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Pharmacotherapy for hypertension in women of different races (Review)

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[Intervention Review]

Pharmacotherapy for hypertension in women of different races

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ABSTRACT

Background

Although hypertension treatment in women is recommended to decrease the risk of cardiovascular disease (Wenger 1993, Kaplan 1995, Kuhn 1993, Hayes 1998, JNCVI,1997), the evidence for treatment benefit is primarily based on combined results for men and women (Collins 1990, Insua 1994, Mulrow 1994, Psaty 1997).

Objectives

To assess whether the relative and absolute benefit of hypertension treatment in women varies with age or race.

Search methods

Literature search of studies from 1966 to 1998 using MEDLINE, reviews, and consultation with experts.

Selection criteria

Studies were eligible if they were randomized controlled trials of pharmacological treatment of primary hypertension, with cardiovascular morbidity and mortality outcomes, and with over one hundred women enrolled.

Data collection and analysis

The pooled population included 23,000 women. Relative risks were combined for each endpoint to form summary risk ratios (RR) using meta-analytic techniques based on a random-effects model. Summary RR's were converted to numbers needed to treat (NNT). Data were dichotomized by age to approximate menopausal status (30 to 54 years, and 55 years and older), and by race (white and African American).

Main results

In women ages 55 years or older (90% white), hypertension treatment results in a 38% risk reduction in fatal and nonfatal cerebrovascular events (95% confidence interval (CI) 27-47%, 5 year NNT 78), a 25% reduction in fatal and nonfatal cardiovascular events (95% CI 17-33%, 5 year NNT 58), and a 17% reduction in cardiovascular mortality (95% CI 3-29%, 5 year NNT 282). In women ages 30 to 54 years (79% white), hypertension treatment results in a 41% risk reduction in fatal and nonfatal cerebrovascular events (95% CI

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8-63%, 5 year NNT 264), and a 27% risk reduction in fatal and nonfatal cardiovascular events (95% CI 4-44%, 5 year NNT 259). Hypertension treatment in African American women (mean age 52 years) reduced the risk of fatal and nonfatal cerebrovascular events by 53% (95% CI 29-69%, 5 year NNT 39), fatal and nonfatal cardiovascular events by 45% (95% CI 18-63%, 5 year NNT 21), fatal and nonfatal coronary events by 33% (95% CI 6-52%, 5 year NNT 48), and all cause mortality by 34% (95% CI 14-49%, 5 year NNT 32). Analyses in white women 30 to 54 years old did not show any statistically significant treatment benefit or harm.

Authors' conclusions

Hypertension treatment lowers the relative and absolute risk of cardiovascular morbidity and mortality in women ages 55 years and older, and in African American women of all ages. A greater effort should be made to increase awareness and treatment in these groups of women. Although relative risk reductions for cerebrovascular and cardiovascular events are similar for younger and older women, the NNT of younger women is at least 4 times higher. Decisions for treatment of hypertension in younger white women should be influenced by the individual patient's absolute risk of cardiovascular disease.

PLAIN LANGUAGE SUMMARY

Treating hypertension greatly reduces the risk of serious health problems such as heart disease or stroke in African American women and in older women

Hypertension (high blood pressure) is a risk factor for heart disease and stroke. Several treatments exist, including many drugs, to try to lower blood pressure and reduce the risk of serious health problems. Hypertension is a significant risk for heart disease in women, and certain groups such as African American women or older women (over 55 years) are more likely to suffer from hypertension. The review found that treating women for hypertension greatly reduced the risk of heart disease and stroke in older women and in African American women of all ages. Treating hypertension in these women is therefore important.

BACKGROUND

Although hypertension treatment in women is recommended to decrease the risk of cardiovascular disease (Wenger 1993, Kaplan 1995, Kuhn 1993, Hayes 1998, JNCVI,1997). The evidence for treatment benefit is primarily based on combined results for men and women (Collins 1990, Insua 1994, Mulrow 1994, Psaty 1997). Recently the INDANA group assessed the benefit of hypertension treatment in women by pooling data for women participants from seven randomized controlled trials(Gueyffier 1997). Results showed a significant 29% risk reduction in fatal cerebrovascular events, 38% risk reduction for non-fatal and fatal cerebrovascular events, and 26% risk reduction for cardiovascular events in women the magnitude of the risk reduction was similar to that in men, although hypertension treatment in men also significantly decreased fatal and non-fatal coronary events and total mortality.

Although the INDANA study is the most complete quantitative review of hypertension treatment in women to date, data confirming a significant clinical benefit in younger women are lacking (Anastos 1991, Schnall 1984, Hayes 1998). Subgroup analyses according to gender in the Medical Research Council (MRC 1985, MRC) and Hypertension Detection and Follow-up Program (HDFP) trials, both with a mean population age of 51 years, suggest an increase in total mortality ranging from 2.5% to 26% among women treated for hypertension. In contrast, a subgroup analysis of men in the same trials shows significant risk reduction in mortality and cerebrovascular events(HDFP). Although these subgroup analyses in younger women have inadequate statistical power to allow a meaningful conclusion, the lack of a clear treatment benefit and the possibility of harm raise the question of whether treating hypertension in a low cardiovascular risk group, such as young women, is clinically beneficial.

Subgroup analyses of African American women from individual studies show a trend towards benefit with hypertension treatment, but the statistical significance of the analyses were not published (HDFP, Shep). Data from randomized studies have not been pooled to determine a more stable risk estimate in African American women treated for hypertension. Yet, the magnitude of treatment benefit is an important clinical issue since hypertension is a major health problem in African American women. The prevalence of hypertension in African American women (23%) is nearly double that of white women (12%) (Burt 1995). The higher prevalence and earlier onset of hypertension in African American

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women contribute to a more severe course and a higher incidence of cardiovascular morbidity and mortality at younger ages, including higher rates of stroke mortality, coronary disease mortality, and end-stage renal disease, compared to non-hypertensives (Croog 1990, Saunders 1985, Sixth report 1997).

OBJECTIVES

We used meta-analytic techniques to combine data from randomized controlled trials to determine whether the benefit of treating hypertension in women differed significantly between younger versus older women, and between white versus African American women. We also calculated the number needed to treat (NNT) according to age and race to assess the absolute clinical benefit of treating hypertension in these subgroups of women.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled studies

Types of participants

The population included greater than 100 women with essential hypertension. Hypertension was defined as diastolic > 89 mm Hg, systolic > 139 mm Hg or isolated systolic > 159 mm Hg with < 90 mm Hg diastolic

Types of interventions

An intervention group received treatment with either a single or multiple pharmacologic agents, and a control group received either placebo or standard of care,

Types of outcome measures

To be included, we required individual patient endpoints to be available according to gender and/or race. Study outcomes were defined similarly to previous hypertension meta-analyses 8, 10 according to cardiovascular morbidity and mortality events: 1) fatal cerebrovascular events, 2) combined fatal and non-fatal cerebrovascular events, excluding transient ischemic attacks 3) fatal coronary events, defined as either myocardial infarction or sudden cardiac death, 4) combined fatal coronary events and non-fatal myocardial infarctions, 5) combined fatal cardiovascular events, including category one and three above and fatal pulmonary embolus and ruptured aortic aneurysm, 6) combined fatal and non-fatal cardiovascular events (non-fatal cerebrovascular accidents and non-fatal myocardial infarctions), and 7) death from any cause. A cerebrovascular event was defined as a persistent neurologic deficit lasting 24 hours or more with or without verification by radiological imaging, and myocardial infarction was defined as persistent ischemic electrocardiogram changes, or verified enzyme elevation.

Search methods for identification of studies

We performed a literature search of studies published between 1966 and September, 1998 using the MEDLINE computer database and the following MESH terms: HYPERTENSION, WOMEN, and MORTALITY or STROKE, and RANDOMIZED CONTROLLED TRIAL and ENGLISH. Additional studies were identified from review articles and consultation with experts. In the case of multiple publications from a single study, we used the most recent publication.

Through our MEDLINE search, we retrieved 270 articles. Seven more articles (Australian, Helgeland 1980, Kuramoto 1981, Wolff 1966, VA115-129, VA90-114, VAfeasibility) were found from references in review articles. Of the 277 eligible articles, forty-four articles were multiple publications from the same studies. The other major reasons for study exclusion are shown in Table 1. Thirty-four randomized controlled studies of treatment for essential hypertension were identified. After applying inclusion criteria, only eleven studies remained eligible (MRC 1985, HDFP, Shep, MRC 1985, older 1992, Perry 1989, Casiglia 1994, Staessen 1997, Australian, Amery 1985, Coope 1986, Dahlof 1991). Of the twenty-three other studies, seven studies included no women, (Helgeland 1980, Veterans 1967, Veterans 1970, VA-NHLBI 1978, Wikstrand 1998, Wilhelmsen 1987, MRFIT) and five studies included fewer than 100 women (Kuramoto 1981, Wolff 1966, Smith 1977, Barraclough, Sprackling 1981) The other eleven randomized controlled trials with cardiovascular outcomes were not included because studies are currently ongoing, (Davis 1996, Malacco 1994, Dahlof 1991, Wing 1997, Lindholm 1996) data were unattainable from primary authors, (Neaton 1993) or two treatment groups were compared, rather than comparing a treatment group to placebo or usual care (Hannson 1994, BBB, IPPPSH, Hansson 1998, HOT, Estacio 1998, Tatti 1998).

Table 1: Reasons for Exclusion of Studies

Primary Reason for Exclusion	Number of Reports
Not a randomized controlled trial	18
No women included	7
Fewer than 100 women in study	5
Not essential hypertension	91
No pharmacological intervention/no control	29
No cardiovascular morbidity or mortality outcomes	66
Data still in collection phase	5
No data available by gender and age	1

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(Multiple 1982) publications 44
Total 266

Data collection and analysis

We performed a literature search of studies published between 1966 and September, 1998 using the MEDLINE computer database and the following MESH terms: HYPERTENSION, WOMEN, and MORTALITY or STROKE, and RANDOMIZED CONTROLLED TRIAL and ENGLISH. Additional studies were identified from review articles and consultation with experts. In the case of multiple publications from a single study, we used the most recent publication.

Retrieved articles were selected if they met all of the following criteria: 1) the study was a randomized controlled trial, 2) the population included greater than 100 women with essential hypertension, 3) hypertension was defined as diastolic > 89 mm Hg, systolic > 139 mm Hg or isolated systolic > 159 mm Hg with < 90 mm Hg diastolic, 4) an intervention group received treatment with either a single or multiple pharmacologic agents, 5) a control group received either placebo or standard of care, 6) individual patient endpoints were available according to gender and/or race, and 7) study outcomes included cardiovascular morbidity and mortality outcomes.

Study outcomes were defined similarly to previous hypertension meta-analyses 8, 10 according to cardiovascular morbidity and mortality events: 1) fatal cerebrovascular events, 2) combined fatal and non-fatal cerebrovascular events, excluding transient ischemic attacks 3) fatal coronary events, defined as either myocardial infarction or sudden cardiac death, 4) combined fatal coronary events and non-fatal myocardial infarctions, 5) combined fatal cardiovascular events, including category one and three above and fatal pulmonary embolus and ruptured aortic aneurysm, 6) combined fatal and non-fatal cardiovascular events (non-fatal cerebrovascular accidents and non-fatal myocardial infarctions), and 7) death from any cause. A cerebrovascular event was defined as a persistent neurologic deficit lasting 24 hours or more with or without verification by radiological imaging, and myocardial infarction was defined as persistent ischemic electrocardiogram changes, or verified enzyme elevation. The definition of major outcomes of cardiovascular morbidity and mortality were similar for each study, except for the Australian Study (Australian), 21 which reported three non-fatal outcomes that differed from the other trials (transient ischemic attacks, congestive heart failure, and evidence of hypertensive end-organ damage) and the HDPF 14 (HDFP) which measured all cause mortality as a primary outcome, and assessed cause-specific outcomes according to coding on death certificates and retrospective patient interviews. Only fatal endpoints from the Australian Study (Australian) (cerebrovascular events, coronary events, and cardiovascular mortality) were incorporated into the meta-analysis. For HDPF (HDFP), all results were incorporated into the meta-analysis.

Study eligibility was assessed by two reviewers according to an abstraction form designed prior to the literature search. Results for women participants in studies were available from publications, (MRC 1985, MRC 1985, older, 1992) primary authors, (Perry 1989, Casiglia 1994, Staessen 1997) and from the INDANA hypertension database, (Gueyffier 1997) which had independently collected individual patient outcome data from two of the published studies, (MRC 1985, MRC 1985, older 1992) as well as six other eligible studies. (HDFP,Shep, Australian, Amery 1985, Coope 1986, Dahlof 1991) Only five studies clearly specified the race of individual patients (HDFP, Perry 1989, Casiglia 1994, Shep, Staessen 1997). All women in the Castel and Syst-Eur studies (CASTEL, Syst-eur) were white (personal communication). (Casiglia 1994, Staessen 1997, Sixth report 1997) other three studies are from the United States, and have only two race categories, "white" and "black". The other six studies did not designate race, but were conducted in geographic areas of Caucasian predominance. Thus, the race subgroups in our review will be designated as African American and "white," the latter of which encompasses patients of any other unspecified race included in the studies.

