

Cardiovascular Event Risk Increases More Sharply for Men Than Women at Very Low Average Blood Pressure

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Key Findings

- The risks of myocardial infarction (MI), ischemic stroke, and hemorrhagic stroke are increased for patients with high or low average systolic blood pressure (BP). The risks are greater at very low systolic BP than at very high systolic BP.
- At an average systolic BP <90 mmHg, risk of hemorrhagic stroke was 166% greater in men and 67% greater in women compared to those with an average systolic BP of 115–119 mmHg. Risk of MI and ischemic stroke at very low average systolic BP was also more pronounced for men than women.

Blood pressure (BP) is a key modifiable risk factor for cardiovascular disease (CVD). Prior research has highlighted that both low BP and high BP can increase risk of adverse cardiovascular events, but less is known about whether this risk differs between men and women.¹ Sex-based physiological differences, including vascular stiffness and hormonal factors, may contribute to different susceptibility to myocardial infarction (MI) and stroke.²

To better understand whether there are differing cardiovascular outcomes between sexes, we studied 22,070,072 patients aged 18 to 95 who had at least one outpatient BP measurement between May 1, 2019, and April 30, 2022, to calculate a historical average BP. An additional outpatient BP measurement between May 1, 2022, and April 30, 2023, served as the index value for stratifying patients by systolic BP levels. Patients were observed for one year for MI and stroke. We accounted for demographics, comorbidities, historical average BP, and medication use. Outcomes were defined as the first occurrence of MI, ischemic stroke, or hemorrhagic stroke.

Relative risk for MI increased at both BP extremes for men and women, but the increase was more pronounced in men for very low average systolic BP. Men with an average systolic BP <90 mmHg had a 142% greater risk of MI compared to men with an average systolic BP of 115–119 mmHg. For women, the risk was 102% greater at an average systolic BP <90 mmHg compared to women with an average systolic BP of 115–119 mmHg. At ≥160 mmHg, risks were similar between men (56% greater risk) and women (55% greater risk).

