COMMENT ON BUCKLEY ET AL.

Intensive Versus Standard Blood Pressure Control in SPRINT-Eligible Participants of ACCORD-BP. Diabetes Care 2017;40:1733–1738

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Buckley et al. (1) suggest that Systolic Blood Pressure Intervention Trial (SPRINT)-eligible patients from the Action to Control Cardiovascular Risk in Diabetes Blood Pressure (ACCORD-BP) trial who did not receive intensive glycemic control may have benefited from intensive blood pressure (BP) control and that therefore the studies share consistent results. Here, we report results of a similar analysis comparing SPRINT and ACCORD with a different conclusion. We specifically address whether varying patient characteristics between the trials account for the clear benefit of intensive BP control in SPRINT and the lack of benefit in ACCORD.

We compared SPRINT-eligible ACCORD patients with ACCORD-eligible SPRINT patients by applying the inclusion and exclusion criteria from both trials to each other (2,3). Of note, we excluded those with a history of stroke and used the Framingham 10-year cardiovascular disease (CVD) risk calculator for eligibility (4). We then calculated propensity scores for the likelihood of being assigned to one trial over another and used stepwise selection to include in the propensity model only variables that were associated with all-cause mortality, which were age, sex, race, number of BP medications taken at baseline, smoking status, history of clinical CVD, history of subclinical CVD, BMI, estimated glomerular filtration rate, and albuminuria.

We constructed increasingly similar cohorts by selecting patients with similar propensity scores (5). In Trim 1, we excluded patients from each trial with propensity scores more extreme than the range of the other. In Trim 2, we further excluded patients with propensity scores more extreme than the top and bottom 1% of the other trial. In Trim 3 and 4, we repeated this process with 3% and 5% cutoffs, respectively. We then calculated Cox proportional hazards regression models for all cohorts stratified by site and by glycemic control intensity, when applicable.

As expected, with successive trimmed cohorts, key predictors that differed substantially at baseline became more similar. For example, we observed progressively smaller differences in moving from the dual-eligible cohort to the most trimmed cohort for the SPRINT versus ACCORD comparison for mean age (66.5 vs. 63.2 years to 65.4 vs. 64.4 years), female sex (36.3% vs. 46.4% to 39.8% vs. 42.4%), number of BP medications (1.86 vs. 1.57 to 1.75 vs. 1.60), current smoking (15.6% vs. 13.1% to 13.4% vs. 13.7%), history of clinical CVD (19.6% vs. 29.3% to 22.5% vs. 22.3%), mean estimated glomerular filtration rate (75.4 vs. 91.1 mL/min/1.73 m^2 to 78.6 vs. 83.0 mL/min/1.73 m^2), and mean urine albumin-to-creatinine ratio (33.4 vs. 87.4 mg/g to 30.1 vs. 48.5 mg/g). BMI and race were also much more similar in the most trimmed cohort.

Despite having more similar patient characteristics, the hazard ratios (HRs) for mortality associated with intensive BP control in SPRINT remained close to that of the original population: HR 0.69 (95% CI 0.50–0.95) for the dual-eligible cohort, 0.71 (0.50–1.00) for the Trim 2 cohort, 0.70 (0.48–1.03) for the Trim 3 cohort, and 0.71 (0.46–1.08) for the Trim 4 cohort. Likewise, the same trend was observed for the HRs from ACCORD: HR 1.00 (95% CI 0.78–1.29) for the dual-eligible cohort, 0.93 (0.69–1.24) for the Trim 2 cohort, 1.01 (0.73–1.39) for the Trim 3 cohort, and 0.89 (0.62–1.27) for the Trim 4 cohort. Furthermore, in a Cox model using all SPRINT and ACCORD patients and controlling for the above predictors of mortality along with an indicator variable for intensive glycemic control, the HRs were 0.71 (95% CI 0.58–0.88) and 1.02 (0.81–1.30), respectively, with a *P* value for interaction of 0.02.

Our analysis suggests that differences in the demographics and comorbidities between SPRINT and ACCORD do not clearly explain the all-cause mortality benefit for intensive BP control in the former and not the latter. Of note, our analysis differs from that of Buckley et al. (1) in at least three ways: *1*) our exclusion criteria match the trials' somewhat better; *2*) we include both ACCORD glycemic control arms to better reflect real-life practice, which includes patients with good control; and *3*) we focus on total mortality, which is least prone to misclassification and most clearly highlights the differences between the two trials. On the basis of our results, we cannot attribute the

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differential benefit of intensive BP control between the two trials to features of the populations aside from diabetes. Other differences, including important distinctions in how BP was managed, remain alternative explanations for this disparity.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

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