

Letters

RESEARCH LETTER

High Blood Pressure in Childhood and Premature Cardiovascular Disease Mortality

High blood pressure (BP) is a major modifiable risk factor for cardiovascular disease (CVD). Although there is growing recognition that early-life elevations in BP may confer lifetime risk for CVD and CVD mortality, the evidence for long-term mortality risk is limited.^{1,2} This is particularly important because the prevalence of elevated BP in children is increasing.^{3,4} This study examined the association between BP at age 7 years and CVD mortality in a large, diverse sample of US children, with follow-up into the sixth decade of life.

Methods | From March to July 2025, data were analyzed from a prospective cohort of children born to women enrolled in the US Collaborative Perinatal Project (CPP) between 1959 and 1965

at 12 sites; participants in the CPP provided verbal consent.⁵ At age 7 years, a single BP was obtained by a pediatrician or nurse using a manual sphygmomanometer. Systolic BP (SBP) and diastolic BP (DBP) were converted to age-, sex-, and height-specific percentiles and categorized as normal (<90th percentile), elevated (90th-94th percentile), or hypertension (≥95th percentile), per American Academy of Pediatrics guidelines.⁶ The children’s vital status (and for decedents, cause of death) through 2016 was ascertained via probabilistic linkage to the National Death Index.

Survival analysis was used to estimate associations of childhood BP with CVD and non-CVD mortality, using age as the time scale and a robust variance estimator to account for sibling clusters. Models were adjusted for childhood body mass index; maternal race, education, and marital status; and study site. In a sensitivity analysis, fixed-effects regression was used to estimate associations within sibling clusters, controlling for shared familial and environmental characteristics. Differences in cumulative incidence functions by BP category were compared

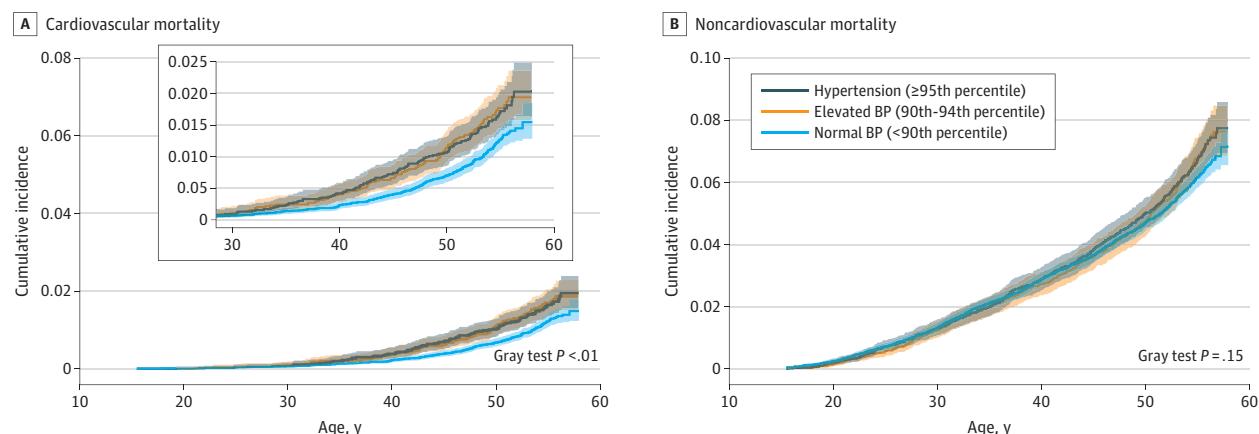
Table. Demographic and Clinical Characteristics of the Study Sample

