# The Effects of Calcium Channel Blockers in the Prevention of Stroke in Adults with Hypertension: A Meta-Analysis of Data from 273,543 Participants in 31 Randomized Controlled Trials

# Gui Jv Chen, Mao Sheng Yang\*

Laboratory of Disorder Genes and Department of Pharmacology, College of Pharmacy, Chongqing Medical University, Chongqing, People's Republic of China

## Abstract

**Background:** Hypertension is a major risk factor for the development of stroke. It is well known that lowering blood pressure decreases the risk of stroke in people with moderate to severe hypertension. However, the specific effects of calcium channel blockers (CCBs) against stroke in patients with hypertension as compared to no treatment and other antihypertensive drug classes are not known.

*Methods and Findings:* This systematic review and meta-analysis of randomized controlled trials (RCTs) evaluated CCBs effect on stroke in patients with hypertension in studies of CCBs versus placebo, angiotensin-converting-enzyme inhibitors (ACEIs),  $\beta$ -adrenergic blockers, and diuretics. The PUBMED, MEDLINE, EMBASE, OVID, CNKI, MEDCH, and WANFANG databases were searched for trials published in English or Chinese during the period January 1, 1996 to July 31, 2012. A total of 177 reports were collected, among them 31 RCTs with 273,543 participants (including 130,466 experimental subjects and 143,077 controls) met the inclusion criteria. In these trials a total of 9,550 stroke events (4,145 in experimental group and 5,405 in control group) were reported. CCBs significantly decreased the incidence of stroke compared with placebo (OR = 0.68, 95% CI 0.61–0.75, p<1×10<sup>-5</sup>),  $\beta$ -adrenergic blockers combined with diuretics (OR = 0.89, 95% CI 0.83–0.95, p = 7×10<sup>-5</sup>) and  $\beta$ -adrenergic blockers (OR = 0.79, 95% CI 0.72–0.87, p<1×10<sup>-5</sup>), statistically significant difference was not found between CCBs and ACEIs (OR = 0.92, 95% CI 0.8–1.02, p = 0.12) or diuretics (OR = 0.95, 95% CI 0.84–1.07, p = 0.39).

**Conclusion:** In a pooled analysis of data of 31 RCTs measuring the effect of CCBs on stroke, CCBs reduced stroke more than placebo and  $\beta$ -adrenergic blockers, but were not different than ACEIs and diuretics. More head to head RCTs are warranted.

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\* E-mail: yangmaosheng@hotmail.com

# Introduction

Hypertension (MIM #14500) is one of the most common chronic diseases, and the most frequent reason for people to consult their doctor and take medication. Hypertension can burst a blood vessel or/and accelerate narrowing of arteries in the brain to cause a stroke which, if not lethal, can result in many catastrophic complications such as paralysis, aphasia, coma and so forth. The damage to the brain cannot be repaired, so the only rational approach is prevention. Hypertension is a major risk factor for the development of stroke. In 1964, it was first demonstrated that antihypertensive agents could reduce the risk of strokes [1]. It is well known that lowering blood pressure decreases the risk of stroke in people with moderate to severe hypertension [2]. There are eight classifications of antihypertensive agents in use today:  $\alpha$ -adrenergic blockers, angiotensinconverting enzyme inhibitors (ACEIs), angiotensin II receptor antagonists, antiadrenergic agents,  $\beta$ -adrenergic blockers or  $\beta$ blockers, calcium channel blockers (CCBs), diuretics, and vasodilators. Despite the widespread use of blood-pressure-lowering agents which one is better against the development of stroke is unclear [3]. Controlling blood pressure in the patients with hypertension or/and stroke has important clinical implications including improved prognosis, reduced mortality and so on [4]. Angiotensin-converting enzyme inhibitors,  $\beta$ -adrenergic blockers, calcium channel blockers and diuretics are used extensively and listed as the first-line agents in the 1989 WHO/International Society of Hypertension Guidelines [5]. Because each study may have insufficient power to detect the effect of calcium channel blockers against stroke in the patients with hypertension; a metastudy to accumulate data from different studies may address this issue, and the specific effects of CCBs against stroke in patients with hypertension as compared to no treatment and other antihypertensive drug classes are not known. Therefore, the major goal of this work was to perform a systematic review and a metaanalysis of the published data and to figure out whether calciumchannel blockers are better than other first-line antihypertensive

agents in the prevention of stroke, as well as to quantify the potential heterogeneity between different studies.

# Methods

#### Data Sources

The PUBMED, MEDLINE, EMBASE, OVID, CNKI, MEDCH, and WANFANG databases were searched for trials published in English or Chinese during the period January 1, 1996 to July 31, 2012. In addition, all references cited in these studies and previously published review articles were reviewed to identify additional works not indexed by the above databases. Search terms were "antihypertensive agents", "placebo", "hypertension", "diuretics", "beta-blockers" or " $\beta$ -adrenergic blockers", "angiotensin-converting-enzyme inhibitors", "calcium channel blockers", "vasodilator agents", and "stroke". Bibliographies of studies were also reviewed.

### **Study Selection**

A total of 177 published studies were identified using the screening procedure shown in Figure 1 (see Supplementary Information online). Among them, fifty-eight are systematic reviews and meta-analyses, one hundred and nineteen are randomized controlled trials. After searching, the following information was extracted: author, ethnicity of research subjects, year of publication, numbers of hypertension- and stroke-cases, medicine of treatment, age of patients, and years of followed-up. Studies were eligible for inclusion if they were randomized controlled trials and reported on stroke risk associated with the current use of the first-line antihypertensive agents in population settings.

#### Quality Assessment

Eligible studies must meet the following inclusion criteria: (1) with original data being independent among studies if more than one studies have overlapping subjects, only the study with bigger/ biggest sample size was selected; (2) with the numbers of hypertension- and stroke-cases clearly provided; (3) with data of the first-line antihypertensive agents and/or placebo; (4) with the research design of randomized controlled trials, which is the best approach to evaluating new treatments, to challenging the efficacy of the old one, and to comparing the efficacy of different treatments [6–7]. All the available information was independently extracted by two investigators and no inconsistency was discovered. The quality assessment of evidence and an overall risk of bias assessment for each included study were evaluated by GRADE-profiler software version 3.2.2 and RevMan version 5.0 (see Supplementary Information online), respectively.

#### Statistical Analysis

Publication bias was detected by Egger's linear regression test, which measures funnel plot asymmetry on the scale of odds ratio (OR) [8]. Heterogeneity between studies was tested by Cochran's Q-statistic test [9] and  $I^2 = 100\% \times (Q-df) \div Q$  [10], respectively. The  $\vec{I}^2$  metric is independent of the number of studies in the metaanalysis, and ranges between 0 and 100% ( $I^2 < 25\%$ : no heterogeneity;  $I^2 = 25\% - 50\%$ : moderate heterogeneity;  $I^2 = 50\% - 75\%$ : high heterogeneity;  $I^2 > 75\%$ : extreme heterogeneity). Heterogeneity was considered statistically significant when  $p \le 0.05$  [11]. If results were heterogeneous, the random effects model was used for meta-analysis. OR was pooled using the method of DerSimonian and Laird, and 95% confidence interval (CI) was constructed using Woolf's method. The statistical analysis was conducted by the statistical package RevMan version 5.0 (The Cochrane collaboration, Oxford, England). A  $\not p$  value of less than 0.05 was considered as statistical significant.

## Results

The derivation of the databases and published articles is described in Figure 1. A total of one hundred and seventy-seven studies concerning the stroke risk associated with the use of antihypertensive agents in the patients with hypertension were identified. Among them, one hundred and forty-six studies were excluded for (1) No numbers of hypertension- and stroke-cases; (2) Data duplication; (3) Not written in English or Chinese; (4) No randomized controlled trials; (5) Data missing or lacking; (6) No control group. Therefore, thirty-one studies [3-5,12-39] and a total of 273,543 participants (including 130,466 experimental subjects and 143,077 controls) matched the inclusion criteria and were selected for the statistical test; and a total of 9.550 stroke events (4,145 in experimental group and 5,405 in control group) were reported (see Table 1). The quantity and quality of original investigations play an important role in determining the quality of the meta-analysis. To controlling the publication bias, the funnel test was performed (see Figure 2). No evidence of publication bias was found for the included thirty-one studies. Our analysis also indicated that the heterogeneity between studies was not statistical significance (p > 0.05), therefore, the fixed effects model was used for the meta-analysis. The results of quality assessment for each included study indicated that among the included thirty-one studies, twenty-eight reports [3-5,12-15,17-25,27-32,34-39] were high quality and the remaining three studies [16,26,33] were moderate quality (see Table 1 and Supplementary Information online). The overall quality of the evidence was high in our statistical tests.

The issue of lost to follow-up or withdrew was identified as follows: 1) six studies [4,24,29,32,34,37] reported that no patient was lost to follow-up or withdrew; 2) eight studies [14,17–18,23,25,35–36,38] did not report the information of the patient's follow-up or withdrew; 3) the remaining seventeen studies [3,5,12–13,15–16,19–22,26–28,30–31,33,39] reported that some patients were lost to follow-up or withdrew but not gave out the reasons, and the rate of lost to follow-up was not significantly difference between the experimental and control groups (see Supplementary Information online). Therefore, we did not perform the comparisons of incidence of withdrawals due to adverse effects for CCBs versus other drugs, because it was easy to result in a bias.

The results from the risk of bias assessment for each included study indicated that among the included thirty-one studies, fifteen reports [3,5,14,17,20–22,27,29–33,37,39] were low risk of bias, thirteen reports [4,12,13,15,18,19,23,25,28,34–36,38] were unclear risk of bias, and the remaining three studies [16,26,33] were high risk of bias (see Table 1 and Supplementary Information online).

There are two types of stroke, ischemic stroke (80%) and hemorrhagic stroke (20%). A total of 60-80% of hypertension patients (blood pressure >140/90 mmHg) face the risk of stroke. Hypertension is associated with ischemic- and hemorrhagic-stroke [40]. The detailed information of ischemic- or hemorrhagic-stroke was not presented in most original studies. The authors of included thirty-one studies have contact. Six reports authors could not contacted, nine reports authors did not response to us, five reports authors responded to us with the information we need, and eleven reports authors responded to us but did not give back the information we need. Therefore, we can not perform sub-groups analysis.