Data Synthesis

Analysis of baseline characteristics and multivariate logistic regressions were conducted in collaboration with INDANA. Percentages and means for baseline characteristics were calculated by combining individual patient data from all studies that met inclusion criteria except for SHEP pilot, CASTEL, and Syst-Eur (CASTEL,Syst-eur, Shep Pilot) from which baseline data were not available.

To estimate the benefit of treating hypertension in women, we performed a meta-analysis using a DerSimion Laird (DL) random-effects model. Relative risks were calculated for each study and then combined to calculate summary risk ratios (RR) and 95% confidence intervals (CI) for each cardiovascular outcome. Summary estimates were calculated based on age (30 to 54 years versus 55 years and older) and race (white versus African American) in the same pooled population of women. We dichotomized the data at age 55 because by this age, 90% of women are menopausal, (Stanford 1987, Whelan 1990) after which cardiovascular risk begins to rise (US Dept 1991). A Chi-squared test for homogeneity was performed for all summary estimates. P values less than or equal to 0.1 were considered statistically significant.

Summary risk ratios (RRDL) were converted to numbers needed to treat (NNT) estimates, which is the number of patients who must be treated to prevent one adverse outcome Rajkumar 1996, Sinclair 1994, Cook 1995, McQuay 1997). The NNT was determined by calculating the absolute risk and then calculating the NNT using the following formulas where p'(C) is a pooled estimate for the proportion of events in the control group, and is calculated using the proportion of events in the control group p(C), variance (p(C)), total number of control patients n(C), and weight from individual studies.

Variance(p(C)) =(p(C)*(1- p(C)))/n(C)

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Weight = 1/var (p(C))
p'(C) = sum (w* p(C))/sum(w)
The risk difference, or absolute risk for the pooled estimate is obtained using:
Absolute Risk = p'(C)* (RRDL) - p'(C)
NNT = 1/(Absolute Risk)
We standardized the NNT to 5 years, as most studies had a 5 year follow-up.
Standard NNT = NNT (length of follow-up/standard years)
The pooled length of follow-up was weighted by dividing the sum of patient years from each study by the total number of women in each subgroup. Thus, to standardize to a 5 year NNT, if the pooled length of follow-up was 4.3 years, we multiplied the calculated NNT by (4.3/5).
To test the robustness of our results for younger and older women, we conducted a multivariate analysis using a logistic regression model using pooled data with adjustment for differences in the following baseline characteristics: age, systolic and diastolic hypertension levels, cholesterol level, smoking status, diabetes mellitus, and history of prior myocardial infarction or cerebrovascular accident. A multivariate analysis was also performed to test the robustness of our results according to race adjusting for the above characteristics. P levels were calculated for interactions between age group and treatment in the age analysis and between race and treatment in the race analysis.

RESULTS

Description of studies

Eligible studies are summarized in the section of Included Studies. Studies recruited women from 30 to 98 years old, with the mean age of women across trials ranging from 50.4 to 75 years. Mean follow-up of studies ranged from 2 to 12 years. Each study used a diuretic or beta-blocker as first line therapy, except for the CASTEL study (Casiglia 1994), which allowed clonidine or nifedipine, and the Syst-Eur study (Staessen 1997) which used nitrendipine. Table 3 shows the number of women from each study dichotomized by age and race. There were approximately 8,500 women aged 30 to 54 years, and 17,600 women 55 years and older. When the same pooled group of women are dichotomized by race, there were 23,000 white women, compared to 3,200 African American women.

Risk of bias in included studies

See above under the Methods of the Review section.

Effects of interventions

Table 4 summarizes pooled baseline characteristics of control and treated groups by age and race. Data on baseline characteristics were not available from CASTEL, Syst-eur and SHEP Pilot (CASTEL, Syst-eur, Shep Pilot) studies and information on other cardiovascular risk factors, such as left ventricular hypertrophy or obesity were not collected for all of the studies. Among women 30 to 54 years (79% white) the control group had a slightly higher percentage of smokers than the treated group (33% versus 31%, P = 0.025). Among women 55 years and older (90% white) there were no significant differences in mean age, systolic and diastolic blood pressure, total cholesterol, or prevalence of smoking, diabetes, and history of cerebrovascular accidents or coronary events. When baseline characteristics of the women were examined according to race, white women treated for hypertension had a slightly higher percentage of prior myocardial infarction than the control group (1.7% versus 1.3%, P = 0.02). In comparison to white women, African American women were younger (mean age 52 years), with a higher percentage of smokers, diabetics, and history of prior myocardial infarction or cerebrovascular accident. There were no significant differences in baseline characteristics between the treated and control groups of African American women.
The summary relative risk estimates according to major cardiovascular events are shown according to age in Figures 1 and 2, and according to race in Figures 3 and 4, with vertical lines delineating the 95% CI. All combined results were found to be homogeneous (P value > 0.1). In women aged 30 to 54 years treated for hypertension (N= 8,565), there was a statistically significant reduction in fatal and non-fatal cerebrovascular events (RR 0.59, 95% CI 0.37 to 0.92), and fatal and non-fatal cardiovascular events (RR 0.73, 95% CI 0.56 to 0.96). (Figure 1) There was no significant reduction or increase in coronary morbidity or mortality, cardiovascular mortality, or all cause mortality outcomes with hypertension treatment.
Figure 2 shows the summary estimates for cardiovascular outcomes in women aged 55 years and older (N= 17,604). Hypertension treatment resulted in a significant risk reduction in fatal and non-fatal cerebrovascular accidents (RR 0.62, 95% CI 0.53 to 0.73), and fatal and non-fatal cardiovascular events (RR 0.75, 95% CI 0.67 to 0.83). In addition, women aged 55 years and older treated for hypertension had a risk reduction in fatal cardiovascular events (RR 0.83, 95% CI 0.71 to 0.97) and bordered on significance for all cause mortality (RR 0.89, 95% CI 0.80-1.0). The summary estimates for coronary events were not statistically significant.
Figures 3 and 4 show the summary estimates for cardiovascular outcomes according to race. Summary estimates in white women (N= 22,963) were significant for fatal and non-fatal cerebrovascular events (RR 0.65, 95% CI 0.55-0.77), and fatal and non-fatal cardiovascular events (RR 0.78, 95% CI 0.7-0.86). However, hypertension treatment in white women of all ages did not demonstrate a reduction in coronary morbidity or mortality, cardiovascular mortality, or all cause mortality. In comparison, hypertension

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treatment in African American women (N= 3,206) resulted in substantial risk reduction in fatal and non-fatal cerebrovascular outcomes (RR 0.47, 95% CI 0.31-0.71), fatal and non-fatal coronary events (RR 0.67, 95% CI 0.48-0.94), fatal cardiovascular events (RR 0.65, 95% CI 0.45-0.95), fatal and non-fatal cardiovascular events (RR 0.55, 95% CI 0.37-0.82), and all cause mortality (RR 0.66, 95% CI 0.51-0.86).

When data were analysed for white women aged 30 to 54 years (N= 6,731), there were no statistically significant reductions in cardiovascular morbidity or mortality, although the trends are similar to the results in all women aged 30 to 54 years. For fatal and non-fatal cerebrovascular events, the RR was 0.62 (95%CI 0.24-1.59); for combined fatal and nonfatal coronary events, the RR was 1.4 (95% CI 0.62 -3.16); for combined fatal and non-fatal cardiovascular events, the RR was 0.74 (95% CI 0.51-1.08), and for all cause mortality, the RR was 1.08 (95% CI 0.73-1.58).

The 5 year NNT by age and race are shown in Table 5. In women aged 55 years and older, the 5 year NNT is 78 to prevent a fatal or non-fatal cerebrovascular event compared to 264 women aged 30 to 54 years. For combined fatal and non-fatal cardiovascular events, older women have a 5 year NNT of 58 versus a 259 in women aged 30 to 54 years. In the race analysis, 39 African American women need to be treated to prevent a fatal or non-fatal cerebrovascular events, 48 women for fatal and non-fatal coronary events, 98 women for fatal cardiovascular events, 21 women for fatal and non-fatal cardiovascular events, and 32 women for all cause mortality. For white women, the 5 year NNT for fatal and non-fatal cerebrovascular events is 178 women, and for fatal and non-fatal cardiovascular events, 158 women. NNT's for white women 30 to 54 years old could not be calculated since summary estimates were not statistically significant.

A multivariate pooled analysis adjusting for baseline age, systolic and diastolic blood pressure, cholesterol levels, smoking status, diabetes mellitus, and history of myocardial infarction or cerebrovascular accident yielded odds ratios (Table 6) similar to the summary relative risk estimates shown in Figures 1 to 4. After adjusting for baseline characteristics, there were no significant interactions in the treatment effect between age groups (30 to 54 years versus 55 years and older) for any cardiovascular outcome. In contrast, in the race analysis, after adjustment for baseline characteristics, there was a significant difference between groups. Compared to white women, African American women treated for hypertension had a greater risk reduction in fatal cardiovascular events (p = 0.05), fatal and nonfatal cardiovascular events (P = 0.04), and all cause mortality (p = 0.003).

DISCUSSION

Case-control and cohort studies consistently show that diastolic and isolated systolic hypertension are risk factors for cardiovascular disease in women (Fiebach 1989, Nielsen 1995, Sigurdsson 1984, Perlman 1988). Furthermore, combined data from women in randomized controlled trials show that treating hypertension in women reduces the risk of fatal and non-fatal cerebrovascular and cardiovascular events. (Gueyffier 1997) Our study adds to this body of knowledge by quantitating the treatment benefit in women according to age and race. Our results demonstrate a significant relative risk reduction in cardiovascular outcomes in both younger and older women, and both white and African American women. African American women had the greatest magnitude of relative risk reduction in cardiovascular outcomes. We also found that the greatest absolute benefit occurs in African American women and women 55 years and older. In comparison, younger white women, who have a lower prevalence of cardiovascular disease, have 5 year NNT's 3 to 4 times higher than older women.

Our results affirm that hypertension treatment markedly decreases the risk of cerebrovascular and cardiovascular morbidity and mortality in women 55 years and older. By this age, 90% of women are likely post-menopausal with cardiovascular risk approaching the level of age-matched men ([Stanford 1987, Whelan 1990). Although results combined for both men and women demonstrated a reduction in coronary events, (Insua 1994, Mulrow 1994, Lever 1995, MacMahon 1993), we did not observe a significant coronary risk reduction in older women. Since the confidence intervals for the summary estimate for coronary events are wide, we may have inadequate numbers to provide statistical power to demonstrate a significant reduction in coronary death.

For cerebrovascular and cardiovascular outcomes, our group of older women had similar relative risk reductions but slightly higher 5 year NNT's, compared to other studies in elderly hypertensive men and women. (Mulrow 1994, Lever 1995, MacMahon 1993, Staessen 1997) For instance, in all cardiovascular events, the 5 year NNT was 18 in a meta-analysis of elderly hypertensive men and women (Mulrow 1994) and was 18.5 in the Syst-Eur randomized trial of elderly hypertensives, (Staessen 1997) compared to 58 in our older women. Likewise, for all cerebrovascular events, the 5 year NNT was 43 for elderly men and women (Mulrow 1994) and 34.5 in Syst-Eur, (Staessen 1997) compared to 78 in our older women. The difference in magnitude of benefit may, in part, be due to a lower mean age in our pooled older women (mean age 66 years), (Mulrow 1994) compared to the elderly population in the meta-analysis (mean age 72 years) and in (Syst-eur) (mean age 70.2 years) (Staessen 1997). Besides a lower mean age, our pooled population of older women also had lower rates of comorbidities, such as prior myocardial infarction, cerebrovascular accidents, or diabetes. Comparatively, in the Syst-eur Study (Syst-eur) alone, 30% of the enrolled population had a history of cardiovascular complications, and thus higher baseline risk for a repeat cardiovascular event. Thus, our 5 year NNT numbers are best applied to women in the community with mild hypertension.

Age subgroup analyses from INDANA and (Syst-eur) suggest an upper limit to the mortality treatment benefit for hypertension

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(Gueyffier 1997, Staessen 1997). Both studies did not find a mortality benefit with hypertension treatment in men and women beyond the age of 80. There was, however, significant risk reduction in cardiovascular and cerebrovascular morbidity in both studies. In our group of older women (mean age 66), the relative risk reduction in cardiovascular mortality was statistically significant, and the risk reduction of all cause mortality bordered on statistical significance. Unfortunately, we lacked the power to analyzer results by decade of age to determine a specific age threshold above which hypertension treatment no longer affects mortality.

