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SYSTEMATIC REVIEW AND META-ANALYSIS

Global Burden, Regional Differences, Trends, and Health Consequences of Medication Nonadherence for Hypertension During 2010 to 2020: A Meta-Analysis Involving 27 Million Patients

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BACKGROUND: Nonadherence to antihypertensive medications is the leading cause of poor blood pressure control and thereby cardiovascular diseases and mortality worldwide.

METHODS AND RESULTS: We investigated the global epidemiology, regional differences, and trend of antihypertensive medication nonadherence via a systematic review and meta-analyses of data from 2010 to 2020. Multiple medical databases and clinicaltrials.gov were searched for articles. Observational studies reporting the proportion of patients with anti-hypertensive medication nonadherence were included. The proportion of nonadherence, publication year, year of first recruitment, country, and health outcomes attributable to antihypertensive medication nonadherence were extracted. Two reviewers screened abstracts and full texts, classified countries according to levels of income and locations, and extracted data. The Joanna Briggs Institute prevalence critical appraisal tool was used to rate the included studies. Prevalence meta-analyses were conducted using a fixed-effects model, and trends in prevalence were analyzed using meta-regression. The certainty of evidence concerning the effect of health consequences of nonadherence was rated according to Grading of Recommendations, Assessment, Development and Evaluations. A total of 161 studies were included. Subject to different detection methods, the global prevalence of anti-hypertensive medication nonadherence was 27% to 40%. Nonadherence was more prevalent in low- to middle-income countries than in high-income countries, and in non-Western countries than in Western countries. No significant trend in prevalence was detected between 2010 and 2020. Patients with antihypertensive medication nonadherence had suboptimal blood pressure control, complications from hypertension, all-cause hospitalization, and all-cause mortality.

CONCLUSIONS: While high prevalence of anti-hypertensive medication nonadherence was detected worldwide, higher prevalence was detected in low- to middle-income and non-Western countries. Interventions are urgently required, especially in these regions. Current evidence is limited by high heterogeneity.

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Key Words: adherence ■ compliance ■ hypertension ■ meta-analyses ■ prevalence

Medication adherence is defined as the "extent to which patients take their medication as prescribed."[1,2] Although hypertension is one of the most common chronic conditions and a leading cause of death globally,[3] medication nonadherence among patients with hypertension is highly prevalent. Up to 50%

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CLINICAL PERSPECTIVE

What Is New?

- Anti-hypertensive medication nonadherence was common globally (27%–40%), was more prevalent in low- to middle income and non-Western countries, and did not improve between 2010 and 2020.

What Are the Clinical Implications?

- Policymakers and clinicians should incorporate validated methods (eg, validated questionnaires, medication procession ratio, pill counting, electronic pills or pillbox, and biochemical detection by drug assays) into health care systems to routinely detect anti-hypertensive medication nonadherence.
- Once detected, clinicians could conceptualize the reasons for nonadherence, using the World Health Organization model, and manage them accordingly.

Nonstandard Abbreviations and Acronyms

MMAS	Morisky Medication Adherence Scale
MPR	medication possession ratio
WHO	World Health Organization

of patients stop taking their prescribed antihypertensive medications within 1 year of initiation.[4] The high prevalence of antihypertensive medication nonadherence has contributed to poor blood pressure (BP) control worldwide. Accordingly, optimal control of BP is attained in less than one-third and one-tenth of patients with hypertension in high-income and low- to middle-income countries, respectively.[1,3] This poor control has consequently led to a high global burden of cardiovascular diseases, chronic kidney disease, dementia, and mortality.

The World Health Organization (WHO) has provided a conceptual framework to explain the multifactorial reasons underlying antihypertensive medication nonadherence, including socioeconomic factors (eg, age, sex, and educational status), patient-related factors (eg, readiness to change and self-efficacy), therapy-related factors (eg, complexity of treatment and out-of-pocket costs), comorbidities (eg, comorbid cardiovascular diseases and mental illnesses), and health care system factors (eg, doctor-patient relationships and doctors' burnout).[5] Clinically, antihypertensive medication nonadherence is detected by various methods, including validated self-reported questionnaires, pill counting (by counting the pills left over since the last prescription), prescription refills (eg, medication possession ratio [MPR] and proportion of days covered by prescriptions by reviewing medication databases), electronic pill boxes (typically detect the opening of the pill box), blood/urine biomarkers or drug assays (detect the presence of drug metabolites in biological samples), and, recently, electronic medication monitors that directly detect gastric juice.[2]

Despite the importance of antihypertensive medication nonadherence, a comprehensive meta-analysis investigating its global epidemiology is yet to be conducted. Previous meta-analyses included only certain countries or populations, for example, low- to middle-income countries and only patients with resistant hypertension.[6-9] Furthermore, previous meta-analyses only included self-reported questionnaires or used both validated and nonvalidated methods to define medication nonadherence.[6-10] Moreover, the high heterogeneity of results from previous meta-analyses has not been adequately investigated using subgroup analyses or meta-regressions, despite the presence of multiple and complex factors associated with medication adherence.[6,7,10] Finally, although trends and regional prevalence of uncontrolled hypertension have been well studied, there is a lack of similar research on anti-hypertensive medication nonadherence.[3]

Therefore, the primary objective of this meta-analysis was to estimate the global prevalence of antihypertensive medication nonadherence. Additionally, the prevalence was compared among different regions and countries. We hypothesized that antihypertensive medication nonadherence would be more prevalent in low- to middle-income countries, attributable to lower availability and affordability of medication, and in non-Western countries, attributable to different beliefs/cultures.[11] Trends in antihypertensive medication nonadherence from 2010 to 2020 were also examined. We hypothesized that because of the considerable research efforts and development of interventions for antihypertensive medication nonadherence over time, its prevalence would have decreased in the previous decade.[12,13] Additionally, the health consequences of antihypertensive medication nonadherence (eg, poor BP control) were investigated. The results of this study can inform patients, physicians, researchers, and policymakers regarding managing antihypertensive medication nonadherence.

METHODS

This meta-analysis was registered in the International Prospective Register of Systematic Reviews (CRD42021259860) and reported according to the Meta-Analyses of Observational Studies in Epidemiology standard of reporting and Preferred

Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[14] Two of the authors (E.K.P.L. and P.P.) had full access to all the data and take full responsibility for its integrity and analysis. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Study Eligibility

Observational studies were included if they (1) included patients with hypertension; (2) reported prevalence of antihypertensive medication nonadherence; (3) included ≥100 participants; (4) measured antihypertensive medication adherence using at least 1 of the following methods: validated questionnaire (eg, 4-item or 8-item Morisky Medication Adherence Scale [MMAS]), pill counting, prescription refills, electronic pill boxes, biochemical assays, or electronic medication monitoring[1,2]; (5) used the validated or conventional cutoff of these methods (eg, scores of MMAS-8 <6); and (6) were published in Chinese or English. The eligibility criteria were determined before the assessment of study eligibility (Table S1).[2,15] Studies were excluded if they included patients who (1) were aged <18 years, (2) had no hypertension, (3) received no antihypertensive medications, and (4) were pregnant.[7] Furthermore, studies that included only patients with resistant hypertension were excluded because these patients may have a higher prevalence of nonadherence and represent a different spectrum of nonadherence behaviors. Interventional trials, qualitative studies, animal studies, commentaries, and reviews were also excluded.

Information Sources

Chinese and English databases, such as the Cumulated Index to Nursing and Allied Health Literature Complete, Cochrane Library, Embase, Ovid Medline, PubMed, Scopus, Web of Science, and China Academic Journals Full-text Database were searched for articles published up to December 2020.

Search Strategy

Keywords such as *medication adherence*, *compliance*, *hypertension*, *antihypertensive medications*, and *medication adherence scale*, were used as search terms (Table S2). The search was limited to studies of adults. In addition to English, studies published in Chinese were also included. Additionally, reference lists of relevant published systematic reviews were searched.[6,7,10] Clinicaltrials.gov was searched for unpublished trials, and the authors were contacted whenever possible.

Selection Process

All studies from the search were entered into the Covidence program (Covidence Systematic Review Software, Veritas Health Innovation, Melbourne, Australia; available at www.covidence.org). Two reviewers (from among E.K.P.L., P.P., Y.B., M.T.Z., and A.C.H.N.) independently assessed the eligibility of studies by screening the title/abstracts followed by the full texts in Covidence.

Data Collection Process

Data were dual extracted by reviewers (2 from among E.K.P.L., P.P., Y.B., M.T.Z., and A.C.H.N.) independently into Covidence. Discrepancies were compared and resolved by 2 reviewers (E.K.P.L. and P.P.).

Data Items

Extracted data included (1) details of the studies (eg, sample size, country, settings [ie, specialist center/hospital settings versus other settings], study design, inclusion/exclusion criteria). Countries were classified independently by 2 reviewers (from among E.K.P.L., P.P., M.T.Z., and A.C.H.N.) as Western or non-Western (Western countries included Australia, New Zealand, Canada, all member countries of the European Union, the European microstates, the United Kingdom, and the United States) and high- or low- to middle-income (as defined by the World Bank); (2) details of anti-hypertensive medication nonadherence (methods used, cutoff, prevalence); (3) details for trend analyses (year of first recruitment and publication year); (4) socioeconomic and demographic variables of the participants that may affect adherence as defined by the WHO (age/sex, proportion with tertiary education or above, presence of cardiovascular diseases/renal diseases/diabetes/hyperlipidemia, number of years since hypertension diagnosis, the use of single-pill combination and once-daily medications, number of antihypertension classes, and proportion of current smokers); and (5) health consequences of nonadherence (systolic BP and diastolic BP differences between adherent and nonadherent participants and odds ratios [ORs] of suboptimal BP).

For cohort or case–control studies, health consequences, including ORs of suboptimal BP control, cardiovascular diseases, renal diseases, hospitalization, and death were also extracted. For cohort studies that reported adherence at multiple time points, the baseline value was used for analysis of comparability with cross-sectional studies.

When only abstracts were found, the authors of the papers were contacted for published reports or articles. Abstracts were included only if they provided adequate information (ie, clear inclusion criteria, definition of anti-hypertensive medication nonadherence, number of participants, and proportion of participants with antihypertensive medication nonadherence). For duplicated studies and cohort studies using potentially

overlapping databases with overlapping dates, the latest study with the most extractable data was selected by 2 reviewers (E.K.P.L and P.P.).

Furthermore, the study by Saleem and colleagues was excluded post hoc because it reported a 100% nonadherence rate at a predetermined cutoff and could not be analyzed in Stata.[16]

Study Risk-of-Bias Assessment

The Joanna Briggs Institute prevalence critical appraisal tool, a validated instrument, was used to rate the included studies.[17] Included studies were rated as having a low risk of bias only when no concern was raised regarding all questions in the instrument. All other included studies were rated as having unknown risk or high risk of bias. Quality assessments were conducted by 2 independent reviewers (from among E.K.P.L., P.P., Y.B., M.T.Z., and A.C.H.N.), and all discrepancies were resolved through discussion with E.K.P.L. and P.P. The certainty of evidence concerning the effect of health consequences of nonadherence was rated according to Grading of Recommendations, Assessment, Development and Evaluations.

Data Analysis

All meta-analyses were conducted using Stata software (Stata Statistical Software: Release 15, StataCorp LLC, College Station, TX).

Global prevalence was estimated through the "metaprop" function, using a fixed-effects model, which is the recommended and valid method to estimate prevalence from given populations.[18] Subgroup analyses were conducted on the basis of (1) the methods used to define nonadherence (eg, questionnaires, biochemical assays), (2) the countries where the studies were performed (Western versus non-Western), and (3) the income level of these countries (high- versus low- to middle-income). The nonadherence trend was analyzed using publication year and year of first recruitment. Heterogeneity, differences, and trends were further investigated by meta-regression analyses using the "metareg" function. Heterogeneity across studies was assessed using I^2 statistics and P values. Furthermore, the effect of nonadherence on BP level and OR was investigated by comparing between adherent and nonadherent patients using the "metan" function and a random-effects model because of a difference in population characteristics in the included studies. P values were 2-tailed, considering those <0.05 to be statistically significant. Examples of the Stata commands can be found in Data S1.

Sensitivity analyses were conducted to include only studies with a low risk of bias and larger studies (n>500 and n>3000 [when an adequate number of studies were available]). Within the subgroup of studies that used questionnaires, sensitivity analyses were conducted by (1) replacing studies in which the MMAS-8 cutoff was <6 with studies that used cutoffs of ≤6; (2) including only studies that used MMAS-4; and (3) including only studies that used MMAS-8 because MMAS-4 and MMAS-8 were the most commonly used questionnaires. For cohort studies that reported adherence data after 1 year, the prevalence of nonadherence at the last follow-up was used for the sensitivity analysis. For health consequences attributable to anti-hypertensive medication nonadherence, sensitivity analysis was conducted using results from cohort studies only.

Publication bias was assessed by visual examination of a funnel plot, plotting the log of prevalence against the standard error of prevalence, and Egger's test.

RESULTS

Characteristics of Included Studies and Population

Of the 7004 studies identified, a total of 161 studies from 68 countries were included, with a sample size ranging from 100 to 23 833 000 (Figure 1). Over half of the included studies were conducted in low- to middle-income countries (n=88). Only a few studies used biochemical assays (n=5), pill counting (n=4), and electronic pill boxes (n=3) to detect nonadherence. Therefore, meaningful corresponding subgroup and meta-regression analyses in these subgroups was not possible. Furthermore, studies in low- to middle-income and non-Western countries predominantly used questionnaires to measure adherence during the study period, with no studies using biochemical assays or electronic pill boxes. Moreover, the sample size of studies conducted in low- to middle-income countries was small, and only 1 had a sample size of >3000. Among the studies that used questionnaires, the MMAS-8 (n=73) and MMAS-4 (n=45) questionnaires were most commonly used (Table S5). Only 23 studies were rated as having a low risk of bias (Tables S6 through S8). Our study population consisted of 27 785 595 patients with hypertension, with a mean age of 57 (42.9% men). Other demographic data and the list of included studies are presented in Tables S3 and S4.

Global Prevalence, Regional Differences, and Trends in Antihypertensive Medication Nonadherence

The prevalence varied with methods used to define nonadherence: 40% by questionnaires (95% CI, 40%–40%), 28% by prescription refill (95% CI, 28%–28%),

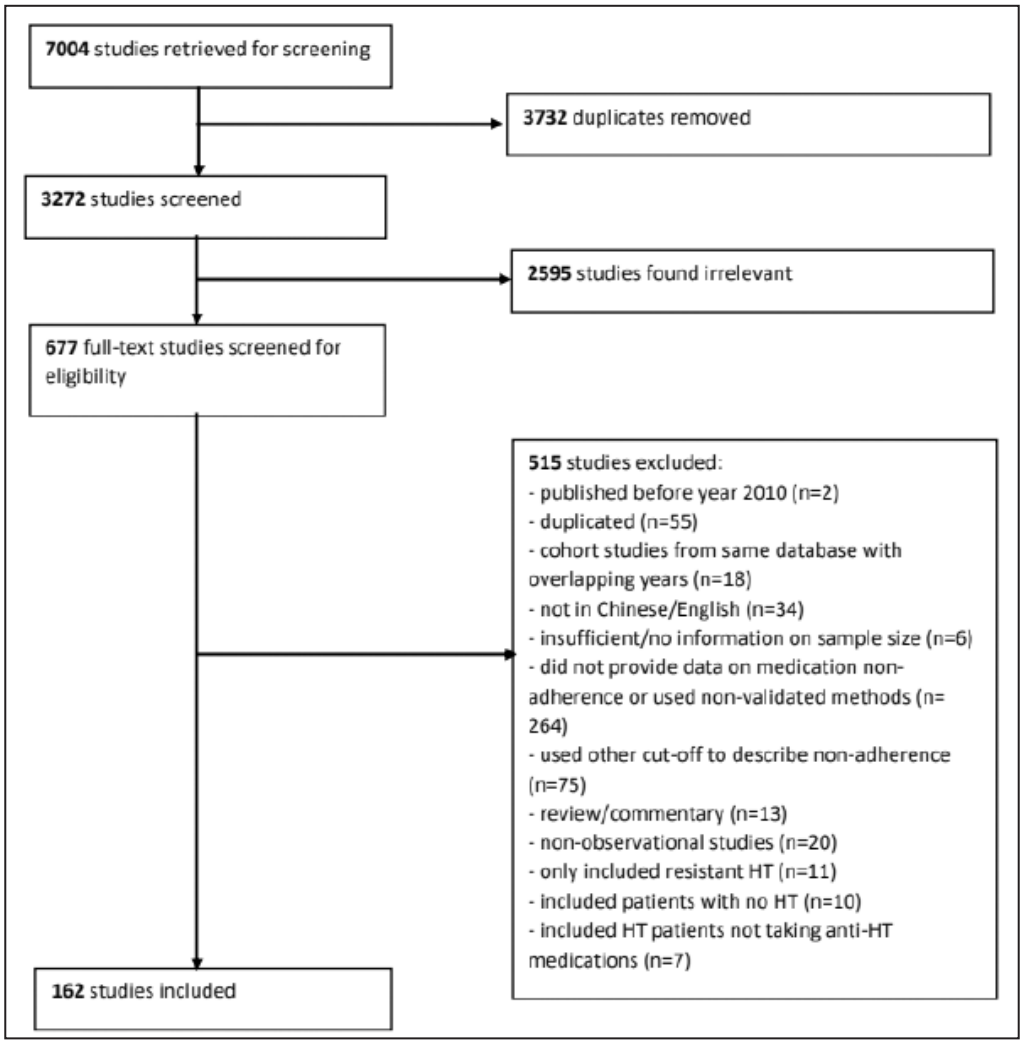

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flowchart.
HT indicates hypertension.

28% by pill counting (95% CI, 26%–29%), 28% by electronic pill boxes (95% CI, 25%–31%), and 27% by biochemical assays (95% CI, 26%–29%) (Figure 2, Table S9).

Nonadherence was more prevalent in low- to middle-income countries than in high-income countries, when defined by questionnaires (43% versus 38%; *P*=0.145), prescription refill (50% versus 28%; *P*=0.37), and pill counting (66% versus 25%; *P*=0.382). Similarly, nonadherence was more prevalent in non-Western countries than in Western countries, when defined by questionnaires (43% versus 38%; *P*=0.108), and prescription refill (49% versus 26%; *P*=0.086; Figure 2, Table S9). Although nonadherence was less prevalent in non-Western countries than in Western countries when pill counting was used, this included only 4 unclear to high risk-of-bias studies (22% versus 49%; *P*=0.974; Figure S1). Depending on the method used to define nonadherence, the prevalence of nonadherence ranged from 20% to 49% among continents (Tables S9 through S13, Figure S1).

No significant trend in antihypertensive medication nonadherence was detected over the past decade in all meta-regression analyses, including subgroup analyses, using publication year or year of first recruitment (Figure 3, Tables S14 and S15).

When using meta-regression to explore heterogeneity, in the subgroup analysis of studies using the prescription refill method of adherence, nonadherence was less common in older patients (*P*=0.001), patients receiving free medical service or insurance (*P*=0.044), and patients receiving more classes of antihypertensive medications (*P*=0.014; Table S16). Other factors, such as the presence of cardiovascular diseases and medication frequency, were not significantly associated with the prevalence of nonadherence (Table S16).

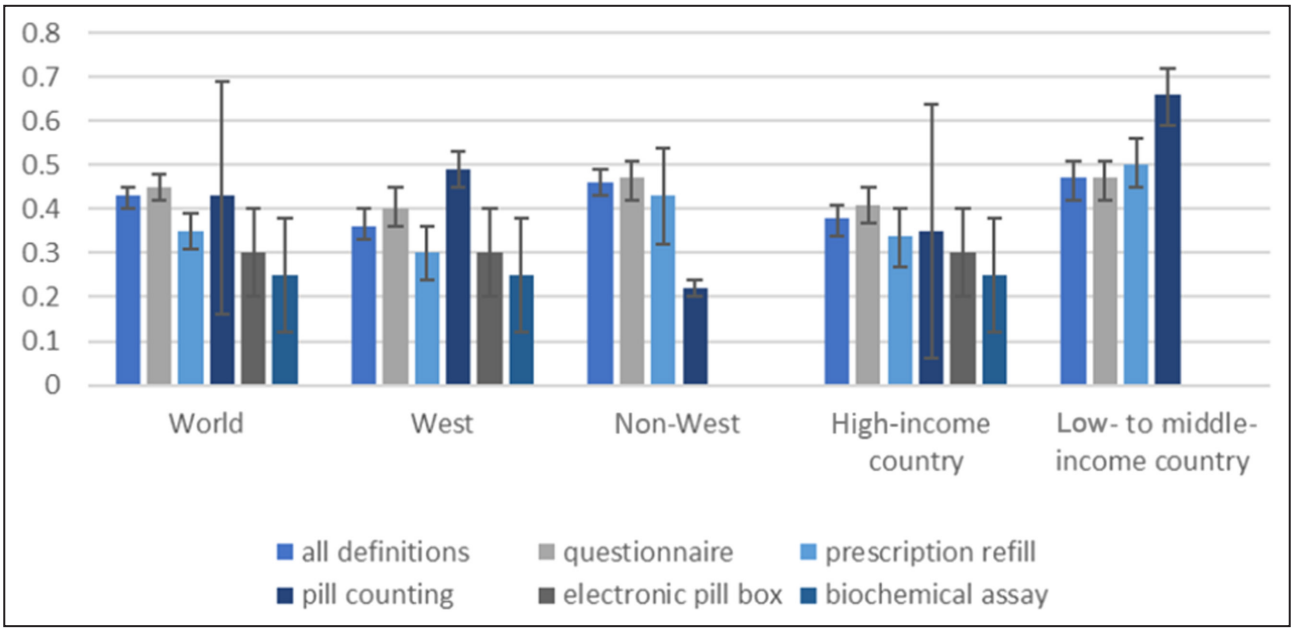

Figure 2. Prevalence of nonadherence presented with 95% CIs (subgroup: nonadherence definitions, West vs non-West, income levels).

These meta-regression analyses did not explain the heterogeneity, and all residual I^2 remained >95%.

Consequences of Antihypertensive Medication Nonadherence

Compared with adherent patients, patients with antihypertensive medication nonadherence had higher systolic BP (mean difference, 3.76 mm Hg [95% CI, 2.23–5.28 mm Hg]; I^2, 87.1%; P<0.001), and diastolic BP (mean difference, 3.11 mm Hg [95% CI, 2.24–3.99 mm Hg]; I^2, 76%; P<0.001; Figure 4).[19-39] Furthermore, patients with antihypertensive medication nonadherence had increased odds of having suboptimal BP control (OR, 2.15 [95% CI, 1.84–2.5]; I^2, 97.4%; P<0.001), complications from hypertension (OR, 2.08 [95% CI, 0.99–4.35]; I^2, 94.2%; P<0.001), all-cause hospitalization (OR, 1.38 [95% CI, 1.35–1.41]; I^2, 0; P=0.64), and all-cause mortality (OR, 1.38 [95% CI, 1.35–1.41]; I^2, 0; P=0.509; Figure 5).[19,21,33–35,40–70] Sensitivity and subgroup analyses revealed similar results but did not resolve high heterogeneity (Figures S2 and S3, Tables S17 and S18). According to Grading of Recommendations, Assessment, Development and Evaluations, the certainty of evidence was low for all health outcomes, owing to inclusion of observational studies only.

Sensitivity Analyses

Sensitivity analyses generally showed a decrease in nonadherence prevalence when only larger studies were included. This result is congruent with our findings on regional differences because larger studies were predominantly from high-income countries. Moreover, almost all sensitivity analyses consistently found lower nonadherence prevalence in Western and high-income countries. For instance, this was observed when only low-risk-of-bias and questionnaire studies (prevalence, 38% [95% CI, 37%–39%]; Figure S3), and only studies using MMAS-4 (prevalence, 41% [95% CI, 41%–42%]; Figure S3) were included. The differences in systolic BP/diastolic BP and health outcomes between adherent and nonadherent participants remained similar in the sensitivity analyses. Moreover, no significant trend in prevalence of nonadherence was detected in various sensitivity analyses (Tables S17 and S18, Figure S3). However, no sensitivity analysis adequately explained the results' high heterogeneity (Tables S17 and S18, Figure S3).

Publication Bias

The funnel plots and Egger's test did not show a significant small study bias (Egger's test, P=0.332; Figure S4).

DISCUSSION

Main Findings and Comparison With Previous Literature

Subject to different detection methods, the global prevalence of antihypertensive medication nonadherence

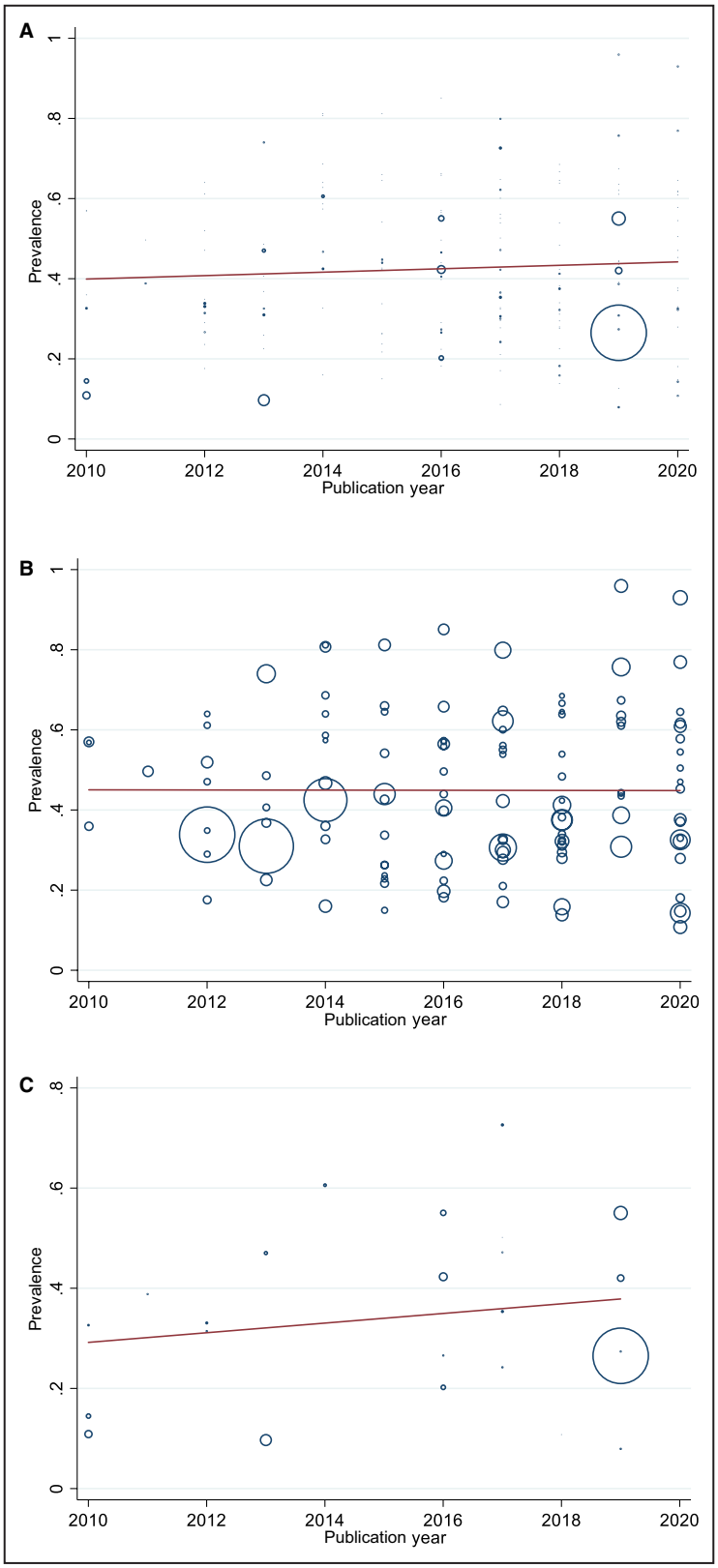

Figure 3. Trend of medication nonadherence according to nonadherence prevalence and included studies' publication year.
A, By any definition: regression coefficient: 0.004, *P*=0.434; (**B**) by questionnaires: regression coefficient: –0.0002, *P*=0.977; (**C**) by prescription refills: meta-regression coefficient: 0.010, *P*=0.416. DBP indicates diastolic blood pressure; HT, hypertension; and SBP, systolic blood pressure.

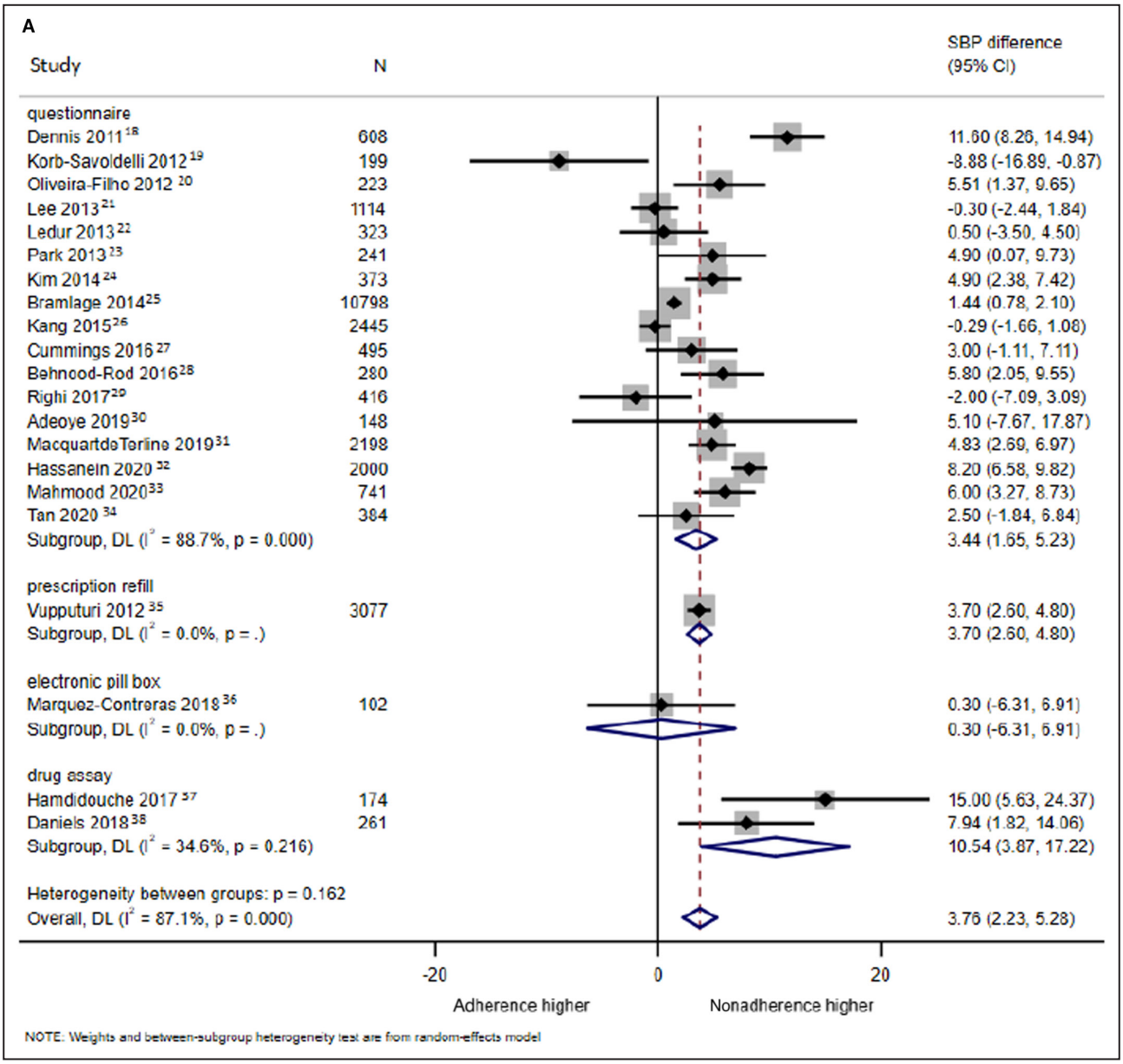

Figure 4. Blood pressure difference attributable to medication nonadherence.
A, Systolic blood pressure difference attributable to medication nonadherence; (**B**) diastolic blood pressure difference attributable to medication nonadherence.

ranged from 27% to 40%. Furthermore, antihypertensive medication nonadherence was more prevalent in low- to middle-income countries and non-Western countries. For instance, using our results from prescription refill and the latest WHO data, this translates to ≈426 million people from low- to middle-income countries, and 119 million people from high-income countries.[71] Our results are similar to those of another meta-analysis that reported a global prevalence of 45%, but that meta-analysis included only studies that used MMAS.[10] Our results are also similar to those of previous large observational studies revealing that antihypertensive medication nonadherence led to poor BP control, higher health care resource use, cardiovascular complications, and death.[72,73] However, this is the first study to suggest that, in addition to the known factors of underdiagnosis and undertreatment, nonadherence plays an important role in the differential poor hypertension control in low- to middle-income countries.[3] The exact reasons underlying these regional differences cannot be determined from our data, but they could be attributed to differences in cultures, beliefs, the use of alternative medicine, health care systems, and drug affordability and availability.[32] To date, there has been a lack of primary studies that directly investigate regional differences (eg, Western versus non-Western or

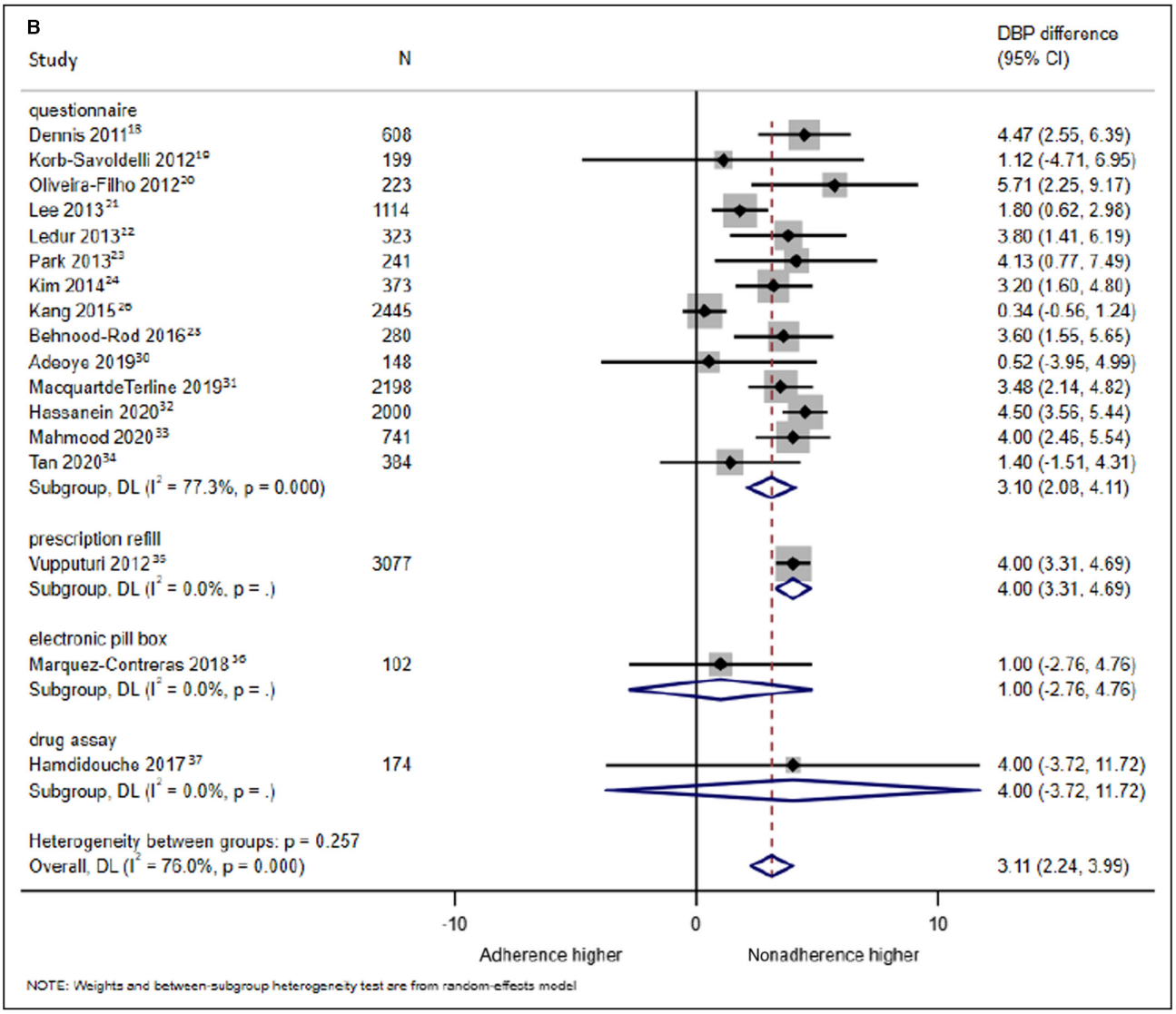

Figure 4. Continued.

high-income versus low- to middle-income countries) in antihypertensive medication nonadherence.

Although a decreasing trend in nonadherence has been described in a few US studies, this trend has not been observed globally.[74,75] This suggests that, although evidence-based interventions, such as reduction in daily number of pills and single-pill combinations, can reduce medication nonadherence, they were not adequately implemented in clinical practice.[13,76,77] A Cochrane review also suggested that significant improvements in adherence and clinical outcomes were uncommon in well-conducted randomized controlled trials, and these called for advances and more interventional studies in the field.[78]

Our results also suggested that the prevalence of nonadherence was generally lower when more objective detection methods were used (ie, electronic pill boxes and biochemical assays). However, these studies were conducted only in Western and high-income countries. This difference could, therefore, be attributable to the regional differences described. These differences could also result from the Hawthorne effect, that is, an improved nonadherence rate when patients know that they are being monitored.[79] In the current study, nonadherence was detected by these objective methods in only 8 studies, and no study used electronic medications.

Clinical and Research Implications

Our results are consistent with international guidelines that state that antihypertensive medication nonadherence is highly prevalent and clinicians treating hypertension should screen for nonadherence during every clinician visit.[80] However, clinicians' predictions of drug nonadherence are known to be no better than "a coin toss." Therefore, policymakers and clinicians should incorporate validated methods into health care systems

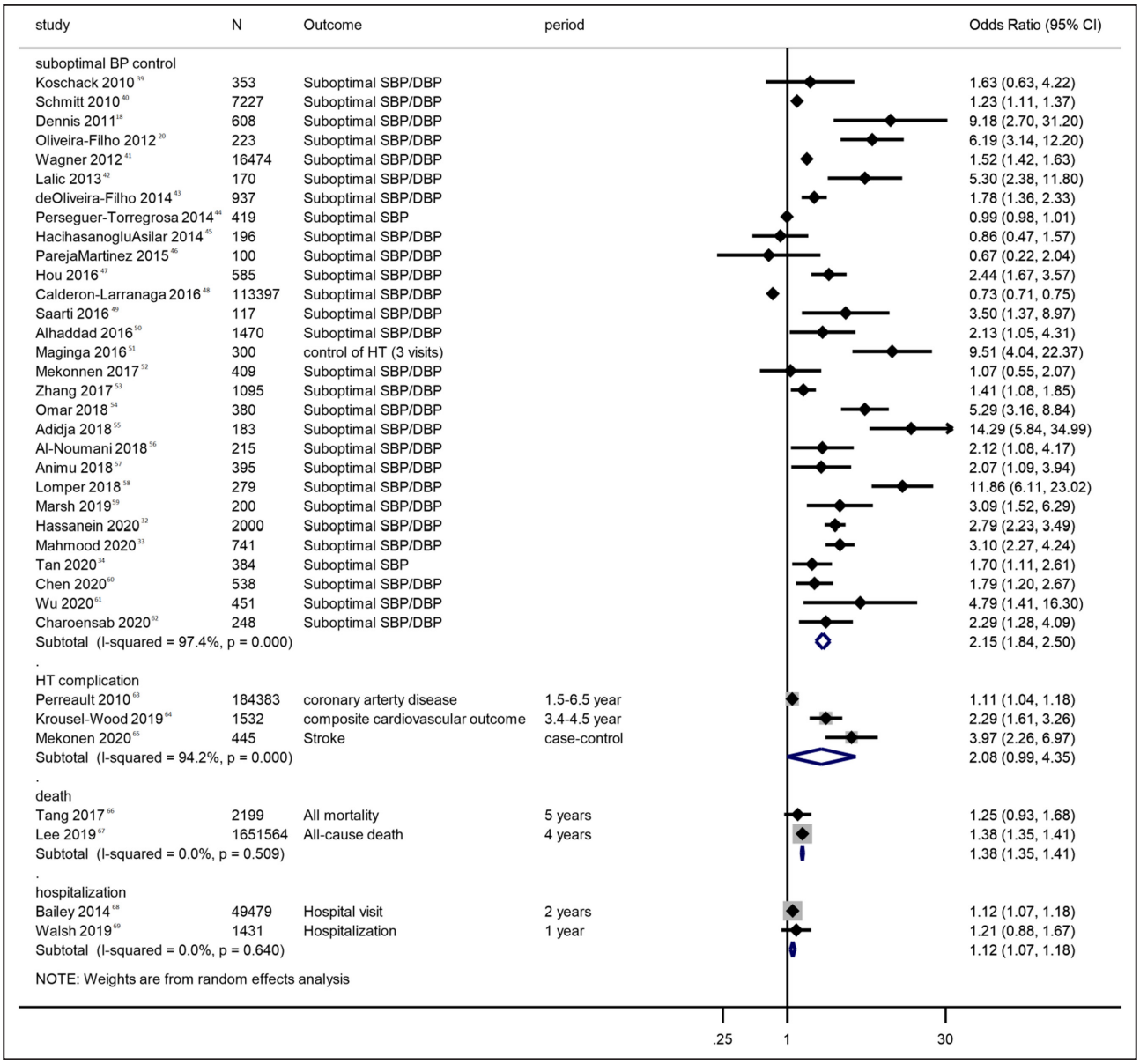

Figure 5. Health consequence attributable to medication nonadherence.
DBP indicates diastolic blood pressure; DL, xxx; and SBP, systolic blood pressure.

to routinely detect anti-hypertensive medication nonadherence.[81] However, all existing methods, including the use of questionnaires, calculation of MPR, or telemonitoring by electronic pill boxes, would require extra time and resources, which could be difficult to implement. Newer methods, including the use of dried blood samples and oral fluid assays, are being developed and investigated to provide reliable and quick methods for clinicians to routinely detect nonadherence.[82,83] Once detected, clinicians could conceptualize the reasons for nonadherence, using the WHO model, and manage them accordingly.[5]

Our results also call for implementation research to examine how the latest evidence can be translated into clinical practice and trials to investigate interventions that can effectively improve medication adherence and clinical outcomes.[78] While most existing research investigated single interventions, clinical practice guidelines suggest that complex interventions combining several interventions to target the factors listed by the WHO are most likely needed.[80] However, real-life data concerning such complex interventions are scarce. Furthermore, there is still no reference standard for the detection of medication nonadherence. Even biochemical assays, which are one of the most objective measures, suffer from the white-coat adherence effect, in which patients have improved adherence only before doctor visits.[84] A feasible, affordable, and reliable

reference standard to define nonadherence would facilitate research and its clinical detection. Additionally, existing validated antihypertensive medication nonadherence detection methods could not provide a comprehensive assessment of patients' adherence behaviors, which include the processes of "initiation," "implementation," and "discontinuation."[85] For instance, although 90% MPR signified good medication adherence using a conventional cutoff, the missing 10% can represent both occasional drug holidays or complete discontinuation. Moreover, the reasons for the higher nonadherence prevalence in low- to middle-income and non-Western countries could be explored and examined further. Finally, large population-based studies on antihypertensive medication nonadherence from low- to middle-income countries are lacking.

