

# Effect of Intensive Versus Standard Blood Pressure Control on Depression and Health-Related Quality of Life in Type 2 Diabetes

The ACCORD trial

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**OBJECTIVE**—We tested the hypothesis that intensive (systolic blood pressure [SBP] <120 mmHg) rather than standard (SBP 130–139 mmHg) blood pressure (BP) control improves health-related quality of life (HRQL) in those with type 2 diabetes.

**RESEARCH DESIGN AND METHODS**—Subjects were 1,028 ACCORD (Action to Control Cardiovascular Risk in Diabetes) BP trial HRQL substudy participants who completed baseline and one or more 12-, 36-, or 48-month HRQL evaluations. Multivariable linear regression assessed impact of BP treatment assignment on change in HRQL.

**RESULTS**—Over 4.0 years of follow-up, no significant differences occurred in five of six HRQL measures. Those assigned to intensive (vs. standard) BP control had statistically significant worsening of the Medical Outcomes Study 36-item short-form health survey (SF36) physical component scores (−0.8 vs. −0.2;  $P = 0.02$ ), but magnitude of change was not clinically significant. Findings persisted across all prespecified subgroups.

**CONCLUSIONS**—Intensive BP control in the ACCORD trial did not have a clinically significant impact, either positive or negative, on depression or patient-reported HRQL.

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In those with type 2 diabetes (T2DM), adequate blood pressure (BP) control may enhance control of hypertension (HT)-related symptoms and reduce the risk of major vascular events that impair health-related quality of life (HRQL) (1,2). However, the net impact of BP treatment on HRQL in patients with T2DM is determined by the balance of treatment burden,

hypotension-related adverse events, and BP medication side effects on the one hand and potential reductions of cardiovascular disease (CVD) and microvascular events on the other (3).

In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, intensive BP control did not reduce the main prespecified, composite macrovascular

outcome, or reduce mortality or myocardial infarctions, although intensive BP treatment did reduce the rate of strokes (4,5). In light of mixed clinical results, the impact of BP interventions on HRQL may inform the selection of optimal BP targets by clinicians and patients.

## RESEARCH DESIGN AND METHODS

The ACCORD BP HRQL substudy reported here was designed to prospectively quantify the impact of intensive versus standard BP treatment on validated measures of depression and HRQL in adults with T2DM over 4 years of follow-up. In the ACCORD BP trial, 4,733 subjects with T2DM, high cardiovascular risk, and uncontrolled HT were randomized to either standard (systolic blood pressure [SBP] goal 130–139 mmHg) or intensive (SBP goal <120 mmHg) BP control (6). A subsample of 1,028 ACCORD BP trial participants was randomly selected for the ACCORD BP HRQL substudy, described in detail elsewhere (7). All HRQL substudy participants were assessed for HRQL, depression status, and other specified measures at baseline and 12, 36, and 48 months throughout the duration of the full ACCORD trial. We hypothesized that compared with standard BP treatment, those treated intensively would 1) reduce symptoms and other medication side effects as assessed by the Symptoms Distress in Diabetes Questionnaire (8), 2) improve physical and mental composite scores as assessed by the Medical Outcomes Study 36-item short-form health survey (SF36) version 2 (9), 3) increase treatment satisfaction as assessed by the Diabetes Treatment Satisfaction Questionnaire (10), and 4) decrease depression scores as measured by the Patient Health Questionnaire-9 (PHQ-9) (11). The first three of these four hypotheses were prespecified in the study protocol. HRQL measures were self-administered by participants after careful review of instructions with trained research team members at baseline

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and at 12, 36, and 48 months throughout the ACCORD clinic visits. All measures that were completed before 30 June 2009 were used in the analysis. Completion varied somewhat across instruments.