Our study is the first to combine data from randomized controlled trials to quantitate the benefit of treating hypertension in African American women. Our results show a substantial benefit in African American women treated for hypertension in the outcomes of cerebrovascular events, coronary events, cardiovascular mortality, and all-cause mortality. Despite a mean age of 52 years, African American women in our study have an absolute benefit comparable to elderly men and women with a mean age of 72 years treated for hypertension (Mulrow 1994). Since the treatment benefit appears to extend to both younger and older African American women, we recommend that African American women with hypertension be

treated irrespective of their age.

The treatment benefit stems, in part, from the higher absolute risk for cardiovascular disease in the pooled African American women compared to white women (Table 4). However, even after adjusting for differences in baseline characteristics, African American women treated for hypertension have a statistically significant greater relative risk reduction than white women in cardiovascular and mortality outcomes (Table 6). The reasons for a larger hypertension treatment benefit among African American women are unclear, but may be related to a higher inherent cardiovascular risk even after adjustment for baseline characteristics, a better response to treatment, or both.

Since 85% of the African American women were from the HDFP study (HDFP) alone, the greater treatment benefit may also stem from non-drug interventions afforded to the treatment arm of the HDFP study, such as greater access of care. A unique aspect of the HDFP design was that patients were not randomized to simple treatment and placebo groups, but to "stepped care" (SC) and "referred care" (RC) groups. The SC patients were treated according to a formal plan of "steps" which added medications as necessary to maintain blood pressure control, while the RC group was released to the care of their individual doctors for "usual care" of hypertension treatment. The SC medication plan achieved higher rates of blood pressure control compared to the RC group (68% vs. 44%), possibly due to additional benefits given to the SC group including measures to improve compliance, such as pill counts, shorter appointment waiting times, formal counseling on other cardiovascular risk factors, and subsidized medications, laboratory tests, and transportation. The greater access to care for SC patients also may have improved overall health status and contributed to improved cardiovascular outcomes. On the other hand, since the (HDFP) study had no true placebo group, the true size of the hypertension treatment effect was blunted by the large numbers of RC patients on medication (60% of RC African American women on medication by year 5, with 44% at goal blood pressure) (HDFP). Thus, the treatment benefit with hypertension treatment may even be greater than reported in our study.

Despite similar relative risk reductions in cardiovascular and cerebrovascular outcomes in women 30 to 54 compared to women over 55 years, the 5 year NNT's are 3-4 times higher in the younger women, reflecting their lower cardiovascular risk (Jackson 1993, Alderman 1993, Cook 1995). Undoubtedly, the significant relative risk reductions seen in cerebrovascular and cardiovascular outcomes in women 30 to 54 years are partially driven by the African American women, who comprised 21% of the younger subgroup of women. Unfortunately, there were not enough events in white women aged 30 to 54 years to obtain a stable summary risk estimate. Thus, in treatment of hypertension in younger white women, our results support neither benefit nor harm, as suggested by subgroup analysis of white women in MRC and HDFP (MRC 1985, HDFP) studies. However, a true treatment benefit may have been blunted in younger white women by two factors: the partial treatment of control groups and the low cardiovascular risk status of young women enrolled in the studies. In the MRC (MRC 1985) and Australian Studies (Australian), 10-12% of control patients received medication, and in the HDFP study (HDFP), 64% of RC patients received medication. However, a large absolute benefit from hypertension treatment was observed among older women and African American women, who had similar rates of hypertension treatment in control groups. Thus, the higher NNT's in younger women in our results probably reflect a lower prevalence of cardiovascular disease, not an underestimation of treatment effect from contamination of the control group. Also, the three studies with women under 55 years (MRC 1985, HDFP, Australian) recruited people through community screening and excluded many with significant systemic disease, so the NNT calculated for women aged 30 to 54 years in our study pertains to a relatively healthy population of younger women.

The higher NNT to prevent a cardiovascular event in younger white women results in higher costs per event prevented than treating older women or African American women. In general, $50,000 per year of life gained is considered an accepted cost for a medical intervention. One cost analysis of hypertension treatment based on a meta-analysis of hypertension trials estimates a cost of $229,000 per life-year gained for treating a 40 year old hypertensive woman, compared with a savings of $161,000 to treat a 70 year old woman with hypertension (Johannesson 1993, Johannesson 1993). These cost analyses did not consider race.

Since the data for white women aged 30 to 54 years is not as

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convincing as for older women or African American women, risk stratification of younger white women with hypertension would help to identify the younger women who may benefit most from treatment (Jackson 1993, Kannel 1992, Anderson 1991, Cook 1995). For example, a 40 year old woman with a blood pressure of 160/95 but no other cardiovascular risk factors has less than a 5% chance of a cardiovascular event within 10 years; if she is diabetic with evidence of LVH, her chance increases to 33%. In comparison, a 60 year old woman with a blood pressure of 160/90 has a baseline 20% risk of a cardiovascular event within 10 years; with diabetes, her risk approaches 40% (Anderson 1991). The new Joint National Committee (JNC) VI hypertension guidelines advocate a risk stratification with lifestyle modification for up to a year in those with mild hypertension (<160/<100) and no risk factors or end organ disease.[JNC VI, 1997]

Our study has several limitations. First there were too few events in women for several outcomes, limiting our ability to detect a significant effect. This was most problematic in coronary outcomes and all outcomes in younger white women. Also, evidence of end organ damage, such as LVH, was not included as a study outcome. These subclinical events may be more likely in younger hypertensive women than severe cardiovascular events in the first five years of treatment. Thus, a greater treatment benefit may have been noted in younger women if subclinical events were included as outcomes. We were not able to evaluate the long-term benefit or harm of treating younger women since the follow-up period for most studies ranged from 2.2 to 5 years. The only study with a 12 year follow-up period was in an elderly population. (Casiglia 1994) It is possible that treatment of hypertension in young women would result in decreased risk of cardiovascular events over a longer period of time. Of note, however, hypertension trials in the elderly clearly demonstrate that a significant risk reduction is attainable within a few years with initiation of treatment at older ages. (Sixth report 1997, Australian) and European Working Party Hypertension trial in the Elderly (Amery 1985) both stopped following patients after a nonfatal event, which may result in an underestimation for mortality outcomes. However, the underestimation should equally affect both control and treated populations and consequently should influence only the confidence intervals surrounding the summary estimates, not the summary estimates themselves. We were not able to obtain results according to gender from one eligible study, the Treatment of Mild Hypertension Study (Tomhs) (Neaton 1993). However, the Tomhs trial included only 345 women, who had low event rates and would not likely influence our results. As mentioned, our pooled data for African American women came only from three studies, (HDFP,Shep, Perry 1989) as did the data for women 30 to 54 years old, (MRC 1985, HDFP, Australian) with the majority of data for African American women from HDFP (HDFP) (85%), and the majority of data for younger women from (MRC 1985) (75%). Therefore, our results for African American and younger women are most generalizable to hypertensive women who are similar to the study populations enrolled in (HDFP) and (MRC 1985), respectively.

AUTHORS' CONCLUSIONS

Implications for practice

In conclusion, hypertension treatment greatly decreases the relative and absolute risk of cerebrovascular and cardiovascular outcomes in women 55 years and older and in both younger and older African American women. African American women treated for hypertension also have significant risk reduction in coronary and all cause mortality outcomes. A greater effort should be made to treat hypertension in these groups of women. In contrast, treatment of hypertension in white women aged 30 to 54 years old did not show statistically significant benefit or harm. Decisions for treatment of hypertension in younger white women should be influenced by the individual patient's absolute risk of cardiovascular disease.

Implications for research

Clearly, many other questions remain outside the scope of the present data on women and hypertension. Hopefully future studies will enrol greater numbers of younger and non-white patients in order to further clarify not only the effect of hypertension treatment, but the most effective medication choices for different subgroups, the optimal age to start or stop treatment, treatment effects in patients with specific comorbidities, and patient utility and compliance with treatment options.

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REFERENCES

References to studies included in this review

Australian *{published and unpublished data}*
The Australian therapeutic trial in mild hypertension. Report by the Management Committee. *Lancet* 1980;**1**: 1261–7.

CASTEL *{published and unpublished data}*
Casiglia E, Spolaore P, Mazza A, et al. Effect of two different therapeutic approaches on total and cardiovascular mortality in a cardiovascular study in the elderly. *Jpn Heart J* 1994; **35**:589–600.

Coope *{published and unpublished data}*
Coope J, Warrender TS. Randomised trial of treatment of hypertension in elderly patients in primary care. *Br Med J (Clin Res Ed)* 1986;**293**:1145–51.

EWPHE *{published and unpublished data}*
Amery A, Birkenhager W, Brixko P, et al. Mortality and morbidity results from the European Working Party on High Blood Pressure in the Elderly trial. *Lancet* 1985;**1**: 1349–54.

HDFP *{published and unpublished data}*
Five-year findings of the hypertension detection and follow-up program. I. Reduction in mortality of persons with high blood pressure, including mild hypertension. Hypertension Detection and Follow-up Program Cooperative Group. *Jama* 1979;**242**:2562–71.

MRC *{published and unpublished data}*
MRC trial of treatment of mild hypertension: principal results. Medical Research Council Working Party. *Br Med J (Clin Res Ed)* 1985;**291**:97–104.

MRC elderly *{published and unpublished data}*
Medical Research Council. Medical Research Council trial of treatment of hypertension in older adults: principal results. *BMJ* 1992;**304**:405–12.

Shep *{published and unpublished data}*
Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension. Final results of the Systolic Hypertension in the Elderly Program (SHEP). SHEP Cooperative Research Group [see comments]. *Jama* 1991;**265**:3255–64.

Shep Pilot *{unpublished data only}*
Perry HM, Jr. Smith WM, McDonald RH, et al. Morbidity and mortality in the Systolic Hypertension in the Elderly Program (SHEP) pilot study. *Stroke* 1989;**20**:4–13.

STOP *{published and unpublished data}*
Dahlof B, Lindholm LH, Hansson L, Schersten B, Ekbom T, Wester PO. Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension) [see comments]. *Lancet* 1991;**338**:1281–5.

Syst-eur *{published and unpublished data}*
Staessen JA, Fagard R, Thijs L, et al. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators [see comments]. *Lancet* 1997;**350**:757–64.

References to studies excluded from this review

Barraclough *{published data only}*
Barraclough M, Joy M, MacGregor G, et al. Control of Moderately Raised Blood Pressure: Report of a Co-Operative Randomized, Controlled Trial. *British Medical Journal* 1973;**3**:434–36.

BBB *{published data only}*
Hannson L. The BBB Study: the effect of intensified antihypertensive treatment on the level of blood pressure, side-effects, morbidity and mortality in "well-treated" hypertensive patients. Behandla Blodtryck Battre. *Blood Press* 1994;**3**:248–54.

Estacio *{published data only}*
Estacio RO, Jeffers BW, Hiatt WR, Biggerstaff SL, Gifford N, Schrier RW. The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension [see comments]. *N Engl J Med* 1998;**338**:645–52.

FACET *{published data only}*
Tatti P, Pahor M, Byington RP, et al. Outcome results of the Fosinopril Versus Amlodipine Cardiovascular Events Randomized Trial (FACET) in patients with hypertension and NIDDM [see comments]. *Diabetes Care* 1998;**21**: 597–603.

HAPPHY *{published data only}*
Wilhelmsen L, Berglund G, Elmfeldt D, et al. Beta-blockers versus diuretics in hypertensive men: main results from the HAPPHY trial. *J Hypertens* 1987;**5**:561–72.

HOT *{published data only}*
Hansson L, Zanchetti A, Carruthers SG, et al. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group [see comments]. *Lancet* 1998;**351**: 1755–62.

IPPPSH *{published data only}*
Myocardial infarctions and cerebrovascular accidents in relation to blood pressure control. The IPPPSH

Copyright © 2010 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Collaborative Group. *J Hypertens Suppl* 1985;**3 Suppl 3**: S513–8.

kuramoto *{published data only}*
Kuramoto K, Matsushita S, Kuwajima I, Murakami M. Prospective study on the treatment of mild hypertension in the aged. *Jpn Heart J* 1981;**22**:75–85.

MAPHY *{published data only}*
Wikstrand J, Warnold I, Olsson G, Tuomilehto J, Elmfeldt D, Berglund G. Primary prevention with metoprolol in patients with hypertension. Mortality results from the MAPHY study. *Jama* 1988;**259**:1976–82.

MRFIT *{published data only}*
Multiple risk factor intervention trial. Risk factor changes and mortality results. Multiple Risk Factor Intervention Trial Research Group. *Jama* 1982;**248**:1465–77.

Oslo *{published data only}*
Helgeland A. Treatment of mild hypertension: a five year controlled drug trial. The Oslo study. *Am J Med* 1980;**69**: 725–32.

Smith *{published data only}*
Smith WM. Treatment of mild hypertension: results of a ten-year intervention trial. *Circ Res* 1977;**40**:I98–105.