Strengths and Limitations

This study has many strengths. This is the first meta-analysis that describes not only global prevalence but also regional differences and trends in antihypertensive medication nonadherence in the previous decade. This study represented the best available evidence in view of the lack of similar primary research across continents with different income levels. Our meta-analysis also involved a comprehensive search, including Chinese databases, with the largest number of studies among similar meta-analyses. Meta-regressions were conducted to investigate the relationship between prevalence of nonadherence and patients' determining factors (eg, presence of cardiovascular diseases), and treatment factors (eg, once-daily or combined-pill treatments, number of medications; Table S16). There was no significant publication bias, and the sensitivity analyses showed congruent results.

However, all results were highly heterogeneous because studies included different populations, used different definitions of nonadherence, and included diverse factors that this study could not encompass (eg, characteristics of health care and insurance systems, quality of doctor-patient relationships, and level of doctors' burnout). Furthermore, questionnaires had different sensitivities and specificities to detect medication nonadherence and measured different aspects of nonadherence (beliefs, barriers, and actual use of medications), which could partially explain the statistical heterogeneity.[86] To minimize heterogeneity, we included only studies that used validated or conventional definitions and cutoffs for antihypertensive medication nonadherence. Relevant subgroups, meta-regression, and sensitivity analyses were also used to investigate heterogeneity; however, these did not adequately explain the heterogeneity. Although the use of only population-based samples may further reduce heterogeneity (a methodology commonly used in other meta-analyses that investigated hypertension epidemiology), this was not possible because large studies from low- to middle-income countries were not available. For instance, only 1 study from a low- to middle-income country had a sample size >3000.[3] Moreover, our sensitivity analyses, which included only large studies, did not resolve heterogeneity (Tables S17 and S18, Figure S3).

Second, methods including prescription refills, pill counting, electronic pill boxes, and biochemical assays were rarely used in studies from non-Western or low- to middle-income countries. These precluded comparative analyses or statistical significance in several subgroups. Therefore, prevalence estimates from these countries were derived primarily using questionnaire methods, which are prone to self-reporting bias and have poor agreement with objective methods.[87] Furthermore, many questionnaires, such as MMAS-8, cannot provide the exact timing and number of doses missed. However, since questionnaires tended to underestimate nonadherence as compared with objective methods (eg, biochemical assays), this strengthens our conclusion that nonadherence was more prevalent in non-Western or low- to middle-income countries.[2] Third, we included only studies published in English or Chinese. Nevertheless, of the 677 full-text studies screened, only 34 were excluded because of language issues. Fourth, interventional trials were excluded because patients who volunteered and consented to these trials (especially trials to improve drug adherence) could be systematically different from other patients with hypertension. Strict inclusion and exclusion criteria of randomized controlled trials often results in the selection of patients with similar characteristics, which may bias our results. Nevertheless, including baseline data from these intervention trials could further enhance our comprehensiveness and sample size. Fifth, high heterogeneity of the results could hinder the detection of trends of antihypertensive medication nonadherence in the meta-regression analysis.

Sixth, although we used the most validated and conventional cutoffs for questionnaires and MPR, these cutoffs can still be questioned. For example, at a cutoff of 6, MMAS-8 has only a sensitivity and specificity to detect nonadherence of ≈0.43 and 0.74, respectively.[15] Similarly, the MPR cutoff of 0.82, instead of 0.80, may be more appropriate to detect antihypertensive medication nonadherence.[88] However, alternate cutoffs (eg, MPR <0.82), were not used by the current studies and therefore could not be used in the current meta-analyses. We have presented questionnaire data using MMAS-8 <6 and ≤6 (sensitivity analysis in Tables S17 and S18 and Figure S3). Finally, although the results of the health consequences of antihypertensive medication nonadherence were rated low according to Grading of Recommendations, Assessment,

Development and Evaluations because of the inclusion of only observational studies, this matter is difficult and unethical to investigate using clinical trials.

CONCLUSIONS

Globally, ≈27% to 40% of patients with hypertension are nonadherent to their medications. A higher prevalence of antihypertensive medication nonadherence was detected in low- to middle-income and non-Western countries. Interventions are urgently required to detect antihypertensive medication nonadherence and improve medication adherence, especially in countries where antihypertensive medication adherence is suboptimal.

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Supplemental Material

Data S1
Tables S1–S18
Figures S1–S4
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SUPPLEMENTAL MATERIAL

Data S1. Stata commands

For meta-analysis of prevalence,

metaprop baselinenumberofpatients n, fixed by (west_vs_non_west) nowt xlabel (0, 0.5, 0.8) graphregion(color(white)) xtitle("Prevalence",size(2)) astext(70)

baselinenumberofpatients = number of patients with non-adherence
n= total number of patients in the studies
west_vs_non_west = western or non-west countries

For meta-regressions

After running relevant meta-analysis as above,

1/generate meandiff = _ES

2/ generate semeandiff=_seES

3/ metareg _ES west_1 , wsse(_seES) graph

West_1 = western or non-western countries

For meta-analysis for SBP values

metan sbp_na_n sbp_mean_na sbp_na_sd sbp_a_n sbp_mean_a sbp_a_sd, random by(detection_ways) sortby (publication_year_sort) favours (adherence higher #non-adherence higher) nostandard nowt effect (SBP difference) graphregion (color(white)) lcols (study n)

sbp_na_n = number of non-adherent patients
sbp_mean_na = mean of SBP of non-adherent patients
sbp_na_sd = standard deviation of SBP of non-adherent patients
sbp_a_n = number of adherent patients
sbp_mean_a = mean of SBP of adherent patients
sbp_a_sd = standard deviation of SBP of adherent patients

Table S1. Cut-off to define medication non-adherence

Validated questionnaires		
Scale	**Cut-off**	**Reference**
Morisky Medication Adherence Scale -8 (MMAS-8)	<6	[15]
	≤6	(sensitivity analysis)
Morisky-Green-Levine test/ MMAS-4	>0	[88]
Hill-Bone medication adherence scale (9-item)	>9	[39]
Medication Adherence Report Scale-5	<25	[89]
Krousel-Wood Medication Adherence Scale (K-WoodMAS-4)	>=1	[90]
Adherence to Refills and Medications scale (ARMS)	<16	[91]
6-item Girerd compliance test	"no" to all 6 items	[92]
Drug Attitude Inventory (DAI-10)	>5	[93]
H-scale	<21	[94]
MAR-scale	''none of the time'' or ''a little of the time'' for all the 15 items	[95]
QAM-Q	80%-120% of drug intake	[96]
Indirect methods		
Medication possession ratio	<0.8	
Pill count	<0.8	
Proportion of days covered (PDC)	<0.8	
Direct methods		
Electronic caps	<0.8	
Electronic pills	<0.8	
Blood/urine sample	Absence of ≥1 drug in assay	

Table S2 Search Strategy

Search strategy for Ovid MEDLINE

1	Medication Adherence/ or Drug Monitoring/ or Patient Compliance/
2	(drug adherence or patient adherence or medication adherence or medication compliance or medication persistence).mp.
3	Hypertension/
4	(hypertension or hypertensive or high blood pressure or uncontrolled blood pressure).mp.
5	Antihypertensive Agents/
6	(antihypertensive drug* or antihypertensive medication*).mp.
7	"Surveys and Questionnaires"/ or Patient Reported Outcome Measures/ or Monitoring, Ambulatory/ or Electronics, Medical/ or self report/ or Biosensing Techniques/
8	((Adherence to Refills and Medication Scale) or Hill-Bone scale or A-14 scale or Morisky Medication Adherence Scale or MMAS or Medication Adherence Scale or Morisky questionnaire or Morisky scale or interview or questionnaire or survey or pill count or capsule count or medication possession ratio or prescription refills data or dispensed drug or dispensed prescription or dispensed supply or MEMS or Medication Event Monitoring System or electronic monitoring system or electronic adherence monitoring or liquid chromatography-mass spectrometry or drug metabolite or directly observed therapy or digital medicine or ingestible sensor or Proteus or digital medicine offering or electronic medication monitor or pill bottle memory cap or Medication Event Monitoring System).mp.
9	1 OR 2
10	3 OR 4
11	5 OR 6
12	7 OR 8
13	9 and 10 and 11 and 12

The same group of keywords and equivalent subject headings (e.g. Emtree of Embase) were used for searching other databases.

For the China Academic Journals Full-text Database, the following search strategy was used:

AB=' 高血壓' and AB=' 降壓藥物' and AB=' 依從性'

Included studies

Table S3. characteristics of included studies

Characteristics of studies/population		Number of studies
Region/country	China	23
	USA	21
	Brazil	10
	Ethiopia	7
	South Korea	6
	Poland	5
	Spain	5
	India	5
	Canada	4
	Nigeria	4
	Hong Kong	4
	Lebanon	4
	Taiwan	3
	Germany	3
	Iran	3
	France	3
	Turkey	3
	Others	48
Settings	Specialist setting/hospital	102
	Other settings	55
	Not mentioned	4
Continent	Asia	68
	North America	25
	Europe	32
	Africa	23

	South America	12
	Oceania	1
Level of regional income	high	73
	Middle	77
	Low	11
Study design	Cross-sectional	128
	Retrospective cohort study	17
	Prospective cohort study	14
	Case-control study	2
Main method to detect non-adherence	Questionnaire	124
	Prescription refill	24
	Drug assay	5
	Pill counting	4
	Electronic pill box	3

Table S4. characteristics of participants

Characteristic		N	Number of studies reporting this characteristic
Total population		27,785,595	161
Mean age (years)		56.995	123
Sex (%)	Male	42.9%	154
Presence of co-morbidities	Diabetes Mellitus	18.7%	60
	Hyperlipidaemia	32%	34
	Mental illness	10.5%	19
	Cardiovascular diseases	17.1%	35
	Renal diseases	18.2%	28
With insurance or free medical service		94.6%	40
Years of HT diagnosis (years)		0.32	41
receiving single pill combination (%)		20.2%	13
classes of antihypertensive medications (n)		2.08	32
Receiving ≥2 anti-hypertensive medications (%)		66.5%	56
Once daily anti-hypertensive medications (%)		69.1%	17
Tertiary education or above (%)		29.8%	75
Current smoker (%)		19.7%	52

Table S5 characteristics and list of individual included studies

Study	Design	definition of non-adherence	Inclusion/exclusion criteria	Number of participants	Mean age	% of male
Argentina – South America, middle income, non-West						
Espeche 2020[97]	cross-sectional	MMAS-8 <6	Inclusion: hypertension on drugs for ≥6 months, exclusion: lack of BP measurements	1111	62.6	0.5
Austria – Europe, high income, West						
Lotsch 2015[98]	cross-sectional	MMAS-4 >0	Inclusion: ≥18 years of age, had hypertension and taking anti-HT medications by self Exclusion: psychiatric illnesses or living in nursing home	323	62	0.55
Bramlage 2014 [25] (also include Belgium, Germany, Netherland and Switzerland)	cross-sectional	MMAS-8 <6	Inclusion: ≥18 years of age, had hypertension Exclusion: contraindications to anti-HT medications, moderate to severe liver impairment, pregnancy, haemodynamically unstable	10798	64	0.54
Morrison 2015[99] (also include Belgium, England, Germany, Greece, Hungary, Netherlands, Poland, Wales)	cross-sectional	MMAS-4>0	Inclusion: ≥18 years of age, consented, self-reported diagnosed hypertension for ≥ 3 months, prescribed antihypertensive, and personally responsible for administering the antihypertensive Exclusion: self-reported diagnosed psychiatric condition, living in a nursing home (or similar facility)	2595	58.96	0.51
Bangladesh – Asia, middle income, non-West						

Amin 2018[100]	cross-sectional	MMAS<6	Inclusion: ≥ 18 years of age, diagnosed hypertension ≥ 6 months before recruitment, receiving antihypertensive and willing to participate	253	49.2	0.55
Jafar 2018[101]	cross-sectional	MMAS<6	Inclusion: ≥ 40 years of age, residing in the selected clusters, and have hypertension as defined by either persistently elevated BP (SBP ≥140 or DBP ≥90) based on mean BP of last 2 of 3 measurements on 2 separate days or currently on antihypertensive Exclusion: permanently bed-ridden, too ill, with advanced medical disease (on dialysis, liver failure, other systemic disease), pregnant, mentally compromised, or unable to give informed consent	1718	59.7	0.3
Benin – Africa, low income, non-West						
MacquartdeTerline 2019 [31] (also include Cameroon, Congo(Brazzaville), Democratic Republic of the Congo, Gabon, Guinea, Cote d'IvoireIvoire, Mauritania, Mozambic, Niger, Senegal, Togo)	cross-sectional	MMAS <6	Inclusion: ≥ 18 years of age and diagnosed hypertension	2198	58.3	0.4
Brazil – South America – middle income, non-West						

Barreto 2015[102]	cross-sectional	Questionnaire of non-adherence to Medicines of the Qualiaids Team (QAM-Q) <80 to ≥120%	Inclusion: ≥18 years of age and in drug treatment for ≥ 1 year Exclusion: with contraindication of anti-hypertensive therapy and diagnosed mental disorder in the acute phase	422	63.25	0.41
Demoner 2012[103]	cross-sectional	MMAS-4>0	Inclusion: >18 years of age and had hypertension treated with medications	150		0.32
Ledur 2013 [22]	cross-sectional	MMAS-4 >0	Inclusion: <65 years of age, had hypertension (defined as current use of at least one antihypertensive or self-reported hypertension), type 2 diabetes (defined as current use of at least one antidiabetic agent or self-reported diabetes) Exclusion: BMI>35, diagnosed chronic illness, arrhythmias (atrial fibrillation) that could interfere with BP measurement, and ABPM records with <6 and 18 measures during the night and the day periods respectively	323	56.5	0.35
Aielo 2019[104]	cross-sectional	MMAS-4>0	Inclusion: diagnosed hypertension under specific drug treatment	411	54	0.47
Righi 2017 [29]	cross-sectional	MMAS-8<6	Inclusion: ≥18 years of age, on antihypertensive with >1 previous follow-up consultation	416	65	0.32
Oliveira-Filho 2012[20]	cross-sectional	MMAS-8<6	Inclusion: ≥18 years of age, diagnosed hypertension, treated at the USF, used antihypertensive Exclusion: secondary hypertension confirmed by medical records, had purchased ≥1	223	57.18	0.29

			antihypertensive drug in the thirty days preceding the interview			
deOliveira-Filho 2014[43]	cross-sectional	MMAS-8<6	Inclusion: ≥18 years of age, taking ≥1 medication to control hypertension	937	57.1	0.29
Ben 2012[105]	cross-sectional	MMAS-4>0	Inclusion: hypertensive people enrolled ≥6 months in the program to assist hypertensive and diabetic individuals (Hiperdia), in basic health units of the city of Porto Alegre, Southern Brazil Exclusion: cognitive deficit, resident of other areas, death, not reached, not hypertensive, participating in other research and refusal	206	66.6	0.35
Ungari 2010[106]	cross-sectional	MMAS-4>0	Inclusion: ≥ 20 years of age, diagnosed hypertension, taking antihypertensive drugs for ≥6 months prior to the study, able to understand, verbalize and answer the questionnaire and give written informed consent	109		0.16
TizatoFeriato 2018[107]	cross-sectional	MMAS-4 >0	Inclusion: workers of the hospital who mentioned the diagnosis of hypertension	108	44.2	0.24
Cameroon, Africa -middle income, non-West						
Akoko 2017[108]	cross-sectional	MMAS-8 <6	Inclusion: ≥21 years of age at diagnosis, on antihypertensive for ≥6 months, and resided in communities in the various health areas in the Bamenda Health District of Cameroon Exclusion: hypertensive patients not on pharmacological treatment	221	62.86	0.44

Adidja 2018[55]	cross-sectional	MMAS-8 <6	Inclusion: ≥ 21 years of age, provided consent, with hypertension, on hypertensive medication(s) for ≥1 month Exclusion: pregnant women, self-reported hypertension but no proof on or had been prescribed drugs, ever smoked, consumed alcohol or other cardio-stimulants 30 mins prior to data collection, and could not express themselves in either English or French	183		0.36
Canada – North America, high income, West						
Natarajan 2013[109]	cross-sectional	MMAS-4>0	Inclusion: provided consent, could understand English, available for follow-up for >1 year, diagnosed with type 2 DM and hypertension, had BP measured with the BpTRU (an automated oscillometric instrument) by their family physicians or nurse practitioners within the past 6 months	527	66	0.52
Gentil 2017[110]	Retrospective cohort study	MPR <0.8	Inclusion: diagnosed hypertension; ≥2 physician claims within 2 years, or 1 inpatient hospital discharge report listing hypertension as a diagnosis with ICD-9 or ICD-9-CM: 401-405, and taking antihypertensive agents registered in RAMQ or MedEcho database Exclusion: severe or moderate cognitive problems with Mini-Mental State Examination (score<22), with a private drug insurance plan	926		0.25
Perreault 2010[63]	Case-control study	MPR <0.8	Inclusion: 45-85 years of age, newly treated (had not taken any AH agent in the 2 years prior to entry into the cohort) with either diuretics (excluding high ceiling diuretics), b-blockers, ACEIs, CCBs, ARBs or a combination between 1/1/1999 and 31/12/2004, diagnosed with essential hypertension (ICD-9 code 401), had filled ≥3	184383	67	0.34

			antihypertensive prescriptions within the 6 months after their entry into the cohort, and had a medical visit with their doctor and to have filled ≥1 antihypertensive prescription for each period of 1.5 years Exclusion: CVD as evidenced by the absence of a related diagnosis or medical procedure in the last 5 years, and any vascular drug marker in the 2 years prior to the cohort entry date, marker of CVD such as: (i) CAD: diagnosis of myocardial infarction or angina; vascular medical procedure, e.g. coronary artery bypass grafting, angiography, or angioplasty or stent, or use of nitrate, including nitroglycerin; (ii)cerebrovascular disease: diagnosis or vascular medical procedures or use of nimodipine; (iii) peripheral arterial disease: diagnosis of a peripheral vascular disease, medical procedure of noncoronary angioplasty or use of pentoxifylline; (iv) chronic heart failure or the use of furosemide alone or with digoxin, ACEIs, spironolactone orb-blockers; (v) arrhythmia: diagnosis, a medical procedure involving a pacemaker or the use of drugs for cardiac arrhythmias; or (vi) valvular heart disease; with diseases such as a renal disease, a related medical procedure, or drugs that may have caused secondary hypertension; received other drugs such as antiplatelets (excluding a low dose of aspirin), or anticoagulants during the 2 years preceding the cohort entry date			
Tang 2017[66]	Prospective cohort study	PDC <0.8	Inclusion: ≥65 years if age, Manitoba residents, with incident hypertension, with an index date of diagnosis between 1/4/2004 and 31/3/2005	2199	75.2	0.45

			Exclusion: without at least 1 prescription refill within 1 year after the first prescription fill in any of the five antihypertensive medication classes of interest (thiazide-type diuretics, beta blockers [BB], calcium channel blockers [CCB], angiotensin converting enzyme inhibitors or angiotensin receptor blockers [ACEI/ARB], or a combination containing ≥ 1 of the above classes; died within 1 year of the first prescription fill			
China – Asia, middle income, non-West						
Lee 2017[111]	cross-sectional	MMAS-4>0	Inclusion: had essential hypertension Exclusion: secondary hypertension	2342	58.6	0.41
Zhao 2015[112]	cross-sectional	MMAS-8<6	Inclusion: diagnosed essential hypertension, receiving ≥1 antihypertensive for ≥1 month, with no mental illness	236	64.1	0.47
Wu 2020[61]	cross-sectional	MMAS-8<6	Inclusion: ≥ 40 years of age, essential hypertension, living in the area, on antihypertensive for ≥3 months Exclusion: secondary hypertension, serious mental illnesses, did not finish the questionnaire, serious physical illnesses	451		0.52
Shen 2020[113]	cross-sectional	MMAS-8<6	Inclusion: ≥18 years of age, diagnosed with hypertension by a cardiologist, antihypertensive for ≥2 weeks, speak Chinese and communicated well with others, understood the purpose and process of the study and agreed to participate Exclusion: had other serious diseases, such as cancer, acute myocardial infarction, cerebral hemorrhage or	790		0.54

			chronic renal failure, had secondary hypertension, such as elevated blood pressure caused by chronic renal dysfunction diseases, diagnosed as psychological or mental impairment according to ICD guideline, on the psychotherapy treatment			
Shi 2019[114]	cross-sectional	MMAS-8 <6	Inclusion: ≥18 years of age, diagnosed hypertension according to the 2011 prevention and treatment guidance for hypertension in China i.e. SBP≥140 mmHg and/or DBP ≥90 mmHg, on antihypertensive for ≥2 weeks, could speak Chinese and communicate well with others Exclusion: severe or acute hypertension or other unstable and uncontrolled cardiovascular and cerebrovascular diseases, psychological and mental illness or pharmacotherapy for mental health conditions, hearing and communication disabilities, dementia or cognitive impairment, cancer, New York Heart Association Class III or IV heart failure, unstable angina, severe disease of other organs or systems	420	60.6	0.53
Tam 2017[115]	cross-sectional	MMAS-4 >0	Inclusion: hypertension for ≥1.5 years, hypertension on medications Exclusion: mental illnesses or cognitive impairment	287	72.53	0.53
Yue 2015[116]	cross-sectional	MMAS<6	Inclusion: outpatients diagnosed with primary hypertension and under antihypertensive drug treatment for ≥1 month Exclusion: have difficulty in understanding or communicating with the investigator, with severe acute diseases, too weak to join	232	64.15	0.47

Ting 2017[117]	cross-sectional	MMAS-4 >0	Inclusion: hypertensive patients on antihypertensive	956	49	0.49
Pan 2017[118]	cross-sectional	MMAS-4>0	Inclusion: ≥18 years of age, hypertensive patients. agreed to attend the study, took antihypertensive during hospitalization, diagnosed with stroke by neurological physician, had a telephone contact records in their medical charts Exclusion: brain tumor or traumatic hemorrhagic stroke, cannot communicate due to physical or mental problems, pregnant women	440		0.55
Hou 2016[47]	cross-sectional	MMAS-8<6	Inclusion: ≥60 years of age, from one specialty outpatient clinic and three inpatient wards of the vasculo-cardiology department of the University Hospital and 15 urban communities in Suzhou, taking ≥1 long-term antihypertensive which effect could last more than 24hrs, able to communicate Exclusion: dementia or cognitive impairment, cancer, New York Heart Association Class III or IV heart failure, unstable angina	585	68.4	0.6
Song 2016[119]	cross-sectional	MMAS-8<6	Inclusion: diagnosed hypertension with ≥2 weeks of antihypertensive medications, normal vision, hearing and comprehensive ability Exclusion: not on medications or received <2 weeks of medications, severe cognitive or mental disorders	156	67	0.47
Ha 2012[120]	cross-sectional	MMAS-4>0	Inclusion: hypertensives in the hospital	162		0.56

Zhang 2017[53]	cross-sectional	MMAS-4>0	Inclusion: ≥18 years of age, primary hypertensive patients included in chronic non-epidemic disease system management Exclusion: with other physical disease, such as cerebral apoplexy, diabetes, tumor, thyroid disease, with family history of psychosis, psychosis disease patents who could not properly answer questions due to physical disability and cognitive impairment	1095		0.46
Wong 2018[121]	cross-sectional	MMAS-4 >0	Inclusion: hypertensive patients in the community	202	70.82	0.32
Yang 2016[122]	cross-sectional	MMAS-4 >0	Inclusion: ≥ 18 years of age, confirmed hypertension patients taking ≥1 kind of antihypertensive	745	56.4	0.46
Lau 2010[123]	cross-sectional	MMAS-4>0	Inclusion: hypertensive patients	526		0.73
Chan 2015[124]	cross-sectional	MMAS-4>0	Inclusion: ≥18 years of age, ≥3 months of HT Exclusion: family history of mental illness, other serious illnesses, cognitive or physical impairment	235	51.3	0.52
Ko 2017[125]	cross-sectional	MMAS-4>0	Inclusion: hypertensive patients on any of 5 commonly used antihypertensives, normal cognitive function, co-operative	3663		0.42
Li 2016[126]	cross-sectional	MMAS-4 >0	Inclusion: ≥60 years of age, hypertension, taking ≥1 antihypertensive for ≥1 month, communicable, provided consent	1316	72.93	0.42

Long 2020[127]	cross-sectional	MMAS-4 >0	Inclusion: ≥ 18 years of age, has hypertension >1 year; antihypertensive use >6 months, speak a Chinese dialect, communicable, provided consent Exclusion: serious complications, cancers, family history of mental illnesses	642	65.36	0.41
Chui 2015[128]	cross-sectional	MMAS-4>0	Inclusion: essential hypertension, hospitalized	220	53.6	0.48
Chan 2018[129]	cross-sectional	MMAS-4>0	Inclusion: >18 years of age, hypertension, on antihypertensives for >6 months Exclusion: secondary hypertension, with serious illnesses, not on antihypertensive or <6 months, unwilling to join	110		
Li 2015[130]	cross-sectional	MMAS-8 <6	Inclusion: ≥30 years of age, with hypertension Exclusion: secondary hypertension (such as pregnancy induced hypertension), stroke, senile dementia, severe mental disorder, language barriers	474		0.36
Democratic Republic of Congo – Africa, low income, non-West						
Lulebo 2015[131]	cross-sectional	MMAS-4 >0	Inclusion: >18 years of age, hypertensive patients, on antihypertensive drugs for ≥1 month Exclusion: pregnant women	395	63.3	0.24
Egypt – Africa, middle income, non-West						
Hassanein 2020 [32]	cross-sectional	MMAS-8<6	Inclusion: >21 years of age, essential hypertension who were prescribed antihypertensive with FDC for ≥3 months, willing to give written informed consent Exclusion: severe renal impairment (GFR < 30 ml/min), pregnancy, lactation, secondary	2000	55.8	0.52

			hypertension, hypersensitivity to the used medications, or participating in other clinical studies			
Ethiopia – Africa, low income, non-West						
Mekonen 2020[65]	Case-control study	MMAS-8 <6	Inclusion: Cases: adult hypertensive patients with stroke diagnosed by the neurologist (consultant internist) or confirmed by brain imaging (CT-scan) or MRI, Controls: adult hypertensive patients without clinical evidence of stroke and without a history of stroke available in ACSH during the data collection period Exclusion: cases with less than three follow-up for hypertension treatment before first stroke occurrence and controls with less than three follow-up for hypertension treatment, pregnant mothers	445	52.78	0.49
G/Tsadik 2020[132]	cross-sectional	MMAS-8 <6	Inclusion: ≥ 18 years of age, hypertension confirmed by a physician, on antihypertensive for ≥3 months, can give consent, with no acute distress related to any disease during recruitment Exclusion: pregnant women, cannot give consent, have hearing and/or speaking problems	989	57.6	0.47
Asgedom 2018[133]	cross-sectional	MMAS-8<6	Inclusion: ≥ 18 years of age, hypertensive patients aged, had a regular follow-up for ≥12 months at the clinic, used an antihypertensive for hypertension, medical records contained complete data, willing to participate Exclusion: seriously ill patients who were not able to finish the interview, on DASH therapy alone, patients without complete medical records	280	55.05	0.53

Mekonnen 2017[52]	cross-sectional	MMAS-8<6	Inclusion: ≥ 18 years of age, hypertensive patient, have been taking antihypertensive medications for ≥1 month Exclusion: not capable of hearing and speaking, known mental disorders or serious illness	409	54.5	0.58
Berhe 2017[134]	cross-sectional	MMAS-8 <6	Inclusion: ≥ 18 years of age, hypertensive patients, received ≥1 antihypertensive from the same hospital previously, as reported by the patient and/or recorded in their appointment card (verified patient medical record), gave informed consent Exclusion: medical records were unavailable or incomplete, proved not to be hypertensive after review of medication record, unable to complete MMAS-8 questionnaire	925	57	0.37
Animu 2018[57]	cross-sectional	MMAS-4>0	Inclusion: adult hypertensive patients who were on outpatient follow-up for ≥6 months, had ≥1 documented BP measurement result	395	57	0.38
Kebede 2020[135]	cross-sectional	MMAS-8 <6	Inclusion: ≥18 years of age, confirmed diagnosis of hypertension, receiving drugs for hypertensin for ≥3 months before data collection, have follow-up at outpatient chronic care unit Exclusion: having psychiatric co-morbidity/ mental illness, pregnant women	153	46.85	0.54
France – Europe, high income, West						
Korb-Savoldelli 2012 [19]	cross-sectional	MMAS-8<6	Inclusion: >18 years of age, treated with antihypertensive, able to read French, signed a written consent	199	55.7	0.57

Lefort 2018[136]	cross-sectional	Girerd compliance test >= 1 "yes" answer	Inclusion: ≥55 years of age, declared being treated for hypertension, answered the adherence questionnaire	2370		0.48
Hamdidouche 2017[37]	cross-sectional	absence of any drug in urine	Inclusion: ≥ 18 years of age, consecutive outpatients attending the hypertension clinic of one physician (S.L.) at the hypertension department of the Pompidou university hospital in Paris, prescribed ≥1 antihypertensive, had essential hypertension Exclusion: severe uncontrolled hypertension (SBP>=200 mmHg and/or DBP>=130mmHg), severe reduced kidney function that may influence renal excretion of antihypertensive, serious physical or psychiatric impairment that limited ability to self-administer antihypertensive medications	174	67	0.43
Germany – Europe, high income, West						
Breitscheidel 2012[137]	Retrospective cohort study	MRP<0.8	Inclusion: diagnosed hypertension (ICD-10 code I10), with treatment data for period 09/2009 to 08/2010, prescriptions of ARBs as single-agents or in combination (fixed-dose or unfixed) with other antihypertensive drugs (e.g., diuretics, CCBs, beta-blockers [BBs], ACEIs)	17310	65.9	0.45
Koschack 2010 [39]	cross-sectional	MMAS-4>0	Inclusion: diagnosis of hypertension on the electronic patient record Exclusion: unconfirmed hypertension diagnosis, emergency visits or practice visits made during times when the practitioner has been temporarily replaced by a locum, mental or terminal disease, with difficulties on verbal communication	353	64	0.51

Schulz 2016[138]	Retrospective cohort study	MPR <0.8	Inclusion: on antihypertensive as monotherapy in first-line treatment Exclusion: prescriptions of loop diuretics, mineralocorticoid receptor antagonists, or any antihypertensive which was not approved for hypertension as single drug product (monotherapy) or fixed dose combinations of loop diuretics or mineralocorticoid receptor antagonists, with a prescription within 12 months prior to the first prescription of one of the antihypertensives included, prescribed parenteral or liquid formulations, with a prescription of a different antihypertensive between first and index prescription, switching the index antihypertensive substance/ fixed combination during the observation period, changed insurance company or died during the study period, no prescription for any medication between 24 and 36 months following the index prescription has been claimed	255501		
Ghana – Africa, Middle income, non-West						
Kretchy 2014[139]	cross-sectional	MMAS-8 <6	Inclusion: ≥ 18 years of age, Ghanaian patients diagnosed as hypertensive only or hypertensive with other co-morbid conditions, reported for treatment at KBTH and KATH, report prescription of ≥1 antihypertensive Exclusion: in-patients, pregnant women, incapacitated people	400		0.37

Sarkodie 2020[140]	cross-sectional	MMAS-8 <6	Inclusion: ≥ 18 years of age, diagnosed hypertension for ≥6 months, on medication during the period of data collection Exclusion: pregnancy induced hypertensive patients, did not consent	370		0.24
Greece – Europe, high income, West						
Stavropoulou 2012[141]	cross-sectional	MMAS-4>0	Inclusion: hypertensive patients	743	61	0.4
Hong Kong – Asia, high income, non-West						
Lee 2013 [21]	cross-sectional	MMAS<=6	Inclusion: ≥ 18 years of age, taking ≥1 long-term antihypertensive, able to communicate and understand Cantonese	1114	65.7	0.42
Kang 2015 [26]	cross-sectional	MMAS <=6	Inclusion: ≥ 18 years of age. hypertensive patients, taking ≥1 type antihypertensive, able to communicate in Cantonese	2445	65.5	0.44
Wong 2010[142]	Retrospective cohort study	MPR <0.8	Inclusion: attended the public primary care practice and received a single antihypertensive prescription in the public sector Exclusion: paid only one clinic visit where anti-hypertensive drugs were prescribed	83884	64.25	0.43
Lo 2016[143]	cross-sectional	MMAS-4>0	Inclusion: ≥65 years of age, had a diagnosis of essential hypertension, attended regular medical consultations for essential hypertension, received ≥1 type of antihypertensive, understood and spoke Cantonese, willing to participate	195	76.4	0.21

			Exclusion: secondary hypertension, psychiatric illness or mental impairment, were unable to give informed consent			
Li 2016[144]	cross-sectional	MMAS-8 <= 6	Inclusion: ≥ 18 years of age, Chinese patients, with physician-diagnosed hypertension including both essential and secondary hypertension, already on antihypertensive regime for ≥4 weeks before the study, mentally capable to communicate in Chinese, willing to give written informed consent Exclusion: newly diagnosed hypertension on the day of the recruitment	2445	65.3	0.46
India – Asia, middle income, non-West						
Sarika 2020[145]	cross-sectional	MMAS-8<=6	Inclusion: hypertensive patients	254		0.63
Meena 2018[146]	Prospective cohort study	MMAS-8<6	Inclusion: hypertensive patients enrolled at NCD clinic	940		
Dennis 2011 [18]	cross-sectional	BMQ>0	Inclusion: hypertensive adults having a treatment history of ≥6 months Exclusion: pregnant women, unable to attend the interview, not willing to give informed consent, having severe complications including coronary artery disease and end organ damage	608	58.4	0.51
Balasubramanian 2018[147]	cross-sectional	MMAS-4>0	Inclusion: ≥30 years of age, diagnosed with hypertension for ≥6 months, resided in the study area for ≥6 months Exclusion: bedridden patients, pregnant women	189	65.12	0.49
Sheilini 2018[148]	cross-sectional	MMAS-8 <6	Inclusion: ≥ 60 years of age, with or without comorbidities like diabetes mellitus, chronic	800		0.52

			Ischaemic Heart Diseases, dyslipidaemias, chronic rheumatism and any other chronic conditions; able to manage taking medications, able to read, write, and converse in English/ Kannada, diagnosed with Stage I (SBP and DBP ranging between 140-159 mmHg and 90-99 mmHg) and Stage II (SBP and DBP ranging between 160-180 mmHg and 100-110 mmHg) according to the Joint National Committee-VII report Exclusion: Stage III hypertension (SBP and DBP ranging between >180 mmHg and >110 mmHg), renal failure, acute stroke, IHD, major psychiatric disorders, dementia or delirium			
Indonesia – Asia, middle income, non-West						
Athiyah 2013[149]	cross-sectional	MMAS-8<6; pill count <0.8	Inclusion: have hypertension, visited Primary Health Centers in five regions of Surabaya during February 2015, on antihypertensive ≥2 weeks, had an ability to communicate well, willing to become the respondents	204		0.27
Sulistiyowatiningsih 2017[150]	cross-sectional	MMAS-8 <6	Inclusion: ≥ 18 years of age, confirmed diagnosis of hypertension, treated at primary health care, on antihypertensive Exclusion: secondary hypertension, with diabetes mellitus, heart disease, hyperlipidemia, stroke, and renal failure confirmed by medical records	233		0.36
Iran – Asia, middle income, non-West						

Heizomi 2020[151]	cross-sectional	MMAS-4 >0	Inclusion: ≥30 years of age, confirmed systolic and/or diastolic BP>120/80 mmHg on two separate occasions in a seated position (Based on the Eighth Joint National Committee (JNC 8), diagnosed in the last six months, resident of study areas ≥6 months, without comorbidities including diabetes mellitus, rheumatoid arthritis, osteoarthritis, coronary heart disease, and hyperlipidemia	300	56.7	0.49
Mamaghani 2020[152]	cross-sectional	MMAS-8<6	Inclusion: diagnosed hypertensive patients	238	57.4	0.32
Behnood-Rod 2016[28]	cross-sectional	MMAS-8<6	Inclusion: adult patients who had documented hypertension and were taking antihypertensive	280	60.3	0.42
Ireland – Europe, high income, West						
Dillon 2019[153]	Prospective cohort study	MPR <0.8	Inclusion: ≥65 years of age, on ≥1 medication for hypertension, community dwelling, able to speak and understand English, with no evidence of cognitive impairment as judged by the pharmacist Exclusion: had incomplete pharmacy records, including participants who reported attending other pharmacies from which pharmacy records were not captured	905	76.39	0.47
Walsh 2019[69]	Prospective cohort study	PDC<0.8	Inclusion: ≥ 50 years of age (at time of CAPI), had participated in wave 1 of TILDA, have a general medical services (GMS) card, received ≥3 pharmacy claims for an antihypertensive within the 12 months preceding the time referred to in the CAPI interview in wave 1	1431	74	0.46
Japan – Asia, high income, non-West						

