# Q/ Is lower BP worth it in higher-risk patients with diabetes or coronary disease?

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## EVIDENCE-BASED ANSWER

A/ **There is no simple answer;** the risk/benefit picture is complicated. Controlling blood pressure to a target of 130/80 mm Hg or lower produces mixed results in patients with diabetes and coronary disease equivalents (chronic kidney disease [CKD], coronary artery disease, peripheral arterial disease, and previous stroke).

No evidence indicates that patients with diabetes or most patients with CKD have better outcomes if their blood pressure is controlled below 140/90 mm Hg. Patients with diabetes controlled to lower systolic blood pressure targets (below 120 mm Hg) have fewer strokes, but more serious adverse events. Achieving diastolic blood pressure targets below 80 mm Hg doesn't reduce mortality, strokes, myocardial infarction, or congestive heart failure (strength of recommendation [SOR]: **A**, systematic review of randomized controlled trials [RCTs]).

Tight blood pressure control (approximately 130/80 mm Hg or lower) reduces the risk of kidney failure by 27% in CKD patients with proteinuria at baseline. In patients without proteinuria, it doesn't add benefit over standard blood pressure control (140/90 mm Hg) for reducing kidney failure, mortality, or cardiovascular events (SOR: **A**, meta-analysis of RCTs).

Controlling hypertension to 130/80 mm Hg or lower in patients with coronary artery disease reduces heart failure (27%) and stroke (18%) but increases the incidence of hypotensive episodes (220%) when compared with standard 140/90 mm Hg target blood pressure. Lower target pressures don't affect total or cardiovascular mortality, myocardial infarction, or angina, but do increase the need for revascularization in 6% of patients (SOR: **A**, meta-analysis of RCTs).

Controlling systolic blood pressure to a target of 120 mm Hg, compared with the standard target of 140 mm Hg, reduces a composite outcome (myocardial infarction, acute coronary syndrome, stroke, congestive heart failure, or cardiovascular death) by 25% and a secondary outcome of all-cause mortality by 27% in patients ages 50 and older with cardiovascular risk factors (but not diabetes or previous stroke).

However, intensive control doesn't significantly improve the composite outcome in patients who are female, black, or younger than 75 years, or who have systolic blood pressures above 132 mm Hg, previous CKD, or previous cardiovascular disease. Intensive control causes more hypotension, syncope, and electrolyte abnormalities, but not falls resulting in injuries (SOR: **B**, large RCT).

No evidence-based studies exist to guide BP control in patients with peripheral artery disease or previous stroke. Current guidelines recommend treating hypertension to a target of 140/90 mm Hg in these patients.

## Evidence summary

A Cochrane systematic review of 5 RCTs with a total of 7314 patients evaluated cardiovascular outcomes after 4.7 years follow-up in patients with diabetes who were treated for hypertension to either "lower" or "standard"

**While the SPRINT study found that targeting systolic BP below 120 mm Hg reduced a composite outcome that included cardiovascular death, it didn't improve this outcome in certain patient subgroups.**

target blood pressures.[1]

One trial in the review (ACCORD, 4734 patients) compared outcomes from significantly lower and standard systolic blood pressures (119/64 mm Hg vs 134/71 mm Hg; *P*<.0001) in patients with diabetes and either cardiovascular disease or 2 risk factors for cardiovascular disease. The authors evaluated outcomes based on achieved systolic blood pressures rather than intention to treat.

They found a reduced incidence of stroke (risk ratio [RR]=0.58; 95% confidence interval [CI], 0.39-0.88; *P*=.009; number needed to treat [NNT]=91) but no change in mortality (RR=1.05; 95% CI, 0.84-1.30) at lower blood pressures. Achieving the lower systolic blood pressure increased the number of serious adverse effects, however (RR=2.58; 95% CI, 1.70-3.91; *P*<.0001; absolute risk increase=2%; number needed to harm=50).

Four RCTs (2580 patients) in the systematic review compared clinical outcomes produced by achieving significantly lower or standard diastolic blood pressure targets (128/76 mm Hg vs 135/83 mm Hg; *P*<.0001). The trials found no significant difference in total mortality (RR=0.73; 95% CI, 0.53-1.01), stroke (RR=0.67; 95% CI, 0.42-1.05), myocardial infarction (RR=0.95; 95% CI, 0.64-1.40), or congestive heart failure (RR=1.06; 95% CI, 0.58-1.92). Sensitivity analysis of trials comparing diastolic blood pressure targets below 80 mm Hg and below 90 mm Hg showed similar results.

The 4 RCTs didn't report end-stage renal failure or total serious adverse events. The authors stated that there was a high risk of selection bias in favor of lower blood pressure targets.

### Patients with CKD

A systematic review and meta-analysis of 11 RCTs (9287 patients) compared outcomes of achieving lower blood pressure targets or standard targets in patients with CKD. Intensive blood pressure treatment reduced the risk of kidney failure only in patients with proteinuria at baseline (hazard ratio [HR]=0.73; 95% CI, 0.62-0.86; 5 trials, 1703 patients).[2] Investigators didn't report the degree of proteinuria for all the trials, but in one trial, patients had proteinuria of 1 to 3 g/d.