Sprackling *{published data only}*
Sprackling ME, Mitchell JR, Short AH, Watt G. Blood pressure reduction in elderly: a randomised controlled trial of methyldopa. *Br Med J (Clin Res Ed)* 1981;**283**:1151–3.

TOMHS *{published data only}*
Neaton JD, Grimm RH, Jr. Prineas RJ, et al. Treatment of Mild Hypertension Study. Final results. *Jama* 1993;**270**: 713–24.

VA115-129 *{published data only}*
Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension: results in patients with diastolic blood pressures averaging 115 through 129 mm hg. *JAMA* 1967; **202**:116–122.

VA90-114 *{published data only}*
Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment , II: results in patients with diastolic blood pressures averaging 90 through 114 mm hg. *JAMA* 1970;**213**:1143–1152.

VAfeasibility *{published data only}*
Evaluation of drug treatment in mild hypertension: VA-NHLBI feasibility trial. Plan and preliminary results of a two-year feasibility trial for a multicenter intervention study to evaluate the benefits versus the disadvantages of treating mild hypertension. Prepared for the Veterans Administration-National Heart, Lung, and Blood Institute Study Group for Evaluating Treatment in Mild Hypertension. *Ann N Y Acad Sci* 1978;**304**:267–92.

Wolff *{published data only}*
Wolff FW, Lindeman RD. Effects of treatment in hypertension. Results of a controlled study. *J Chronic Dis* 1966;**19**:227–40.

References to ongoing studies

ALLHAT *{published data only}*
Davis BR, Cutler JA, Gordon DJ, et al. Rationale and design for the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Am J Hypertens* 1996;**9**:342–60.

ANBP2 *{published data only}*
Wing LM, Reid CM, Ryan P, et al. Second Australian National Blood Pressure Study (ANBP2). Australian Comparative Outcome Trial of ACE inhibitor- and diuretic-based treatment of hypertension in the elderly. Management Committee on behalf of the High Blood Pressure Research Council of Australia. *Clin Exp Hypertens* 1997;**19**:779–91.

LIFE *{published data only}*
Dahlof B, Devereux R, de Faire U, et al. The Losartan Intervention For Endpoint reduction (LIFE) in Hypertension study: rationale, design, and methods. The LIFE Study Group. *Am J Hypertens* 1997;**10**:705–13.

SHELL *{published data only}*
Malacco E, Gnemmi AE, Romagnoli A, Coppini A. Systolic hypertension in the elderly: long-term lacidipine treatment. Objective, protocol, and organization. SHELL Study Group. *J Cardiovasc Pharmacol* 1994;**23**(5):S62–6.

STOPhtn2 *{published data only}*
Lindholm LH, Hansson L, Dahlof B, et al. The Swedish Trial in old patients with hypertension-2 (STOP-hypertension-2): a progress report. *Blood Press* 1996;**5**: 300–4.

Additional references

Alderman 1993
Alderman, MH. Blood pressure management: individualized treatment based on absolute risk and the potential for benefit. *Ann Intern Med* 1993;**119**:329–35.

Amery 1985
Amery, A, Birkenhager, W, Brixko, P, Bulpitt, C, Clement, D, Deruyttere, M, De Schaepdryver, A, Dollery, C, Fagard, R, Forette, F, et al. Mortality and morbidity results from the European Working Party on High Blood Pressure in the Elderly trial. *Lancet* 1985;**1**:1349–54.

Anastos 1991
Anastos, K, Charney, P, Charon, RA, Cohen, E, Jones, CY, Marte, C, Swiderski, DM, Wheat, ME, Williams. S. Hypertension in women: what is really known? The Women's Caucus, Working Group on Women's Health of the Society of General Internal Medicine. *Ann Intern Med* 1991;**115**:287–93.

Anderson 1991
Anderson, KM, Wilson, PW, Odell, PM, Kannel. WB. An updated coronary risk profile. A statement for health professionals. *Circulation* 1991;**83**:356–62.

Australian 1980
The Australian therapeutic trial in mild hypertension. Report by the Management Committee. *Lancet* 1980;**1**: 1261–7.

Copyright © 2010 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Burt 1995
Burt, VL, Culter, JA, Higgins, M, Horan, MJ, Labarthe, D, Whelton, P, Brown, C, Roccella. EJ. Trends in the prevalence, awareness, treatment, and control of hypertension in the adult US Population. Data From the Health Examinination Surveys, 1960 to 1991. *Hypertension* 1995;**26**:60–9.

Casiglia 1994
Casiglia, E, Spolaore, P, Mazza, A, Ginocchio, G, Colangeli, G, Onesto, C, Di Menza, G, Pegoraro, L, Ambrosio. GB. Effect of two different therapeutic approaches on total and cardiovascular mortality in a cardiovascular study in the elderly. *Jpn Heart J* 1994;**35**:589–600.

Collins 1990
Collins, R, Peto, R, MacMahon, S, Hebert, P, Fiebach, NH, Eberlein, KA, Godwin, J, Qizilbash, N, Taylor, JO, Hennekens. CH. Blood pressure, stroke, and coronary heart disease. Part 2, Short-term reductions in blood pressure: overview of randomised drug trials in their epidemiological context. *Lancet* 1990;**335**:827–38.

Cook 1995
Cook, RJ, Sackett. DL. The number needed to treat: a clinically useful measure of treatment. *BMJ* 1995;**310**: 452–4.

Coope 1986
Coope, J, Warrender, TS. Randomised trial of treatment of hypertension in elderly patients in primary care. *Br Med J (Clin Res Ed)* 1986;**293**:1145–51.

Croog 1990
Croog, SH, Kong, BW, Levine, S, Weir, MR, Baume, RM, Saunders. E. Hypertensive black men and women. Quality of life and effects of antihypertensive medications. *Arch Intern Med* 1990;**150**:1733–41.

Dahlof 1991
Dahlof, B, Lindholm, LH, Hansson, L, Schersten, B, Ekbom, T, Wester. PO. Morbidity and mortality in the Swedish Trial in Old Patients with Hypertension (STOP-Hypertension)b. *Lancet* 1991;**338**:1281–5.

Dahlof 1997
Dahlof, B, Devereux, R, de Faire, U, Fyhrquist, F, Hedner, T, Ibsen, H, Julius, S, Kjeldsen, S, Kristianson, K, Lederballe-Pedersen, O, Lindholm, LH, Nieminen, MS, Omvik, P, Oparil, S, Wedel. H. The Losartan Intervention For Endpoint reduction (LIFE) in Hypertension study: rationale, design, and methods. The LIFE Study Group. *Am J Hypertens* 1997;**10**:705–13.

Davis 1996
Davis, BR, Cutler, JA, Gordon, DJ, Furberg, CD, Wright, JT, Jr, Cushman, WC, et al. Rationale and design for the Antihypertensive and Lipid Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *Am J Hypertens* 1996;**9**: 342–60.

Estacio 1998
Estacio, RO, Jeffers, BW, Hiatt, WR, Biggerstaff, SL, Gifford, N, Schrier. RW. The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension. *N Engl J Med* 1998;**338**:645–52.

Fiebach 1989
Fiebach, NH, Hebert, PR, Stampfer, MJ, Colditz, GA, Willett, WC, Rosner, B, Speizer, FE, Hennekens. CH. A prospective study of high blood pressure and cardiovascular disease in women. *Am J Epidemiol* 1989;**130**:646–54.

Gueyffier 1995
Gueyffier, F, Boutitie, F, Boissel, JP, Coope, J, Cutler, J, Ekbom, T, Fagard, R, Friedman, L, Perry, HM, Pocock, S, et al. INDANA: a meta-analysis on individual patient data in hypertension. *Therapie* 1995;**50**:353–62.

Gueyffier 1997
Gueyffier, F, Boutitie, F, Boissel, JP, Pocock, S, Coope, J, Cutler, J, Ekbom, T, Fagard, R, Friedman, L, Perry, M, Prineas, R, Schron. E. Effect of antihypertensive drug treatment on cardiovascular outcomes in women and men: a meta-analysis of individual patient data from randomized, controlled trials. *Ann Intern Med* 1997;**126**:761–7.

Gueyffier 1999
Gueyffier, F, Bulpitt, C, Boissel, JP, Schron, E, Ekbom, T, Fagard, R, Casiglia, E, Kerlikowske, K, Coope, J. Antihypertensive drugs in very old people: a subgroup meta-analysis of randomised controlled trials. *Lancet* 1999; **353**(9155):793–96.

Hannson 1994
Hannson, L. The BBB Study: the effect of intensified antihypertensive treatment on the level of blood pressure, side-effects, morbidity and mortality in "well-treated" hypertensive patients. Behandla Blodtryck Battre. *Blood Press* 1994;**3**:248–54.

Hansson 1998
Hansson, L, Zanchetti, A, Carruthers, SG, Dahlof, B, Elmfeldt, D, Julius, S, Menard, J, Rahn, KH, Wedel, H, Westerling. S. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. HOT Study Group. *Lancet* 1998; **351**:1755–62.

Hayes 1998
Hayes, SN, Taler. SJ. Hypertension in women: current understanding of gender differences. *Mayo Clin Proc* 1998; **73**:157–65.

Helgeland 1980
Helgeland, A. Treatment of mild hypertension: a five year controlled drug trial. The Oslo study. *Am J Med* 1980;**69**: 725–32.

Insua 1994
Insua, JT, Sacks, HS, Lau, TS, Lau, J, Reitman, D, Pagano, D, Chalmers. TC. Drug treatment of hypertension in the elderly: a meta-analysis. *Ann Intern Med* 1994;**121**:355–62.

Jackson 1993
Jackson, R, Barham, P, Bills, J, Birch, T, McLennan, L, MacMahon, S, Maling. T. Management of raised blood pressure in New Zealand: a discussion document. *BMJ* 1993;**307**:107–10.

Copyright © 2010 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Johannesson 1993
Johannesson, M, Dahlof, B, Lindholm, LH, Ekbom, T, Hansson, L, Oden, A, Schersten, B, Wester, PO, Jonsson. B. The cost-effectiveness of treating hypertension in elderly people--an analysis of the Swedish Trial in Old Patients with Hypertension (STOP Hypertension). *J Intern Med* 1993; **234**:317–23.

Johannesson 1994
Johannesson, M. The impact of age on the cost-effectiveness of hypertension treatment: an analysis of randomized drug trials. *Med Decis Making* 1994;**14**:236–44.

Kannel 1992
Kannel, WB, Wolf. PA. Pulling it all together: changing the cardiovascular outlook [editorial]. *Am Heart J* 1992;**123**: 264–7.

Kaplan 1995
Kaplan, NM. The treatment of hypertension in women. *Arch Intern Med* 1995;**155**:563–7.

Kuhn 1993
Kuhn, FE, Rackley. CE. Coronary artery disease in women. Risk factors, evaluation, treatment, and prevention. *Arch Intern Med* 1993;**153**:2626–36.

Kuramoto 1981
Kuramoto, K, Matsushita, S, Kuwajima, I, Murakami. M. Prospective study on the treatment of mild hypertension in the aged. *Jpn Heart J* 1981;**22**:75–85.

Lindholm 1996
Lindholm, LH, Hansson, L, Dahlof, B, Ekbom, T, Hedner, T, De Faire, U, Schersten, B, Wester. PO. The Swedish Trial in old patients with hypertension-2 (STOP-hypertension-2): a progress report. *Blood Press* 1996;**5**:300–4.

MacMahon 1993
MacMahon, S, Rodgers. A. The effects of blood pressure reduction in older patients: an overview of five randomized controlled trials in elderly hypertensives. *Clin Exp Hypertens* 1993;**15**:967–78.

Malacco 1994
Malacco, E, Gnemmi, AE, Romagnoli, A, Coppini. A. Systolic hypertension in the elderly: long-term lacidipine treatment. Objective, protocol, and organization. SHELL Study Group. *J Cardiovasc Pharmacol* 1994;**23**(5):S62–6.

McQuay 1997
McQuay, HJ, Moore. RA. Using numerical results from systematic reviews in clinical practice. *Ann Intern Med* 1997;**126**:712–20.

MRC 1985
Medical Research Council Working Party. MRC trial of treatment of mild hypertension: principal results. *Br Med J (Clin Res Ed)* 1985;**291**:97–104.

MRC 1992
Medical Research Council Working Party. Medical Research Council trial of treatment of hypertension in older adults: principal results. *BMJ* 1992;**304**:405–12.

Mulrow 1994
Mulrow, CD, Cornell, JA, Herrera, CR, Kadri, A, Farnett, L, Aguilar. C. Hypertension in the elderly. Implications and generalizability of Randomized Trials. *JAMA* 1994; **272**:1932–8.

Neaton 1993
Neaton, JD, Grimm, RH, Jr, Prineas, RJ, Stamler, J, Grandits, GA, Elmer, PJ, et al. Treatment of Mild Hypertension Study. Final results. *JAMA* 1993;**270**: 713–24.

