Glycemia Treatment Strategies in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) Trial

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There is an independent progressive epidemiologic relation between glycemia and cardiovascular disease (CVD) events; however, whether lowering glucose levels with currently available therapies can reduce CVD events remains unknown. The Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial is designed to answer this question in high-risk patients with type 2 diabetes mellitus. In ACCORD, 10,251 patients with type 2 diabetes and other CVD risk factors or CVD were randomly allocated to intensive glycemic control, targeting a glycosylated hemoglobin (HbA_{1c}) level <6%, or standard glycemic control, targeting an HbA_{1c} level of 7.0%–7.9%. All participants are provided with diabetes education, glucose-monitoring equipment, and antidiabetic medications. All participants in the intensive glycemic control group are started on ≥2 classes of agents. Doses are intensified or a new medication class is added every month if HbA_{1c} levels are ≥6% or if >50% of premeal or postmeal capillary glucose readings are >5.6 mmol/L (100 mg/dL) or >7.8 mmol/L (140 mg/dL), respectively. All drug combinations are permitted, and drugs are reduced only because of side effects or contraindications. Annual training, menus of approaches for intensification, regular electronic messaging, audits of achieved glycemia, and central feedback to sites support glycemic intensification strategies in intensive participants. In participants in the standard glycemic control group, therapy is intensified whenever HbA_{1c} is ≥8%, and antihyperglycemic drugs that promote hypoglycemia (ie, insulin or insulin secretagogues) are reduced if HbA_{1c} persistently decreases to <7% in the setting of hypoglycemia. ACCORD addresses the hypothesis that aggressive glucose lowering prevents CVD events in patients with type 2 diabetes. It is focused on the levels of glycemia achieved using a variety of strategies, not on the specific therapies used. It will also provide information on how to safely approach near-normal levels of glucose control in clinical practice and evidence to support future clinical guidelines for diabetes management in older adults. **(Am J Cardiol 2007;99[suppl]:34i–43i)**

Diabetes mellitus is a metabolic disease characterized by hyperglycemia that is now established as a strong independent risk factor for incident cardiovascular disease (CVD).[1] This risk has been attributed to a high prevalence of many CVD risk factors, including hypertension and dyslipidemia, in addition to hyperglycemia. Indeed, several epidemiologic analyses of large databases have reported that the risk for CVD increases with the degree of hyperglycemia.[2–5] They have also shown that the link between glucose levels or glycosylated hemoglobin (HbA_{1c}) levels (a measure corre-

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Table 1
United Kingdom Prospective Diabetes Study (UKPDS) major composite outcomes

Composite Outcome	Absolute Risk*		RR (95% CI)	p Value
	Intensive (n = 2,729)	Conventional (n = 1,138)		
Any diabetes mellitus–related end point	40.9	46.0	0.88 (0.79–0.99)	0.029
Diabetes-related deaths	10.4	11.5	0.90 (0.73–1.11)	0.3
All-cause death	17.9	18.9	0.94 (0.80–1.10)	0.4
Myocardial infarction	14.7	17.4	0.84 (0.71–1.00)	0.052
Stroke	5.6	5.0	1.11 (0.81–1.51)	0.5
Amputation or PVD death	1.1	1.6	0.65 (0.36–1.18)	0.15
Microvascular end point	8.6	11.4	0.75 (0.60–0.93)	0.0099

CI = confidence interval; PVD = peripheral vascular disease; RR = relative risk.
* Absolute risk is expressed per 1,000 person-years.
Adapted from *Lancet*.[8]

Table 2
United Kingdom Prospective Diabetes Study (UKPDS) components of the microvascular outcome

Composite Outcome	Absolute Risk*		RR (99% CI)	p Value
	Intensive (n = 2,729)	Conventional (n = 1,138)		
Retinal photocoagulation	7.9	11.0	0.71 (0.53–0.96)	0.0031
Vitreous hemorrhage	0.7	0.9	0.77 (0.28–2.11)	0.5
Renal failure	0.6	0.8	0.73 (0.25–2.14)	0.45
Renal death	0.3	0.2	1.63 (0.21–12.49)	0.5

