A Review of Blood Pressure Goals for Patients with Diabetes Mellitus

Ethan J. Sebring, PharmD Candidate, Class of 2015. (843) 450-5606. sebring@musc.edu, South Carolina College of Pharmacy, MUSC Campus

Kristy L. Brittain, PharmD, BCPS, CDE. Assistant Professor – Clinical Pharmacy and Outcome Sciences. (843) 792-0050. brittain@musc.edu, South Carolina College of Pharmacy, MUSC Campus

Stephanie E. Kirk, PharmD, BCACP, CDE. Assistant Professor – Clinical Pharmacy and Outcome Sciences. (843) 876-5270. kirks@musc.edu, South Carolina College of Pharmacy, MUSC Campus

Abstract

Objectives

1) Recognize the prevalence of hypertension among the population of patients with diabetes
2) Identify the benefits associated with the treatment of hypertension among patients with diabetes
3) Review the current blood pressure goals as described in recent hypertension and diabetes guidelines
4) Evaluate the evidence supporting specified blood pressure goals among patients with diabetes
5) Select an acceptable and evidence-based blood pressure goal for a patient with diabetes

Keywords: blood pressure goal, diabetes, systolic goal, diastolic goal, JNC8, ADA

Introduction

Hypertension (HTN) is currently the chronic medical condition that is most frequently treated in the United States. It is defined as a blood pressure (BP) of ≥ 140/90 mmHg. Patients may also have isolated systolic hypertension at a BP of ≥ 140 and less than 90 mmHg or isolated diastolic hypertension at a BP of less than 140 and ≥ 90 mmHg. Therefore, a diagnosis of HTN may be made based on either an elevated systolic blood pressure (SBP) or elevated diastolic blood pressure (DBP) if noted during repeat assessments over time. If left untreated, HTN is associated with significant morbidity and mortality, placing patients at an increased risk for stroke, kidney damage, and myocardial infarction (MI).

Patients with diabetes mellitus type 1 or type 2 are subject to the development of HTN sometime over the course of their lifetime. The incidence of HTN rises from 5% at 10 years after diagnosis to 70% at 40 years after diagnosis among patients with type 1 diabetes (T1DM). According to the Center for Disease Control (CDC), 71% of patients with diabetes from 2009-2012 had concomitant HTN. Additionally, in 2010, patients with diabetes were 1.5 times more likely to suffer a stroke and 1.8 times more likely to have a MI as...
compared to healthy individuals. Data from 2003-2006 showed that patients with diabetes had a risk of cardiovascular (CV) death 1.7 times among patients without diabetes. Diabetes also predisposes patients to chronic kidney disease (CKD), and almost 50% of the new cases in 2011 were in patients with diabetes. There are several factors thought to play a role in the development of HTN in patients with diabetes, which include nephropathy, volume expansion, arterial rigidity and hyperinsulinemia.

Development of HTN in patients with T1DM correlates with albuminuria, which typically presents a few years before an elevation in BP. Blood pressure elevation increases with the severity of nephropathy. The relationship between albuminuria and HTN in patients with type 2 diabetes (T2DM) is less pronounced. One study showed that almost 40% of patients with newly diagnosed T2DM already have HTN. Furthermore, 50% of this group of patients developed albuminuria sometime after they developed HTN. A marked correlation existed between obesity and increased BP in this population, and risk of CV events and CV disease were increased.

A second factor, volume expansion, is related to glucose and insulin. Hyperglycemia causes more glucose to be filtered and then reabsorbed via a sodium-glucose cotransporter in the proximal tubule of the kidney. This leads to sodium retention and an increase in volume, both of which may elevate a patient’s BP. Insulin itself may also promote sodium retention and increase volume and therefore BP.

A third factor, arterial rigidity, is related to the glycation of proteins and presence of atherosclerotic plaques. Patients with diabetes or glucose intolerance may have elevated SBP due to decreased elasticity of the arteries. This characteristic also increases the mortality of these patients.

Hyperinsulinemia is believed to be another factor contributing to elevated BP in patients with diabetes. This relationship is typically due to administration of insulin in T1DM and insulin resistance in T2DM. Insulin is capable of causing sodium retention and increasing sympathetic activity in the body, resulting in heightened BP.