Nielsen 1995
Nielsen, WB, Vestbo, J, Jensen. GB. Isolated systolic hypertension as a major risk factor for stroke and myocardial infarction and an unexploited source of cardiovascular prevention: a prospective population-based study. *J Hum Hypertens* 1995;**9**:175–80.

Perlman 1988
Perlman, JA, Wolf, PH, Ray, R, Lieberknecht. G. Cardiovascular risk factors, premature heart disease, and all-cause mortality in a cohort of northern California women. *Am J Obstet Gynecol* 1988;**158**:1568–74.

Perry 1989
Perry, HM, Jr, Smith, WM, McDonald, RH, Black, D, Cutler, JA, Furberg, CD, et al. Morbidity and mortality in the Systolic Hypertension in the Elderly Program (SHEP) pilot study. *Stroke* 1989;**20**:4–13.

Psaty 1997
Psaty, BM, Smith, NL, Siscovick, DS, Koepsell, TD, Weiss, NS, Heckbert, SR, Lemaitre, RN, Wagner, EH, Furberg. CD. Health outcomes associated with antihypertensive therapies used as first line agents. *JAMA* 1997;**277**:739–45.

Rajkumar 1996
Rajkumar, SV, Sampathkumar, P, Gustafson. AB. Number needed to treat is a simple measure of treatment efficacy for clinicians. *J Gen Intern Med* 1996;**11**:357–9.

Report 1986
Report of the Task Force on Black and Minority Health. *Cardiovascular and Cerebrovascular Disease, Part 2. US Department of Health and Human Services.* Vol. **IV**, Washington DC: US Government Printing Office, 1986: I–1-I-21.

Schnall 1984
Schnall, PL, Alderman, MH, Kern. R. An analysis of the HDFP trial. Evidence of adverse effects of antihypertensive treatment on white women with moderate and severe hypertension. *N Y State J Med* 1984;**84**:299–301.

Sigurdsson 1984
Sigurdsson, JA, Bengtsson, C, Lapidus, L, Lindquist, O, Rafnsson. V. Morbidity and mortality in relation to blood pressure and antihypertensive treatment. A 12-year follow-up study of a population sample of Swedish women. *Acta Med Scand* 1984;**215**:313–22.

Sinclair 1994
Sinclair, JC, Bracken. MB. Clinically useful measures of effect in binary analyses of randomized trials. *J Clin Epidemiol* 1994;**47**:881–9.

Sixth report 1997
Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. The sixth

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report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Arch Intern Med* 1997;**157**:2413–46.

Smith 1977
Smith, WM. Treatment of mild hypertension: results of a ten-year intervention trial. *Circ Res* 1977;**40**:I98–105.

Sprackling 1981
Sprackling, ME, Mitchell, JR, Short, AH, Watt. G. Blood pressure reduction in elderly: a randomised controlled trial of methyldopa. *Br Med J (Clin Res Ed)* 1981;**283**:1151–3.

Staessen 1997
Staessen, JA, Fagard, R, Thijs, L, Celis, H, Arabidze, GG, Birkenhager, WH, Bulpitt, CJ, de Leeuw, PW, Dollery, CT, Fletcher, AE, Forette, F, Leonetti, G, Nachev, C, ET, OB, Rosenfeld, J, Rodicio, JL, Tuomilehto, J, Zanchetti. A. Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. *Lancet* 1997;**350**:757–64.

Staessen 1998
Staessen, JA, Fagard, R, Thijs, L, Celis, H, Birkenhager, WH, Bulpitt, CJ, et al. Subgroup and per-protocol analysis of the randomized European Trial on Isolated Systolic Hypertension in the Elderly. *Arch Intern Med* 1998;**158**: 1681–91.

Stanford 1987
Stanford, JL, Hartge, P, Brinton, LA, Hoover, RN, Brookmeyer. R. Factors influencing the age at natural menopause. *J Chron Dis* 1987;**40**:995–1002.

Tatti 1998
Tatti, P, Pahor, M, Byington, RP, Di Mauro, P, Guarisco, R, Strollo, G, Strollo. F. Outcome results of the Fosinopril Versus Amlodipine Cardiovascular Events Randomized Trial (FACET) in patients with hypertension and NIDDM. *Diabetes Care* 1998;**21**:597–603.

US Dept 1991
US Department of Commerce, Economics, and Statistics Administration and Bureau of the Census. Vital statistics: statistical abstract of the United States. *Vital statistics: statistical abstract of the United States*. 11th Edition. Washington DC: Government Printing Office, 1991:84.

VA-NHLBI 1978
Evaluation of drug treatment in mild hypertension: VA-NHLBI feasibility trial. Plan and preliminary results of a two-year feasibility trial for a multicenter intervention study to evaluate the benefits versus the disadvantages of treating mild hypertension. Prepared for the Veterans Administration-National Heart, Lung, and Blood Institute Study Group for Evaluating Treatment in Mild Hypertension. *Ann N Y Acad Sci* 1978;**304**:267–92.

Veterans 1967
Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment on morbidity in hypertension: results in patients with diastolic blood pressures averaging 115 through 129 mm hg. *JAMA* 1967; **202**:116–22.

Veterans 1970
Veterans Administration Cooperative Study Group on Antihypertensive Agents. Effects of treatment , II: results in patients with diastolic blood pressures averaging 90 through 114 mm hg. *JAMA* 1970;**213**:1143–52.

Wenger 1993
Wenger, NK, Speroff, L, Packard. B. Cardiovascular health and disease in women. *N Engl J Med* 1993;**329**:247–56.

Whelan 1990
Whelan, EA, Sandler, DP, McConnaughey, DR, Weinberg. CR. Menstrual and reproductive characteristics and age at natural menopause. *Am J Epidemiol* 1990;**131**:625–32.

Wikstrand 1998
Wikstrand, J, Warnold, I, Olsson, G, Tuomilehto, J, Elmfeldt, D, Berglund. G. Primary prevention with metoprolol in patients with hypertension. Mortality results from the MAPHY study. *JAMA* 1988;**259**:1976–82.

Wilhelmsen 1987
Wilhelmsen, L, Berglund, G, Elmfeldt, D, Fitzsimons, T, Holzgreve, H, Hosie, J, Hornkvist, PE, Pennert, K, Tuomilehto, J, Wedel. H. Beta-blockers versus diuretics in hypertensive men: main results from the HAPPHY trial. *J Hypertens* 1987;**5**:561–72.

Wing 1997
Wing, LM, Reid, CM, Ryan, P, Beilin, LJ, Brown, MA, Jennings, GL, et al. Second Australian National Blood Pressure Study (ANBP2). Australian Comparative Outcome Trial of ACE inhibitor- and diuretic-based treatment of hypertension in the elderly. Management Committee on behalf of the High Blood Pressure Research Council of Australia. *Clin Exp Hypertens* 1997;**19**:779–91.

Wolff 1966
Wolff, FW, Lindeman. RD. Effects of treatment in hypertension. Results of a controlled study. *J Chronic Dis* 1966;**19**:227–40.

References to other published versions of this review

Saunders 1985
Saunders, E, Shulman NB, Ed. *Hypertension in Blacks: Epidemiology, Pathophysiology and Treatment.*. Chicago: Ill: Year Book Medical Publishers, 1985:17–36.

* *Indicates the major publication for the study*

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CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Australian

Methods	RCT	
Participants	community, primary htn 1456 white women mean age 50.4	
Interventions	Chlorothiazide vs placebo	
Outcomes	CV M&M	
Notes	2.9 yrs f/u	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	A - Adequate

CASTEL

Methods	RCT	
Participants	424 white women mean age 74 yrs	
Interventions	clonidine or nifedipine vs placebo	
Outcomes	CV m&m	
Notes	12 yrs f/u	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

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Coope

Methods	RCT	
Participants	611 women mean age 68 yrs	
Interventions	atenolol vs placebo	
Outcomes	CV m&m	
Notes	4.5 yr f/u	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

EWPHE

Methods	RCT	
Participants	community, primary htn 586 women mean age 72 yrs	
Interventions	HCTZ/triamterene (maxide) vs placebo	
Outcomes	CV M&M	
Notes	4.6 yrs f/u	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

HDFP

Methods	RCT of Stepped care vs Usual care
Participants	5030 total women 2726 black women mean age 52.3
Interventions	Chlorthalidone first step vs usual care in community, htn rx allowed

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HDFP (*Continued*)

Outcomes	primary:all cause mortality secondary other cv M&M	
Notes	F/u 4.9 yrs	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

MRC

Methods	RCT	
Participants	primary htn, community centers N women 8306, mean age 51 yrs	
Interventions	bendrufluazide or propranolol vs placebo	
Outcomes	CV M&M	
Notes	5 yrs f/u	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

MRC elderly

Methods	RCT,
Participants	British, community centers, primary htn 2560 white wom mean age 70 yrs
Interventions	Hctz/amiloride or atenolol vs placebo
Outcomes	CV mortality and morbidity
Notes	f/u 5.9 yrs
Risk of bias	

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MRC elderly (*Continued*)

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Shep

Methods	RCT
Participants	1019 women total 444 African American women mean age 75 years
Interventions	chlortalidone vs placebo
Outcomes	CV m&m
Notes	4.4 yrs f/u

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

Shep Pilot

Methods	RCT
Participants	349 women total African American women n = 67 mean age 72 yrs
Interventions	chlorthalidone vs placebo
Outcomes	CV m&m
Notes	f/u 2.8 yrs

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	D - Not used

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STOP

Methods	RCT	
Participants	1019 women mean age 72	
Interventions	hctz/amiloride, metoprolol, pindolol, or atenolol	
Outcomes	CV m&m	
Notes	f/u 2.2 yrs	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Syst-eur

Methods	RCT	
Participants	3138 women mean age 70.5 yrs	
Interventions	nitrendipine vs placebo	
Outcomes	CV m&m	
Notes	2 yrs f/u	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	D - Not used

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Barraclough	Fewer than 100 women included
BBB	Compared two treatment groups, no placebo or usual care
Estacio	Compared two treatment groups, nisoldipine vs enalapril in NIDDM and htn, no placebo or usual care

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(*Continued*)

FACET	Compared two treatment groups, fosinopril vs amlodipine in NIDDM and htn, no placebo or usual care
HAPPHY	No women included
HOT	Compared two treatment groups, no placebo or usual care
IPPPSH	Compared two treatment groups, no placebo or usual care
kuramoto	Fewer than 100 women included
MAPHY	No women included
MRFIT	No women included
Oslo	No women included
Smith	Fewer than 100 women included
Sprackling	Fewer than 100 women included
TOMHS	Contacted authors, declined to contribute data on women (JDN, RHG)
VA115-129	No women included
VA90-114	No women included
VAfeasibility	No women included
Wolff	Fewer than 100 women included

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DATA AND ANALYSES

Comparison 1. Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Fatal Cerebrovascular Events	3	8558	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.51 [0.24, 1.08]
2 Fatal and Non-Fatal Cerebrovascular Accidents	3	8269	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.59 [0.38, 0.91]
3 Fatal Coronary Heart Disease	3	8565	Peto Odds Ratio (Peto, Fixed, 95% CI)	1.38 [0.77, 2.48]
4 Fatal and Nonfatal Coronary Heart Disease	3	8304	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.80 [0.56, 1.14]
5 Fatal Cardiovascular Events	3	8565	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.93 [0.61, 1.43]
6 Fatal and Nonfatal Cardiovascular Events	3	8317	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.72 [0.55, 0.95]
7 All Cause Mortality	3	8565	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.91 [0.68, 1.22]

Comparison 2. Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Fatal Cerebrovascular Events	11	17604	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.75 [0.56, 1.00]
2 Fatal and Non-Fatal Cerebrovascular Accidents	11	17328	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.61 [0.52, 0.72]
3 Fatal Coronary Heart Disease	11	17604	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.82 [0.66, 1.02]
4 Fatal and Nonfatal Coronary Heart Disease	11	17344	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.85 [0.72, 1.00]
5 Fatal Cardiovascular Events	11	17604	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.81 [0.69, 0.94]
6 Fatal and Nonfatal Cardiovascular Events	11	17402	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.72 [0.64, 0.80]
7 All Cause Mortality	11	17604	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.89 [0.79, 1.00]

Comparison 3. White Women: Hypertension Treatment versus Placebo or Usual Care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Fatal Cerebrovascular Events	11	22937	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.75 [0.56, 1.00]
2 Fatal and Non-Fatal Cerebrovascular Accidents	11	22673	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.64 [0.54, 0.75]
3 Fatal Coronary Heart Disease	11	22963	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.89 [0.72, 1.11]