| Source vear [reference]                | 6thnicity | Ethnicity Treatment                  | Cases of Hypertension    | tension             | Age of Cases<br>(Mean±SD) |              | Years of<br>followed | Cases of<br>Stroke |         | Incidence of<br>Stroke (%) | Quality<br>of the<br>evidenc | e,         | Overall<br>risk of bias<br>assessment |
|--|-----------|--------------------------------------|--------------------------|---------------------|---------------------------|--------------|----------------------|--------------------|---------|----------------------------|------------------------------|------------|---------------------------------------|
|  |           |                                      | Experimental<br>(Male %) | Control<br>(Male %) | Experimental              | Control      | ŀ                    | Experimental       | Control | Experimental Control       |                              | (GRADE) (  | (RevMan)                              |
| CCBs vs Placebo                        |           |                                      |                          |                     |                           |              |                      |                    |         |                            |                              |            |                                       |
| Poole-Wilson PA et al 2004 [16] Europe | ] Europe  | Nifedipine vs Placebo 3825(80)       | o 3825(80)               | 3840(79)            | 63.5±9.3                  | 63.4±9.3     | ≥4.9                 | 77                 | 66      | 2 2.6                      |                              | Moderate H | High                                  |
| Lubsen J et al 2005 [14]               | Europe    | Nifedipine vs Placebo 1795           | o 1795                   | 2002                | 61.8±9.4                  | 65.0±8.9     | ≥5.5                 | 123                | 171     | 6.9 8.5                    | High                         |            | Low                                   |
| Turnbull F 2003 [23]                   | Europe    | CCBs vs Placebo                      | 3794                     | 3688                | 65                        | 65           | ≥4                   | 76                 | 119     | 2 3.2                      | e High                       |            | Unclear                               |
| Liu L et al 2005 [21]                  | Asia      | Felodipine vs Placebo 4841(61.8)     | o 4841(61.8)             | 4870(60.5)          | 61.5±7.1                  | 61.5±7.2     | ≥3.5                 | 177                | 251     | 3.7 5.2                    | High                         |            | Low                                   |
| Berl T et al 2003 [37]                 | Europe    | Amlodipine vs Placebo567(63)         | 00567(63)                | 569(71)             | 59.1±7.9                  | 58.3±8.2     | ≥2.6                 | 15                 | 26      | 2.6 4.6                    | High                         |            | Low                                   |
| Tuomilehto J et al 1999 [38]           | Europe    | Nitrendipine vs<br>Placebo           | 2146                     | 2057                | ≥60                       | 80           | ≥2                   | 42                 | 62      | 2 3                        | High                         |            | Unclear                               |
| Dens JA et al 2001 [25]                | Europe    | Nisoldipine vs Placebo 408(82)       | 00 408(82)               | 411(79)             | 60±9                      | 60±9         | ۲)<br>ا              | 4                  | 7       | 1 1.7                      | ' High                       |            | Unclear                               |
| Gong L et al 1996 [26]                 | Asia      | Nifedipine vs Placebo 817            | o 817                    | 815                 | 66.2±5.1                  | 66.7±5.4     | ≥2.5                 | 16                 | 36      | 2 4.4                      |                              | Moderate H | High                                  |
| Liu L et al 1998 [15]                  | Asia      | Nitrendipine vs<br>Placebo           | 1253(65.0)               | 1141(63.6)          | 66.7±5.7                  | 66.4±5.4     | 54                   | 45                 | 59      | 3.6 5.2                    | High                         |            | Unclear                               |
| Staessen JA et al 1998 [12]            | Europe    | Nitrendipine vs<br>Placebo           | 2398(32.5)               | 2297(33.8)          | 70.2±6.7                  | 70.3±6.7     | ≥2                   | 47                 | 77      | 2 3.4                      | High                         |            | Unclear                               |
| Total                                  |           |                                      | 21844                    | 21690               |                           |              |                      | 622                | 907     | 2.8 4.2                    |                              |            |                                       |
| <b>CCBs vs ACEIs</b>                   |           |                                      |                          |                     |                           |              |                      |                    |         |                            |                              |            |                                       |
| Estacio RO et al 1998 [35]             | Europe    | Nisoldipine vs Enalapril235(68.1)    | ıril235(68.1)            | 235(66.8)           | 57.2±8.2                  | 57.7±8.4     | ≥5                   | 11                 | 7       | 4.7 3                      | High                         |            | Unclear                               |
| Leenen FH et al 2005 [20]              | Europe    | Amlodipine vs<br>Lisinopril          | 9048(52.7)               | 9054(53.8)          | 66.8±7.8                  | 66.8±7.8     | ≥4                   | 377                | 457     | 4.2 5                      | High                         |            | Low                                   |
| Fukui T et al 2003 [36]                | Asia      | Amlodipine vs<br>Candesartan         | 2349                     | 2354                | 20–85                     | 20-85        | ≥3.2                 | 60                 | 47      | 2.6 2                      | High                         |            | Unclear                               |
| Song Y et al 2011 [4]                  | Asia      | Levamlodipine<br>Beaylate vs Enapril | 69(52.2)                 | 68(51.5)            | 63.32±6.15                | 61.85±5.19≥1 | 9≥1                  | 6                  | 11      | 13 16.2                    | .2 High                      |            | Unclear                               |
| Tatti P et al 1998 [13]                | Europe    | Amlodipine vs<br>Fosinopril          | 191 (55.5)               | 189(63.5)           | 62.8±0.5                  | 63.3±0.4     | ≥3.5                 | 10                 | 4       | 5.2 2.1                    | High                         |            | Unclear                               |
| Hansson L et al 1999 [29]              | Europe    | CCBs vs ACEIs                        | 2196(34.0)               | 2205(33.7)          | 75.9                      | 76.1         | ≥5                   | 207                | 215     | 1 9.8                      | 8 High                       |            | Low                                   |
| Schrader J et al 2005 [39]             | Europe    | Nitrendipine vs<br>Eprosartan        | 671 (54.8)               | 681 (53.6)          | 67.7±10.4                 | 68.1±9.5     | ≥2.5                 | 39                 | 31      | 5.8 4.6                    | High                         |            | Low                                   |
| Ekbom T et al 2004 [18]                | Europe    | CCBs vs ACEIs                        | 752(26.6)                | 772(26.8)           | 76.5                      | 76.6         | ≥5                   | 15                 | 16      | 2 2.1                      | High                         |            | Unclear                               |
| Total                                  |           |                                      | 15511                    | 15558               |                           |              |                      | 728                | 788     | 4.7 5.1                    |                              |            |                                       |
| CCBs vs β blockers or/and<br>Diuretics |           |                                      |                          |                     |                           |              |                      |                    |         |                            |                              |            |                                       |
| ALLHAT 2002 [27]                       | Europe    | Amlodipine vs<br>Chlorthalidone      | 9048(52.7)               | 15255(53.0)         | 66.9±7.7                  | 66.9±7.7     | ≥4.9                 | 377                | 675     | 4.2 4.4                    | High                         |            | Low                                   |
| Rothwell PM et al 2010 [17]            | Europe    | Amlodipine vs<br>Atenolol            | 9302                     | 9228                | 40–78                     | 40–78        | ≥2                   | 279                | 350     | 3.8                        | High                         |            | Low                                   |

Table 1. Characteristics of 31 randomized controlled trials included in the meta-analyses.

Table 1. Cont.

| Source year [reference]      | Ethnicity | Ethnicity Treatment                             | Cases of Hyper           | pertension          | Age of Cases<br>(Mean±SD) |          | Years of<br>followed<br>up | Cases of<br>Stroke |         | Incidence of<br>Stroke (%) | Quainty<br>of the<br>evidence | Uverall<br>risk of bias<br>assessment |
|------------------------------|-----------|---|--------------------------|---------------------|---------------------------|----------|----------------------------|--------------------|---------|----------------------------|-------------------------------|---------------------------------------|
|                              |           |   | Experimental<br>(Male %) | Control<br>(Male %) | Experimental              | Control  |                            | Experimental       | Control | Experimental Control       | trol (GRADE)                  | (RevMan)                              |
| Dahlöf B et al 2005 [19]     | Europe    | Amlodipine vs<br>Atenolol                       | 9639(77)                 | 9618(77)            | 63.0±8.5                  | 63.0±8.5 | ≥5.5                       | 327                | 422     | 3.4 4.4                    | High                          | Unclear                               |
| Turnbull F 2003 [23]         | Europe    | CCBs vs diuretic and $\beta$ 31031 blocker      | β31031                   | 37418               | 65                        | 65       | 4                          | 666                | 1358    | 3.2 3.6                    | High                          | Unclear                               |
| Black HR et al 2003 [28]     | Europe    | Verapamil vs Atenolol 8179(43.8)<br>and         | ol 8179(43.8)            | 8297(44.2)          | 65.6±7.4                  | 65.6±7.4 | 33                         | 133                | 118     | 1.6 1.4                    | High                          | Unclear                               |
|                              |           | Hydrochlorothiazide                             |                          |                     |                           |          |                            |                    |         |                            |                               |                                       |
| Hansson L et al 1999 [29]    | Europe    | CCBs vs diuretic and $\beta$ 2196(34.0) blocker | β2196(34.0)              | 2213(32.0)          | 75.9                      | 76       | ≥5                         | 207                | 237     | 9.4 10.7                   | High                          | Low                                   |
| Brown MJ et al 2000 [30]     | Europe    | Nifedipine vs Co-<br>amilozide                  | 3157(46.1)               | 3164(46.6)          | 55-80                     | 55-80    | ≥3.5                       | 67                 | 74      | 2.1 2.3                    | High                          | Low                                   |
| Pepine CJ et al 2003 [31]    | Europe    | Verapamil vs Atenolol 11267(48.1)               | 시 11267(48.1)            | 11309(47.7)         | 66.0±9.7                  | 66.1±9.8 | ≥4                         | 176                | 201     | 1.6 0.2                    | High                          | Low                                   |
| Borhani NO et al 1996 [32]   | Europe    | Isradipine vs<br>Hydrochlorothiazide            | 442(79.9)                | 441 (75.7)          | 58.2±8.3                  | 58.7±8.7 | N<br>1                     | 9                  | ε       | 0.1 0.07                   | High                          | Low                                   |
| Wang Y et al 1998 [24]       | Asia      | Nitrendipine vs<br>Diuretics                    | 141(62.4)                | 120(63.3)           | 56±11                     | 54±13    | ≥5.1                       | 0                  | £       | 0 2.5                      | High                          | Low                                   |
| Hansson L et al 2000 [5]     | Europe    | Diltiazem vs Diuretic and $\beta$ -blocker      | 5410(48.5)               | 5471(48.7)          | 60.5±6.5                  | 60.3±6.5 | ≥4.5                       | 159                | 196     | 2.9 3.6                    | High                          | Low                                   |
| NICS-EH Study Group 1999 [3] | Asia      | Nicardipine vs<br>Trichlormethiazide            | 204(40.2)                | 210(26.2)           | 69.7±6.5                  | 69.9±6.4 | ≥4.2                       | -                  | 0       | 0.5 0                      | High                          | Low                                   |
| Malacco E et al 2003 [33]    | Europe    | Lacidipine vs<br>Chlorthalidone                 | 942(39.6)                | 940(37.8)           | 72.3±7.5                  | 72.4±7.6 |                            | 37                 | 38      | 4                          | Moderate                      | High                                  |
| Ekbom T et al 2004 [18]      | Europe    | CCBs vs diuretic and $\beta752(26.6)$ blocker   | β752(26.6)               | 756(21.8)           | 76.5                      | 76.6     | l∧5                        | 15                 | 20      | 2 2.6                      | High                          | Low                                   |
| Zanchetti A et al 2002 [22]  | Europe    | Lacidipine vs Atenolol 1177(54.2)               | ol 1177(54.2)            | 1157(55.4)          | 55.9±7.5                  | 56.1±7.5 | ≥4                         | 6                  | 14      | 0.8 1.2                    | High                          | Low                                   |
| Zanchetti A et al 1998 [34]  | Europe    | Verapamil vs<br>Chlorthalidone                  | 224(53.1)                | 232(51.3)           | 54.2±6.8                  | 53.9±7.2 | ≥2                         | ĸ                  | -       | 1.3 0.4                    | High                          | Unclear                               |
| Total                        |           |   | 93111                    | 105829              |                           |          |                            | 2795               | 3710    | 3 3.5                      |                               |                                       |
|                              |           |   |                          |                     |                           |          |                            |                    |         |                            |                               |                                       |
| Overall                      |           |   | 130466                   | 143077              |                           |          |                            | 4145               | 5405    |                            |                               |                                       |

an important impact on our confidence in the estimate of effect and may change the estimate. Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change

the estimate. Very low quality: We are very uncertain about the estimate. The risk of bias assession quality: We are very uncertain about the estimate. The risk of bias assession and risk of bias for one or more key domains (within a study), and most information is from studies at low or unclear risk of bias for one or more key domains (within a study), and most information is from studies at low or unclear risk of bias for one or more key domains (within a study), and most information is from studies at low or unclear risk of bias for one or more key domains (within a study), and most information is from studies at low or unclear risk of bias for one or more key domains (within a study), and most information is from studies at low or unclear risk of bias for one or more key domains (within a study), the proportion of information from studies at high risk of bias is sufficient to affect the interpretation of results (across studies).

Calcium Channel Blockers and Stroke Prevention

## Stroke Events of CCBs vs Placebo

Ten studies were included in this test [12,14–16,21,23,25–26,37–38], which consisted of 21,844 experimental subjects and 21,690 controls, and 1,574 stroke events (622 in experimental group and 907 in control group). Statistic test revealed that the CCBs could significantly decline the stroke risk (OR = 0.68, 95% CI 0.61–0.75, p<1×10<sup>-5</sup>) compared with that of placebo (see Figure 3a). The incidence of stroke in CCBs group was decreased

by 33.33% [(4.2%-2.8%)  $\div$  4.2% × 100%] compared with that of placebo group (see Table 1).

# Stroke Events of CCBs vs ACEIs

Eight studies with a total of 15,511 experimental subjects and 15,558 controls were included in this analysis [4,13,18,20,29,35–36,39], and 1446 stroke events were reported (728 in experimental group and 788 in control group). No statistically significant

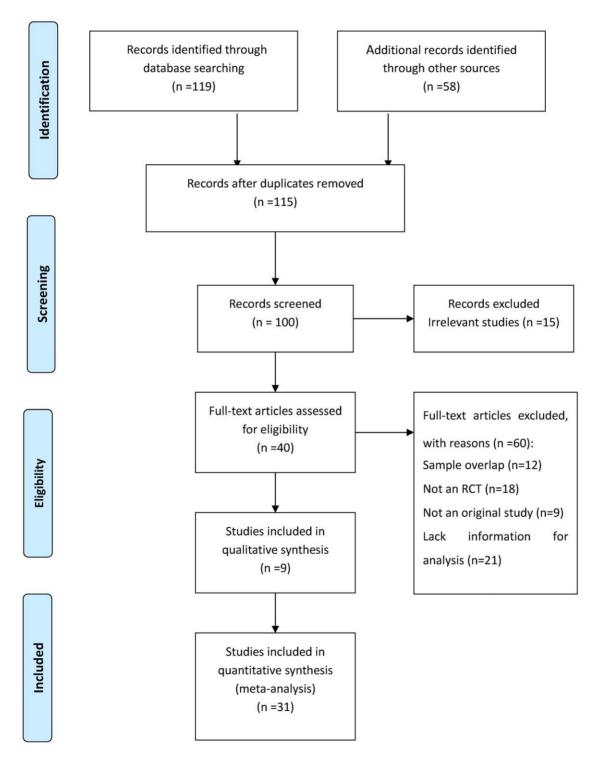
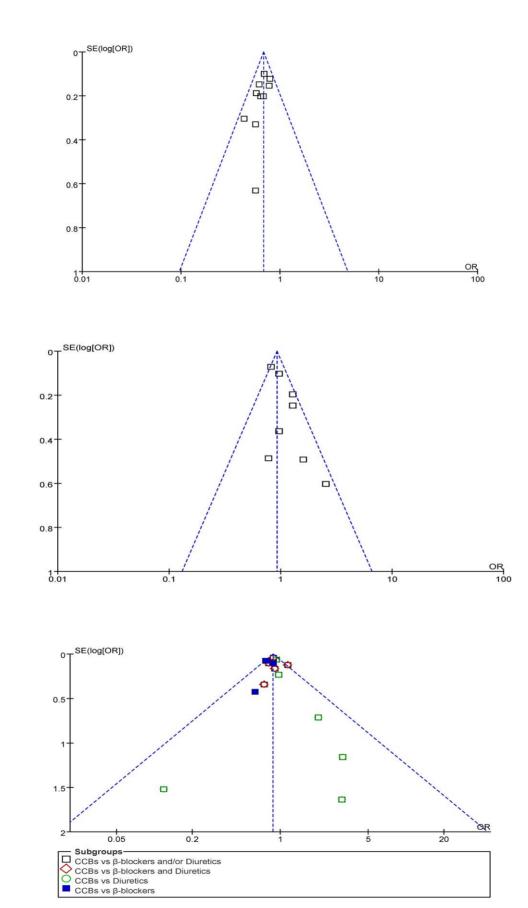