MI Risk by Average Systolic BP and Sex

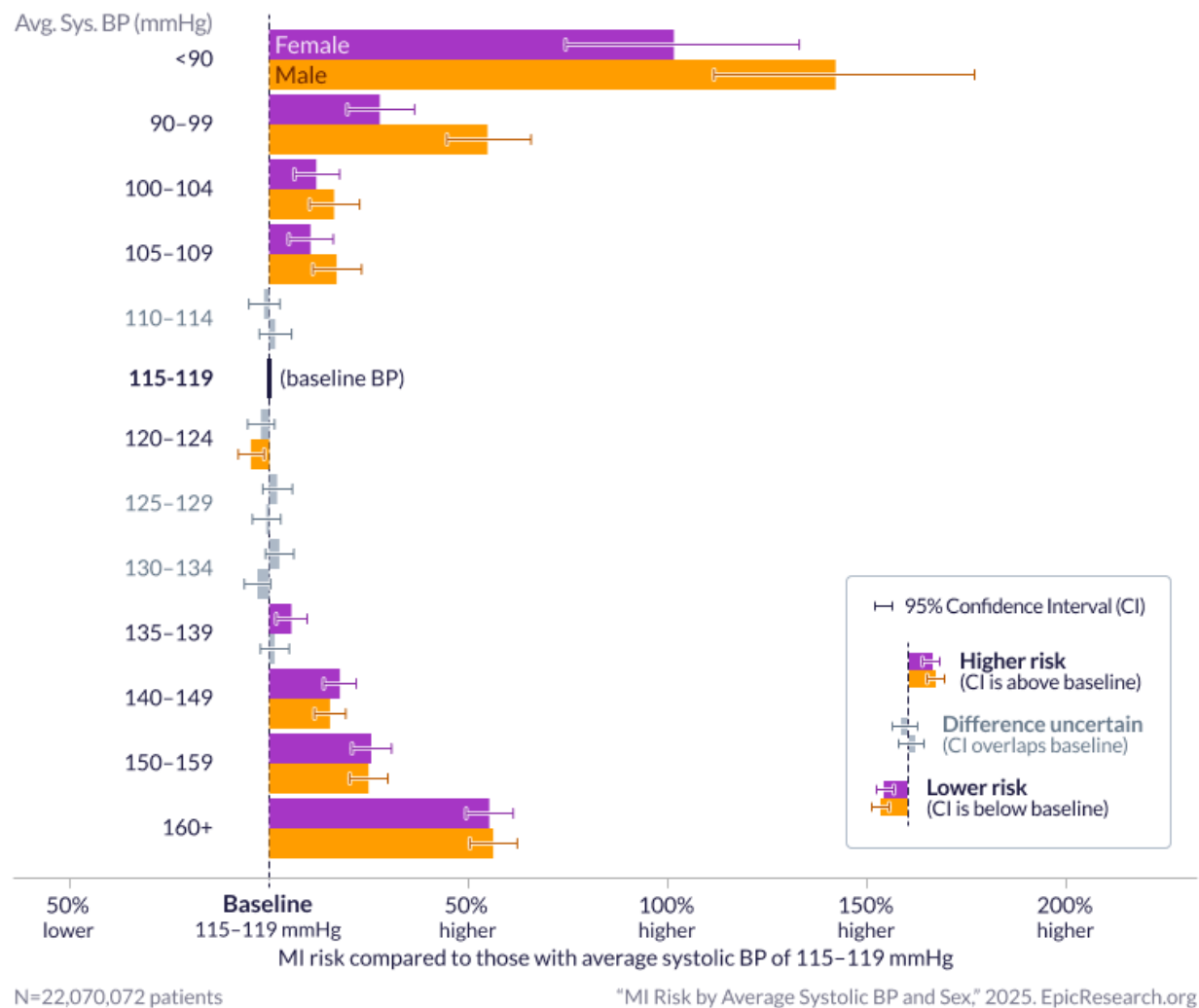


Figure 1. The risk of a patient experiencing an MI stratified by their average systolic BP and sex.

Similarly, both sexes showed higher ischemic stroke risk at both BP extremes, with a greater increase in men at very low average systolic BP. At <90 mmHg, the risk was 142% higher for men and 106% higher for women (compared with an average systolic BP of 115-119). The difference between sexes was smaller at ≥160 mmHg (71% greater for men and 59% greater for women).