Saito 2016[154]	Retrospective cohort study	PDC <0.8	Inclusion: <75 years of age, prescribed with anti-HT	2132	58.9	0.68
Kenya – Africa, middle income, non-West						
Otenyo 2018[155]	cross-sectional	MMAS-8<6	Inclusion: ≥18 years of age, with chronic kidney disease who had also been diagnosed with hypertension	144		0.52
Latvia – Europe, high income, West						
Gavrilova 2019[156]	cross-sectional	MMAS-8 <6	Inclusion: >18 years of age, with diagnosis of arterial hypertension, taking antihypertensive for ≥1 year	171	64.36	0.25
Lebanon – Asia, middle income, non-West						
Yassine 2016[157]	cross-sectional	MMAS-8<6	Inclusion: Lebanese adult outpatients (P18 years), diagnosed with essential (primary) hypertension by a cardiovascular physician. taking ≥1 antihypertensive Exclusion: secondary hypertension, pregnant women, taking other drugs that could increase BP, hypertensive patients taking no medication	210	59.33	0.41
BouSerhal 2018[158]	cross-sectional	MMAS-8 <6	Inclusion: ≥ 18 years of age, Lebanese, with primary hypertension diagnosed ≥6 months, treated with antihypertensives for ≥ 6 weeks, having signed the informed consent Exclusion: secondary hypertension, pregnant women, being hospitalized, dementia, mentally disabled, physical disability, any infection affecting blood pressure	404	65.05	0.49
Saarti 2016[49]	cross-sectional	MMAS-8<6	Inclusion: ≥18 years of age, hypertensive patients (diagnosed with hypertension ≥3 months before	117		0.5

			recruitment), had been taking ≥1 antihypertension drug for ≥3 months Exclusion: secondary hypertension, cognitive disease, unable to recognise their antihypertension medications from the total medications they were taking daily			
Farah 2016[159]	cross-sectional	MMAS-8 <6	Inclusion: ≥40 years of age, diagnosed with hypertension by a physician, taking antihypertensive	562	63.7	0.5
Alhaddad 2016[50] (and Jordan)	Prospective cohort study	MMAS-4>0	Inclusion: ≥21 years of age, newly diagnosed with hypertension, uncontrolled hypertension on medication after being treated for ≥6 months Exclusion: secondary hypertension, acute illnesses, psychiatric diseases, pregnant women, nursing mothers, unable to provide informed consent	1470	54.69	0.57
Malaysia – Asia, middle income, non-West						
Tan 2020 [34]	cross-sectional	MMAS-8<6	Inclusion: ≥ 18 years of age, diagnosed with hypertension by a registered medical practitioner for ≥3 months (verified by patients appointment card), prescribed with ≥1 antihypertensive for the past 3 months, able to communicate in English or Malay Exclusion: severe enduring health problems or cognitive impairment	384	56.8	0.4
Nepal – Asia, middle income, non-West						
Shakya 2020[160]	cross-sectional	Hill Bone Compliance>9	Inclusion: ≥20 years of age, diagnosed with hypertension, on antihypertensive therapy for ≥6 months,	204	60	0.51

			attending the OPD in MCVTC, can communicate in Nepali, willing to participate Exclusion: hospitalised, medically unstable (having high BP, symptoms like headache, dizziness at the time of interview), unable to communicate			
Netherland – Europe, high income, West						
VanKleef 2019[161]	cross-sectional	quantitative LC-MS/MS in plasma - concentration ratio (CR) of at least one of the prescribed drugs ≤0.3	Inclusion: newly referred hypertensive patients prescribed with ≥1 antihypertensive	197	56	0.49
New Zealand – Oceania, high income, West						
Warren 2011[162]	Retrospective cohort study	MPR <0.8	Inclusion: >20 years of age, had ≥1 antihypertensive prescription in the period 1/7/2007 to 31/12/2008	1475		
Nigeria – Africa, middle income, non-West						
Akintunde 2015[163]	cross-sectional	MMAS-8 <6	Inclusion: adult hypertensive patients, on medications for ≥ 1 year, has been attending the clinic from which they were recruited for ≥3 months before the recruitment, willing to participate Exclusion: any behavioural or social issues that might affect medication adherence, declined to participate, with serious medical or surgical issues requiring admission into the hospital	114	62.7	

Adeoye 2019 [30]	cross-sectional	MMAS-4>0	Inclusion: ≥18 years of age, ≥1 year duration of hypertension on treatment, provided consent, on ≥1 antihypertensive with BP ≥140/90mmHg at recruitment, with two or three previous clinic visits Exclusion: had kidney transplantation, refused to consent	148	61.06	0.48
Ekanem 2020[164]	cross-sectional	MMAS-8<6	Inclusion: adult hypertensive patients who presented at designated outpatient clinics for 3 months (May to July) 2018, outpatient treatment for ≥6 months and recorded ≥2 clinic visits, not critically ill, had no conditions that affect cognition e.g. psychiatric illnesses	379	60.75	0.75
Okwuonu 2014[165]	cross-sectional	MMAS-8<6	Inclusion: ≥18 years of age, provided consent, with a previous diagnosis of hypertension made by medical personnel, on antihypertensive Exclusion: psychiatric illness, an appearance of being chronically ill, known hypertensive emergency	252	56.6	0.57
Oman – Asia, high income, non-West						
Al-Noumani 2018[56]	cross-sectional	MMAS-8 <6	Inclusion: ≥21 years of age, Omanis. diagnosed with hypertension for ≥3 months, taking ≥1 antihypertensive	215	53.6	0.34
Pakistan – Asia, middle income, non-West						
Saleem 2012[166]	cross-sectional	DAI-10<=5	Inclusion: ≥18 years of age, with confirmed diagnosis of hypertension, using antihypertensive for the last six months, familiar with the national language of Pakistan (Urdu)	385	39.02	0.69

			Exclusion: aged <18 or >80 years, with co-morbidities and mental impairments, immigrants from other countries, pregnant ladies			
Saqlain 2019[167]	cross-sectional	MMAS-4>0	Inclusion: ≥65 years of age, diagnosed with hypertension, taking ≥1 medication for the previous one month Exclusion: cognitive impairment and psychiatric illness, visiting hospital due to exacerbation of acute illness that might lead to hospital admission	262		0.36
Mahmood 2020 [33]	cross-sectional	MMAS-8 <6	Inclusion: ≥ 18 years of age, diagnosed with essential hypertension at any time; on ≥1 antihypertensive for the past 6 months, able to communicate in Urdu language, attending one of the participating healthcare facilities Exclusion: pregnant women, mental disorders such as dementia, could not communicate in Urdu	741	53.6	0.53
Palestine – Asia, middle income, non-West						
Zyoud 2013[168]	cross-sectional	MMAS-8 <6	Inclusion: ≥ 18 years of age, diagnosed with hypertension ≥6 months before recruitment, treated for hypertension with anti-hypertensive, able to recognise their medications from the total medications that they took daily, willing to participate, given verbal consent	410	58.38	0.48
Peru – South America, middle income, non-West						
Fernandez-Arias 2014[169]	cross-sectional	MMAS-8 <6	Inclusion: adult patients in the waiting rooms of the cardiology and endocrinology clinics that admitted having a medical diagnosis of hypertension, take ≥1 antihypertensive	115	62.7	0.33

			Exclusion: patients that were not responsible for their own medication, unable to understand questionnaires			
Poland – Europe, high income, West						
Jankowska-Polanska 2017[170]	cross-sectional	MMAS-8<6	Inclusion: ≥18 years of age, diagnosis of hypertension in line with the guidelines of the ESH, treatment with ≥1 antihypertensive for the past year, provided informed consent Exclusion: other serious diseases (cardiac insufficiency, renal insufficiency, and neoplasms) and severe cardiovascular complications or other severe concomitant diseases	620	58	0.46
Pluta 2020[171]	cross-sectional	MMAS-8<6	Inclusion: ≥ 18 years of age, clinically diagnosed hypertension, provided consent	200	49.1	0.43
Wilinski 2013[172]	cross-sectional	MMAS-4>0	Inclusion: arterial hypertension with the pharmacotherapy containing ramipril (Pi-ramil, Sandoz Polska, Poland) in the daily dose of 10 mg which has been introduced within the last 3 months Exclusion: standard contraindications for the ACE inhibitors use	1467	59.5	0.49
Jankowska-Polanska 2016[173]	cross-sectional	MMAS-8 <6	Inclusion: ≥ 60 years of age, clinically confirmed hypertension, provided written informed consent Exclusion: moderate to severe dementia (defined as Mini-Mental score <15), previous stroke, not provided consent	296	68.8	0.44
Lomper 2018[58]	cross-sectional	ARMS >=16	Inclusion: >18 years of age, diagnosed with hypertension in accordance with the European Society of Hypertension	279	66.5	0.41

			guidelines (BP value the mean of two measurements with an interval of 1-2 minutes; third measurement was done in patients whose difference in measurements was >10 mmHg), had been treated with ≥1 antihypertensive for ≥6 months, had no mental disorders or cognitive impairment with dementia Exclusion: limited cognitive function (score showing cognitive impairment with dementia on the Mini-Mental State Examination, cutoff at 23 points), did not provide informed consent in writing, had an exacerbation of concurrent severe chronic diseases (cancer, respiratory failure, or cardiac decompensation)			
Portugal - Europe, high income, West						
Cabral 2018[174]	cross-sectional	MMAS-8 <6	Inclusion: >18 years of age, taking ≥1 antihypertensive drug	472	68.2	0.49
Russia – Asia, middle income, non-West						
Efanov 2018[175]	Prospective cohort study	MMAS-8 <6	Inclusion: arterial hypertension, visited one of the outpatient departments in Tyumen region, Russia	256		
Saudi Arabia – Asia, high income, non-West						
Fatani 2019[176]	cross-sectional	MMAS-8<6	Inclusion: ≥18 years of age, hypertensive adult patients, all nationalities who have an access on any of social media	276		0.42
Khayyat 2017[177]	cross-sectional	MMAS-8 <6	Inclusion: >18 years of age, confirmed diagnosis of hypertension for >6 months, taking ≥1 antihypertensive, able to communicate in Arabic	204	59.1	0.28

			Exclusion: pregnant women, patients with mental health issues and dementia			
Serbia – Europe, middle income, West						
Lalic 2013[42]	cross-sectional	MMAS-8<=6	Inclusion: outpatients with hypertension (II-IV degree), treated in the primary healthcare	170	64.5	0.34
Singapore – Asia, high, non-West						
Kang 2020[178]	cross-sectional	MARS-5 <25	Inclusion: 31-80 years of age, diagnosis of essential hypertension, with ≥1 antihypertensive prescription in the past 12 months in their electronic health records (EHR) and prescription records, multi-ethnic Asian adults Exclusion: debilitating conditions which rendered them incapable of providing informed consent, treated for hypertension by healthcare providers other than those at Sengkang Polyclinic	395	61	0.48
Slovenia – Europe, high income, West						
Janezic 2014[179]	cross-sectional	MMAS-8<6	Inclusion: adult Slovenian speaking patients dispensed ≥1 antihypertensive	468		0.42
South Africa – Africa, middle income, non-West						
Olowe 2017[180]	cross-sectional	MMAS-8<6	Inclusion: >18 years of age, hypertension, had been collecting hypertensive medication from the PHC clinic for ≥1 year Exclusion: <18 years of age, not willing to participate	348		0.22
South Korea – Asia, high income, non-West						

Choi 2018[181]	Prospective cohort study	pill counting of <0.80	Inclusion: ≥20 years of age at diagnosis, prescribed angiotensin II receptor blockers (ARBs) for the first time, both newly treated hypertensive patients and those who were already on antihypertensive medication other than ARBs	1523		0.6
Kim 2016[182]	Retrospective cohort study	MPR<0.8	Inclusion: ≥20 years of age, patients with hypertension whose major diagnoses included ICD-10 code: I10 -I15, excluding I14, newly diagnosed hypertension who have not used medical services for the past year, filed claims for health insurance coverage for hypertension more than once in the year 2008, prescribed anti-hypertensive drugs at least once Exclusion: patients with newly diagnosed hypertension who died within 2 years after they received their first prescription, suffered complications such as stroke or ischemic heart disease within one year before medication was first prescribed and two years following the first prescription	564782	58.8	0.48
Choi 2017[183]	Retrospective cohort study	MPR<0.8	Inclusion: newly diagnosed uncomplicated hypertensive adult patients who started antihypertensive monotherapy in 2012 Exclusion: had been prescribed any antihypertensive medication within 1 year before the index date, previously diagnosed with cardiovascular disease (I20-I25, I30-I52, Z95), cerebrovascular disease (G45, I60-I69), peripheral vascular disease (I7X), renal disease (N03-N05, N18, N19, Z49, Z94.0, Z99.2), diabetes mellitus (E08-E11, E13), and pregnancy (O00-O9A), prescribed only 1 dose of	20067	68.5	0.27

			antihypertensive or who had taken the medications for a period of <7 days, had been hospitalized for >7 days within 1 year, claims data were discontinued before the end of the follow-up period			
Park 2013 [23]	cross-sectional	MMAS-4>0	Inclusion: ≥65 years of age, attended a large senior centre in Seoul, having regular follow-up care at the clinic for treatment of hyper-tension (at least once every 6 months), diagnosed with hypertension for ≥1 year before completing the study, prescribed antihypertensive medication	241		0.6
Lee 2019[67]	Retrospective cohort study	MPR<0.8	Inclusion: 30 to 80 years of age, newly treated for primary hypertension (ICD-10 code I10 with antihypertensive medication) from 1/1/2004 to 31/12/2007 Exclusion: prior diagnosis or medication for any hypertensive disease, prior myocardial infarction, heart failure, or stroke, <2 prescriptions during the first year of treatment, died or had a CVD event within 2 years following the index date, with incomplete income information including medical aid beneficiaries	1651564	53	0.52
Kim 2014 [24]	cross-sectional	MMAS-8 <6	Inclusion: >30 years of age, able to communicate in the Korean language, receipt of a prescription for antihypertensive at the clinics during the 30 days before the study began, no signs or symptoms of severe health problems such as cancer or chronic heart failure	373	57.2	0.55
Spain – Europe, high income, West						

Perseguer-Torregrosa 2014[44]	Prospective cohort study	Pill counting: <80% of prescribed drugs	Inclusion: ≥50 years of age, hypertensive patients, taking antihypertensive for ≥3 months, visited the pharmacy during the study period, gave informed consent Exclusion: dementia or severe diseases or any mental, pathological, or social issue that could prevent adequate completion of the data collection notebook or pill count, pregnant women, participants in other research studies, persons living with somebody else taking the same antihypertensive treatments, treatment distributed over several locations, did not have a telephone contact number	419	64.7	0.44
Marquez-Contreras 2012[184]	Prospective cohort study	Pill Box: percentage of compliance < 80%	Inclusion: >18 years of age, had been diagnosed as having hypertension (according to the 2007 ESH/ESC criteria), receiving antihypertensive therapy for ≥3 months prior to the initiation of the study, provided written informed consent, receiving treatment with an ACE inhibitor or an ARB Exclusion: secondary hypertension, pregnant or breastfeeding, had some disease that the investigator considered could interfere with the course of the study, participating in other research studies, living with someone who was taking the same antihypertensive agent	701	63.7	0.53
Marquez-Contreras 2018 [36]	Prospective cohort study	Pill box: MEMS<0.8	Inclusion: 40 to 80 years of age, diagnosed with mild to moderate essential hypertension, on antihypertensive therapy, with the diagnosis of hypertension registered in the medical record and incorporated in thee-prescription program ≥3 months before study baseline	102	61.06	0.31

			Exclusion: pregnant or breastfeeding, disabling diseases (e.g. dementia, Alzheimer's disease, neurological diseases, terminal cancer, disabling heart disease), inability or unwillingness to give informed consent, participating in other research studies; or living with someone taking the same antihypertensive medications			
ParejaMartinez 2015[46]	cross-sectional	MMAS-8<6	Inclusion: >18 years of age, had been prescribed antihypertensive therapy Exclusion: pregnant women, had problems with communication (deaf-mute, foreigners who did not speak Spanish)	100	65.5	0.57
Calderon-Larranaga 2016[48]	cross-sectional	MPR<0.8	Inclusion: ≥ 18 years of age, with a diagnosis of hypertension Exclusion: no unique GP identifier, not having ≥2 valid blood pressure measurements, not having ≥2 refills of either TD, BB, CCB, ACEI/ARB	113397	70.5	0.44
Sudan – Africa, low income, non-West						
Omar 2018[54]	cross-sectional	MMAS-4 >0	Inclusion: ≥20 years of age, hypertensive Sudanese patients Exclusion: pregnant women, poor cognitive functions	380	57.8	0.38
Taiwan – Asia, high income, non-west						
Chen 2020[60]	cross-sectional	ChMAR-Scale, any answer that is not “never”	Inclusion: ≥20 years of age, diagnosed with high blood pressure by a physician, had taken blood pressure medicine	538		0.55

			Exclusion: inability to communicate in Chinese			
Lee 2013[185]	Retrospective cohort study	MPR <0.8	Inclusion: ≥30 years of age, received ambulatory care following a principal diagnosis of hypertension between 2004 and 2007, receiving ≥1 antihypertensive Exclusion: hospitalised during the previous 12 months (from January to December 2003) for diabetes mellitus, ischaemic heart disease, pulmonary circulation diseases, other forms of heart disease (including dysrhythmia and heart failure) or other causes, only visited their clinic once and did not have a follow-up medical visit within six months	78558	61.8	0.5
Ho 2017[186]	Retrospective cohort study	MPR <0.8	Inclusion: 18-80 years of age, diagnoses of hypertension taking ≥1 antihypertensive medication Exclusion: diagnoses of cancer during the study, MPR of any antihypertensive drug <10%	19859	56	0.54
Tanzania – Africa, middle income, non-West						
Maginga 2016[51]	cross-sectional	MMAS-4>0	Inclusion: ≥18 years of age, previously diagnosed with hypertension, had attended ≥2 prior clinic encounters, had been prescribed antihypertensive Exclusion: cognitive impairment that made it impossible to conduct a reliable and private interview	300	54	0.35
Thailand – Asia, middle income, non-West						
Charoensab 2020[62]	cross-sectional	MMAS-4>0	Inclusion: 18-65 years of age, diagnosed as having hypertension for ≥3 months	248	58.8	0.44

Turkey – Europe, middle income, West						
Cinar 2020[187]	cross-sectional	MMAS-4>0	Inclusion: ≥ 18 years of age, having a diagnosis of hypertension (according to the 2018 European Society of Cardiology [ESC]/European Society of Hypertension [ESH] Guidelines for the management of arterial hypertension (Williams et al., 2018), using ≥1 antihypertensive for ≥6 months before the commencement of the study, able to speak, read, and write in Turkish, provided consent Exclusion: diagnosed with major psychiatric diseases, cognitive impairment, concurrent terminal illness, clinically unstable, inability to give informed consent	200	61.9	0.19
Baran 2017[188]	cross-sectional	MMAS-8 <6	Inclusion: hypertensive patients in a family clinic Exclusion: <18 years of age, pregnant or breastfeeding, having neurological disease that could cause communication problems, mental retardation or hearing loss, inability to participate in the study, unable to answer the questions	465	61.02	0.36
HacihasanogluAsilar 2014[45]	cross-sectional	MMAS-8 <6	Inclusion: ≥18 years of age, ability to communicate, diagnosed essential hypertension for ≥1 year, having started antihypertensive treatment Exclusion: mental retardation, psychological disorder, pregnancy	196	61.8	0.39
Uganda – Africa, low income, non-West						

Okello 2016[189]	cross-sectional	MMAS-8 <6	Inclusion: enrolled in the clinic ≥6 months prior to this study, filled a prescription of antihypertensive therapy at least once within 2 weeks prior to this study	329	55	0.31
United Kingdom – Europe, high income, West						
Khan 2014[190]	cross-sectional	MMAS-4>0	Inclusion: 18-60 years of age, diagnosed hypertension, on antihypertensive (at least one) for last 6 months Exclusion: pregnancy induced hypertension, diagnosed with hypertension <6 months, hypertensive patients in an inpatient setting	200		0.39
Gupta 2017[191] (with Czech Republic)	cross-sectional	absence of at least 1 prescribed BP-lowering medications/their metabolites in body fluids on biochemical analysis	Inclusion: suspected therapeutic nonadherence by a referring clinician or difficulty to manage hypertension/suboptimal BP control	1348	55.1	0.53
Sandy 2015[192] (with Germany, Italy, and Spain)	cross-sectional	MARS-5<25	Inclusion: self-reported hypertension and treatment with ≥1 antihypertensive	353		
United States of America – North America, high income, West						
Siddiqui 2019[193]	cross-sectional	24-Hour Urine High-Performance LC-MS/MS, fewer medications	Inclusion: Patients with AOBP controlled (<135/85 mmHg) on antihypertensive medications, having been seen by a hypertension specialist for ≥3 follow-up visits	158	59.57	0.55

		detected than prescribed were classified as partially adherent	Exclusion: chronic kidney disease stage 4 or 5 (estimated glomerular filtration rate <30 mL/min per 1.73 m2), pregnancy			
Chang 2019[194]	Retrospective cohort study	MPR <0.8	Inclusion: continuously enrolled in a health insurance plan within the database, have a prescription fill measurement period ≥90 days, and have no stays ≥90 days at long-term care facilities during 2015, have ≥2 prescription fills for a qualifying medication class identified using the Uniform System of Classification system10 (ACE [angiotensin-converting enzyme] inhibitors, angiotensin II receptor blockers, renin-angiotensin system antagonists [ACE inhibitor + angiotensin II receptor blocker + direct renin inhibitor], beta blockers, calcium channel blockers, diuretics, other antihypertensives), diagnosed hypertension Exclusion: with any Medicare-paid claims in the MarketScan Medicare Supplemental dataset	23833000		0.42
Bailey 2014[68]	Retrospective cohort study	MPR <0.8	Inclusion: 18-64 years of age in each study year, noninstitutionalized persons with continuous eligibility (320 days per year) throughout the 2-year study period, lack of Medicare eligibility, yearly diagnosis of essential hypertension (any International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] diagnosis code 401.x for any professional or inpatient claim), receipt of ≥1 antihypertensive medication prescription for each of the 2 baseline years	49479	48.5	0.32

			Exclusion: died or had a stroke during their baseline 2-year period			
Sim 2013[195]	Retrospective cohort study	PDC <0.8	Inclusion: ≥18 years of age, with ≥4 months continuous membership in the health plan, had documented hypertension and a blood pressure measurement, have ≥2 visits with ICD-9 codes to determine prevalent hypertension during the study period Exclusion: did not have a blood pressure measurement, diagnosed with secondary hypertension (ICD-9 codes for renovascular disease, adrenal disorders, Cushing's syndrome, aortic coarctation, and secondary hypertension not specified)	395482	65	0.45
Cummings 2013[196]	Prospective cohort study	MMAS-4>0	Inclusion: ≥ 45 years of age, reported in their telephone interview that a physician had told them they had hypertension/ high blood pressure and who also had a home visit evaluation that included documentation of antihypertensive medications Exclusion: race other than African-American or white, active treatment for cancer, medical conditions that would prevent long-term participation, cognitive impairment judged by the telephone interviewer, residence in or inclusion on a waiting list for a nursing home, or inability to communicate in English	15071	66.16	0.43
Vupputuri 2012 [35]	Retrospective cohort study	MPR<0.8	Inclusion: >18 years of age, 2 outpatient diagnosis of CKD in 2008-2009, ≥2 fills of ACEi/ARB, with ≥1 year of continuous membership and prescription benefits prior to 01/01/08, have no history of end-stage renal disease	3077	64.1	0.47

Bautista 2012[197]	Prospective cohort study	Pill counting: missed pills >20%	Inclusion: 20-70 years of age, with essential hypertension who had been taking medication for up to 1 week. Exclusion: pregnant women, with self-reported history of cancer, diabetes, rheumatoid arthritis, psychiatric disease requiring drug treatment, coronary heart disease, congestive heart failure, chronic kidney disease, hepatitis, taking mood-modifying medications	178	49.9	0.58
Lor 2019[198]	cross-sectional	MMAS-8<6	Inclusion: ≥18 years of age, English or Spanish speaking, Hispanic, self-reporting hypertension	1355	62.27	0.24
Al-Ruthia 2017[199]	cross-sectional	MMAS-8<6	Inclusion: ≥60 years of age with self-reported hypertension	190		0.23
Tajeu 2019[200]	Retrospective cohort study	PDC <0.8	Inclusion: US adults <65 years of age who initiated antihypertensive medication between 2007 and 2014 using deidentified Truven Health MarketScan Commercial Claims Data; diagnoses of 401.x (malignant, benign, or unspecified essential hypertension), ≥7 days apart, during the look-back period. Exclusion: beneficiaries who were ≥65 years of age at the end of the follow-up period to focus on the population of adults who would not be eligible for Medicare coverage due to age during the follow-up period; beneficiaries with any claims for antihypertensive medication fills during the look-back period.	379658	50.29	0.51
Wagner 2012[41]	cross-sectional	MMAS-4>0	US adults 18 years and older had a self-reported diagnosis of hypertension and reported use of antihypertensive prescription medication	16474	59.4	0.51

Daniels 2018 [38]	cross-sectional	absence of drug in blood assay	Inclusion: Adult patients (≥ 18 years old) who were seen in the VUMC Adult ED from July 1, 2012 to April 25, 2013, were eligible if they had a diagnosis of hypertension recorded in their electronic medical record, were prescribed at least one of 14 common antihypertensive medications detected by the mass spectrometry assay and had a VUMC primary care provider Exclusion: did not have a peripheral IV or declined a blood draw, were pregnant, were unable to provide consent, had previously been enrolled in this study, sought care in the ED for acute stroke or alcohol withdrawal, or had been in the ED for more than36 hours.	261	59.2	0.47
Silver 2019[201]	cross-sectional	K-Wood-MAS-4>=1	stablished hypertension, age 55 and older, recruited through a commercial health insurance partner and via community outreach in the Greater New Orleans area.	199	64	0.5
Breaux-Shropshire 2012[202]	cross-sectional	MMAS-8 <6	city workers who reported having been diagnosed with hypertension and who attended the screening for their health risk assessment	149	47	0.85
Gallagher 2015[203]	cross-sectional	MMAS-8 <6, electronic pill box opening <0.8	Inclusion: ≥ 18 years of age, had an established relationship with a primary care provider who was enrolled in the study, spoke English or Spanish, were prescribed ≥1 antihypertensive; had uncontrolled hypertension at the baseline study visit and at their previous clinic visit as defined by criteria from the Seventh Joint National Committee report: SBP ≥140 mmHg or DBP ≥90 mmHg in patients without diabetes mellitus or chronic kidney disease (CKD), estimated glomerular filtration rate (eGFR) below 60 ml/min	149	64	0.28

			per 1.73 m2; SBP ≥130 mmHg or DBP ≥80 mmHg in patients with diabetes mellitus or CKD Exclusion: severe uncontrolled hypertension (SBP ≥200 mmHg or DBP ≥130 mmHg), severe physical, cognitive, or psychiatric impairment that limited ability to self-administer antihypertensive medications, terminal non-cardiovascular illness, unavailability for follow-up, enrollment in another cardiovascular clinical trial			
Krousel-Wood 2019[90]	Prospective cohort study	K-Wood-MAS-4 >=1	Inclusion: ≥65 years of age with essential hypertension	1532	76.3	0.39
Marsh 2019[59]	cross-sectional	K-Wood-MAS-4>0	Inclusion: ≥55 years of age	200	64.2	0.5
Schmitt 2010[40]	Retrospective cohort study	MPR<0.8	Inclusion: who sought ambulatory care at the Cincinnati VA Medical Center between 1/1/2006 and 31/12/2007, had ≥1 available estimated GFR measurement of <60 ml/ min/1.73 m2 during the study period, also received ≥1 antihypertensive prescription Exclusion: lack information on either serum creatinine or other data to calculate glomerular filtration rate (GFR) by using the four-variable MDRD equation, had an antihypertensive prescription filled only once, the prescription was discontinued by the provider	7227	71.3	0.97
Cummings 2016 [27]	cross-sectional	MMAS-8 <6	Inclusion: ≥1 visit in the last year with an uncontrolled systolic BP measurement, diagnosis of hypertension and an uncontrolled systolic BP >150 mmHg	495	57.3	0.32

Rajpura 2014[204]	cross-sectional	MMAS-4 >0	Inclusion: ≥55 years of age, self-reported hypertensive, prescribed ≥1 antihypertensive medication to be taken daily	117		0.64
Fortuna 2018[205]	cross-sectional	MMAS-8 <6	Inclusion: previously received care for high blood pressure, have received a prescription for medicine to help control blood pressure, hypertensive patients seeking care at three urban safety-net practices in upstate New York	2128	50.4	0.4
Vietnam – Asia, middle income, non-West						
Nguyen 2017[206]	Prospective cohort study	PDC<0.8	Inclusion: newly diagnosed hypertensive patients, medication prescription for ≥1 month, had ≥90 days of follow up since the first prescription. Exclusion: history of myocardial infarction or other serious heart disease(s), or any heart diseases which need to be treated in second-line facilities, referral to second-line if, despite strictly following the prescribed regimen, BP was inadequately controlled or organ damage was suspected, referral to second-line because patients requested it, generally thinking that their hypertension would be better managed there, had moved to another place to live, no longer needed to take antihypertensive drugs, missed getting a prescription for ≥2 months between two doses	315	53.7	0.54

ARMS: Adherence to Refills and Medication Scale; BMQ – Beliefs about medicines questionnaire; ChMAR-Scale: Chinese version of Medication Adherence Reasons Scale; DAI-10: Drug Attitude Inventory-10; PDC: Proportion of days covered; K-Wood-MAS-4: 4-item Krouse-Wood Medication Adherence Scale; MARS: The Medication Adherence Report Scale; MEMS: medication event monitoring system; MMAS-4: 4-item Morisky Medication-taking Adherence Scale; MMAS-8: 8-item Morisky Medication-taking Adherence Scale; MPR: medication possession ratio

Further details of individual studies can be obtained by contacting the corresponding author

Quality Assessment of included studies

Table S6. Quality assessments of cross-sectional studies

Study	*Q1. appropriate sampling frame?*	*Q2. appropriate way to sample?*	*Q3. adequate sample size?*	*Q4. Setting/ subjects described in detail?*	*Q5. sufficient coverage of identified sample?*	*Q6. valid method to identify condition?*	*Q7. Standardized/ reliable way to identify condition?*	*Q8. appropriate statistical analysis?*	*Q9. adequate response rate?*	*Overall*
Adeoye 2019	●	●	●	●	●	●	●	●	●	●
Adidja 2018	●	●	●	●	●	●	●	●	●	●
Aielo 2019	●	●	●	●	●	●	●	●	●	●
Akintunde 2015	●	●	●	●	●	●	●	●	●	●
Akoko 2017	●	●	●	●	●	●	●	●	●	●
Al-Noumani 2018	●	●	●	●	●	●	●	●	●	●
Al-Ruthia 2017	●	●	●	●	●	●	●	●	●	●
Amin 2018	●	●	●	●	●	●	●	●	●	●
Animu 2018	●	●	●	●	●	●	●	●	●	●
Asgedom 2018	●	●	●	●	●	●	●	●	●	●
Athiyah 2013	●	●	●	●	●	●	●	●	●	●
Balasubramanian 2018	●	●	●	●	●	●	●	●	●	●
Baran 2017	●	●	●	●	●	●	●	●	●	●
Barreto 2015	●	●	●	●	●	●	●	●	●	●
Behnood-Rod 2016	●	●	●	●	●	●	●	●	●	●
Ben 2012	●	●	●	●	●	●	●	●	●	●
Berhe 2017	●	●	●	●	●	●	●	●	●	●
BouSerhal 2018	●	●	●	●	●	●	●	●	●	●

Bramlage 2014	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🟢	🟢	🟡
Breaux-Shropshire 2012	🟢	🟡	🔴	🟡	🟢	🟢	🟡	🟢	🟡	🔴
Cabral 2018	🟢	🟡	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🟡
Calderon-Larranaga 2016	🟢	🟢	🟢	🟢	🔴	🟢	🟢	🟢	🟢	🔴
Charoensab 2020	🟢	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🟡	🔴
Chen 2020	🟢	🔴	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🔴
Cinar 2020	🟢	🟡	🔴	🟢	🟢	🟢	🟢	🟢	🟡	🔴
Cummings 2016	🟡	🟡	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟡
Daniels 2018	🟡	🔴	🔴	🟢	🟢	🟢	🟢	🟢	🔴	🔴
Demoner 2012	🟢	🟢	🔴	🟢	🟢	🟢	🟡	🟢	🟡	🔴
Dennis 2011	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🟡
deOliveira-Filho 2014	🟢	🟢	🟢	🔴	🟢	🟢	🟢	🟢	🟡	🔴
Ekanem 2020	🟢	🟢	🟢	🔴	🟢	🟢	🟢	🟢	🟡	🔴
Espeche 2020	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🟢	🟡	🟡
Farah 2016	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🟡
Fatani 2019	🔴	🟡	🔴	🟢	🟡	🟢	🟢	🟢	🟡	🔴
Fernandez-Arias 2014	🟢	🔴	🔴	🟢	🟢	🟢	🟡	🟢	🟡	🔴
Fortuna 2018	🟡	🟡	🟢	🔴	🟢	🟢	🟡	🟢	🔴	🔴
G/Tsadik 2020	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢
Gallagher 2015	🟢	🟡	🔴	🟢	🟢	🟢	🟢	🟢	🟡	🔴
Gavrilova 2019	🟢	🟡	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🔴
Gupta 2017	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🔴
HacihasanogluAsilar 2014	🟢	🟡	🔴	🟡	🟢	🟢	🟢	🟢	🟡	🔴
Hamdidouche 2017	🔴	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🟡	🔴
Hassanein 2020	🟢	🟡	🟢	🟡	🟢	🟢	🟢	🟢	🟡	🟡
Heizomi 2020	🟢	🟢	🔴	🟢	🟡	🟢	🟢	🟢	🟢	🔴

Hou 2016	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🔴
Jafar 2018	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢
Janezic 2014	🟢	🟡	🟢	🟡	🟡	🟢	🟡	🟡	🟡	🟡
Jankowska-Polanska 2016	🟢	🔴	🔴	🟢	🟢	🟢	🟡	🟢	🟡	🔴
Jankowska-Polanska 2017	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🔴
Kang 2015	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🟡
Kang 2020	🟢	🟡	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🟡
Kebede 2020	🟢	🟡	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🔴
Khan 2014	🟢	🔴	🟡	🔴	🟡	🟢	🟡	🟢	🟡	🔴
Khayyat 2017	🟢	🔴	🔴	🟢	🟢	🟢	🟢	🟢	🟡	🔴
Kim 2014	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢
Korb-Savoldelli 2012	🟡	🟡	🔴	🟡	🟢	🟢	🟢	🟢	🟡	🔴
Koschack 2010	🟢	🟡	🟢	🟡	🟢	🟢	🟡	🟢	🔴	🔴
Kretchy 2014	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🟡
Lalic 2013	🟢	🟡	🔴	🟡	🟢	🟢	🟡	🟢	🟡	🔴
Ledur 2013	🔴	🟢	🟡	🟢	🟢	🟢	🟡	🟢	🟡	🔴
Lee 2013	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🟡
Lefort 2018	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢
Li 2015	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🔴
Li 2016	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢
Li 2016	🟢	🟡	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟡
Lo 2016	🟢	🔴	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🔴
Lomper 2018	🟢	🟡	🔴	🔴	🟢	🟢	🟢	🟢	🟢	🔴
Lor 2019	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🔴
Lotsch 2015	🟢	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🟡	🔴
Lulebo 2015	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢

MacquartdeTerline 2019	●	●	●	●	●	●	●	●	●	●
Maginga 2016	●	●	●	●	●	●	●	●	●	●
Mahmood 2020	●	●	●	●	●	●	●	●	●	●
Mamaghani 2020	●	●	●	●	●	●	●	●	●	●
Marsh 2019	●	●	●	●	●	●	●	●	●	●
Mekonnen 2017	●	●	●	●	●	●	●	●	●	●
Morrison 2015	●	●	●	●	●	●	●	●	●	●
Natarajan 2013	●	●	●	●	●	●	●	●	●	●
Okello 2016	●	●	●	●	●	●	●	●	●	●
Okwuonu 2014	●	●	●	●	●	●	●	●	●	●
Oliveira-Filho 2012	●	●	●	●	●	●	●	●	●	●
Olowe 2017	●	●	●	●	●	●	●	●	●	●
Omar 2018	●	●	●	●	●	●	●	●	●	●
Otenyo 2018	●	●	●	●	●	●	●	●	●	●
Pan 2017	●	●	●	●	●	●	●	●	●	●
ParejaMartinez 2015	●	●	●	●	●	●	●	●	●	●
Park 2013	●	●	●	●	●	●	●	●	●	●
Pluta 2020	●	●	●	●	●	●	●	●	●	●
Rajpura 2014	●	●	●	●	●	●	●	●	●	●
Righi 2017	●	●	●	●	●	●	●	●	●	●
Saarti 2016	●	●	●	●	●	●	●	●	●	●
Saleem 2012	●	●	●	●	●	●	●	●	●	●
Sandy 2015	●	●	●	●	●	●	●	●	●	●
Saqlain 2019	●	●	●	●	●	●	●	●	●	●
Sarika 2020	●	●	●	●	●	●	●	●	●	●
Sarkodie 2020	●	●	●	●	●	●	●	●	●	●
Shakya 2020	●	●	●	●	●	●	●	●	●	●
Sheilini 2018	●	●	●	●	●	●	●	●	●	●

Shen 2020	🟢	🟡	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟡
Shi 2019	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢
Siddiqui 2019	🟢	🟡	🟡	🟢	🟢	🟢	🟢	🟢	🟡	🟡
Silver 2019	🟢	🟡	🔴	🔴	🟡	🟢	🟡	🟡	🟡	🔴
Stavropoulou 2012	🟡	🟢	🟢	🔴	🟢	🟢	🟡	🟢	🔴	🔴
Sulistiyowatiningsih 2017	🟢	🟡	🔴	🟢	🔴	🟢	🟢	🟢	🟢	🔴
Tan 2020	🟢	🟡	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🔴
TizatoFeriato 2018	🔴	🟢	🔴	🟢	🔴	🟢	🟢	🟢	🟡	🔴
Ungari 2010	🟢	🟢	🔴	🟢	🟢	🟢	🟡	🟢	🟡	🔴
VanKleef 2019	🟡	🟡	🔴	🟡	🟡	🟢	🟢	🟢	🟡	🔴
Wagner 2012	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🔴
Wilinski 2013	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🟢	🟢	🟡
Yang 2016	🟢	🟡	🟢	🔴	🟢	🟢	🟢	🟢	🟡	🔴
Yassine 2016	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🔴
Yue 2015	🟢	🟡	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🔴
Zhang 2017	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🟢	🔴
Zhao 2015	🟢	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🟡	🔴
Zyoud 2013	🟢	🔴	🟢	🟢	🟢	🟢	🟢	🟢	🟡	🔴
Ting 2017	🟢	🟡	🟢	🔴	🟢	🟢	🟡	🟢	🟡	🔴
Lau 2010	🟢	🟡	🟢	🟢	🟢	🟢	🟡	🟢	🟡	🟡
Ha 2012	🟢	🟡	🔴	🔴	🟢	🟢	🟡	🟢	🟢	🔴
Song 2016	🟢	🟡	🔴	🔴	🔴	🟢	🟢	🟢	🟡	🔴
Chui 2015	🟢	🟡	🔴	🔴	🟡		🟡	🟡	🟡	🔴
Lee 2017	🟢	🟡	🟢	🔴	🟢		🔴	🟢	🟡	🔴
Wong 2018	🟢	🟡	🟡	🟡	🟢		🟡	🟢	🟡	🟡
Wu 2020	🟢	🟡	🟢	🟢	🟢		🟢	🟢	🟡	🟡
Tam 2017	🟢	🟡	🔴	🔴	🟢		🟡	🟢	🟡	🔴
Chan 2018	🟢	🟡	🔴	🔴	🟡		🟡	🔴	🟡	🔴

Chan 2015	●	●	●	●	●		●	●	●	●
Ko 2017	●	●	●	●	●		●	●	●	●
Long 2020	●	●	●	●	●		●	●	●	●

●high risk; ●unknown risk; ● low risk

Table S7. Quality assessments of cohort studies

Study	*Q1. both groups from same population?*	*Q2. exposure measured similarly for both groups?*	*Q3. exposure measured in valid/ reliable way?*	*Q4. confound-ing factors identified?*	*Q5. strategy to deal with confound-ing?*	*Q6. groups free of outcomes at beginning of study?*	*Q7. outcomes measured in valid/ reliable way?*	*Q8. follow-up time long enough?*	*Q9. follow-up complete?*	*Q10. strategies to address incomplete follow-up?*	*Q11. appropriate statistical analysis?*	*Overall*
Alhaddad 2016	●	●	●	●	●	●	●	●	●	●	●	●
Bailey 2014	●	●	●	●	●	●	●	●	●	●	●	●
Bautista 2012	●	●	●	●	●	●	●	●	●	●	●	●
Breitscheidel 2012	●	●	●	●	●	●	●	●	●	●	●	●
Chang 2019	●	●	●	●	●	●	●	●	●	●	●	●
Choi 2017	●	●	●	●	●	●	●	●	●	●	●	●
Choi 2018	●	●	●	●	●	●	●	●	●	●	●	●
Cummings 2013	●	●	●	●	●	●	●	●	●	●	●	●
Dillon 2019	●	●	●	●	●	●	●	●	●	●	●	●
Efanov 2018	●	●	●	●	●	●	●	●	●	●	●	●
Gentil 2017	●	●	●	●	●	●	●	●	●	●	●	●
Ho 2017	●	●	●	●	●	●	●	●	●	●	●	●
Kim 2016	●	●	●	●	●	●	●	●	●	●	●	●
Krousel-Wood 2019	●	●	●	●	●	●	●	●	●	●	●	●
Lee 2013	●	●	●	●	●	●	●	●	●	●	●	●
Lee 2019	●	●	●	●	●	●	●	●	●	●	●	●
Marquez-Contreras 2012	●	●	●	●	●	●	●	●	●	●	●	●
Marquez-Contreras 2018	●	●	●	●	●	●	●	●	●	●	●	●

