Treatment of hypertension in patients with diabetes mellitus

AUTHOR: George L Bakris, MD
SECTION EDITORS: David M Nathan, MD, William B White, MD
DEPUTY EDITORS: Karen Law, MD, John P Forman, MD, MSc

All topics are updated as new evidence becomes available and our peer review process is complete.

Literature review current through: **Aug 2023.**
This topic last updated: **Feb 08, 2023.**

INTRODUCTION

Diabetes mellitus is a common disorder, affecting nearly half a billion people worldwide and 8 to 9 percent of the population in the United States.

- (See "Type 2 diabetes mellitus: Prevalence and risk factors", section on 'Prevalence'.)
- (See "Epidemiology, presentation, and diagnosis of type 1 diabetes mellitus in children and adolescents", section on 'Epidemiology'.)

Hypertension occurs frequently in patients with diabetes and, together, diabetes and hypertension substantially increase the risk of cardiovascular and kidney disease. Effective treatment of hypertension in such patients reduces cardiovascular risk. (See "Overview of established risk factors for cardiovascular disease".)

The pathogenesis, epidemiology, and choice of antihypertensive therapy in patients with diabetes mellitus are presented in this topic. The diagnosis of hypertension and goal blood pressure in patients with diabetes are discussed separately:

- (See "Blood pressure measurement in the diagnosis and management of

hypertension in adults".)

- (See "Goal blood pressure in adults with hypertension", section on 'Patients with diabetes mellitus'.)

PATHOGENESIS

In addition to the development of kidney disease, at least two other factors have been proposed to contribute to hypertension in diabetes: extracellular fluid volume expansion and increased arterial stiffness [1].

Sodium retention and volume expansion may be induced both by insulin and the hyperglycemia-induced increase in the filtered glucose load [2,3]. The excess filtered glucose is reabsorbed in the proximal tubule via a sodium-glucose cotransporter, resulting in a parallel rise in sodium reabsorption [3]. Thus, salt loading tends to raise the blood pressure, an effect that can be reversed by salt restriction.

Patients with diabetes have increased vascular stiffness [1], which is thought to be a consequence of increased protein glycation and, at a later stage, atheromatous disease. The reduction in arterial distensibility, which is seen with both impaired glucose tolerance and overt diabetes, can contribute to the rise in systolic pressure disproportionately to diastolic pressure and is associated with increased blood pressure variability and mortality risk [4,5].

EPIDEMIOLOGY

Hypertension is a common problem in patients with both type 1 and type 2 diabetes, but the time course in relation to the duration of diabetes is different [2,6-9].

Among those with type 1 diabetes, the incidence of hypertension rises from 5 percent at 10 years, to 33 percent at 20 years, and to 70 percent at 40 years [2]. There is a close relation between the prevalence of hypertension and increasing albuminuria. The blood pressure typically begins to rise within the normal range at or within a few years after the onset of moderately increased albuminuria (the new term for what was previously called "microalbuminuria" and what is also sometimes called "high albuminuria") [7]. Blood pressure then increases progressively as the kidney disease progresses. (See "Moderately

increased albuminuria (microalbuminuria) in type 1 diabetes mellitus", section on 'Risk factors'.)

These features were illustrated in a study of 981 patients who had type 1 diabetes for five or more years [8]. Hypertension was present in 19 percent of patients with normoalbuminuria, 30 percent with moderately increased albuminuria, and 65 percent with severely increased albuminuria (the new term for what was previously called "macroalbuminuria" and what is sometimes called "very high albuminuria") [7]. The incidence of hypertension eventually reaches 75 to 85 percent in patients with progressive diabetic nephropathy [10]. The risk of hypertension is highest in Black individuals, who are also at much greater risk for kidney failure due to diabetic kidney disease. (See "Diabetic kidney disease: Pathogenesis and epidemiology".)

The findings are different in patients with type 2 diabetes [11-13]. In a series of over 3500 newly diagnosed patients, 39 percent were already hypertensive [11]. In approximately one-half of these patients, the elevation in blood pressure occurred before the onset of moderately increased albuminuria. Hypertension was strongly associated with obesity, and not surprisingly, the hypertensive patients were at increased risk for cardiovascular morbidity and mortality. Among patients with diabetes in general (regardless of vintage) in the United States, the prevalence of hypertension is nearly 70 percent. (See "Moderately increased albuminuria (microalbuminuria) in type 2 diabetes mellitus".)

GOAL BLOOD PRESSURE

UpToDate recommendations on goal blood pressure in hypertensive patients with diabetes mellitus are presented in detail elsewhere. In general, patients with diabetes are at higher cardiovascular risk compared with the general population, and therefore we suggest more intensive, rather than less intensive, blood pressure control. (See "Goal blood pressure in adults with hypertension", section on 'Patients with diabetes mellitus'.)

Goal blood pressure also depends upon the method by which it is measured (table 1). (See "Goal blood pressure in adults with hypertension", section on 'Importance of how blood pressure is measured'.)

Our recommendations are broadly consistent with the 2017 American College of Cardiology/American Heart Association (ACC/AHA) hypertension guidelines [14], as well as

the American Diabetes Association (ADA) guidelines that suggest a goal blood pressure of less than 130/80 mmHg in patients with diabetes mellitus who have greater than a 10 percent 10-year cardiovascular risk [15].

Support for these recommendations comes from randomized trials, meta-analyses, and large observational studies [16-19]. A detailed presentation of the rationale for our approach, including a discussion of the Action to Control Cardiovascular Risk in Diabetes blood pressure trial (ACCORD BP) [20], is found in a separate topic. (See "Goal blood pressure in adults with hypertension", section on 'Patients with diabetes mellitus'.)

APPROACH TO LOWERING BLOOD PRESSURE

Since hypertension magnifies cardiovascular risk among those with diabetes, all patients with diabetes and persistently elevated blood pressure should be started on antihypertensive drug therapy [21-25]. Drug therapy in patients with diabetes and hypertension is unequivocally protective [16,26-32]. (See 'Choice of antihypertensive drug therapy' below.)

In addition, all patients with diabetes and elevated blood pressure should be counseled on lifestyle modification to reduce blood pressure. Successful implementation of nonpharmacologic therapy may permit later reduction in the dose or number of antihypertensive agents. (See 'Nonpharmacologic therapy (lifestyle modification)' below and "Can drug therapy be discontinued in well-controlled hypertension?".)

Nonpharmacologic therapy (lifestyle modification) — Nonpharmacologic interventions to prevent and treat hypertension include lifestyle modifications such as (table 2):

- Salt restriction (see "Salt intake, salt restriction, and primary (essential) hypertension")
- Weight reduction (see "Overweight, obesity, and weight reduction in hypertension")
- Increased consumption of fresh fruits, vegetables, and low-fat dairy products (see "Diet in the treatment and prevention of hypertension")
- Increased exercise (see "Exercise in the treatment and prevention of hypertension")
- Avoidance of smoking and excess alcohol ingestion (see "Smoking and hypertension"

and "Overview of hypertension in adults", section on 'Nonpharmacologic therapy')

We agree with the American Diabetes Association (ADA) 2020 guidelines, which advise that, among patients with a systolic blood pressure ≥120 mmHg or a diastolic pressure ≥80 mmHg, such nonpharmacologic methods should be used to reduce blood pressure [33].

