

Disease Burden and Unmet Need in Hypertension



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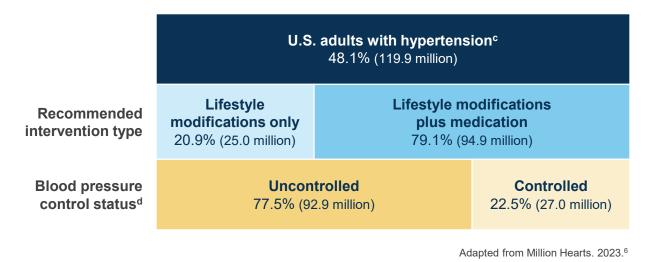




Uncontrolled hypertension is a global public health crisis¹ despite available therapies, many patients do not reach and maintain blood pressure targets, which leads to substantial morbidity and mortality

In the U.S., ~50% of adults are hypertensive, with approximately 80% of those individuals remaining uncontrolled^{2,a}

- Treated patients with uncontrolled hypertension have increased risk of mortality³
- In hypertension clinical trials using ACEis or ARBs, there remains a 90–92% residual risk of CV events, despite achieving risk factor targets (eg, BP)⁴
 - The ACC/AHA 2017 guideline defines CV events as coronary heart disease, congestive heart failure, and stroke⁵



^aUncontrolled hypertension is defined as individuals with a BP ≥130/80 mmHg. ^bAmong adults aged 18 years or older. Estimates are rounded and may not equal 100%. ^cBP ≥130/80 mmHg or currently using prescription to lower BP. ^dControlled is defined as a blood pressure <130/80 mmHg. All adults recommended lifestyle modifications only are considered uncontrolled as their BP lies above the threshold.

ACC, American College of Cardiology; ACEi, angiotensin-converting enzyme inhibitor; AHA, American Heart Association; ARB, angiotensin II receptor blocker; BP, blood pressure; CV, cardiovascular; RNAi, RNA interference. 1. World Health Organization. A global brief on hypertension. Published June 25, 2013. Accessed October 11, 2023. <u>https://www.who.int/publications/i/item/a-global-brief-on-hypertension-silent-killer-global-public-health-crisis-world-health-day-2013</u>. 2. Million Hearts. Estimated hypertension prevalence, treatment, and control among U.S. adults: tables. Accessed October 26, 2023. <u>https://millionhearts.hhs.gov/files/Estimated-Hypertension-Prevalence-tables-508.pdf</u>. 3. Zhou D, et al. *Sci Rep.* 2018;8: 9418. 4. Ferrario CM, et al. *Curr Hypertens Rep.* 2022;24(12):709-721. 5. Whelton PK, et al. *J Am Coll Cardiol.* 2018; 71:e127-e248; 6. Million Hearts. Estimated hypertension prevalence, treatment, and control among U.S. adults. Last updated May 2023. Accessed August 30, 2023. <u>https://millionhearts.hhs.gov/files/Estimated-hypertension-prevalence.html</u>



Hypertension in U.S. Adults^{6,b}

3



Risk of mortality in patients with treated but uncontrolled hypertension^{1,a}:

Data is based on a study of 13,947 U.S. adults aged ≥18 years, enrolled in the Third National Health and Nutrition Examination Survey (1988–1994).



1.62x

risk of all-cause mortality (95% CI: 1.35–1.95; *P* < 0.001)



2.19x

risk of heart disease–specific mortality (95% CI: 1.57–3.05; *P* < 0.001)

2.23x

risk of cardiovascular disease– specific mortality (95% CI: 1.66–2.99; *P* < 0.001)



3.01x

risk of cerebrovascular disease–specific mortality (95% CI: 1.91–4.73; *P* < 0.001)



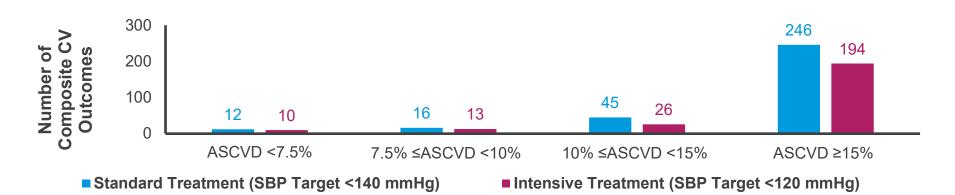


High CV risk patients with hypertension have a greater likelihood of serious CV events and experience greater financial burdens

High CV risk patients are defined:

- By the 2017 ACC/AHA guidelines as individuals with¹:
 - Clinical ASCVD (first CHD death, non-fatal MI, or fatal or non-fatal stroke)
 - An estimated 10-year risk of ASCVD ≥10%
 - Hypertension with comorbid diabetes mellitus and/or chronic kidney disease

In a post-hoc analysis of 9,361 patients with hypertension, CV outcomes^a increased with worsening ASCVD scores, regardless of patients being placed on standard or intensive treatment plans^{2,b}