Meena 2018	●	●	●	●	●	●	●	●	●	●	●	●
Nguyen 2017	●	●	●	●	●	●	●	●	●	●	●	●
Perseguer-Torregrosa 2014	●	●	●	●	●	●	●	●	●	●	●	●
Saito 2016	●	●	●	●	●	●	●	●	●	●	●	●
Schmitt 2010	●	●	●	●	●	●	●	●	●	●	●	●
Schulz 2016	●	●	●	●	●	●	●	●	●	●	●	●
Sim 2013	●	●	●	●	●	●	●	●	●	●	●	●
Tajeu 2019	●	●	●	●	●	●	●	●	●	●	●	●
Tang 2017	●	●	●	●	●	●	●	●	●	●	●	●
Vupputuri 2012	●	●	●	●	●	●	●	●	●	●	●	●
Walsh 2019	●	●	●	●	●	●	●	●	●	●	●	●
Warren 2011	●	●	●	●	●	●	●	●	●	●	●	●
Wong 2010	●	●	●	●	●	●	●	●	●	●	●	●

●high risk; ●unknown risk; ● low risk

Table S8. Quality assessment of case-control studies

Study	*Q1. were groups comparable?*	*Q2. case and control matched appropriately?*	*Q3. same criteria used for identification case/control?*	*Q4. exposure measured in standardized / valid/ reliable way?*	*Q5. exposure measured in same way for cases/ controls?*	*Q6. confound-ing factors identified?*	*Q7. strategies to deal with confound-ing factors?*	*Q8. outcomes assessed in standardized/ valid/ reliable way?*	*Q9. exposure period long enough?*	*Q10. appropriate statistical analysis?*	*Overall*
Mekonen 2020	●	●	●	●	●	●	●	●	●	●	●
Perreault 2010	●	●	●	●	●	●	●	●	●	●	●

●high risk; ●unknown risk; ● low risk

Results of meta-analyses

Table S9 summary of meta-analyses of prevalence of medication non-adherence

Questionnaires

	prevalence	Lower 95%CI	Upper 95%CI	N
World	0.40	0.40	0.40	125
West	0.38	0.37	0.38	34
non-West	0.43	0.43	0.44	91
high income country	0.38	0.38	0.38	40
low-to-middle income country	0.43	0.43	0.43	85
Africa	0.41	0.41	0.42	23
Asia	0.45	0.45	0.46	56
Europe	0.43	0.42	0.43	21
North America	0.35	0.34	0.35	13
Oceania	No study			
South America	0.34	0.33	0.35	12

Prescription refill

	prevalence	Lower 95%CI	Upper 95%CI	N
World	0.28	0.28	0.28	24
West	0.26	0.26	0.26	16
non-West	0.49	0.49	0.49	8
high income country	0.28	0.28	0.28	23
low-to-middle income country	0.5	0.45	0.56	1
Africa	No study			
Asia	0.49	0.49	0.49	8
Europe	0.40	0.40	0.40	6
North America	0.26	0.26	0.26	9
Oceania	0.39	0.36	0.41	1
South America	No study			

* NA due to inadequate numbers of studies

Pill counting

	Prevalence	Lower 95%CI	Upper 95%CI	N
World	0.28	0.26	0.29	4
West	0.49	0.45	0.53	2
non-West	0.22	0.2	0.24	2
high income country	0.25	0.23	0.27	3
low-to-middle income country	0.66	0.59	0.72	1
Africa	No study			
Asia	0.22	0.2	0.24	2
Europe	0.63	0.58	0.67	1
North America	0.24	0.18	0.3	1
Oceania	No study			
South America	No study			

* NA due to inadequate numbers of studies

Electronic pill box

	Prevalence	Lower 95%CI	Upper 95%CI	N
World	0.28	0.25	0.31	3
West	0.28	0.25	0.31	3
non-West	No study			
high income country	0.28	0.25	0.31	3
low-to-middle income country	No study			
Africa	No study			
Asia	No study			
Europe	0.26	0.23	0.29	2
North America	0.42	0.35	0.5	1
Oceania	No study			
South America	No study			

* NA due to inadequate numbers of studies

Biochemical Assay

	prevalence	Lower 95%CI	Upper 95%CI	N
World	0.27	0.26	0.29	5
West	0.27	0.26	0.29	5
non-West	No study			
high income country	0.27	0.26	0.29	5
low-to-middle income country	No study			
Africa	No study			
Asia	No study			
Europe	0.30	0.28	0.32	3
North America	0.2	0.16	0.24	2
Oceania	No study			
South America	No study			

* NA due to inadequate numbers of studies

Table S10. Meta-regression analysis of prevalence studies in accordance to subgroup (i) income level and (ii) West versus non-West

	questionnaires		**prescription refill**	
	meta-regression coefficient	p-value	meta-regression coefficient	P-value
high vs low-to-middle income country	-0.05	0.145	-0.16	0.37
west versus non-west	-0.06	0.108	-0.12	0.086

Table S11. meta-analysis of prevalence of medication non-adherence in table format (by questionnaires; subgroup: West versus non-West)

Study	prevalence	Lower 95%CI	Upper 95% CI	%weight
West				
Koschack 2010	0.36	0.31	0.41	0.30
Breaux-Shropshire 20	0.35	0.28	0.43	0.13
Korb-Savoldelli 2012	0.18	0.13	0.23	0.27
Stavropoulou 2012	0.52	0.48	0.56	0.58
Wagner 2012	0.34	0.33	0.35	14.45
Cummings 2013	0.31	0.30	0.32	13.84
Wilinski 2013	0.74	0.72	0.76	1.50
Natarajan 2013	0.23	0.19	0.26	0.59
HacihasanogluAsilar	0.59	0.52	0.65	0.16
Bramlage 2014	0.42	0.42	0.43	8.68
Janezic 2014	0.16	0.13	0.20	0.68
Rajpura 2014	0.81	0.73	0.87	0.15
Khan 2014	0.64	0.57	0.70	0.17
Perseguer-Torregrosa	0.36	0.32	0.41	0.36
Sandy 2015	0.66	0.61	0.71	0.31
ParejaMartinez 2015	0.15	0.09	0.23	0.15
Gallagher 2015	0.23	0.17	0.30	0.17
Lotsch 2015	0.34	0.29	0.39	0.28
Morrison 2015	0.44	0.42	0.46	2.07
Cummings 2016	0.40	0.36	0.44	0.41
Jankowska-Polanska 2	0.18	0.14	0.23	0.39
Al-Ruthia 2017	0.21	0.16	0.27	0.22
Jankowska-Polanska 2	0.30	0.26	0.33	0.59
Lomper 2018	0.48	0.43	0.54	0.22
Lefort 2018	0.38	0.36	0.40	1.98
Fortuna 2018	0.38	0.35	0.40	1.78
Cabral 2018	0.28	0.24	0.32	0.46
Krousel-Wood 2019	0.39	0.36	0.41	1.27
Silver 2019	0.44	0.37	0.51	0.16
Marsh 2019	0.44	0.37	0.50	0.16
Lor 2019	0.76	0.73	0.78	1.45
Gavrilova 2019	0.44	0.37	0.52	0.14
Pluta 2020	0.33	0.27	0.40	0.18
Cinar 2020	0.55	0.48	0.61	0.16
Sub-total				
Fixed pooled ES	0.38	0.37	0.38	54.40
non-west				
Ungari 2010	0.57	0.48	0.66	0.09
Lau 2010	0.57	0.53	0.61	0.42
Dennis 2011	0.50	0.46	0.54	0.48
Oliveira-Filho 2012	0.47	0.41	0.54	0.18

Ben 2012	0.61	0.54	0.68	0.17
Demoner 2012	0.64	0.56	0.71	0.13
Ha 2012	0.29	0.23	0.36	0.15
Zyoud 2013	0.37	0.32	0.42	0.35
Park 2013	0.41	0.35	0.47	0.20
Ledur 2013	0.49	0.43	0.54	0.25
Kim 2014	0.33	0.28	0.38	0.33
deOliveira-Filho 201	0.47	0.44	0.50	0.74
Kretchy 2014	0.81	0.77	0.84	0.51
Fernandez-Arias 2014	0.57	0.48	0.66	0.09
Okwuonu 2014	0.69	0.63	0.74	0.23
Li 2015	0.81	0.77	0.84	0.61
Akintunde 2015	0.24	0.17	0.32	0.12
Zhao 2015	0.26	0.21	0.32	0.24
Yue 2015	0.26	0.21	0.32	0.24
Chui 2015	0.65	0.58	0.71	0.19
Lulebo 2015	0.54	0.49	0.59	0.31
Chan 2015	0.22	0.17	0.27	0.27
Barreto 2015	0.43	0.38	0.47	0.34
Farah 2016	0.20	0.17	0.23	0.70
Hou 2016	0.66	0.62	0.70	0.51
Behnood-Rod 2016	0.50	0.44	0.55	0.22
Saarti 2016	0.29	0.22	0.38	0.11
Okello 2016	0.85	0.81	0.89	0.51
Song 2016	0.57	0.49	0.65	0.13
Athiyah 2013	0.57	0.50	0.64	0.16
Yassine 2016	0.22	0.17	0.28	0.24
Alhaddad 2016	0.41	0.38	0.43	1.20
Maginga 2016	0.44	0.38	0.50	0.24
Yang 2016	0.57	0.53	0.60	0.60
Li 2016	0.27	0.25	0.30	1.30
Lo 2016	0.56	0.49	0.63	0.16
Righi 2017	0.17	0.14	0.21	0.58
Akoko 2017	0.56	0.50	0.62	0.18
Berhe 2017	0.42	0.39	0.45	0.74
Olowe 2017	0.32	0.28	0.38	0.31
Khayyat 2017	0.54	0.47	0.61	0.16
Sulistiyowatiningsih	0.60	0.54	0.66	0.19
Mekonnen 2017	0.33	0.28	0.37	0.36
Baran 2017	0.28	0.24	0.32	0.46
Tam 2017	0.55	0.49	0.61	0.23
Ting 2017	0.80	0.77	0.82	1.17
Zhang 2017	0.30	0.27	0.33	1.02
Ko 2017	0.31	0.29	0.32	3.38
Lee 2017	0.62	0.60	0.64	1.96
Pan 2017	0.65	0.60	0.69	0.38

Sheilini 2018	0.16	0.14	0.19	1.18
Adidja 2018	0.67	0.60	0.73	0.16
Meena 2018	0.32	0.29	0.35	0.85
Al-Noumani 2018	0.32	0.26	0.39	0.19
Asgedom 2018	0.38	0.33	0.44	0.23
BouSerhal 2018	0.14	0.11	0.18	0.66
Jafar 2018	0.41	0.39	0.44	1.39
Amin 2018	0.34	0.28	0.40	0.22
Otenyo 2018	0.42	0.35	0.51	0.12
Efanov 2018	0.32	0.27	0.38	0.23
Animu 2018	0.31	0.27	0.36	0.36
Omar 2018	0.29	0.25	0.34	0.36
Balasubramanian 2018	0.54	0.47	0.61	0.15
Chan 2018	0.65	0.55	0.73	0.09
Wong 2018	0.64	0.57	0.70	0.17
TizatoFeriato 2018	0.69	0.59	0.77	0.10
MacquartdeTerline 20	0.31	0.29	0.33	2.02
Fatani 2019	0.67	0.62	0.73	0.25
Shi 2019	0.64	0.59	0.68	0.36
Adeoye 2019	0.96	0.91	0.98	0.75
Saqlain 2019	0.61	0.55	0.67	0.22
Aielo 2019	0.62	0.57	0.67	0.34
Chen 2020	0.62	0.58	0.66	0.45
Shakya 2020	0.50	0.44	0.57	0.16
Kang 2020	0.45	0.40	0.50	0.31
Tan 2020	0.58	0.53	0.63	0.31
Sarkodie 2020	0.11	0.08	0.14	0.75
G/Tsadik 2020	0.32	0.29	0.35	0.89
Mahmood 2020	0.38	0.34	0.41	0.62
Hassanein 2020	0.33	0.31	0.35	1.79
Wu 2020	0.28	0.24	0.32	0.44
Mekonen 2020	0.37	0.33	0.42	0.37
Ekanem 2020	0.15	0.12	0.19	0.59
Shen 2020	0.61	0.57	0.64	0.65
Kebede 2020	0.47	0.39	0.55	0.12
Espeche 2020	0.14	0.12	0.16	1.78
Mamaghani 2020	0.18	0.14	0.23	0.32
Heizomi 2020	0.93	0.90	0.95	0.91
Long 2020	0.77	0.74	0.80	0.71
Charoensab 2020	0.65	0.58	0.70	0.21
Sub-total				
Fixed pooled ES	0.43	0.43	0.44	45.60
Overall				
Fixed pooled ES	0.40	0.40	0.40	100.00

Meta-regression coefficient: -0.061, p=0.108

Table S12. meta-analysis of prevalence of medication non-adherence in table format (by questionnaires; subgroup: income level)

Study	prevalence	Lower 95%CI	Upper 95% CI	%weight
High				
Koschack 2010	0.36	0.31	0.41	0.30
Breaux-Shropshire 20	0.35	0.28	0.43	0.13
Korb-Savoldelli 2012	0.18	0.13	0.23	0.27
Stavropoulou 2012	0.52	0.48	0.56	0.58
Wagner 2012	0.34	0.33	0.35	14.45
Cummings 2013	0.31	0.30	0.32	13.84
Park 2013	0.41	0.35	0.47	0.20
Wilinski 2013	0.74	0.72	0.76	1.50
Natarajan 2013	0.23	0.19	0.26	0.59
Kim 2014	0.33	0.28	0.38	0.33
Bramlage 2014	0.42	0.42	0.43	8.68
Janezic 2014	0.16	0.13	0.20	0.68
Rajpura 2014	0.81	0.73	0.87	0.15
Khan 2014	0.64	0.57	0.70	0.17
Perseguer-Torregrosa	0.36	0.32	0.41	0.36
Sandy 2015	0.66	0.61	0.71	0.31
ParejaMartinez 2015	0.15	0.09	0.23	0.15
Gallagher 2015	0.23	0.17	0.30	0.17
Lotsch 2015	0.34	0.29	0.39	0.28
Morrison 2015	0.44	0.42	0.46	2.07
Cummings 2016	0.40	0.36	0.44	0.41
Jankowska-Polanska 2	0.18	0.14	0.23	0.39
Lo 2016	0.56	0.49	0.63	0.16
Al-Ruthia 2017	0.21	0.16	0.27	0.22
Jankowska-Polanska 2	0.30	0.26	0.33	0.59
Khayyat 2017	0.54	0.47	0.61	0.16
Lomper 2018	0.48	0.43	0.54	0.22
Lefort 2018	0.38	0.36	0.40	1.98
Fortuna 2018	0.38	0.35	0.40	1.78
Cabral 2018	0.28	0.24	0.32	0.46
Al-Noumani 2018	0.32	0.26	0.39	0.19
Krousel-Wood 2019	0.39	0.36	0.41	1.27
Silver 2019	0.44	0.37	0.51	0.16
Marsh 2019	0.44	0.37	0.50	0.16
Lor 2019	0.76	0.73	0.78	1.45
Gavrilova 2019	0.44	0.37	0.52	0.14
Fatani 2019	0.67	0.62	0.73	0.25
Chen 2020	0.62	0.58	0.66	0.45
Kang 2020	0.45	0.40	0.50	0.31
Pluta 2020	0.33	0.27	0.40	0.18
Sub-total				

Fixed pooled ES	0.38	0.38	0.38	56.13
low to middle				
Ungari 2010	0.57	0.48	0.66	0.09
Lau 2010	0.57	0.53	0.61	0.42
Dennis 2011	0.50	0.46	0.54	0.48
Oliveira-Filho 2012	0.47	0.41	0.54	0.18
Ben 2012	0.61	0.54	0.68	0.17
Demoner 2012	0.64	0.56	0.71	0.13
Ha 2012	0.29	0.23	0.36	0.15
Zyoud 2013	0.37	0.32	0.42	0.35
Ledur 2013	0.49	0.43	0.54	0.25
deOliveira-Filho 201	0.47	0.44	0.50	0.74
Kretchy 2014	0.81	0.77	0.84	0.51
Fernandez-Arias 2014	0.57	0.48	0.66	0.09
HacihasanogluAsilar	0.59	0.52	0.65	0.16
Okwuonu 2014	0.69	0.63	0.74	0.23
Li 2015	0.81	0.77	0.84	0.61
Akintunde 2015	0.24	0.17	0.32	0.12
Zhao 2015	0.26	0.21	0.32	0.24
Yue 2015	0.26	0.21	0.32	0.24
Chui 2015	0.65	0.58	0.71	0.19
Lulebo 2015	0.54	0.49	0.59	0.31
Chan 2015	0.22	0.17	0.27	0.27
Barreto 2015	0.43	0.38	0.47	0.34
Farah 2016	0.20	0.17	0.23	0.70
Hou 2016	0.66	0.62	0.70	0.51
Behnood-Rod 2016	0.50	0.44	0.55	0.22
Saarti 2016	0.29	0.22	0.38	0.11
Okello 2016	0.85	0.81	0.89	0.51
Song 2016	0.57	0.49	0.65	0.13
Athiyah 2013	0.57	0.50	0.64	0.16
Yassine 2016	0.22	0.17	0.28	0.24
Alhaddad 2016	0.41	0.38	0.43	1.20
Maginga 2016	0.44	0.38	0.50	0.24
Yang 2016	0.57	0.53	0.60	0.60
Li 2016	0.27	0.25	0.30	1.30
Righi 2017	0.17	0.14	0.21	0.58
Akoko 2017	0.56	0.50	0.62	0.18
Berhe 2017	0.42	0.39	0.45	0.74
Olowe 2017	0.32	0.28	0.38	0.31
Sulistiyowatiningsih	0.60	0.54	0.66	0.19
Mekonnen 2017	0.33	0.28	0.37	0.36
Baran 2017	0.28	0.24	0.32	0.46
Tam 2017	0.55	0.49	0.61	0.23
Ting 2017	0.80	0.77	0.82	1.17
Zhang 2017	0.30	0.27	0.33	1.02

Ko 2017	0.31	0.29	0.32	3.38
Lee 2017	0.62	0.60	0.64	1.96
Pan 2017	0.65	0.60	0.69	0.38
Sheilini 2018	0.16	0.14	0.19	1.18
Adidja 2018	0.67	0.60	0.73	0.16
Meena 2018	0.32	0.29	0.35	0.85
Asgedom 2018	0.38	0.33	0.44	0.23
BouSerhal 2018	0.14	0.11	0.18	0.66
Jafar 2018	0.41	0.39	0.44	1.39
Amin 2018	0.34	0.28	0.40	0.22
Otenyo 2018	0.42	0.35	0.51	0.12
Efanov 2018	0.32	0.27	0.38	0.23
Animu 2018	0.31	0.27	0.36	0.36
Omar 2018	0.29	0.25	0.34	0.36
Balasubramanian 2018	0.54	0.47	0.61	0.15
Chan 2018	0.65	0.55	0.73	0.09
Wong 2018	0.64	0.57	0.70	0.17
TizatoFeriato 2018	0.69	0.59	0.77	0.10
MacquartdeTerline 20	0.31	0.29	0.33	2.02
Shi 2019	0.64	0.59	0.68	0.36
Adeoye 2019	0.96	0.91	0.98	0.75
Saqlain 2019	0.61	0.55	0.67	0.22
Aielo 2019	0.62	0.57	0.67	0.34
Shakya 2020	0.50	0.44	0.57	0.16
Tan 2020	0.58	0.53	0.63	0.31
Sarkodie 2020	0.11	0.08	0.14	0.75
G/Tsadik 2020	0.32	0.29	0.35	0.89
Mahmood 2020	0.38	0.34	0.41	0.62
Hassanein 2020	0.33	0.31	0.35	1.79
Wu 2020	0.28	0.24	0.32	0.44
Mekonen 2020	0.37	0.33	0.42	0.37
Ekanem 2020	0.15	0.12	0.19	0.59
Shen 2020	0.61	0.57	0.64	0.65
Kebede 2020	0.47	0.39	0.55	0.12
Espeche 2020	0.14	0.12	0.16	1.78
Mamaghani 2020	0.18	0.14	0.23	0.32
Heizomi 2020	0.93	0.90	0.95	0.91
Long 2020	0.77	0.74	0.80	0.71
Cinar 2020	0.55	0.48	0.61	0.16
Charoensab 2020	0.65	0.58	0.70	0.21
Sub-total				
Fixed pooled ES	0.43	0.43	0.43	43.87
Overall				
Fixed pooled ES	0.40	0.40	0.40	100.00

Meta-regression coefficient: -0.05, p=0.145

Table S13. meta-analysis of prevalence of medication non-adherence in table format (by questionnaires; subgroup: continent)

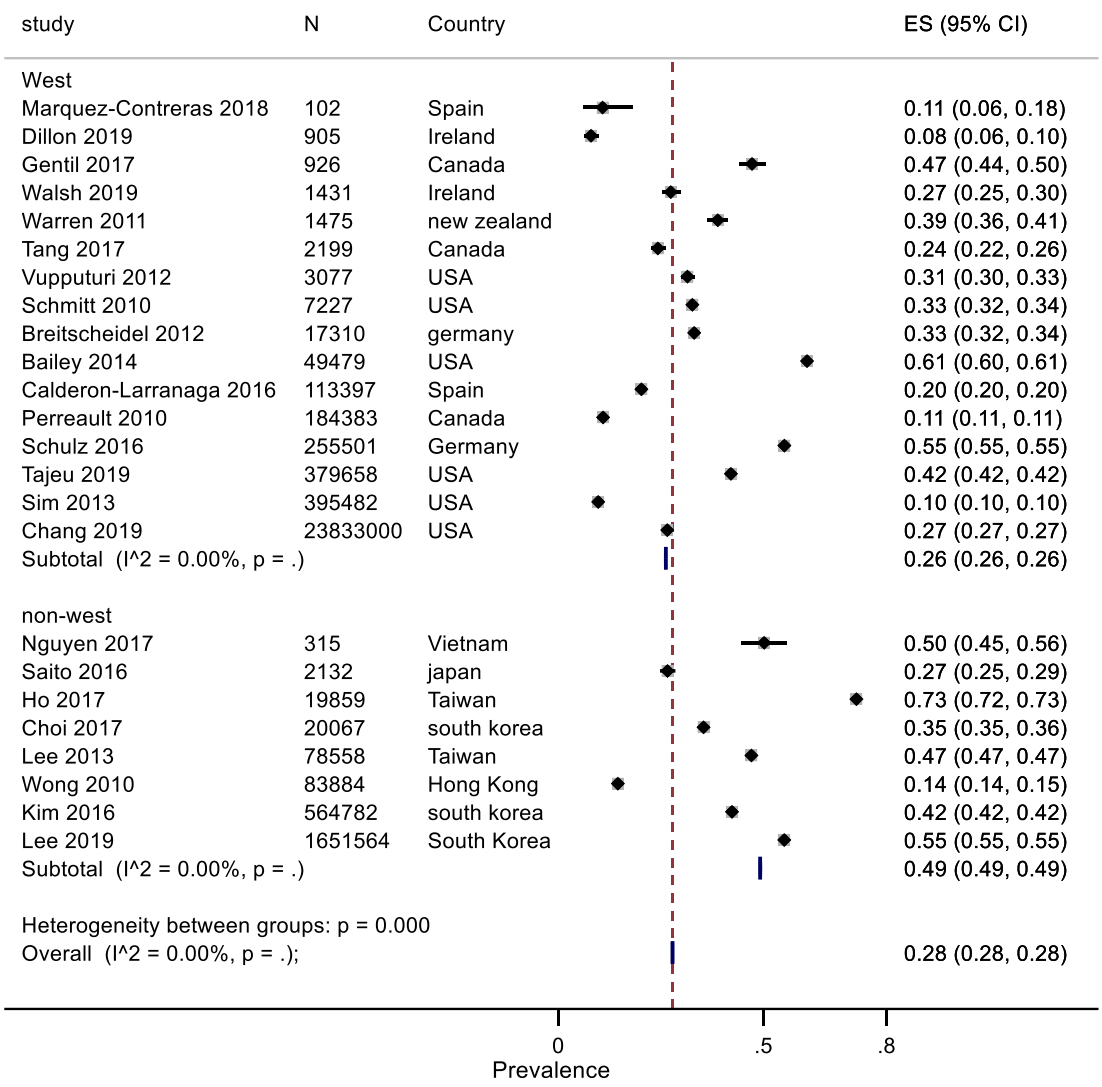
Study	prevalence	Lower 95%CI	Upper 95% CI	%weight
Europe				
Koschack 2010	0.36	0.31	0.41	0.30
Korb-Savoldelli 2012	0.18	0.13	0.23	0.27
Stavropoulou 2012	0.52	0.48	0.56	0.58
Wilinski 2013	0.74	0.72	0.76	1.50
HacihasanogluAsilar	0.59	0.52	0.65	0.16
Bramlage 2014	0.42	0.42	0.43	8.68
Janezic 2014	0.16	0.13	0.20	0.68
Khan 2014	0.64	0.57	0.70	0.17
Perseguer-Torregrosa	0.36	0.32	0.41	0.36
Sandy 2015	0.66	0.61	0.71	0.31
ParejaMartinez 2015	0.15	0.09	0.23	0.15
Lotsch 2015	0.34	0.29	0.39	0.28
Morrison 2015	0.44	0.42	0.46	2.07
Jankowska-Polanska 2	0.18	0.14	0.23	0.39
Jankowska-Polanska 2	0.30	0.26	0.33	0.59
Lomper 2018	0.48	0.43	0.54	0.22
Lefort 2018	0.38	0.36	0.40	1.98
Cabral 2018	0.28	0.24	0.32	0.46
Gavrilova 2019	0.44	0.37	0.52	0.14
Pluta 2020	0.33	0.27	0.40	0.18
Cinar 2020	0.55	0.48	0.61	0.16
Sub-total				
Fixed pooled ES	0.43	0.42	0.43	19.63
Asia				
Lau 2010	0.57	0.53	0.61	0.42
Dennis 2011	0.50	0.46	0.54	0.48
Ha 2012	0.29	0.23	0.36	0.15
Zyoud 2013	0.37	0.32	0.42	0.35
Park 2013	0.41	0.35	0.47	0.20
Kim 2014	0.33	0.28	0.38	0.33
Li 2015	0.81	0.77	0.84	0.61
Zhao 2015	0.26	0.21	0.32	0.24
Yue 2015	0.26	0.21	0.32	0.24
Chui 2015	0.65	0.58	0.71	0.19
Chan 2015	0.22	0.17	0.27	0.27
Farah 2016	0.20	0.17	0.23	0.70
Hou 2016	0.66	0.62	0.70	0.51
Behnood-Rod 2016	0.50	0.44	0.55	0.22
Saarti 2016	0.29	0.22	0.38	0.11
Song 2016	0.57	0.49	0.65	0.13
Athiyah 2013	0.57	0.50	0.64	0.16

Yassine 2016	0.22	0.17	0.28	0.24
Alhaddad 2016	0.41	0.38	0.43	1.20
Yang 2016	0.57	0.53	0.60	0.60
Li 2016	0.27	0.25	0.30	1.30
Lo 2016	0.56	0.49	0.63	0.16
Khayyat 2017	0.54	0.47	0.61	0.16
Sulistiyowatiningsih	0.60	0.54	0.66	0.19
Baran 2017	0.28	0.24	0.32	0.46
Tam 2017	0.55	0.49	0.61	0.23
Ting 2017	0.80	0.77	0.82	1.17
Zhang 2017	0.30	0.27	0.33	1.02
Ko 2017	0.31	0.29	0.32	3.38
Lee 2017	0.62	0.60	0.64	1.96
Pan 2017	0.65	0.60	0.69	0.38
Sheilini 2018	0.16	0.14	0.19	1.18
Meena 2018	0.32	0.29	0.35	0.85
Al-Noumani 2018	0.32	0.26	0.39	0.19
BouSerhal 2018	0.14	0.11	0.18	0.66
Jafar 2018	0.41	0.39	0.44	1.39
Amin 2018	0.34	0.28	0.40	0.22
Efanov 2018	0.32	0.27	0.38	0.23
Balasubramanian 2018	0.54	0.47	0.61	0.15
Chan 2018	0.65	0.55	0.73	0.09
Wong 2018	0.64	0.57	0.70	0.17
Fatani 2019	0.67	0.62	0.73	0.25
Shi 2019	0.64	0.59	0.68	0.36
Saqlain 2019	0.61	0.55	0.67	0.22
Chen 2020	0.62	0.58	0.66	0.45
Shakya 2020	0.50	0.44	0.57	0.16
Kang 2020	0.45	0.40	0.50	0.31
Tan 2020	0.58	0.53	0.63	0.31
Mahmood 2020	0.38	0.34	0.41	0.62
Wu 2020	0.28	0.24	0.32	0.44
Shen 2020	0.61	0.57	0.64	0.65
Mamaghani 2020	0.18	0.14	0.23	0.32
Heizomi 2020	0.93	0.90	0.95	0.91
Long 2020	0.77	0.74	0.80	0.71
Charoensab 2020	0.65	0.58	0.70	0.21
Sub-total				
Fixed pooled ES	0.45	0.45	0.46	28.78
north america				
Breaux-Shropshire 20	0.35	0.28	0.43	0.13
Wagner 2012	0.34	0.33	0.35	14.45
Cummings 2013	0.31	0.30	0.32	13.84
Natarajan 2013	0.23	0.19	0.26	0.59
Rajpura 2014	0.81	0.73	0.87	0.15

Gallagher 2015	0.23	0.17	0.30	0.17
Cummings 2016	0.40	0.36	0.44	0.41
Al-Ruthia 2017	0.21	0.16	0.27	0.22
Fortuna 2018	0.38	0.35	0.40	1.78
Krousel-Wood 2019	0.39	0.36	0.41	1.27
Silver 2019	0.44	0.37	0.51	0.16
Marsh 2019	0.44	0.37	0.50	0.16
Lor 2019	0.76	0.73	0.78	1.45
Sub-total				
Fixed pooled ES	0.35	0.34	0.35	34.77
south america				
Ungari 2010	0.57	0.48	0.66	0.09
Oliveira-Filho 2012	0.47	0.41	0.54	0.18
Ben 2012	0.61	0.54	0.68	0.17
Demoner 2012	0.64	0.56	0.71	0.13
Ledur 2013	0.49	0.43	0.54	0.25
deOliveira-Filho 201	0.47	0.44	0.50	0.74
Fernandez-Arias 2014	0.57	0.48	0.66	0.09
Barreto 2015	0.43	0.38	0.47	0.34
Righi 2017	0.17	0.14	0.21	0.58
TizatoFeriato 2018	0.69	0.59	0.77	0.10
Aielo 2019	0.62	0.57	0.67	0.34
Espeche 2020	0.14	0.12	0.16	1.78
Sub-total				
Fixed pooled ES	0.34	0.33	0.35	4.78
Africa				
Kretchy 2014	0.81	0.77	0.84	0.51
Okwuonu 2014	0.69	0.63	0.74	0.23
Akintunde 2015	0.24	0.17	0.32	0.12
Lulebo 2015	0.54	0.49	0.59	0.31
Okello 2016	0.85	0.81	0.89	0.51
Maginga 2016	0.44	0.38	0.50	0.24
Akoko 2017	0.56	0.50	0.62	0.18
Berhe 2017	0.42	0.39	0.45	0.74
Olowe 2017	0.32	0.28	0.38	0.31
Mekonnen 2017	0.33	0.28	0.37	0.36
Adidja 2018	0.67	0.60	0.73	0.16
Asgedom 2018	0.38	0.33	0.44	0.23
Otenyo 2018	0.42	0.35	0.51	0.12
Animu 2018	0.31	0.27	0.36	0.36
Omar 2018	0.29	0.25	0.34	0.36
MacquartdeTerline 20	0.31	0.29	0.33	2.02
Adeoye 2019	0.96	0.91	0.98	0.75
Sarkodie 2020	0.11	0.08	0.14	0.75
G/Tsadik 2020	0.32	0.29	0.35	0.89

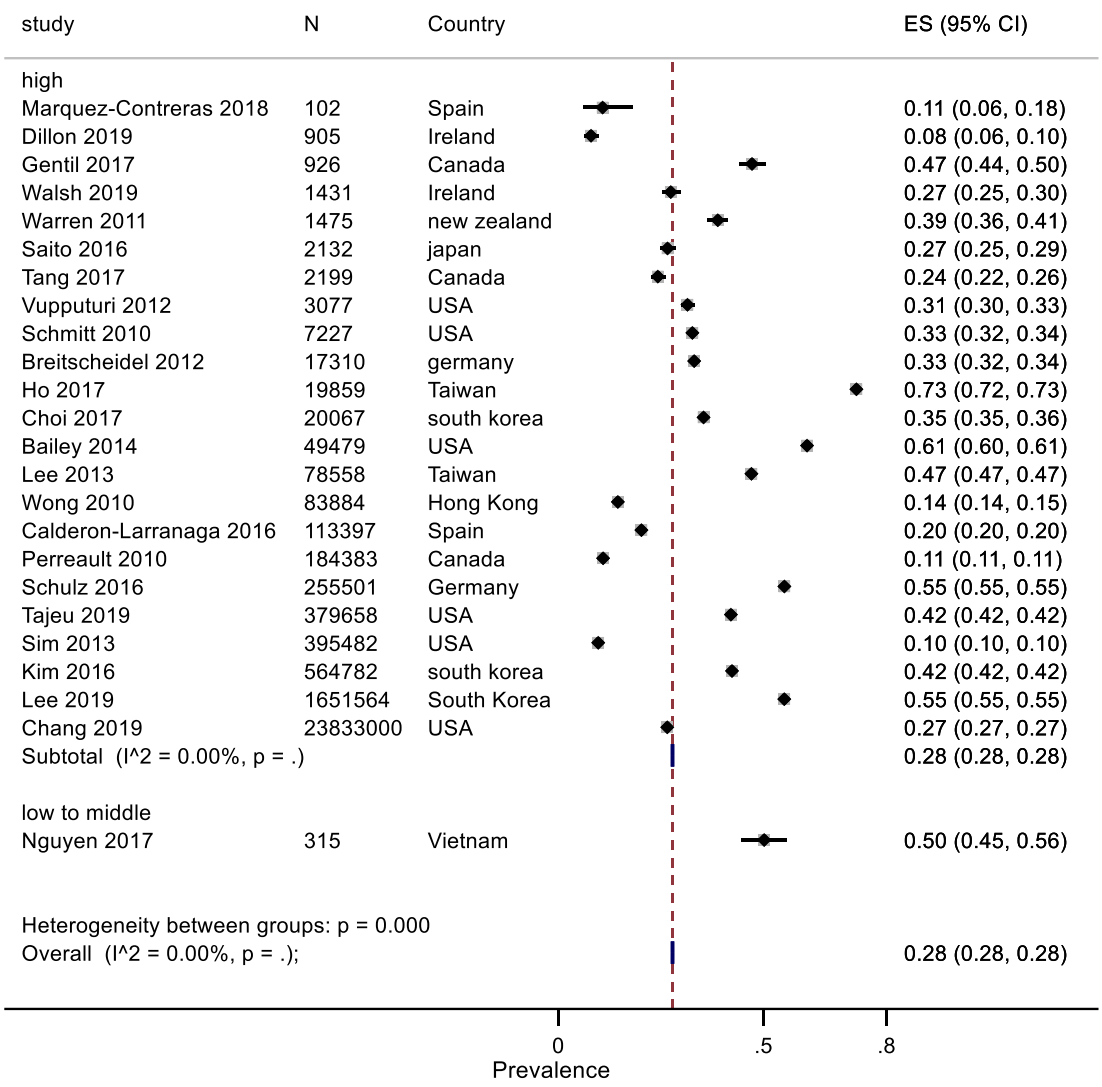
Hassanein 2020	0.33	0.31	0.35	1.79
Mekonen 2020	0.37	0.33	0.42	0.37
Ekanem 2020	0.15	0.12	0.19	0.59
Kebede 2020	0.47	0.39	0.55	0.12
Sub-total				
Fixed pooled ES	0.41	0.41	0.42	12.04
Overall				
Fixed pooled ES	0.40	0.40	0.40	100.00

Figure S1a. meta-analysis of prevalence of medication non-adherence in forest plot (by prescription refill; subgroup: West versus non-West)



In between group difference: meta-regression coefficient: -0.12, p=0.086

Figure S1b. meta-analysis of prevalence of medication non-adherence in forest plot (by prescription refill; subgroup: income level)



In between group difference: meta-regression coefficient = -.16, p=0.37

Figure S1c. meta-analysis of prevalence of medication non-adherence in forest plot (by prescription refill; subgroup: continents)