Treatment of HTN in patients with diabetes is of utmost importance. Reduced BP has been associated with decreases in both macrovascular and microvascular complications. Macrovascular complications include events such as MI and stroke, whereas microvascular complications include retinopathy (eye damage) and nephropathy (kidney damage). Therapy can consist of lifestyle interventions with or without pharmacotherapy. Lifestyle interventions include dietary changes, exercise, weight loss, smoking cessation, and consumption of alcohol in moderation. Various drugs can be used to treat diabetic HTN, such as angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptor blockers, calcium channel blockers, thiazide diuretics, beta-blockers, and other classes. Upon reaching a SBP greater than 120 mmHg or a DBP greater than 80 mmHg or both, the American Diabetes Association (ADA) recommends initiating lifestyle modifications. Once a patient’s BP is greater than 140/80 mmHg, the ADA recommends initiating drug therapy.

Several trials have demonstrated the benefits associated with BP lowering among patients with diabetes. The Hypertension Optimal Treatment (HOT) trial demonstrated that reducing BP is associated with a significant decrease in the relative risk of experiencing CV complications. The United Kingdom Prospective Diabetes Study 38 (UKPDS 38) reported fewer deaths, strokes, and CV complications, along with less nephropathy and retinopathy. The Action in Diabetes and Vascular disease: preterAx and diamicroN-MR Controlled Evaluation (ADVANCE) trial showed a decrease in both macrovascular and microvascular issues.

Summary of Recommendations

Several organizations have published detailed guidelines on the management of HTN in patients with diabetes mellitus. Some of these organizations include the American Diabetes Association (ADA), the Joint National Committee (JNC), the Canadian Hypertension Education Program (CHEP), the European Society of Hypertension/European Society of Cardiology (ESH/ESC), and the United Kingdom’s National Institute for Health and Care Excellence (NICE). Guidelines also exist for HTN management in diabetes with chronic kidney disease (CKD); these include the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI) and the Kidney Disease: Improving Global Outcomes (KDIGO) guidelines. The recommended goal BP varies by each organiza-
tion and therefore the objective of this article is to discuss the rationale behind such recommendations. Table 1 summarizes the recommended goals by their associated organization.

This article will focus on recommendations set forth by the ADA and the JNC 8 as these two guidelines are commonly referenced in several primary and tertiary sources.

**ADA Recommendations and Evidence**

The ADA Standards of Medical Care in Diabetes-2014 Position Statement is designed to provide clinicians with recommendations regarding the diagnosis, therapy, and treatment goals as related to diabetes. The ADA formulated an evidence scale of A, B, C, and E; this grading system is summarized in Table 2. The ADA currently recommends a SBP goal of less than 140 mmHg and a DBP goal of less than 80 mmHg (ADA Level of Evidence: B). The guideline also includes an optional SBP goal of less than 130 mmHg in patients who may tolerate this intensity. This population may likely include younger patients and those whose BP does not require excessive therapy (ADA Level of Evidence: C).12

Several studies have shown that patients with diabetes have increased morbidity and mortality at BP greater than 115/75 mmHg. Additional studies show that a reduction of BP to less than 140/80 mmHg is associated with improvements in nephropathy and macrovascular outcomes.11,12,15,22-24 One of the significant trials quoted by the ADA is the Action to Control Cardiovascular Risk in Diabetes blood pressure (ACCORD-BP) trial.25 This trial was a randomized, multicenter study designed to determine if intensive antihypertensive therapy provides additional benefits as compared to traditional therapy. The study allocated 4,733 patients to either the intensive (SBP goal of < 120 mmHg) or the standard (SBP goal of < 140 mmHg) treatment arm. Patients were followed for an average of 4.7 years, and the primary outcome was the occurrence of a composite of “nonfatal MI, nonfatal stroke, or CV death”. Some of the secondary outcomes included “fatal or nonfatal stroke, nonfatal stroke, death from any cause, and death from CV causes”. Adverse effects were also assessed in this trial. Of note, the average BP for all patients in this study was less than 140/80 mmHg prior to the start of the study.25 The intensive group achieved an average SBP of 119.3 mmHg, and the standard group achieved an average SBP of 133.5 mmHg; the average between-group difference was 14.2 mmHg. There were no significant differences in the occurrence of the primary outcome or the rates of death between the 2 groups. The only differences seen regarding the secondary outcomes were related to stroke. Regarding nonfatal stroke, a rate of 0.30%/yr was seen in the intensive group compared to 0.47%/yr in the standard group. Regarding overall stroke, patients in the intensive group experienced a rate of 0.32%/yr compared with 0.53%/yr in the standard group. This study showed that 89 patients would need to be treated to the lower BP goal for 5 years to prevent one stroke in one individual. Another positive effect seen in the intensive group was a reduction in macroalbuminuria; this occurred in 6.6% of patients in the intensive group vs. 8.7% in the standard group. Regarding adverse effects, significant differences between groups were observed for estimated glomerular filtration rate (eGFR) and medication-related side effects. 4.2% of intensive-arm patients and 2.2% of standard-arm patients experienced at least one episode of eGFR

