 mg/dL, and (ii) HDL-C <55 mg/dL for women or African Americans or HDL-C <50 mg/dL for all other sex and race groups, and triglycerides <750 mg/dL (1 mg/dL = 0.01129 mmol/L) on no therapy or <400 mg/dL on treatment with lipid-lowering drugs
   2. Exclusion criteria for lipid intervention include known hypersensitivity to statins or fibrates; requirements for use of erythromycin, clarithromycin, cyclosporine, systemic azole antifungals, or nefazodone or trazodone (all of which have reported interactions with either statins or fibrates); refusal to stop current lipid-lowering drugs; history of pancreatitis; untreated or inadequately treated thyroid disease; breastfeeding; documented previous occurrence of myositis/myopathy; preexisting gallbladder disease

D. Additional BP trial criteria (for entry into blood pressure trial)
   1. To be eligible, systolic BP can be
      a. 130–160 mm Hg, inclusive, if the participant is on 0, 1, 2, or 3 antihypertensive medications,
      b. 161–170 mm Hg, inclusive, if the participant is on 0, 1, or 2 antihypertensive medications, or
      c. 171–180 mm Hg, inclusive, if the patient is on 0 or 1 antihypertensive medication
   2. The dipstick protein in a spot urine test must be <2+, the protein/creatinine ratio in a spot urine test must be <700 mg/g creatinine, and the 24-hr protein excretion must be <1.0 g/24 hr
   3. For screenees who are not currently on BP-lowering medication, there must be documentation of systolic BP ≥130 mm Hg on ≥2 occasions

ADA = American Diabetes Association; BMI = body mass index; BP = blood pressure; CVD = cardiovascular disease; ECG = electrocardiography; HbA_{1c} = glycosylated hemoglobin; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; MI = myocardial infarction; NYHA = New York Heart Association.

Table 5
Baseline description of randomized Action to Control Cardiovascular Risk in Diabetes (ACCORD) participants

Characteristic	Overarching Glycemia Trial (n = 10,251)	BP Trial (n = 4,733)	Lipid Trial (n = 5,518)
Mean age (yr)	62.2	62.2	62.3
Women (%)	38.6	47.7	30.7
Race/ethnicity			
White (%)	64.8	60.5	68.4
Black (%)	19.3	24.1	15.1
Hispanic (%)	7.2	7.0	7.4
Highest level of education			
Less than high school (%)	14.8	16.3	13.6
High school graduate (%)	26.4	26.9	26.0
Some college (%)	32.8	32.4	33.1
College graduate or more (%)	26.0	24.5	27.3
Cigarette smoker			
Current (%)	14.0	13.3	14.6
Former (%)	44.4	42.1	46.3
Never (%)	41.6	44.6	39.0
Secondary prevention (%)	35.2	33.6	36.6
Mean HbA_{1c} (%)	8.3	8.3	8.3
Median HbA_{1c} (%)	8.1	8.1	8.1
Mean fasting serum glucose, mg/dL (mmol/L)	175.3 (9.7)	174.7 (9.7)	175.8 (9.8)
Median duration of diabetes (yr)	10	10	9
Mean weight, lb (kg)	206.2 (93.5)	202.8 (92.0)	209.1 (94.8)
Mean body mass index	32.2	32.2	32.3
Mean waist circumference, in (cm)	42.0 (106.6)	41.6 (105.6)	42.4 (107.7)
Mean systolic BP (mm Hg)	136.4	139.2	133.9
Mean diastolic BP (mm Hg)	74.9	76.0	74.0
Use of any antihypertensive (%)	85.4	87.3	83.8
Use of ACE inhibitor (%)	52.9	52.0	53.6
Use of β-blocker (%)	29.2	25.4	32.5
Mean LDL-C, mg/dL (mmol/L)	104.9 (2.71)	110.0 (2.84)	100.6 (2.60)
Mean HDL-C, mg/dL (mmol/L)			
Women	47.0 (1.22)	51.3 (1.33)	41.4 (1.07)
Men	38.6 (1.00)	41.7 (1.08)	36.6 (0.95)
Mean total cholesterol, mg/dL (mmol/L)	183.3 (4.74)	192.8 (4.99)	175.2 (4.53)
Median triglyceride, mg/dL (mmol/L)	155 (1.74)	147 (1.65)	162 (1.81)
Use of statins (%)	59.3	61.1	57.7
Mean potassium (mmol/L)	4.5	4.5	4.5
Mean serum creatinine, mg/dL (μmol/L)	0.9 (80)	0.9 (80)	0.9 (80)