Figure 1. A schematic diagram for the search strategy of published reports. doi:10.1371/journal.pone.0057854.g001



b

a



Figure 2. Funnel plots of odds ratios for all studies in the meta-analyses. (a) Calcium channel blockers vs Placebo, (b) Calcium channel blockers vs ACEIs, and (c) Calcium channel blockers vs Diuretics or/and  $\beta$  blockers. No evidence of publication bias was found in any of them. doi:10.1371/journal.pone.0057854.g002

|  | Experin  | nental  | Cont  | rol   |   | Odds R   |  |  | Odds Ratio                              |
|--|--|---|---|---|---|--|--|--|---|
| tudy or Subgroup   | Events   |   | Events  |   |   | M-H, Fixed   |  | N  | A-H. Fixed, 95% CI                      |
| Berl T et al 2003<br>Dens JA et al 2001  | 15   | 567<br>408  | 26  | 569<br>411  | 2.9%  |  | 30, 1.08]  |  |   |
| Song L et al 1996  | 4  | 817   | 36  | 815   | 4.0%  |  | 24, 0.79]  |  |   |
| iu L et al 1998  | 45   | 1253  | 59  | 1141  | 6.8%  |  | 46, 1.02]  |  | -                                       |
| iu L et al 2005  | 177  | 4841  | 251   | 4870  | 27.6%   | 0.70 [0.   | 57, 0.85]  |  |   |
| ubsen J et al 2005   | 123  | 1795  | 171   | 2002  | 17.3%   | 0.79 [0.   | 52, 1.00]  |  | -                                       |
| Poole-Wilson PA et al2004  | 77   | 3825  | 99  | 3840  | 11.1%   |  | 57, 1.05]  |  | *                                       |
| Staessen JA et al 1997   | 47   | 2398  | 77  | 2297  | 8.8%  |  | 40, 0.83]  |  | -                                       |
| uomilehto J et al 1999   | 42   | 2146  | 62  | 2057  | 7.1%  |  | 43, 0.95]  |  | 1                                       |
| umbull F 2003  | 76   | 3794  | 119   | 3688  | 13.5%   | 0.61 [0.4  | 46, 0.82]  |  |   |
| otal (95% CI)  |  | 21844   |   | 21600   | 100.0%  | 0.68 [0.6  | 1 0 751  |  | •                                       |
| lotal events   | 622  | 21044   | 907   | 21030   | 100.036   | 0.00 [0.0  | 1, 0.10]   |  |   |
| leterogeneity: Chi <sup>2</sup> = 6.18, (  |  | 0.72)-12  |   |   |   |  |  | H  |   |
| est for overall effect: Z = 7.   |  |   | - 970   |   |   |  |  | 0.005 0.   |   |
|  |  |   |   |   |   |  | P  | avours experi  | imental Favours control                 |
|  |  |   |   |   |   |  |  |  |   |
| 1  | Experime   | ntal  | Contro  | ol  |   | Odds R   |  |  | Odds Ratio                              |
| Study or Subgroup  | Events   | Total I   | Events  | Total   | Neight  | M-H. Fixed   | 1. 95% C   |  | M-H. Fixed. 95% Cl                      |
| Ekborn T et al 2004  | 15   | 752   | 16  | 772   | 2.1%  | 0.96 [0.4  | 47, 1.96]  |  | -                                       |
| Estacio RO et al 1998  | 11   | 235   | 7   | 235   | 0.9%  |  | 51, 4.20]  |  | +                                       |
| Fukui T et al 2003   | 60   | 2349  | 47  | 2354  | 6.2%  |  | 87, 1.89]  |  | +-                                      |
| Hansson L et al 1999   | 207  | 2196  | 215   | 2205  | 26.2%   |  | 79, 1.18]  |  |   |
| eenen FH et al 2005  | 377  | 9048  | 457   | 9054  | 20.2%   |  |  |  |   |
|  |  |   |   |   |   |  | 71, 0.94]  |  |   |
| Schrader J et al 2005  | 39   | 671   | 31  | 681   | 3.9%  |  | 80, 2.10]  |  |   |
| Song Y et al 2011  | 9  | 69  | 11  | 68  | 1.3%  |  | 30, 2.02]  |  |   |
| atti P et al 1998  | 10   | 191   | 4   | 189   | 0.5%  | 2.56 [0.]  | 79, 8.29]  |  |   |
| Total (95% CI)   |  | 5511  |   | 5558  | 100.0%  | 0.92 [0.8  | 3 1 021  |  |   |
| fotal events   | 728  |   | 788   | 0000  |   | 0.02 [0.0  |  |  |   |
| Heterogeneity: Chi <sup>2</sup> = 12.0   | 2, df = 7 (  |   |   | %   |   |  |  | 0.01 0.1   | 1 1 10 10                               |
| est for overall effect: Z =  | 1.54 (P =  | 0.12)   |   |   |   |  | F  |  | rimental Favours control                |
|  |  |   |   |   |   |  |  |  |   |
|  | E  | perime  | ntal  | Con   | trol  |  | Odd  | s Ratio  | Odds Ratio                              |
| Study or Subgroup  | E  | rents   | Total   | Events  |   | Weight   |  | ixed, 95% C  |   |
| .2.1 CCBs vs β-blocke  |  |   |   |   |   |  |  |  |   |
| ALLHAT 2002  |  | 377   | 9048  | 675   | 15255   | 7.3%   | 0.94   | [0.83, 1.07]   | 1                                       |
| Black H et al R2003  |  | 133   | 8179  | 118   | 8297  | 1.8%   | 1.15   | [0.89, 1.47]   | +                                       |
| Borhani NO et al 1996  |  | 6   | 442   | 3   | 441   | 0.0%   |  | [0.50, 8.08]   |   |
| Brown MJ et al 2000  |  | 67  | 3157  | 74  | 3164  | 1.1%   |  | [0.65, 1.26]   | 1                                       |
| Dahlöf B et al 2005  |  | 327   | 9639  | 422   | 9618  | 6.2%   |  | [0.66, 0.89]   |   |
| Ekbom T et al 2004<br>Hansson L et al 1999   |  | 15  | 752   | 20 237  | 756<br>2213   | 0.3%   |  | [0.38, 1.47] [0.71, 1.06]  |   |
|  |  |   |   |   | 2213  |  |  |  |   |
|  |  | 207   | 2196  |   |   |  |  |  | -                                       |
| Hansson L et al 2000   |  | 159   | 2196<br>5410<br>942   | 196   | 5471<br>940   | 2.9%   | 0.81   | [0.66, 1.01]   | -                                       |
| Hansson L et al 2000<br>Malacco E et al 2003   | 999  |   | 5410  | 196   | 5471  | 2.9%   | 0.81<br>0.97   | [0.66, 1.01]<br>[0.61, 1.54]   |   |
| Hansson L et al 2000   | 999  | 159<br>37<br>1  | 5410<br>942   | 196<br>38   | 5471<br>940   | 2.9%<br>0.6%   | 0.81<br>0.97<br>3.10 [   | [0.66, 1.01]<br>[0.61, 1.54]<br>0.13, 76.62]   |   |
| Hansson L et al 2000<br>Malacco E et al 2003<br>NICS-EH Study Group 19   | 999  | 159<br>37<br>1  | 5410<br>942<br>204  | 196<br>38<br>0  | 5471<br>940<br>210  | 2.9%<br>0.6%<br>0.0%   | 0.81<br>0.97<br>3.10 [<br>0.88   | [0.66, 1.01]<br>[0.61, 1.54]   |   |
| Hansson L et al 2000<br>Malacco E et al 2003<br>NICS-EH Study Group 19<br>Pepine CJ et al 2003   | 999  | 159<br>37<br>1<br>176<br>279  | 5410<br>942<br>204<br>11267   | 196<br>38<br>0<br>201   | 5471<br>940<br>210<br>11309   | 2.9%<br>0.6%<br>0.0%<br>3.0%   | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78   | [0.66, 1.01]<br>[0.61, 1.54]<br>0.13, 76.62]<br>[0.72, 1.08]   |   |
| Hansson L et al 2000<br>Malacco E et al 2003<br>NICS-EH Study Group 19<br>Pepine CJ et al 2003<br>Rothwell PM et al 2010<br>Furnbull F 2003<br>Nang Y et al 1998   | 999  | 159<br>37<br>1<br>176<br>279  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141   | 196<br>38<br>0<br>201<br>350  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120   | 2.9%<br>0.6%<br>0.0%<br>3.0%<br>5.2%<br>18.1%<br>0.1%  | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.88<br>0.12   | [0.66, 1.01]<br>[0.61, 1.54]<br>0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]   |   |
| Hansson L et al 2000<br>Malacco E et al 2003<br>NICS-EH Study Group 19<br>Pepine CJ et al 2003<br>Rothwell PM et al 2010<br>Furnbull F 2003<br>Wang Y et al 1998<br>Zanchetti A et al 1998   | 999  | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224  | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232  | 2.9%<br>0.6%<br>0.0%<br>3.0%<br>5.2%<br>18.1%<br>0.1%<br>0.0%  | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.12<br>3.14 [   | [0.66, 1.01]<br>[0.61, 1.54]<br>0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>0.32, 30.37]   |   |
| Hansson L et al 2000<br>Malacco E et al 2003<br>VICS-EH Study Group 19<br>Pepine CJ et al 2003<br>Rothwell PM et al 2010<br>Furnbull F 2003<br>Wang Y et al 1998<br>Zanchetti A et al 1998<br>Zanchetti A et al 2002   | 999  | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177  | 196<br>38<br>0<br>201<br>350<br>1358<br>3   | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157  | 2.9%<br>0.6%<br>0.0%<br>3.0%<br>5.2%<br>18.1%<br>0.1%<br>0.0%<br>0.2%  | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.12<br>3.14 [<br>0.63   | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>[0.32, 30.37]<br>[0.27, 1.46]  |   |
| Hansson L et al 2000<br>Malacco E et al 2003<br>VICS-EH Study Group 15<br>Pepine CJ et al 2003<br>Nothwell PM et al 2010<br>Furmbul F 2003<br>Nang Y et al 1998<br>Zanchetti A et al 1998<br>Zanchetti A et al 2002<br>Subtotal (95% CI)   |  | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224  | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232  | 2.9%<br>0.6%<br>0.0%<br>3.0%<br>5.2%<br>18.1%<br>0.1%<br>0.0%  | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.12<br>3.14 [<br>0.63   | [0.66, 1.01]<br>[0.61, 1.54]<br>0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>0.32, 30.37]   |   |
| Hansson L et al 2000<br>Malacco E et al 2003<br>VICS-EH Study Group 19<br>Pepine CJ et al 2003<br>Rothwell PM et al 2010<br>Furnbull F 2003<br>Vang Y et al 1998<br>Zanchetti A et al 1998<br>Zanchetti A et al 2002<br>Subtotal (95% CI)<br>Total events  |  | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9<br>9   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157  | 2.9%<br>0.6%<br>0.0%<br>3.0%<br>5.2%<br>18.1%<br>0.1%<br>0.0%<br>0.2%  | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.12<br>3.14 [<br>0.63   | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>[0.32, 30.37]<br>[0.27, 1.46]  |   |
| tansson L et al 2000<br>falacco E et al 2003<br>(ICS-EH Study Group 11<br>Pepine CJ et al 2003<br>tothwell PM et al 2010<br>umbull F 2003<br>Vang Y et al 1998<br>anchetti A et al 1998<br>anchetti (a et al 2002<br>ubtotal (95% CI)<br>"otal events<br>tetrogeneity: Chi <sup>2</sup> = 17.  | 02, df = 1   | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9<br>9<br>2795<br>5 (P = 0   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>.32); I <sup>2</sup> =   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157  | 2.9%<br>0.6%<br>0.0%<br>3.0%<br>5.2%<br>18.1%<br>0.1%<br>0.0%<br>0.2%  | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.12<br>3.14 [<br>0.63   | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>[0.32, 30.37]<br>[0.27, 1.46]  |   |
| tansson L et al 2000<br>Malacco E et al 2003<br>Malacco E et al 2003<br>ICS-EH Study Group 11<br>Pepine CJ et al 2003<br>tothwell PM et al 2010<br>umbull F 2003<br>Vang Y et al 1998<br>(anchetti A et al 1998<br>(anchetti A et al 1998<br>(anchetti A et al 2002<br>uibtotat (95% Cl)<br>total events<br>telerogeneity: Ch <sup>p</sup> = 17,<br>est for overall effect: Z =  | 02, df = 1<br>= 5.39 (P -  | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9<br>2795<br>5 (P = 0<br>< 0.0000  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>.32); I <sup>2</sup> =   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157  | 2.9%<br>0.6%<br>0.0%<br>3.0%<br>5.2%<br>18.1%<br>0.1%<br>0.0%<br>0.2%  | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.12<br>3.14 [<br>0.63   | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>[0.32, 30.37]<br>[0.27, 1.46]  |   |
| Iansson L et al 2000<br>Malacco E et al 2003<br>(ICS-EH Study Group 11<br>Pepine CJ et al 2003<br>Othwell PM et al 2010<br>Yung Y et al 2010<br>Yung Y et al 1998<br>Zanchetti A et al 2002<br>Wang Y et al 2002<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction<br>Construction   | 02, df = 1<br>= 5.39 (P -  | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9<br>2795<br>5 (P = 0<br>< 0.0000  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>.32); I <sup>2</sup> =   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%   | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157  | 2.9%<br>0.6%<br>0.0%<br>3.0%<br>5.2%<br>18.1%<br>0.1%<br>0.0%<br>0.2%  | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.12<br>3.14 [<br>0.63<br>0.87   | [0.66, 1.01]<br>[0.61, 1.54]<br>0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>0.32, 30.37]<br>[0.27, 1.46]<br>[0.83, 0.92]   |   |