**Table 1** – Blood pressure goals for both T1DM and T2DM by organization16

<table>
<thead>
<tr>
<th>Organization</th>
<th>Systolic BP Goal (mmHg)</th>
<th>Diastolic BP Goal (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADA12</td>
<td>&lt;140</td>
<td>&lt;80</td>
</tr>
<tr>
<td>JNC 8</td>
<td>&lt;140</td>
<td>&lt;90</td>
</tr>
<tr>
<td>CHEP17</td>
<td>&lt;130</td>
<td>&lt;80</td>
</tr>
<tr>
<td>ESH/ESC18</td>
<td>&lt;140</td>
<td>&lt;85</td>
</tr>
<tr>
<td>NICE19 – T2DM</td>
<td>&lt;140</td>
<td>&lt;80</td>
</tr>
<tr>
<td>NF KDOQI20</td>
<td>&lt;130</td>
<td>&lt;80</td>
</tr>
<tr>
<td>KDIGO21 &lt;30 mg/24 hr: ≤140</td>
<td>Urine albumin excretion</td>
<td>Urine albumin excretion</td>
</tr>
<tr>
<td></td>
<td>&gt; 30 mg/24 hr: ≤130</td>
<td>&lt; 30 mg/24 hr: ≤90</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&gt; 30 mg/24 hr: ≤80</td>
</tr>
</tbody>
</table>
less than 30 mL/min/1.73 m². When evaluating the data from ACCORD BP, 50 patients would need to be treated more intensively for 5 years in order to decrease eGFR in one patient. Of note, this decrease in eGFR was not necessarily chronic. 3.3% of intensive-group patients vs. 1.27% of standard group patients experienced a serious adverse event related to antihypertensive therapy; these events included: “hypotension, syncope, bradycardia or arrhythmia, hyperkalemia, angioedema, and renal failure”, which translates to 1 patient experiencing an adverse event for every 49 patients treated to a lower BP goal. The investigators concluded that more intensive BP lowering does not reduce the rate of a composite of CV events more than standard BP lowering. 25

Another randomized controlled trial (RCT) referenced by the ADA is the ADVANCE trial. 12,15 The aim of this study was to determine how BP lowering with an ACEI (perindopril) and a thiazide diuretic (indapamide) affected macro- and microvascular events in patients with T2DM. Composites of macro- and microvascular outcomes were designated as the primary outcomes of this study. Macrovascular outcomes included: “CV death, non-fatal MI, or non-fatal stroke”; microvascular outcomes included “new or worsening nephropathy or retinopathy”. Secondary outcomes included: “all-cause mortality, CV death, total coronary events, total cerebrovascular events, new or worsening nephropathy, new or worsening retinopathy,” and others. The study followed 11,140 patients for an average of 4.3 years. BP in the treatment arm was lowered on average to 136/73 mmHg and BP in the control arm was lowered on average to 140/73 mmHg. This shows an average SBP change of 5.6 mmHg and an average DBP change of 2.2 mmHg. The treatment arm had 9% fewer primary outcome events as compared to the placebo arm (15.5% vs. 16.8%). Over a period of five years, 66 patients would need to be treated to avoid one of these events. Also, 14% fewer deaths were reported in the treatment arm (7.3% vs. 8.5%). Therefore, the treatment group would prevent one death per 66 patients treated to a lower BP goal during a five-year period. Other benefits of treatment include 21% fewer renal events (22.3% vs. 26.9%), and 21% less cases of microalbuminuria (19.6% vs. 23.6%). Over five years, 20 patients would need to be treated to the lower BP goal to prevent one renal complication, with this statistic largely applicable to new onset microalbuminuria. No significant difference in adherence between the treatment and control arms was
observed (73% vs. 74%, respectively). Also, only 3.6% of patients in the treatment arm discontinued the study drug due to intolerance of the adverse effects. Although this study had several statistically significant morbidity and mortality benefits, there was no specific BP goal defined in the study. Nonetheless, one can conclude that lowering BP to <140/80 mmHg does provide substantial benefits in patients with T2DM.15

