Individualizing Blood Pressure Targets for People With Diabetes and Hypertension Comparing the ADA and the ACC/AHA Recommendations

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People with diabetes are at high risk for cardiovascular diseases, kidney disease, and retinopathy, all of which may be reduced with appropriate blood pressure (BP) management.¹ Therefore, the American Diabetes Association (ADA) includes recommendations for the diagnosis and management of hypertension in its annual Standards of Medical Care in Diabetes.² In addition, the ADA published a position statement on diabetes and hypertension in September 2017,¹ and the American College of Cardiology (ACC) and American Heart Association (AHA) published the 2017 Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults.³

Recommendations from the ADA and the ACC/AHA have similarities and differences. For example, both groups emphasize the importance of proper BP measurement and encourage home BP monitoring, and the classes of recommended antihypertensive medications are aligned. On the other hand, there are substantial differences with regard to target BP thresholds for hypertension treatment as well as BP thresholds used to diagnose hypertension.

The ADA recommendations include a BP target of less than 14O/90 mm Hg for most patients with diabetes and emphasize the need to individualize specific BP targets for each patient.^{1,2} Individualization includes the possibility of a lower BP target, and a target of less than 13O/80 mm Hg is explicitly suggested as a consideration for patients who are at high risk of cardiovascular or kidney disease and are able to tolerate this target without undue adverse effects. Age is listed as a factor that may influence selection of a BP target, particularly as age relates to cardiovascular risk, comorbidity, and polypharmacy, although age-specific targets are not advocated. The ADA recommendations urge that a shared decisionmaking process be applied to select each individual's optimal BP target.

To arrive at these recommendations, the writing group of the ADA's position statement on diabetes and hypertension and the ADA Professional Practice Committee reviewed all pertinent literature published through the middle of 2017. Recommendations were based on an extensive review of the clinical diabetes literature and supplemented with input from ADA staff and the medical community at large through an open-commentary process. There is strong evidence supporting treatment of patients with diabetes and BP of 140/90 mm Hg or higher with a goal to lower BP to less than 140/90 mm Hg.⁴ To evaluate lower BP targets, particular attention was paid to the Action to Control Cardiovascular Risk in Diabetes-blood pressure (ACCORD-BP) trial,⁵ which tested targeting a systolic BP less than 120 mm Hg vs less than 140 mm Hg among participants with type 2 diabetes at high risk for cardiovascular events. In the ACCORD-BP trial,⁵ there was no significant difference between the 2 BP treatment groups in the primary composite cardiovascular outcome, which included myocardial infarction, stroke, and death from cardiovascular causes, with annual rates of 1.87% vs 2.09% in a group targeting less than 120 mm Hg vs a group targeting less than 140 mm Hg (hazard ratio, 0.88; 95% CI, 0.73-1.06; P = .20). Benefits with regard to the secondary outcome of stroke prevention were counterbalanced by an increased risk of adverse events (including elevations in serum creatinine and electrolyte abnormalities) in the group targeting BP less than 120 mm Hg.

In meta-analyses of clinical trials that enrolled individuals with diabetes, more intensive BP treatment was clearly associated with improved cardiovascular outcomes for trials with mean baseline systolic BP of 140 mm Hg or higher or with mean systolic BP attained by the intensively treated group of 130 mm Hg or higher.⁴ On the other hand, for trials with mean baseline systolic BP less than 140 mm Hg or mean attained systolic BP for the intensively treated group of less than 130 mm Hg, more intensive BP treatment was associated with modest improvements in stroke prevention and albuminuria reduction but no significant difference in coronary heart disease, heart failure, composite cardiovascular events, or death.⁴

Data from populations without diabetes were also reviewed. The Systolic Blood Pressure Intervention Trial (SPRINT), which excluded individuals with diabetes, demonstrated that targeting a systolic BP less than 120 mm Hg can improve cardiovascular outcomes among patients with hypertension and high cardiovascular risk, albeit with increased risk of some adverse events (including hypotension, syncope, electrolyte abnormalities, and acute kidney injury).⁶ In the Heart Outcomes Prevention Education-3 trial of people at intermediate cardiovascular risk, among whom 6% had uncomplicated diabetes treated with diet, a fixed-dose combination of candesartan plus hydrochlorothiazide reduced cardiovascular risk only among participants with baseline systolic BP in the upper third (>143.5 mm Hg).⁷ A recent metaanalysis including 74 trials and more than 300 000 participants found significant heterogeneity by baseline BP, with no benefit to antihypertensive therapy in trials with mean baseline systolic BP less than 140/90 mm Hg.⁸

Overall, available evidence suggests that BP targets lower than less than 14O/90 mm Hg yield cardiovascular benefits for some populations but increase adverse events. The evidence suggests that patients with higher baseline cardiovascular risk and higher baseline BP may derive greater relative and absolute benefits. Patient factors determining adverse effects have not been well described. The extent to which the benefits and risks of intensive BP reduction extrapolate from clinical trials to clinical care also remain to be seen. In addition to strict protocols and intensive follow-up, ACCORD-BP⁵ and SPRINT⁶ each applied rigorous monitoring methods that are not currently used in usual practice and yield BP values that are generally lower than typical office BP readings by approximately 5 to 10 mm Hg.³