| iansson L et al 2000<br>Malacco E et al 2003<br>WICS-EH Study Group 11<br>Pepine CJ et al 2003<br>Softweil FM et al 2010<br>Turnbuil F 2003<br>Mang Y et al 1998<br>Zanchetti A et al 1998<br>Zanchetti A et al 2002<br>Subtotal (95% CI)<br>Fotal events<br>Heterogeneity: Chi <sup>p</sup> = 17.<br>Test for overall effect. Z =<br>1.2.2 CCBs vs β-blocke<br>Jack H et al R2003   | 02, df = 1<br>= 5.39 (P -  | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9<br>2795<br>5 (P = 0<br>< 0.0000<br>uretics   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>.32); I <sup>2</sup> =   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%   | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157<br>105829<br>8297  | 2.9%<br>0.6%<br>0.0%<br>3.0%<br>5.2%<br>0.1%<br>0.1%<br>0.2%<br>50.0%  | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.12<br>3.14 [<br>0.63<br>0.87   | [0.66, 1.01]<br>[0.61, 1.54]<br>(0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>(0.32, 30.37]<br>[0.27, 1.46]<br>[0.83, 0.92]   |   |
| iansson L et al 2000<br>Malacco E et al 2003<br>(ICS-EH Study Group 1f<br>Pepine CJ et al 2003<br>Softwell FM et al 2010<br>Journbull F 2003<br>Mang Y et al 1998<br>Zanchetti A et al 1998<br>Zanchetti A et al 2002<br>Subtotal (195% CI)<br>Total events<br>Idetrogeneity: ChF = 17.<br>Fest for overall effect: Z =<br>1.2.2 CCBs vs β-blocke  | 02, df = 1<br>= 5.39 (P -  | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9<br>2795<br>5 (P = 0<br>< 0.0000<br>uretics<br>133  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>.32); I <sup>2</sup> =   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%   | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157<br>105829  | 2.9%<br>0.6%<br>3.0%<br>5.2%<br>18.1%<br>0.1%<br>0.2%<br>50.0%   | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.12<br>3.14 [<br>0.63<br>0.87<br>1.15<br>0.91   | [0.66, 1.01]<br>[0.61, 1.54]<br>0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>0.32, 30.37]<br>[0.27, 1.46]<br>[0.83, 0.92]   |   |
| iteration L et al 2000<br>MicSc-EH Study Group 11<br>Opino CJ et al 2003<br>ViCS-EH Study Group 12<br>Opino CJ et al 2003<br>Softwell PM et al 2010<br>Vang Y et al 1998<br>Zanchetti A et al 1998<br>Zanchetti A et al 1998<br>Zanchetti A et al 1998<br>Canchetti A et al 1998<br>Canchetti A et al 1998<br>Sanchetti A et al 1998<br>Sanchetti A et al 2002<br>Victoria ventis<br>Fest for overall effect: Z = 1<br>1.2.2 CCBs vs β-blocke<br>Slack H et al 2000  | 02, df = 1<br>= 5.39 (P -  | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9<br>0<br>3<br>9<br>5 (P = 0<br>< 0.0000<br>uretics<br>133<br>67   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>.32); F =<br>11)<br>8179<br>3157<br>752<br>2196  | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157<br>105829<br>8297<br>3164<br>756<br>2213   | 2.9%<br>0.6%<br>0.0%<br>3.0%<br>5.2%<br>18.1%<br>0.1%<br>0.2%<br>50.0%   | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.12<br>3.14 [<br>0.63<br>0.87<br>1.15<br>0.91<br>0.75   | [0.66, 1.01]<br>[0.61, 1.54]<br>0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>0.32, 30.37]<br>[0.27, 1.46]<br>[0.83, 0.92]<br>[0.89, 1.47]<br>[0.65, 1.26]   |   |
| Innson Let al 2000<br>MIGS-EH Study Group 11<br>Papine CJ et al 2003<br>WIGS-EH Study Group 12<br>Papine CJ et al 2003<br>Winny T et al 1968<br>Canchetti et al 1968<br>Canchetti et al 1968<br>Canchetti et al 2002<br>Subtolal (95% CI)<br>Colal events<br>Actor overall effect; Z =<br>1.2.2 CCBs vs β-blocke<br>Back H et al 2004  | 02, df = 1<br>= 5.39 (P -  | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9<br>2795<br>5 (P = 0<br>< 0.0000<br>uretics<br>133<br>67<br>15<br>207<br>159  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>32); P =<br>11)<br>8179<br>3157<br>752<br>2196<br>5410   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>20  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157<br>105829<br>8297<br>3164<br>756<br>2213<br>5471   | 2.9%<br>0.6%<br>0.0%<br>5.2%<br>18.1%<br>0.0%<br>0.2%<br>50.0%   | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.88<br>0.88<br>0.12<br>3.14 [<br>0.63<br>0.87<br>1.15<br>0.97<br>0.75<br>0.87   | [0.66, 1.01]<br>[0.61, 1.54]<br>(0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>(0.27, 1.46]<br>[0.83, 0.92]<br>[0.89, 1.47]<br>[0.65, 1.26]<br>[0.63, 1.47]  |   |
| dranson Let al 2000<br>MIGS-EH Shudy Group II<br>Macco Et al 2003<br>MIGS-EH Shudy Group II<br>Pagine CJ et al 2003<br>Softwall PM et al 2003<br>Unitodial PM et al 2003<br>Unitodial (9% CI)<br>Colad eventis<br>Atelerogenety: Ch <sup>2</sup> = 17,<br>Colad eventis<br>Atelerogenety: Ch <sup>2</sup> = 14,<br>22, CCBs vs $\beta$ -blocke<br>Black H et al R2003<br>Show M Let al R2003<br>Chow MJ et al 2000<br>Chow MJ et al 2000<br>Chow MJ et al 2000   | 02, df = 1<br>= 5.39 (P ·  | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9<br>2795<br>5 (P = 0<br>< 0.0000<br>uretics<br>133<br>67<br>15<br>207<br>159<br>999   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>.32); P =<br>11)<br>8179<br>3157<br>752<br>2196<br>5410<br>31031   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>20<br>237   | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157<br>105829<br>8297<br>3164<br>756<br>2213<br>5471<br>37418  | 2.9%<br>0.6%<br>0.0%<br>5.2%<br>18.1%<br>0.0%<br>50.0%<br>1.8%<br>1.1%<br>0.3%<br>3.3%<br>2.9%<br>8.1%   | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.88<br>0.12<br>3.14 [<br>0.63<br>0.87<br>1.15<br>0.91<br>0.75<br>0.87<br>0.87<br>0.88   | [0.66, 1.01]<br>[0.61, 1.54]<br>(0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>(0.27, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 1.26]<br>[0.38, 1.47]<br>[0.71, 1.06]<br>[0.68, 1.01]<br>[0.68, 1.01]<br>[0.68, 1.01]  |   |
| Imason Let al 2000<br>MIGS-EH Study Group II<br>Allacob E et al 2003<br>VICS-EH Study Group II<br>Penne CJ et al 2003<br>Softweil PM et al 2003<br>Vang Y et al 1998<br>Eanchett A et al 2002<br>Autotal (95% C)]<br>Total events<br>deterogeneity: Chi'r = 17.<br>Test for overall effect: Z -<br>I.22 CCBs vs β-blocks<br>Mack H et al 2004<br>Hansson L et al 1999<br>Easch H et al 2004<br>Hansson L et al 2004<br>Vansson L et al 2004  | 02, df = 1<br>= 5.39 (P<br>rs and Di   | 159<br>37<br>1<br>176<br>279<br>999<br>0<br>3<br>9<br>2795<br>5 (P = 0<br>< 0.0000<br>uretics<br>133<br>67<br>15<br>207<br>159<br>999   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>32); P =<br>11)<br>8179<br>3157<br>752<br>2196<br>5410   | 196<br>38<br>0<br>201<br>3500<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>20<br>237<br>196<br>1358   | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157<br>105829<br>8297<br>3164<br>756<br>2213<br>5471   | 2.9%<br>0.6%<br>0.0%<br>5.2%<br>18.1%<br>0.0%<br>0.2%<br>50.0%   | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.88<br>0.12<br>3.14 [<br>0.63<br>0.87<br>1.15<br>0.91<br>0.75<br>0.87<br>0.87<br>0.88   | [0.66, 1.01]<br>[0.61, 1.54]<br>(0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>(0.27, 1.46]<br>[0.83, 0.92]<br>[0.89, 1.47]<br>[0.65, 1.26]<br>[0.38, 1.47]<br>[0.71, 1.06]<br>[0.71, 1.06]  |   |
| $\label{eq:constraints} \\ \begin{tabular}{lllllllllllllllllllllllllllllllllll$  | 02, df = 1<br>= 5.39 (P<br>rs and Di   | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 5 \ (P=0\\ 0,0000\\ uretics\\ 133\\ 67\\ 15\\ 207\\ 159\\ 999\\ 1580\\ \end{array}$  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>.32): F =<br>11)<br>8179<br>3157<br>752<br>2196<br>5410<br>31031<br>50725  | 196<br>38<br>0<br>2011<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>200<br>237<br>196<br>1358<br>2003  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157<br>105829<br>8297<br>3164<br>756<br>2213<br>5471<br>37418  | 2.9%<br>0.6%<br>0.0%<br>5.2%<br>18.1%<br>0.0%<br>50.0%<br>1.8%<br>1.1%<br>0.3%<br>3.3%<br>2.9%<br>8.1%   | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.88<br>0.12<br>3.14 [<br>0.63<br>0.87<br>1.15<br>0.91<br>0.75<br>0.87<br>0.87<br>0.88   | [0.66, 1.01]<br>[0.61, 1.54]<br>(0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>(0.27, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 1.26]<br>[0.38, 1.47]<br>[0.71, 1.06]<br>[0.68, 1.01]<br>[0.68, 1.01]<br>[0.68, 1.01]  |   |
| Iamson Let al 2000<br>MICS-EH Study Group MICS-EH Study Group Mang Y et al 1998<br>Canchetti A et al 2003<br>Mang Y et al 1998<br>Canchetti A et al 2002<br>MICS-EH Study Group MICS-CH Study MICS-<br>Total events<br>deterogeneity: ChIF = 17.<br>Test for overall effect: Z -<br>2.2 CCBw sp. Biotocke<br>MICS-CH Study MICS-<br>MICS-MICS-MICS-<br>MICS-MICS-MICS-<br>MICS-MICS-MICS-<br>MICS-MICS-MICS-<br>MICS-MICS-<br>MICS-MICS-<br>MICS-MICS-<br>MICS-MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>MICS-<br>M | 02, df = 1<br>= 5.39 (P -<br>rs and Di<br>4, df = 5 (  | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 2795\\ 5\ (P=0\\ 0\\ 0\\ 00000\\ uretics\\ 133\\ 67\\ 15\\ 207\\ 159\\ 999\\ 1580\\ P=0.42\\ \end{array}$  | 5410<br>942<br>204<br>11267<br>9302<br>331031<br>141<br>224<br>1177<br>933111<br>322; P =<br>1177<br>933111<br>332; P =<br>1177<br>933111<br>332; P =<br>2196<br>5410<br>31031<br>50725<br>2196<br>2410<br>31031<br>31031<br>2196<br>219 - 219<br>2196<br>219 - 219<br>2196<br>219 - 219<br>2196<br>219 - 219<br>2197<br>2196<br>2197<br>2197<br>2197<br>2197<br>2197<br>2197<br>2197<br>2197   | 196<br>38<br>0<br>2011<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>200<br>237<br>196<br>1358<br>2003  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157<br>105829<br>8297<br>3164<br>756<br>2213<br>5471<br>37418  | 2.9%<br>0.6%<br>0.0%<br>5.2%<br>18.1%<br>0.0%<br>50.0%<br>1.8%<br>1.1%<br>0.3%<br>3.3%<br>2.9%<br>8.1%   | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.88<br>0.12<br>3.14 [<br>0.63<br>0.87<br>1.15<br>0.91<br>0.75<br>0.87<br>0.87<br>0.88   | [0.66, 1.01]<br>[0.61, 1.54]<br>(0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>(0.27, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 1.26]<br>[0.38, 1.47]<br>[0.71, 1.06]<br>[0.68, 1.01]<br>[0.68, 1.01]<br>[0.68, 1.01]  |   |
| dranson Let al 2000<br>MIGS-EH Shudy Group II<br>Macco Et al 2003<br>MIGS-EH Shudy Group II<br>Pagine CJ et al 2003<br>Softwall PM et al 2003<br>Unitodial PM et al 2003<br>Unitodial (9% CI)<br>Colad eventis<br>Atelerogenety: Ch <sup>2</sup> = 17,<br>Colad eventis<br>Atelerogenety: Ch <sup>2</sup> = 14,<br>22, CCBs vs $\beta$ -blocke<br>Black H et al R2003<br>Show M Let al R2003<br>Chow MJ et al 2000<br>Chow MJ et al 2000<br>Chow MJ et al 2000   | 02, df = 1<br>= 5.39 (P<br>rs and Di<br>4, df = 5 (<br>= 3.37 (P   | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 2795\\ 5\ (P=0\\ 0\\ 0\\ 00000\\ uretics\\ 133\\ 67\\ 15\\ 207\\ 159\\ 999\\ 1580\\ P=0.42\\ \end{array}$  | 5410<br>942<br>204<br>11267<br>9302<br>331031<br>141<br>224<br>1177<br>933111<br>322; P =<br>1177<br>933111<br>332; P =<br>1177<br>933111<br>332; P =<br>2196<br>5410<br>31031<br>50725<br>2196<br>2410<br>31031<br>31031<br>2196<br>219 - 219<br>2196<br>219 - 219<br>2196<br>219 - 219<br>2196<br>219 - 219<br>2197<br>2196<br>2197<br>2197<br>2197<br>2197<br>2197<br>2197<br>2197<br>2197   | 196<br>38<br>0<br>2011<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>200<br>237<br>196<br>1358<br>2003  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157<br>105829<br>8297<br>3164<br>756<br>2213<br>5471<br>37418  | 2.9%<br>0.6%<br>0.0%<br>5.2%<br>18.1%<br>0.0%<br>50.0%<br>1.8%<br>1.1%<br>0.3%<br>3.3%<br>2.9%<br>8.1%   | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.88<br>0.12<br>3.14 [<br>0.63<br>0.87<br>1.15<br>0.91<br>0.75<br>0.87<br>0.87<br>0.88   | [0.66, 1.01]<br>[0.61, 1.54]<br>(0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>(0.27, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 1.26]<br>[0.38, 1.47]<br>[0.71, 1.06]<br>[0.68, 1.01]<br>[0.68, 1.01]<br>[0.68, 1.01]  |   |