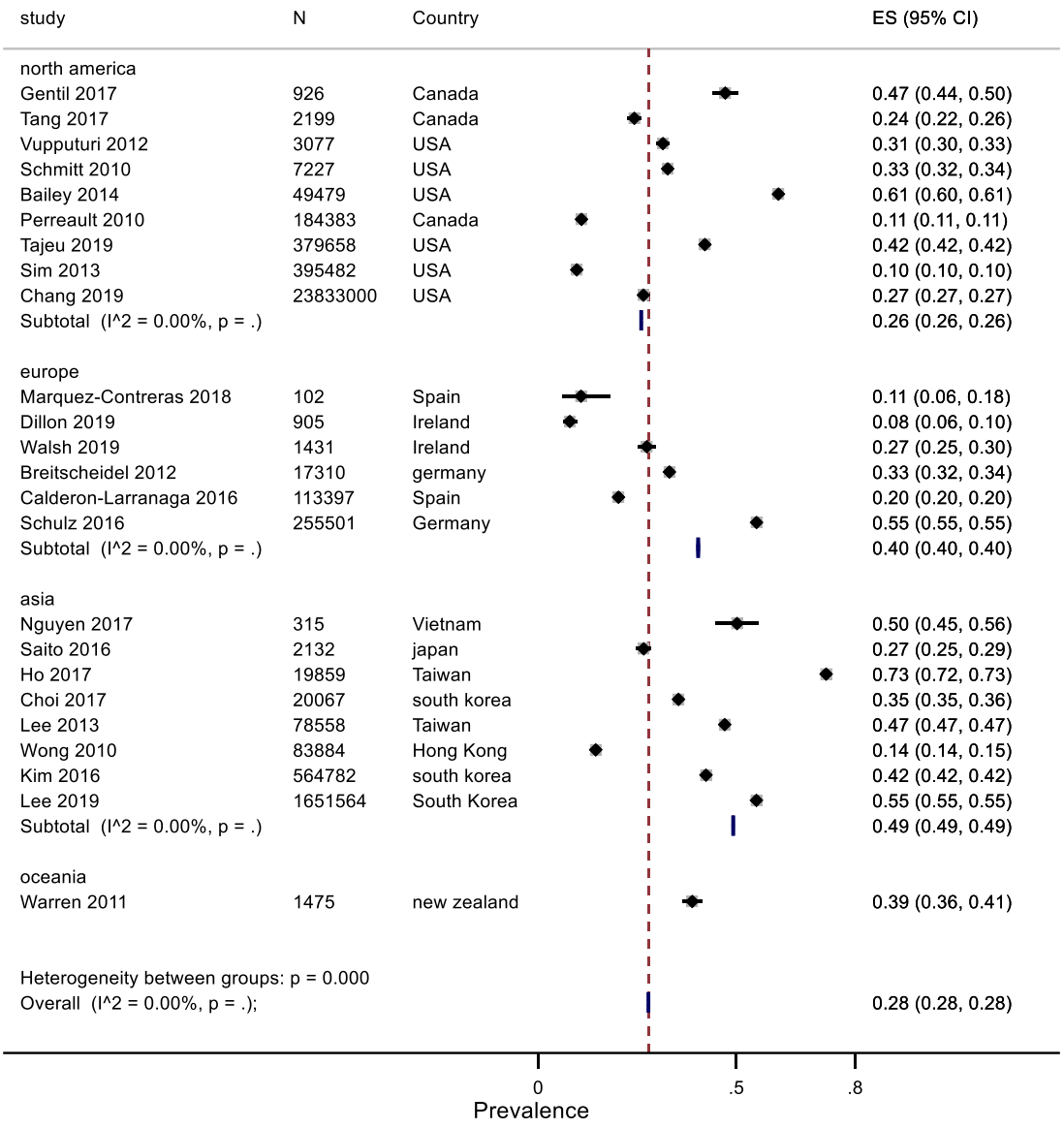
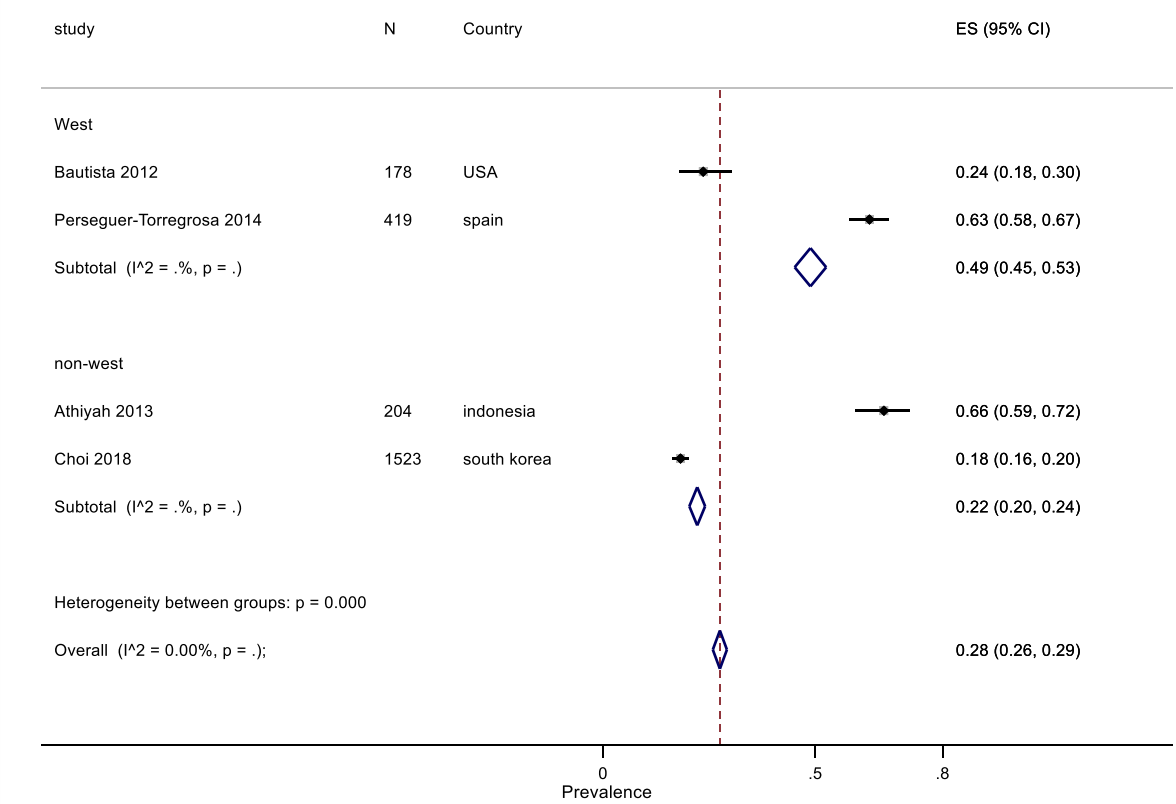
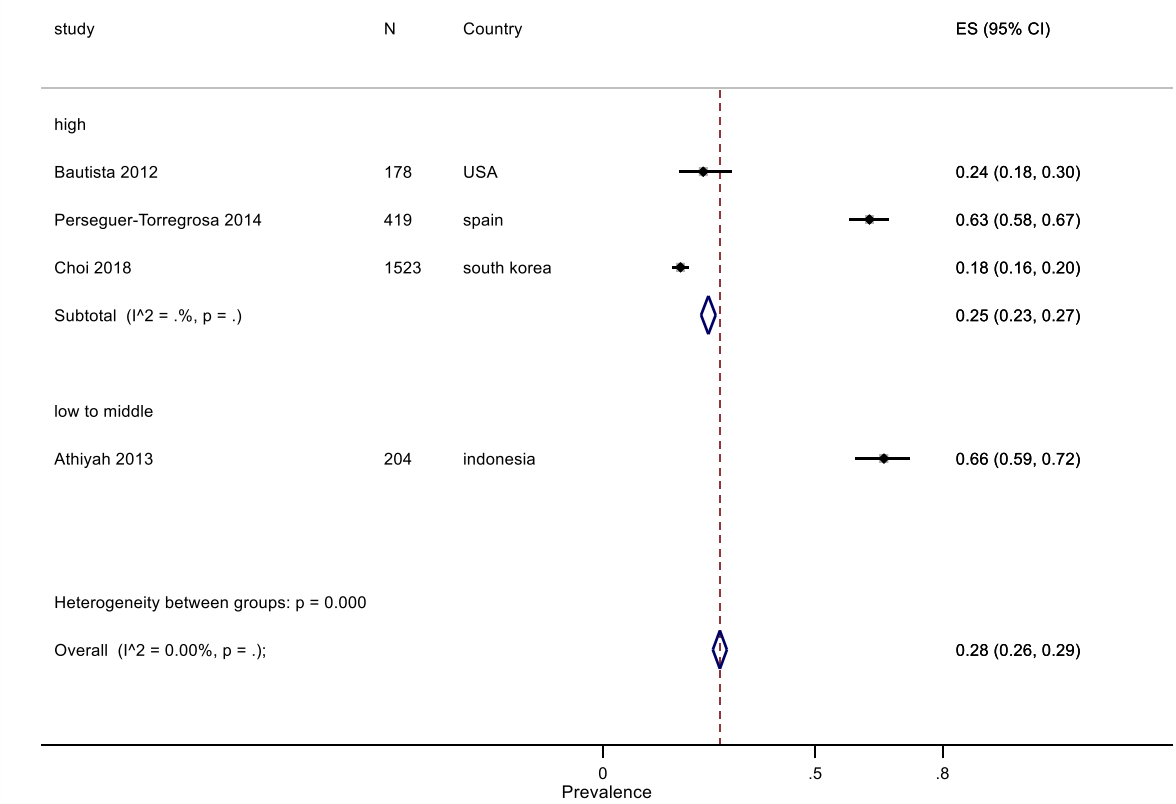


Figure S1d. meta-analysis of prevalence of medication non-adherence in forest plot (by pill counting; subgroup: West vs non-West)



Between group difference - meta-regression coefficient: 0.01, p = 0.974

Figure S1e. meta-analysis of prevalence of medication non-adherence in forest plot (by pill counting; subgroup: income level)



Between-group difference – meta-regression coefficient = 0.31, p = 0.382

Figure S1f. meta-analysis of prevalence of medication non-adherence in forest plot (by pill counting; subgroup: continent)

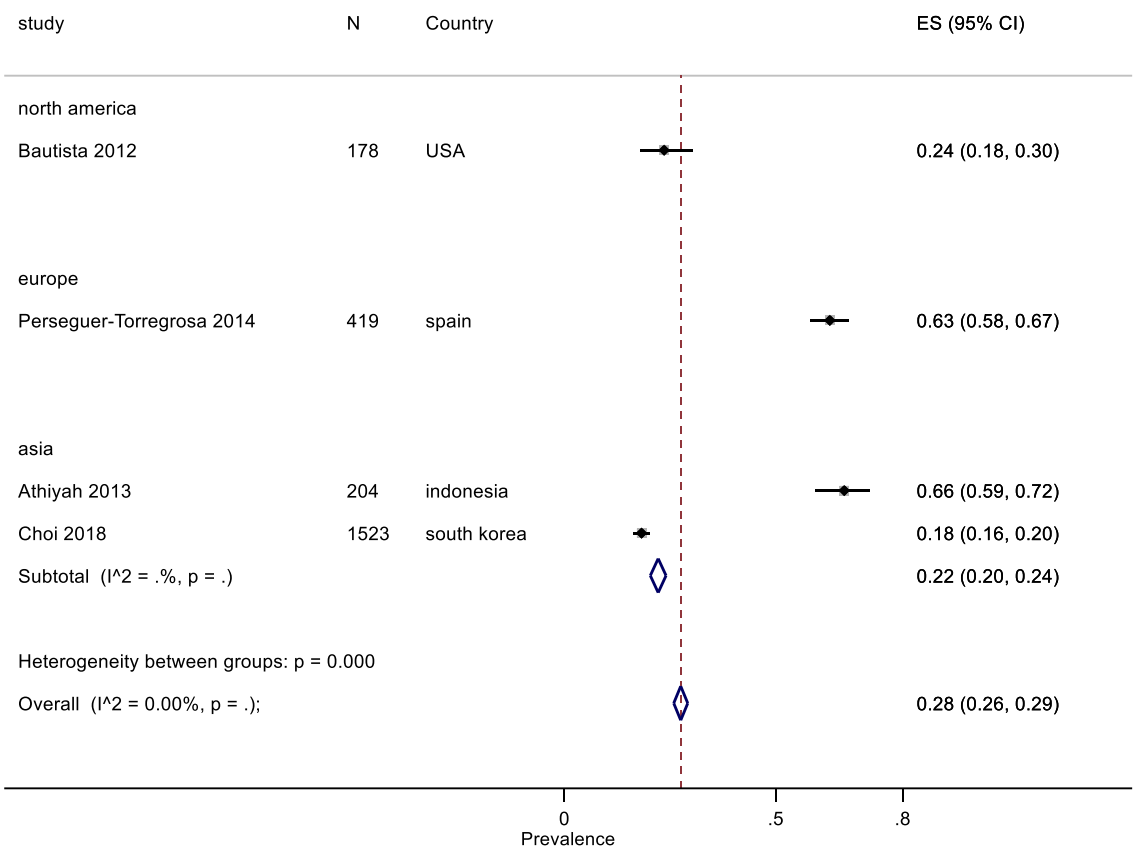


Figure S1g. meta-analysis of prevalence of medication non-adherence in forest plot (by electronic pill box; subgroup: West vs non-West)

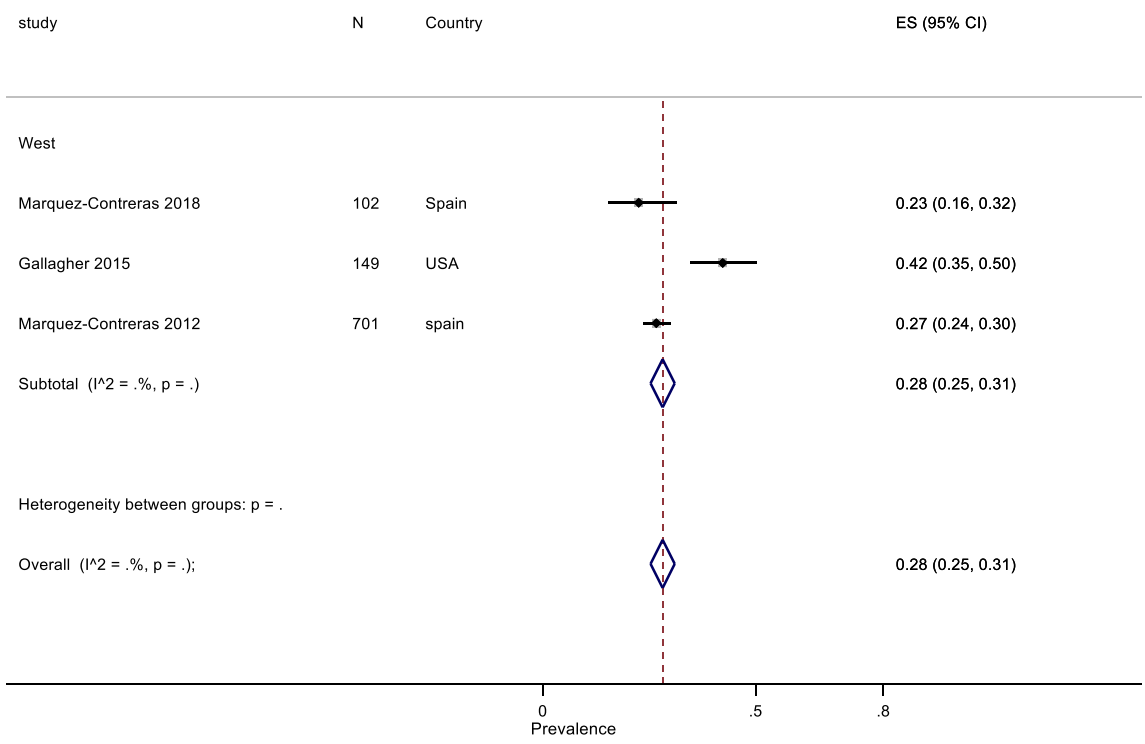


Figure S1h. meta-analysis of prevalence of medication non-adherence in forest plot (by electronic pill box; subgroup: income level)

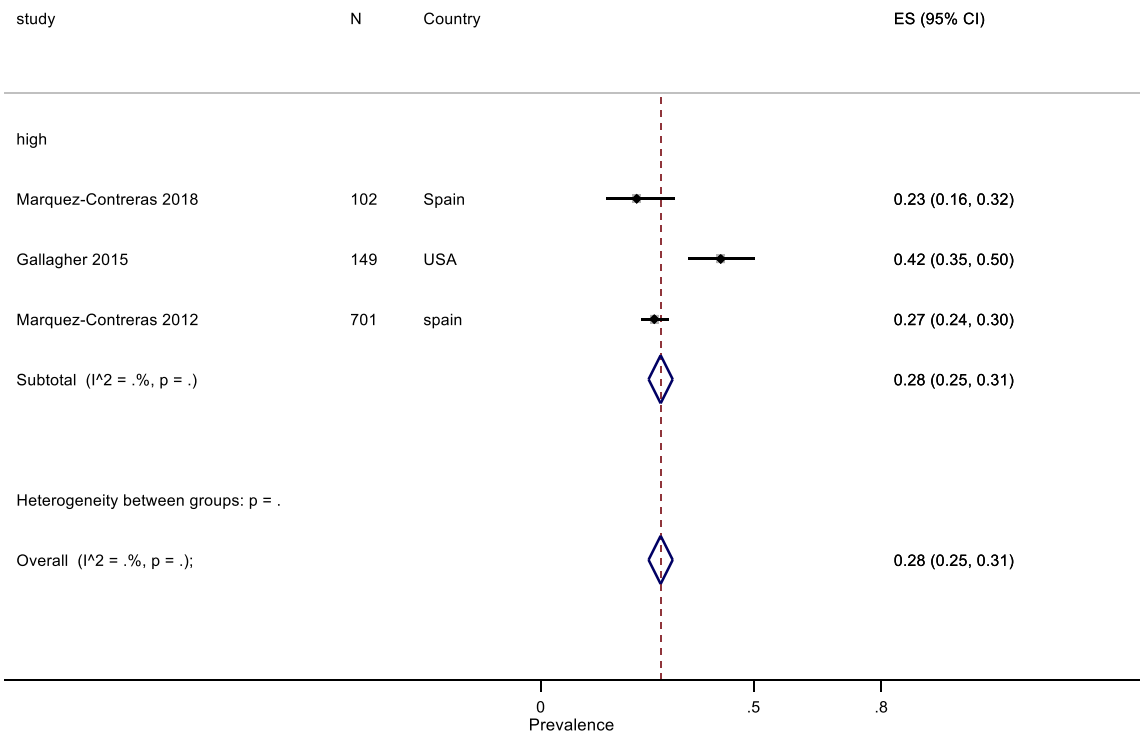


Figure S1i. meta-analysis of prevalence of medication non-adherence in forest plot (by electronic pill box; subgroup: continent)

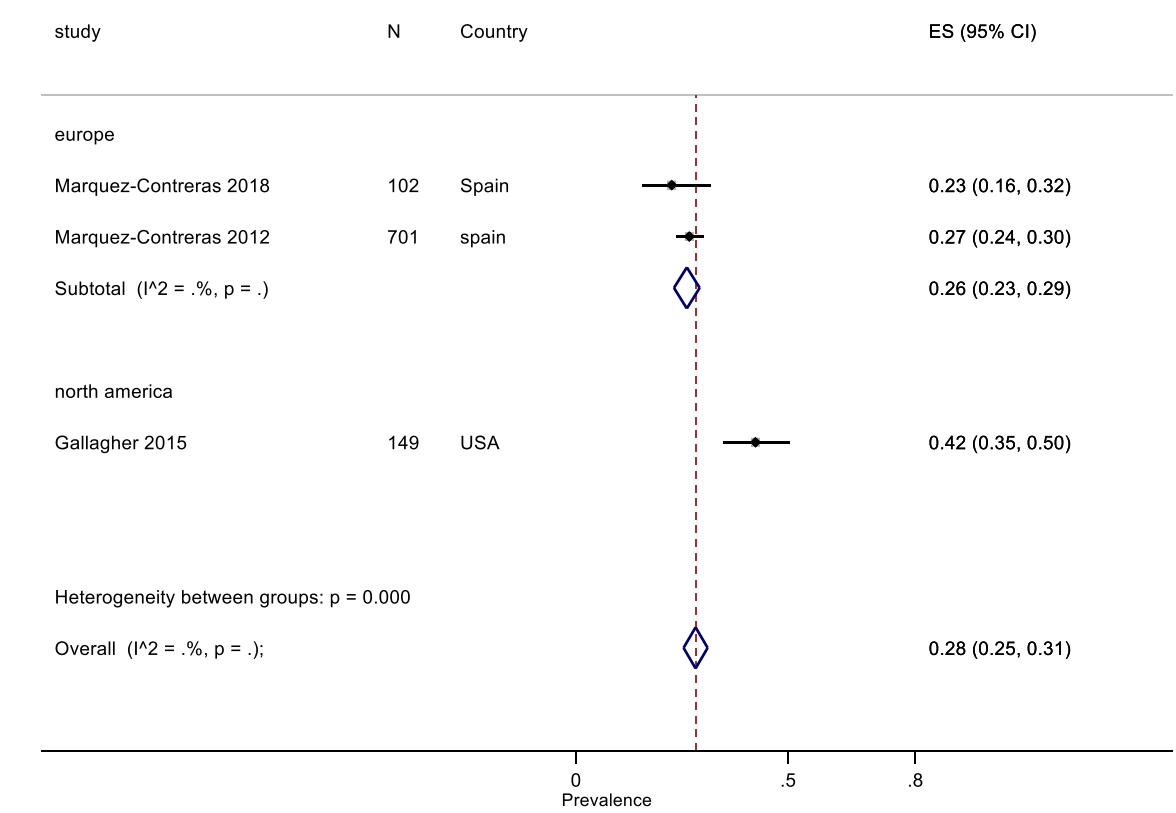


Figure S1j. meta-analysis of prevalence of medication non-adherence in forest plot (by biochemical assay; subgroup: West vs non-West)

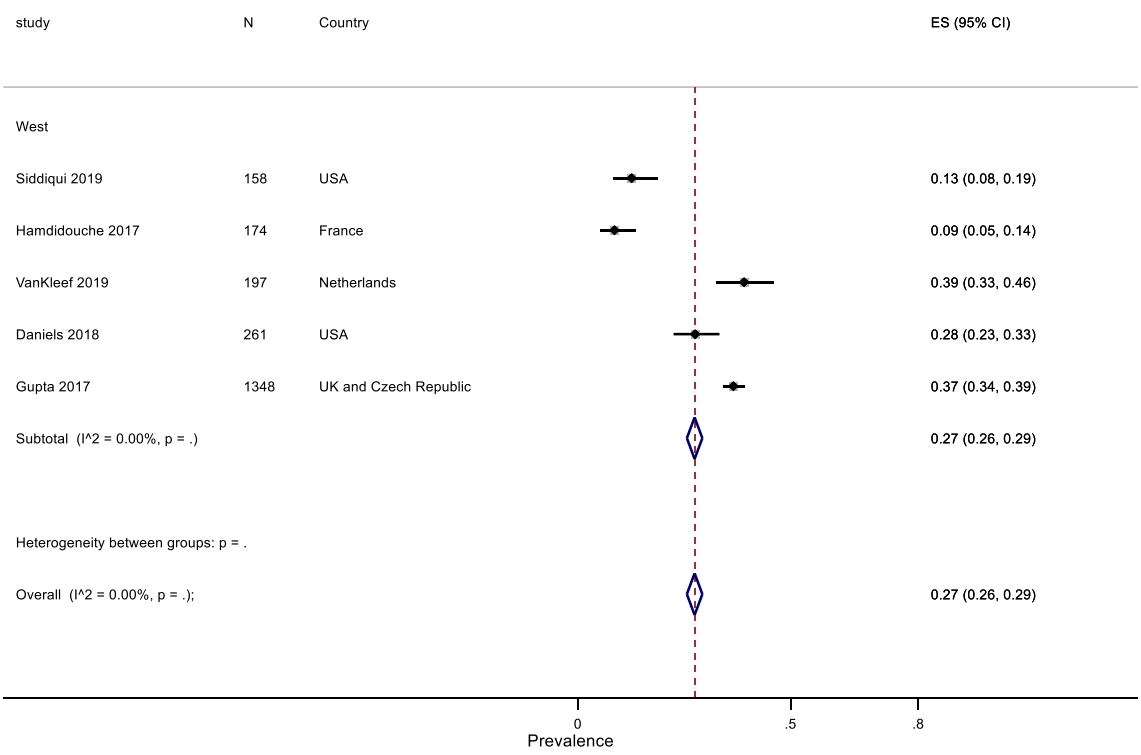


Figure S1k. meta-analysis of prevalence of medication non-adherence in forest plot (by biochemical assay; subgroup: income level)

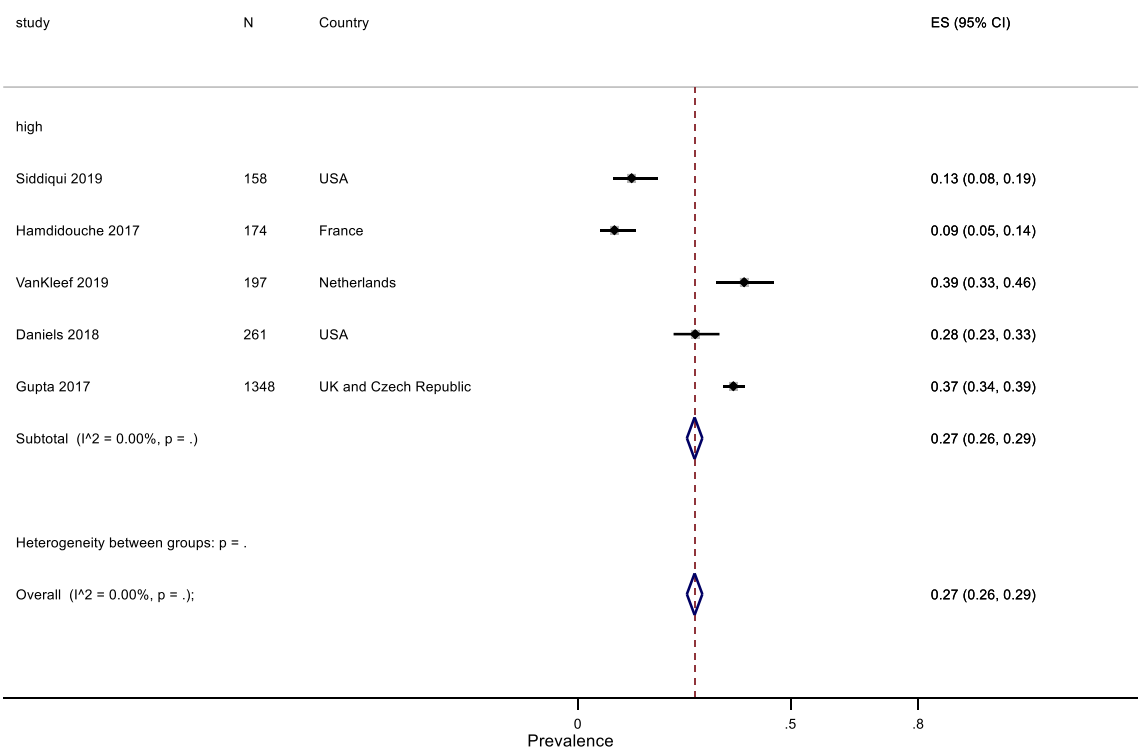
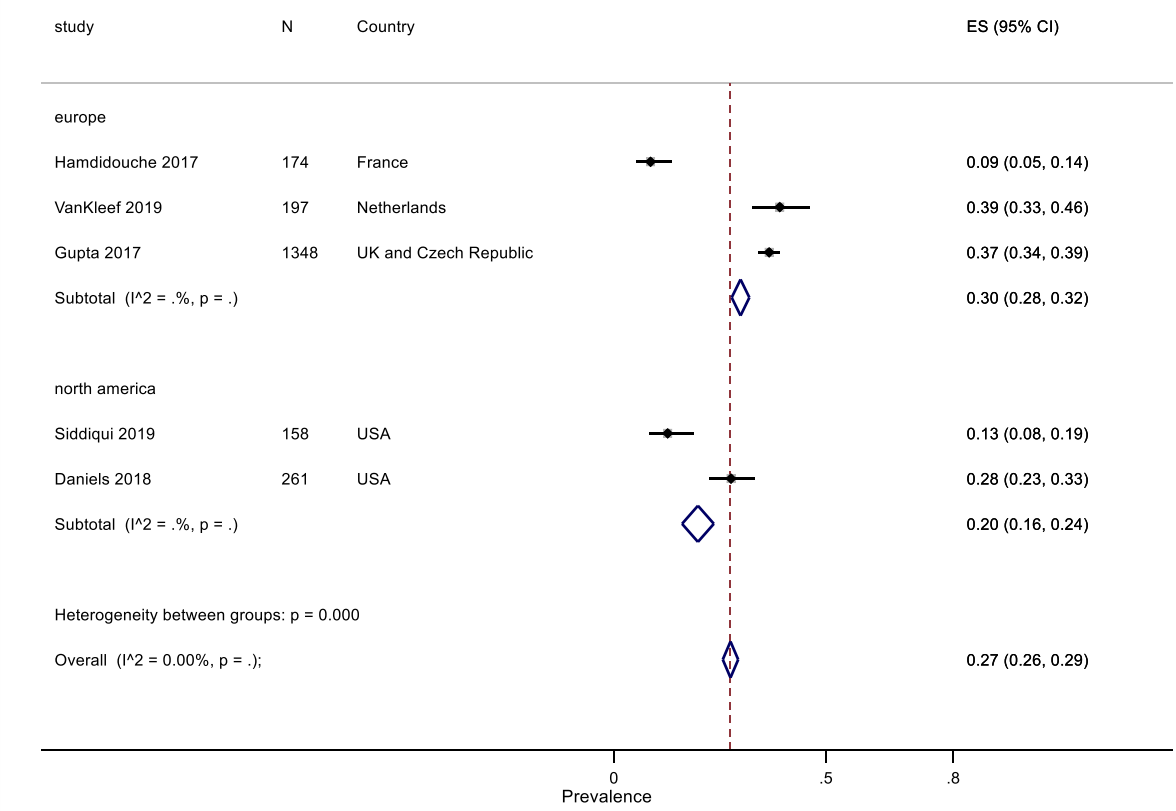


Figure S1l. meta-analysis of prevalence of medication non-adherence in forest plot (biochemical assay; subgroup: continent)



Trend of medication non-adherence

Table S14. Trend of medication non-adherence as defined by publication year

		Meta-regression Co-efficient	***trend meta-regression p-value***
Questionnaire	Overall	0	0.977
	West	0.005	0.661
	Non-west	-0.006	0.473
	High income country	0.01	0.291
	Low to middle income country	-0.009	0.307
Prescription refill	Overall	0.01	0.416
	West	-0.002	0.862
	Non-west	0.04	0.092
	High income country	0.009	0.477
	Low to middle income country	(not available)	

Table S15. Trend of medication non-adherence as defined by year of first recruitment

		Meta-regression Co-efficient	*trend meta-regression p-value*
Questionnaire	Overall	0	0.984
	West	0.003	0.745
	Non-west	-0.006	0.451
	High income country	0.007	0.346
	Low to middle income country	-0.01	0.220
Prescription refill	Overall	-0.012	0.127
	West	-0.014	0.067
	Non-west	-0.007	0.792
	High income country	-0.012	0.127
	Low to middle income country	(not available)	

Table S16. regression analyses between demographic data and non-adherence

	questionnaires		**prescription refill**	
	Meta-regression coefficient	p-value	Meta-regression coefficient	p-value
mean age of participants	0	0.456	-0.015	**0.001***
proportion of male	-0.2	0.178	0.111	0.678
diabetes mellitus	-0.1	0.523	-0.679	0.260
Hyperlipidaemia	0	0.992	-0.608	0.237
mental illnesses	-0.29	0.166	1.356	0.088
cardiovascular diseases	0.2	0.234	-0.159	0.708
renal diseases	-0.07	0.729	-0.864	0.342
insurance/free health service	0.05	0.701	0.368	**0.044***
years of diagnosis	-0.02	0.071	-0.042	0.146
single combination pills	0.08	0.793	-0.268	0.729
average number of anti-hypertensive classes	-0.02	0.641	-1.589	**0.014***
tertiary or above education	-0.05	0.658	NA**	NA
>=2 antihypertensive classes	-0.07	0.539	-0.05	0.829
current smoker	0.19	0.374	NA**	
once daily medication	0.33	0.197	NA**	
Specialist settings vs other settings	-0.02	0.628	-0.017	0.927

**Not applicable due to inadequate number of studies

Blood pressure difference (in various subgroups)

Figure S2a Systolic blood pressure difference due to medication non-adherence (Subgroup: west versus non-west)

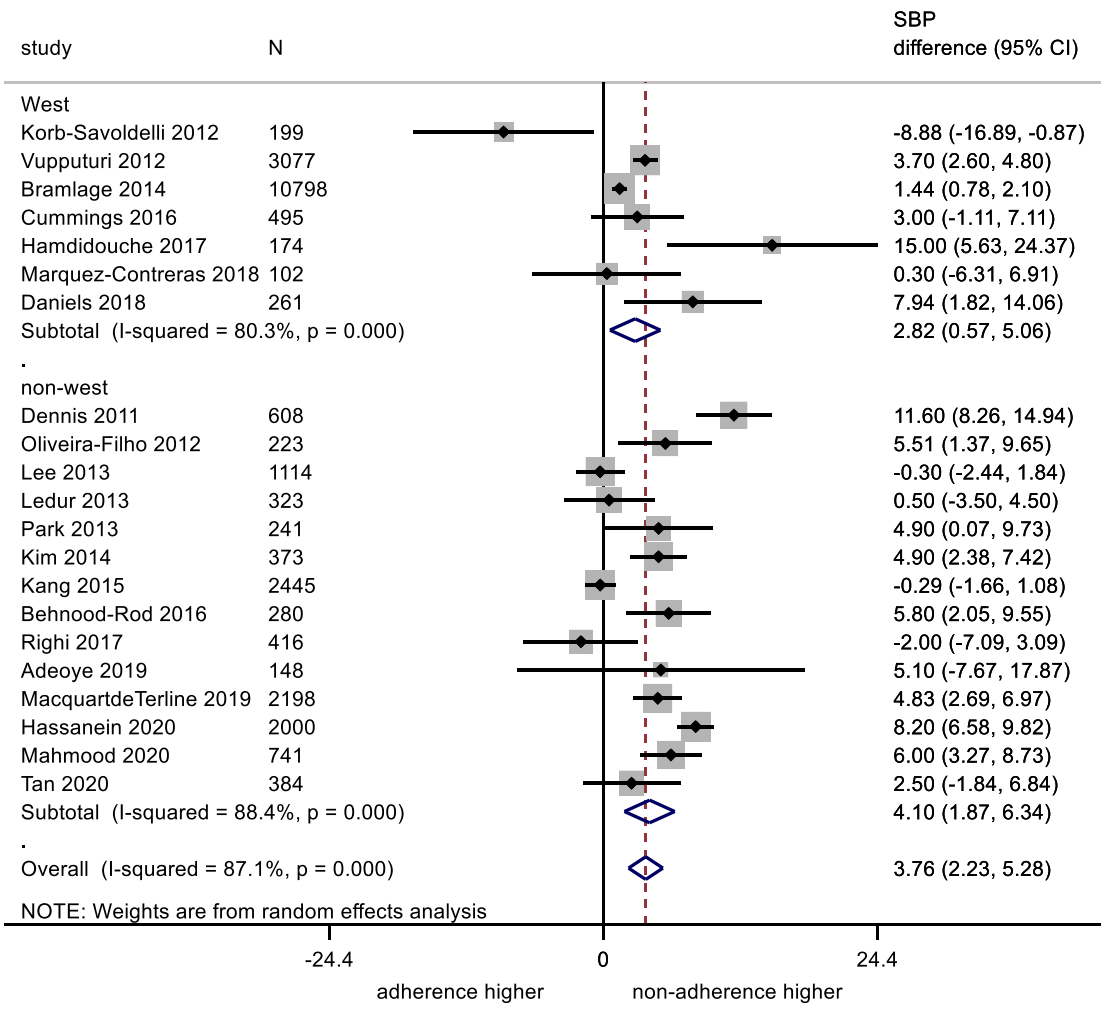


Figure S2b Systolic blood pressure difference due to medication non-adherence (Subgroup: income level)

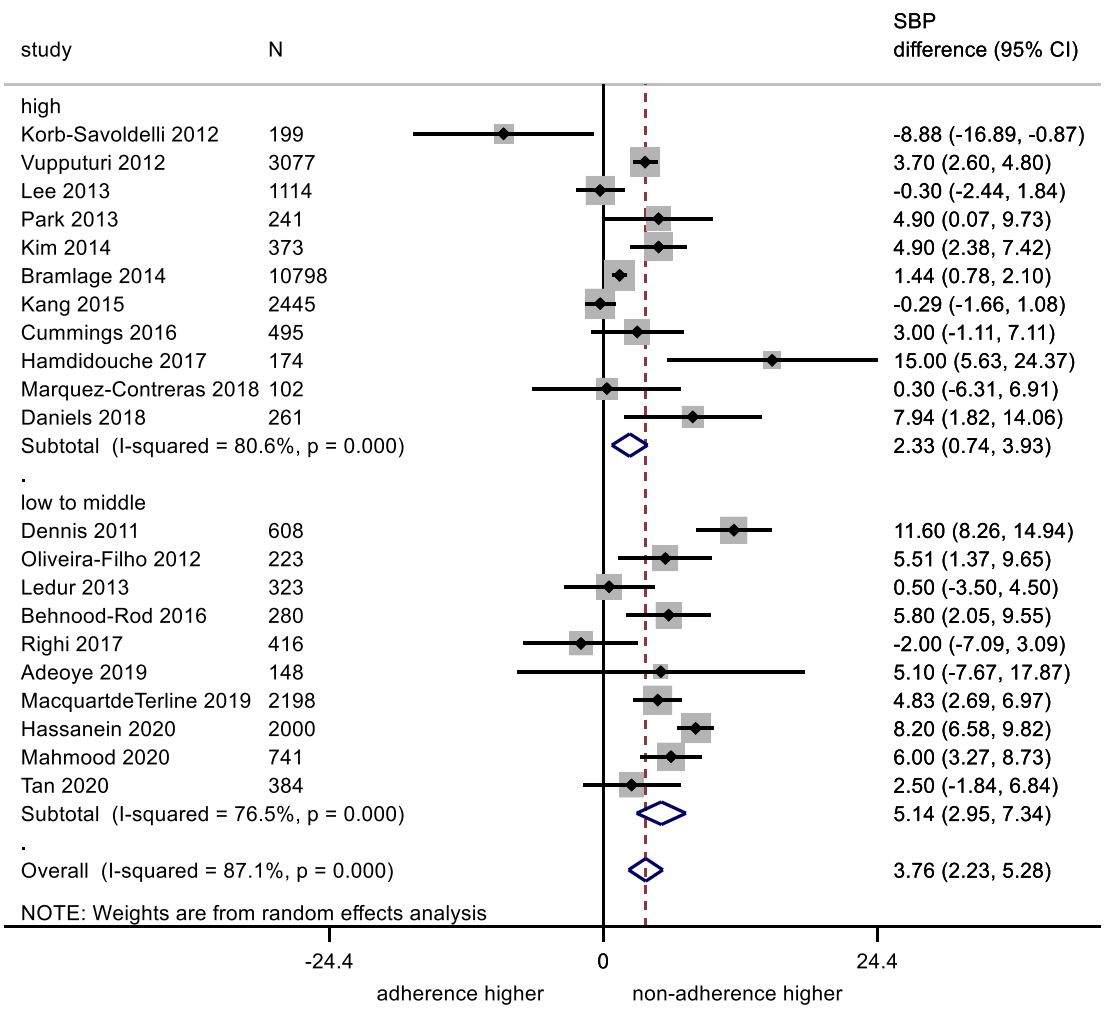


Figure S2c Diastolic blood pressure difference due to medication non-adherence (Subgroup: west versus non-west)

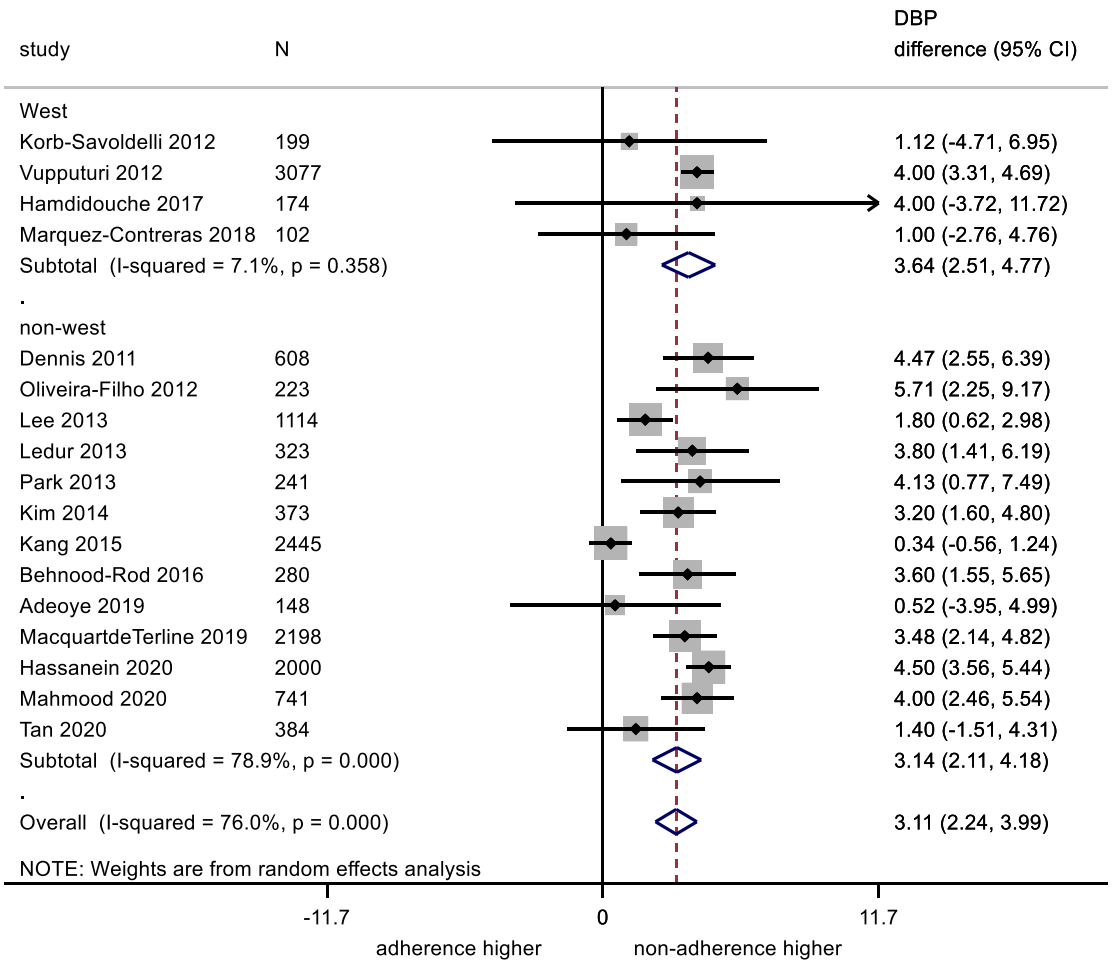
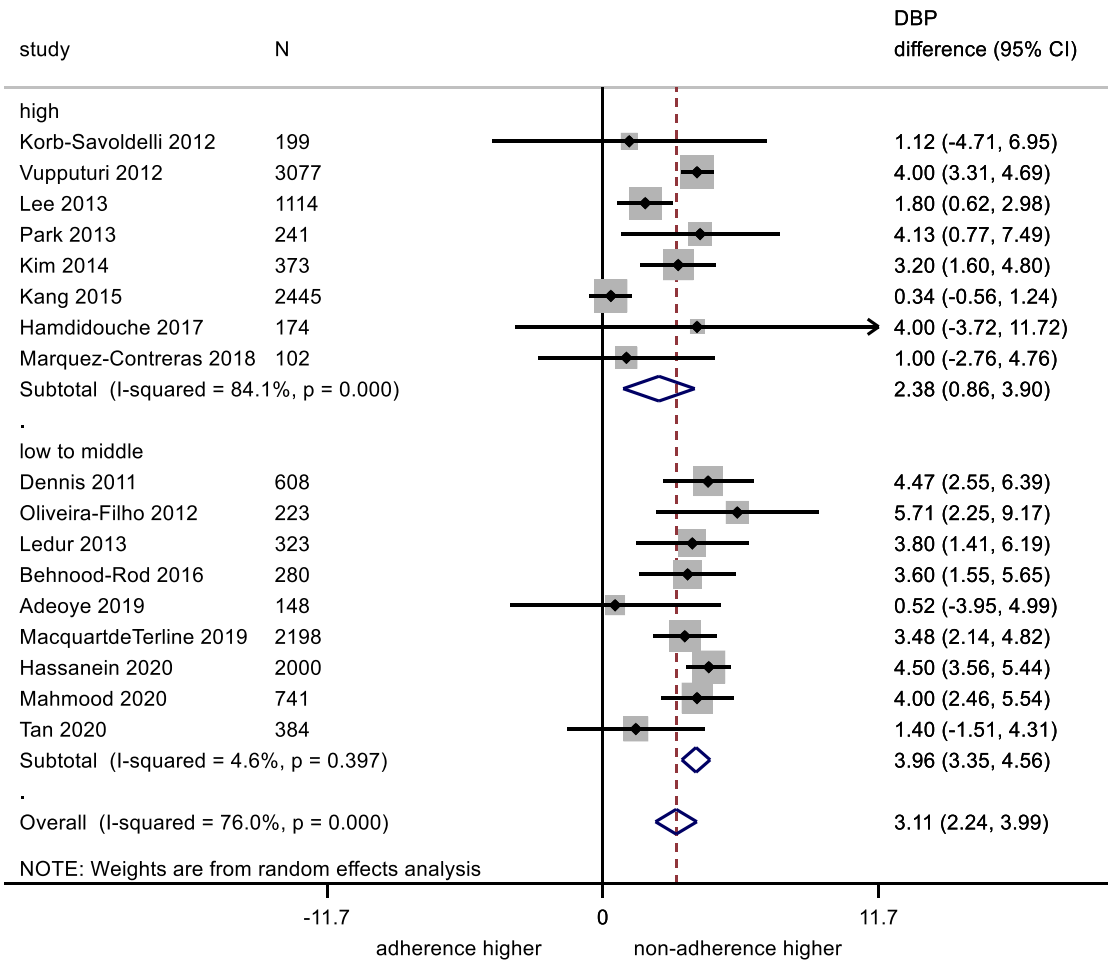