Several other trials were quoted in the ADA position statement that support a BP goal of less than 140/80 mmHg. One meta-analysis demonstrated that SBP lowering to less than 130 mmHg resulted in fewer deaths and strokes and improved albuminuria. However, patients in the lower-goal arm experienced more adverse effects with no change in non-stroke cardiovascular outcomes, neuropathy, or retinopathy. The authors of this study concluded that a SBP goal of 130-135 mmHg was adequate.26 Another trial in patients with concomitant coronary artery disease (CAD) showed that a SBP goal of 130-140 mmHg was non-inferior to a SBP goal of less than 130 mmHg.27 Yet another study reported less incidence of stroke but increased cardiac complications in patients treated to a SBP goal of less than 115 mmHg.28 Ultimately, the ADA concludes that a SBP goal of <140 mmHg is appropriate for the majority of patients with diabetes. A SBP of less than 130 mmHG may be justified for patients considered to be at a high risk for stroke, those with a considerable life expectancy or patients that can be treated with low quantities of medications and little adverse effects.12

JNC 8 Recommendations and Evidence

The JNC 8 published evidence-based HTN guidelines in February 2014. The authors of this guideline examined only RCTs that contained specific subpopulations (e.g., CAD, diabetes, CKD, heart failure, etc.) and reported outcomes such as mortality and cardiac events. The authors conducted their own meta-analysis of the selected trials. Recommendations within the report were given a strength score of A-E or N, with A representing the strongest evidence, E representing expert opinion, and N representing no recommendation. Table 3 provides additional details regarding this rating scale. The recommendation of the panel is to treat patients ≥18 years old with diabetes to a goal BP of less than 140/90 mmHg and to initiate medication therapy at a BP of ≥140/90 mmHg.2 Pharmacotherapy may be started once either the SBP or DBP exceeds the recommended level. This recommendation includes summative discussions of the ACCORD BP, HOT, and UKPDS 38 trials.2,13,14,25 The ACCORD BP trial (discussed above) is largely responsible for the committee’s recommendation of SBP less than 140 mmHg as opposed to even lower goals.2 Other trials, including Systolic Hypertension in the Elderly Program (SHEP) and Systolic Hypertension in Europe (Syst-Eur), are briefly quoted in the recommendation summary due to their data on the benefits of

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>Strong Very likely to have a significant net benefit</td>
</tr>
<tr>
<td>B</td>
<td>Moderate Likely to have a moderate or moderate to high net benefit</td>
</tr>
<tr>
<td>C</td>
<td>Weak Likely that a small net benefit is present.</td>
</tr>
<tr>
<td>D</td>
<td>Against Likely that there is no net benefit or risks outweigh the benefits</td>
</tr>
<tr>
<td>E</td>
<td>Expert Opinion (Evidence may be ambiguous or even lacking) Net benefit is ambiguous. Risk vs. benefit cannot be fully determined, but the committee believed a decision was necessary. Potential for additional research exists.</td>
</tr>
<tr>
<td>N</td>
<td>No decision for or against (Evidence may be ambiguous, contradictory, or lacking) Net benefit is ambiguous. Risk vs. benefit cannot be fully determined, but the committee believed no decision could be made. Potential for additional research exists.</td>
</tr>
</tbody>
</table>

Table 3 – JNC 8 recommendation grading schematic2
lowering SBP to less than 150 mmHg.\textsuperscript{29,30} Results of the ADVANCE trial were not included in their analysis “because participants were eligible irrespective of baseline BP, and there were no randomized BP treatment thresholds or goal”.\textsuperscript{2}