| $\label{eq:constraints} \begin{array}{l} \mbox{diascot} \in t \neq al 2000 \\ \mbox{diascot} \in t \neq al 2003 \\ \mbox{discot} = t \neq al 2004 \\ \mbo$   | 02, df = 1<br>= 5.39 (P<br>rs and Di<br>4, df = 5 (<br>= 3.37 (P   | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 2795\\ 5\ (P=0\\ 0\\ 0\\ 00000\\ uretics\\ 133\\ 67\\ 15\\ 207\\ 159\\ 999\\ 1580\\ P=0.42\\ \end{array}$  | 5410<br>942<br>204<br>11267<br>9302<br>331031<br>141<br>224<br>1177<br>933111<br>322; P =<br>1177<br>933111<br>332; P =<br>1177<br>933111<br>332; P =<br>2196<br>5410<br>31031<br>50725<br>2196<br>2410<br>31031<br>31031<br>2196<br>219 - 219<br>2196<br>219 - 219<br>2196<br>219 - 219<br>2196<br>219 - 219<br>2197<br>2196<br>2197<br>2197<br>2197<br>2197<br>2197<br>2197<br>2197<br>2197   | 196<br>38<br>0<br>2011<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>200<br>237<br>196<br>1358<br>2003  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>1157<br>105829<br>8297<br>3164<br>756<br>2213<br>5471<br>37418  | 2.9%<br>0.6%<br>0.0%<br>5.2%<br>18.1%<br>0.0%<br>50.0%<br>1.8%<br>1.1%<br>0.3%<br>3.3%<br>2.9%<br>8.1%   | 0.81<br>0.97<br>3.10 (<br>0.88<br>0.78<br>0.88<br>0.78<br>0.87<br>3.14 (<br>0.63<br>0.87<br>1.15<br>0.91<br>0.75<br>0.87<br>0.87<br>0.88<br>0.89   | [0.66, 1.01]<br>[0.61, 1.54]<br>(0.13, 76.62]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>(0.27, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 1.26]<br>[0.38, 1.47]<br>[0.71, 1.06]<br>[0.68, 1.01]<br>[0.68, 1.01]<br>[0.68, 1.01]  | +++++++++++++++++++++++++++++++++++++++ |
| Iamson Let al 2000<br>MICS-EH Study Group II<br>Alacco E et al 2003<br>MICS-EH Study Group II<br>Combul F 2003<br>Vang Y et al 1998<br>Canchetti A et al 2003<br>Vang Y et al 1998<br>Canchetti A et al 2002<br>Vathotal (95% C)<br>Total events<br>deterogeneity: Chi" = 17.<br>Test for overall effect: Z -<br>2.2 CCBw sp. Biotock-<br>theory and the 2003<br>Yanson L et al 2004<br>Vansson L et al 2  | 02, df = 1<br>= 5.39 (P<br>rs and Di<br>4, df = 5 (<br>= 3.37 (P   | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\$   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>   | 196<br>38<br>0<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>200<br>237<br>196<br>1358<br>2003<br>%   | 5471<br>940<br>11309<br>9228<br>37418<br>120<br>232<br>1157<br>3164<br>756<br>2213<br>3764<br>756<br>2213<br>37418<br>577319  | 2.9%<br>0.6%<br>0.0%<br>5.2%<br>18.1%<br>0.1%<br>0.2%<br>50.0%<br>1.8%<br>50.0%<br>1.8%<br>3.3%<br>2.9%<br>18.1%<br>27.4%  | 0.81<br>0.97<br>3.10 (<br>0.88<br>0.78<br>0.88<br>0.12<br>3.14 (<br>0.63<br>0.87<br>1.15<br>0.91<br>0.75<br>0.91<br>0.75<br>0.87<br>0.88<br>0.88<br>0.88<br>0.88   | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.67, 0.92]<br>[0.67, 0.92]<br>[0.72, 1.08]<br>[0.01, 2.32]<br>[0.32, 0.37]<br>[0.27, 1.46]<br>[0.83, 0.92]<br>[0.65, 1.26]<br>[0.65, 1.26]<br>[0.66, 1.01]<br>[0.66, 1.01]<br>[0.66, 0.95]<br>[0.83, 0.95]   |   |
| Imason Let al 2000<br>MIGS-EH Study Group J<br>MIGS-EH Study Group J<br>Penne CJ et al 2003<br>Softwall PM et al 2010<br>Tumbul IF 2003<br>Wang Y et al 1998<br>Earnchett A et al 2003<br>Earnchett A et al 2003<br>Work CM et al 1999<br>Earnchett A et al 2004<br>Heterogeneity: C/H" = 17.<br>Fest for overall effect: Z<br>subtotal (95% C)]<br>Total events<br>Heterogeneity: C/H" = 14.<br>2004<br>Hansson L et al 2004<br>Wansson L et al 2004<br>Wansson L et al 2004<br>Wansson L et al 2004<br>Wansson L et al 2004<br>Fest for overall effect: Z<br>subtotal (95% C)]<br>Total events<br>Heterogeneity: C/H" = 4.9<br>Fest for overall effect: Z<br>subtotal (95% C)]<br>Total events<br>Heterogeneity: C/H" = 4.9<br>Fest for overall effect: Z<br>subtotal (95% C)]<br>Total events<br>Heterogeneity: C/H" = 4.9<br>Fest for overall effect: Z<br>subtotal (95% C)]   | 02, df = 1<br>= 5.39 (P<br>rs and Di<br>4, df = 5 (<br>= 3.37 (P   | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 153\\ 07\\ 15\\ 207\\ 159\\ 999\\ 1580\\ P=0.42\\ 0.0007\\ 377\\ \end{array}$  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>933111<br>8179<br>93117<br>752<br>2196<br>031031<br>3157<br>752<br>2196<br>031031<br>31057<br>5410  | 196<br>38<br>0<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>200<br>237<br>196<br>1358<br>2003<br>%   | 5471<br>940<br>210<br>11309<br>9228<br>33418<br>120<br>2322<br>1157<br>105829<br>8297<br>3164<br>2213<br>5471<br>35471<br>3748<br>57319   | 2.9%<br>0.6%<br>5.2%<br>18.1%<br>0.1%<br>0.2%<br>50.0%<br>1.8%<br>2.9%<br>18.1%<br>2.7.4%  | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.78<br>0.88<br>0.72<br>0.83<br>0.83<br>0.87<br>1.15<br>0.97<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.8  | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.72, 1.03]<br>[0.72, 1.03]<br>[0.72, 1.03]<br>[0.71, 1.03]<br>[0.71, 1.03]<br>[0.71, 1.03]<br>[0.71, 1.03]<br>[0.72, 1.46]<br>[0.74, 1.46]<br>[0.74, 1.46]<br>[0.74, 1.46]<br>[0.74, 1.46]<br>[0.74, 1.46]<br>[0.83, 0.95]<br>[0.83, 0.95]   |   |
| Imason Let al 2000<br>MIGS-EH Study Group II<br>Papine CJ et al 2003<br>Softwali PM et al 2010<br>Immbil E 2003<br>Softwali PM et al 2010<br>Immbil E 2003<br>Mang Y et al 1998<br>Earnchetti A et al 2002<br>Subtotal (19% C)<br>Total events<br>Heterogenetic: Lohir = 17.<br>Test for overall effect: Z<br>1.2 2 CCBs vs β-blocket<br>Statom T et al 2003<br>Subtotal (19% C)<br>Total events<br>Heterogenetic: Lohir = 17.<br>Cala events<br>Heterogenetic: Lohir = 17.<br>Cala events<br>Heterogenetic: Lohir = 17.<br>Cala events<br>Heterogenetic: Lohir = 4.<br>Subtotal (19% C)<br>Test for overall effect: Z<br>1.2 3 CCBs vs Dutrettics<br>Luhhan IXO et al 1996<br>Malacco Et al 1996<br>Malacco Et al 1996<br>Malacco Et al 2003  | 02, df = 1<br>= 5.39 (P<br>rs and Di<br>4, df = 5 (<br>= 3.37 (P   | $\begin{array}{c} 159\\ 37\\ 1\\ 1\\ 176\\ 279\\ 999\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\$   | 5410<br>942<br>204<br>11267<br>9302<br>204<br>11267<br>9302<br>204<br>1177<br>93157<br>752<br>2196<br>5410<br>9048<br>442<br>942<br>942   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>20<br>237<br>196<br>1358<br>2003<br>%   | 5471<br>940<br>11309<br>9228<br>9228<br>2322<br>1157<br>3164<br>5213<br>5471<br>37418<br>57319<br>15255<br>441<br>940<br>210  | 2.9%<br>0.6%<br>0.0%<br>3.0%<br>5.2%<br>18.1%<br>0.1%<br>5.2%<br>18.1%<br>0.0%<br>50.0%<br>50.0%<br>7.3%<br>0.0%<br>0.2%   | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.72<br>3.14 [<br>0.63<br>0.87<br>1.15<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87   | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.12, 7, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.93]<br>[0.83, 0.95]<br>[0.83, 0.95]<br>[0.83, 0.95]  |   |
| Iamson Let al 2000<br>MICS-EH Study Group J<br>MICS-EH Study Group J<br>Compane CJ et al 2003<br>Varbauel IPM et al 2010<br>Varbauel IPM et al 2010<br>Varbauel A et al 2003<br>Varbauel A et al 2003<br>Varbauel A et al 2004<br>Varbauel K et al 2004<br>Varbauel K et al 2004<br>Varbauel K et al 2004<br>Varbauel A et al 2003<br>Varbauel A et al 2003<br>VARDA et al 1096  | 02, df = 1<br>= 5.39 (P<br>rs and Di<br>4, df = 5 (<br>= 3.37 (P   | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 9999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\$  | 5410<br>942<br>204<br>11267<br>9302<br>9302<br>9302<br>1141<br>224<br>1177<br>1375<br>2196<br>31177<br>117<br>3157<br>752<br>2196<br>31031<br>3157<br>752<br>2196<br>31031<br>31031<br>31031<br>2197<br>9048<br>442<br>942<br>204   | 196<br>38 8<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>200<br>237<br>196<br>1358<br>2003<br>%  | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>232<br>232<br>213<br>5471<br>105829<br>8297<br>3164<br>57319<br>57319<br>15255<br>57319   | 2 9%<br>0.6%<br>0.0%<br>5.2%<br>18.1%<br>0.2%<br>52.0%<br>18.1%<br>0.2%<br>50.0%<br>1.8%<br>0.2%<br>50.0%<br>1.8%<br>0.3%<br>1.8%<br>2.7.4%  | 0.81<br>0.97<br>0.888<br>0.788<br>0.888<br>0.888<br>0.889<br>0.887<br>0.83<br>0.83<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.89<br>0.89<br>0.89<br>0.89<br>0.89<br>0.94<br>0.89<br>0.94<br>0.89<br>0.94<br>0.89<br>0.94<br>0.89<br>0.94<br>0.89<br>0.94<br>0.88<br>0.88<br>0.72<br>0.75<br>0.75<br>0.75<br>0.75<br>0.75<br>0.75<br>0.75<br>0.75 | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>[0.27, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 1.07]<br>[0.76, 1.60]<br>[0.86, 1.01]<br>[0.86, 1.01]<br>[0.83, 0.95]<br>[0.83, 0.95]   |   |
| Imason Let al 2000<br>MIGS-EH Study Group II<br>Papine CJ et al 2003<br>VICS-EH Study Group II<br>Tumbuli E 2003<br>Vahag Y et al 2003<br>Vahag Y et al 1998<br>Eanchetti A et al 2003<br>Vahag Y et al 1998<br>Eanchetti A et al 2004<br>Vahag Y et al 1998<br>Stutchal (95% C)<br>Total events<br>Heterogeneity: Chif = 17,<br>Test for overall effect: 2<br>J 2.2 CCBs vo β-blocket<br>Manson L et al 1999<br>Stutchal (95% C)<br>Total events<br>Heterogeneity: Chif = 4<br>Test for overall effect: 2<br>J 2.3 CCBs vo further<br>La C CBS vo Further<br>La C C CBS vo Further<br>La C C CBS vo Further<br>La C C C C C C C C C C C C C C C C C C C   | 02, df = 1<br>= 5.39 (P<br>rs and Di<br>4, df = 5 (<br>= 3.37 (P   | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\$   | 5410<br>942<br>204<br>11267<br>9302<br>204<br>11267<br>9302<br>204<br>1117<br>303111<br>32); P =<br>117<br>33111<br>32); P =<br>117<br>33111<br>32); P =<br>117<br>3157<br>752<br>2196<br>5410<br>31031<br>50725<br>219<br>9048<br>442<br>942<br>204<br>1411<br>224   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>20<br>237<br>196<br>1358<br>2003<br>%   | 5471<br>940<br>11309<br>9228<br>37418<br>37418<br>120<br>232<br>232<br>21157<br>3164<br>756<br>57319<br>15255<br>441<br>15255<br>441<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>21   | 2 9%<br>0 6%<br>0 0%<br>3 0%<br>5 2%<br>18.1%<br>0 1%<br>5 2%<br>18.1%<br>0 2%<br>5 0.0%<br>1.8%<br>27.4%<br>7.3%<br>0.6%<br>0.6%<br>0.0%<br>0.6%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0 | 0.81<br>0.97<br>0.82<br>0.82<br>0.78<br>0.88<br>0.78<br>0.88<br>0.87<br>0.83<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87   | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.12, 7, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.93]<br>[0.83, 0.95]<br>[0.83, 0.95]<br>[0.83, 0.95]<br>[0.13, 76.62]<br>[0.13, 76.62]<br>[0.13, 76.62]   |   |
| Intescon Let al 2000<br>IIICSE-IEL Study Group III<br>Pepine C2 et al 2003<br>IIICSE-IEL Study Group III<br>Pepine C2 et al 2003<br>Vang Y et al 1998<br>anchetti A et al 2003<br>Vang Y et al 1998<br>anchetti A et al 2004<br>Vatotal (195% C)<br>Otal events<br>Ieterogeneity: Chi" = 17.<br>est for overall effect: Z -<br>Z CCBW vs β-biocke<br>Itack H et al 72004<br>Vatotal (195% C)<br>Otal events<br>Ieterogeneity: Chi" = 14.<br>2004<br>Imasson L et al 2004<br>Vatotal (195% C)<br>Otal events<br>Ieterogeneity: Chi" = 4.<br>2 est for overall effect: Z -<br>2 est for overall effect: Z -<br>2.3 CCBW vs Diuretics<br>LLHAT 2002<br>UICSE-IEI Study Group 15<br>Vang Y et al 1998<br>anchetti A et al 1998<br>anchetti A et al 1998<br>unchetti A et al 1998  | 02, df = 1<br>= 5.39 (P<br>rs and Di<br>4, df = 5 (<br>= 3.37 (P   | $\begin{array}{c} 159\\ 37\\ 1\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 5\\ (P=0, 0, 000)\\ uretics\\ 133\\ 67\\ 15\\ 207\\ 15\\ 999\\ 9\\ 999\\ 9\\ 1580\\ 377\\ 6\\ 37\\ 1\\ 0\\ 3\\ 3\end{array}$   | 5410<br>942<br>204<br>11267<br>9302<br>9302<br>9302<br>1141<br>224<br>1177<br>1375<br>2196<br>31177<br>117<br>3157<br>752<br>2196<br>31031<br>3157<br>752<br>2196<br>31031<br>31031<br>31031<br>2197<br>9048<br>442<br>942<br>204   | 196<br>38 8<br>0<br>201<br>1358<br>3<br>1<br>1<br>4<br>3710<br>12%<br>118<br>74<br>200<br>237<br>196<br>1358<br>2003<br>%<br>675<br>3<br>38<br>0<br>0<br>3<br>1   | 5471<br>940<br>210<br>11309<br>9228<br>37418<br>120<br>232<br>232<br>232<br>213<br>5471<br>105829<br>8297<br>3164<br>57319<br>57319<br>15255<br>57319   | 2 9%<br>0.6%<br>0.0%<br>5.2%<br>18.1%<br>0.2%<br>52.0%<br>18.1%<br>0.2%<br>50.0%<br>1.8%<br>0.2%<br>50.0%<br>1.8%<br>0.3%<br>1.8%<br>2.7.4%  | 0.81<br>0.97<br>0.82<br>0.82<br>0.78<br>0.88<br>0.78<br>0.88<br>0.87<br>0.83<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87   | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.67, 0.92]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>[0.81, 0.96]<br>[0.01, 2.32]<br>[0.27, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 1.07]<br>[0.76, 1.60]<br>[0.86, 1.01]<br>[0.86, 1.01]<br>[0.83, 0.95]<br>[0.83, 0.95]   |   |