 Based on a study from 2009 in the U.S., individuals with hypertension who also suffered from ≥1 CV event experienced significantly greater total healthcare costs (ie, inpatient, outpatient, and drug costs) for any one CV event, ranging from \$502-\$1,688 per member per month, compared to patients with no previous CV event^{3,c}

^aCV outcomes considered were a composite of nonfatal myocardial infarction, acute coronary syndrome not resulting in myocardial infarction, stroke, acute decompensated heart failure, or death from CV causes. ^bIn the Systolic Blood Pressure Intervention Trial (SPRINT), 9361 nondiabetic patients without a history of stroke were randomized into standard-treatment had a SBP target of <140 mmHg. Patients randomized into intensive-treatment had a SBP target of <120 mmHg. All major classes of antihypertensive drugs were included and medications were adjusted according to target each SBP goal. ^cEstimated regression-adjusted per-member-per-month healthcare costs after CV events is based on claims data from privately insured individuals with hypertension diagnoses in 2004-2006.

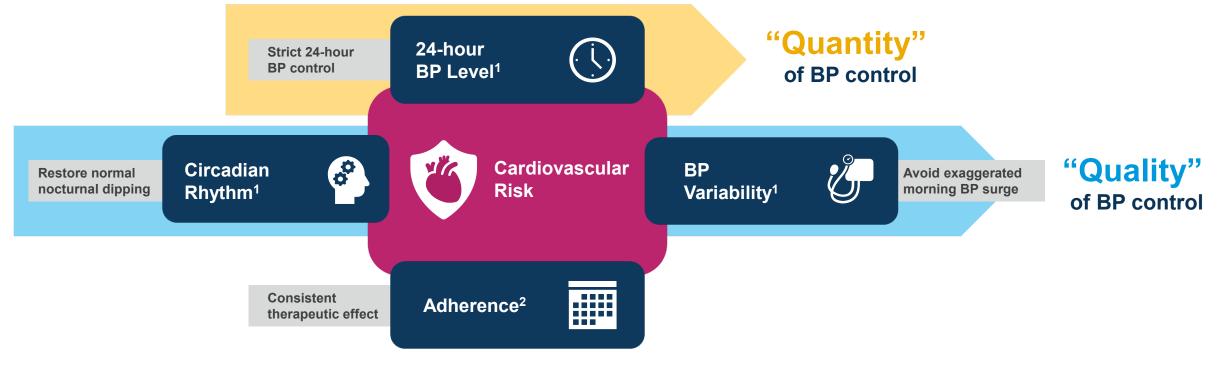
ACC, American College of Cardiology; AHA, American Heart Association; ASCVD, atherosclerotic cardiovascular disease; CHD coronary heart disease; CV, cardiovascular; MI, myocardial infarction; RNAi, RNA interference; SBP, systolic blood pressure. 1. Whelton PK, et al. J Am Coll Cardiol. 2018; 71:e127-e248. 2. Alborzi A, et al. Cardiol Res Pract. 2021:2021:6635345. 3. Duh MS, et al. Am J Hypertens. 2009;3(6):403-415.



5



Lack of consistent tonic blood pressure control in patients with hypertension contributes to organ damage, CV events, and death



Koche

Adapted from Kario K. Prog Cardiovasc Dis. 2016;59:262-281.1

6



| | Tonic Blood Pressure Control

24-hour BP Level



Circadian Rhythm

BP Variability

Adherence

•

A global longitudinal population-based cohort study of 11,135 adults from 1988–2010 showed that **24hour SBP** (increasing increments of 20 mmHg) is significantly associated with an **increased risk of CV outcomes (HR = 1.45), CV mortality (HR = 1.48), and total mortality** (HR = 1.22)¹ In a prospective ABPM study of 6,359 Japanese patients, **disrupted circadian BP rhythm** (riser pattern), significantly **increased overall CV risk by 1.48x** (*P* = 0.024) and heart **failure by 2.45x** (*P* = 0.004), compared with normal circadian rhythm² A 10-year follow-up of 689,051 U.S. veterans found that patients with hypertension and **BP rates consistently within therapeutic range** had an **all-cause mortality of 6.5%**, compared to those with **BP rates consistently above** (21.9%) or below (33.1%) **the therapeutic range** (*P* < 0.0001)³ A meta-analysis of 44 prospective epidemiological studies found that ≥80% adherence to antihypertensive medications lowered CV risk by 19% and all-cause mortality by 29%, compared to <80% adherence⁴

"Quantity" of BP control⁵

"Quality" of BP control⁵

ABPM, ambulatory blood pressure monitoring; BP, blood pressure; CV, cardiovascular; HR, hazard ratio; SBP, systolic blood pressure.

1. Yang WY, et al. JAMA. 2019;322(5):409-420. 2. Kario K, et al. Circulation. 2020;142(19):1810-1820. 3. Doumas M, et al. J Am Heart Assoc. 2017;6(11):e007131. 4. Chowdhury R, et al. Eur Heart J. 2013;34(38):2940-2948; 5. Kario K. Prog Cardiovasc Dis. 2016;59:262-281.