Achieved blood pressures in the intensive therapy group averaged 7.7/4.9 mm Hg lower, with pressures typically ranging from 75 to 80 mm Hg diastolic and 125 to 135 mm Hg systolic. Intensive blood pressure lowering didn't reduce kidney failure in patients without baseline proteinuria (HR=1.12; 95% CI, 0.67-1.87; 3 trials, 1218 patients). Nor did it reduce death (RR=0.94; 95% CI, 0.84-1.05; 10 trials, 6788 patients) or major cardiovascular outcomes (RR=1.09; 95% CI, 0.83-1.42; 5 trials, 5308 patients).

### Patients with coronary artery disease

A meta-analysis of 15 RCTs (66,504 patients) that evaluated tight control of hypertension (≤130/80 mm Hg) compared with standard control (<140/90 mm Hg) in patients with coronary artery disease found reduced rates of heart failure (RR=0.73; 95% CI, 0.64-0.84; 10 trials, 37,990 patients) and stroke (RR=0.82; 95% CI, 0.69-0.98; 9 trials, 8344 patients) but increased rates of hypotension (RR=2.19; 95% CI, 1.80-2.66; 6 trials, 17,836 patients).[3]

Achieving lower blood pressure targets didn't reduce all-cause mortality (RR=0.96; 95% CI, 0.89-1.04; 13 trials, 39,262 patients), cardiovascular mortality (RR=0.96; 95% CI, 0.86-1.07; 11 trials, 38,452 patients), myocardial infarction (RR=0.92; 95% CI, 0.85-1.00; 14 trials, 39,696 patients), or angina (RR=0.92; 95% CI, 0.84-1.0; 11 trials, 28,007 patients). But it slightly increased the need for revascularization (RR=1.06; 95% CI, 1.01-1.12; 11 trials, 38,450 patients).

### The SPRINT trial: Promising results for intensive treatment of some patients

The Systolic Blood Pressure Intervention Trial (SPRINT), a large RCT, found that targeting systolic blood pressures below 120 mm Hg (compared with a target below 140 mm Hg) in middle-aged and older patients with increased cardiovascular risk reduced a composite outcome that included cardiovascular death by 25%.[4]

Researchers recruited 9361 patients older than 50 years (mean age 68 years; >28% older than 75 years) with systolic blood pressure between 130 and 180 mm Hg and increased cardiovascular risk defined by one or more of the following: preexisting cardiovascular dis-

ease, CKD with estimated glomerular filtration rate between 20 and 60 mL/min/1.73 $m^2$, age >75 years, and Framingham 10-year risk of 15% or more. They excluded patients with diabetes or previous stroke.

Patients were randomized to intensive treatment (target systolic BP <120; mean achieved 121.4) or standard treatment (target systolic BP <140; mean achieved 136.2). Treatment typically comprised 3 (intensive) or 2 (standard) agents. The primary outcome was a composite of myocardial infarction, acute coronary syndrome, stroke, congestive heart failure, or cardiovascular death.

The study, which was originally intended to run for 5 years, was stopped at 3.26 years based on positive results. Intensive treatment improved the primary composite outcome overall (1.65% vs 2.19%; HR=0.75; 95% CI, 0.64-0.89; *P*<.001; NNT=61 over 3.26 years), all-cause mortality (HR=0.73; 95% CI, 0.60-0.90; *P*=.003; NNT=90), and cardiovascular death (HR=0.57; 95% CI, 0.38-0.85; *P*=.005; NNT=172).

However, intensive treatment didn't significantly improve the primary composite outcome in these subgroups:

- female patients (HR=0.84; 95% CI, 0.62-1.14)
- black patients (HR=0.77; 95% CI, 0.55-1.06)
- patients with preexisting CKD (HR=0.82; 95% CI, 0.63-1.07) or cardiovascular disease (HR=0.83; 95% CI, 0.62-1.09)
- patients younger than 75 years (HR=0.80; 95% CI, 0.64-1.00)
- patients with systolic blood pressures higher than 132 mm Hg (BP >132 to <145 mm Hg, HR=0.77; 95% CI, 0.57-1.03; BP ≥145 mm Hg, HR=0.83; 95% CI, 0.63-1.09).

Intensive treatment also produced more net serious adverse events (HR=1.88; 4.7% vs 2.5%; *P*<.001), including: ≥30% decrease of glomerular filtration rates to values below 60 mL/min/1.73 $m^2$ (HR=3.49; 95% CI, 2.44-5.10; *P*<.001), syncope (HR=1.44; 3.5% vs 2.4%; *P*=.003), hypotension (HR=1.70; 3.4% vs 2.0%; *P*<.001), and electrolyte abnormalities (HR=1.38; 3.8% vs 2.8%; *P*=.006). It didn't cause injurious falls (HR=1.00; *P*=.97) or orthostatic hypotension in clinic (HR=0.88; 16.6% vs 18.3%; *P*=.01).

## Guidelines for patients with peripheral artery disease, previous stroke

A national guideline by an expert panel recommended treating patients with hypertension who have peripheral artery disease or previous stroke to standard values for the general population: <140/90 mm Hg if ages 60 years or younger, <150/90 mm Hg if older than 60 years.[5] JFP


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