When to initiate antihypertensive drug therapy — The decision to initiate drug therapy should be individualized and involve shared decision-making between patient and provider. In general, however, we suggest that antihypertensive drug therapy be initiated in the following hypertensive patients (our suggestions broadly agree with those recommendations made by the 2017 American College of Cardiology/American Heart Association [ACC/AHA] guidelines and by the 2020 ADA guidelines) [14,33,34] (see "Overview of hypertension in adults", section on 'Who should be treated with pharmacologic therapy?'):

- Patients with out-of-office daytime blood pressure ≥135 mmHg systolic or ≥85 mmHg diastolic (or an average office blood pressure ≥140/90 mmHg if out-of-office readings are not available)
- Patients with an out-of-office daytime blood pressure ≥130 mmHg systolic or ≥80 mmHg diastolic (or an average of appropriately measured office blood pressures ≥130/80 mmHg if out-of-office readings are not available) who, in addition, have one or more of the following:
  - Established clinical cardiovascular disease (eg, chronic coronary syndrome [stable ischemic heart disease], heart failure, carotid disease, previous stroke, or peripheral arterial disease)
  - Type 2 diabetes mellitus
  - Chronic kidney disease
  - Age 65 years or older
  - An estimated 10-year risk of atherosclerotic cardiovascular disease of at least 10 percent (calculator 1)

These recommendations differ slightly from the 2020 ADA guidelines; specifically, the ADA suggests not starting antihypertensive drug therapy in a patient with type 2 diabetes and blood pressure <140/<90 mmHg if the predicted 10-year risk is <10 percent.

Early treatment of hypertension is particularly important in patients with diabetes both to

prevent cardiovascular disease and to minimize progression of kidney disease and diabetic retinopathy [35]. This is exemplified by the 21-year follow-up of the Steno diabetes study; specifically, appropriate management of systolic blood pressure, glycated hemoglobin (A1C), and low-density lipid (LDL) cholesterol resulted in a 20 percent absolute risk reduction at 13 years, a benefit that was persistent at 21 years [36,37].

Choice of antihypertensive drug therapy — The choice of antihypertensive agents in patients with diabetes is based upon their ability to do the following:

- Prevent mortality
- Prevent adverse cardiovascular events, such as myocardial infarction, stroke, and heart failure
- Prevent the progression of kidney disease, if present

The choice is not based upon retinopathy endpoints, since comparative trials have not demonstrated superiority of one agent over another for retinopathy. (See "Diabetic retinopathy: Prevention and treatment", section on 'Good blood pressure control'.)

Overview of our approach — Major guidelines including the 2017 ACC/AHA, European Society of Hypertension/European Society of Cardiology (ESH/ESC), ADA, and Canadian guidelines all conclude that the degree of blood pressure reduction is the major determinant of reduction in cardiovascular risk in both younger and older patients with hypertension (including patients with diabetes), **not** the choice of antihypertensive drug; this is also true in patients with diabetes [38]. (See "Choice of drug therapy in primary (essential) hypertension".)

However, in patients with diabetic kidney disease, renin-angiotensin system inhibitors (angiotensin-converting enzyme [ACE] inhibitors or angiotensin receptor blockers [ARBs]) may slow kidney disease progression more effectively than other antihypertensive drugs. In addition to kidney disease, placebo-controlled trials of ACE inhibitors and ARBs in high-risk patients have led some experts to conclude that these agents have a unique cardiovascular benefit in this setting [39,40]. However, the available data are more consistent with the conclusion that the achieved blood pressure, rather than the specific drug or drug class used, is the principal determinant of cardiovascular benefit. (See "Choice of drug therapy in primary (essential) hypertension".)

Based upon the effects of ACE inhibitors and ARBs on kidney disease progression, our

overall approach in patients with diabetes who require antihypertensive therapy is as follows:

- In patients with severely increased albuminuria, ≥300 mg/day (formerly called "macroalbuminuria" and sometimes called "very high albuminuria"), we treat with an ACE inhibitor or an ARB as part of the regimen to achieve the blood pressure goal. (See 'Severely increased albuminuria (300 mg/day or higher)' below.)

- We also use these drugs in patients with moderately increased albuminuria (formerly called "microalbuminuria" and sometimes called "high albuminuria") who are hypertensive, even though the benefits of angiotensin inhibition on kidney disease progression in such patients are unproven. (See 'Moderately increased albuminuria (30 to 299 mg/day)' below.)

- In patients without increased albuminuria, initial monotherapy can consist of an ACE inhibitor, ARB, thiazide diuretic, or calcium channel blocker. However, because thiazide diuretics have the disadvantage of an adverse effect on glucose metabolism, many experts will choose an ACE inhibitor, ARB, or calcium antagonist as initial therapy.

- In patients whose blood pressure is >20/10 mmHg above their goal, initial combination therapy (with a single pill, if available) should be prescribed. In addition, among patients with diabetes initiated on monotherapy, a second agent will often be required to attain goal blood pressure. In these settings (ie, when two antihypertensive drugs are needed), we generally treat with an ACE inhibitor or ARB plus a long-acting dihydropyridine calcium channel blocker. The combination of an ACE inhibitor or ARB with a diuretic is an acceptable alternative, and may be preferred in patients with edema; however, the Avoiding Cardiovascular Events through Combination Therapy in Patients Living with Systolic Hypertension (ACCOMPLISH) trial suggested that combining an ACE inhibitor or ARB with a long-acting dihydropyridine calcium channel blocker was superior to the combination with a thiazide diuretic [41], including among patients with diabetes [42]. (See "Choice of drug therapy in primary (essential) hypertension".)

  When using two antihypertensive medications, a single-pill combination is usually preferred since it is associated with better medication adherence. (See "Patient adherence and the treatment of hypertension", section on 'Methods to improve

adherence'.)

If an ACE inhibitor or ARB is indicated but cannot be used, alternative first-line agents include calcium channel blockers and diuretics. However, in patients with severely increased albuminuria, nondihydropyridine agents (eg, diltiazem, verapamil) are generally preferred over dihydropyridine drugs (eg, amlodipine, felodipine) since nondihydropyridine calcium channel blockers can reduce albuminuria [43,44].

Major side effects of ACE inhibitors and ARBs are reviewed separately. (See "Major side effects of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers".)

Severely increased albuminuria (300 mg/day or higher) — In hypertensive patients with diabetes who have severely increased albuminuria, defined as a measured (eg, with a 24-hour urine collection) or estimated (eg, using a random urine albumin-to-creatinine ratio [ACR]) albumin excretion ≥300 mg/day, we recommend treatment with an ACE inhibitor or an ARB rather than other antihypertensive agents. Other drugs can be added, as needed, to attain the blood pressure goal.

This approach is based upon high-quality, randomized trials demonstrating that these agents slow the progression of kidney disease compared with alternative therapy [45-48]. In addition, indirect evidence from trials of nondiabetic individuals supports the conclusion that ACE inhibitors and ARBs reduce the risk of kidney failure among those with severely increased albuminuria [49,50]. However, ACE inhibitors and ARBs do not appear to decrease all-cause mortality or the incidence of major cardiovascular events compared with other antihypertensive drugs.

- Type 1 diabetes – The best data supporting angiotensin inhibition in patients with type 1 diabetes come from a trial of 409 adult participants who had urine protein excretion ≥500 mg/day and a serum creatinine ≤2.5 mg/dL (221 micromol/L) [45,46]. Patients were randomly assigned to captopril (25 mg three-times daily) or placebo; other antihypertensive drugs, except for calcium channel blockers, were added if needed. Captopril reduced the rate of death or end-stage kidney disease (ESKD; 11 versus 21 percent) at three years, reduced the likelihood of doubling of serum creatinine (12 versus 21 percent), and slowed the annual loss of creatinine clearance (11 versus 17 percent per year). Smaller trials similarly concluded that ACE inhibitor slow the progression of kidney disease in patients with type 1 diabetes [51,52].