Ischemic Stroke Risk by Average Systolic BP and Sex

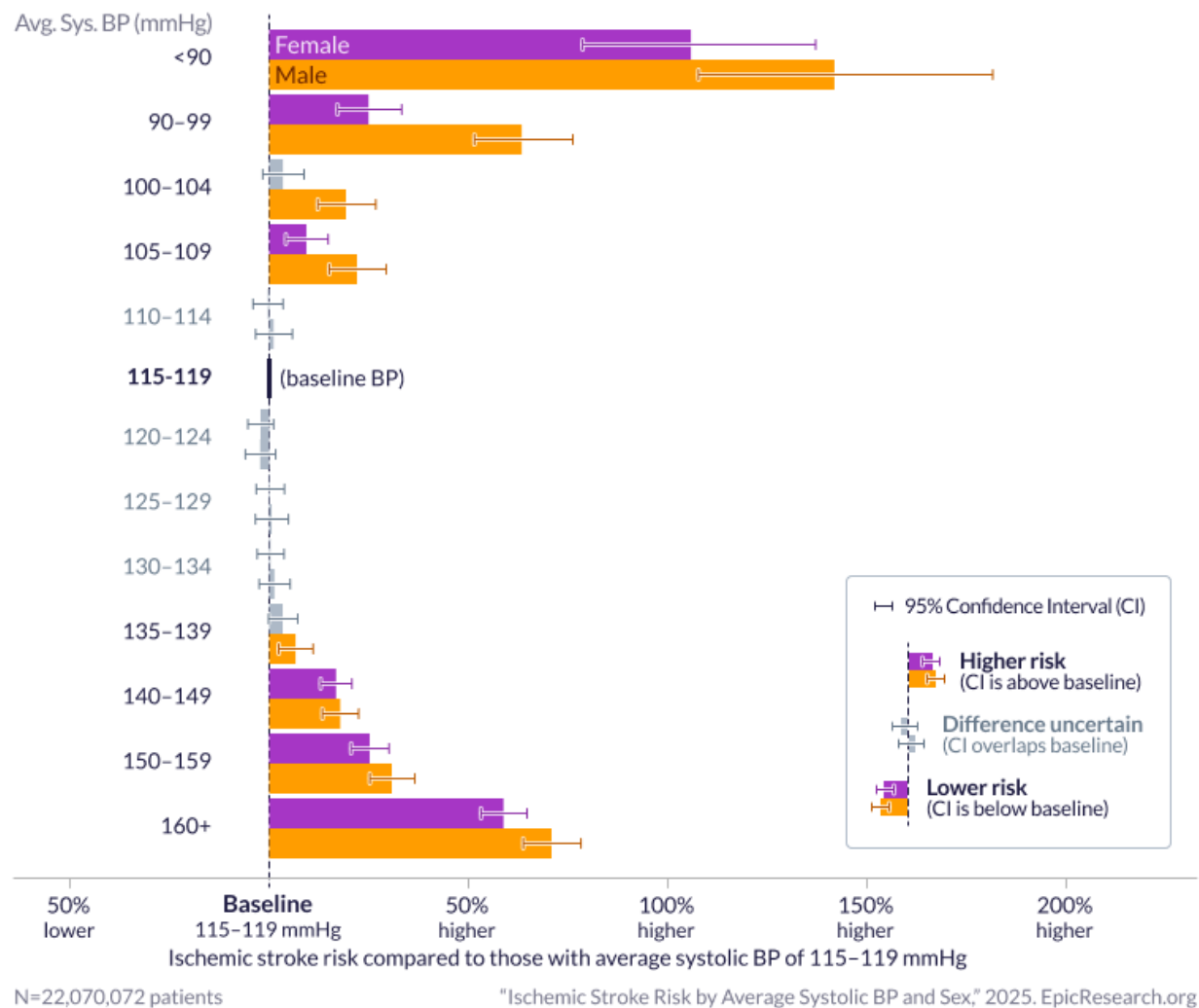


Figure 2. The risk of a patient experiencing an ischemic stroke by their average systolic BP and sex.

Men had a sharper increase in hemorrhagic stroke risk at low average systolic BP than women. At an average systolic BP <90 mmHg, men had a 166% greater risk, versus a 67% greater risk for women, compared to those with an average systolic BP of 115-119 mmHg. At the highest average BP (≥ 160 mmHg), risk converged (24% for men, 26% for women).