The UK Prospective Diabetes Study (UKPDS) 38 trial was constructed to determine the effect of strict BP management on macro- and microvascular events in patients with T2DM. Patients were stratified to treatment goals of either less than 150/85 mmHg or less than 180/105 mmHg. Treatment in the lower-goal arm consisted of captopril and atenolol while treatment in the higher-goal arm consisted of any antihypertensives except an ACEI or a beta-blocker. The primary outcome was defined as the time to the occurrence of a composite of CV or diabetic complications or death. Secondary endpoints included additional macro- and microvascular complications. This trial followed 1,148 patients for an average of 8.4 years.\textsuperscript{14} The average BP in the lower-goal arm was 144/82 mmHg while the average BP in the higher-goal arm was 154/87 mmHg. The lower-goal group provided a 24\% decrease in any diabetic complication (34\% vs. 44\%) and a 32\% decrease in diabetes-related mortality (11\% vs. 16\%). The authors calculated that 15 patients would need to be treated to this lower-goal over a 10-year period to prevent one diabetes-related death. Furthermore, the study demonstrated a 34\% decrease in all macrovascular events and a 44\% decrease in stroke (5\% vs. 9\%) in the lower-goal group. Microvascular endpoints were shown to have a 37\% reduction (9\% vs. 14\%). The investigators calculated that 6.1 patients would need to be treated with lower-goal for 10 years to prevent one diabetes-related death. Furthermore, the study demonstrated a 34\% decrease in diabetes-related complications and deaths. Of note, 29\% of patients in the lower-goal arm used at least 3 medications for BP control.\textsuperscript{11} The JNC 8 investigators did not use this evidence to determine a specific DBP goal since the trial looked at both SBP and DBP lowering.\textsuperscript{2} Therefore, clinical outcomes cannot necessarily be attributed to the lowering of one over the other or both. Also, UKPDS 38 was designed to compare a DBP goal of less than 85 mmHg to a DBP goal of less than 105 mmHg, making it impractical to extrapolate this data to compare a goal of <85 mmHg to a goal of less than 90 mmHg.\textsuperscript{2,14}

The HOT trial was conducted to determine the most appropriate DBP goal in hypertensive patients. The study was broken into three treatment arms based on DBP goals: ≤ 80 mmHg, ≤ 85 mmHg, and ≤ 90 mmHg. Concomitant diabetes mellitus was present in only 8\% of patients in each treatment arm. Medication regimens consisted of felodipine initially, followed by the addition of an ACEI or beta-blocker, if necessary, and then addition of a diuretic, if necessary. The authors defined major CV events as “all MI, all stroke, and all other CV deaths”. Patients were followed for a period of 3 years.\textsuperscript{13} At the end of the study, BP averages in the ≤ 80 mmHg, ≤ 85 mmHg, and ≤ 90 mmHg groups were 81.1 mmHg, 83.2 mmHg, and 85.2 mmHg, respectively. In the subset of patients with diabetes, major CV event risk in the ≤ 80 mmHg group was roughly 50\% of the risk in the ≤ 90 mmHg group (22 events vs. 45 events, respectively). Additionally, CV mortality was significantly decreased in the ≤ 80 mmHg group when compared to the ≤ 90 mmHg group. The occurrence of side effects gradually improved over the course of the study, with 16.9\% of patients experiencing them at the 3-month visit, and 2.2\% of patients experiencing them at the final visit. Overall, the authors concluded that BP lowering to less than 140/85 mmHg is associated with significant macrovascular benefits.\textsuperscript{13} The SBP value associated with the lowest stroke risk was 142.2 mmHg while the DBP value associated with this decrease was beneath 80 mmHg. Risk of cardiovascular death was at its lowest at a SBP of 138.8 mmHg and a DBP of 86.5 mmHg. Based on the information provided from the diabetic subset, one may conclude that a DBP goal of ≤ 80 mmHg has added macrovascular benefits in this population.\textsuperscript{13} However, given that the average DBP overall in this arm was only 81.1 mmHg (average value in the subpopulation with diabetes was not reported), one may instead conclude that treatment to the lower end of the 80-89 mmHg range may be sufficient for the macrovascular benefits in patients with diabetes. Of note, the JNC 8 panel considered the evidence from this trial low- quality since the subpopulation of patients with diabetes was not prespecified in the study plan.\textsuperscript{2}