ACE = angiotensin-converting-enzyme; BP = blood pressure; HbA_{1c} = glycosylated hemoglobin; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; statin = 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor.

dial band to a level more than twice the upper limit of normal). Q-wave MI is defined as the development of new significant Q waves. Silent MI is diagnosed when new (compared with the previous 12-lead electrocardiogram) significant Q waves are detected by surveillance electrocardiography performed every 2 years and at study end in all participants. Stroke is diagnosed by a focal neurologic deficit that lasts >24 hours, associated with evidence of brain infarction or hemorrhage by computed tomography, MRI, or autopsy.

The secondary end points are (1) an expanded macrovascular outcome, specifically the combination of the primary end point plus any revascularization and hospitalization for congestive heart failure; (2) total mortality; (3) cardiovascular mortality; (4) major coronary artery disease events, specifically fatal events, nonfatal MI, and unstable angina; (5) total stroke (combined fatal and nonfatal); (6) congestive heart failure death or hospitalization for heart failure (with documented clinical and radiologic evidence); (7) the main microvascular outcome of ACCORD and the primary outcome of ACCORD-EYE, namely, the combined outcome of progression of diabetic retinopathy of ≥3 stages on the Early Treatment Diabetic Retinopathy Study (ETDRS) scale, photocoagulation, or vitrectomy for diabetic retinopathy, which will be determined only in the 3,537 participants in ACCORD-EYE[19]; (8) a second composite microvascular end point, to be examined in the entire ACCORD population, namely, fatal or nonfatal renal failure or retinal photocoagulation or vitrectomy for diabetic retinopathy; and (9) outcomes related to health-related quality of life and cost-effectiveness.[21]

Table 6
Measures

1. Questionnaires
   a. Sociodemographics: age, ethnicity, sex, level of education, persons living with participants, and US zip code/Canadian postal code; Social Security number, Medicare number, Canadian Social Insurance number, or Provincial Health Insurance number was collected for tracking purposes
   b. Medical history: detailed initial medical history; follow-up abbreviated interval history focused on eligibility criteria, allergies, CVD, smoking status, and diabetes mellitus
   c. Concomitant medications: all standing therapies, with the emphasis placed on concurrent antihypertensive, glycemic, and lipid-lowering therapy, as well as background risk reduction (eg, aspirin) therapy
   d. Diet*
   e. Physical activity*
   f. Health-related quality of life substudy*
   g. Cost-effectiveness substudy*
   h. ACCORD Eye Study* (ACCORD-EYE)
   i. ACCORD Memory in Diabetes Study* (ACCORD-MIND)
2. Physical examination measures
   a. Anthropometric measurements: standing height, weight, and waist circumference
   b. BP and pulse
   c. Systems physical examination: general survey, skin, head, ears, eyes, nose, throat, neck, chest, heart, abdomen, musculoskeletal/extremities, pulse assessment, and neurologic (including lower extremity)
   d. Visual acuity
3. Laboratory measures
   a. HbA_{1c}
   b. Electrocardiogram
   c. Fasting serum glucose
   d. Potassium, creatinine
   e. Fasting lipid panel
   f. Alanine transaminase, creatine phosphokinase*
   g. Urine albumin–creatinine ratio
   h. Stored samples: serum, urine, WBCs for DNA extraction (the latter only with participant consent)

ACCORD = Action to Control Cardiovascular Risk in Diabetes; BP = blood pressure; CVD = cardiovascular disease; HbA_{1c} = glycosylated hemoglobin; WBC = white blood cell.

* Measured in subsets of patients.

Analysis Plan

The primary ACCORD hypotheses are as follows: In middle-aged or older patients with type 2 diabetes who are at high risk for having a CVD event,

1. Does a therapeutic strategy that targets an HbA_{1c} level of $<6.0\%$ reduce the rate of CVD events more than a strategy that targets an HbA_{1c} level of 7.0%–7.9% (with the expectation of achieving a median level of 7.5%)?
2. In the context of good glycemic control, does a therapeutic strategy that uses a fibrate to increase HDL cholesterol and lower triglyceride levels together with a 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitor (statin) to lower LDL cholesterol reduce the rate of CVD events compared with a strategy that uses a statin plus a placebo?
3. In the context of good glycemic control, does a therapeutic strategy that targets a systolic blood pressure level of <120 mm Hg reduce the rate of CVD events compared with a strategy that targets a systolic blood pressure level of <140 mm Hg?