CI = confidence interval; RR = relative risk.
* Absolute risk is expressed per 1,000 person-years.
Adapted from *Lancet*.[8]

lated with mean glucose levels over the preceding 2–3 months) and CVD extends well below glucose levels that are used to diagnose diabetes and that the risk for CVD increases approximately 20% for every 1% increase in HbA_{1c} level >5.0%.[2,3,6] Indeed, ≥2 reports have shown that that the relation between HbA_{1c} level and CVD is independent of the presence or absence of a diagnosis of diabetes.[2,7]

Previous Relevant Clinical Trials

Although measures of glycemia progressively predict the risk for CVD, clinical trials to date have not demonstrated that the degree of hyperglycemia is a modifiable risk factor for CVD in patients with type 2 diabetes—ie, that achieving either nondiabetic or normal glucose levels can reduce the risk for CVD in these individuals. The United Kingdom Prospective Diabetes Study (UKPDS) allocated patients with newly diagnosed diabetes to a policy of either intensive glycemic control (which targeted a fasting plasma glucose level ≤6 mmol/L [108 mg/dL]) or conventional glycemic control (which had an "action required" fasting plasma glucose level ≥15 mmol/L [270 mg/dL]) and measured cardiovascular outcomes.[8] Participants in the intensive and conventional groups achieved median HbA_{1c} levels of 7.0% and 7.9%, respectively, during 10 years of follow-up. These levels were not stable, however, and increased progressively over time in the 2 groups. Nevertheless, the intensive policy reduced the risk for the first occurrence of any of 7 diabetes-related events by 12% compared with the conventional policy. Much of this benefit was due to a 25% reduction in the development of the microvascular composite outcome comprising laser therapy, vitreous bleed, or renal failure. Tables 1 and 2 list the key results of the UKPDS.[8]

The UKPDS did not demonstrate a significant benefit of glycemic control on macrovascular disease, but it did show a trend toward benefit for the intensive glycemic control group: a 16% reduction in myocardial infarction (MI) that was just short of statistical significance (p = 0.052). This lack of statistical significance is not surprising, because the UKPDS participants were at relatively low risk for cardiovascular events, and the study was not designed to test the effects of glucose lowering on CVD events. Specifically, participants were newly diagnosed, the mean age at randomization was only 53 years, and participants were excluded from the study if they had histories of recent MIs or >1 previous vascular event, current angina, or heart failure. Thus, the annualized risk for MI was only 1.7% per year, and the study did not have adequate power to detect clinically important macrovascular benefits.

The results of the small feasibility phase of the Veterans Affairs Cooperative Study on Glycemic Control and Complications in Type II Diabetes Mellitus (VA CSDM) suggested a different conclusion. This 27-month study included 153 men and achieved a 2% separation of HbA_{1c} between a conventionally treated group and a group that was more intensively treated. This preliminary study was not powered to assess cardiovascular outcomes, but there was a trend toward more CVD-related mortality in the intensively treated group.[9]

In light of the inconclusive results of the UKPDS and other studies, it remains uncertain whether targeting near-normal glycemic control will reduce CVD in patients with type 2 diabetes and, if it does, whether the magnitude of benefit will exceed the potential risks, such as those related to hypoglycemia. These questions are being addressed by the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial.

Description of the Action to Control Cardiovascular Risk in Diabetes Trial Glycemia Intervention

ACCORD is an open-label, multicenter clinical trial of 10,251 middle-aged and older patients with type 2 diabetes at high risk for CVD events due to CVD risk factors or previous CVD events, whose baseline HbA_{1c} levels are $\geq$7.5%. It is explicitly testing the hypothesis that a therapeutic strategy designed to lower HbA_{1c} to $<$6.0% will reduce CVD event rates to a greater extent than a strategy that lowers and/or maintains HbA_{1c} at 7.0%–7.9%, with the expectation of achieving a median level of 7.5%. It is also indirectly testing the hypothesis that it is possible to safely achieve an HbA_{1c} level $<$6% in intensively treated high-risk patients with type 2 diabetes using contemporary therapeutic approaches.