Overall, given the somewhat conflicting data included in the JNC 8 summary, the authors decided on a BP goal of less than 140/90 mmHg based primarily on expert opinion. There is currently insufficient high-quality evidence pointing towards a SBP goal of less than 130 mmHg. Additionally, the authors were unable to identify any “good- or fair-quality RCTs” that measured mortality
in relation to DBP goals less than 90 mmHg compared to even lower goals.²

**Conclusions/Summary**

Hypertension in diabetes is associated with significant macro- and microvascular complications, and lowering of BP has been shown to significantly reduce these events. However, multiple organizations have developed recommended goal values for patients with diabetes, and sometimes these values differ. This article focused on the reasoning behind the goals included in the ADA position statement and the JNC 8 HTN management guidelines. These guidelines recommend a goal of less than 140/80 mmHg and less than 140/90 mmHg, respectively. There is sufficient data to conclude that a SBP goal of less than 140 mmHg is non-inferior to even lower goals as trials such as ACCORD BP and Cooper-DeHoff, et al. showed minimal differences in overall CV outcomes. However, these trials did show significantly fewer strokes. On the other hand, the HOT trial, which examined various DBP goals, did not provide high-quality evidence. Furthermore, the ADA DBP goal of less than 80 mmHg appears to be based on the diastolic values in the ACCORD BP trial. Patients in this study had an average DBP below 80 mmHg before and after the study; therefore, positive outcomes may have been more attributable to SBP lowering. Some trials also reported results with SBP and DBP lowering, making it more difficult to determine which BP value was responsible for the clinical benefits. Table 4 provides a summary of the trials discussed in this article. Furthermore, of the trials discussed, only the ACCORD BP study reported thorough data on the serious

<table>
<thead>
<tr>
<th>Trial</th>
<th>Outcome (Goal)</th>
<th>NNT/NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACCORD²</td>
<td>Decreased stroke rate (&lt;120 mmHg)</td>
<td>89</td>
</tr>
<tr>
<td></td>
<td>Reduced eGFR (&lt;120 mmHg)</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Increase in adverse effects (&lt;120 mmHg)</td>
<td>49</td>
</tr>
<tr>
<td>ADVANCE¹³</td>
<td>Decreased mortality (&lt;140 mmHg)</td>
<td>75</td>
</tr>
<tr>
<td></td>
<td>Fewer renal complications (&lt;140 mmHg)</td>
<td>20</td>
</tr>
<tr>
<td>HOT ¹³</td>
<td>Reduction in major CV events, not including silent MI (≤ 80 mmHg)</td>
<td>272</td>
</tr>
<tr>
<td></td>
<td>Reduction in major CV events, including silent MI (≤ 80 mmHg)</td>
<td>348</td>
</tr>
<tr>
<td></td>
<td>Reduction in CV mortality (≤ 80 mmHg)</td>
<td>448</td>
</tr>
<tr>
<td>UKPDS 38¹⁴</td>
<td>Fewer diabetes-related deaths (&lt;150/85 mmHg)</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Reduced microvascular events (&lt;150/85 mmHg)</td>
<td>6.1</td>
</tr>
</tbody>
</table>
adverse effects experienced by patients. This makes it difficult to make a conclusion about the true prevalence of side effects when treating to a lower BP goal.

Additionally, these studies did not extensively report the effects of various socioeconomic factors such as cost, increased medication burden, overall tolerability, and adherence. The use of additional medications to further lower BP may be too expensive for some patients. The increased number of medications and/or increased frequency may make the medication regimen too difficult for a patient to understand. Patients may also not tolerate the side effects of a medication. Collectively, these factors can all negatively affect the patient’s adherence to his or her medication regimen.