Figure S2d Diastolic blood pressure difference due to medication non-adherence (Subgroup: income level)



Sensitivity analysis

Table S17 summary of sensitivity analysis

	Estimated prevalence	95% CI	I^2 statistics	p-value
Any definition				
Original	0.28	0.28-0.28		
Included only larger studies (n>500)	0.28	0.28-0.28		
Included only larger studies (n>3000)	0.28	0.28-0.28		
Included only low risk of bias studies	0.34	0.34-0.34		
Questionnaire				
Original	0.40	0.40-0.40		
Included only larger studies (n>500)	0.39	0.38-0.39		
Included only larger studies (n>3000)	0.34	0.34-0.35		
Included only low risk of bias studies	0.38	0.37-0.39		
If MMAS-8 cut off used at ≤6 instead of <6	0.42	0.41-0.42		
Include MMAS-4>0 only	0.41	0.41-0.42		
Include MMAS-8 <6 only	0.38	0.38-0.39		
Prescription refill				
Original	0.28	0.28-0.28		
Included only larger studies (n>500)	0.28	0.28-0.28		
Included only larger studies (n>3000)	0.28	0.28-0.28		
Included only low risk of bias studies	0.34	0.34-0.34		
Used last data end-point rather than baseline non-adherence proportion	0.25	0.17-0.34		

Systolic blood pressure				
Original	3.76mmHg	2.23-5.28mmHg	87.1%	<0.001
Included only larger studies (n>500)	4.19mmHg	1.98-6.4mmHg	94.4%	<0.001
Included only low risk of bias studies	3.66mmHg	-0.35-7.66mmHg	38.5%	<0.001
Diastolic blood pressure				
Original	3.11mmHg	2.24-3.99mmHg	76%	<0.001
Included only larger studies (n>500)	3.18mmHg	1.88-4.49mmHg	89.9%	<0.001
Included only low risk of bias studies	2.79mmHg	1.10-4.47mmHg	10.3%	<0.001

*Not applicable due to inadequate number of studies. (N=2, Hsu 2015 reported a prevalence of 71%)

Table S17 (cont)

Trend of non-adherence

By publication year				
	Questionnaire		**Prescription refill**	
	Co-efficient	trend meta-regression p-value	Co-efficient	p-value
only larger studies (n>500)	-0.003	0.731	0.012	0.323
only larger studies (n>3000)	N/A	N/A	0.27	0.06
only low risk of bias	0.016	0.391	0.033	0.113

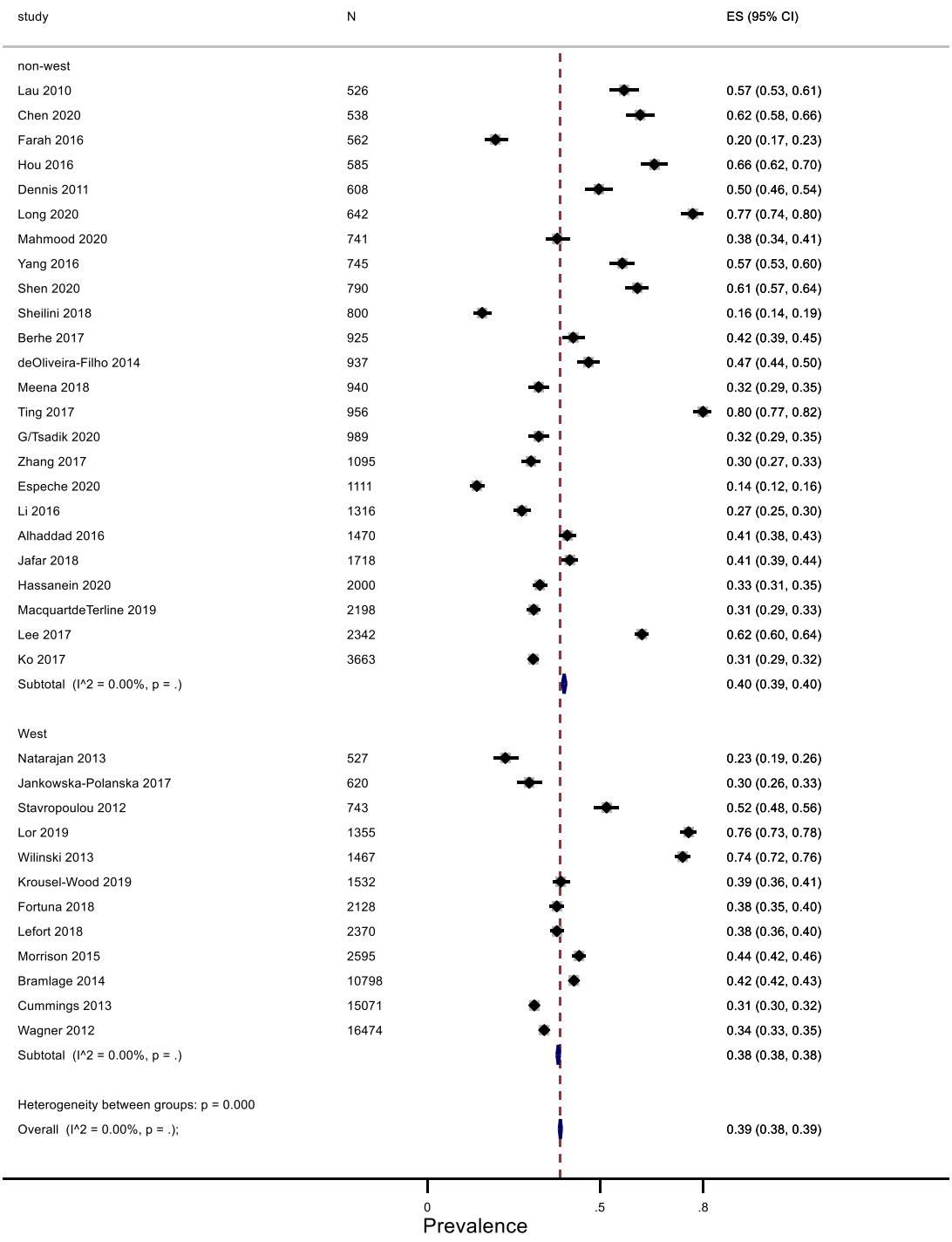
*N/A due to inadequate number of studies

By year of recruitment				
	Questionnaire		**Prescription refill**	
	Co-efficient	trend meta-regression p-value	Co-efficient	p-value
only larger studies (n>500)	0	0.974	-0.011	0.171
only larger studies (n>3000)	N/A	N/A	-0.007	0.49
only low risk of bias	-0.006	0.636	0.006	0.732

*N/A due to inadequate number of studies

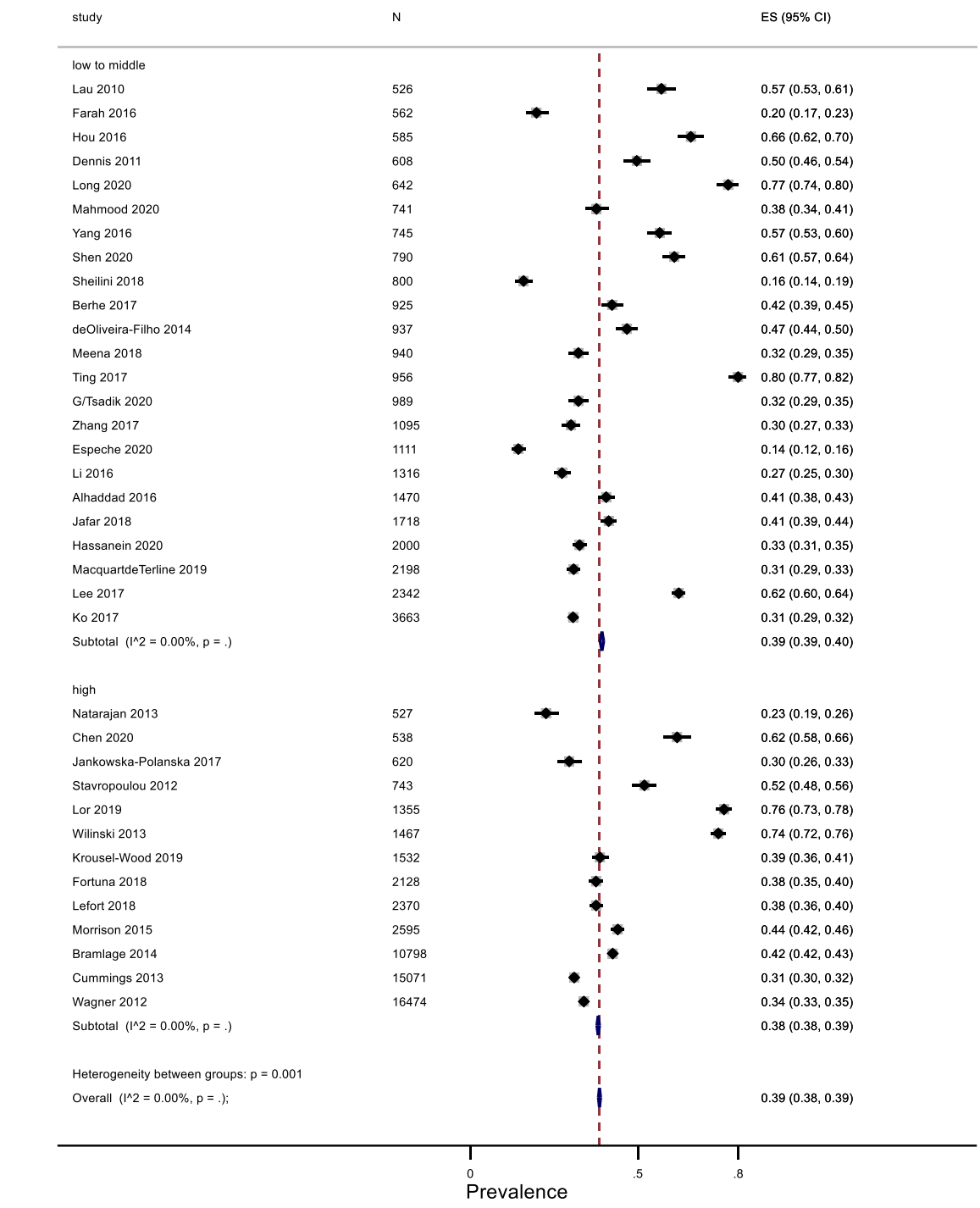
Figure S3a. prevalence using questionnaires and only included larger studies (n>500)

(i) West versus non-west



Meta-regression coefficient: -0.002, p=0.966

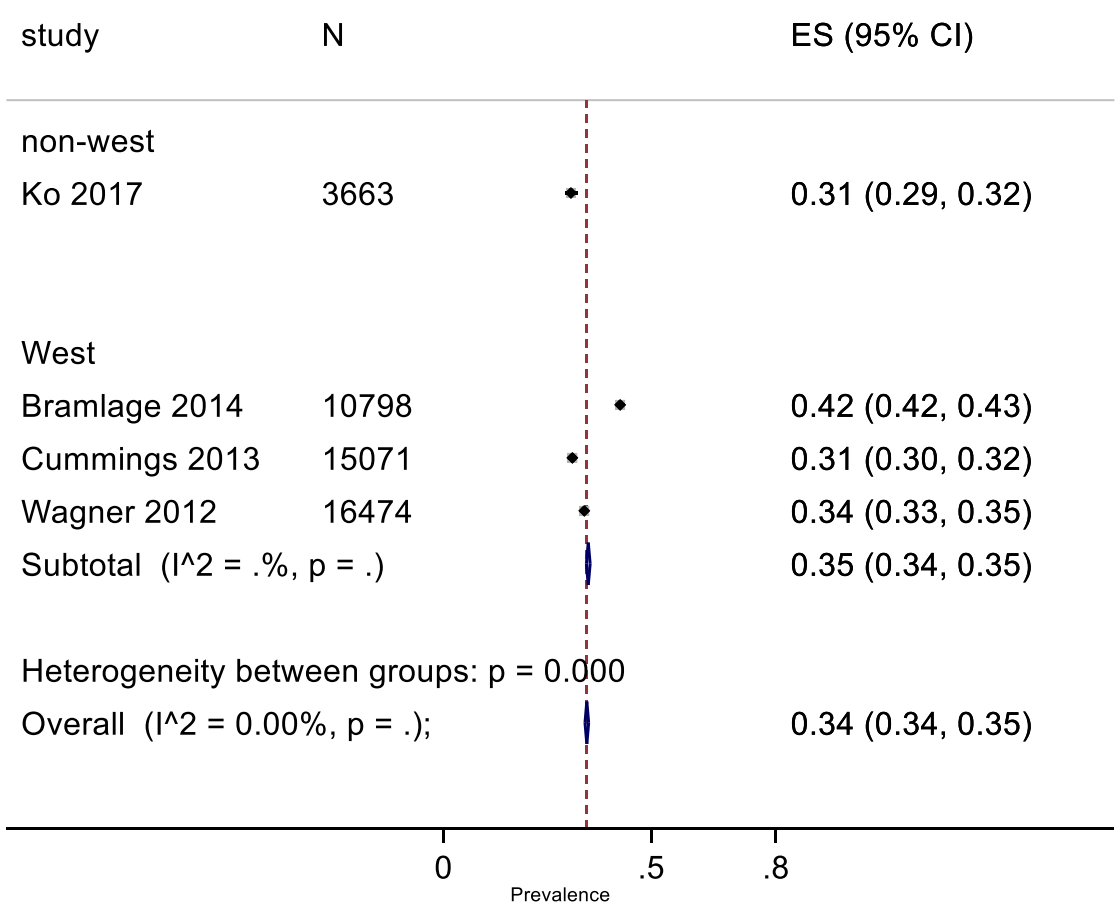
(ii) Income level



Meta-regression coefficient: 0.019, p = 0.756

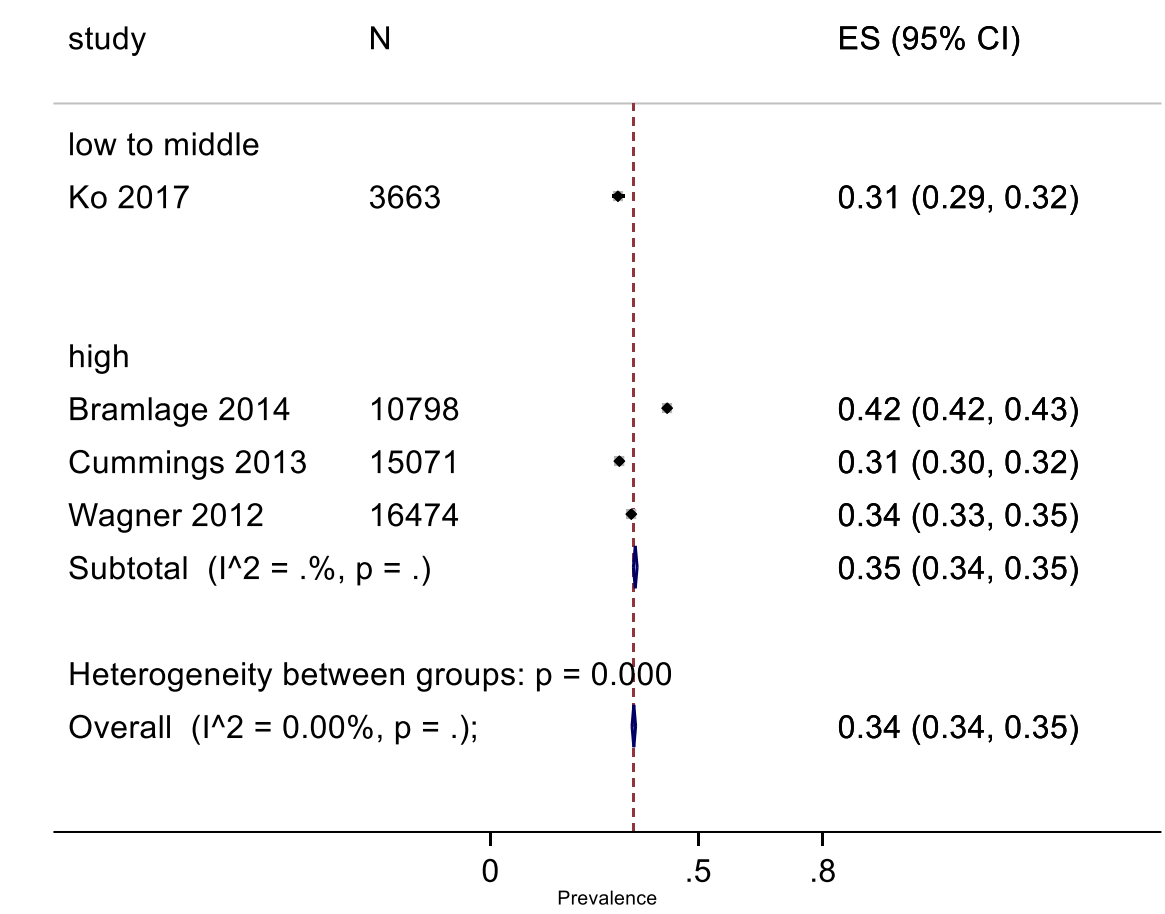
Figure S3b. prevalence using questionnaires and only included larger studies (n>3000)

(i) West vs non-west



Meta-regression coefficient: 0.051, p=0.537

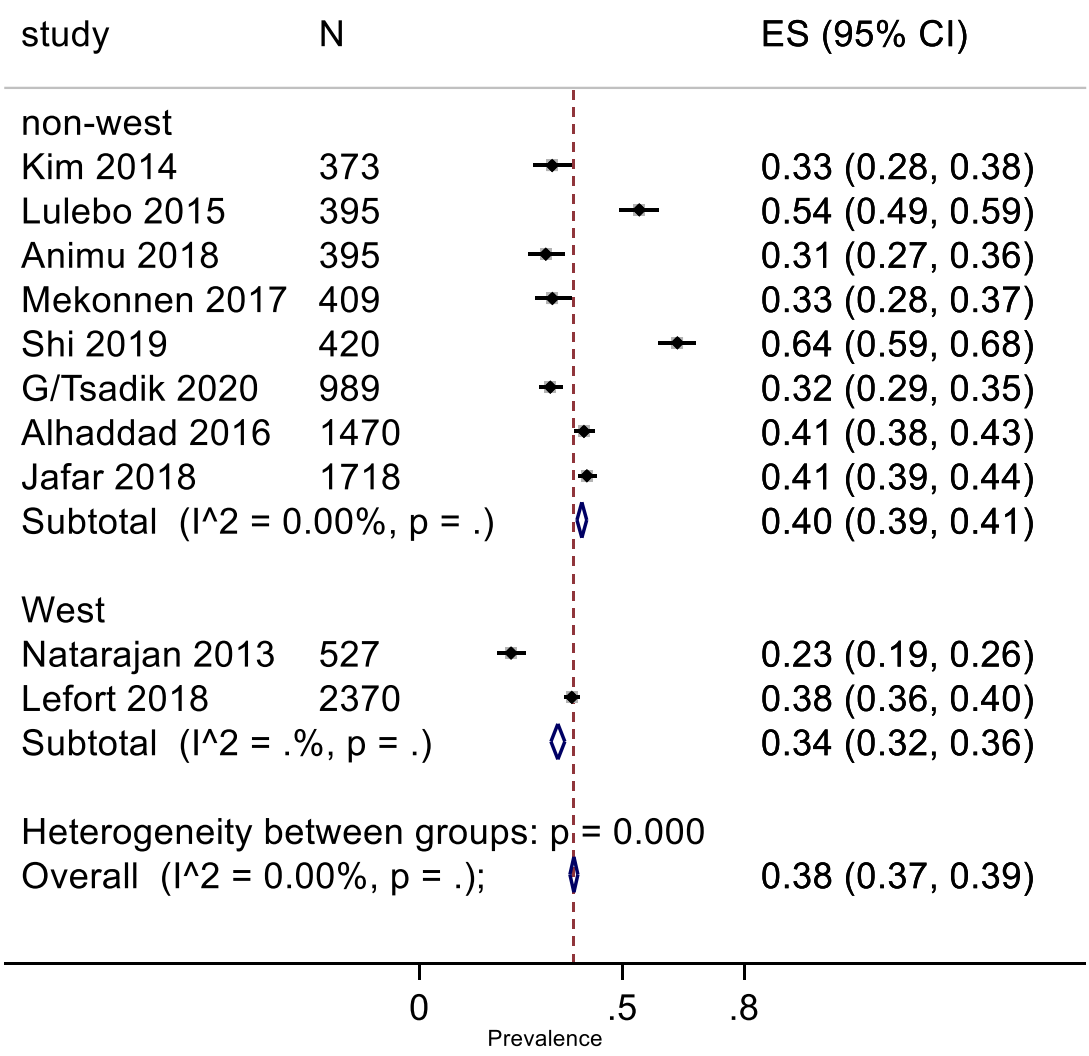
(ii) Income level



Meta-regression coefficient: 0.051, p=0.537

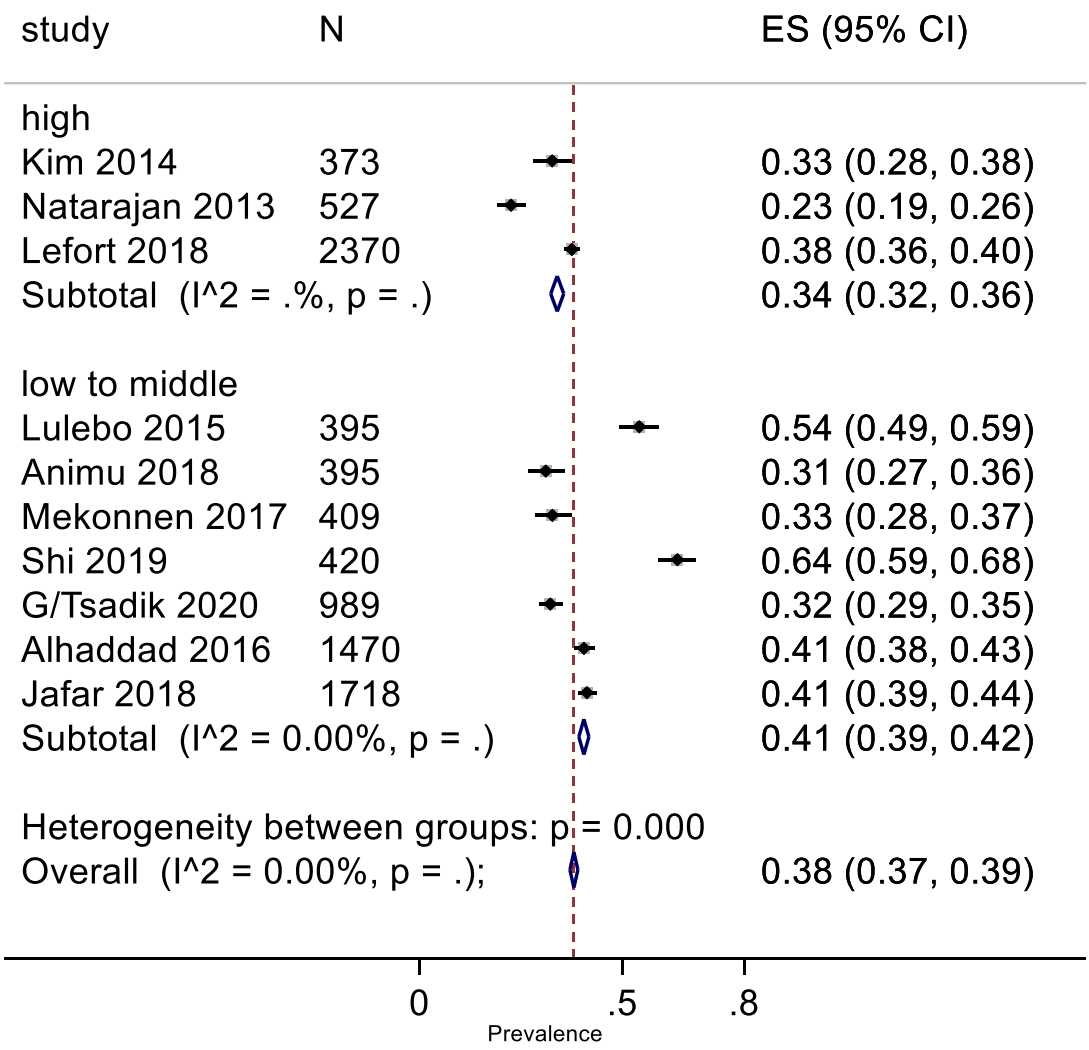
Figure S3c. prevalence using questionnaires and only low-risk-of-bias studies

(i) West vs non-west



Meta-regression co-efficient: -0.10, p = 0.271

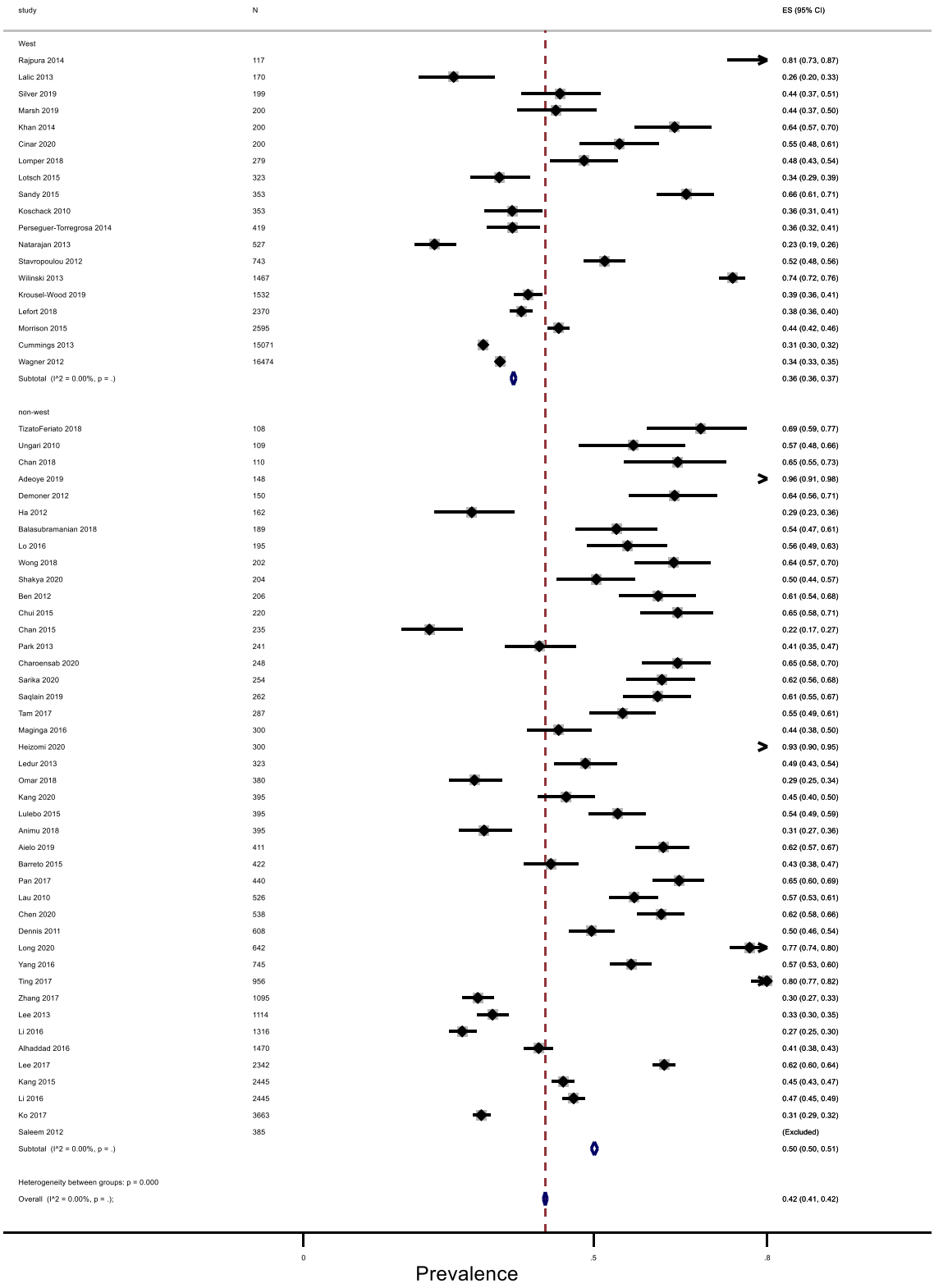
(ii) Income level



Meta-regression co-efficient: -0.112, p=0.188

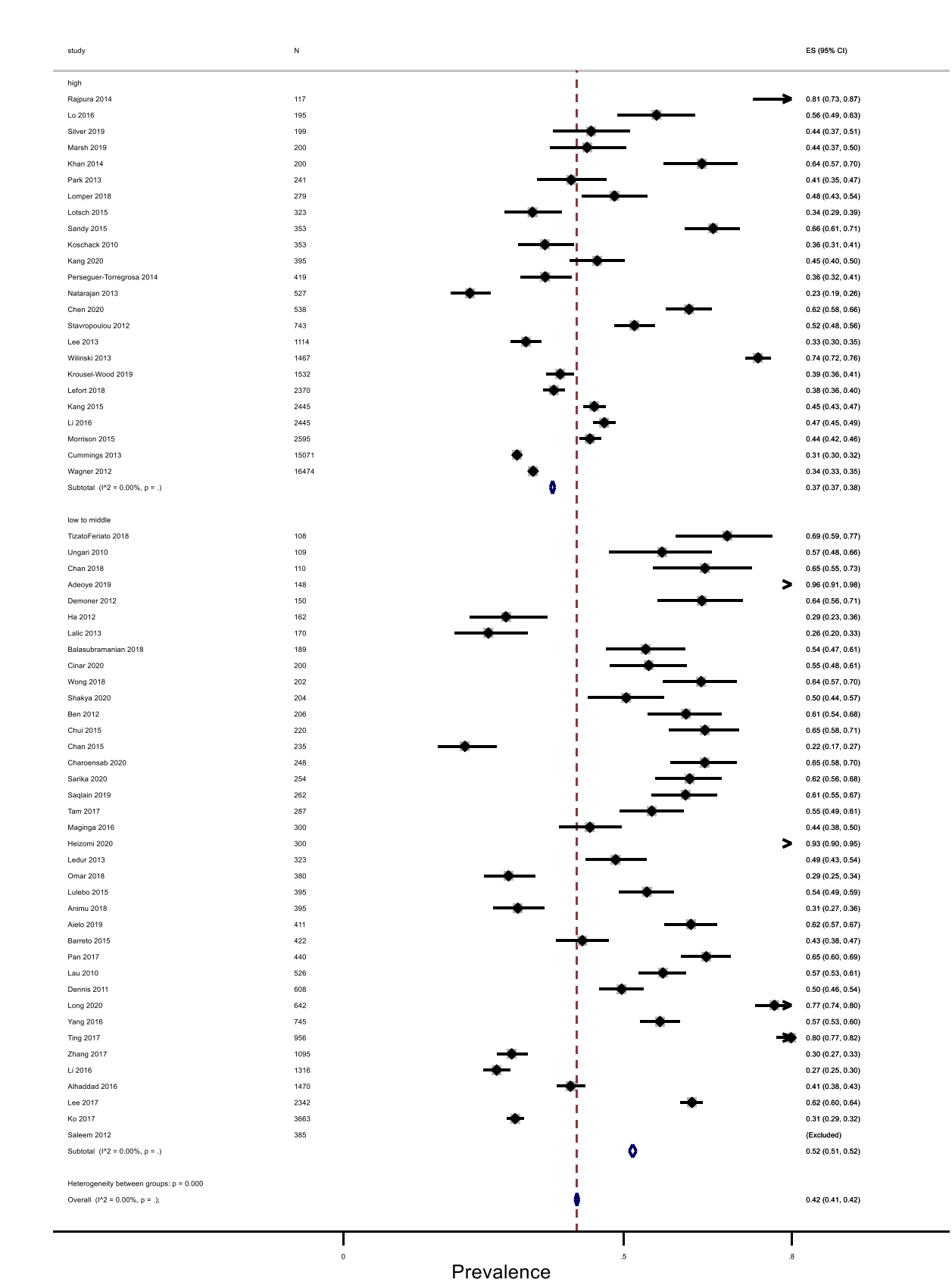
Figure S3d. prevalence using questionnaires and if MMAS-8 cut off used at ≤6 than <6

(i) West versus non-west



Meta-regression coefficient: -0.079, p = 0.094

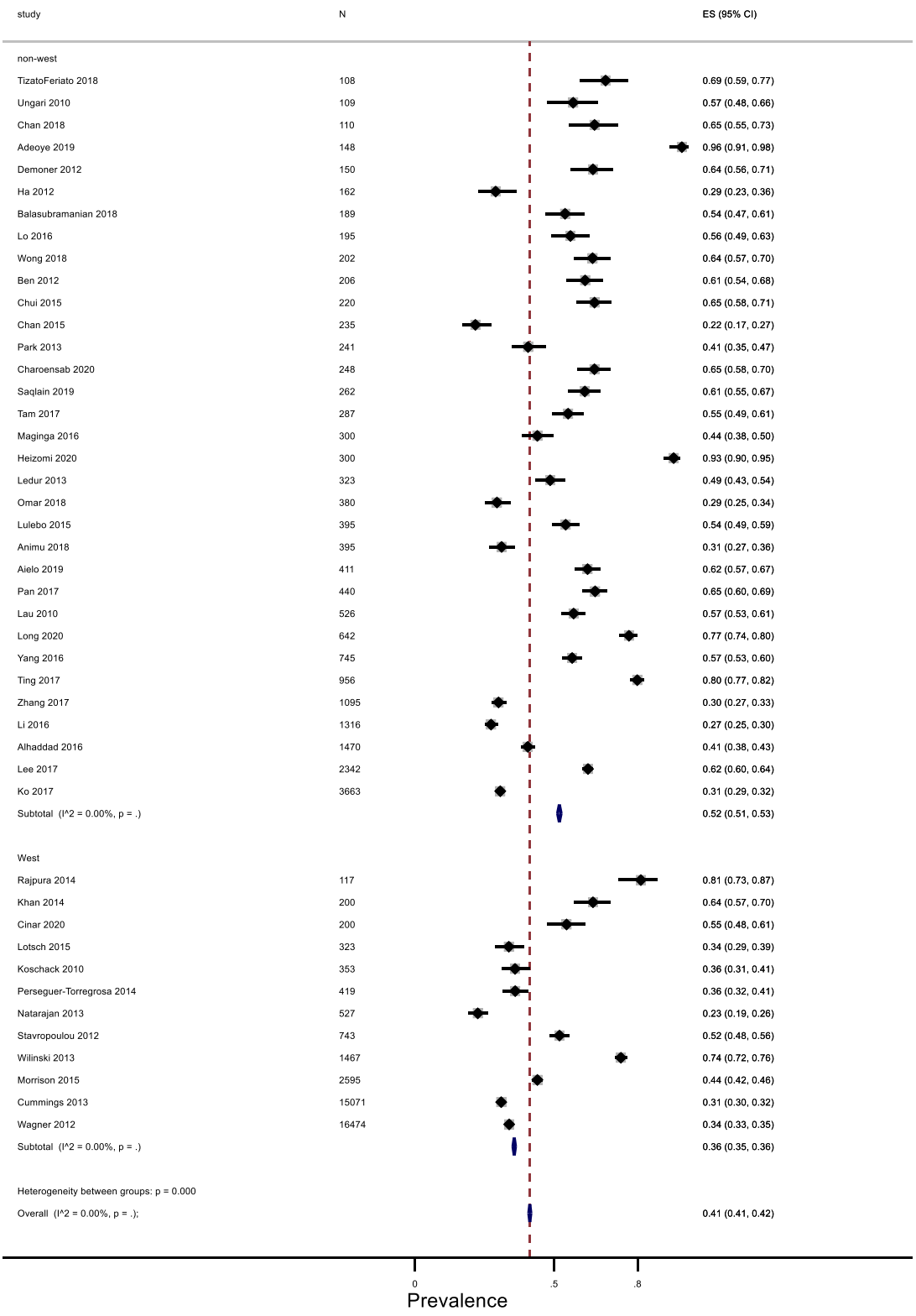
(ii) Income level



meta-regression coefficient: -0.074, p=0.097

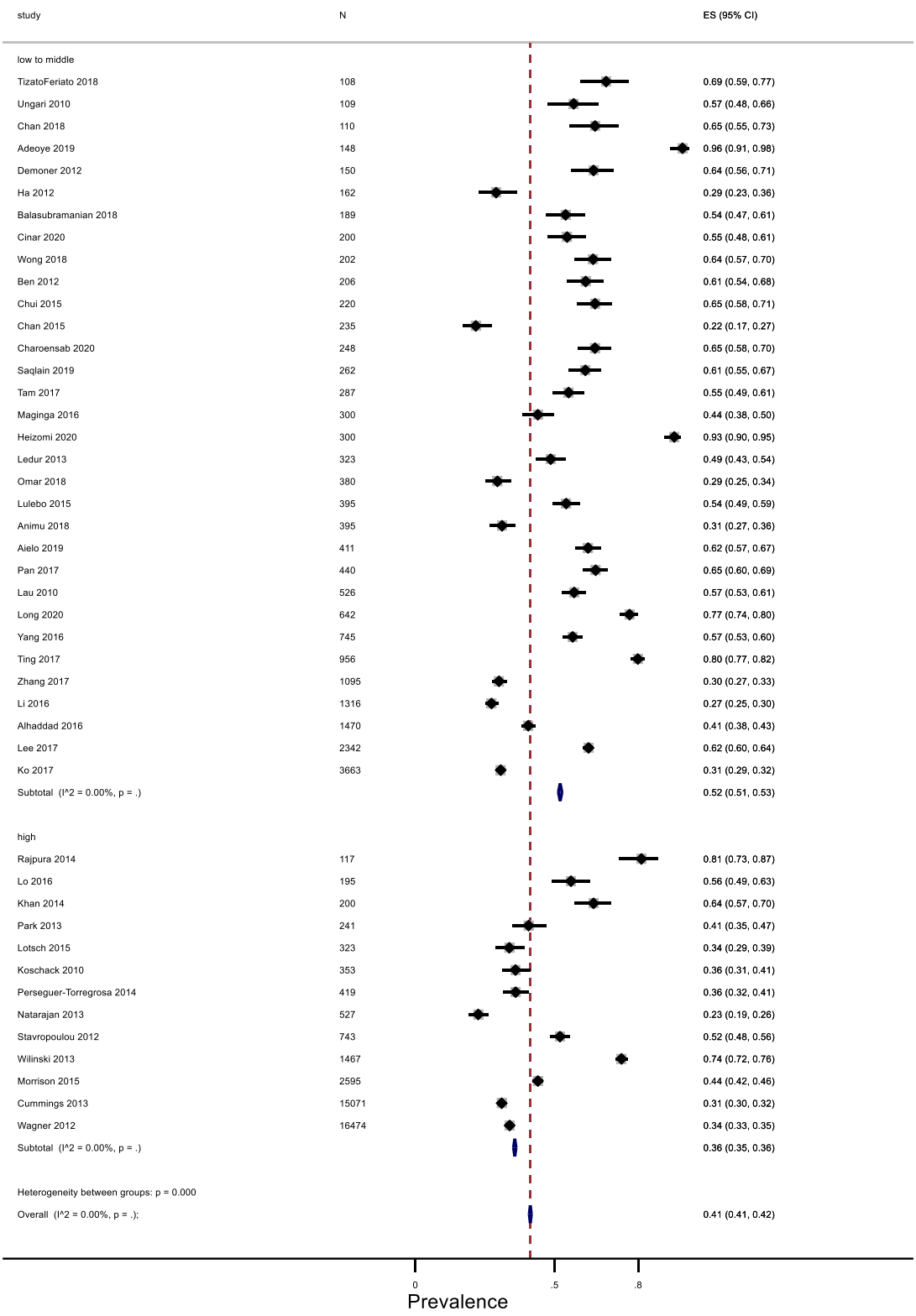
Figure S3e. prevalence using questionnaires and only MMAS-4 and cut-ff at >0