Rationale for the glycemic targets in ACCORD: Normoglycemia (a "nondiabetic" HbA_{1c} level $<$6%) is being targeted in the "experimental" or intensive glycemic control group for several reasons. First, it will clearly and stringently test the glycemia hypothesis in patients with diabetes. Second, it allows ACCORD to test the effects of glucose lowering within an HbA_{1c} range in which epidemiologic studies have demonstrated a progressive relation between HbA_{1c} levels and cardiovascular risk. Third, the growing range of drug classes for the treatment of patients with type 2 diabetes has made it possible to seek such an aggressive target with an acceptable level of risk for hypoglycemia. Fourth, it allows ACCORD to target a conventional-group HbA_{1c} level that has been shown to reduce the risk for microvascular events relative to the participants' risk before entry into the trial while generating sufficient contrast with the intensive-group HbA_{1c} target to test the primary hypothesis. Finally, the choice of the HbA_{1c} target for intensive treatment is highly relevant to clinical practice, because various groups are already recommending that all patients with diabetes seek normal glucose levels, despite a lack of strong clinical trial evidence regarding the risks and benefits of doing so.

The goal selected for the "control" or standard group is an HbA_{1c} level of 7.0%–7.9%, with an expected median value of 7.5%. This goal was chosen because the randomized comparison of treatments in the UKPDS[8] as well as the epidemiologic analyses[10] suggested that higher levels might lead to an unacceptable risk for microvascular events. As shown in Figure 1,[10] the relation between microvascular end points and HbA_{1c} is curvilinear, with the risk for microvascular events increasing steeply as the HbA_{1c} increases to $>$8%. Values $<$7% only modestly reduce the absolute risk for microvascular events, while they substantially increase the risk for severe hypoglycemia.

The targets chosen for the standard-control and intensive-control arms of the glycemia comparison in ACCORD should generate a median HbA_{1c} contrast of 1.0%–1.5%. A recent meta-analysis of prospective studies of patients with diabetes reported that a 1.0% difference in HbA_{1c} leads to an 18% reduction in cardiovascular risk.[3] ACCORD was designed to be powered to detect a 15% reduction in cardiovascular events. Therefore, aiming for a contrast of 1.5% ensures that the final achieved HbA_{1c} contrast will be large enough to test the glycemia hypothesis definitively. Even if intensive treatment does not achieve a median HbA_{1c} level $<$6.0%, the trial is designed to allow an adequate HbA_{1c} contrast of $\geq$1% without relaxing the HbA_{1c} target in the standard glycemic control group.

Risk for hypoglycemia: Epidemiologic studies and clinical trials have shown that the risk for hypoglycemia is proportional to the achieved level of glycemic control: the closer the mean glucose or HbA_{1c} level is to normal, the greater the risk.[11] In patients with type 2 diabetes, those using insulin have the highest risk for hypoglycemia.[12] Most hypoglycemic episodes appear to have no chronic sequelae; however, the long-term consequences of such hypoglycemia on cognitive function, cerebrovascular disease, or CVD have not been carefully studied in older patients with type 2 diabetes at high risk for CVD events (ie, similar to ACCORD participants). This trial will therefore determine whether the possible benefits of intensive glycemic control outweigh its potential risks. An accompanying report in this supplement provides details regarding hypoglycemia prevention, monitoring, and management in ACCORD.[13]

In addition, ACCORD will determine whether the therapeutic approaches being used (ie, combinations of different classes of agents that target different aspects of glucose metabolism) can sustain normal or near-normal glycemia for several years or whether there will be progressive increases in HbA_{1c}, as seen in the UKPDS.[8]