<table>
<thead>
<tr>
<th>Trial</th>
<th>SBP Goal (mmHg)</th>
<th>DBP Goal</th>
<th>Average BP (mmHg)</th>
<th>Key Point(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACCORD\textsuperscript{25}</td>
<td>&lt;120&lt;br&gt;&lt;140</td>
<td>-</td>
<td>119.3&lt;br&gt;133.5</td>
<td>• No significant difference in most outcomes&lt;br&gt;• Significantly fewer strokes in the lower-goal arm&lt;br&gt;• More serious adverse effects in the lower-goal arm</td>
</tr>
<tr>
<td>ADVANCE\textsuperscript{15}</td>
<td>-&lt;br&gt;-&lt;br&gt;-</td>
<td>-</td>
<td>136/73&lt;br&gt;140/73</td>
<td>• Fewer coronary events in the lower-goal arm&lt;br&gt;• Fewer kidney complications in the lower-goal arm&lt;br&gt;• No specific BP goals predefined</td>
</tr>
<tr>
<td>HOT\textsuperscript{13}</td>
<td>-&lt;br&gt;-&lt;br&gt;-</td>
<td>\leq80&lt;br&gt;\leq85&lt;br&gt;\leq90</td>
<td>81.1&lt;br&gt;83.2&lt;br&gt;85.2</td>
<td>• CV risk decreased by 50% in the \leq80 arm compared to the \leq90 arm</td>
</tr>
<tr>
<td>UKPDS 38\textsuperscript{14}</td>
<td>&lt;150&lt;br&gt;&lt;180</td>
<td>&lt;85&lt;br&gt;&lt;105</td>
<td>144/82&lt;br&gt;154/87</td>
<td>• Less diabetes-related morbidity and mortality in the lower-goal arm&lt;br&gt;• Less CV events, including stroke, and less microvascular events in the lower-goal arm</td>
</tr>
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</table>
Nonadherence will likely promote elevated blood pressure, which would decrease the macro- and microvascular benefits associated with antihypertensive therapy. These factors should therefore be taken into consideration when evaluating a patient’s medication regimen in relation to his or her BP goal.

Ultimately, the BP goal should be individualized for each patient. Based on the above evidence, it is reasonable to recommend treating most patients with diabetes to a goal BP of less than 140/90 mmHg as suggested by the JNC 8. This goal has been associated with substantial improvements in macro- and microvascular outcomes and is not associated with unreasonable adverse effects. A goal of less than 140/80 or less than 130/80 mmHg, as suggested by the ADA, may be appropriate in patients who would benefit from an additional decrease in stroke risk and in patients who can tolerate the associated increases in medication burden. Patients who have significant adverse effects or symptoms of hypotension should not be treated to these lower goals. Additionally, patients who have trouble with adherence may also not be candidates for these lower goals. Of note, patients who are already managed at the lower goals without significant tolerance issues may be maintained on their current antihypertensive regimen. Dosages should only be reduced once the effects of treatment become intolerable.

References
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LEARNING ASSESSMENT QUESTIONS:

1. A 32 year-old white male presents to the pharmacy for chronic disease state education. Part of the education session includes a discussion of the specific blood pressure goals for this patient. His past medical history is significant for type 2 diabetes mellitus, hypertension, hyperlipidemia, and obesity. His father also has hypertension, history of stroke and had a myocardial infarction (MI) at the age of 62. His mother has type 2 diabetes also and suffered a stroke 2 years ago. His current medications include metformin 1000 mg twice daily, ramipril 5 mg daily, and atorvastatin 80 mg daily. His morning blood pressure measurement over the past 2 weeks has been 152/96 mm Hg on average.

Based on data from the ACCORD BP trial, which of the following reasons would best justify a blood pressure goal of <130/80 if chosen after a provider-patient discussion?

a. To reduce the risk of MI, given his family history
b. To reduce the risk of arrhythmia, given that he is already taking ramipril
c. To reduce the risk of hyperkalemia, given that he is already taking ramipril
d. To reduce the risk of stroke, given his family history

2. You are a pharmacist in a primary care clinic who sees diabetic patients as part of a collaborative practice agreement. One of the physicians asks if you would recommend treating one of her patients to a lower BP goal. The 82 year-old patient is currently at a BP of 131/78 mmHg. She is taking losartan 100 mg, amlopidine 10 mg, and hydrochlorothiazide 25 mg daily and has not experienced any intolerable side effects.

What would be your response to this physician?

a. Recommend treating her to a SBP goal < 130 mmHg as this will significantly reduce her risk of a heart attack.
b. Recommend treating her to a SBP goal <130 mmHg to reduce her risk of further kidney or eye damage.
c. Recommend leaving her treatment as is, given her age and already significant medication burden.
d. Recommend removing one of her medications to maintain a DBP goal of <90 mmHg.