Each HRQL or depression measure was a dependent variable considered in a separate linear model for repeated measures; no formal adjustments were made for multiple tests. All models included BP trial assignment, glucose trial assignment, and presence or absence of cardiovascular events at baseline. To test whether the effect of the BP treatment arm assignment varied across time, we included an interaction term for BP treatment arm by time. A second set of models tested each HRQL or depression outcome as outlined above but included sex, race, and age at baseline. Finally, we analyzed prespecified subgroups based on age, race/ethnicity, prior CVD, glucose trial assignment, number of BP medications taken just prior to randomization, baseline diastolic BP, and baseline systolic BP levels.

**RESULTS**—Participants randomly assigned to the intensive and standard BP treatment arms of ACCORD had similar baseline demographic and clinical characteristics, except that the proportion of subjects on statin therapy at baseline was 64.2% in the intensive BP treatment arm and 71.2% in the standard BP versus intensive BP treatment arms ( $P = 0.02$ ). At baseline, the six prespecified HRQL and depression outcome measures were not statistically different between subjects randomized to intensive versus standard BP treatment.

Table 1 shows the results of repeated HRQL and depression outcome measure analyses by intensive versus standard BP treatment arm at last available follow-up. Mean follow-up time from randomization to last HRQL assessment was 1,362 days (median 1,461 days, or 4.0 years). No

differences between intensive BP and standard BP treatment group were noted in the change in PHQ-9 scores, SF36 mental component scores, number of symptoms, mean symptom distress, or treatment satisfaction. However, SF36 physical component scores decreased more from baseline to follow-up among the intensive BP treatment group relative to the standard BP treatment group ( $-0.8$  vs.  $-0.2$  units;  $P = 0.02$ ), suggesting worse perceived physical function over time in the intensive BP treatment group.

Results, including the statistically significantly worse SF36 physical component scores, persisted across prespecified subgroups based on age, sex, race, baseline CVD status, glucose trial assignment, BP tertiles at baseline, and baseline number of BP medications (data not shown).

**CONCLUSIONS**—Intensive BP control neither improved nor worsened most measures of health-related quality of life. Although intensive BP control subjects had significantly worse SF36 physical component scores, the magnitude of this difference (less than one point out of 100 on the SF36 physical component score) is less than the five-point change generally considered the minimal clinically important difference for this scale (9). Thus, this degree of difference in SF36 physical component scores, although statistically significant, was not clinically significant.

A recent meta-analysis of 20 studies (using various SF questionnaire versions) reported physical health scores that were 2.43 points lower in hypertensive compared with normotensive patients, but the studies included were heterogeneous (12). The Treatment of Mild Hypertension Study (TOMHS) showed that among adults with HT and no diabetes, actively treated HT patients had better HRQL than those treated with placebo, although the effects of specific classes of HT medications

were mixed (2). However, HRQL data for those with diabetes and comorbid HT are limited. The few observational studies examining the effects of coexisting morbidities (e.g., diabetes and other non-BP cardiovascular risk factors) have shown no consistent pattern of association for BP (and/or HT) and HRQL (13–15). Furthermore, no prior, large, randomized trial has achieved SBP  $<120$  mmHg, so no prior assessment of the impact of such low BP levels on the HRQL of patients with HT is available. Whether the results presented may change with longer-term follow-up is of interest, and follow-up of ACCORD subjects is underway.

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**Table 1—Results of repeated-measures analyses of HRQL and PHQ-9 outcomes by glycemia arm measures taken at years 1, 3, and 4**

Variable	Change in score from baseline across all visits in BP trial		
	Intensive	Standard	P value
SF36 physical component score (SE)	−0.8 (0.19)	−0.2 (0.19)	0.02
SF36 mental component score (SE)	0.5 (0.39)	0.4 (0.40)	0.77
Sum of diabetes symptoms (SE)	−1.4 (0.34)	−1.1 (0.35)	0.48
Diabetes symptom distress (SE)	−0.04 (0.02)	−0.04 (0.02)	0.98
Diabetes treatment satisfaction (SE)	13.3 (0.54)	13.1 (0.55)	0.84
PHQ-9 continuous score (SE)	−1.1 (0.14)	−0.9 (0.14)	0.29

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