Characteristic	No. (%)			
	Total No. (N = 37 081)	Blood pressure category		
		Normal (<90th percentile) (n = 22 479 [60.6%])	Elevated (90th-94th percentile) (n = 6968 [18.8%])	Hypertension (≥95th percentile) (n = 7634 [20.6%])
Offspring characteristics				
Sex				
Male	18 810 (50.7)	11 138 (49.6)	3824 (54.9)	3848 (50.4)
Female	18 271 (49.3)	11 341 (50.4)	3144 (45.1)	3786 (49.6)
Age at baseline, mean (SD), y	7.1 (0.6)	7.1 (0.6)	7.1 (0.6)	7.1 (0.6)
Systolic blood pressure, mean (SD), mm Hg	101.9 (10.2)	96.6 (7.1)	105.5 (6.3)	114.4 (8.5)
Diastolic blood pressure, mean (SD), mm Hg	61.2 (10.0)	56.9 (8.1)	65.9 (6.8)	69.9 (9.8)
BMI, mean (SD)	16.0 (2.0)	15.7 (1.7)	16.1 (1.9)	16.8 (2.7)
BMI category				
Healthy or underweight (BMI <85th percentile)	31 587 (85.2)	20 069 (89.3)	5849 (83.9)	5669 (74.3)
Overweight or obese (BMI ≥85th percentile)	5494 (14.8)	2410 (10.7)	1119 (16.1)	1965 (25.7)
Household sociodemographic characteristics				
Maternal race				
Black	18 392 (49.6)	12 087 (53.8)	3140 (45.1)	3165 (41.5)
White	17 124 (46.2)	9453 (42.0)	3515 (50.4)	4156 (54.4)
Other ^a	1565 (4.2)	939 (4.2)	313 (4.5)	313 (4.1)
Maternal marital status, married	28 627 (77.2)	16 980 (75.5)	5503 (79.0)	6144 (80.5)
Maternal education, y				
<12 (Did not complete high school)	21 170 (57.1)	12 721 (56.6)	3965 (56.9)	4484 (58.7)
12 (Completed high school)	11 790 (31.8)	7111 (31.6)	2245 (32.2)	2434 (31.9)
>12 (More than high school)	4121 (11.1)	2647 (11.8)	758 (10.9)	716 (9.4)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

^a Other includes endorsement of Puerto Rican, Asian, or other (not specified).

Figure. Cumulative Incidence of Cardiovascular and Noncardiovascular Mortality Stratified by Blood Pressure (BP) Category at Age 7 Years



BP categories were based on age-, sex-, and height-specific percentiles according to the 2017 American Academy of Pediatrics guidelines. The shading indicates the 95% CIs. The inset in panel A displays the same data with a magnified y-axis.

using the Gray test. Statistical significance was set at $P < .05$ (eMethods in Supplement 1).

Results | Among 37 081 children, the mean (SD) age was 7.1 (0.6) years, mean SBP was 101.9 (10.2) mm Hg, and mean DBP was 61.2 (10.0) mm Hg at baseline (Table). Approximately 21% of children were classified with hypertension. During a median (IQR) follow-up through age 54 (52-55) years, there were 487 cardiovascular and 2242 noncardiovascular deaths.

A 1-SD higher SBP (unadjusted hazard ratio [HR], 1.15 [95% CI, 1.04-1.26]; adjusted HR [aHR], 1.14 [95% CI, 1.03-1.26]) and DBP (unadjusted HR, 1.17 [95% CI, 1.07-1.29]; aHR, 1.18 [95% CI, 1.07-1.29]) at age 7 years was significantly associated with premature CVD mortality. Findings were also consistent in magnitude and direction in the fixed-effects sibling analysis (359 children in 150 sibling clusters) for SBP (aHR, 1.14 [95% CI, 0.90-1.45]) and DBP (aHR, 1.18 [95% CI, 0.93-1.51]). There was a significant interaction by sex for SBP ($P < .01$), with a stronger magnitude of association in male (aHR, 1.31 [95% CI, 1.14-1.50]) vs female individuals (aHR, 0.97 [95% CI, 0.84-1.11]). Cumulative incidence functions differed by BP category for CVD mortality but not non-CVD mortality (Figure). Elevated BP (unadjusted HR, 1.45 [95% CI, 1.16-1.81]; aHR, 1.48 [95% CI, 1.18-1.86]) and hypertension (unadjusted HR, 1.41 [95% CI, 1.13-1.75]; aHR, 1.40 [95% CI, 1.12-1.76]) at age 7 years were associated with greater risk of CVD mortality.