- Type 2 diabetes – In type 2 diabetes, the best data comparing renin-angiotensin system inhibition with alternative therapy come from the Irbesartan Diabetic Nephropathy Trial (IDNT) and the Reduction of Endpoints in Non-Insulin-Dependent Diabetes Mellitus with the Angiotensin II Antagonist Losartan (RENAAL) trial [47,48]:

  - In IDNT, 1715 participants aged 30 to 70 years with type 2 diabetes, hypertension, urine protein excretion ≥0.9 g/day, and mean serum creatinine of 1.7 mg/dL (150 micromol/L) were randomly assigned to irbesartan (75 to 300 mg once daily), amlodipine (2.5 to 10 mg once daily), or placebo [47]. Target systolic blood pressure was ≤135 mmHg, or 10 mmHg lower than the value at screening (if systolic blood pressure at screening ≥145 mmHg), and target diastolic blood pressure was ≤85 mmHg. At 2.6 years, the likelihood of a doubling of serum creatinine was lower with irbesartan (17 percent) compared with amlodipine (25 percent) and placebo (24 percent); in addition, irbesartan nonsignificantly reduced the incidence of ESKD (14 versus 18 percent with amlodipine and placebo) (figure 1). Patients assigned to placebo had a higher blood pressure throughout the trial than those assigned irbesartan; however, the blood pressure in the irbesartan and amlodipine groups were similar, and therefore the benefits from irbesartan were independent of attained blood pressure [53,54].

  - In RENAAL, 1513 adults with type 2 diabetes, albuminuria >300 mg/day (median urinary ACR of approximately 1250 mg/g), and mean serum creatinine 1.9 mg/dL (168 micromol/L) were randomly assigned to losartan (50 titrating up to 100 mg once daily) or placebo; additional drugs were added as need to attain goal blood pressure [48]. At 3.4 years, the incidence of ESKD was lower with losartan (20 versus 26 percent), as was doubling of serum creatinine (22 versus 26 percent). Unlike IDNT, there was no active comparator, and the mean blood pressure throughout the study was lower among those assigned losartan.

ACE inhibitors and ARBs have similar effects on patient-important outcomes among patients with diabetes as well as among broader populations [55-60]. Thus, in general, either agent can be used when treating patients with diabetes and albuminuria.

Some studies suggest that ACE inhibitors are superior to ARBs in preventing mortality and cardiovascular events in patients with diabetes. As an example, a meta-analysis of 48 trials that compared ACE inhibitors or ARBs with either placebo or another antihypertensive

drug found that ACE inhibitors significantly reduced mortality compared with placebo (9.3 versus 10.5 percent) but that ARBs did not reduce mortality compared with placebo (5 versus 5 percent) [55]. However, both ACE inhibitors and ARBs had similar, nonsignificant benefits on mortality when compared with another antihypertensive drug (10.2 versus 11.9 percent and 8.5 versus 10.5 percent, respectively). The lack of benefit when ARBs were compared with placebo may be due to the fact that one-half of these trials included lower-risk patients (ie, normotensive and/or those with normoalbuminuria). In addition, both drugs had significant benefits on heart failure; ACE inhibitors significantly reduced the risk of myocardial infarction, and ARBs significantly reduced the risk of stroke.

Other meta-analyses that included many of the same trials found that, in contrast to the study mentioned above, ARBs are equivalent to ACE inhibitors. One network meta-analysis, for example, used both direct and indirect comparisons to evaluate trials of antihypertensive therapy in patients with diabetes and found that ACE inhibitors and ARBs had identical effects on mortality and ESKD [56]. In addition, a meta-analysis that included patients with and without diabetes found that ACE inhibitors and ARBs reduced mortality and cardiovascular events to a similar degree [57].

Moderately increased albuminuria (30 to 299 mg/day) — In hypertensive patients with diabetes who have moderately increased albuminuria, defined as a measured (eg, with a 24-hour urine collection) or estimated (eg, using a random urine ACR) albumin excretion 30 to 299 mg/day, we suggest treatment with an ACE inhibitor or ARB rather than other antihypertensive drugs. Additional agents are added, as needed, to attain the blood pressure goal.

The rationale for this approach comes from evidence that ACE inhibitors and ARBs, compared with other antihypertensive agents, can prevent the progression from moderately increased albuminuria to severely increased albuminuria in patients with diabetes [61-63]. In addition, these drugs may slow the rise in serum creatinine [64], and observational data suggest that a reduction in albuminuria is associated with a decreased incidence of ESKD [65].

However, there are **no** high-quality data that, in patients with moderately increased albuminuria, ACE inhibitors and ARBs are superior to other first-line agents in preventing kidney failure, all-cause mortality, or cardiovascular events.

Normoalbuminuria (less than 30 mg/day) — In patients without increased albuminuria

(ie, measured or estimated albumin excretion <30 mg/day), initial monotherapy can consist of an ACE inhibitor, ARB, thiazide diuretic, or calcium channel blocker. However, because thiazide diuretics have the disadvantage of an adverse, albeit minor, effect on glucose metabolism, many experts will choose an ACE inhibitor, ARB, or a calcium antagonist as initial therapy. This approach is generally similar to the selection of antihypertensive therapy in patients without diabetes. (See "Choice of drug therapy in primary (essential) hypertension".)

In patients with diabetes and normoalbuminuria, ACE inhibitors and ARBs do not provide superior protection against ESKD, all-cause mortality, and cardiovascular events, compared with other first-line drugs [14].

Avoid combination renin-angiotensin system inhibition — A separate issue is whether an ARB should be given with an ACE inhibitor since combining these agents provides better blood pressure control compared with monotherapy and also reduces albuminuria to a greater degree [66]. However, based upon high-quality data in patients with diabetes as well as other individuals at high cardiovascular risk, we recommend **against** combination therapy with an ACE inhibitor and ARB or direct renin inhibitor [67].

In the subgroup analysis of the Ongoing Telmisartan Alone and in Combination with Ramipril Global Endpoint Trial (ONTARGET) trial cited above, ramipril, telmisartan, and combination therapy were compared in 6365 patients with diabetes [59]. There was no difference in the composite primary outcome of death from cardiovascular causes, myocardial infarction, stroke, or hospitalization for heart failure among these groups. However, in the entire cohort, which comprised 25,620 patients with vascular disease or diabetes, there was an increase in adverse side effects (including a possible increase in mortality) in patients who received both agents, compared with those who received ramipril alone [59,60]. (See "Major side effects of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers".)

In addition, the combination of an ACE inhibitor with an ARB or with a direct renin inhibitor in two other large trials of patients with diabetic chronic kidney disease (Aliskiren Trial in Type 2 Diabetes Using Cardiovascular and Renal Disease Endpoints [ALTITUDE] and Veterans Affairs Nephropathy in Diabetes [VA NEPHRON-D]) was not superior to ACE inhibitor monotherapy and produced more side effects. (See "Treatment of diabetic kidney disease".)

A subsequent multiple-treatment comparison (network) meta-analysis suggested that combination therapy with an ACE inhibitor and ARB was superior to placebo in preventing ESKD in patients with diabetes and hypertension [68]. However, monotherapy with either an ACE inhibitor or an ARB produced similar benefits compared with placebo, and combination therapy produced more adverse effects.