| Iamson Let al 2000<br>MICS-EH Study Group II<br>Macro E et al 2003<br>MICS-EH Study Group II<br>mubuli F 2003<br>Vang Y et al 1098<br>Canchetti A et al 2003<br>Vang Y et al 1098<br>Canchetti A et al 2002<br>Vathoral (45% C)<br>Vathal (41)<br>Vathal (41)<br>Vathal (41)<br>Vathal (41)<br>Vathal (42)<br>Vathal  | 02, df = 1<br>= 5.39 (P<br>rs and Di<br>= 3.37 (P<br>=   | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 2795\\ 5\ (P=0\\ c\ 0.0000\\ urretics\\ 133\\ 67\\ 15\\ 207\\ 15\\ 999\\ 999\\ 1580\\ P=0.42\\ c\\ 377\\ 6\\ 37\\ 1\\ 0\\ 3\\ 424 \end{array}$   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>1224<br>1177<br>93111<br>32), P =<br>11)<br>3157<br>752<br>2196<br>5410<br>50725<br>2); P = 0'<br>9048<br>442<br>942<br>204<br>141<br>224<br>11001   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>20<br>237<br>796<br>1358<br>2003<br>%<br>675<br>3<br>38<br>0<br>33<br>1<br>1<br>720   | 5471<br>940<br>11309<br>9228<br>37418<br>37418<br>120<br>232<br>232<br>21157<br>3164<br>756<br>57319<br>15255<br>441<br>15255<br>441<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>21   | 2 9%<br>0 6%<br>0 0%<br>3 0%<br>5 2%<br>18.1%<br>0 1%<br>5 2%<br>18.1%<br>0 2%<br>5 0.0%<br>1.8%<br>27.4%<br>7.3%<br>0.6%<br>0.6%<br>0.0%<br>0.6%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0 | 0.81<br>0.97<br>0.82<br>0.82<br>0.78<br>0.88<br>0.78<br>0.88<br>0.87<br>0.83<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87   | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.12, 7, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.93]<br>[0.83, 0.95]<br>[0.83, 0.95]<br>[0.83, 0.95]<br>[0.13, 76.62]<br>[0.13, 76.62]<br>[0.13, 76.62]   |   |
| Intescon Let al 2000<br>IIICS-EIL Study Group III<br>Pepine C2 et al 2003<br>IIICS-EIL Study Group III<br>Pepine C2 et al 2003<br>Iothwell PM et al 2010<br>Iothwell A et al 2003<br>Iothwell A et al 2003<br>Iothotal (45% C)<br>Iotal events<br>Ieterogeneity: Chil" = 17.<br>est for overall effect: Z<br>- 22 CCBW vs β-blocka<br>Itack H et al 7800<br>Intesch H et al 2004<br>Imbulctal (45% C)<br>Iotal events<br>Ieterogeneity: Chil" = 17.<br>est for overall effect: Z<br>- 23 CCBW vs Di-Iotack<br>Intesch H et al 2004<br>Imbulctal (45% C)<br>Iotal events<br>Ieterogeneity: Chil" = 14.<br>est for overall effect: Z<br>- 23 CCBW vs Diuretics<br>LLHAT 2002<br>IUCS-EIT Study Group SI<br>Iotacco E et al 2003<br>IUCS-EIT Study Group SI<br>Iotacco E et al 2003<br>IUCS-EIT Study Group SI<br>Iotacit A et al 1989<br>Interting V et al 1996<br>Iotacit A et al 1989<br>Interting V et al 1996<br>Iotacit A et al 1989<br>Interting V et al 1996<br>Iotacit A et al 1989<br>Interting V C(L)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interting V C)<br>Cal events<br>Ieterogeneity: Chil" et A et al 1984<br>Interti   | 02, df = 1<br>5,39 (P<br>4, df = 5<br>5,37 (P<br>9<br>9<br>9<br>9<br>9<br>9<br>9<br>9<br>9<br>9<br>9<br>9<br>9<br>9  | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\$   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>1224<br>1177<br>93111<br>32), P =<br>11)<br>3157<br>752<br>2196<br>5410<br>50725<br>2); P = 0'<br>9048<br>442<br>942<br>204<br>141<br>224<br>11001   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>20<br>237<br>796<br>1358<br>2003<br>%<br>675<br>3<br>38<br>0<br>33<br>1<br>1<br>720   | 5471<br>940<br>11309<br>9228<br>37418<br>37418<br>120<br>232<br>232<br>21157<br>3164<br>756<br>57319<br>15255<br>441<br>15255<br>441<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>21   | 2 9%<br>0 6%<br>0 0%<br>3 0%<br>5 2%<br>18.1%<br>0 1%<br>5 2%<br>18.1%<br>0 2%<br>5 0.0%<br>1.8%<br>27.4%<br>7.3%<br>0.6%<br>0.6%<br>0.0%<br>0.6%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0 | 0.81<br>0.97<br>0.82<br>0.82<br>0.78<br>0.88<br>0.78<br>0.88<br>0.87<br>0.83<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87   | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.12, 7, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.93]<br>[0.83, 0.95]<br>[0.83, 0.95]<br>[0.83, 0.95]<br>[0.13, 76.62]<br>[0.13, 76.62]<br>[0.13, 76.62]   |   |
| Imason Let al 2000<br>MIGS-EH Study Group II<br>Alacco E et al 2003<br>VIGS-EH Study Group II<br>Penne CJ et al 2003<br>Softwall PM et al 2010<br>Xanchetti A et al 2003<br>Xanchetti A et al 2003<br>Xanchetti A et al 2003<br>Vibrotal (95% C)]<br>Total events<br>deterogeneity: C/H* = 17.<br>Test for overall effect: Z +<br>Xanson L et al 2004<br>Amason L et al 2004<br>Amason L et al 2004<br>Vibrotal (95% C)]<br>Total events<br>deterogeneity: C/H* = 4.9<br>Vibrotal (95% C)]   | 02, df = 1<br>5,39 (P<br>4, df = 5<br>3,37 (P<br>4<br>999)<br>2, df = 5 (<br>909)  | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\$   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>1224<br>1177<br>93111<br>32), P =<br>11)<br>3157<br>752<br>2196<br>5410<br>50725<br>2); P = 0'<br>9048<br>442<br>942<br>204<br>141<br>224<br>11001   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>20<br>237<br>796<br>1358<br>2003<br>%<br>675<br>3<br>38<br>0<br>33<br>1<br>1<br>720   | 5471<br>940<br>11309<br>9228<br>37418<br>37418<br>120<br>232<br>232<br>21157<br>3164<br>756<br>57319<br>15255<br>441<br>15255<br>441<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>21   | 2 9%<br>0 6%<br>0 0%<br>3 0%<br>5 2%<br>18.1%<br>0 1%<br>5 2%<br>18.1%<br>0 2%<br>5 0.0%<br>1.8%<br>27.4%<br>7.3%<br>0.6%<br>0.6%<br>0.0%<br>0.6%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0 | 0.81<br>0.97<br>0.82<br>0.82<br>0.78<br>0.88<br>0.78<br>0.88<br>0.87<br>0.83<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87   | [0.66, 1.01]<br>[0.61, 1.54]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.72, 1.08]<br>[0.12, 7, 1.46]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.92]<br>[0.83, 0.93]<br>[0.83, 0.95]<br>[0.83, 0.95]<br>[0.83, 0.95]<br>[0.13, 76.62]<br>[0.13, 76.62]<br>[0.13, 76.62]   |   |
| Imason Let al 2000<br>MIGS-EH Study Group MIGS-EH Study MIGS-MIGS-MIGS-MIGS-MIGS-MIGS-MIGS-MIGS-   | 02, df = 1<br>5,39 (P<br>4, df = 5<br>3,37 (P<br>4<br>999)<br>2, df = 5 (<br>909)  | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\$   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>1224<br>1177<br>93111<br>32), P =<br>11)<br>3157<br>752<br>2196<br>5410<br>50725<br>2); P = 0'<br>9048<br>442<br>942<br>204<br>141<br>224<br>11001   | 196<br>38<br>0<br>201<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>20<br>237<br>796<br>1358<br>2003<br>%<br>675<br>3<br>38<br>0<br>33<br>1<br>1<br>720   | 5471<br>940<br>11309<br>9228<br>37418<br>37418<br>120<br>232<br>232<br>21157<br>3164<br>756<br>57319<br>15255<br>441<br>15255<br>441<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>210<br>21   | 2 9%<br>0 6%<br>0 0%<br>3 0%<br>5 2%<br>18.1%<br>0 1%<br>5 2%<br>18.1%<br>0 2%<br>5 0.0%<br>1.8%<br>27.4%<br>7.3%<br>0.6%<br>0.6%<br>0.0%<br>0.6%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0.0%<br>0 | 0.81<br>0.97<br>3.10 [<br>0.88<br>0.87<br>0.86<br>0.12<br>0.87<br>0.81<br>0.91<br>0.75<br>0.87<br>0.81<br>0.87<br>0.81<br>0.83<br>0.87<br>0.83<br>0.87<br>0.84<br>0.88<br>0.89<br>0.84<br>0.88<br>0.89<br>0.94<br>0.95   | [0.68, 101]<br>0.61, 1.54]<br>0.61, 1.54]<br>0.61, 1.54]<br>0.61, 0.54]<br>0.61, 0.62]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.63, 0.62]<br>0.63, 0.62]<br>0.63, 0.63]<br>0.63, 0.63]<br>0.63, 0.63]<br>0.63, 0.63]<br>0.64, 1.67]<br>0.63, 0.63]<br>0.64, 1.67]<br>0.64, 1.67]<br>0.65, 1.68]<br>0.65,                         |   |
| Imason Let al 2000<br>MIGS-EH Study Group II<br>Adacob E et al 2003<br>VIGS-EH Study Group II<br>Penne CJ et al 2003<br>Softweil PM et al 2010<br>Xanbett A et al 2003<br>Xanbett A et al 2003<br>Xanbett A et al 2004<br>Xanbetta (16% C)<br>Total events<br>Iderogeneity: C/H = 17.<br>Test for overall effect: Z -<br>12.2 CCBs vs D-balcods<br>Jack H et al 72004<br>Xanbetta (16% C)<br>Total events<br>Iderogeneity: C/H = 41.<br>Ziback H et al 72004<br>Xanbotta (16% C)<br>Total events<br>Iderogeneity: C/H = 4.<br>Zibacka (2005   | 02, df = 1<br>5,39 (P<br>4, df = 5<br>3,37 (P<br>4<br>999)<br>2, df = 5 (<br>909)  | $\begin{array}{c} 159\\ 37\\ 1\\ 1\\ 76\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\$  | 5410<br>942<br>204<br>11267<br>9302<br>9302<br>9302<br>31031<br>141<br>224<br>1177<br>752<br>2196<br>55410<br>31031<br>3157<br>752<br>2196<br>55410<br>31031<br>9048<br>442<br>204<br>141<br>224<br>141<br>224<br>141<br>1001   | 196<br>38<br>0<br>201<br>1350<br>33<br>1<br>14<br>3710<br>12%<br>118<br>74<br>200<br>237<br>196<br>675<br>3<br>38<br>6<br>753<br>338<br>0<br>3<br>1<br>1358<br>720  | 54717<br>940<br>210<br>9228<br>37418<br>2028<br>223<br>223<br>223<br>223<br>221<br>3164<br>57319<br>15255<br>441<br>57319<br>15255<br>441<br>2210<br>221<br>27198   | 2 9%<br>2 0%<br>0 6%<br>0 0%<br>5 2%<br>18.1%<br>0 0%<br>5 2%<br>18.1%<br>0 0%<br>5 2%<br>5 2%<br>5 2%<br>5 2%<br>5 2%<br>5 2%<br>5 2%<br>5 2  | 0.81<br>0.97<br>0.97<br>0.97<br>0.88<br>0.88<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.8  | [0.66, 101]<br>[0.61, 154]<br>[0.61, 154]<br>[0.67, 022]<br>[0.67, 022]<br>[0.61, 056]<br>[0.61, 056]<br>[0.61, 056]<br>[0.63, 052]<br>[0.63, 052]<br>[0.63, 052]<br>[0.63, 053]<br>[0.63, 055]<br>[0.63, 055]<br>[0.61, 154]<br>[0.61, 154]<br>[0.61, 154]<br>[0.61, 154]<br>[0.62, 0.65]<br>[0.64, 0.65]<br>[0.64, 0.65]   |   |
| Hansson Let al 2000       Malacob E et al 2003       MUGS-EH Study Group II       Marchand E et al 2003       Softwall PM et al 2010       Softwall PM et al 2010       Stanchetti A et al 2003       Stanchetti A et al 1098       Zanchetti A et al 2003       Stanchetti A et al 2004       Stanchetti A et al 2005       Stanchetti A et al 2004       Stanchetti A et al 2005       Stanchetti A et al 2004       Stanchetti A et al 2002       Stomm T et al 2004       Hansson L et al 2004       Hansson L et al 2004       Stomm T et al 2004       Hansson L et al 1098       Stommanne L et al 2004       Hansson L et al 2004       Hansson L et al 2004       Stommanne L et al 2004       Hansson L et al 2004       Stommanne L et al 2004       Malacoc E et al 2003       Malacoc E et al 2004       Malaco E et al 2005       Malaco E et al 2004       Malaco E et al 2005       Malaco E et al 2004   | 02, df = 1<br>5,39 (P<br>4, df = 5<br>3,37 (P<br>4<br>999)<br>2, df = 5 (<br>909)  | $\begin{array}{c} 159\\ 37\\ 1\\ 1\\ 76\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\$  | 5410<br>942<br>204<br>11267<br>204<br>11267<br>204<br>11267<br>2105<br>31031<br>31031<br>3127<br>2196<br>33111<br>3157<br>752<br>2196<br>31031<br>3157<br>752<br>2196<br>31031<br>31031<br>31057<br>31031<br>31057<br>9048<br>442<br>204<br>141<br>224<br>11001<br>3); I <sup>2</sup> = 0'<br>9048<br>942<br>942<br>204<br>9639   | 196<br>38<br>0<br>2011<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>237<br>196<br>1358<br>2003<br>%<br>675<br>3<br>3<br>8<br>0<br>3<br>1<br>720<br>422<br>422   | 54717<br>940<br>2100<br>9228<br>37418<br>120<br>9228<br>37418<br>1157<br>105829<br>2213<br>37418<br>577319<br>15255<br>441<br>577319<br>15255<br>441<br>1202<br>232<br>232<br>217198  | 2.9%<br>0.05%<br>0.05%<br>5.02%<br>18.15%<br>0.1%<br>0.0%<br>50.0%<br>50.0%<br>18.15%<br>50.0%<br>7.3%<br>0.0%<br>0.0%<br>0.0%<br>8.0%   | 0.81<br>0.97<br>0.97<br>0.97<br>0.88<br>0.88<br>0.88<br>0.87<br>0.87<br>0.87<br>0.87<br>0.8  | [0.66, 101]<br>[0.61, 154]<br>[0.61, 154]<br>[0.67, 022]<br>[0.67, 022]<br>[0.61, 056]<br>[0.72, 108]<br>[0.61, 056]<br>[0.61, 056]<br>[0.63, 0.62]<br>[0.63, 0.62]<br>[0.63, 0.62]<br>[0.63, 0.63]<br>[0.63, 0.63]<br>[0.63, 0.63]<br>[0.63, 0.64]<br>[0.61, 154]<br>[0.61, 154]<br>[0.61, 154]<br>[0.61, 154]<br>[0.61, 154]<br>[0.61, 154]<br>[0.62, 0.69]<br>[0.62, 0.68]<br>[0.72, 108]<br>[0.67, 022]  |   |