Discussion | In a large sample of US children born between 1959 and 1966, higher BP at age 7 years was associated with greater risk of premature CVD mortality. These findings build upon prior research that linked childhood SBP with fatal CVD in young adulthood, but that sample had a follow-up duration through a mean age of only 46 years.² This study extends that work with follow-up into the mid-50s and demonstrated consistency in the magnitude of the associations within siblings, which mitigates concerns regarding unmeasured confounding due to shared family or lifestyle characteristics. Limitations include that outcomes were restricted to fatal events

ascertained through 2016, reflecting premature mortality. Childhood BP was based on a single measurement, although hypertension rates aligned with nationally representative data from the same period.³ CPP study participants were predominantly Black or White, so findings may not generalize to other groups. Overall, the findings underscore the importance of early-life cardiovascular health promotion, with a focus on monitoring and modifying BP-associated risk beginning as early as age 7 years.

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Accepted for Publication: July 30, 2025.

Published Online: September 7, 2025. doi:10.1001/jama.2025.14405

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Statistical analysis: Freedman, Gilman.

Obtained funding: Freedman, Gilman.

Administrative, technical, or material support: Ernst.

Supervision: Ernst, Borders, Miller, Gilman, Khan.

Conflict of Interest Disclosures: Dr Freedman reported receiving grants from the National Institutes of Health/National Heart, Lung, and Blood Institute (NIH/NHLBI; KO1HL165038) during the conduct of the study. Dr Perak reported receiving grants from NIH/NHLBI related to youth heart health (R34 HL171722) during the conduct of the study. Dr Allen reported receiving grants from NIH during the conduct of the study. Dr Khan reported receiving grants from NHLBI outside the submitted work. No other disclosures were reported.

Funding/Support: The Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) supported data acquisition (project ZIAHD008976).

Role of the Funder/Sponsor: The Intramural Research Program of NICHD had no role in the design and conduct of the study; management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Meeting Presentation: This paper was presented at the American Heart Association Scientific Sessions; September 7, 2025; Baltimore, Maryland.

Data Sharing Statement: See [Supplement 2](#).

1. Yang L, Sun J, Zhao M, Liang Y, Bovet P, Xi B. Elevated blood pressure in childhood and hypertension risk in adulthood: a systematic review and meta-analysis. *J Hypertens*. 2020;38(12):2346-2355. doi:10.1097/HJH.0000000000002550
2. Jacobs DR Jr, Woo JG, Sinaiko AR, et al. Childhood cardiovascular risk factors and adult cardiovascular events. *N Engl J Med*. 2022;386(20):1877-1888. doi:10.1056/NEJMoa2109191
3. Din-Dzietham R, Liu Y, Bielo MV, Shamsa F. High blood pressure trends in children and adolescents in national surveys, 1963 to 2002. *Circulation*. 2007;116(13):1488-1496. doi:10.1161/CIRCULATIONAHA.106.683243
4. Ruan X, Zhu A, Wang T, et al. Global prevalence of hypertension in children and adolescents younger than 19 years: a systematic review and meta-analysis. *JAMA Pediatr*. 2025:e252206. doi:10.1001/jamapediatrics.2025.2206
5. Niswander KR. *The Women and Their Pregnancies: The Collaborative Perinatal Study of the National Institute of Neurological Diseases and Stroke*. Saunders; 1972.
6. Flynn JT, Kaelber DC, Baker-Smith CM, et al; Subcommittee on Screening and Management of High Blood Pressure in Children. Clinical practice guideline for screening and management of high blood pressure in children and adolescents. *Pediatrics*. 2017;140(3):e20171904. doi:10.1542/peds.2017-1904