Analyses of each primary hypothesis will be conducted within separate models to test each intervention as a comparison of the marginal (main) effect for each of the 3 research hypotheses separately, not as comparisons among the individual cells of the double 2×2 design. The 1,174 participants entered during the vanguard phase are included in all the planned analyses along with the 9,077 entered during the main trial phase, yielding the total number of 10,251 participants. All of these participants will be included in the analysis for the glycemia hypothesis. Primary analyses will be performed according to the intention-to-treat principle (ie, all randomized participants will be analyzed according to their intervention assignment at randomization, regardless of adherence). Each hypothesis will be tested using a 2-sided probability of type 1 error of 0.05. The main analyses will be based on survival analysis methods, with failure time measured from the time of randomization. Proportional hazards models will be used,[22] incorporating adjustment for the prespecified covariates listed below.

Glycemia hypothesis: The glycemia hypothesis will be tested in all 10,251 randomized participants. The model to be fit will contain separate indicator variables that identify participants (1) in the blood pressure trial, (2) in the blood pressure trial and randomized to the intensive blood pressure control intervention, (3) in the lipid trial, (4) in the lipid trial and randomized to fibrate, and (5) randomized to intensive glycemic control.

In addition to these variables, indicator variables will be included that identify secondary prevention participants (variable 6) and clinical center networks (CCNS) (variable 7). The main comparison in this model will be based on the χ^2 statistic from a likelihood ratio test obtained from proportional-hazards models with or without variable 5.

Lipid hypothesis: The lipid hypothesis will be tested in the 5,518 lipid trial participants. The model to be fit will contain variables 4, 5, 6, and 7. This hypothesis will be tested using a likelihood ratio test for models with or without variable 4.

Blood pressure hypothesis: The blood pressure hypothesis will be tested in the 4,733 participants in the blood pressure trial. The model to be fit will contain the variables 2, 5, 6, and 7. This hypothesis will be tested using a likelihood ratio test for models with or without variable 2.

Kaplan-Meier[23] estimates of survival will be obtained for the intervention and control groups for each hypothesis. Estimates of the proportion of participants who remain

event free at prespecified time points, and the associated confidence intervals, will be constructed.[24] The hazard functions will be assessed for proportionality using log/log plots of survival and Schoenfeld residuals. Unadjusted analyses (ie, log-rank tests) will also be performed.

All of the secondary outcomes and the 2 substudies (ACCORD-MIND and ACCORD-EYE) also will be analyzed as marginal (main) effects, with the glycemia, lipid, and blood pressure trials analyzed separately. Two subgroup hypotheses for the glycemia intervention are to determine whether the effects of glycemic control on the primary outcome are the same across baseline levels of HbA_{1c} and if the effects of glycemic control on the primary outcome are independent of effects due to the blood pressure and lipid interventions. Three subgroup hypotheses for the lipid intervention are to determine whether the benefits of fibrate (in the context of desirable levels of LDL cholesterol and good glycemic control) are equal across levels of LDL cholesterol, HDL cholesterol, and triglycerides measured before the initiation of fibrate therapy. The consistency of the effects for the glycemia, lipid, and blood pressure interventions will also be examined in subgroups defined by sex, age, race or ethnicity, and the presence of clinical CVD at baseline (ie, primary and secondary prevention participants), and the presence or absence of the other interventions.

The ACCORD study was designed to have 89% power to detect a 15% treatment effect of intensive glycemic control compared with standard glycemic control, 87% power to detect a 20% treatment effect of lipid treatment with fibrate compared with placebo (on a background of statin treatment for LDL cholesterol), and 94% power to detect a 20% treatment effect of intensive blood pressure control compared with standard blood pressure control. The original sample size and power determinations for each intervention were made under the assumption that the other 2 interventions would produce the effect sizes for which they were powered. The ACCORD clinic investigators are masked to all CVD outcome measurements until the end of the trial, when data analysis is complete.

Management

The ACCORD organizational structures and responsibilities are similar to those of other large, multicenter clinical trials sponsored by government or industry. Seven CCNs and the Coordinating Center are contracted by the NHLBI to work together through the Steering Committee to successfully design and conduct the trial. In addition, the Central Chemistry Laboratory and the ECG Reading Center are subcontracted by the Coordinating Center. The Drug Distribution Center is funded by a governmental interagency agreement. Each CCN comprises a network of collaborating clinical sites, which include medical facilities and/or individual practices that enroll and treat participants in the trial. In all, there are 77 such active clinical sites located across the United States and Canada.