INDICATIONS FOR ALTERNATIVE ANTIHYPERTENSIVE DRUGS

The choice of initial antihypertensive therapy may vary from the approach described above if the patient has one of the following disorders:

- A recent myocardial infarction (ie, in the previous three years) (see 'Patients with a recent myocardial infarction' below)
- Heart failure (see 'Patients with heart failure' below)

Patients with a recent myocardial infarction — Beta blockers, while generally not recommended as initial monotherapy or as part of combination therapy in patients with hypertension, are indicated in patients who have had a myocardial infarction in the previous three years. Patients who have had a myocardial infarction are also frequently prescribed an angiotensin-converting enzyme (ACE) inhibitor or angiotensin receptor blocker (ARB), regardless of whether they have albuminuria. (See "Acute myocardial infarction: Role of beta blocker therapy", section on 'Long-term therapy' and "Angiotensin converting enzyme inhibitors and receptor blockers in acute myocardial infarction: Recommendations for use".)

Although there are concerns about masking of hypoglycemic symptoms and possible exacerbation of peripheral artery disease, beta blockers can effectively lower blood pressure in patients with diabetes. Among beta blockers, carvedilol, a combined nonselective beta- and alpha-1 adrenergic antagonist that improves survival in patients with heart failure, may have certain advantages compared with other beta blockers in patients with diabetes [69,70]. However, bisoprolol and metoprolol extended release are reasonable alternatives.

This issue was best addressed in the Glycemic Effects in Diabetes Mellitus: Carvedilol-Metoprolol Comparison in Hypertensives (GEMINI) trial of 1235 patients with hypertension (>130/80 mmHg) and type 2 diabetes; all patients were treated with an ACE inhibitor or

ARB, while other antihypertensive drugs were discontinued [69]. The patients were then randomly assigned to carvedilol (6.25 to 25 mg twice daily) or metoprolol (50 to 200 mg twice daily); hydrochlorothiazide and a dihydropyridine calcium channel blocker were added as necessary to achieve a blood pressure below 130/80 mmHg.

Carvedilol was associated with the following significant benefits at five months; the blood pressure was similar in the two groups:

- No change in glycated hemoglobin (A1C) compared with a mean 0.15 percent increase with metoprolol and an increase in insulin sensitivity (9.1 percent) and compared with no change with metoprolol. In addition, fewer patients withdrew from the trial because of worsening glycemic control (0.6 versus 2.2 percent).
- A lower rate of progression to moderately increased albuminuria in patients in whom this was not present at baseline (6.6 versus 11.1 percent with metoprolol) and a 16 percent relative reduction in albumin excretion.

The modest worsening of glycemic control seen with metoprolol has also been noted in studies of other beta blockers [71-73].

In the United Kingdom Prospective Diabetes Study (UKPDS) study of patients with type 2 diabetes, atenolol was as effective as captopril in terms of both blood pressure lowering and protection against microvascular disease [74]. In the Losartan Intervention for Endpoint Reduction in Hypertension (LIFE) diabetic parallel study, however, losartan provided significantly more protection from adverse cardiovascular outcomes than atenolol [75].

Patients with heart failure — Heart failure is common in patients with diabetes. Those who have heart failure with reduced ejection fraction (HFrEF) are typically treated with renin-angiotensin system inhibitors (ACE inhibitors, ARBs, or angiotensin receptor-neprilysin inhibitors [ARNIs]) whether or not they have albuminuria, since these drugs reduce mortality and morbidity in the setting of HFrEF. Patients who have heart failure with preserved ejection fraction (HFpEF) are often prescribed mineralocorticoid receptor antagonists because these agents may reduce morbidity in that population. Frequently, patients with HFpEF require multiple antihypertensive medications to control their blood pressure, and among those with diabetes, agent selection should follow the same approach as described above. (See 'Overview of our approach' above.)

Detailed discussions of pharmacologic therapy in patients with heart failure are presented elsewhere:

- HFrEF (see "Primary pharmacologic therapy for heart failure with reduced ejection fraction" and "Secondary pharmacologic therapy for heart failure with reduced ejection fraction")
- HFpEF (see "Treatment and prognosis of heart failure with preserved ejection fraction")

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Hypertension in adults" and "Society guideline links: Diabetes mellitus in adults".)

SUMMARY AND RECOMMENDATIONS

- Contributors to hypertension in patients with diabetes include kidney disease, extracellular fluid volume expansion, and increased arterial stiffness. Hypertension is common problem in patients with both type 1 and type 2 diabetes, but the time course in relation to the duration of diabetes is different. In type 1 diabetes, the prevalence of hypertension at the time of diagnosis is low, increasing subsequently over several decades. In type 2 diabetes, a substantial proportion of patients already have hypertension at the time of diabetes diagnosis. (See 'Pathogenesis' above and 'Epidemiology' above.)
- In general, patients with diabetes are at higher cardiovascular risk compared with the general population, and therefore we target more intensive, rather than less intensive, blood pressure control. Our recommendations on goal blood pressure in hypertensive patients with diabetes mellitus are presented in detail elsewhere. Goal blood pressure also depends upon the method by which it is measured (table 1). (See "Goal blood pressure in adults with hypertension", section on 'Patients with diabetes mellitus'.)
- Nonpharmacologic interventions should be prescribed, as appropriate, to all patients

with hypertension. These include salt restriction; weight reduction; increased consumption of fresh fruits, vegetables, and low-fat dairy products; increased exercise; and avoidance of smoking and excess alcohol ingestion.

- The decision to initiate drug therapy should be individualized and involve shared decision-making between patient and provider. In general, however, we initiate antihypertensive drug therapy in patients with diabetes who have an out-of-office daytime blood pressure ≥130 mmHg systolic or ≥80 mmHg diastolic (or an average of appropriately measured office blood pressures ≥130/80 mmHg if out-of-office readings are not available). (See 'When to initiate antihypertensive drug therapy' above and "Overview of hypertension in adults", section on 'Who should be treated with pharmacologic therapy?'.)

- Our approach to the choice of antihypertensive therapy depends in part upon the degree of the patient's urine albumin excretion (see 'Overview of our approach' above and "Treatment of diabetic kidney disease", section on 'Severely increased albuminuria: Treat with angiotensin inhibition'):

  - In patients with severely increased albuminuria, ≥300 mg/day (formerly called "macroalbuminuria" and sometimes called "very high albuminuria"), we treat with an angiotensin-converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB) as part of the regimen to achieve the blood pressure goal. (See 'Severely increased albuminuria (300 mg/day or higher)' above.)

  - We also use these drugs in patients with moderately increased albuminuria (formerly called "microalbuminuria" and sometimes called "high albuminuria") who are hypertensive, even though the benefits of angiotensin inhibition on kidney disease progression in such patients are unproven. (See 'Moderately increased albuminuria (30 to 299 mg/day)' above.)

  - In patients without increased albuminuria, initial monotherapy can consist of an ACE inhibitor, ARB, thiazide diuretic, or calcium channel blocker. However, because thiazide diuretics have the disadvantage of an adverse effect on glucose metabolism, albeit minor, many experts will choose an ACE inhibitor, ARB, or calcium antagonist as initial therapy. (See 'Normoalbuminuria (less than 30 mg/day)' above.)

- In patients whose blood pressure is >20/10 mmHg above their goal, initial combination therapy (with a single pill, if available) should be prescribed. In addition, among patients with diabetes initiated on monotherapy, a second agent will often be required to attain goal blood pressure. In these settings (ie, when two antihypertensive drugs are needed), we generally treat with an ACE inhibitor or ARB plus a long-acting dihydropyridine calcium channel blocker. (See "Choice of drug therapy in primary (essential) hypertension".)