| Imasch Let al 2000 VICS-EH Study Group II VICS-EH Study EI   | 02, df = 1<br>5,39 (P<br>4, df = 5<br>3,37 (P<br>4<br>999)<br>2, df = 5 (<br>909)  | $\begin{array}{c} 159\\ 37\\ 1\\ 1\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 999\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\$   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>752<br>2196<br>5410<br>31031<br>300725<br>2196<br>5410<br>31031<br>300725<br>2196<br>5410<br>31031<br>300725<br>2196<br>9048<br>442<br>204<br>11001<br>30, P = 0'<br>9639<br>11267<br>9302<br>217<br>1177   | 196<br>38<br>0<br>201<br>1350<br>33<br>1<br>14<br>3710<br>12%<br>118<br>74<br>20<br>237<br>7<br>196<br>1358<br>2003<br>3<br>8<br>675<br>3<br>38<br>8<br>0<br>3<br>1<br>1<br>720<br>%  | 54717<br>940<br>2100<br>11309<br>9228<br>37418<br>120<br>232<br>2157<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>57319<br>15255<br>541<br>17198<br>9618<br>11309<br>9228 | 2.9%<br>0.0%<br>0.0%<br>5.2%<br>1.1%<br>0.2%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>6.2%<br>8.0%   | 0.81<br>0.87<br>0.97<br>0.97<br>0.87<br>0.88<br>0.82<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87   | [0.66, 101]<br>0.61, 1.54]<br>0.61, 1.54]<br>0.61, 1.54]<br>0.61, 0.52]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.63, 0.62]<br>0.63, 0.62]<br>0.63, 0.63]<br>0.61, 1.64]<br>0.65, 0.63]<br>0.64, 1.07]<br>0.65, 1.03<br>0.65, 1.03<br>0.03, 1.67<br>0.03, 1.67<br>0.0 |   |
| tansson Let al 2000       Malacco E et al 2003       MCS-EH Study Group III       Marchan E et al 2003       Softwall PM et al 2010       Softwall PM et al 2010       Starbwell PM et al 2000       Starbwell PM et al 2000       Garashett et al 2004       Starbottal (95% CI)       Total events       Stelerogeneity: Chif" = 4.1       Starbottal (95% CI)       Total events       Stelerogeneity: Chif" = 4.1       Starbottal (95% CI)       Total events       Stelerogeneity: Chif" = 4.1       Starbottal (950 vs Diurettics       LLHAT 2002       Starbottal (950 vs Diurettics       LLHAT 2005       Starbottal (950 vs Diurettics       LLA CCBS vs Diots       Starbottal (950 vc)   | 02, df = 1<br>5,39 (P<br>4, df = 5<br>3,37 (P<br>4<br>999)<br>2, df = 5 (<br>909)  | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 0\\ 0\\ 3\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\ 9\\$   | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1177<br>93111<br>3157<br>752<br>2196<br>5410<br>9048<br>442<br>204<br>141<br>1277<br>9048<br>442<br>204<br>141<br>1224<br>11001<br>9048<br>942<br>204<br>204<br>942<br>942<br>204<br>204<br>204<br>204<br>204<br>204<br>204<br>204<br>204<br>2  | 1966<br>38<br>0<br>2011<br>35<br>3<br>1<br>14<br>3710<br>12%<br>118<br>74<br>2003<br>3<br>6755<br>3<br>8<br>0<br>3<br>3<br>1<br>4<br>2003<br>3<br>4<br>2003<br>3<br>4<br>2003<br>3<br>4<br>2003<br>3<br>1<br>1<br>5<br>8<br>2003<br>3<br>1<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>1<br>5<br>8<br>200<br>207<br>1<br>1<br>208<br>200<br>207<br>1<br>208<br>200<br>207<br>207<br>1<br>208<br>200<br>207<br>207<br>207<br>1<br>208<br>200<br>207<br>207<br>207<br>207<br>207<br>207<br>207   | 54717<br>940<br>2100<br>11309<br>9228<br>9228<br>9228<br>120<br>2322<br>1157<br>3164<br>2105<br>829<br>756<br>2213<br>37418<br>57319<br>15255<br>441<br>1940<br>210<br>1202<br>232<br>217198<br>9618<br>9139  | 2.9%<br>0.0%<br>0.0%<br>5.2%<br>1.1%<br>0.2%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>6.2%<br>8.0%   | 0.81<br>0.87<br>0.97<br>0.97<br>0.87<br>0.88<br>0.82<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87   | [0.66, 101]<br>[0.61, 154]<br>[0.61, 154]<br>[0.67, 022]<br>[0.67, 022]<br>[0.61, 056]<br>[0.72, 108]<br>[0.61, 056]<br>[0.61, 056]<br>[0.63, 0.62]<br>[0.63, 0.62]<br>[0.63, 0.62]<br>[0.63, 0.63]<br>[0.63, 0.63]<br>[0.63, 0.63]<br>[0.63, 0.64]<br>[0.61, 154]<br>[0.61, 154]<br>[0.61, 154]<br>[0.61, 154]<br>[0.61, 154]<br>[0.61, 154]<br>[0.62, 0.69]<br>[0.62, 0.68]<br>[0.72, 108]<br>[0.67, 022]  |   |
| Imason Let al 2000<br>MIGS-EH Study Group II<br>Papine CJ et al 2003<br>Softweil PM et al 2013<br>Softweil PM et al 2013<br>Canchetti A et al 2003<br>Stutheal (9%% C)<br>Total events<br>Intercomment (100 mm)<br>Stutheal (9%% C)<br>Total events<br>Intercomment (100 mm)<br>Stutheal (9%% C)<br>Call events<br>Intercomment (100 mm)<br>Stutheal (9%% C)<br>Coll events<br>Intercomment (100 mm)<br>Stutheal (9%% C)<br>Coll events<br>Intercomment (100 mm)<br>Stutheal (9%% C)<br>Coll events  | 2, df = 5<br>39 (P<br>4, df = 5<br>3, 37 (P<br>4, df = 5<br>3, 37 (P<br>4<br>3<br>3999<br>22, df = 5<br>3, 66 (P<br>7<br>15<br>3<br>3<br>3<br>3<br>3<br>3<br>3<br>3<br>3<br>3<br>3<br>3<br>3<br>3<br>3<br>3<br>3<br>3  | $\begin{array}{c} 159\\ 37\\ 1\\ 176\\ 279\\ 999\\ 0\\ 3\\ 9\\ 999\\ 0\\ 0\\ 3\\ 9\\ 9\\ 999\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 3\\ 7\\ 1\\ 5\\ 999\\ 9\\ 999\\ 1\\ 158\\ 0\\ 999\\ 9\\ 1580\\ 0\\ 1580\\ 0\\ 1580\\ 0\\ 1580\\ 0\\ 377\\ 6\\ 377\\ 1\\ 0\\ 3\\ 377\\ 6\\ 377\\ 1\\ 0\\ 3\\ 327\\ 1\\ 176\\ 6\\ 279\\ 9\\ 9\\ 9\\ 791\\ \end{array}$ | 5410)<br>942<br>204<br>11267<br>9302<br>9302<br>931031<br>1127<br>1127<br>93117<br>1177<br>752<br>2196<br>31031<br>31031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>30031<br>3003100000000 | 1966<br>38<br>0<br>2011<br>350<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>2003<br>3<br>2003<br>3<br>8<br>0<br>3<br>3<br>8<br>0<br>3<br>3<br>8<br>0<br>237<br>196<br>1358<br>2003<br>3<br>3<br>8<br>0<br>201<br>201<br>201<br>201<br>201<br>201<br>201   | 54717<br>940<br>2100<br>11309<br>9228<br>37418<br>120<br>232<br>2157<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>57319<br>15255<br>541<br>17198<br>9618<br>11309<br>9228 | 2.9%<br>0.0%<br>0.0%<br>5.2%<br>1.1%<br>0.2%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>6.2%<br>8.0%   | 0.81<br>0.87<br>0.97<br>0.97<br>0.87<br>0.88<br>0.82<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87   | [0.66, 101]<br>0.61, 1.54]<br>0.61, 1.54]<br>0.61, 1.54]<br>0.61, 0.52]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.63, 0.62]<br>0.63, 0.62]<br>0.63, 0.63]<br>0.61, 1.64]<br>0.65, 0.63]<br>0.64, 1.07]<br>0.65, 1.03<br>0.65, 1.03<br>0.03, 1.67<br>0.03, 1.67<br>0.0 |   |
| Hansson Let al 2000       Malcso E et al 2003       MUGS-EH Study Group III       Marchard E H and 2003       Softwall PM et al 2004       March et al 2002       Softwall PM et al 2004       Softwall PM et al 2004       Hansson L et al 1999       Softwall PM et al 2004       Hansson L et al 2004       Winbell PC 2003       Softwall PM et al 2004       Hansson L et al 2004       Hansson L et al 2004       Malcoco E et al 2003       Softwall PM et al 2004  | 02, df = 1<br>5 39 (P<br>rs and Di<br>4, df = 5<br>3 3.37 (P<br>999<br>2, df = 5<br>0.86 (P<br>rs<br>7, df = 3 (2  | $\begin{array}{c} 159\\ 37\\ 1\\ 1\\ 79\\ 999\\ 0\\ 3\\ 9\\ 999\\ 0\\ 0\\ 3\\ 9\\ 999\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\$  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1127<br>31031<br>1177<br>3111<br>32), P =<br>1117<br>3157<br>752<br>2196<br>3157<br>752<br>2196<br>3157<br>752<br>2196<br>3157<br>752<br>2196<br>3157<br>752<br>2196<br>9072<br>9048<br>442<br>942<br>9048<br>442<br>942<br>9048<br>442<br>942<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>907<br>907<br>907<br>907<br>907<br>907<br>907<br>907<br>907<br>90   | 1966<br>38<br>0<br>2011<br>350<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>2003<br>3<br>2003<br>3<br>8<br>0<br>3<br>3<br>8<br>0<br>3<br>3<br>8<br>0<br>237<br>196<br>1358<br>2003<br>3<br>3<br>8<br>0<br>201<br>201<br>201<br>201<br>201<br>201<br>201   | 54717<br>940<br>2100<br>11309<br>9228<br>37418<br>120<br>232<br>2157<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>57319<br>15255<br>541<br>17198<br>9618<br>11309<br>9228 | 2.9%<br>0.0%<br>0.0%<br>5.2%<br>1.1%<br>0.2%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>6.2%<br>8.0%   | 0.81<br>0.87<br>0.97<br>0.97<br>0.87<br>0.88<br>0.82<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87   | [0.66, 101]<br>0.61, 1.54]<br>0.61, 1.54]<br>0.61, 1.54]<br>0.61, 0.52]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.63, 0.62]<br>0.63, 0.62]<br>0.63, 0.63]<br>0.61, 1.64]<br>0.65, 0.63]<br>0.64, 1.07]<br>0.65, 1.03<br>0.65, 1.03<br>0.03, 1.67<br>0.03, 1.67<br>0.0 |   |
| Iamson Let al 2000<br>MICS-EH Study Group II<br>Paper Ca Let al 2003<br>MICS-EH Study Group II<br>mubuli F 2003<br>Vang Y et al 1998<br>Canchetti A et al 2003<br>Vang Y et al 1998<br>Canchetti A et al 2003<br>Vang Y et al 1998<br>Canchetti A et al 2002<br>Vang Y et al 1998<br>Canchetti A et al 2002<br>Vang Y et al 2004<br>Vang Y et al 1998<br>Canchetti A et al 1999<br>Vang Y et al 1998<br>Vang Y et al 2005<br>Vang Y et al 2004<br>Vang Y et al 2005<br>Vang Y et al 200   | 02, df = 1<br>5 39 (P<br>rs and Di<br>4, df = 5<br>3 3.37 (P<br>999<br>2, df = 5<br>0.86 (P<br>rs<br>7, df = 3 (2  | $\begin{array}{c} 159\\ 37\\ 1\\ 1\\ 79\\ 999\\ 0\\ 3\\ 9\\ 999\\ 0\\ 0\\ 3\\ 9\\ 999\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\$  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1127<br>31031<br>1177<br>3111<br>32), P =<br>1117<br>3157<br>752<br>2196<br>3157<br>752<br>2196<br>3157<br>752<br>2196<br>3157<br>752<br>2196<br>3157<br>752<br>2196<br>9072<br>9048<br>442<br>942<br>9048<br>442<br>942<br>9048<br>442<br>942<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>9048<br>3157<br>752<br>219<br>907<br>907<br>907<br>907<br>907<br>907<br>907<br>907<br>907<br>90   | 1966<br>38<br>0<br>2011<br>350<br>350<br>1358<br>3<br>1<br>14<br>3710<br>12%<br>2003<br>3<br>2003<br>3<br>8<br>0<br>3<br>3<br>8<br>0<br>3<br>3<br>8<br>0<br>237<br>196<br>1358<br>2003<br>3<br>3<br>8<br>0<br>201<br>201<br>201<br>201<br>201<br>201<br>201   | 54717<br>940<br>2100<br>11309<br>9228<br>37418<br>120<br>232<br>2157<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>547<br>105829<br>3164<br>57319<br>15255<br>541<br>17198<br>9618<br>11309<br>9228 | 2.9%<br>0.0%<br>0.0%<br>5.2%<br>1.1%<br>0.2%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>50.0%<br>7.3%<br>6.2%<br>8.0%   | 0.81<br>0.87<br>0.97<br>0.97<br>0.87<br>0.88<br>0.82<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87<br>0.87   | [0.66, 101]<br>0.61, 1.54]<br>0.61, 1.54]<br>0.61, 1.54]<br>0.61, 0.52]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.61, 0.63]<br>0.63, 0.62]<br>0.63, 0.62]<br>0.63, 0.63]<br>0.61, 1.64]<br>0.65, 0.63]<br>0.64, 1.07]<br>0.65, 1.03<br>0.65, 1.03<br>0.03, 1.67<br>0.03, 1.67<br>0.0 |   |
| Iamson Let al 2000<br>MICS-EH Study Group 1<br>Alacco E et al 2003<br>MICS-EH Study Group 1<br>Combul F 2003<br>Vang Y et al 1998<br>Enchetti A et al 2003<br>Vang Y et al 1998<br>Enchetti A et al 2003<br>Vang Y et al 1998<br>Extension I et al 2004<br>Vathotal (95% C)]<br>Cital events<br>detergameliy: (Chi" = 17.<br>"est for overall effect: Z<br>vathotal (95% C)]<br>Cital events<br>detergameliy: (Chi" = 41.<br>2004<br>Vathotal (95% C)]<br>Cital events<br>detergameliy: (Chi" = 41.<br>2005<br>Vathotal (95% C)]<br>Cital events<br>detergameliy: (Chi" = 41.<br>2005<br>Vathotal (95% C)]<br>Cital events<br>detergameliy: (Chi" = 4.<br>2.3 CCBs vs Diuritots<br>LLHAT 2002<br>Vathotal (95% C)]<br>Cital events<br>detergameliy: (Chi" = 4.<br>2.<br>3.2 CCBs vs Diuritots<br>LLHAT 2002<br>Vathotal (95% C)]<br>Cital events<br>detergameliy: (Chi" = 4.<br>2.<br>3.2 CCBs vs Diuritots<br>LLHAT 2002<br>Vathotal (95% C)]<br>Cital events<br>detergameliy: (Chi" = 4.<br>2.<br>3.4 CCBs vs Diacos<br>Papine C) et al 2003<br>Vathotal (95% C)]<br>Cital events<br>detergameliy: (Chi" = 4.<br>2.<br>3.4 CCBs vs Diacos<br>Papine C) et al 2003<br>Vathotal (95% C)]<br>Cital events<br>detergameliy: (Chi" = 4.<br>2.<br>3.<br>3.<br>3.<br>4.<br>3.<br>3.<br>3.<br>3.<br>3.<br>3.<br>3.<br>3.<br>3.<br>3.<br>3.<br>3.<br>3.   | 02, df = 1<br>5 39 (P = 5<br>4, df = 5 (1 = 5<br>3, 37 (P = 1<br>5) (2 = 1 | $\begin{array}{c} 159\\ 37\\ 17\\ 279\\ 999\\ 0\\ 3\\ 9\\ 999\\ 0\\ 0\\ 3\\ 9\\ 999\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\ 0\\$  | 5410<br>942<br>204<br>11267<br>9302<br>31031<br>141<br>224<br>1127<br>31031<br>1177<br>3111<br>32), P 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Figure 3. OR and 95% Cl of individual studies and pooled data against stroke in the patients with hypertension. (a) Calcium channel blockers vs Placebo, (b) Calcium channel blockers vs ACEIs, and (c) Calcium channel blockers vs Diuretics or/and  $\beta$  Blockers. doi:10.1371/journal.pone.0057854.q003