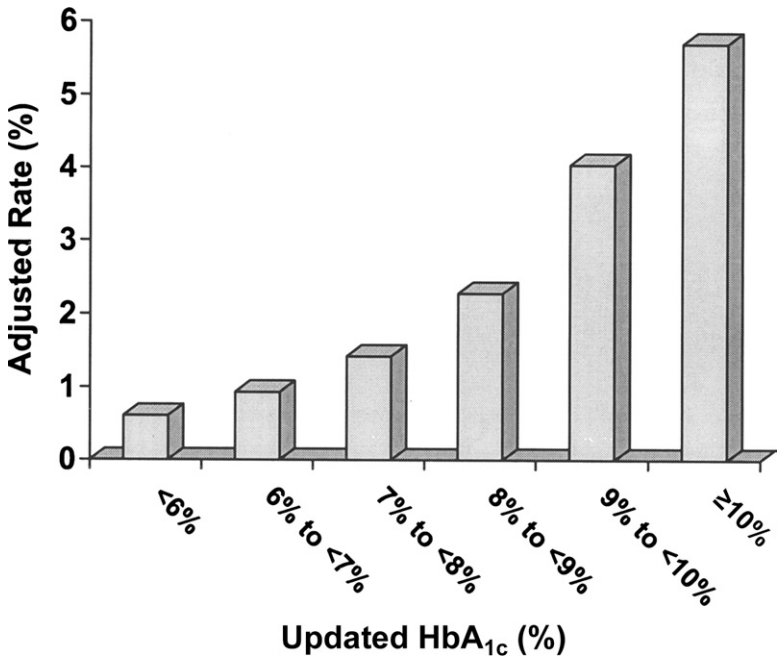

Figure 1. Link between glycosylated hemoglobin (HbA_{1c}) and microvascular end points in the United Kingdom Prospective Diabetes Study (UKPDS). The graph shows the epidemiologic relation between the updated HbA_{1c} levels of participants in the UKPDS and the point estimate of the 10-year rate of the composite microvascular end point (laser therapy, vitreous bleed, or renal failure). The rates are adjusted to reflect the experience of white men aged 50–54 years at diagnosis of diabetes mellitus. (Adapted from *BMJ*.[10])

Methods

Details regarding the overall design of ACCORD are described elsewhere in this supplement.[14] All ACCORD participants are provided with education regarding diet and lifestyle, glucose monitoring and therapy, and the avoidance and treatment of hypoglycemia. They are also provided with antidiabetic medications from a formulary of drugs, as well as glucose-monitoring equipment. The ACCORD formulary contains the following drugs, representing several classes of antihyperglycemic agents: glimepiride (a sulfonylurea), repaglinide (a rapid-acting secretagogue), metformin (a biguanide), rosiglitazone (a thiazolidinedione), acarbose (an α-glucosidase inhibitor), glargine, neutral protamine Hagedorn and premixed insulins (longer-acting insulins), and aspart and regular insulin (shorter-acting insulins).

Participants randomly allocated to the intensive treatment group are scheduled for monthly visits for the first 4 months and bimonthly visits thereafter, with ≥1 extra visit or between-visits phone call. Participants in the standard glycemic control group are seen at 1 month and then every 2–4 months depending on whether they are also allocated to the intensive blood pressure control arm of ACCORD, as described in the report on the trial's overall design elsewhere in this supplement.[14] Additional interactions with either group are scheduled at the discretion of the clinical site. HbA_{1c} levels are measured at a central laboratory every 4 months, and the results are promptly reported back to clinical sites and to the central database. A Bayer DCA 2000 point-of-care measurement device (Bayer AG, Leverkusen, Germany) is also available at each site to immediately estimate participants' HbA_{1c} results when indicated (see the following discussion).