The ADA position statement on diabetes and hypertension and standards of medical care in diabetes assert that the best approach to determine treatment goals in the setting of incompletely defined benefits and risks that appear to vary across patients is to embrace individualization of treatment for each patient.^{1,2} In a relevant comparison, the ADA standards of medical care in diabetes acknowledge that the benefits and risks of glucose-lowering therapy vary according to patient characteristics and recommend individualization of hemoglobin A_{1c} targets.⁹ To individualize hemoglobin A_{1c} targets, the ADA recommends considering factors that modify both benefits of glucose-lowering treatment (such as anticipated lifespan and stage of existing diabetes complications) and risks of glucose-lowering treatment (such as comorbidity, intensity of treatment required to achieve goals, and observed adverse effects).

The ADA position statement on diabetes and hypertension and standards of medical care in diabetes recommend that BP targets be individualized for patients with hypertension in a manner similar to that used for establishing individual hemoglobin A_{1c} targets.^{1,2} In addition to reflecting the uncertainty of available evidence for lowering BP, individualization is consistent with a patientfocused approach to care that values patient priorities and physician judgment. Ideally, in the current era of precision medicine, more methods will become available to help guide clinicians and patients in this process by identifying individuals most likely to benefit or least likely to be harmed by intensive BP control. Adverse effects may play a prominent role in individualizing BP targets, as they do hemoglobin A_{1c} targets,⁹ and 1 potential risk of the uniform treatment target of less than 130/80 mm Hg recommended in the ACC/AHA guideline is overtreatment of patients with comorbidities, frailty, and increased risk of medication adverse effects.¹ Because of this concern, the ADA did not adopt the ACC/AHA recommendation to target BP less than 130/80 mm Hg for all patients with hypertension.³

The ADA recommendations distinguish BP thresholds used to diagnose hypertension from those used as treatment targets,^{1,2} as they distinguish hemoglobin A_{1c} thresholds used to diagnose diabetes from those used as treatment targets.⁹ With this view, there is no clear rationale to change the BP thresholds used to define hypertension from 140/90 mm Hg or higher (as recommended in ADA guidelines and others) to 130/80 mm Hg or higher (as recommended by the ACC/AHA guidelines).³ Among people with diabetes and most other conditions with high cardiovascular risk, the prevalence of hypertension is already high and would not increase substantially by applying lower BP thresholds. Rather, most adults newly classified as having hypertension using newly proposed BP thresholds (ie, with systolic BP 130-139 mm Hg or diastolic BP 80-89 mm Hg but not \geq 140/90 mm Hg) would be at markedly lower cardiovascular risk than those currently diagnosed as having hypertension. For most of these adults, lifestyle modification would be indicated and is already recommended by most professional societies.1-3

Consensus is important to most effectively guide patients and clinicians in treatment. To this end, open discussion and debate regarding the diagnosis and treatment of hypertension are essential, as is ongoing research to define optimal diagnostic and therapeutic approaches. As the process proceeds, individualization of patient goals and targets should be placed at the center of discussion.

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REFERENCES

1. de Boer IH, Bangalore S, Benetos A, et al. Diabetes and hypertension: a position statement by the American Diabetes Association. *Diabetes Care*. 2017;40(9):1273-1284.

2. American Diabetes Association. 9. Cardiovascular disease and risk management: standards of medical care in diabetes-2018. *Diabetes Care*. 2018; 41(suppl 1):S86-S104.

3. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines [published online November 13, 2017]. *Hypertension*. doi:10.1161/HYP.000000000000065

4. Emdin CA, Rahimi K, Neal B, Callender T, Perkovic V, Patel A. Blood pressure lowering in type 2 diabetes: a systematic review and meta-analysis. *JAMA*. 2015;313(6):603-615. 5. Cushman WC, Evans GW, Byington RP, et al; ACCORD Study Group. Effects of intensive blood-pressure control in type 2 diabetes mellitus. *N Engl J Med*. 2010;362(17):1575-1585.

6. Wright JT Jr, Williamson JD, Whelton PK, et al; SPRINT Research Group. A randomized trial of intensive versus standard blood-pressure control. *N Engl J Med*. 2015;373(22):2103-2116.

7. Lonn EM, Bosch J, López-Jaramillo P, et al; HOPE-3 Investigators. Blood-pressure lowering in intermediate-risk persons without cardiovascular disease. *N Engl J Med*. 2016;374(21):2009-2020.

8. Brunstrom M, Carlberg B. Association of blood pressure lowering with mortality and cardiovascular disease across blood pressure levels: a systematic review and meta-analysis. *JAMA Intern Med.* 2018; 178(1):28-36.

9. American Diabetes Association. 6. Glycemic targets: standards of medical care in diabetes-2018. *Diabetes Care*. 2018;41(suppl 1): S55-S64.