(i) West versus non-west



Meta-regression: -0.08, p = 0.202

(ii) Income level



Meta-regression co-efficient: -0.087, p=0.152

Table S18. prevalence using questionnaires and only MMAS-8 and cut-ff at <6

(i) west versus non-west

Study	prevalence	Lower 95%CI	Upper 95%CI
West			
ParejaMartinez 2015	0.15	0.09	0.23
Breaux-Shropshire 20	0.35	0.28	0.43
Gallagher 2015	0.23	0.17	0.30
Gavrilova 2019	0.44	0.37	0.52
Al-Ruthia 2017	0.21	0.16	0.27
HacihasanogluAsilar	0.59	0.52	0.65
Korb-Savoldelli 2012	0.18	0.13	0.23
Pluta 2020	0.33	0.27	0.40
Jankowska-Polanska 2	0.18	0.14	0.23
Janezic 2014	0.16	0.13	0.20
Cabral 2018	0.28	0.24	0.32
Cummings 2016	0.40	0.36	0.44
Jankowska-Polanska 2	0.30	0.26	0.33
Lor 2019	0.76	0.73	0.78
Fortuna 2018	0.38	0.35	0.40
Bramlage 2014	0.42	0.42	0.43
Sub-total			
Fixed pooled ES	0.41	0.40	0.42
non-west			
Akintunde 2015	0.24	0.17	0.32
Fernandez-Arias 2014	0.57	0.48	0.66
Saarti 2016	0.29	0.22	0.38
Otenyo 2018	0.42	0.35	0.51
Kebede 2020	0.47	0.39	0.55
Song 2016	0.57	0.49	0.65
Adidja 2018	0.67	0.60	0.73
Athiyah 2013	0.57	0.50	0.64
Khayyat 2017	0.54	0.47	0.61
Yassine 2016	0.22	0.17	0.28
Al-Noumani 2018	0.32	0.26	0.39
Akoko 2017	0.56	0.50	0.62
Oliveira-Filho 2012	0.47	0.41	0.54
Yue 2015	0.26	0.21	0.32
Sulistiyowatiningsih	0.60	0.54	0.66
Zhao 2015	0.26	0.21	0.32
Mamaghani 2020	0.18	0.14	0.23
Okwuonu 2014	0.69	0.63	0.74
Amin 2018	0.34	0.28	0.40
Efanov 2018	0.32	0.27	0.38
Fatani 2019	0.67	0.62	0.73
Behnood-Rod 2016	0.50	0.44	0.55
Asgedom 2018	0.38	0.33	0.44
Okello 2016	0.85	0.81	0.89

Olowe 2017	0.32	0.28	0.38
Sarkodie 2020	0.11	0.08	0.14
Kim 2014	0.33	0.28	0.38
Ekanem 2020	0.15	0.12	0.19
Tan 2020	0.58	0.53	0.63
Kretchy 2014	0.81	0.77	0.84
BouSerhal 2018	0.14	0.11	0.18
Mekonnen 2017	0.33	0.28	0.37
Zyoud 2013	0.37	0.32	0.42
Righi 2017	0.17	0.14	0.21
Shi 2019	0.64	0.59	0.68
Mekonen 2020	0.37	0.33	0.42
Wu 2020	0.28	0.24	0.32
Baran 2017	0.28	0.24	0.32
Li 2015	0.81	0.77	0.84
Farah 2016	0.20	0.17	0.23
Hou 2016	0.66	0.62	0.70
Mahmood 2020	0.38	0.34	0.41
Shen 2020	0.61	0.57	0.64
Sheilini 2018	0.16	0.14	0.19
Berhe 2017	0.42	0.39	0.45
deOliveira-Filho 201	0.47	0.44	0.50
Meena 2018	0.32	0.29	0.35
G/Tsadik 2020	0.32	0.29	0.35
Espeche 2020	0.14	0.12	0.16
Jafar 2018	0.41	0.39	0.44
Hassanein 2020	0.33	0.31	0.35
MacquartdeTerline 20	0.31	0.29	0.33
Sub-total			
Fixed pooled ES	0.36	0.36	0.37
Overall			
Fixed pooled ES	0.38	0.38	0.39

Meta-regression co-efficient: -0.076, p=0.156

(ii) income level

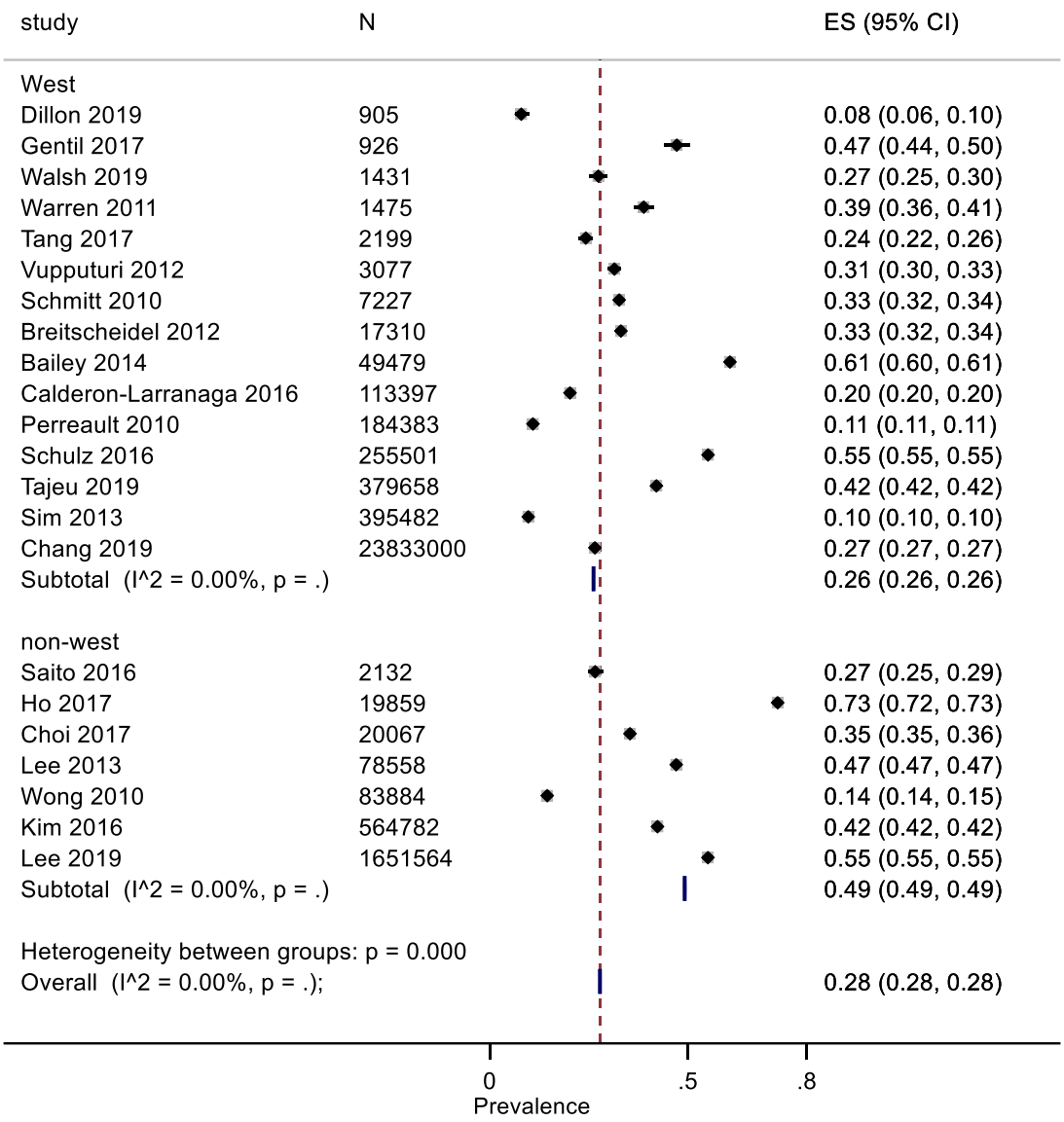
Study	prevalence	Lower 95%CI	Upper 95%CI
High			
ParejaMartinez 2015	0.15	0.09	0.23
Breaux-Shropshire 20	0.35	0.28	0.43
Gallagher 2015	0.23	0.17	0.30
Gavrilova 2019	0.44	0.37	0.52
Al-Ruthia 2017	0.21	0.16	0.27
Korb-Savoldelli 2012	0.18	0.13	0.23
Pluta 2020	0.33	0.27	0.40
Khayyat 2017	0.54	0.47	0.61
Al-Noumani 2018	0.32	0.26	0.39
Fatani 2019	0.67	0.62	0.73
Jankowska-Polanska 2	0.18	0.14	0.23
Kim 2014	0.33	0.28	0.38
Janezic 2014	0.16	0.13	0.20
Cabral 2018	0.28	0.24	0.32
Cummings 2016	0.40	0.36	0.44
Jankowska-Polanska 2	0.30	0.26	0.33
Lor 2019	0.76	0.73	0.78
Fortuna 2018	0.38	0.35	0.40
Bramlage 2014	0.42	0.42	0.43
Sub-total			
Fixed pooled ES	0.41	0.40	0.42
low to middle			
Akintunde 2015	0.24	0.17	0.32
Fernandez-Arias 2014	0.57	0.48	0.66
Saarti 2016	0.29	0.22	0.38
Otenyo 2018	0.42	0.35	0.51
Kebede 2020	0.47	0.39	0.55
Song 2016	0.57	0.49	0.65
Adidja 2018	0.67	0.60	0.73
HacihasanogluAsilar	0.59	0.52	0.65
Athiyah 2013	0.57	0.50	0.64
Yassine 2016	0.22	0.17	0.28
Akoko 2017	0.56	0.50	0.62
Oliveira-Filho 2012	0.47	0.41	0.54
Yue 2015	0.26	0.21	0.32
Sulistiyowatiningsih	0.60	0.54	0.66
Zhao 2015	0.26	0.21	0.32
Mamaghani 2020	0.18	0.14	0.23
Okwuonu 2014	0.69	0.63	0.74
Amin 2018	0.34	0.28	0.40
Efanov 2018	0.32	0.27	0.38
Behnood-Rod 2016	0.50	0.44	0.55
Asgedom 2018	0.38	0.33	0.44
Okello 2016	0.85	0.81	0.89
Olowe 2017	0.32	0.28	0.38

Sarkodie 2020	0.11	0.08	0.14
Ekanem 2020	0.15	0.12	0.19
Tan 2020	0.58	0.53	0.63
Kretchy 2014	0.81	0.77	0.84
BouSerhal 2018	0.14	0.11	0.18
Mekonnen 2017	0.33	0.28	0.37
Zyoud 2013	0.37	0.32	0.42
Righi 2017	0.17	0.14	0.21
Shi 2019	0.64	0.59	0.68
Mekonen 2020	0.37	0.33	0.42
Wu 2020	0.28	0.24	0.32
Baran 2017	0.28	0.24	0.32
Li 2015	0.81	0.77	0.84
Farah 2016	0.20	0.17	0.23
Hou 2016	0.66	0.62	0.70
Mahmood 2020	0.38	0.34	0.41
Shen 2020	0.61	0.57	0.64
Sheilini 2018	0.16	0.14	0.19
Berhe 2017	0.42	0.39	0.45
deOliveira-Filho 201	0.47	0.44	0.50
Meena 2018	0.32	0.29	0.35
G/Tsadik 2020	0.32	0.29	0.35
Espeche 2020	0.14	0.12	0.16
Jafar 2018	0.41	0.39	0.44
Hassanein 2020	0.33	0.31	0.35
MacquartdeTerline 20	0.31	0.29	0.33
Sub-total			
Fixed pooled ES	0.36	0.36	0.37
Overall			
Fixed pooled ES	0.38	0.38	0.39

Meta-regression coefficient: -0.06, p=0.230

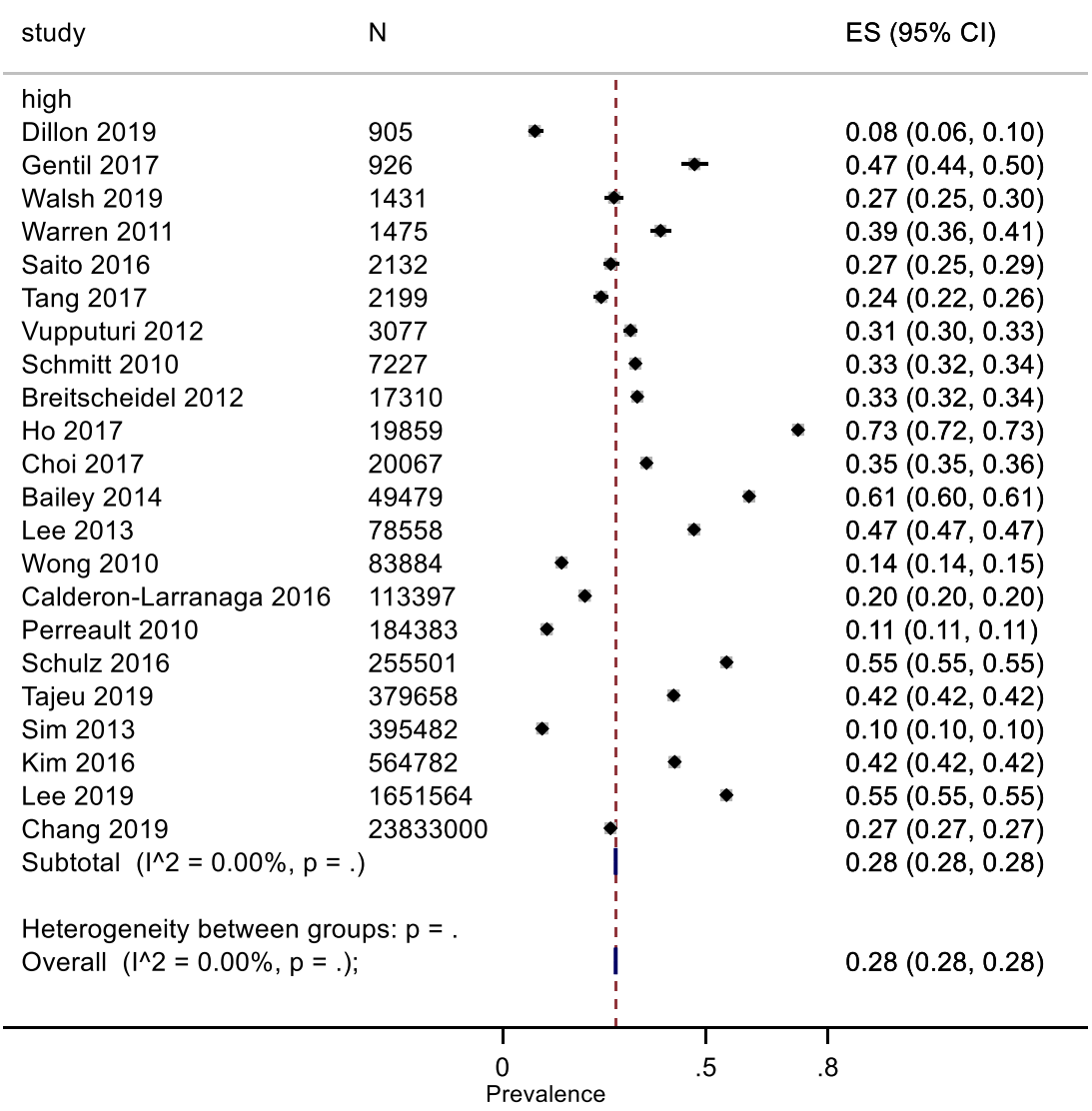
Figure S3f prevalence using prescription refill and only included larger studies (n>500)

(i) West versus non-west



Meta-regression coefficient: -0.107, p= 0.178

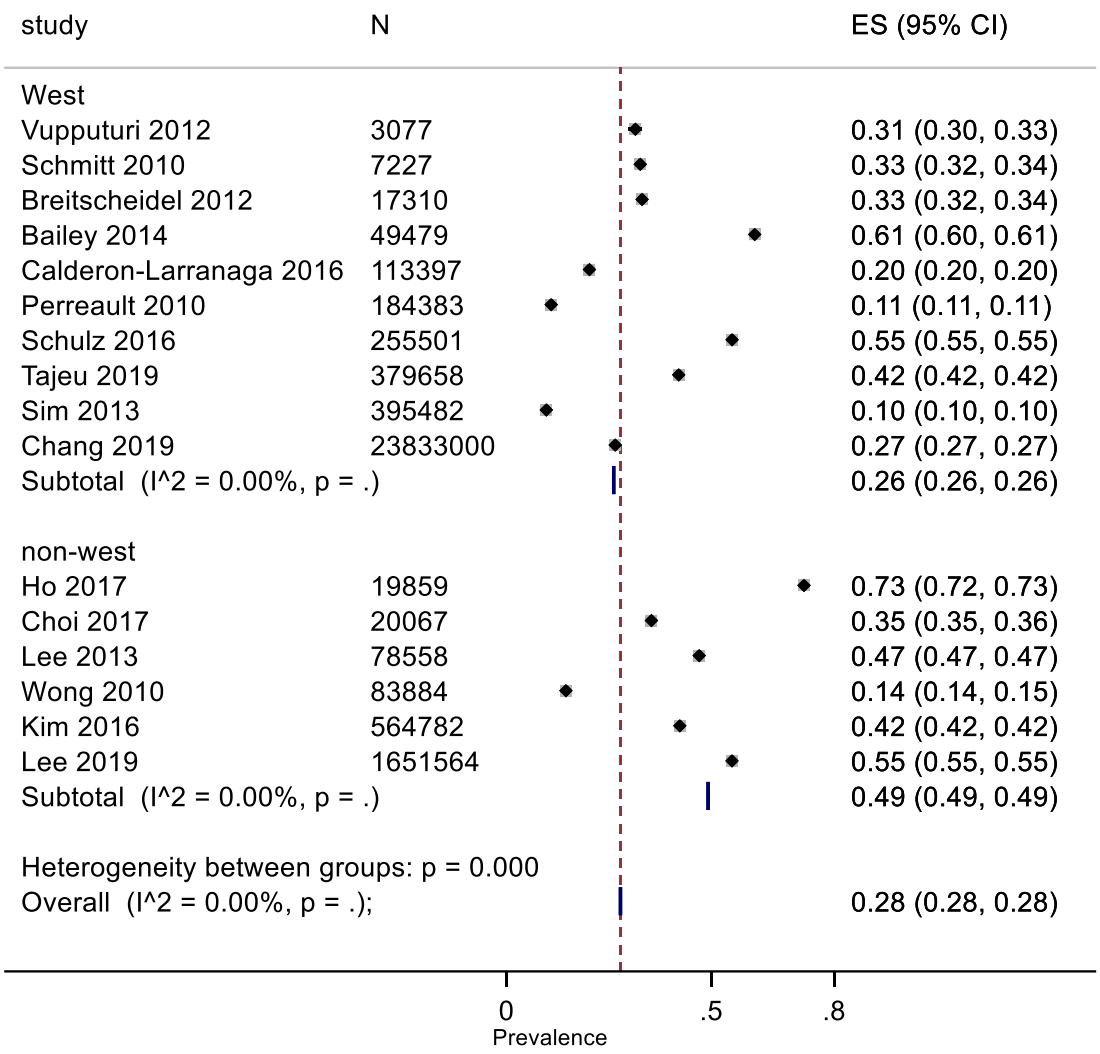
(ii) Income level



Meta-regression NA

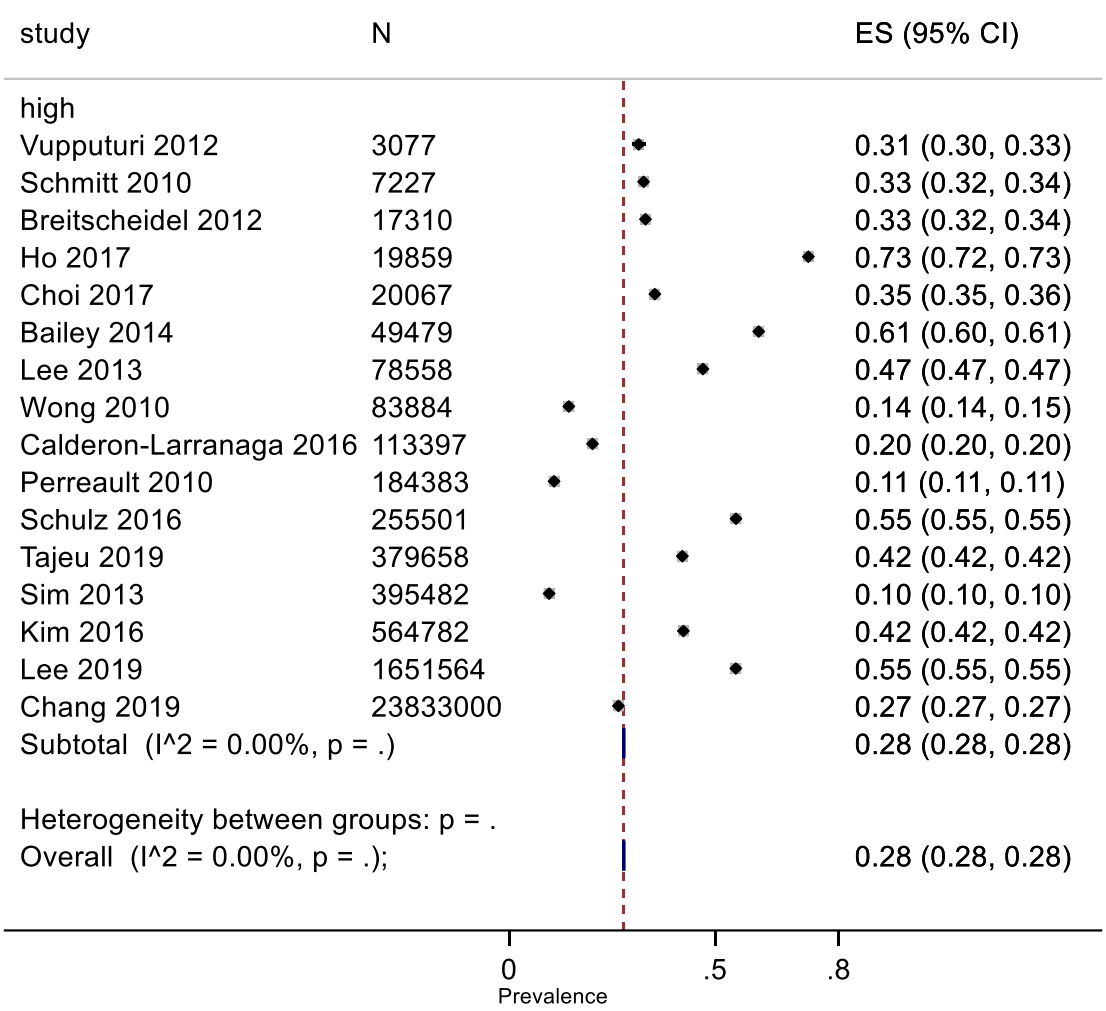
Figure S3g. Prevalence using prescription refill and only included larger studies (n>3000)

(i) West vs non-west



Meta-regression coefficient: -0.122, p= 0.205

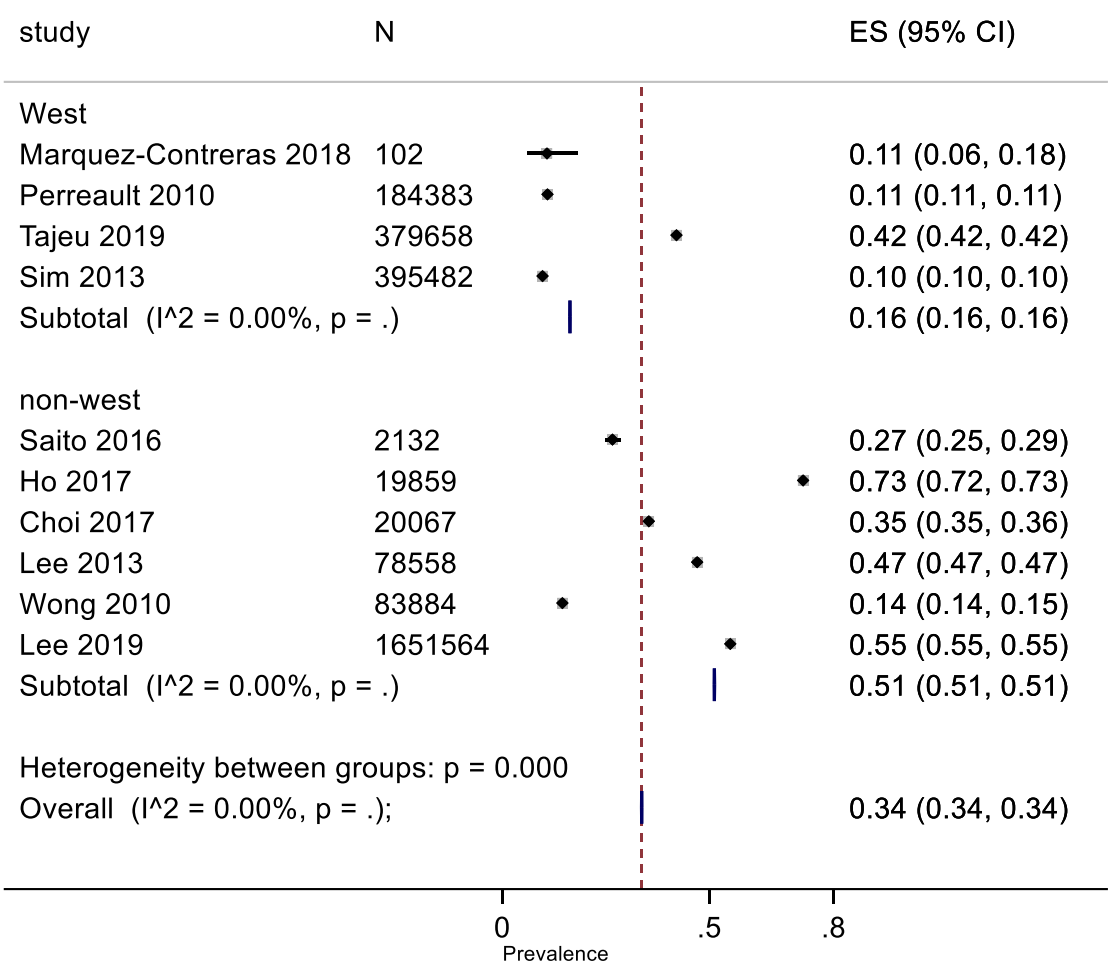
(ii) Income level



Meta-regression NA

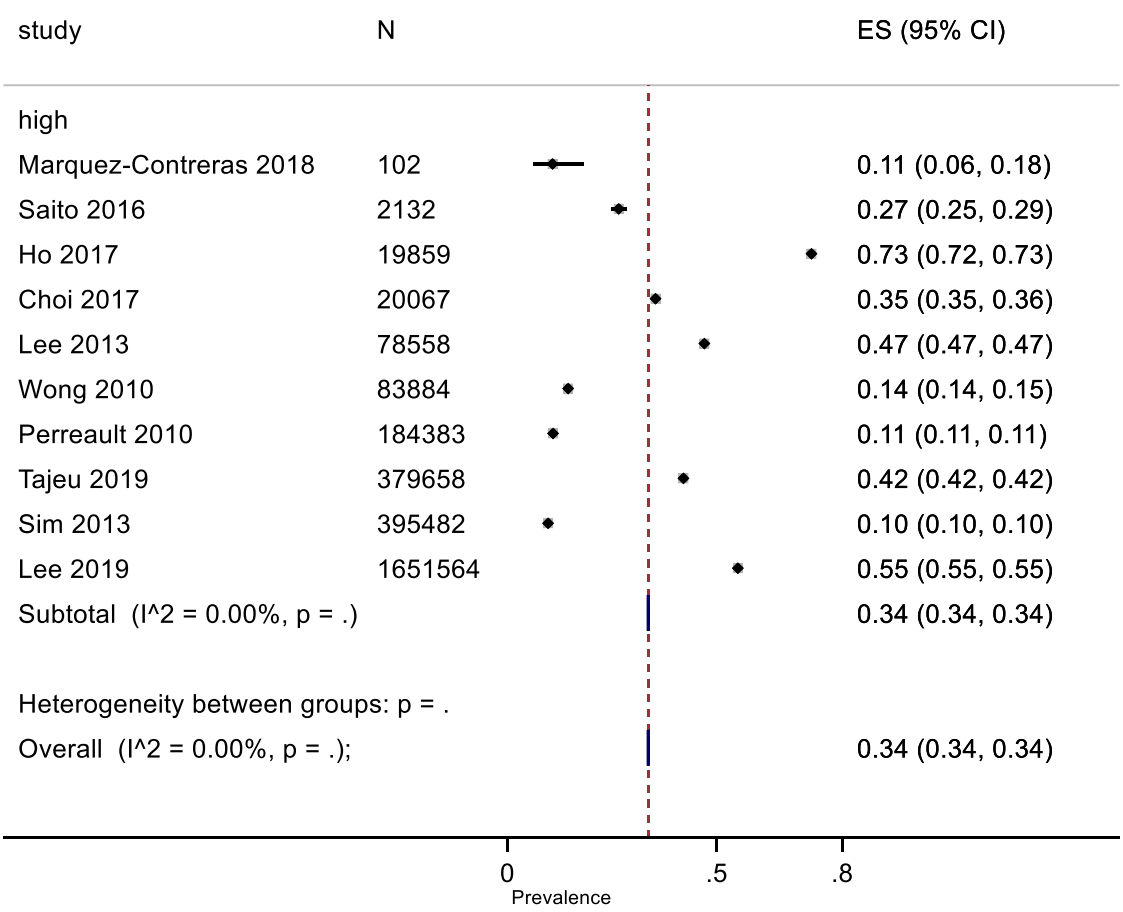
Figure S3h. prevalence using prescription refill and only low-risk-of-bias studies

(i) West versus non-west



Regression co-efficient: -0.234, p=0.094

(ii) Income level



Meta-regression N/A

Figure S3i. prevalence using prescription refill and if using end-point rather than baseline data

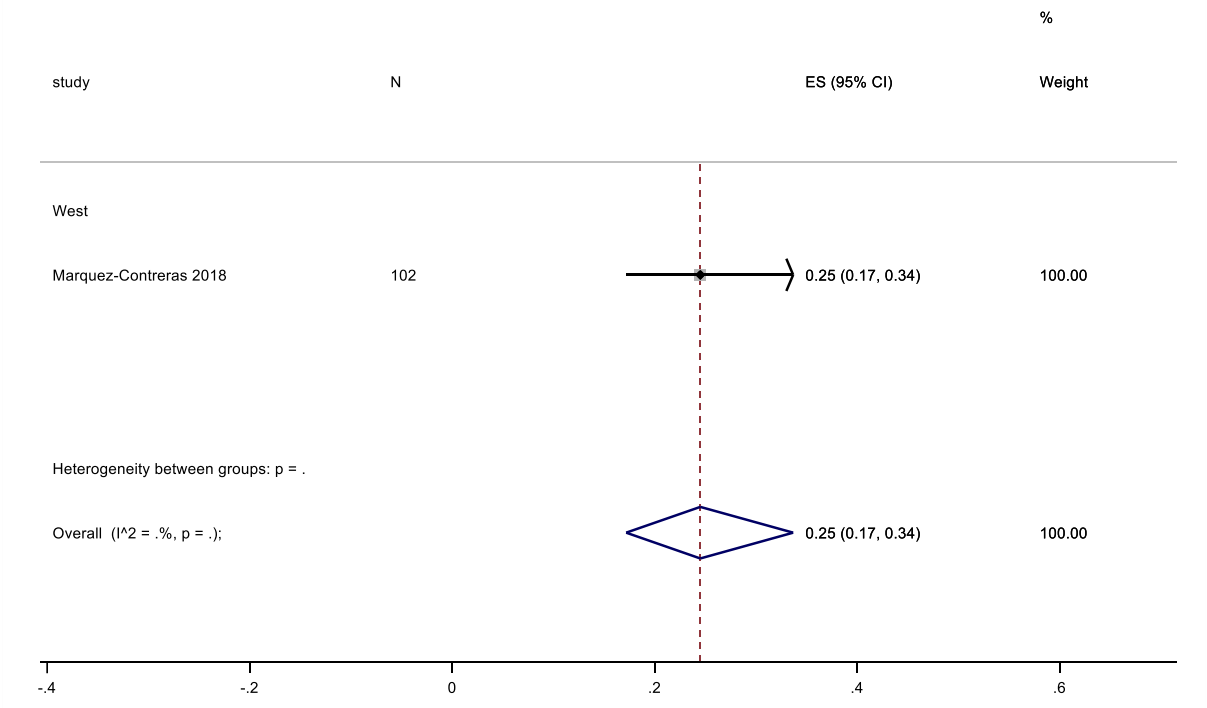


Figure S3j. systolic blood pressure difference and used only larger studies (n>500)

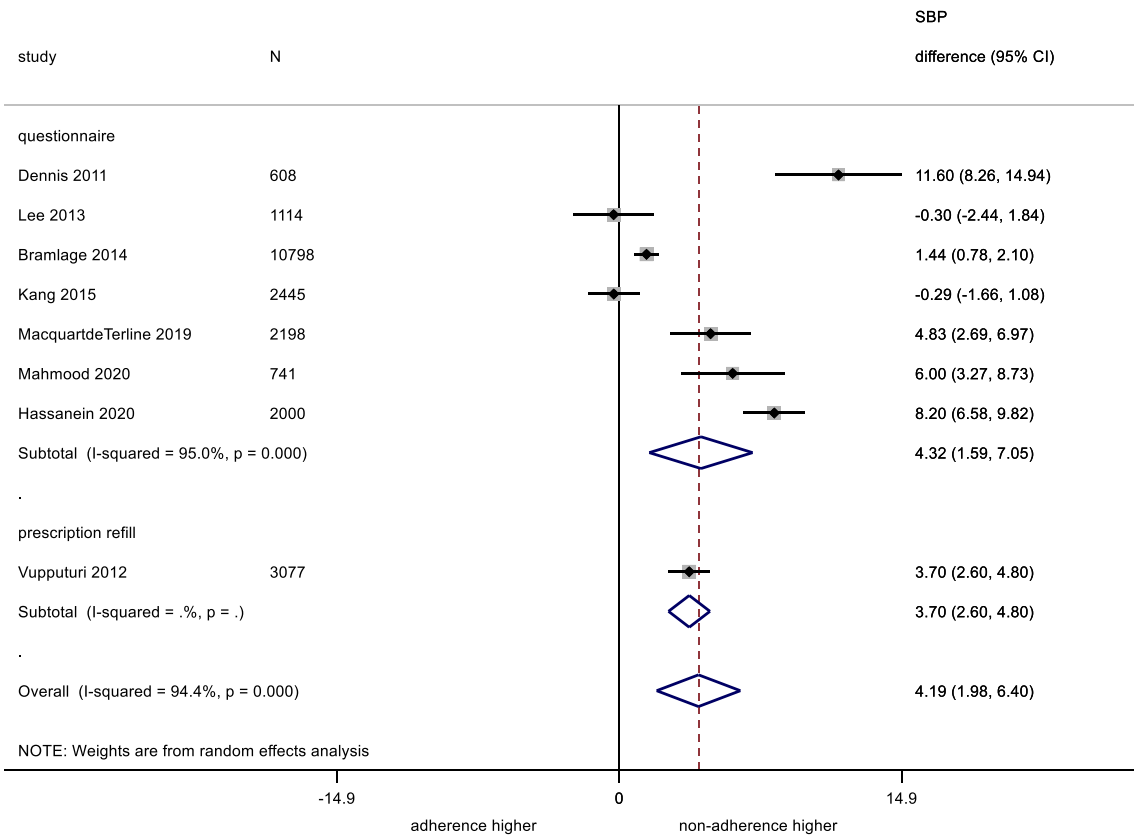


Figure S3k. systolic blood pressure difference and used only only low-risk-of-bias studies

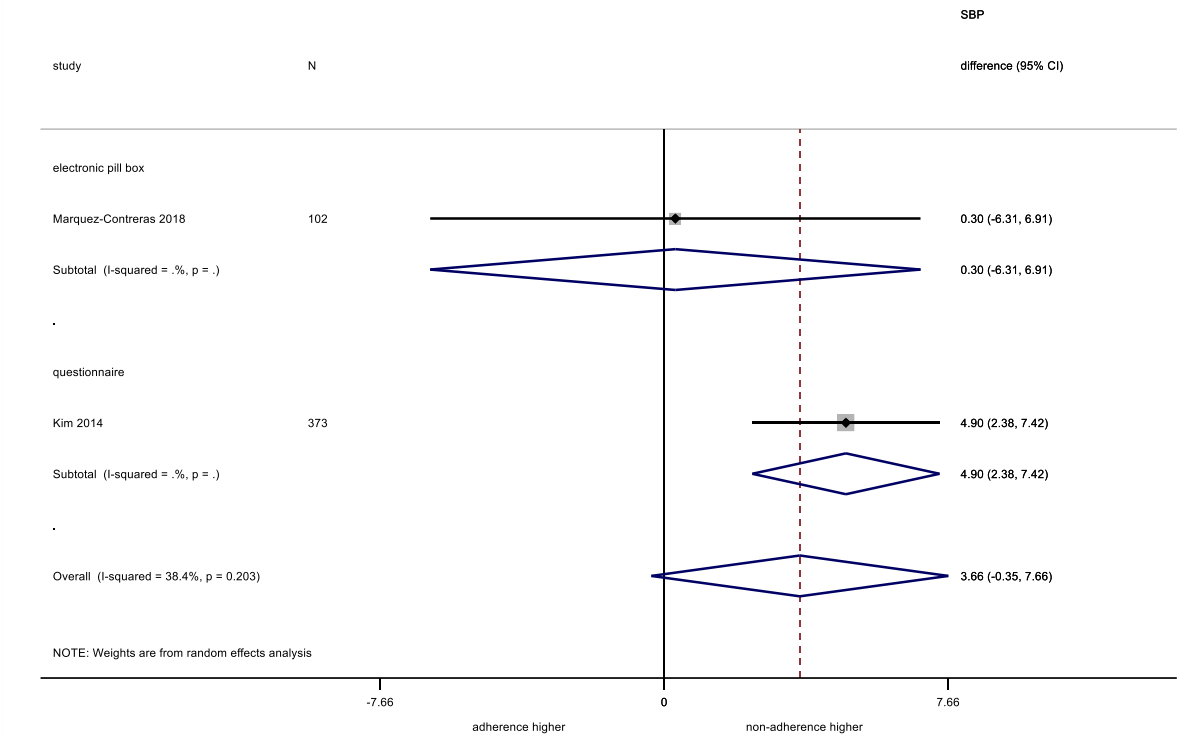


Figure S3l. diastolic blood pressure difference and used only larger studies (n>500)

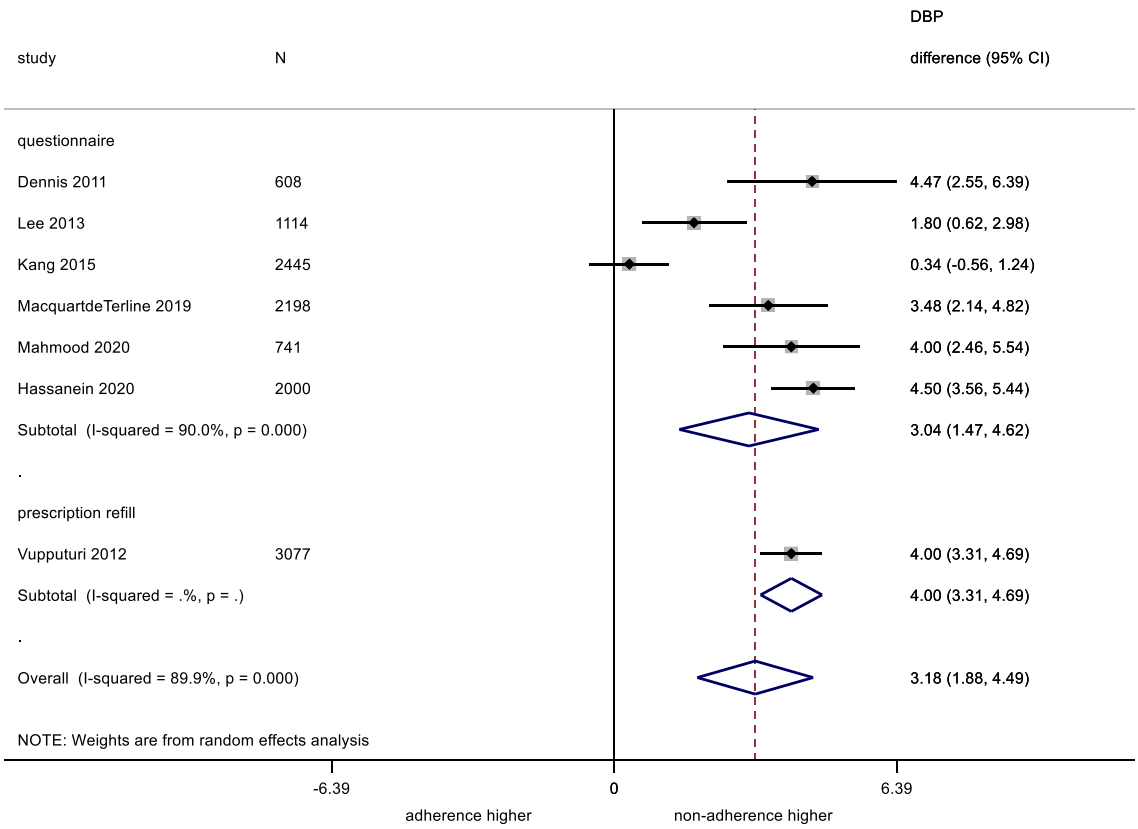


Figure S3m. diastolic blood pressure difference and used only only low-risk-of-bias studies