As noted in the inclusion criteria, described in this supplement,[14] all participants' HbA_{1c} levels must be documented to be ≥7.5% before randomization. Thus, glycemic interventions are adjusted with the aim of reducing all of the intensive-group participants' HbA_{1c} levels to <6% and to either maintain or reduce standard-group participants' HbA_{1c} levels at 7.0%–7.9%. Investigators and research staff members are all provided with guidelines regarding diabetes care and are given flexibility to individualize interventions (including lifestyle approaches, behavioral therapies, and self-titration and the adjustment of any of the glucose-lowering drugs) needed to achieve the glycemic targets of the group to which each participant has been allocated. Thus, ACCORD is a trial in which 2 different treatment policies or strategies (with differing HbA_{1c} targets and not mandated differential medication use) are being compared.

Intensive glycemic control: In addition to lifestyle approaches, the pharmacologic antihyperglycemic regimen of intensive-group participants is initially adjusted so that ≥2 classes of agents are provided. As noted in Table 3, the dosage of ≥1 class is to be increased, or an agent of another class is to be added at each visit, whenever (1) the central laboratory–measured or point-of-care HbA_{1c} level is ≥6%, (2) >50% of self-monitored premeal capillary glucose readings are >5.6 mmol/L (100 mg/dL), or (3) >50% of postmeal capillary glucose readings are >7.8 mmol/L (140

Table 3
Glycemic targets and thresholds for action in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial

Therapy	Target HbA_{1c}	"Action Required" Thresholds	
		HbA_{1c}	>50% of SMBG Results/4 Days
Standard	7%–7.9%	>7.9%* or ≤6.5%† (anytime) or 6.6%–6.9%† (twice consecutively)	Fasting/ac <90 mg/dL (5.0 mmol/L)†
Intensive	<6.0%	≥6.0%*	Fasting/ac >100 mg/dL (5.6 mmol/L) or 2-hr pc >140 mg/dL (7.8 mmol/L)*

ac = antecibal; HbA_{1c} = glycosylated hemoglobin; pc = postcibal; SMBG = self-monitoring of blood glucose.
* Antihyperglycemic therapy will be advanced if either the HbA_{1c} or the SMBG "action required" criteria are met at any participant encounter.
† Therapy with drugs that increase the risk for hypoglycemia (eg, insulin, sulfonylureas, meglitinides) will be reduced to avoid hypoglycemia if these criteria are met.

Table 4
Differences in glycemic approach for the 2 treatment groups

Element of Approach	Standard Group	Intensive Group
Visits (first 4 mo)	Monthly to every 4 mo*	Monthly
Visits (>4 mo)	Every 2–4 mo*	Every 2 mo
Phone contact	Participant initiated	Research staff initiated (≥1 between visits)
Supplemental contact	Severe hypoglycemia or HbA_{1c} in "action required" range or >50% of premeal SMBG levels <90 mg/dL (5.0 mmol/L)	Severe hypoglycemia or HbA_{1c}/ SMBG levels in "action required" range
Point-of-care HbA_{1c}	Optional	Mandatory
Routine postprandial SMBG values to guide therapy	No	Yes
SMBG frequency† (not on insulin)	≤7/wk (daily at different times or >1/day on certain days)	≥2/day and 4/day if glucose is greater than target (2 ac/day and 2 pc/day)
SMBG frequency† (on insulin)	≤3/day	4–8/day (≥2 premeal and 2 postmeal); periodic 3 AM test
Self-titration principles	Avoid severe hypoglycemia‡ and premeal SMBG levels <90 mg/dL (5.0 mmol/L)	Avoid severe hypoglycemia‡ and adjust doses every 4 days and use food patterns to adjust mealtime insulin
Initial minimum therapy	Diet/lifestyle	Diet/lifestyle and 2 oral agents
Insulin use (when needed)	Generally ≤2 injections/day	Flexible

ac = antecibal; HbA_{1c} = glycosylated hemoglobin; pc = postcibal; SMBG = self-monitoring of blood glucose.
* Depending on the blood pressure group to which the patient has been assigned.
† Less frequent if goals are achieved.
‡ Including avoiding SMBG levels <70 mg/dL (3.9 mmol/L) on >25% of the readings.

mg/dL). When a new agent is added, previous therapies are continued unless there is a specific reason not to do so. Medications are reduced or withdrawn only because of side effects, severe hypoglycemia,[13] or contraindications. All combinations of drugs are permitted.