The ACCORD Steering Committee provides the overall leadership for the trial and establishes scientific and administrative policy. It is composed of voting members (the principal investigators from the 7 CCNs, the principal investigator from the Coordinating Center, and the NHLBI project officer) and the chairs of the 3 major intervention working groups (glycemia, lipid, and blood pressure), the Steering Committee chair, and the Steering Committee vice chair. Nine standing subcommittees of the Steering Committee are specified in the protocol: Design and Analysis, Medical Interventions, Recruitment and Retention, Measurement Procedures and Quality Control, Morbidity and Mortality, Publications and Presentations, Health-Related Quality of Life/Cost-Effectiveness, Laboratory and Ancillary Studies, and Operations. The Executive Committee acts as the operational arm of the Steering Committee and makes decisions on behalf of the Steering Committee on day-to-day operational issues requiring immediate action as well as study processes and assignments.

The independent Protocol Review Committee, appointed by the director of the NHLBI, reviewed the originally proposed protocol (in mid-2000) and recommended to the NHLBI that a vanguard phase of 1,000 participants be conducted and evaluated before mounting the full-scale trial. The independent DSMB, also appointed by the director of the NHLBI, monitors data and oversees patient safety, meeting twice annually to advise the NHLBI. ACCORD receives contributed resources from industry, including some medications and some supplies. However, the scientific decisions and governance of the trial are determined solely by the Steering Committee.

The ACCORD investigators established a conflict-of-interest policy to meet public standards of conduct and to ensure unbiased and fully informed decision making. To meet these goals, the study obtains full disclosure by all key members of the study regarding their own and their immediate family members' financial relationships with all pharmaceutical and biomedical companies judged to have active or potential interests in the conduct and outcome of the study. Members with significant financial conflicts of interest are required to recuse themselves from voting on issues related to the conflict.

ACCORD is an Internet-based trial, with its home page located at http://www.accordtrial.org. In addition to the public section of the Web site, which contains general information regarding ACCORD, there is a password-protected section used by the CCNs and clinical sites to randomize participants and to enter data. All study documents are found in the password-protected section of the Web site, including the protocol, the manual of procedures, training materials, forms, special notices, Steering Committee minutes, the study directory, quality-control reports, and overall and site-specific reports related to the achievement of recruitment and treatment goals. The current protocol is

posted on the public Web site. It should be recognized that the protocol is a dynamic document that may change over time.

Conclusion

By addressing several important and currently unanswered questions regarding the prevention of CVD in patients with type 2 diabetes, the results of the ACCORD trial should provide substantial direction regarding appropriate targets and techniques of risk factor management in patients with type 2 diabetes for many years to come.

