Hypertension

Association of all-cause and cardiovascular mortality with prehypertension: A meta-analysis

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Background Studies of prehypertension and mortality are controversial after adjusting for other cardiovascular risk factors. This meta-analysis sought to evaluate the association of prehypertension with all-cause and cardiovascular disease (CVD) mortality.

Methods The PubMed, EMBASE, Cochrane Library databases, and conference proceedings were searched for studies with data on prehypertension and mortality. The relative risks (RRs) of all-cause, CVD, coronary heart disease (CHD), and stroke mortality were calculated and presented with 95% CIs. Subgroup analyses were conducted according to blood pressure, age, gender, ethnicity, follow-up duration, participant number, and study characteristics.

Results Data from 1,129,098 participants were derived from 20 prospective cohort studies. Prehypertension significantly increased the risk of CVD, CHD, and stroke mortality (RR 1.28, 95% CI 1.16-1.40; RR 1.12, 95% CI 1.02-1.23; and RR 1.41, 95% CI 1.28-1.56, respectively), but did not increase the risk of all-cause mortality after multivariate adjustment (RR 1.03, 95% CI 0.97-1.10). The difference between CHD mortality and stroke mortality was significant ($P < .001$). Subgroup analyses showed that CVD mortality was significantly increased in high-range prehypertension (RR 1.28, 95% CI 1.16-1.41) but not in low-range prehypertension (RR 1.08, 95% CI 0.98-1.18).

Conclusion Prehypertension is associated with CVD mortality, especially with stroke mortality, but not with all-cause mortality. The risk for CVD mortality is largely driven by high-range prehypertension. (Am Heart J 2014;167:160-168.e1.)

The seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure proposed a new classification, prehypertension, for patients presenting with a systolic blood pressure (BP) of 120 to 139 mm Hg or diastolic BP of 80 to 89 mm Hg.[1] Studies have demonstrated that prehypertension is an independent risk factor for cardiovascular disease (CVD).[2-5] However, reports on the association of prehypertension with all-cause mortality and CVD mortality are inconsistent.[6-9] Furthermore, arguments against using the term "prehypertension" include the fact that there is heterogeneity within this category because the risk of developing CVD may be different in individuals with BP of 130-139/85-89 mm Hg than in those with BP in the range of 120-129/80-84 mm Hg.[10,11]

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These inconsistent results could be clarified by a meta-analysis of prospective cohort studies. Our objective was to evaluate the association of prehypertension with all-cause and CVD mortality, as well as coronary heart disease (CHD) and stroke mortality.