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4 Fatal and Nonfatal Coronary Heart Disease	11	22707	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.89 [0.76, 1.05]
5 Fatal Cardiovascular Events	11	22963	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.86 [0.74, 1.01]
6 Fatal and Nonfatal Cardiovascular Events	11	22580	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.75 [0.67, 0.84]
7 All Cause Mortality	11	22963	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.95 [0.85, 1.07]

Comparison 4. African American Women: Hypertension Treatment versus Placebo or Usual Care

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Fatal Cerebrovascular Events	3	3206	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.55 [0.27, 1.11]
2 Fatal and Non-Fatal Cerebrovascular Accidents	3	2924	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.47 [0.31, 0.70]
3 Fatal Coronary Heart Disease	3	3206	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.79 [0.46, 1.33]
4 Fatal and Nonfatal Coronary Heart Disease	3	2947	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.66 [0.47, 0.93]
5 Fatal Cardiovascular Events	3	3206	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.66 [0.46, 0.96]
6 Fatal and Nonfatal Cardiovascular Events	3	2973	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.58 [0.44, 0.76]
7 All Cause Mortality	3	3206	Peto Odds Ratio (Peto, Fixed, 95% CI)	0.65 [0.49, 0.85]

Analysis 1.1. Comparison 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care, Outcome 1 Fatal Cerebrovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care

Outcome: 1 Fatal Cerebrovascular Events

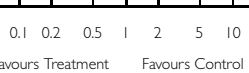
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	1/445	2/416		11.1 %	0.48 [0.05, 4.62]
HDFP	2/1540	7/1561		33.3 %	0.33 [0.09, 1.23]
MRC	6/2319	9/2277		55.5 %	0.66 [0.24, 1.81]
Total (95% CI)	**4304**	**4254**		**100.0 %**	**0.51 [0.24, 1.08]**

Total events: 9 (Treatment), 18 (Control)

Heterogeneity: $Chi^2 = 0.65$, df = 2 (P = 0.72); $I^2 = 0.0\%$

Test for overall effect: Z = 1.77 (P = 0.077)

Test for subgroup differences: Not applicable



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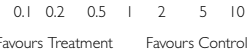
Analysis 1.2. Comparison 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care, Outcome 2 Fatal and Non-Fatal Cerebrovascular Accidents.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care

Outcome: 2 Fatal and Non-Fatal Cerebrovascular Accidents

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	1/445	2/416		3.8 %	0.48 [0.05, 4.62]
HDFP	20/1422	32/1390		64.7 %	0.61 [0.35, 1.06]
MRC	9/2319	16/2277		31.5 %	0.56 [0.25, 1.23]
Total (95% CI)	**4186**	**4083**		**100.0 %**	**0.59 [0.38, 0.91]**
Total events: 30 (Treatment), 50 (Control)					
Heterogeneity: Chi^2 = 0.07, df = 2 (P = 0.97); I^2 =0.0%					
Test for overall effect: Z = 2.36 (P = 0.019)					
Test for subgroup differences: Not applicable					



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Analysis 1.3. Comparison 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care, Outcome 3 Fatal Coronary Heart Disease.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care

Outcome: 3 Fatal Coronary Heart Disease

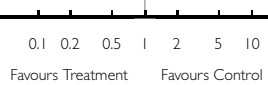
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	0/445	0/416			Not estimable
HDFP	19/1540	15/1568		75.4 %	1.29 [0.66, 2.54]
MRC	7/2319	4/2277		24.6 %	1.70 [0.52, 5.54]
Total (95% CI)	**4304**	**4261**		**100.0 %**	**1.38 [0.77, 2.48]**

Total events: 26 (Treatment), 19 (Control)

Heterogeneity: $Chi^2 = 0.15$, df = 1 (P = 0.70); $I^2 = 0.0\%$

Test for overall effect: Z = 1.08 (P = 0.28)

Test for subgroup differences: Not applicable



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Analysis 1.4. Comparison 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care, Outcome 4 Fatal and Nonfatal Coronary Heart Disease.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care

Outcome: 4 Fatal and Nonfatal Coronary Heart Disease

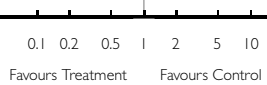
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	0/445	0/416			Not estimable
HDFP	43/1443	59/1404		80.5 %	0.70 [0.47, 1.04]
MRC	14/2319	10/2277		19.5 %	1.37 [0.62, 3.06]
Total (95% CI)	**4207**	**4097**		**100.0 %**	**0.80 [0.56, 1.14]**

Total events: 57 (Treatment), 69 (Control)

Heterogeneity: $Chi^2 = 2.16$, df = 1 (P = 0.14); $I^2 = 54\%$

Test for overall effect: Z = 1.23 (P = 0.22)

Test for subgroup differences: Not applicable



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Analysis 1.5. Comparison 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care, Outcome 5 Fatal Cardiovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care

Outcome: 5 Fatal Cardiovascular Events

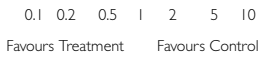
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	1/445	2/416		3.6 %	0.48 [0.05, 4.62]
HDFP	27/1540	28/1568		64.4 %	0.98 [0.58, 1.67]
MRC	13/2319	14/2277		32.0 %	0.91 [0.43, 1.94]
Total (95% CI)	**4304**	**4261**		**100.0 %**	**0.93 [0.61, 1.43]**

Total events: 41 (Treatment), 44 (Control)

Heterogeneity: $Chi^2 = 0.37$, df = 2 (P = 0.83); $I^2 = 0.0\%$

Test for overall effect: Z = 0.31 (P = 0.76)

Test for subgroup differences: Not applicable



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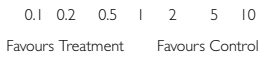
Analysis 1.6. Comparison 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care, Outcome 6 Fatal and Nonfatal Cardiovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care

Outcome: 6 Fatal and Nonfatal Cardiovascular Events

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	1/445	2/416		1.5 %	0.48 [0.05, 4.62]
HDFP	66/1447	92/1413		74.4 %	0.69 [0.50, 0.95]
MRC	23/2319	26/2277		24.1 %	0.87 [0.49, 1.52]
Total (95% CI)	**4211**	**4106**		**100.0 %**	**0.72 [0.55, 0.95]**
Total events: 90 (Treatment), 120 (Control)					
Heterogeneity: Chi^2 = 0.62, df = 2 (P = 0.73); I^2 =0.0%					
Test for overall effect: Z = 2.29 (P = 0.022)					
Test for subgroup differences: Not applicable					



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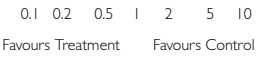
Analysis 1.7. Comparison 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care, Outcome 7 All Cause Mortality.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 1 Women ages 30-54 years: Hypertension Treatment versus Placebo or Usual Care

Outcome: 7 All Cause Mortality

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	1/445	2/416		1.7 %	0.48 [0.05, 4.62]
HDFP	49/1540	66/1568		61.6 %	0.75 [0.52, 1.09]
MRC	38/2319	29/2277		36.7 %	1.29 [0.80, 2.09]
Total (95% CI)	**4304**	**4261**		**100.0 %**	**0.91 [0.68, 1.22]**
Total events: 88 (Treatment), 97 (Control)					
Heterogeneity: Chi^2 = 3.35, df = 2 (P = 0.19); I^2 =40%					
Test for overall effect: Z = 0.65 (P = 0.52)					
Test for subgroup differences: Not applicable					



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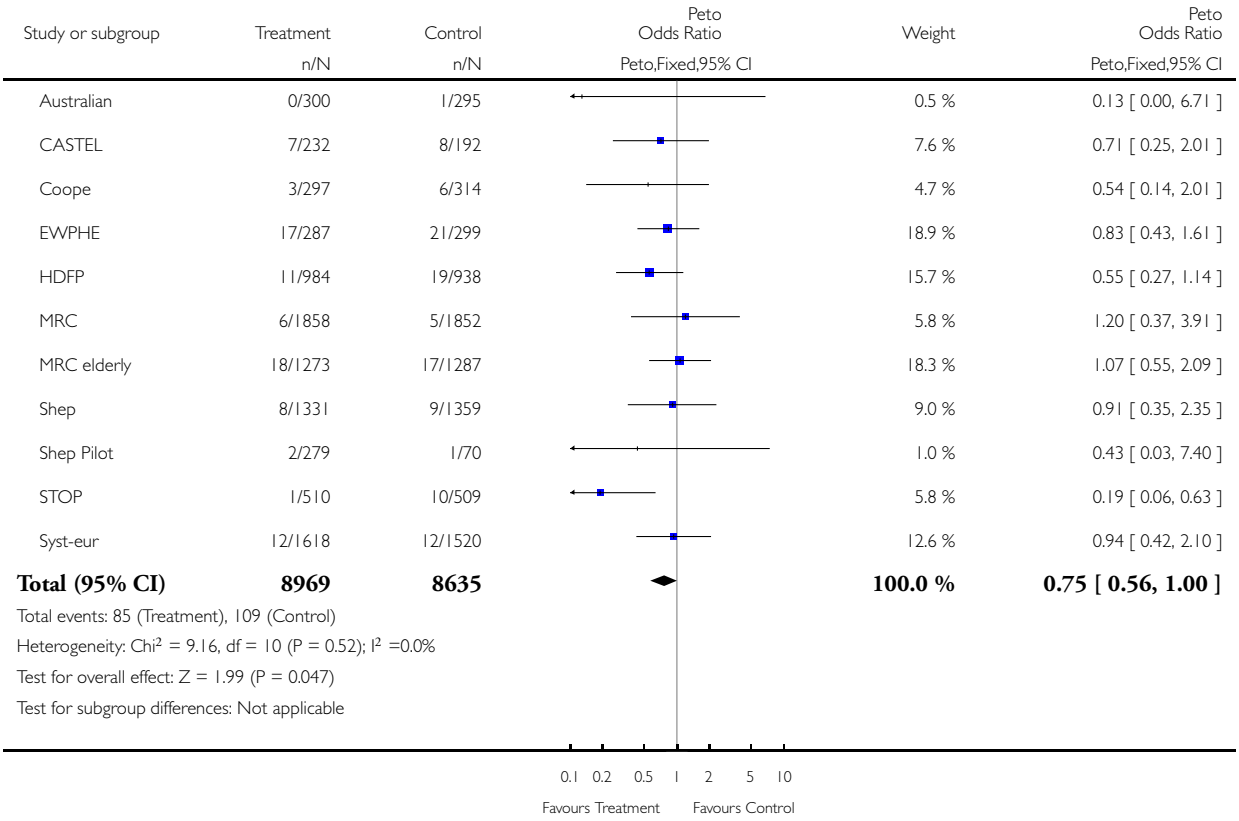
Analysis 2.1. Comparison 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care, Outcome 1 Fatal Cerebrovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care

Outcome: 1 Fatal Cerebrovascular Events



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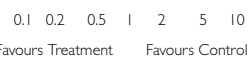
Analysis 2.2. Comparison 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care, Outcome 2 Fatal and Non-Fatal Cerebrovascular Accidents.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care

Outcome: 2 Fatal and Non-Fatal Cerebrovascular Accidents

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	0/300	1/295		0.2 %	0.13 [0.00, 6.71]
CASTEL	9/232	13/192		3.6 %	0.56 [0.24, 1.32]
Coope	13/297	19/314		5.3 %	0.71 [0.35, 1.45]
EWPHE	23/287	30/299		8.5 %	0.78 [0.45, 1.38]
HDFP	23/871	37/775		10.1 %	0.54 [0.33, 0.91]
MRC	14/1858	28/1852		7.3 %	0.51 [0.28, 0.93]
MRC elderly	46/1273	63/1287		18.3 %	0.73 [0.50, 1.07]
Shep	55/1331	87/1359		23.6 %	0.64 [0.45, 0.89]
Shep Pilot	6/279	5/70		1.2 %	0.20 [0.04, 0.88]
STOP	13/510	33/509		7.7 %	0.40 [0.22, 0.73]
Syst-eur	34/1618	50/1520		14.3 %	0.63 [0.41, 0.98]
Total (95% CI)	**8856**	**8472**		**100.0 %**	**0.61 [0.52, 0.72]**
Total events: 236 (Treatment), 366 (Control)					
Heterogeneity: Chi^2 = 7.15, df = 10 (P = 0.71); I^2 =0.0%					
Test for overall effect: Z = 5.89 (P < 0.00001)					
Test for subgroup differences: Not applicable					



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Analysis 2.3. Comparison 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care, Outcome 3 Fatal Coronary Heart Disease.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care