Several tools have been developed to promote the intensification of therapy. These are available to investigators, nurses, dietitians, and research staff members at all sites and include (1) Web-based patient management tools that allow investigators to review the latest HbA_{1c} level and drug regimen of each participant at their sites in comparison with other participants at the sites; (2) automated e-mails when a participant's HbA_{1c} level requires corrective action; (3) dynamic, Web-based reports that allow investigators to view the median achieved HbA_{1c} levels and the frequency and nature of drugs used at their sites relative to other sites in ACCORD; (4) weekly e-mailed tips to all sites suggesting methods to intensify therapy that are prepared by expert ACCORD clinicians and staff members; (5) the regular distribution of achieved HbA_{1c} levels in the intensive group at each site; (6) regular audit and feedback in which the achieved HbA_{1c} levels and antidiabetic regimens used at each site are reviewed by a network expert who is external to the site; and (7) annual training meetings that include

Table 5
Strategies used to intensity glycemic control

- Interact with participants at least once per month in person and/or on the phone
- Reinforce lifestyle and behavioral issues and increment pharmacotherapy at each visit
- Teach and encourage self-titration of insulin and oral agents to achieve capillary goals (at least once per week)
- Review and reinforce adherence at each visit
- Schedule intensive-group participant visits on the same day
- Consider group visits with intensive-group participants to reinforce self-care and allow participants to share experiences
- Add or increment therapy at every visit if the point-of-care or central laboratory HbA_{1c} level is ≥6% or if >50% of premeal capillary glucose levels are >100 mg/dL (5.6 mmol/L) or postmeal levels are >140 mg/dL (7.8 mmol/L)
- Encourage self-monitoring ≥2 times/day if not on insulin and ≥4 times/day if on insulin
- Add and optimize metformin use early
- Start with evening glargine insulin as the basal insulin and target fasting capillary glucose ≤100 mg/dL (5.6 mmol/L)
- Increment insulin doses by ≥10% of total daily dose regularly
- Consider adding prandial aspart insulin if >0.5 U/kg of basal insulin is being used and glycemic targets remain unmet
- Add a thiazolidinedione (rosiglitazone) early
- Do not stop or reduce any therapy when adding or incrementing another one
- Review each participant's HbA_{1c} level in team meetings at least weekly
- Contact participants to increment therapy on the phone if a central laboratory HbA_{1c} level ≥6% is reported if not incremented at the visit when it was drawn

HbA_{1c} = glycosylated hemoglobin.

glycemic management workshops and lectures. Finally, point-of-care HbA_{1c} measurements using the Bayer DCA 2000 are used at each visit to immediately inform changes in antihyperglycemic therapy; such an approach has been shown to lead to better glycemic control than awaiting central laboratory HbA_{1c} levels.[15]

Standard glycemic control: The antihyperglycemic regimen of standard-group participants is adjusted to reach and maintain an HbA_{1c} level of 7.0%–7.9%. Lifestyle and/or pharmacologic therapy is intensified whenever HbA_{1c} is ≥8%, and pharmacologic therapy is relaxed if a participant is experiencing problems with hypoglycemia or other side effects. Moreover, antihyperglycemic drug therapies that promote hypoglycemic episodes (ie, insulin and insulin secretagogues) are reduced or withdrawn if HbA_{1c} levels persistently decrease to <7% in patients who are experiencing hypoglycemia (summarized in Tables 3 and 4).