difference was found (OR = 0.92, 95% CI 0.8–1.02, p = 0.12) between CCBs and ACEIs in their efficiency of against stroke (see Figure 3b). However, the incidence of stroke in CCBs group was decreased by 7.84% [(5.1%-4.7%)  $\div$  5.1% × 100%] compared with that of ACEIs group (see Table 1).

# Stroke Events of CCBs vs Diuretics or/and $\beta\text{-adrenergic}$ Blockers

Sixteen independent reports with 93,111 experimental subjects and 105,829 controls were included in this meta-analysis [3,5,17– 19,22–24,27–34], which consisted of 6,505 stroke events (2795 in experimental group and 3710 in control group). The incidence of stroke in CCBs group was decreased by 14.28% [(3.5%-3%) ÷  $3.5\% \times 100\%$ ] compared with that of diuretics or/and βadrenergic blockers group (see Table 1), and the CCBs were more effective (OR = 0.87, 95% CI 0.83–0.92, p<1×10<sup>-5</sup>) than diuretics or/and β blockers in the prevention of stroke (see Figure 3c). Results of subgroups analyses indicated that the CCBs were more effective than β-adrenergic blockers alone (OR = 0.79, 95% CI 0.72–0.87, p<1×10<sup>-5</sup>), β-adrenergic blockers combined with diuretics (OR = 0.89, 95% CI 0.83–0.95, p = 7×10<sup>-5</sup>), but not diuretics alone (OR = 0.95, 95% CI 0.84–1.07, p = 0.39) in the prevention of stroke (see Figure 3c).

# Discussion

This study demonstrates that the use of calcium channel blockers therapy, compared with placebo therapy (OR, 0.68),  $\beta$ adrenergic blockers therapy (OR, 0.79), diuretics combined with  $\beta$ -adrenergic blockers therapy (OR, 0.89), angiotensin-converting enzyme inhibitors therapy (OR, 0.92), and diuretics therapy (OR, 0.95), was associated with a lower incidence of stroke events in the patients with hypertension. In this combined study of different hypertension populations, the risk of stroke events reduction for patients receiving calcium channel blockers therapy was similar. Due to different sample size in different treatment groups, it is essential to use and interpret the above results with cautions. These findings present new evidence to support the idea that the CCBs reduced stroke more than placebo and β-adrenergic blockers but were not different than ACEIs and diuretics. Hypertension is only one of the major risk factors in the development of stroke, the number of stroke events remains high even though the antihypertensive agents are used extensively [39]. Therefore, other risk factors or/and the biological processes underlying the pathophysiology of stroke warrant further studies in the near future.

The findings of our work indicated that CCBs reduced stroke more than placebo and  $\beta$ -adrenergic blockers, but the detail molecular mechanisms are not well known and remain to be excavated in the future. By now, it can be explained in part by that CCBs can generate stronger antihypertensive effect (by dilating the blood vessels) than that of beta-blockers (by reducing the blood flow of cardiac output) or that of placebo (by confounders). These results reported here provide strong evidence linking controlling hypertension to a reduced risk of stroke. Meanwhile, this study has some limitations and caveats. First, as not all clinical data were available from each original report, other subclasses-stratified analyses could not be performed; the risk of bias assessment in this work could rob the credibility of results. Second, only studies reported in English or Chinese were included, which might be vulnerable to the bias of language and ethnicity. Third, the whole sample size in this study is sufficient for statistic purposes, but the sample size of each subgroup is relatively small and susceptible to false positive or negative results. Fourth, after the treatment of antihypertensive agents, the years of followed-up between studies varied greatly (from 1 to 5.5 years), which also could result in a bias. Finally, only four kinds of antihypertensive agents were tested in this report; addition of other drugs and withdrawals of treatment may also lead to an underestimation of the real differences in stroke risk between the previous reports. Further studies are required to investigate the association between other antihypertensive agents and stroke-risk, and to provide a better estimate the benefits of antihypertensive agents against stroke in the hypertension populations.

In conclusions, the present analysis shows that CCBs, ACEIs, diuretics, and  $\beta$ -adrenergic blockers can decline the incidence of stroke in the hypertension populations. Among them, CCBs reduced stroke more than placebo and  $\beta$ -adrenergic blockers, but were not different than ACEIs and diuretics. More head to head RCTs are warranted. This systematic review and meta-analysis provides a thorough examination of the literature on the effect of first-line antihypertensive agents in the prevention of stroke, and

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provide a foundation of knowledge on which clinical and public health messaging deserves to be further discussed.

## **Supporting Information**

**Supplementary Information S1** The quality assessment of evidence by GRADEprofiler. (DOC)

**Supplementary Information S2** The risk of bias assessment by RevMan.

(DOC)

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#### **Author Contributions**

Conceived and designed the experiments: MSY. Performed the experiments: MSY GJC. Analyzed the data: MSY GJC. Contributed reagents/ materials/analysis tools: MSY GJC. Wrote the paper: MSY GJC.

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