Outcome: 3 Fatal Coronary Heart Disease

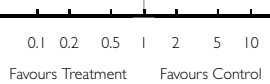
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	0/300	1/295		0.3 %	0.13 [0.00, 6.71]
CASTEL	12/232	15/192		7.5 %	0.64 [0.29, 1.41]
Coope	11/297	10/314		6.1 %	1.17 [0.49, 2.79]
EWPHE	13/287	18/299		8.8 %	0.74 [0.36, 1.53]
HDFP	22/984	24/938		13.5 %	0.87 [0.49, 1.56]
MRC	11/1858	6/1852		5.1 %	1.80 [0.69, 4.67]
MRC elderly	38/1273	40/1287		22.7 %	0.96 [0.61, 1.51]
Shep	22/1331	40/1359		18.2 %	0.56 [0.34, 0.93]
Shep Pilot	11/279	2/70		2.4 %	1.35 [0.34, 5.38]
STOP	6/510	8/509		4.1 %	0.75 [0.26, 2.14]
Syst-eur	17/1618	21/1520		11.3 %	0.76 [0.40, 1.44]
Total (95% CI)	**8969**	**8635**		**100.0 %**	**0.82 [0.66, 1.02]**

Total events: 163 (Treatment), 185 (Control)

Heterogeneity: Chi² = 7.74, df = 10 (P = 0.65); I² =0.0%

Test for overall effect: Z = 1.77 (P = 0.076)

Test for subgroup differences: Not applicable



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Analysis 2.4. Comparison 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care, Outcome 4 Fatal and Nonfatal Coronary Heart Disease.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care

Outcome: 4 Fatal and Nonfatal Coronary Heart Disease

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	0/300	1/295		0.2 %	0.13 [0.00, 6.71]
CASTEL	16/232	19/192		5.5 %	0.67 [0.34, 1.35]
Coope	19/297	16/314		5.7 %	1.27 [0.64, 2.52]
EWPHE	27/287	26/299		8.3 %	1.09 [0.62, 1.92]
HDFP	52/885	54/783		17.0 %	0.84 [0.57, 1.25]
MRC	24/1858	24/1852		8.1 %	1.00 [0.56, 1.76]
MRC elderly	59/1273	59/1287		19.3 %	1.01 [0.70, 1.46]
Shep	42/1329	69/1355		18.2 %	0.61 [0.42, 0.90]
Shep Pilot	15/279	3/70		1.9 %	1.25 [0.38, 4.08]
STOP	12/510	18/509		5.0 %	0.66 [0.32, 1.37]
Syst-eur	30/1618	35/1520		10.9 %	0.80 [0.49, 1.31]
Total (95% CI)	**8868**	**8476**		**100.0 %**	**0.85 [0.72, 1.00]**

Total events: 296 (Treatment), 324 (Control)

Heterogeneity: Chi^2 = 8.26, df = 10 (P = 0.60); I^2 =0.0%

Test for overall effect: Z = 1.94 (P = 0.052)

Test for subgroup differences: Not applicable

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Analysis 2.5. Comparison 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care, Outcome 5 Fatal Cardiovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care

Outcome: 5 Fatal Cardiovascular Events

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	0/300	2/295		0.3 %	0.13 [0.01, 2.13]
CASTEL	38/232	47/192		10.3 %	0.60 [0.37, 0.97]
Coope	19/297	20/314		5.6 %	1.00 [0.53, 1.92]
EWPHE	50/287	63/299		14.0 %	0.79 [0.53, 1.19]
HDFP	42/984	57/938		14.4 %	0.69 [0.46, 1.04]
MRC	17/1858	13/1852		4.6 %	1.30 [0.64, 2.68]
MRC elderly	72/1273	65/1287		19.9 %	1.13 [0.80, 1.59]
Shep	43/1331	62/1359		15.4 %	0.70 [0.47, 1.04]
Shep Pilot	13/279	3/70		1.5 %	1.09 [0.31, 3.80]
STOP	9/510	20/509		4.3 %	0.46 [0.22, 0.96]
Syst-eur	31/1618	34/1520		9.7 %	0.85 [0.52, 1.40]
Total (95% CI)	**8969**	**8635**		**100.0 %**	**0.81 [0.69, 0.94]**

Total events: 334 (Treatment), 386 (Control)

Heterogeneity: Chi^2 = 12.43, df = 10 (P = 0.26); I^2 =20%

Test for overall effect: Z = 2.69 (P = 0.0071)

Test for subgroup differences: Not applicable

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Analysis 2.6. Comparison 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care, Outcome 6 Fatal and Nonfatal Cardiovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care

Outcome: 6 Fatal and Nonfatal Cardiovascular Events

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	0/300	2/295		0.2 %	0.13 [0.01, 2.13]
CASTEL	44/232	56/192		6.4 %	0.57 [0.36, 0.89]
Coope	34/297	39/314		5.4 %	0.91 [0.56, 1.49]
EWPHE	66/287	77/299		9.1 %	0.86 [0.59, 1.26]
HDFP	83/905	103/815		13.9 %	0.70 [0.51, 0.95]
MRC	38/1858	54/1852		7.5 %	0.70 [0.46, 1.06]
MRC elderly	116/1273	127/1287		18.5 %	0.92 [0.70, 1.19]
Shep	100/1331	158/1359		19.6 %	0.62 [0.48, 0.80]
Shep Pilot	21/279	8/70		1.4 %	0.60 [0.23, 1.55]
STOP	26/510	51/509		6.0 %	0.49 [0.31, 0.79]
Syst-eur	66/1618	86/1520		12.1 %	0.71 [0.51, 0.98]
Total (95% CI)	**8890**	**8512**		**100.0 %**	**0.72 [0.64, 0.80]**
Total events: 594 (Treatment), 761 (Control)					
Heterogeneity: Chi^2 = 11.38, df = 10 (P = 0.33); I^2 =12%					
Test for overall effect: Z = 5.78 (P < 0.00001)					
Test for subgroup differences: Not applicable					

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Analysis 2.7. Comparison 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care, Outcome 7 All Cause Mortality.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 2 Women > 55 Years : Hypertension Treatment versus Placebo or Usual Care

Outcome: 7 All Cause Mortality

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	0/300	2/295		0.2 %	0.13 [0.01, 2.13]
CASTEL	55/232	64/192		7.3 %	0.62 [0.41, 0.95]
Coope	32/297	28/314		4.7 %	1.23 [0.72, 2.10]
EWPHE	92/287	104/299		11.2 %	0.88 [0.63, 1.25]
HDFP	78/984	89/938		13.1 %	0.82 [0.60, 1.13]
MRC	53/1858	43/1852		8.1 %	1.23 [0.82, 1.85]
MRC elderly	118/1273	135/1287		19.6 %	0.87 [0.67, 1.13]
Shep	98/1331	120/1359		17.3 %	0.82 [0.62, 1.08]
Shep Pilot	23/279	4/70		1.4 %	1.42 [0.53, 3.79]
STOP	21/510	30/509		4.2 %	0.69 [0.39, 1.21]
Syst-eur	84/1618	75/1520		13.0 %	1.05 [0.77, 1.45]
Total (95% CI)	**8969**	**8635**		**100.0 %**	**0.89 [0.79, 1.00]**

Total events: 654 (Treatment), 694 (Control)

Heterogeneity: Chi^2 = 11.86, df = 10 (P = 0.29); I^2 =16%

Test for overall effect: Z = 1.97 (P = 0.049)

Test for subgroup differences: Not applicable

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Analysis 3.1. Comparison 3 White Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 1 Fatal Cerebrovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 3 White Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 1 Fatal Cerebrovascular Events

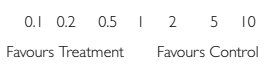
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	1/745	3/711		2.2 %	0.35 [0.05, 2.49]
CASTEL	7/232	8/192		7.8 %	0.71 [0.25, 2.01]
Coope	3/297	6/314		4.8 %	0.54 [0.14, 2.01]
EWPHE	17/287	21/299		19.2 %	0.83 [0.43, 1.61]
HDFP	5/1180	8/1150		7.0 %	0.61 [0.21, 1.82]
MRC	12/4165	14/4115		14.0 %	0.85 [0.39, 1.83]
MRC elderly	18/1273	17/1287		18.7 %	1.07 [0.55, 2.09]
Shep	6/1120	7/1130		7.0 %	0.86 [0.29, 2.57]
Shep Pilot	1/229	1/54		0.7 %	0.13 [0.00, 4.59]
STOP	1/510	10/509		5.9 %	0.19 [0.06, 0.63]
Syst-eur	12/1618	12/1520		12.9 %	0.94 [0.42, 2.10]
Total (95% CI)	**11656**	**11281**		**100.0 %**	**0.75 [0.56, 1.00]**

Total events: 83 (Treatment), 107 (Control)

Heterogeneity: Chi^2 = 8.62, df = 10 (P = 0.57); I^2 =0.0%

Test for overall effect: Z = 1.95 (P = 0.051)

Test for subgroup differences: Not applicable



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Analysis 3.2. Comparison 3 White Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 2 Fatal and Non-Fatal Cerebrovascular Accidents.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 3 White Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 2 Fatal and Non-Fatal Cerebrovascular Accidents

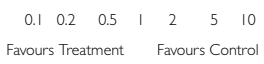
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	1/745	3/711		0.7 %	0.35 [0.05, 2.49]
CASTEL	9/232	13/192		3.7 %	0.56 [0.24, 1.32]
Coope	13/297	19/314		5.5 %	0.71 [0.35, 1.45]
EWPHE	23/287	30/299		8.7 %	0.78 [0.45, 1.38]
HDFP	19/1062	25/978		7.7 %	0.70 [0.38, 1.26]
MRC	23/4177	44/4129		12.0 %	0.53 [0.32, 0.85]
MRC elderly	46/1273	63/1287		18.8 %	0.73 [0.50, 1.07]
Shep	48/1120	66/1130		19.5 %	0.72 [0.50, 1.06]
Shep Pilot	4/229	3/54		0.8 %	0.21 [0.03, 1.39]
STOP	13/510	33/509		7.9 %	0.40 [0.22, 0.73]
Syst-eur	34/1618	50/1520		14.7 %	0.63 [0.41, 0.98]
Total (95% CI)	**11550**	**11123**		**100.0 %**	**0.64 [0.54, 0.75]**

Total events: 233 (Treatment), 349 (Control)

Heterogeneity: $Chi^2 = 6.36$, df = 10 (P = 0.78); $I^2 = 0.0\%$

Test for overall effect: Z = 5.27 (P < 0.00001)

Test for subgroup differences: Not applicable



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Analysis 3.3. Comparison 3 White Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 3 Fatal Coronary Heart Disease.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 3 White Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 3 Fatal Coronary Heart Disease

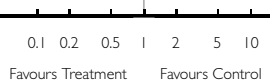
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	0/745	1/711		0.3 %	0.13 [0.00, 6.51]
CASTEL	12/232	15/192		7.8 %	0.64 [0.29, 1.41]
Coope	11/297	10/314		6.3 %	1.17 [0.49, 2.79]
EWPHE	13/287	18/299		9.1 %	0.74 [0.36, 1.53]
HDFP	21/1180	18/1150		11.9 %	1.14 [0.60, 2.15]
MRC	18/4177	10/4129		8.7 %	1.75 [0.84, 3.68]
MRC elderly	38/1273	40/1287		23.5 %	0.96 [0.61, 1.51]
Shep	18/1120	29/1130		14.3 %	0.63 [0.35, 1.12]
Shep Pilot	10/229	2/54		2.2 %	1.18 [0.27, 5.11]
STOP	6/510	8/509		4.3 %	0.75 [0.26, 2.14]
Syst-eur	17/1618	21/1520		11.6 %	0.76 [0.40, 1.44]
Total (95% CI)	**11668**	**11295**		**100.0 %**	**0.89 [0.72, 1.11]**

Total events: 164 (Treatment), 172 (Control)

Heterogeneity: Chi² = 8.02, df = 10 (P = 0.63); I² =0.0%

Test for overall effect: Z = 1.00 (P = 0.32)

Test for subgroup differences: Not applicable



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Analysis 3.4. Comparison 3 White Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 4 Fatal and Nonfatal Coronary Heart Disease.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 3 White Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 4 Fatal and Nonfatal Coronary Heart Disease

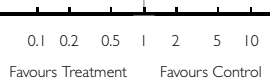
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	0/745	1/711		0.2 %	0.13 [0.00, 6.51]
CASTEL	16/232	19/192		5.5 %	0.67 [0.34, 1.35]
Coope	19/297	16/314		5.7 %	1.27 [0.64, 2.52]
EWPHE	27/287	26/299		8.3 %	1.09 [0.62, 1.92]
HDFP	47/1082	50/992		15.9 %	0.86 [0.57, 1.29]
MRC	38/4177	34/4129		12.3 %	1.11 [0.70, 1.76]
MRC elderly	59/1273	59/1287		19.4 %	1.01 [0.70, 1.46]
Shep	36/1120	54/1130		14.9 %	0.67 [0.44, 1.01]
Shep Pilot	14/229	2/54		1.6 %	1.57 [0.44, 5.65]
STOP	12/510	18/509		5.0 %	0.66 [0.32, 1.37]
Syst-eur	30/1618	35/1520		11.0 %	0.80 [0.49, 1.31]
Total (95% CI)	**11570**	**11137**		**100.0 %**	**0.89 [0.76, 1.05]**