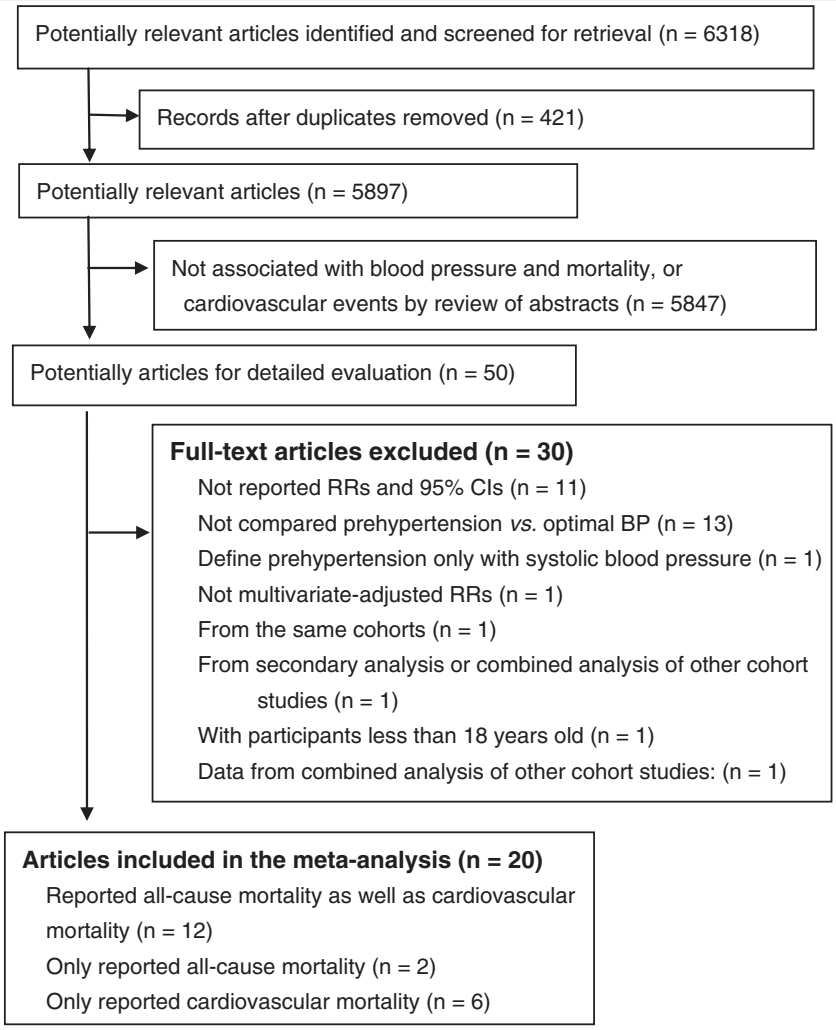
Methods

Search strategy and selection criteria

Electronic databases (PubMed, EMBASE, and the Cochrane Library) were searched to the third week of December 2012 using the following terms: "prehypertension," "prehypertensive," "pre-hypertension," "pre-hypertensive," "high normal blood pressure," "optimal blood pressure," or "borderline hypertension" and "mortality," "death," "deaths," or "fatal." There were no restrictions for language or publication form. In addition, conference proceedings (American College of Cardiology Meeting, American Heart Association Scientific Sessions and European Society of Cardiology Congress, American Hypertension Society, World Hypertension Congress) from the past 10 years, and the reference lists of potentially relevant studies were searched manually.

Studies were included if they met the following criteria: (1) prospective cohort studies and participants ≥18 years; (2) BP and other cardiovascular risk factors evaluated at baseline; (3) follow-up duration ≥2 years and with assessment of cardiovascular mortality, or all-cause mortality; (4) reported the

Figure 1



Flow of articles through review.

multivariate-adjusted relative risks (RRs) and 95% CIs for events associated with prehypertension (BP 120-139/80-89 mm Hg) vs reference (optimal BP, BP < 120/80 mm Hg), or reported RRs and 95% CIs for low-range (BP 120-129/80-84 mm Hg) and high-range prehypertension (BP 130-139/85-89 mm Hg) vs reference, respectively.

Studies were excluded if (1) enrollment depended on having a particular condition or risk factor, such as diabetes mellitus or chronic kidney disease; (2) the RR was adjusted only for age and sex; and (3) data were derived from the same cohort or from a secondary analysis or combined analysis of other cohort studies.

If duplicate studies were from the same cohort and offered the same outcome messages, only the latest published study was included.

Data extraction and quality assessment

Two investigators (Y.H. and S.W.) independently used the search strategy described earlier to identify and screen potentially relevant articles. Full articles of potentially relevant studies were reviewed by predefined eligibility criteria.

The quality of each study was evaluated following the guidelines developed by the US Preventive Task Force and a modified checklist,[12-14] which assessed the following: (1) designation of prospective study; (2) maintenance of comparable groups; (3) adequate adjustment of potential confounders (at least 5 of 6 factors: age, sex, diabetes mellitus, body mass index or other measure of overweight/obesity, cholesterol, and smoking); (4) documented follow-up rate; (5) outcome assessed blind to the baseline status; (6) clear definition of exposures and outcomes; (7) temporality (BP measured at baseline, not at the time of outcomes assessment); and (8) a follow-up of at least 2 years. Quality of studies was graded as good, fair, or poor, if they met 7 to 8, 4 to 6, or <4 criteria, respectively.

Data synthesis and analysis

The primary outcomes were the risk of all-cause and CVD mortality; secondary outcomes were the risks of CHD and stroke

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