- If an ACE inhibitor or ARB is indicated but cannot be used, alternative first-line agents include calcium channel blockers and diuretics. However, in patients with severely increased albuminuria, nondihydropyridine agents (eg, diltiazem, verapamil) are generally preferred over dihydropyridine drugs (eg, amlodipine, felodipine), since nondihydropyridine calcium channel blockers can reduce albuminuria. (See 'Overview of our approach' above.)

- The choice of initial antihypertensive therapy may vary from the approach described above if the patient has one of the following disorders: a recent myocardial infarction (ie, in the previous three years), in which case a beta blocker is appropriate, or heart failure, in which case various antihypertensive agents may be appropriate regardless of the degree of albuminuria. (See 'Indications for alternative antihypertensive drugs' above.)

REFERENCES

1. Jia G, Sowers JR. Hypertension in Diabetes: An Update of Basic Mechanisms and Clinical Disease. Hypertension 2021; 78:1197.
2. Epstein M, Sowers JR. Diabetes mellitus and hypertension. Hypertension 1992; 19:403.
3. Nosadini R, Sambataro M, Thomaseth K, et al. Role of hyperglycemia and insulin resistance in determining sodium retention in non-insulin-dependent diabetes. Kidney Int 1993; 44:139.
4. Cruickshank K, Riste L, Anderson SG, et al. Aortic pulse-wave velocity and its relationship to mortality in diabetes and glucose intolerance: an integrated index of vascular function? Circulation 2002; 106:2085.

5. Viazzi F, Bonino B, Mirijello A, et al. Long-term blood pressure variability and development of chronic kidney disease in type 2 diabetes. J Hypertens 2019; 37:805.
6. van den Boom L, Buchal G, Kaiser M, Kostev K. Multimorbidity Among Adult Outpatients With Type 1 Diabetes in Germany. J Diabetes Sci Technol 2022; 16:152.
7. Chapter 1: Definition and classification of CKD. Kidney Int Suppl (2011) 2013; 3:19.
8. Parving HH, Hommel E, Mathiesen E, et al. Prevalence of microalbuminuria, arterial hypertension, retinopathy and neuropathy in patients with insulin dependent diabetes. Br Med J (Clin Res Ed) 1988; 296:156.
9. Koebnick C, Imperatore G, Jensen ET, et al. Progression to hypertension in youth and young adults with type 1 or type 2 diabetes: The SEARCH for Diabetes in Youth Study. J Clin Hypertens (Greenwich) 2020; 22:888.
10. Mogensen CE, Hansen KW, Pedersen MM, Christensen CK. Renal factors influencing blood pressure threshold and choice of treatment for hypertension in IDDM. Diabetes Care 1991; 14 Suppl 4:13.
11. Hypertension in Diabetes Study (HDS): I. Prevalence of hypertension in newly presenting type 2 diabetic patients and the association with risk factors for cardiovascular and diabetic complications. J Hypertens 1993; 11:309.
12. Raghavan S, Ho YL, Kini V, et al. Association Between Early Hypertension Control and Cardiovascular Disease Incidence in Veterans With Diabetes. Diabetes Care 2019; 42:1995.
13. Kabakov E, Norymberg C, Osher E, et al. Prevalence of hypertension in type 2 diabetes mellitus: impact of the tightening definition of high blood pressure and association with confounding risk factors. J Cardiometab Syndr 2006; 1:95.
14. 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. Hypertension 2018; 71:e13.
15. ElSayed NA, Aleppo G, Aroda VR, et al. 10. Cardiovascular Disease and Risk Management: Standards of Care in Diabetes-2023. Diabetes Care 2023; 46:S158.
16. Emdin CA, Rahimi K, Neal B, et al. Blood pressure lowering in type 2 diabetes: a systematic review and meta-analysis. JAMA 2015; 313:603.

17. Xie X, Atkins E, Lv J, et al. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. Lancet 2016; 387:435.
18. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet 2016; 387:957.
19. Adamsson Eryd S, Gudbjörnsdottir S, Manhem K, et al. Blood pressure and complications in individuals with type 2 diabetes and no previous cardiovascular disease: national population based cohort study. BMJ 2016; 354:i4070.
20. ACCORD Study Group, Cushman WC, Evans GW, et al. Effects of intensive blood-pressure control in type 2 diabetes mellitus. N Engl J Med 2010; 362:1575.
21. Buse JB, Ginsberg HN, Bakris GL, et al. Primary prevention of cardiovascular diseases in people with diabetes mellitus: a scientific statement from the American Heart Association and the American Diabetes Association. Circulation 2007; 115:114.
22. James PA, Oparil S, Carter BL, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). JAMA 2014; 311:507.
23. Mancia G, Fagard R, Narkiewicz K, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens 2013; 31:1281.
24. American Diabetes Association. (8) Cardiovascular disease and risk management. Diabetes Care 2015; 38 Suppl:S49.
25. American Diabetes Association. 10. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes-2019. Diabetes Care 2019; 42:S103.
26. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. UK Prospective Diabetes Study Group. BMJ 1998; 317:703.
27. Executive summary: Standards of medical care in diabetes--2010. Diabetes Care 2010; 33 Suppl 1:S4.
28. Vijan S, Hayward RA. Treatment of hypertension in type 2 diabetes mellitus: blood pressure goals, choice of agents, and setting priorities in diabetes care. Ann Intern

Med 2003; 138:593.

29. Snow V, Weiss KB, Mottur-Pilson C, Clinical Efficacy Assessment Subcommittee of the American College of Physicians. The evidence base for tight blood pressure control in the management of type 2 diabetes mellitus. Ann Intern Med 2003; 138:587.
30. Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. Lancet 1998; 351:1755.
31. Patel A, ADVANCE Collaborative Group, MacMahon S, et al. Effects of a fixed combination of perindopril and indapamide on macrovascular and microvascular outcomes in patients with type 2 diabetes mellitus (the ADVANCE trial): a randomised controlled trial. Lancet 2007; 370:829.
32. Turnbull F, Neal B, Algert C, et al. Effects of different blood pressure-lowering regimens on major cardiovascular events in individuals with and without diabetes mellitus: results of prospectively designed overviews of randomized trials. Arch Intern Med 2005; 165:1410.
33. American Diabetes Association. 10. Cardiovascular Disease and Risk Management: Standards of Medical Care in Diabetes-2020. Diabetes Care 2020; 43:S111.
34. de Boer IH, Bangalore S, Benetos A, et al. Diabetes and Hypertension: A Position Statement by the American Diabetes Association. Diabetes Care 2017; 40:1273.
35. Gaede P, Vedel P, Parving HH, Pedersen O. Intensified multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: the Steno type 2 randomised study. Lancet 1999; 353:617.
36. Gæde P, Oellgaard J, Carstensen B, et al. Years of life gained by multifactorial intervention in patients with type 2 diabetes mellitus and microalbuminuria: 21 years follow-up on the Steno-2 randomised trial. Diabetologia 2016; 59:2298.
37. Oellgaard J, Gæde P, Rossing P, et al. Reduced risk of heart failure with intensified multifactorial intervention in individuals with type 2 diabetes and microalbuminuria: 21 years of follow-up in the randomised Steno-2 study. Diabetologia 2018; 61:1724.
38. Bangalore S, Fakheri R, Toklu B, Messerli FH. Diabetes mellitus as a compelling indication for use of renin angiotensin system blockers: systematic review and meta-analysis of randomized trials. BMJ 2016; 352:i438.

39. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and MICRO-HOPE substudy. Heart Outcomes Prevention Evaluation Study Investigators. Lancet 2000; 355:253.
40. Daly CA, Fox KM, Remme WJ, et al. The effect of perindopril on cardiovascular morbidity and mortality in patients with diabetes in the EUROPA study: results from the PERSUADE substudy. Eur Heart J 2005; 26:1369.
41. Jamerson K, Weber MA, Bakris GL, et al. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. N Engl J Med 2008; 359:2417.
42. Weber MA, Bakris GL, Jamerson K, et al. Cardiovascular events during differing hypertension therapies in patients with diabetes. J Am Coll Cardiol 2010; 56:77.
43. Birkenhäger WH, Staessen JA. Treatment of diabetic patients with hypertension. Curr Hypertens Rep 1999; 1:225.
44. Bakris GL, Weir MR, Secic M, et al. Differential effects of calcium antagonist subclasses on markers of nephropathy progression. Kidney Int 2004; 65:1991.
45. Lewis EJ, Hunsicker LG, Bain RP, Rohde RD. The effect of angiotensin-converting-enzyme inhibition on diabetic nephropathy. The Collaborative Study Group. N Engl J Med 1993; 329:1456.
46. Hebert LA, Bain RP, Verme D, et al. Remission of nephrotic range proteinuria in type I diabetes. Collaborative Study Group. Kidney Int 1994; 46:1688.
47. Lewis EJ, Hunsicker LG, Clarke WR, et al. Renoprotective effect of the angiotensin-receptor antagonist irbesartan in patients with nephropathy due to type 2 diabetes. N Engl J Med 2001; 345:851.
48. Brenner BM, Cooper ME, de Zeeuw D, et al. Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. N Engl J Med 2001; 345:861.
49. Jafar TH, Schmid CH, Landa M, et al. Angiotensin-converting enzyme inhibitors and progression of nondiabetic renal disease. A meta-analysis of patient-level data. Ann Intern Med 2001; 135:73.
50. Kent DM, Jafar TH, Hayward RA, et al. Progression risk, urinary protein excretion, and treatment effects of angiotensin-converting enzyme inhibitors in nondiabetic kidney disease. J Am Soc Nephrol 2007; 18:1959.

51. Kasiske BL, Kalil RS, Ma JZ, et al. Effect of antihypertensive therapy on the kidney in patients with diabetes: a meta-regression analysis. Ann Intern Med 1993; 118:129.
52. Parving HH, Hommel E, Jensen BR, Hansen HP. Long-term beneficial effect of ACE inhibition on diabetic nephropathy in normotensive type 1 diabetic patients. Kidney Int 2001; 60:228.
53. Berl T, Hunsicker LG, Lewis JB, et al. Impact of achieved blood pressure on cardiovascular outcomes in the Irbesartan Diabetic Nephropathy Trial. J Am Soc Nephrol 2005; 16:2170.
54. Pohl MA, Blumenthal S, Cordonnier DJ, et al. Independent and additive impact of blood pressure control and angiotensin II receptor blockade on renal outcomes in the irbesartan diabetic nephropathy trial: clinical implications and limitations. J Am Soc Nephrol 2005; 16:3027.
55. Cheng J, Zhang W, Zhang X, et al. Effect of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers on all-cause mortality, cardiovascular deaths, and cardiovascular events in patients with diabetes mellitus: a meta-analysis. JAMA Intern Med 2014; 174:773.
56. Wu HY, Huang JW, Lin HJ, et al. Comparative effectiveness of renin-angiotensin system blockers and other antihypertensive drugs in patients with diabetes: systematic review and bayesian network meta-analysis. BMJ 2013; 347:f6008.
57. Savarese G, Costanzo P, Cleland JG, et al. A meta-analysis reporting effects of angiotensin-converting enzyme inhibitors and angiotensin receptor blockers in patients without heart failure. J Am Coll Cardiol 2013; 61:131.
58. Barnett AH, Bain SC, Bouter P, et al. Angiotensin-receptor blockade versus converting-enzyme inhibition in type 2 diabetes and nephropathy. N Engl J Med 2004; 351:1952.
59. ONTARGET Investigators, Yusuf S, Teo KK, et al. Telmisartan, ramipril, or both in patients at high risk for vascular events. N Engl J Med 2008; 358:1547.
60. Mann JF, Schmieder RE, McQueen M, et al. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): a multicentre, randomised, double-blind, controlled trial. Lancet 2008; 372:547.
61. Parving HH, Lehnert H, Bröchner-Mortensen J, et al. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. N Engl J Med 2001; 345:870.

62. Makino H, Haneda M, Babazono T, et al. Prevention of transition from incipient to overt nephropathy with telmisartan in patients with type 2 diabetes. Diabetes Care 2007; 30:1577.

63. Ravid M, Savin H, Jutrin I, et al. Long-term stabilizing effect of angiotensin-converting enzyme inhibition on plasma creatinine and on proteinuria in normotensive type II diabetic patients. Ann Intern Med 1993; 118:577.

64. Kidney Disease: Improving Global Outcomes (KDIGO) Diabetes Work Group. KDIGO 2020 Clinical Practice Guideline for Diabetes Management in Chronic Kidney Disease. Kidney Int 2020; 98:S1.

65. Heerspink HJ, Kröpelin TF, Hoekman J, et al. Drug-Induced Reduction in Albuminuria Is Associated with Subsequent Renoprotection: A Meta-Analysis. J Am Soc Nephrol 2015; 26:2055.

66. Mogensen CE, Neldam S, Tikkanen I, et al. Randomised controlled trial of dual blockade of renin-angiotensin system in patients with hypertension, microalbuminuria, and non-insulin dependent diabetes: the candesartan and lisinopril microalbuminuria (CALM) study. BMJ 2000; 321:1440.

67. Gradman AH, Basile JN, Carter BL, et al. Combination therapy in hypertension. J Am Soc Hypertens 2010; 4:90.

68. Palmer SC, Mavridis D, Navarese E, et al. Comparative efficacy and safety of blood pressure-lowering agents in adults with diabetes and kidney disease: a network meta-analysis. Lancet 2015; 385:2047.

69. Bakris GL, Fonseca V, Katholi RE, et al. Metabolic effects of carvedilol vs metoprolol in patients with type 2 diabetes mellitus and hypertension: a randomized controlled trial. JAMA 2004; 292:2227.

70. Giugliano D, Acampora R, Marfella R, et al. Metabolic and cardiovascular effects of carvedilol and atenolol in non-insulin-dependent diabetes mellitus and hypertension. A randomized, controlled trial. Ann Intern Med 1997; 126:955.

71. Messerli FH, Bangalore S, Julius S. Risk/benefit assessment of beta-blockers and diuretics precludes their use for first-line therapy in hypertension. Circulation 2008; 117:2706.

72. Gress TW, Nieto FJ, Shahar E, et al. Hypertension and antihypertensive therapy as risk factors for type 2 diabetes mellitus. Atherosclerosis Risk in Communities Study. N

Engl J Med 2000; 342:905.