3. A patient with hypertension has recently been diagnosed with type 2 diabetes mellitus. He presents to your pharmacy with concerns about his new disease state and medications. He wants to know if diabetes places him at risk for any other issues in the future. What would be the most appropriate counseling point for this patient?

a. Diabetes and hypertension place him at an increased risk of suffering macrovascular complications such as a heart attack or stroke.
b. Diabetes places him at increased risk of microvascular complications such as kidney damage, while hypertension places him at increased risk for a heart attack.
c. Diabetes and hypertension place him at an increased risk of having microvascular complications such as a heart attack or stroke.
d. Diabetes places him at an increased risk of a stroke, while hypertension places him at increased risk for microvascular complications including eye damage.
4. The HOT trial was designed to determine the most appropriate diastolic blood pressure goals in patients with diabetes and hypertension. The authors determined that a diastolic blood pressure goal less than 80 mmHg provided significant reductions in macrovascular complications. Which of the following aspects of this trial is most important when making a conclusion about this result?

a. The majority of patients in the lowest-goal arm achieved blood pressures in the range of 70-75.

b. The average diastolic blood pressure in the lowest-goal arm was above 80 mmHg.

c. The results from the lowest-goal arm excluded data for strokes and therefore cannot be applied to patients at higher risk for these events.

d. Patients in the ≤80 mmHg group had significantly fewer heart attacks than patients in the ≤85 mmHg group – making this the most beneficial diastolic blood pressure goal.

5. A 69 year-old female has been recently diagnosed with hypertension. Aside from her new diagnosis, her past medical history is significant for type 2 diabetes mellitus, hyperlipidemia, COPD, and chronic migraine. Her family history is significant for hypertension and hyperlipidemia in both her father and mother. Her conditions are managed with several medications, and she often feels the side effects of some of her medications are a nuisance. She is open to trying a medication for hypertension, but is hesitant about the potential for more side effects. Her average BP readings are 164/102 mm Hg. What would be the most appropriate blood pressure goal for this patient?

a. <140/90 mmHg

b. <150/90 mmHg

c. <150/80 mmHg

d. <130/80 mmHg

6. A 48 year-old male has a past medical history significant for type 2 diabetes and hypertension. His family history is significant for myocardial infarction and hypertension in his father and diabetes in his mother. He currently takes metformin 1000 mg twice daily, glipizide ER 10 mg daily, and quinapril 10 mg daily. Overall, he tolerates his current medication regimen quite well. His average blood pressure over the past month is 146/84 mm Hg. What would be the most appropriate blood pressure goal for this patient?

a. <120/80 mmHg

b. <130/80 mmHg

c. <140/80 mmHg

d. <150/90 mmHg

7. The ACCORD BP trial is one of the trials the ADA referenced when determining their blood pressure goal of less than 140/80 mmHg. Which of the following is true of this trial and must be considered when applying this trial’s data to a patient?

a. Patients in the trial only had type 1 diabetes mellitus and the data can therefore not be applied to patients with type 2 diabetes mellitus.

b. The lower systolic goal of <120 mmHg was associated with much fewer cases of myocardial infarction than the higher goal of <140 mmHg.

c. Patients in the study had an average blood pressure lower than <140/80 mmHg at the start of the study and therefore likely had decreased risk from the beginning.

d. Many of the patients in the trial had an incidence of reduced eGFR which ultimately led to chronic renal disease.

8. A 54 year-old male with a past medical history for type 2 diabetes mellitus, hypertension, myocardial infarction, and cerebrovascular accident presents to your pharmacy for prescription refills. While at the counter, he mentions his daily blood pressures have been in the low 140s/90s mm Hg and asks if his numbers should be lower. What is the most appropriate response for this patient?

a. No. Given your past medical history and age, it is not likely that you will tolerate a much lower goal.

b. Yes. Given your age, you would be a good candidate for a diastolic goal of <90 mmHg.

c. Yes. Given your past medical history, you would likely benefit from achieving a systolic blood pressure <130 mmHg.

d. No. Despite your medical history, you are already at the recommended goal and there is no high-quality evidence to support a lower blood pressure goal at this time.