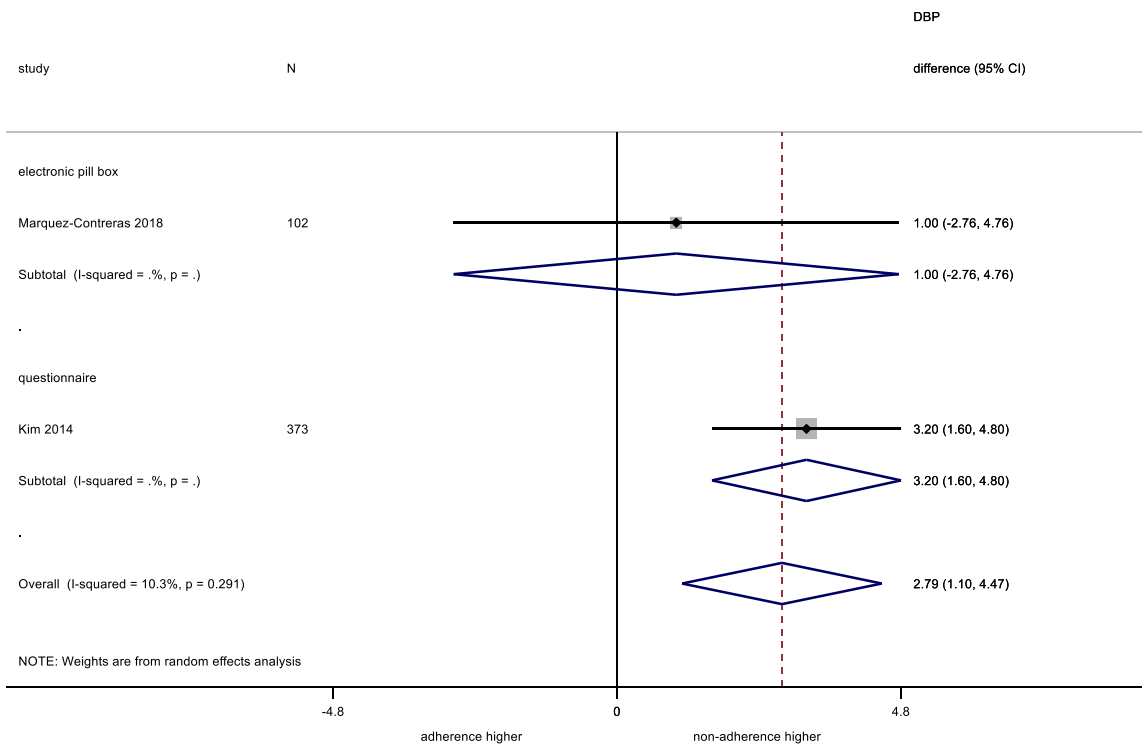


Figure S3n. odd ratio of suboptimal blood pressure and used only larger studies (n>500)

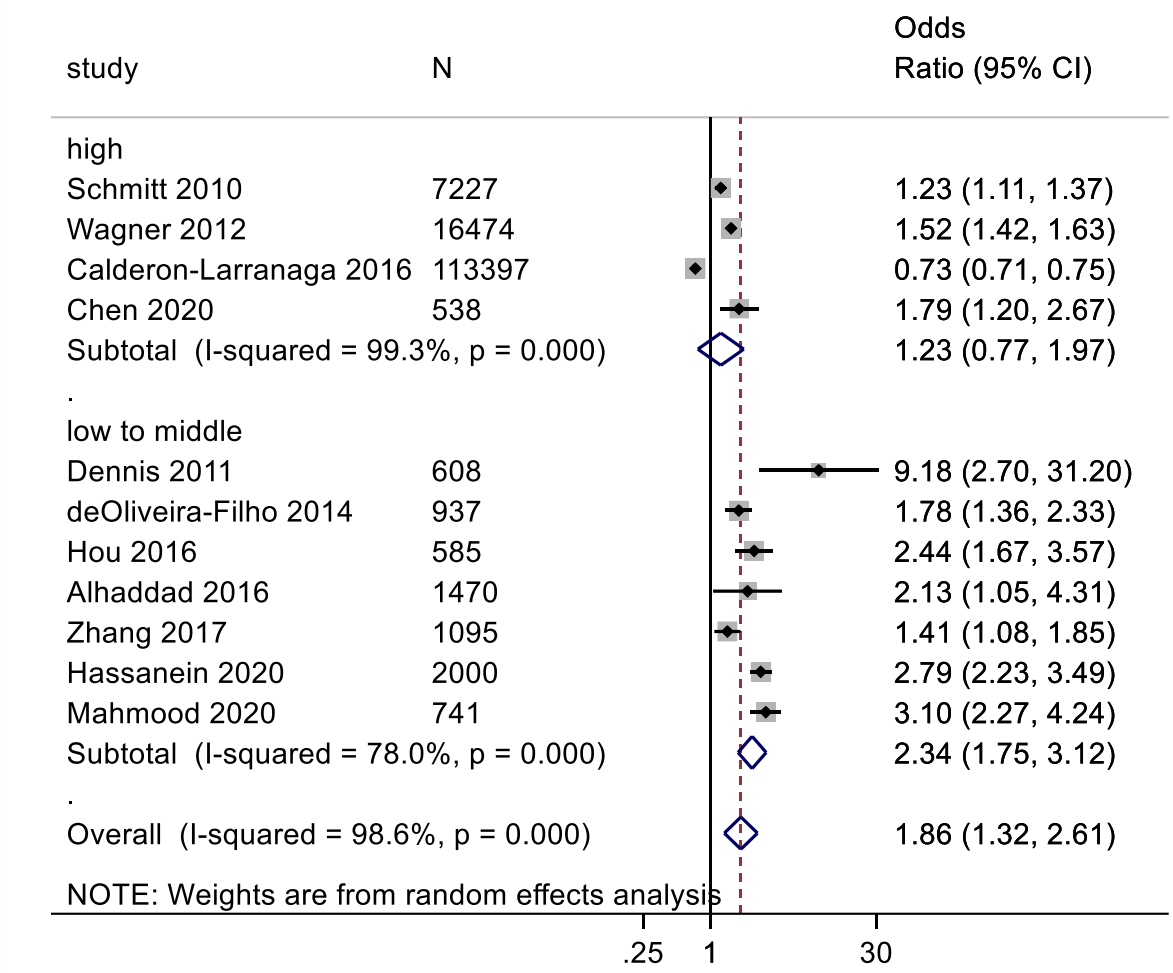


Figure S3o. Odd ratio of suboptimal blood pressure and used only low-risk-of-bias studies

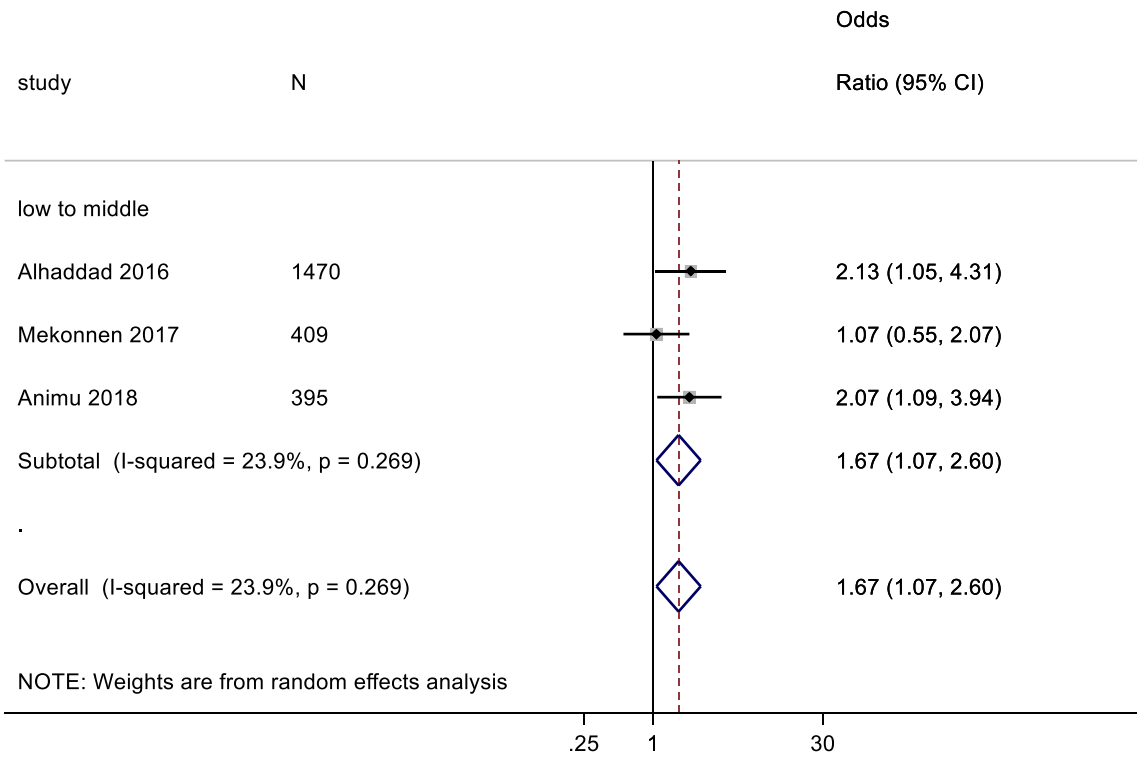


Figure S3p. health consequences of medication non-adherence using only cohort studies

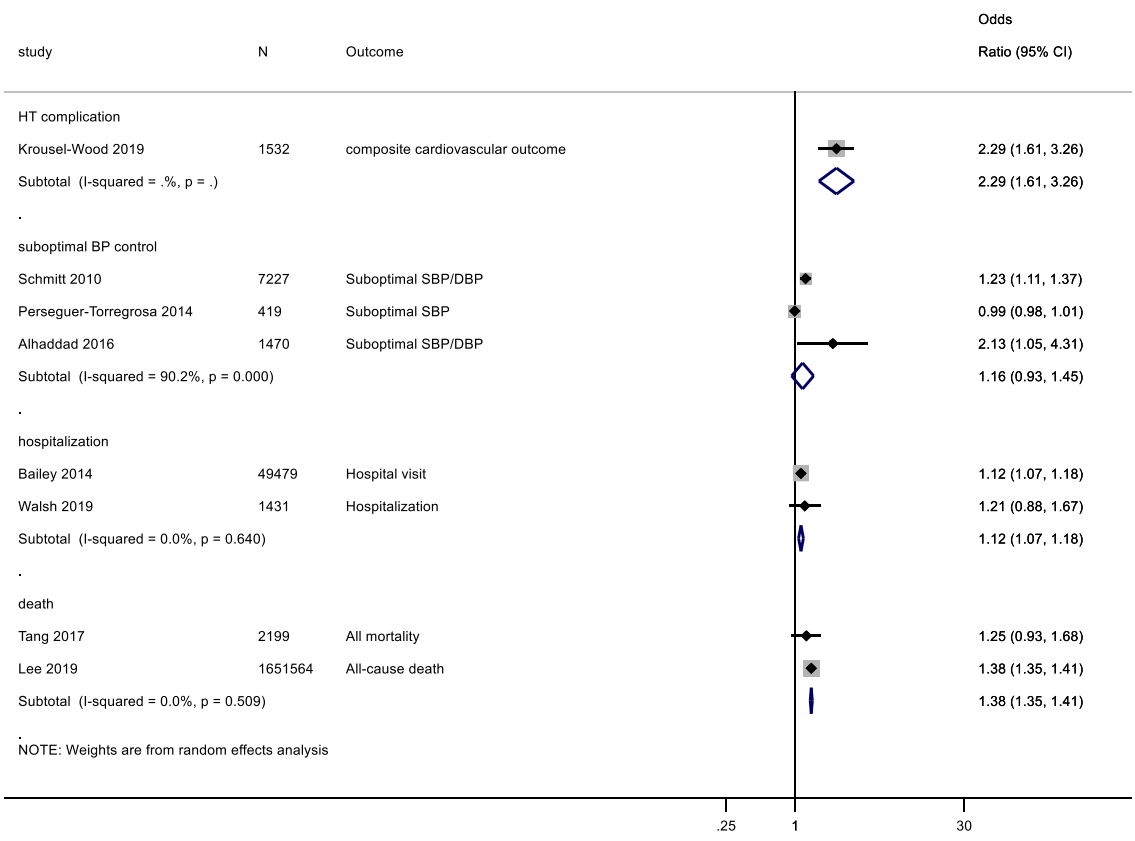
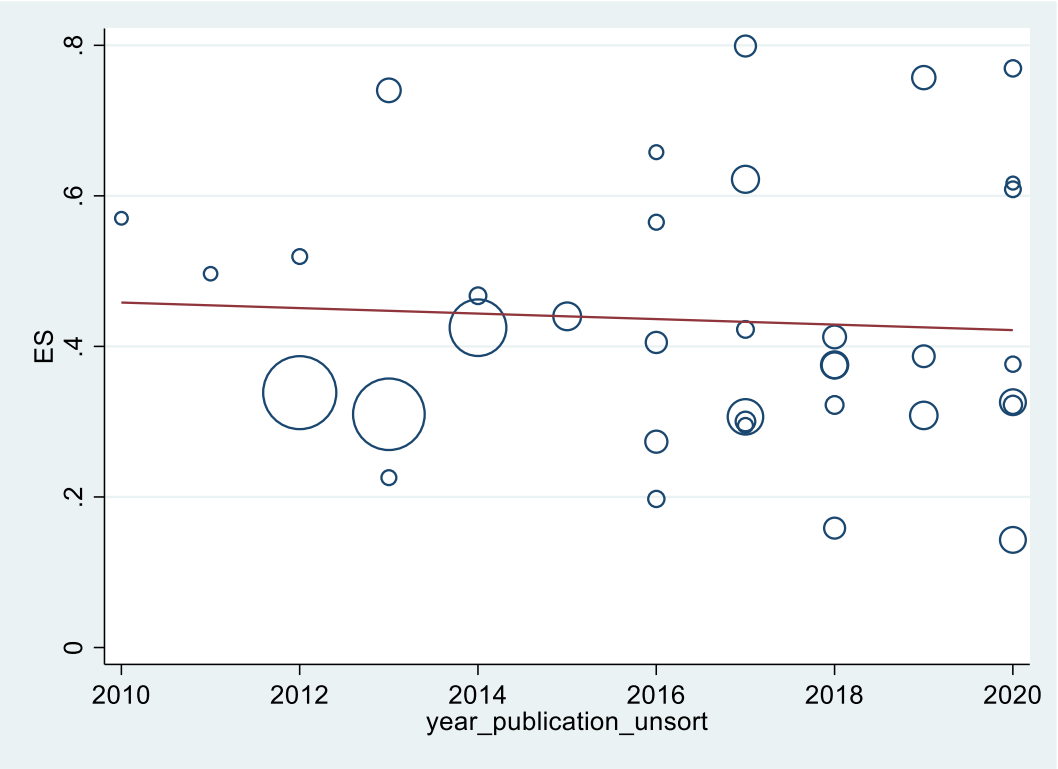
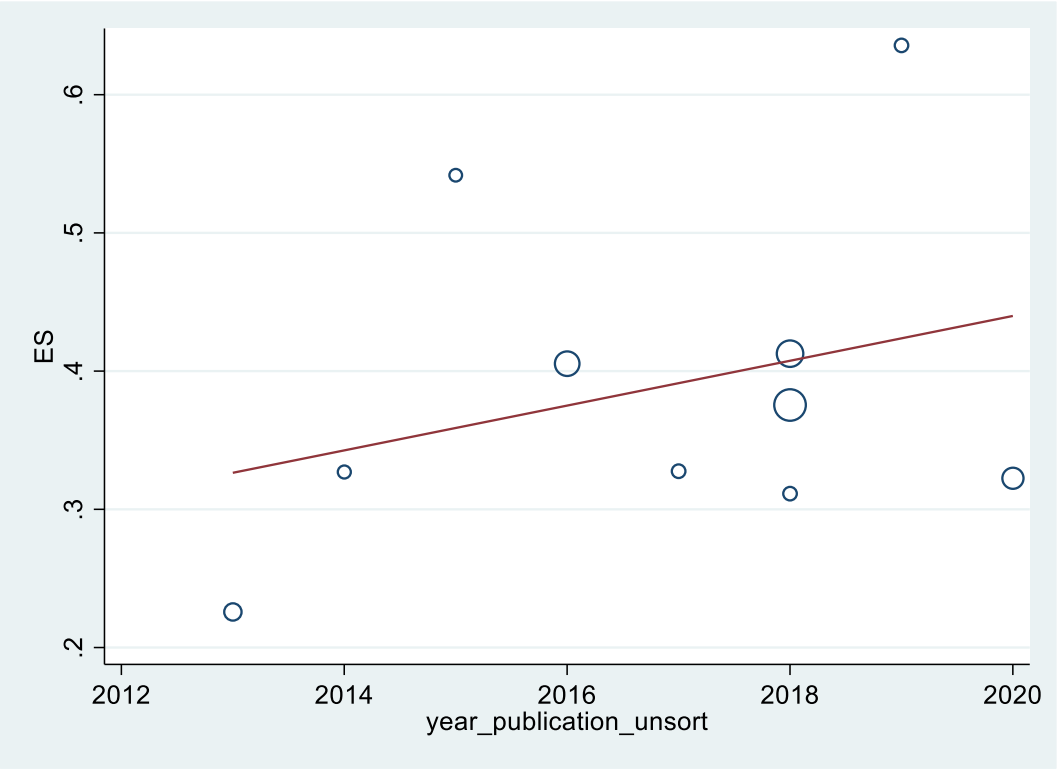


Figure S3q. trend sensitivity analysis using publication year and used only larger studies (n>500, questionnaire)



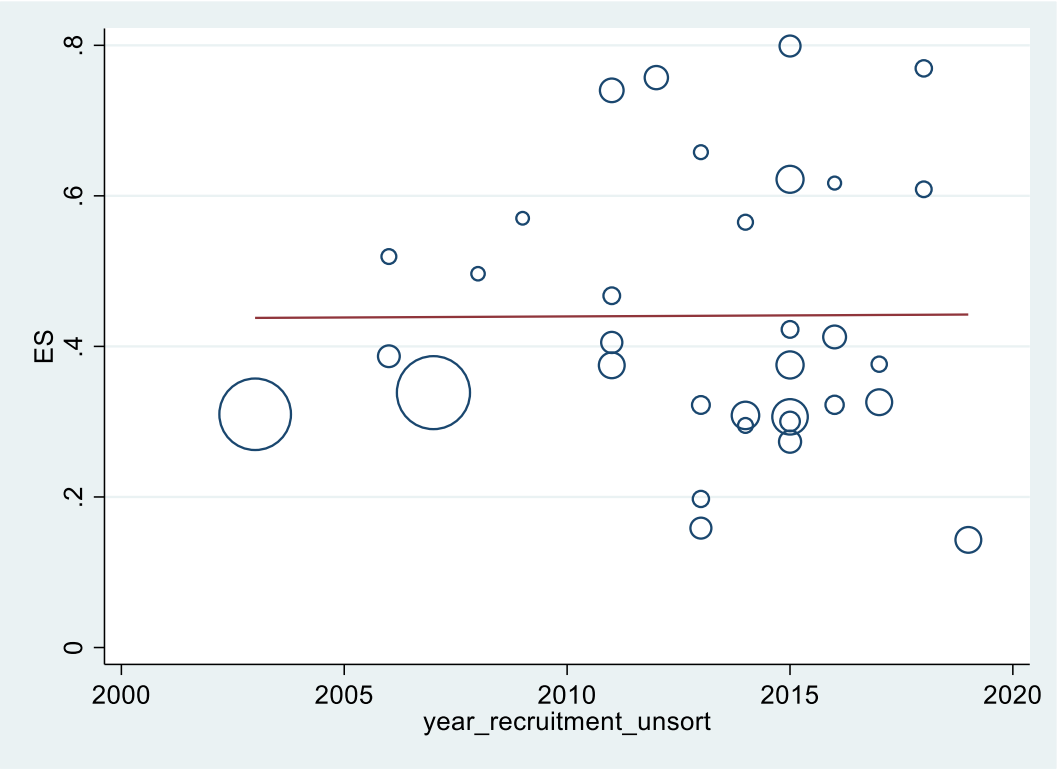
Meta-regression coefficient: -0.003, p=0.731

Figure S3r. trend sensitivity analysis using publication year and used only low-risk-of-bias studies (questionnaire)



Meta-regression coefficient: 0.016, p=0.391

Figure S3s. trend sensitivity analysis using year of first recruitment and used only larger studies (n>500, questionnaire)

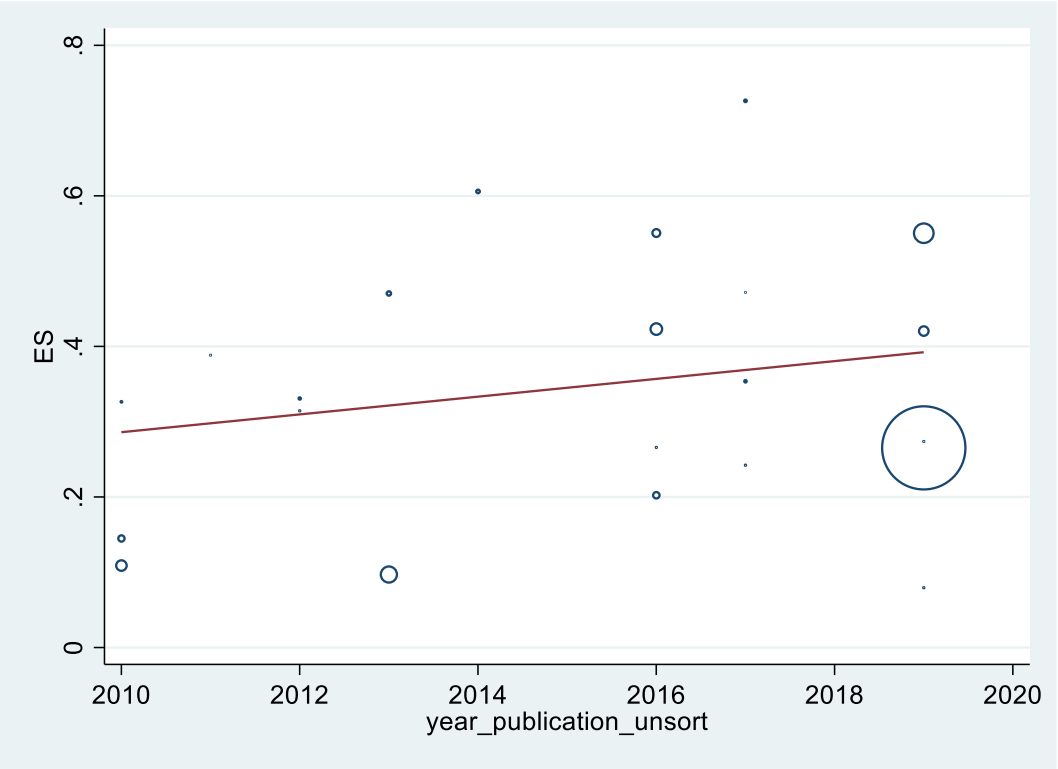


Meta-regression co-efficient: 0, p=0.974

Figure S3t. trend sensitivity analysis using year of first recruitment and used only low-risk-of-bias studies (questionnaire)

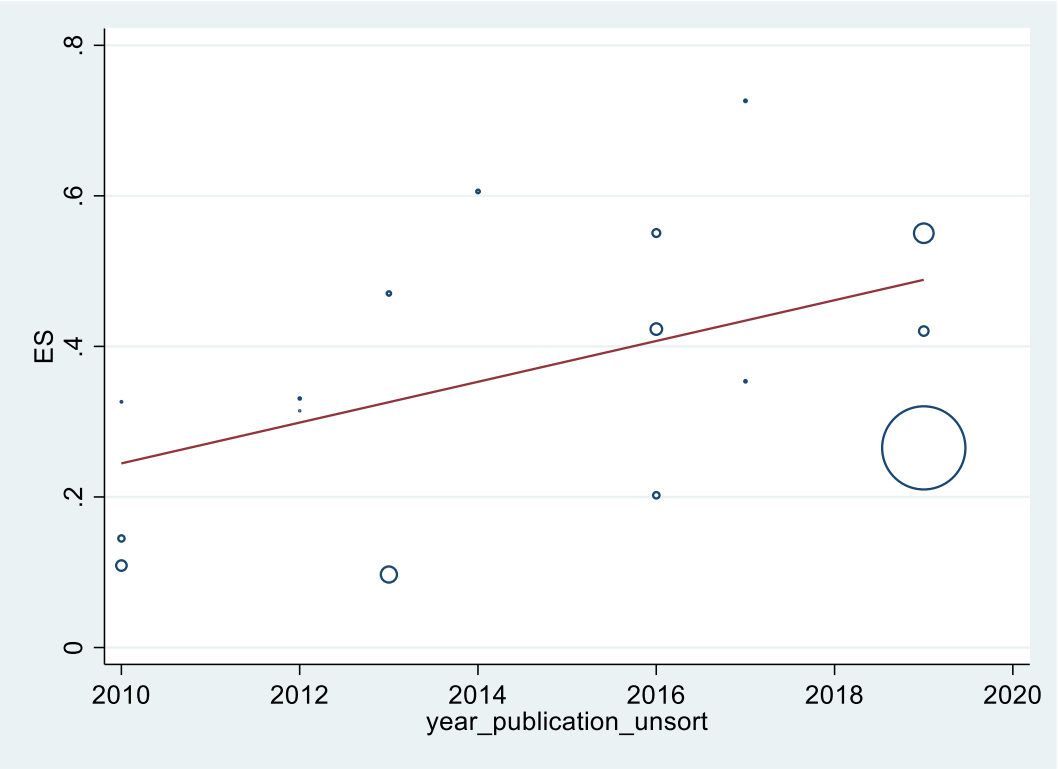
Meta-regression co-efficient: -0.006, p=0.636

Figure S3u. trend sensitivity analysis using publication year and used only larger studies (n>500, prescription refill)



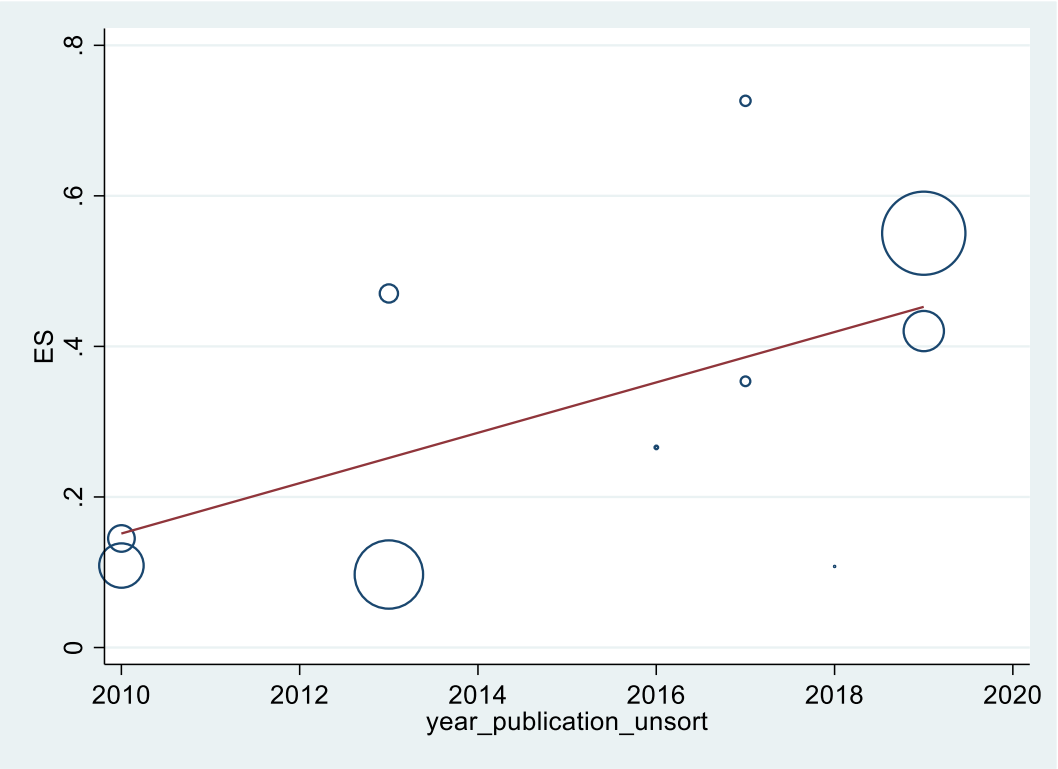
Meta-regression coefficient: 0.012, p=0.323

Figure S3v. trend sensitivity analysis using publication year and used only larger studies (n>3000, prescription refill)



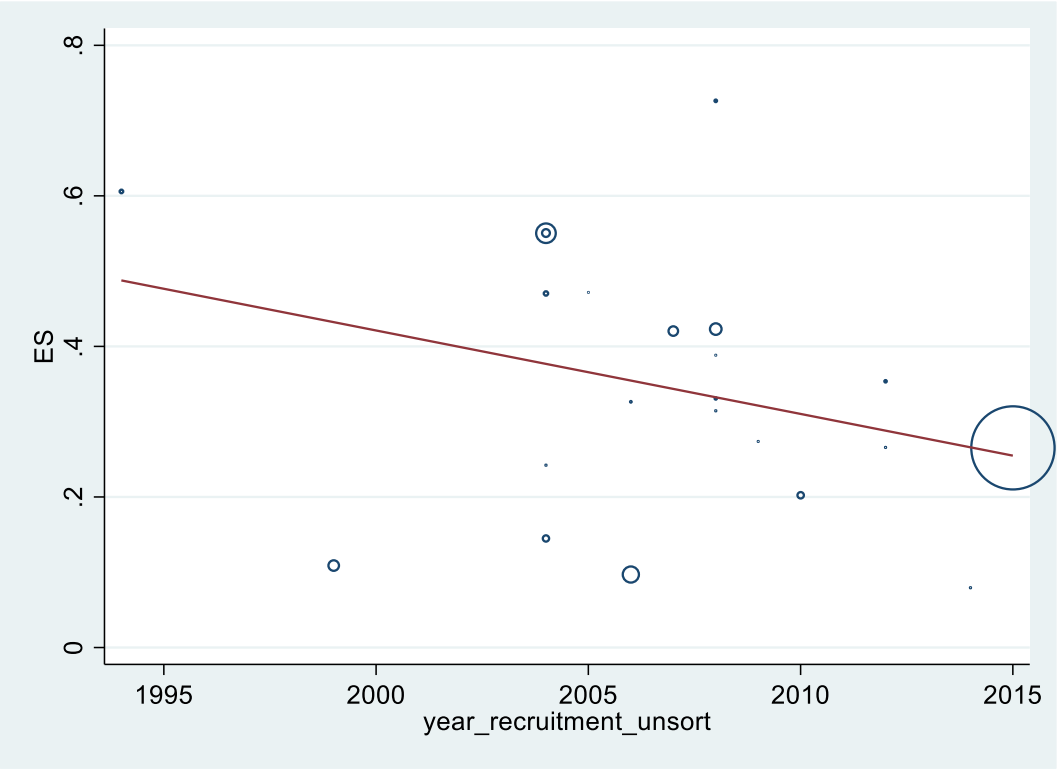
Meta-regression co-efficient: 0.27, p=0.06

Figure S3w. trend sensitivity analysis using publication year and used only low-risk-of-bias studies (prescription refill)



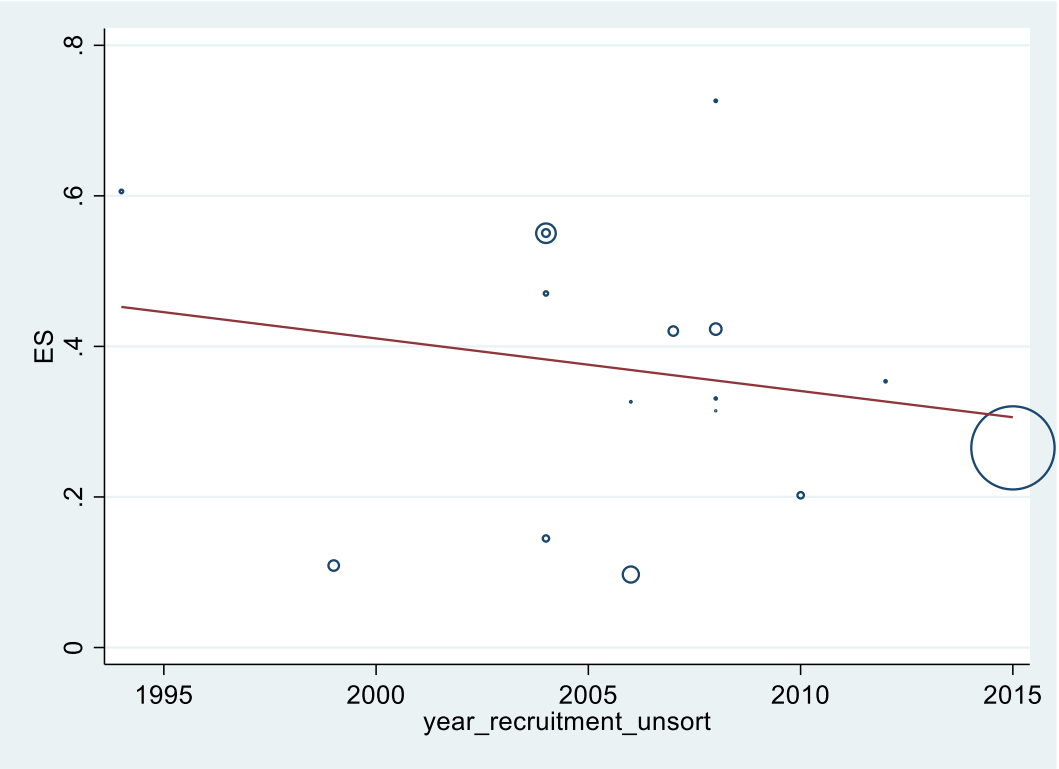
Meta-regression co-efficient: 0.033, p =0.113

Figure S3x. trend sensitivity analysis using year of first recruitment and used only larger studies (n>500, prescription refill)



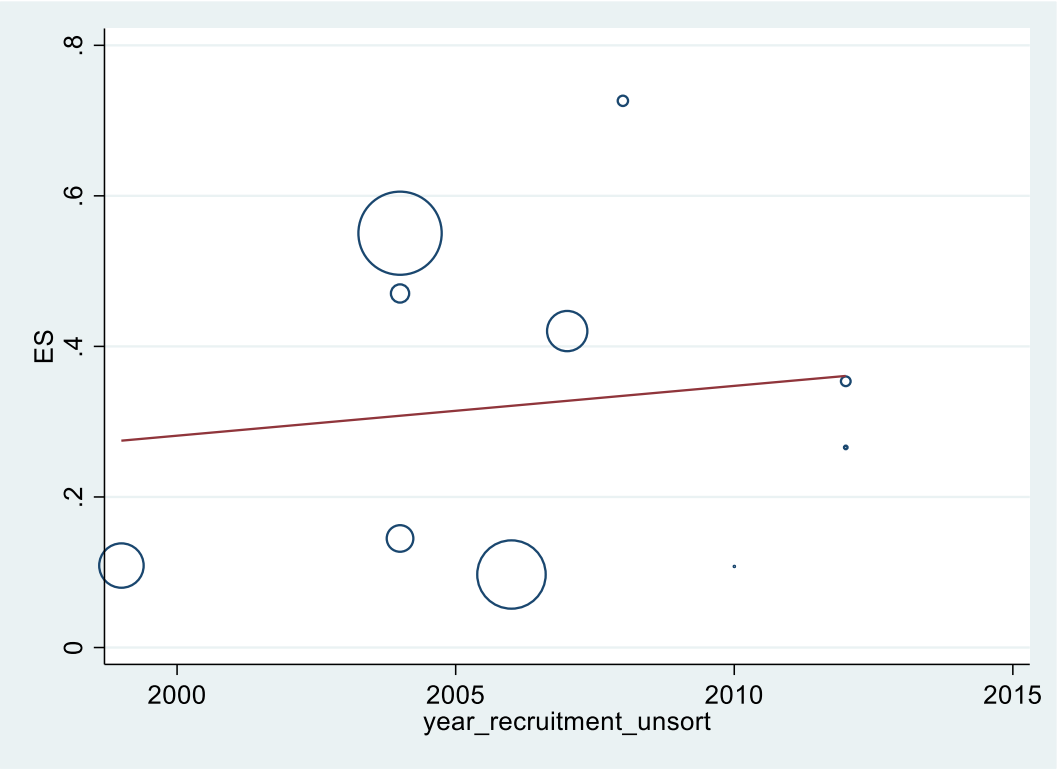
Meta-regression co-efficient: -0.011, p=0.171

Figure S3y. trend sensitivity analysis using year of first recruitment and used only larger studies (n>3000, prescription refill)



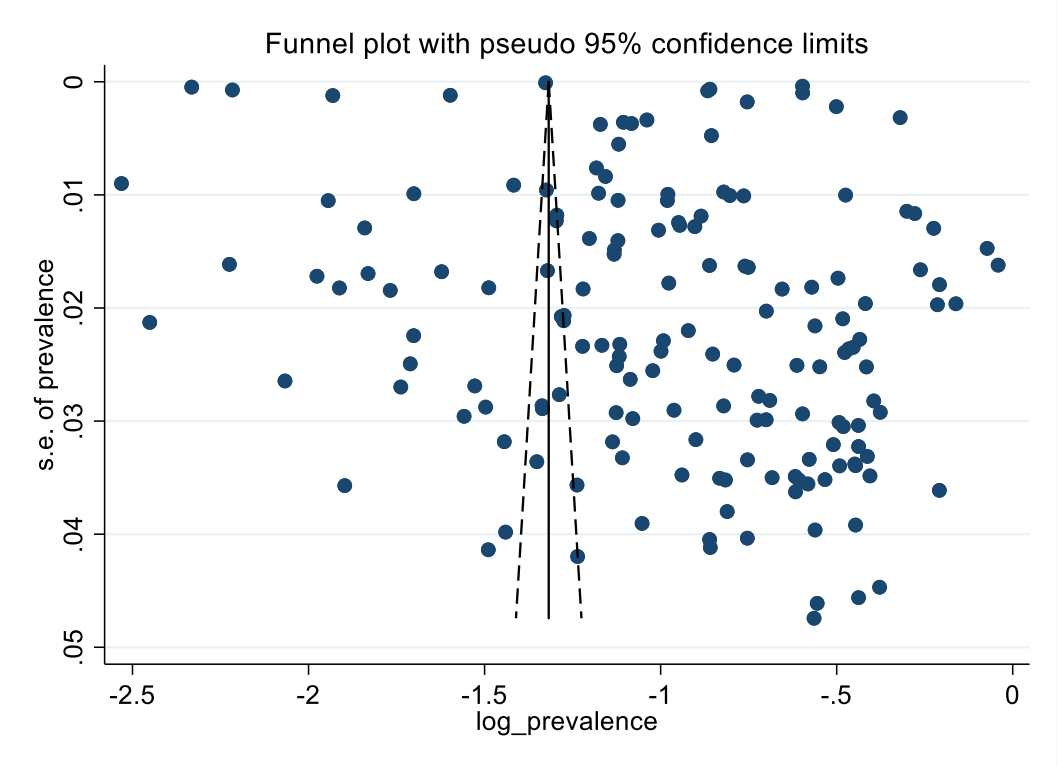
Meta-regression coefficient: -0.007, p=0.49

Figure S3z. trend sensitivity analysis using year of first recruitment and used only low-risk-of-bias studies (prescription refill)



Meta-regression co-efficient: 0.006, p=0.732

Figure S4 funnel plots



Eggers' test by using log of prevalence and standard error, p =0.332