73. Sarafidis PA, Bakris GL. Antihypertensive treatment with beta-blockers and the spectrum of glycaemic control. QJM 2006; 99:431.
74. Efficacy of atenolol and captopril in reducing risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 39. UK Prospective Diabetes Study Group. BMJ 1998; 317:713.
75. Lindholm LH, Ibsen H, Dahlöf B, et al. Cardiovascular morbidity and mortality in patients with diabetes in the Losartan Intervention For Endpoint reduction in hypertension study (LIFE): a randomised trial against atenolol. Lancet 2002; 359:1004.

Topic 3829 Version 49.0

GRAPHICS

Goal blood pressure according to baseline risk for cardiovascular disease and method of measuring blood pressure

	Routine/conventional office blood pressure (manual measurement with stethoscope or oscillometric device)*	Unattended AOBPM, daytime ABPM, or home blood pressure¶
Higher-risk populationΔ		
▪ Known ASCVD◇ ▪ Heart failure ▪ Diabetes mellitus ▪ Chronic kidney disease ▪ Age ≥65 years§ ▪ Calculated 10-year risk of ASCVD event ≥10%¥	125 to 130/<80	120 to 125/<80
Lower-risk‡		
▪ None of the above risk factors	130 to 139/<90	125 to 135/<90

- All target ranges presented above are in mmHg.
- On average, blood pressure readings are 5 to 10 mmHg lower with digital, unattended, or out-of-office methods of measurement (ie, AOBPM, daytime ABPM, home blood pressure) than with routine/standard methods of office measurement (ie, manual auscultatory or oscillometric measurement), presumably due to the "white coat effect." However, it is critical to realize that this average difference in blood pressures according to the methodology of measurement applies to the population and not the individual. Some patients do not experience a white coat effect, and, therefore, there is some uncertainty in setting goals that are specific to the method of measurement.
- When treating to these goals, a patient may (inadvertently) attain a blood pressure below the given target. Provided the patient does not develop symptoms, side effects, or adverse events as a result of the treatment regimen, then reducing or withdrawing antihypertensive medications is unnecessary.
- Less aggressive goals than those presented in the table may be appropriate for specific groups of patients, including those with postural hypotension, the frail older adult patient, and those with side effects to multiple antihypertensive medications.

AOBPM: automated oscillometric blood pressure monitoring; ABPM: ambulatory blood pressure monitoring; ASCVD: atherosclerotic cardiovascular disease; ACC/AHA: American College of Cardiology/American Heart Association.

* Office blood pressure must be performed adequately in order to use such measurements to manage patients. Critical to an adequate office assessment of blood pressure are proper patient positioning (eg, seated in a chair, feet flat on the floor, arm supported, remove clothing covering the location of cuff placement) and proper technique (eg, calibrated device, proper-sized cuff). The average of multiple measurements should be used for management. Refer to UpToDate topics on measurement of blood pressure. Office readings should not be used to manage blood pressure unless it is performed adequately.

¶ Home blood pressure, like office blood pressure, must be performed adequately in order for the measurements to be used to manage patients. First, the accuracy of the home blood pressure device must be verified in the clinician's office. Second, the clinician should verify that the cuff and bladder that the patient will use are the appropriate size. Third, patients should measure their pressure after several minutes of rest and while seated in a chair (back supported and feet flat on the floor) with their arm supported (eg, resting on a table). Fourth, the blood pressure should be measured at different times per day and over multiple days. The average value of these multiple measurements is used for management. Home blood pressure readings should not be used to manage blood pressure unless it is performed adequately and in conjunction with office blood pressure or ambulatory blood pressure.

Δ The level of evidence supporting the lower goal in higher-risk individuals is stronger for some risk groups (eg, patients with known coronary heart disease, patients with a calculated 10-year risk ≥15%, chronic kidney disease) than for other risk groups (eg, patients with diabetes, patients with a prior stroke). Refer to UpToDate topics on goal blood pressure for a discussion of the evidence.

◇ Prior history of coronary heart disease (acute coronary syndrome or stable angina), prior stroke or transient ischemic attack, prior history of peripheral artery disease.

§ In older adults with severe frailty, dementia, and/or a limited life expectancy, or in patients who are nonambulatory or institutionalized (eg, reside in a skilled nursing facility), we individualize goals and share decision-making with the patient, relatives, and caretakers, rather than targeting one of the blood pressure goals in the table.

¥ The 2013 ACC/AHA cardiovascular risk assessment calculator should be used to estimate 10-year cardiovascular disease risk.

‡ In the large subgroup of patients who have an initial (pretreatment) blood pressure ≥140/≥90 mmHg, but who do not have any of the other listed cardiovascular risk factors, some experts would set a more aggressive blood pressure goal of <130/<80 mmHg rather than those presented in the table. This more aggressive goal would likely reduce the chance of developing severe hypertension and ultimately lower the relative risk of cardiovascular events in these lower-risk patients over the long term. However, the absolute benefit of more aggressive blood pressure lowering in these patients is comparatively small, and a lower goal would require more intensive pharmacologic therapy and corresponding side effects.

Graphic 117101 Version 3.0

Best proven nonpharmacologic interventions for prevention and treatment of hypertension*

	Nonpharmacologic intervention	Dose	Approximate impact on S	
			Hypertension	Normotension
Weight loss	Weight/body fat	▪ Best goal is ideal body weight, but aim for at least a 1 kg reduction in body weight for most adults who are overweight. Expect about 1 mmHg for every 1 kg reduction in body weight.	-5 mmHg	-3 mmHg
Healthy diet	DASH dietary pattern	▪ Consume a diet rich in fruits, vegetables, whole grains, and low-fat dairy products, with reduced content of saturated and total fat.	-11 mmHg	-3 mmHg
Reduced intake of dietary sodium	Dietary sodium	▪ Optimal goal is <1500 mg/day, but aim for at least a 1000 mg/day reduction in most adults.	-5 to -6 mmHg	-2 to -3 mmHg

Enhanced intake of dietary potassium	Dietary potassium	▪ Aim for 3500 to 5000 mg/day, preferably by consumption of a diet rich in potassium.	-4 mmHg	-2 mmHg
Physical activity	Aerobic	▪ 90 to 150 minutes/week. ▪ 65 to 75% heart rate reserve.	-5 to -8 mmHg	-2 to -4 mmHg
	Dynamic resistance	▪ 90 to 150 minutes/week. ▪ 50 to 80% of maximum 1 repetition weight. ▪ 6 exercises, 3 sets/exercise, 10 repetitions/set.	-4 mmHg	-2 mmHg
	Isometric resistance	▪ 4 × 2 minutes (hand grip), 1 minute rest between exercises, 30 to 40% maximum voluntary contraction, 3 sessions/week. ▪ 8 to 10 weeks.	-5 mmHg	-4 mmHg
Moderation in alcohol intake	Alcohol consumption	▪ In individuals who drink alcohol, reduce alcohol to:¶ • Men: ≤2 drinks	-4 mmHg	-3 mmHg

		daily. • Women: ≤1 drink daily.			