Total events: 298 (Treatment), 314 (Control)

Heterogeneity: Chi^2 = 7.83, df = 10 (P = 0.65); I^2 =0.0%

Test for overall effect: Z = 1.36 (P = 0.17)

Test for subgroup differences: Not applicable



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Analysis 3.5. Comparison 3 White Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 5 Fatal Cardiovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 3 White Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 5 Fatal Cardiovascular Events

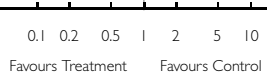
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	1/745	4/711		0.8 %	0.29 [0.05, 1.66]
CASTEL	38/232	47/192		10.7 %	0.60 [0.37, 0.97]
Coope	19/297	20/314		5.8 %	1.00 [0.53, 1.92]
EWPHE	50/287	63/299		14.5 %	0.79 [0.53, 1.19]
HDFP	32/1180	32/1150		9.9 %	0.97 [0.59, 1.60]
MRC	30/4177	27/4129		9.0 %	1.10 [0.65, 1.85]
MRC elderly	72/1273	65/1287		20.7 %	1.13 [0.80, 1.59]
Shep	36/1120	46/1130		12.6 %	0.78 [0.50, 1.22]
Shep Pilot	1/229	3/54		1.3 %	0.85 [0.22, 3.34]
STOP	9/510	20/509		4.5 %	0.46 [0.22, 0.96]
Syst-eur	31/1618	34/1520		10.1 %	0.85 [0.52, 1.40]
Total (95% CI)	**11668**	**11295**		**100.0 %**	**0.86 [0.74, 1.01]**

Total events: 329 (Treatment), 361 (Control)

Heterogeneity: Chi^2 = 10.44, df = 10 (P = 0.40); I^2 =4%

Test for overall effect: Z = 1.90 (P = 0.058)

Test for subgroup differences: Not applicable



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Analysis 3.6. Comparison 3 White Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 6 Fatal and Nonfatal Cardiovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 3 White Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 6 Fatal and Nonfatal Cardiovascular Events

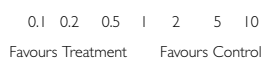
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	1/745	4/711		0.4 %	0.29 [0.05, 1.66]
CASTEL	44/232	56/192		6.5 %	0.57 [0.36, 0.89]
Coope	34/297	39/314		5.5 %	0.91 [0.56, 1.49]
EWPHE	66/287	77/299		9.3 %	0.86 [0.59, 1.26]
HDFP	64/1088	75/1000		11.2 %	0.77 [0.55, 1.09]
MRC	61/4116	80/4049		11.9 %	0.75 [0.54, 1.04]
MRC elderly	116/1273	127/1287		19.0 %	0.92 [0.70, 1.19]
Shep	87/1120	123/1130		16.4 %	0.69 [0.52, 0.92]
Shep Pilot	18/229	5/54		1.1 %	0.83 [0.28, 2.45]
STOP	26/510	51/509		6.1 %	0.49 [0.31, 0.79]
Syst-eur	66/1618	86/1520		12.4 %	0.71 [0.51, 0.98]
Total (95% CI)	**11515**	**11065**		**100.0 %**	**0.75 [0.67, 0.84]**

Total events: 583 (Treatment), 723 (Control)

Heterogeneity: Chi^2 = 9.50, df = 10 (P = 0.49); I^2 =0.0%

Test for overall effect: Z = 4.94 (P < 0.00001)

Test for subgroup differences: Not applicable



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Analysis 3.7. Comparison 3 White Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 7 All Cause Mortality.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 3 White Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 7 All Cause Mortality

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
Australian	1/745	4/711		0.4 %	0.29 [0.05, 1.66]
CASTEL	55/232	64/192		7.5 %	0.62 [0.41, 0.95]
Coope	32/297	28/314		4.8 %	1.23 [0.72, 2.10]
EWPHE	92/287	104/299		11.5 %	0.88 [0.63, 1.25]
HDFP	59/1180	55/1150		9.5 %	1.05 [0.72, 1.53]
MRC	91/4177	72/4129		14.0 %	1.25 [0.92, 1.71]
MRC elderly	118/1273	135/1287		20.0 %	0.87 [0.67, 1.13]
Shep	81/1120	87/1130		13.7 %	0.93 [0.68, 1.28]
Shep Pilot	19/229	3/54		1.1 %	1.46 [0.48, 4.42]
STOP	21/510	30/509		4.3 %	0.69 [0.39, 1.21]
Syst-eur	84/1618	75/1520		13.2 %	1.05 [0.77, 1.45]
Total (95% CI)	**11668**	**11295**		**100.0 %**	**0.95 [0.85, 1.07]**

Total events: 653 (Treatment), 657 (Control)

Heterogeneity: Chi^2 = 12.72, df = 10 (P = 0.24); I^2 =21%

Test for overall effect: Z = 0.85 (P = 0.40)

Test for subgroup differences: Not applicable

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Analysis 4.1. Comparison 4 African American Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 1 Fatal Cerebrovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 4 African American Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 1 Fatal Cerebrovascular Events

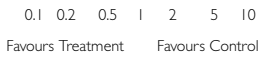
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
HDFP	8/1344	18/1356		84.6 %	0.46 [0.21, 1.00]
Shep	2/211	2/229		13.0 %	1.09 [0.15, 7.77]
Shep Pilot	1/50	0/16		2.4 %	3.74 [0.04, 362.67]
Total (95% CI)	**1605**	**1601**		**100.0 %**	**0.55 [0.27, 1.11]**

Total events: 11 (Treatment), 20 (Control)

Heterogeneity: Chi^2 = 1.32, df = 2 (P = 0.52); I^2 =0.0%

Test for overall effect: Z = 1.67 (P = 0.094)

Test for subgroup differences: Not applicable



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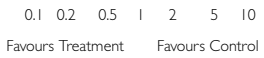
Analysis 4.2. Comparison 4 African American Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 2 Fatal and Non-Fatal Cerebrovascular Accidents.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 4 African American Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 2 Fatal and Non-Fatal Cerebrovascular Accidents

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
HDFP	24/1231	44/1187		69.5 %	0.53 [0.32, 0.85]
Shep	7/211	21/229		27.6 %	0.38 [0.17, 0.81]
Shep Pilot	2/50	2/16		2.9 %	0.23 [0.02, 2.39]
Total (95% CI)	**1492**	**1432**		**100.0 %**	**0.47 [0.31, 0.70]**
Total events: 33 (Treatment), 67 (Control)					
Heterogeneity: Chi^2 = 0.90, df = 2 (P = 0.64); I^2 =0.0%					
Test for overall effect: Z = 3.71 (P = 0.00021)					
Test for subgroup differences: Not applicable					



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Analysis 4.3. Comparison 4 African American Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 3 Fatal Coronary Heart Disease.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 4 African American Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 3 Fatal Coronary Heart Disease

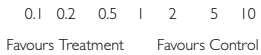
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
HDFP	20/1344	21/1356		72.6 %	0.96 [0.52, 1.78]
Shep	4/211	11/229		26.1 %	0.41 [0.15, 1.16]
Shep Pilot	1/50	0/16		1.3 %	3.74 [0.04, 362.67]
Total (95% CI)	**1605**	**1601**		**100.0 %**	**0.79 [0.46, 1.33]**

Total events: 25 (Treatment), 32 (Control)

Heterogeneity: $Chi^2 = 2.34$, df = 2 (P = 0.31); $I^2 = 14\%$

Test for overall effect: Z = 0.90 (P = 0.37)

Test for subgroup differences: Not applicable



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Analysis 4.4. Comparison 4 African American Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 4 Fatal and Nonfatal Coronary Heart Disease.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 4 African American Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 4 Fatal and Nonfatal Coronary Heart Disease

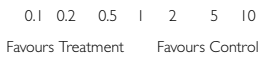
Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
HDFP	48/1246	63/1195		83.2 %	0.72 [0.49, 1.06]
Shep	6/211	15/229		15.7 %	0.44 [0.18, 1.06]
Shep Pilot	1/50	1/16		1.1 %	0.24 [0.01, 6.26]
Total (95% CI)	**1507**	**1440**		**100.0 %**	**0.66 [0.47, 0.93]**

Total events: 55 (Treatment), 79 (Control)

Heterogeneity: Chi^2 = 1.37, df = 2 (P = 0.50); I^2 =0.0%

Test for overall effect: Z = 2.35 (P = 0.019)

Test for subgroup differences: Not applicable



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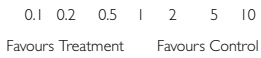
Analysis 4.5. Comparison 4 African American Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 5 Fatal Cardiovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 4 African American Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 5 Fatal Cardiovascular Events

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
HDFP	37/1344	53/1356		78.9 %	0.70 [0.46, 1.06]
Shep	7/211	16/229		19.8 %	0.48 [0.21, 1.11]
Shep Pilot	2/50	0/16		1.3 %	3.82 [0.15, 99.46]
Total (95% CI)	**1605**	**1601**		**100.0 %**	**0.66 [0.46, 0.96]**
Total events: 46 (Treatment), 69 (Control)					
Heterogeneity: Chi^2 = 1.76, df = 2 (P = 0.42); I^2 =0.0%					
Test for overall effect: Z = 2.16 (P = 0.031)					
Test for subgroup differences: Not applicable					



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Analysis 4.6. Comparison 4 African American Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 6 Fatal and Nonfatal Cardiovascular Events.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 4 African American Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 6 Fatal and Nonfatal Cardiovascular Events

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
HDFP	70/1254	101/1213		77.3 %	0.65 [0.48, 0.89]
Shep	13/211	35/229		20.8 %	0.39 [0.22, 0.71]
Shep Pilot	3/50	3/16		2.0 %	0.22 [0.03, 1.53]
Total (95% CI)	**1515**	**1458**		**100.0 %**	**0.58 [0.44, 0.76]**
Total events: 86 (Treatment), 139 (Control)					
Heterogeneity: Chi^2 = 3.17, df = 2 (P = 0.20); I^2 =37%					
Test for overall effect: Z = 3.97 (P = 0.000072)					
Test for subgroup differences: Not applicable					

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Analysis 4.7. Comparison 4 African American Women: Hypertension Treatment versus Placebo or Usual Care, Outcome 7 All Cause Mortality.

Review: Pharmacotherapy for hypertension in women of different races

Comparison: 4 African American Women: Hypertension Treatment versus Placebo or Usual Care

Outcome: 7 All Cause Mortality

Study or subgroup	Treatment n/N	Control n/N	Peto Odds Ratio Peto,Fixed,95% CI	Weight	Peto Odds Ratio Peto,Fixed,95% CI
HDFP	68/1344	100/1356		76.7 %	0.67 [0.49, 0.92]
Shep	17/211	33/229		21.6 %	0.53 [0.30, 0.96]
Shep Pilot	4/50	1/16		1.7 %	1.28 [0.15, 10.56]
Total (95% CI)	**1605**	**1601**		**100.0 %**	**0.65 [0.49, 0.85]**

Total events: 89 (Treatment), 134 (Control)

Heterogeneity: $Chi^2 = 0.88$, df = 2 (P = 0.65); $I^2 = 0.0\%$

Test for overall effect: Z = 3.12 (P = 0.0018)

Test for subgroup differences: Not applicable

WHAT'S NEW

Last assessed as up-to-date: 2 December 1999.

Date	Event	Description
13 August 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 2, 2000

Review first published: Issue 2, 2000

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Date	Event	Description
26 February 2003	Amended	Minor update.

CONTRIBUTIONS OF AUTHORS

A Quan - Formulated the study question, did the literature search, gathered data from multuiple sources, entered and analyzed the data for the meta -analysis models, and wrote the manuscript

K Kerlikowske - Formulated the study question and inclusion/exclusion criteria, evaluation of studies for inclusion, review of data analyses, and review of the manuscript

F Gueyffier - Coordination of the INDANA Steering Committee/ Management of the INDANA data base, Extraction of the INDANA data used in the review/ Analysis of the interactions on indivual patient data, Review of the manuscript

J P Boissel - Research director for INDANA project, Review of th e manuscript

DECLARATIONS OF INTEREST

The INDANA data base was supported by grants from the Association pour la Promotion de la Recherche et de l'Evaluation en Therapeutique, the Societe Francaise d'Hypertension Arterielle, the Fondation pour la Recherche Medicale, and the Hospices Civils de Lyon. However, we do not see any potential conflict of interest through the INDANA grants, or from the conclusions made in our study.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Association pour la Promotion de la Recherche et de l'Evaluation en Therapeutiq, France.
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- Fondation pour la Recherche Medicale, France.
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INDEX TERMS

Medical Subject Headings (MeSH)

*African Continental Ancestry Group; *European Continental Ancestry Group; Age Factors; Antihypertensive Agents [*therapeutic use]; Hypertension [*drug therapy; ethnology; mortality]; Randomized Controlled Trials as Topic; Risk

MeSH check words

Adult; Female; Humans; Middle Aged

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