Central audit of glycemia progress: Median HbA_{1c} levels and the use of antidiabetic therapies that have been recorded at each visit in the intensive-control and standard-control groups are reviewed at least once a month by the ACCORD Glycemia Working Group, comprising diabetologist representatives from each network of ACCORD sites. Its role is to (1) identify and disseminate successful strategies and combinations of drugs, (2) identify and interact with sites that are least successful at achieving the glycemic targets to facilitate their success, (3) recommend the addition of new drugs to the study formulary if they become available, (4) review and assess the impact on ACCORD treatment algorithms of newly published information, and (5) identify and interact with sites reporting episodes of severe hypoglycemia to minimize these rates.

Therapeutic strategies for glycemic management: The ACCORD interventions and the ACCORD hypothesis are focused on the levels of glycemia achieved, not on the nature of the therapies used to achieve these levels. On the basis of the cumulative experience in ACCORD, several strategies are being strongly promoted for glycemic management in the intensive group in ACCORD: (1) ensuring that recruited participants are capable and motivated to use all of the available therapies (especially insulin as needed) to achieve their glycemic goals if they are allocated to the intensive group; (2) excluding patients who are at high risk for hypoglycemia, such as those aged ≥80 years; (3) using ≥2 classes of antihyperglycemic therapies from the time of randomization in addition to reinforcing lifestyle approaches for all intensive-group participants; (4) rapidly titrating and/or adding pharmacologic therapy every 1–2 months; (5) initiating insulin use as early as possible; (6) preferentially using insulin analogues (eg, glargine and aspart) instead of human insulin; (7) combining all classes of antihyperglycemic agents (ie, secretagogues, metformin, thiazolidinediones, α-glucosidase inhibitors, and insulin); and (8) basing immediate changes in the glucose-lowering regimen on point-of-care HbA_{1c} measurements (with phone follow-up if the concomitantly sampled blood for central HbA_{1c} measurements returns discordant values). Tables 4 and 5 list these and other tactics that are currently being used in the intensive glycemic control group.

Finally, as noted in an accompanying report in this supplement on hypoglycemia monitoring,[13] a carefully structured system has been designed to detect and address hypoglycemia within the study to minimize the chance of harm and to decrease therapies in patients who are experiencing problems. Moreover, hypoglycemia (along with other adverse effects) is audited carefully by the external Data and Safety Monitoring Board (DSMB) to ensure that participants are not experiencing unacceptably high or dangerous rates.

Conclusion

The day-to-day challenge of achieving and maintaining 2 different levels of glycemic control during ≥4 years (and up to 8 years) of therapy is an arduous but necessary task for investigators and participants. The fact that successful achievement of the glycemic goals requires many pharmacologic therapies in addition to diet, exercise, and overall behavior modification means that actual adverse effects, concerns over the possibility of adverse effects, nonadherence, and lack of motivation are often encountered. Nevertheless, the strategies outlined in this report have been put into action and are being successfully implemented.

The ACCORD trial will determine whether aggressive glucose lowering that targets an HbA_{1c} level <6% will reduce CVD in patients with type 2 diabetes. It is not designed or powered to test one antihyperglycemic approach against another; however, secondary epidemiologic analyses of ACCORD data will add insight regarding the relative importance of various strategies. It is also not designed to determine whether the results are due to the effect of the interventions on glucose levels as opposed to HbA_{1c} levels. Such a distinction may be important in light of recent evidence that the link between HbA_{1c} levels and diabetes complication rates may be independently affected by patterns of glycemia and by genetic factors.[16–18] Nevertheless, the ACCORD investigators are learning how to target normal-range HbA_{1c} levels in the safest possible way. No previous study has attempted to achieve this degree of glycemic control in thousands of patients over several years. Indeed, the approaches used are evolving as the investigators accumulate experience and modify their approaches in light of this experience. ACCORD is therefore also accumulating important data related to how optimal glycemic control can be obtained and to the rate of side effects of various approaches and combinations of therapies. Once completed, the ACCORD trial will clearly influence the management of patients with type 2 diabetes, regardless of the results.

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