SBP: systolic blood pressure; DASH: Dietary Approaches to Stop Hypertension.
* Type, dose, and expected impact on BP in adults with a normal BP and with hypertension.
¶ In the United States, one "standard" drink contains roughly 14 g of pure alcohol, which is typically found in 12 oz of regular beer (usually about 5% alcohol), 5 oz of wine (usually about 12% alcohol), and 1.5 oz of distilled spirits (usually about 40% alcohol).[14]

Resources:

- *National Heart, Lung, and Blood Institute. Your Guide to Lowering Your Blood Pressure With DASH. Available at: https://www.nhlbi.nih.gov/files/docs/public/heart/new_dash.pdf (Accessed on August 16, 2019).*
- *Top 10 DASH Diet Tips. Available at: http://dashdiet.org/dash_diet_tips.asp (Accessed on September 18, 2017).*

References:

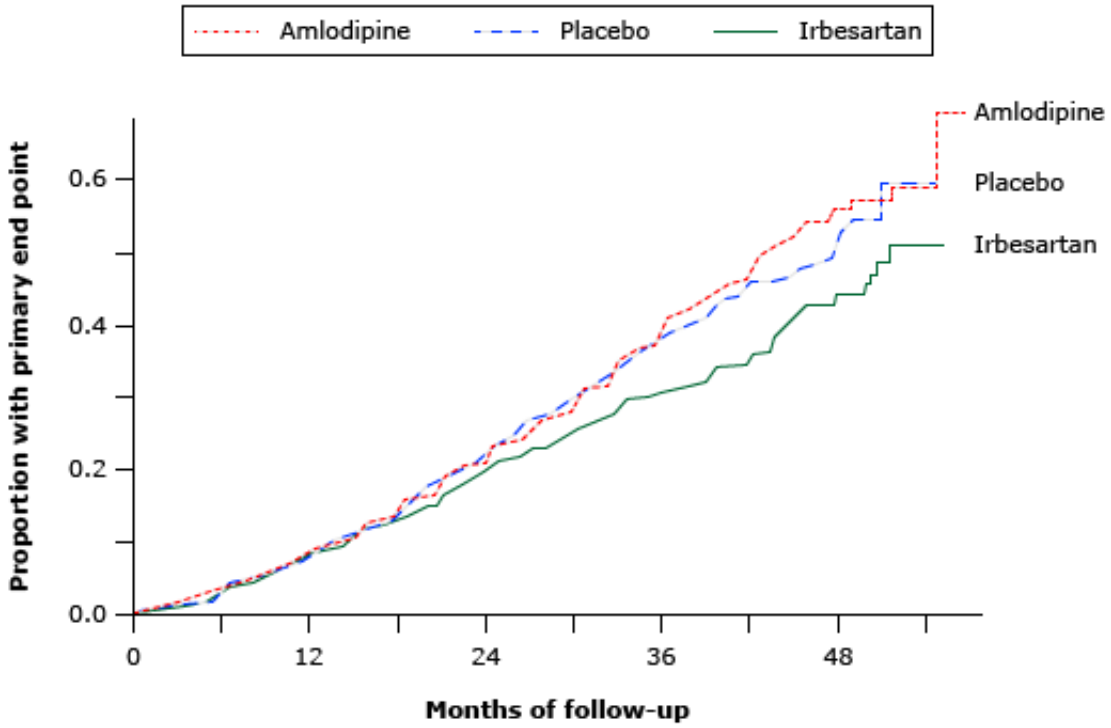
1. *Neter JE, Stam BE, Kok FJ, et al. Influence of weight reduction on blood pressure: a meta-analysis of randomized controlled trials. Hypertension 2003; 42:878.*
2. *Appel LJ, Champagne CM, Harsha DW, et al. Effects of comprehensive lifestyle modification on blood pressure control: main results of the PREMIER clinical trial. JAMA 2003; 289:2083.*
3. *Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. DASH Collaborative Research Group. N Engl J Med 1997; 336:1117.*
4. *Aburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and metaanalyses. BMJ 2013; 346:f1326.*
5. *He FJ, Li J, MacGregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. BMJ 2013; 346:f1325.*
6. *Whelton PK, He J, Cutler JA, et al. Effects of oral potassium on blood pressure. Meta-analysis of randomized controlled clinical trials. JAMA 1997; 277:1624.*
7. *Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc 2013; 2:e004473.*
8. *Whelton SP, Chin A, Xin X, et al. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. Ann Intern Med 2002; 136:493.*
9. *Carlson DJ, Dieberg G, Hess NC, et al. Isometric exercise training for blood pressure management: a systematic review and meta-analysis. Mayo Clin Proc 2014; 89:327.*
10. *Inder JD, Carlson DJ, Dieberg G, et al. Isometric exercise training for blood pressure management: a systematic review and meta-analysis to optimize benefit. Hypertens Res 2016; 39:88.*
11. *Whelton SP, Chin A, Xin X, et al. Effect of aerobic exercise on blood pressure: a meta-analysis of randomized, controlled trials. Ann Intern Med 2002; 136:493.*
12. *Xin X, He J, Frontini MG, et al. Effects of alcohol reduction on blood pressure: a meta-analysis of randomized controlled trials. Hypertension 2001; 38:1112.*
13. *Roerecke M, Kaczorowski J, Tobe SW, et al. The effect of a reduction in alcohol consumption on blood pressure: a systematic review and meta-analysis. Lancet Public Health 2017; 2:e108.*
14. *National Institute on Alcohol Abuse and Alcoholism (NIAAA). What Is A Standard Drink? Available at: https://www.niaaa.nih.gov/alcohol-health/overview-alcohol-consumption/what-standard-drink (Accessed on August 16, 2017).*

Reproduced from: 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. J Am Coll Cardiol 2017. Table used with the permission of Elsevier Inc. All rights reserved.

Graphic 116041 Version 3.0

Irbesartan slows progression of nephropathy in type 2 diabetes



Effect of irbesartan, amlodipine, and placebo on the course of patients with hypertension with nephropathy due to type 2 diabetes; the target blood pressure was similar in the 3 groups. Treatment with irbesartan was associated with a risk of the primary end point (doubling of the baseline serum creatinine, development of end-stage kidney disease, or death from any cause) that was 20% lower than placebo and 23% lower than amlodipine.

Adapted from data published in: Lewis EJ, Hunsicker LG, Clarke WR, et al. N Engl J Med 2001; 345:851.

Graphic 80116 Version 4.0

Contributor Disclosures

George L Bakris, MD Grant/Research/Clinical Trial Support: Bayer [Diabetic nephropathy]; KBP Biosciences [Resistant hypertension]; Novo Nordisk [Diabetic kidney disease]. Consultant/Advisory Boards: Alnylam [Resistant hypertension]; AstraZeneca [Diabetic nephropathy]; Bayer [Nephropathy]; Ionis [Resistant hypertension]; KBP BioSciences [Resistant hypertension]; Vifor [Hyperkalemia]. All of the relevant financial relationships listed have been mitigated. **David M Nathan, MD** No relevant financial relationship(s) with ineligible companies to disclose. **William B White, MD** Consultant/Advisory Boards: AB Science [Alzheimer's disease, mastocytosis]; Alynam [Heart failure]; AstraZeneca [Lupus, lung disease]; Bristol-Myers Squibb [Psoriasis]; Cadence [Oral contraception]; Cerevel Therapeutics [Cancer, schizophrenia]; Chinook [IgA nephropathy]; JAZZ [Narcolepsy]; Marius [Hypogonadism]; Medtronics [Renal denervation]; Takeda [Gout, narcolepsy, cancer]; Travere [IgA nephropathy]; UCB [Psoriasis, arthritis]. All of the relevant financial relationships listed have been mitigated. **Karen Law, MD** No relevant financial relationship(s) with ineligible companies to disclose. **John P Forman, MD, MSc** No relevant financial relationship(s) with ineligible companies to disclose.

Contributor disclosures are reviewed for conflicts of interest by the editorial group. When found, these are addressed by vetting through a multi-level review process, and through requirements for references to be provided to support the content. Appropriately referenced content is required of all authors and must conform to UpToDate standards of evidence.

Conflict of interest policy

→