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1. Stamler J, Vaccaro O, Neaton JD, Wentworth D. Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care* 1993;16:434–444.
2. Turner RC, Millins H, Neil HA, Stratton IM, Manley SE, Matthews DR, Holman RR. Risk factors for coronary artery disease in non-insulin dependent diabetes mellitus: United Kingdom Prospective Diabetes Study (UKPDS: 23). *BMJ* 1998;316:823–828.
3. Centers for Disease Control and Prevention. National diabetes fact sheet: total prevalence of diabetes in the United States, all ages, 2005. Available at: http://www.cdc.gov/diabetes/pubs/estimates05.htm#prev. Accessed June 21, 2006.
4. Engelgau MM, Geiss LS, Saaddine JB, Boyle JP, Benjamin SM, Gregg EW, Tierney EF, Rios-Burrows N, Mokdad AH, Ford ES, Imperatore G, Narayan KM. The evolving diabetes burden in the United States. *Ann Intern Med* 2004;140:945–950.
5. Barrett-Connor E, Giardina EG, Gitt AK, Gudat U, Steinberg HO, Tschoepe D. Women and heart disease: the role of diabetes and hyperglycemia. *Arch Intern Med* 2004;164:934–942.
6. Gilmer TP, O'Connor PJ, Rush WA, Crain AL, Whitebird RR, Hanson AM, Solberg LI. Predictors of health care costs in adults with diabetes. *Diabetes Care* 2005;28:59–64.
7. Hogan P, Dall T, Nikolov P, for the American Diabetes Association. Economic costs of diabetes in the US in 2002. *Diabetes Care* 2003;26:917–932.
8. Imperatore G, Cadwell BL, Geiss L, Saadinne JB, Williams DE, Ford ES, Thompson TJ, Narayan KM, Gregg EW. Thirty-year trends in cardiovascular risk factor levels among US adults with diabetes: National Health and Nutrition Examination Surveys, 1971–2000. *Am J Epidemiol* 2004;160:531–539.
9. Saydah SH, Fradkin J, Cowie CC. Poor control of risk factors for vascular disease among adults with previously diagnosed diabetes. *JAMA* 2004;291:335–342.
10. CDC Diabetes Cost-Effectiveness Group. Cost-effectiveness of intensive glycemic control, intensified hypertension control and serum cholesterol level reduction for type 2 diabetes. *JAMA* 2002;287:2542–2551.
11. Buse JB, Rosenstock J. Prevention of cardiovascular outcomes in type 2 diabetes mellitus: trials on the horizon. *Endocrinol Metab Clin North Am* 2005;34:221–235.
12. Goff DC, Gerstein HC, Ginsberg HN, Cushman WC, Margolis KL, Byington RP, Buse JB, Genuth S, Probstfield JL, Simons-Morton DG, for the ACCORD Study Group. Prevention of cardiovascular disease in persons with type 2 diabetes mellitus: current knowledge and rationale for the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. *Am J Cardiol* 2007;99(suppl):4i–20i.
13. Gerstein, HC, Riddle MC, Kendall DM, Cohen RM, Goland R, Feinglos MN, Kirk JK, Hamilton BP, Ismail-Beigi F, Feeney P, for the ACCORD Study Group. Glycemia treatment strategies in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. *Am J Cardiol* 2007;99(suppl):34i–43i.
14. Ginsberg HN, Bonds DE, Lovato LC, Crouse JR, Elam MB, Linz PE, O'Connor PJ, Leiter LA, Weiss D, Lipkin E, Fleg JL, for the ACCORD Study Group. Evolution of the lipid trial protocol of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. *Am J Cardiol* 2007;99(suppl):56i–67i.
15. Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, Hogg RJ, Perrone RD, Lau J, Eknoyan G. National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classification, and stratification. *Ann Intern Med* 2003;139:137–147.
16. Cushman WC, Grimm RH Jr, Cutler JA, Evans GW, Capes S, Corson MA, Sadler LS, Alderman MH, Peterson K, Bertoni A, Basile JN, for the ACCORD Study Group. Rationale and design for the blood pressure intervention of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. *Am J Cardiol* 2007;99(suppl):44i–55i.
17. Kingry C, Bastien A, Booth G, Geraci TS, Kirpach BB, Lovato LC, Margolis KL, Rosenberg Y, Sperl-Hillen JM, Vargo L, Williamson J, Probstfield JL, for the ACCORD Study Group. Recruitment strategies in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. *Am J Cardiol* 2007;99(suppl):68i–79i.
18. Report of the Special Emphasis Panel on Opportunities and Obstacles to Genetic Research in NHLBI Clinical Studies. http://www.nhlbi.nih.gov/meetings/workshops/opporsep.htm. Accessed June 21, 2006.
19. Chew EY, Ambrosius WT, Howard LT, Greven CM, Johnson S, Danis RP, Davis MD, Genuth S, Domanski M, for the ACCORD Study Group. Rationale, design, and methods of the Action to Control Cardiovascular Risk in Diabetes Eye Study (ACCORD-EYE). *Am J Cardiol* 2007;99(suppl):103i–112i.
20. Williamson JD, Miller ME, Bryan RN, Lazar RM, Coker LH, Johnson J, Cukierman T, Horowitz KR, Murray A, Launer LJ, for the ACCORD Study Group. The Action to Control Cardiovascular Risk in Diabetes Memory in Diabetes Study (ACCORD-MIND): rationale, design, and methods. *Am J Cardiol* 2007;99(suppl):113i–123i.
21. Sullivan MD, Anderson RT, Aron D, Atkinson HH, Bastien A, Chen GJ, Feeney P, Gafni A, Hwang W, Katz LA, et al, for the ACCORD Study Group. Health-related quality of life and cost-effectiveness components of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial: rationale and design. *Am J Cardiol* 2007;99(suppl):90i–102i.
22. Cox DR. Regression models and life tables. *J R Stat Soc* 1972;34B:187–197.
23. Kaplan E, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958;8:699–711.
24. Peto R, Pike MC, Armitage P, Breslow NE, Cox DR, Howard SV, Mantel N, McPherson K, Peto J, Smith PG. Design and analysis of

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