Hemorrhagic Stroke Risk by Average Systolic BP and Sex

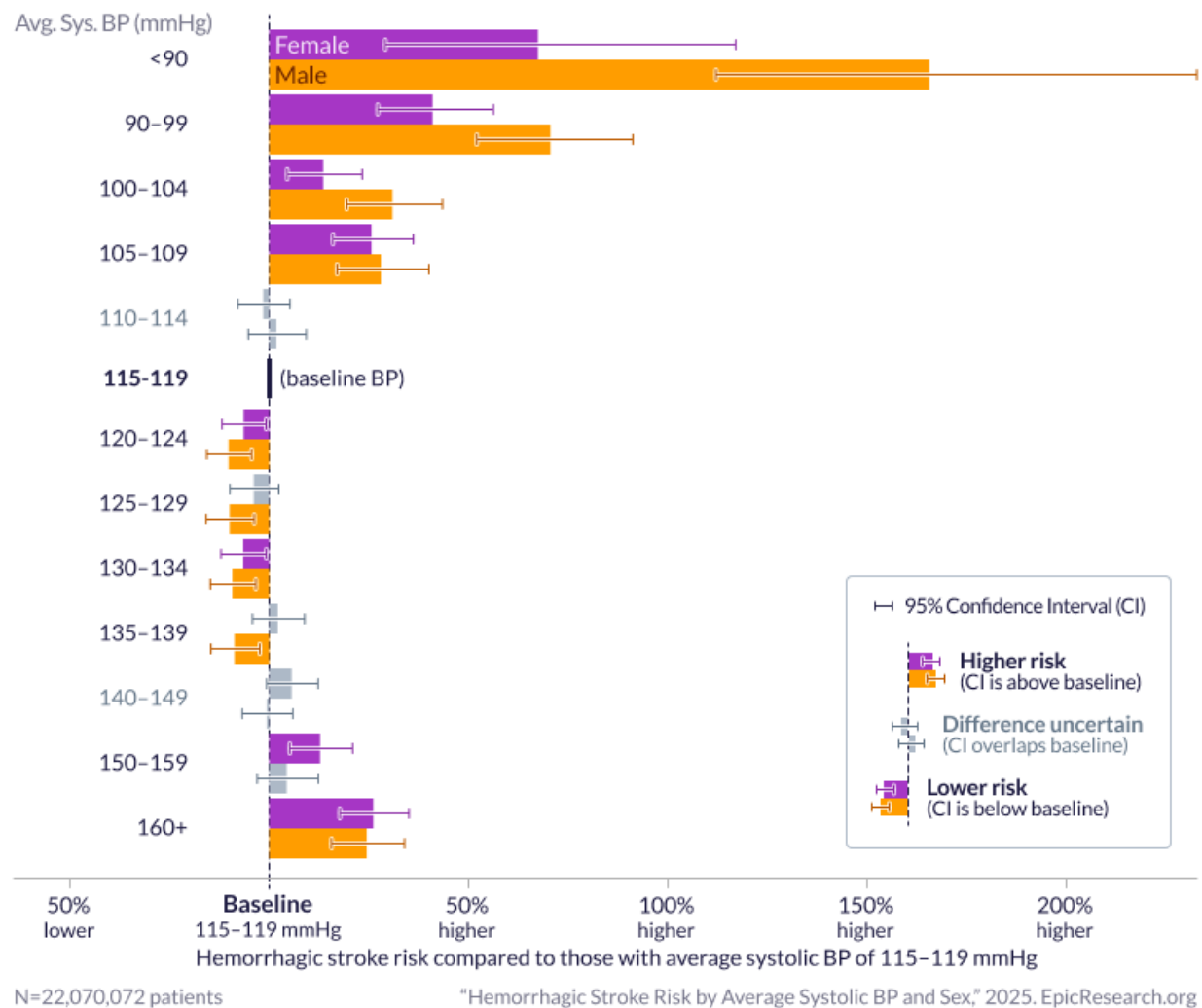


Figure 3. The risk of a patient experiencing a hemorrhagic stroke by their average systolic BP and sex.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 300 million patient records from 1,800 hospitals and more than 41,000 clinics from all 50 U.S. states, Canada, Lebanon, and Saudi Arabia. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. 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: Executive summary. Hypertension. 2018;71(6):1269-1324. doi:10.1161/HYP.0000000000000066
2. Ji H, Kwan AC, Chen MT, et al. Sex differences in myocardial and vascular aging. Circ Res. 2022;130(4):566-577. doi:10.1161/CIRCRESAHA.121.319902.

Data Definitions

Term	Definition
Study period	Pre-study period: BP readings between 5/1/2019 and 4/30/2022 Study period (index date): Random BP reading between 5/1/2022 and 4/30/2023 Follow-up: 5/1/2023 to 5/1/2024, one year after index date
Study population	Inclusion: • More than one outpatient BP reading in pre-study period • More than one outpatient BP reading in study period • Aged 18 to 95 at BP reading during the study period • Outcome after index date or outpatient encounter one to two years after index date Exclusion: • Any outcome prior to index date • First outcome in non-admission encounter • CKD prior to index date: ICD-10-CM code N18* • CHF prior to index date: ICD-10-CM code I50* • Pregnancy during follow-up period
Censoring	Last encounter with a type of Emergency, Office Visit, Well Child, Follow-up, Telemedicine, Urgent Care, or Walk-In First outcome
Exposures	Average systolic blood pressure Legal sex: male or female
Outcomes	The following first observed in an admission: • MI: ICD-10-CM code I21*, I22*, or I23* • Ischemic stroke: ICD-10-CM code I63* • Hemorrhagic stroke: ICD-10-CM code I60*, I61*, or I62*
Confounders	Age: 18-30, 31-45, 46-55, 56-65, 66-70, 71-75, 76-80, 81-85, 86-95) Race and ethnicity (binary flags) Social Vulnerability Index quartile (based on most recent ZIP code) RUCA: Rural (10), Small Town (7-9), Micropolitan (4-6), and Metropolitan (1-3) BMI classification (closest preceding blood pressure) Type 1 diabetes: ICD-10-CM code E10* Type 2 diabetes: ICD-10-CM code E11* Hyperlipidemia: ICD-10-CM code E78.2*-E78.5* or statin medication prescribed between on year before the index date and the index date • Statin: C10AA* CVD: ICD-10-CM code I20*-I26*, I30*-I39*, I40*-I49*, I51*, or I70*-I79* Atrial fibrillation: ICD-10-CM code ICD-10-CM code I48.0*, I48.1*, I48.2*, or I48.91 Hypertension: ICD-10-CM code I10 or antihypertensive prescribed between one year before the index date and the index date identified with ATC codes: • ACE inhibitors: C09B*, C09A* • ARBs: C09D*, C09C* • Beta-blockers: C07* • Diuretics: C03* • Calcium Channel Blockers: C08*

	Average systolic BP from pre-study period • <90 • 90-99 • 100-104 • 105-109 • 110-114 • 115-119 • 120-124 • 125-129 • 130-134 • 135-139 • 140-149 • 150-159 • 160+
Race and ethnicity	Patients were classified based on self-reported race and ethnicity as binary variables. Patients with multiple races were given two values.
International considerations	Yes, patients outside of the U.S. Missing RUCA/SVI handled as an independent category.
Model specifications	Cox Survival Model
Limitations	Cumulative blood pressure is a known risk factor that is not adjusted for.

Table 1. MI Risk by Average Systolic BP and Sex

Systolic BP	Female HR	Female Lower CI	Female Upper CI	Male HR	Male Lower CI	Male Upper CI
<90	2.02	1.74	2.33	2.42	2.12	2.77
90-99	1.28	1.20	1.36	1.55	1.45	1.66
100-104	1.12	1.06	1.18	1.16	1.10	1.23
105-109	1.10	1.05	1.16	1.17	1.11	1.23
110-114	0.99	0.95	1.03	1.01	0.98	1.06
120-124	0.98	0.95	1.01	0.95	0.92	0.99
125-129	1.02	0.98	1.06	0.99	0.96	1.03
130-134	1.03	0.99	1.06	0.97	0.94	1.00
135-139	1.06	1.02	1.10	1.01	0.98	1.05
140-149	1.18	1.14	1.22	1.15	1.11	1.19
150-159	1.26	1.21	1.31	1.25	1.20	1.30
160+	1.55	1.49	1.61	1.56	1.50	1.62

Table 2. Ischemic Stroke Risk by Average Systolic BP and Sex

Systolic BP	Female HR	Female Lower CI	Female Upper CI	Male HR	Male Lower CI	Male Upper CI
<90	2.06	1.79	2.37	2.42	2.08	2.82
90-99	1.25	1.17	1.33	1.63	1.51	1.76
100-104	1.03	0.98	1.09	1.19	1.12	1.27
105-109	1.09	1.04	1.15	1.22	1.15	1.29
110-114	1.00	0.96	1.03	1.01	0.97	1.06
120-124	0.98	0.95	1.01	0.98	0.94	1.02
125-129	1.00	0.97	1.04	1.01	0.97	1.05
130-134	1.00	0.97	1.04	1.01	0.97	1.05
135-139	1.03	1.00	1.07	1.07	1.02	1.11
140-149	1.17	1.13	1.21	1.18	1.13	1.22
150-159	1.25	1.21	1.30	1.31	1.25	1.36
160+	1.59	1.53	1.65	1.71	1.64	1.78

Table 3. Hemorrhagic Stroke Risk by Average Systolic BP and Sex

Systolic BP	Female HR	Female Lower CI	Female Upper CI	Male HR	Male Lower CI	Male Upper CI
<90	1.67	1.29	2.17	2.66	2.12	3.33
90-99	1.41	1.27	1.56	1.71	1.52	1.91
100-104	1.14	1.04	1.23	1.31	1.19	1.43
105-109	1.26	1.16	1.36	1.28	1.17	1.40
110-114	0.98	0.92	1.05	1.02	0.95	1.09
120-124	0.94	0.88	0.99	0.90	0.84	0.96
125-129	0.96	0.90	1.02	0.90	0.84	0.96
130-134	0.93	0.88	0.99	0.91	0.85	0.97
135-139	1.02	0.96	1.09	0.91	0.85	0.98
140-149	1.06	0.99	1.12	0.99	0.93	1.06
150-159	1.13	1.05	1.21	1.04	0.97	1.12
160+	1.26	1.18	1.35	1.24	1.16	1.34