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ORIGINAL RESEARCH

Clinical Outcomes in Hypertensive Emergency: A Systematic Review and Meta-Analysis

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BACKGROUND: To study the prevalence and types of hypertension-mediated organ damage and the prognosis of patients presenting to the emergency department (ED) with hypertensive emergencies.

METHODS AND RESULTS: PubMed was queried from inception through November 30, 2021. Studies were included if they reported the prevalence or prognosis of hypertensive emergencies in patients presenting to the ED. Studies reporting data on hypertensive emergencies in other departments were excluded. The extracted data were arcsine transformed and pooled using a random-effects model. Fifteen studies (n=4370 patients) were included. Pooled analysis demonstrates that the prevalence of hypertensive emergencies was 0.5% (95% CI, 0.40%–0.70%) in all patients presenting to ED and 35.9% (95% CI, 26.7%–45.5%) among patients presenting in ED with hypertensive crisis. Ischemic stroke (28.1% [95% CI, 18.7%–38.6%]) was the most prevalent hypertension-mediated organ damage, followed by pulmonary edema/acute heart failure (24.1% [95% CI, 19.0%–29.7%]), hemorrhagic stroke (14.6% [95% CI, 9.9%–20.0%]), acute coronary syndrome (10.8% [95% CI, 7.3%–14.8%]), renal failure (8.0% [95% CI, 2.9%–15.5%]), subarachnoid hemorrhage (6.9% [95% CI, 3.9%–10.7%]), encephalopathy (6.1% [95% CI, 1.9%–12.4%]), and the least prevalent was aortic dissection (1.8% [95% CI, 1.1%–2.8%]). Prevalence of in-hospital mortality among patients with hypertensive emergency was 9.9% (95% CI, 1.4%–24.6%).

CONCLUSIONS: Our findings demonstrate a pattern of hypertension-mediated organ damage primarily affecting the brain and heart, substantial cardiovascular renal morbidity and mortality, as well as subsequent hospitalization in patients with hypertensive emergencies presenting to the ED.

Key Words: emergency departments ■ hypertension-mediated organ damage ■ hypertensive emergency ■ ischemic stroke ■ malignant hypertension

The 2017 American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines defines hypertensive emergency as systolic blood pressure (BP) >180 mm Hg and diastolic BP >120 mm Hg, along with evidence of new or worsening hypertension-mediated organ damage (HMOD).[1] Hypertensive emergency is a life-threatening condition and has been linked with increased admission rates. It has been estimated that emergency department (ED) visits for hypertensive emergency have increased by 2-fold per million adults from 2006 to 2013.[2] Although a 0.3% reduction in mortality rate over the period of 7 years was observed, 4.5% of ED visits for hypertensive emergency still resulted in death in 2013, either in the ED or during subsequent hospital admission.[2] Despite the increased rate of hypertensive emergency presentations,

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CLINICAL PERSPECTIVE

What Is New?

- Approximately 10% of individuals who were admitted due to hypertensive emergencies died during their hospitalization period.
- Our up-to-date analysis of 15 studies found ischemic stroke as the most prevalent hypertension-mediated organ damage in patients with hypertensive emergency.

What Are the Clinical Implications?

- The rate of subsequent hospitalization in patients with hypertensive emergency was about 84%, showing that patients dismissed after blood pressure management evidently remain at high risk of hospitalization and organ damage.
- Thus, before discharging, a comprehensive review and thorough follow-up are warranted.
- Interventional approaches are essential to address significant acute hypertension and reduce long-term organ failure.

Nonstandard Abbreviations and Acronyms

HMOD	hypertension-mediated organ damage

subsequent morbidity and mortality data to support clinical decision making are still scarce. Hypertensive emergency may originate from poor management of essential hypertension or secondary hypertension, unrecognized hypertension, inadequately managed hypertension, reduced patient compliance, and reduced access to health care. Many people who present with hypertensive emergencies have chronic hypertension. Secondary hypertension can stem from several underlying causes, such as renal disease due to atherosclerosis or fibromuscular dysplasia, endocrine disorders like pheochromocytoma, or medications such as nonsteroidal anti-inflammatory agents and hormonal contraceptives. Malignant hypertension is one of the several forms of hypertensive emergency and is characterized by severe BP spikes and abrupt microvascular injury to a variety of organs, including the retina, brain, and kidney. Analysis of a multiracial population in England reported essential hypertension to be the most common underlying cause of malignant hypertension, whereas secondary hypertension, mainly due to chronic kidney disease, was identified as the cause in about 40% of the patients.[3] Moreover, the incidence rates of malignant hypertension have been documented as 2 new cases per 100 000 people per year, including up to 4 times greater rates (7.3 per 100 000 per year) recorded for self-identified Black individuals.[4] Concerns have been raised that although BP control is often acutely achieved in patients admitted with hypertensive emergencies, sufficient focus is not placed on control of chronic hypertension and prevention of organ damage in the long run.[5,6] Moreover, hypertensive emergency cases are further challenging due to involvement of a variety of organ damages, each of which may complicate the prognosis of the patients. Although some studies have demonstrated prevalence of hypertensive emergencies in patients presenting to the ED, the literature lacks robust estimates of the true prevalence of hypertensive emergencies. Moreover, the estimates available can substantially vary depending on the populations studied and the methods used. In addition, there is a lack of consensus-based guidelines in the management strategies of hypertensive emergencies. In this study, we sought to conduct a systematic review and meta-analysis to assess the prevalence of hypertensive emergency, HMOD, and subsequent hospitalization and in-hospital mortality among patients with hypertensive emergency visiting the ED. Therefore, we aim to provide a review of existing literature, highlight future avenues of research, and find high-powered estimates to evaluate the prevalence of outcomes of interest. Our analysis synthesizes data on the incidence of hypertensive emergency and their related HMOD from multiple studies and reduces the gap in the literature due to a lack of well-powered estimates on prevalence of hypertensive emergency. Hence, these findings will assist policymakers in providing more accurate recommendations about diagnosis, treatment, and management of hypertensive emergency and in developing evidence-based guidelines to improve patient-related outcomes. Moreover, we also highlight the limitations of existing studies and provide recommendations to improve future clinical studies on patients with hypertensive emergency.

METHODS

This systematic review and meta-analysis were conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[7,8] Permission from an ethical review board was not required as the data were publicly available. The data that support the findings of this study are available from the corresponding author upon reasonable request.

Data Sources and Search Strategy

A detailed search for relevant articles was conducted using the PubMed database, from inception until November 30, 2021. The search strategy used in each database is given in Table S1. To make certain no important publication was overlooked, we used the snowballing approach from relevant systematic reviews. All retrieved articles were transferred to Endnote

X7 (Clarivate Analytics, PA) to identify and remove duplicates. Two reviewers (T.J.S. and A.M.R.) independently reviewed the articles for relevance. Any discrepancies were resolved by a third reviewer (M.S.U.). Initially, titles and abstracts were screened, and then the full text was examined. If 2 articles were conducted by the same research group, we examined the likelihood of sample overlap and, if verified, used the most recent published article.

Study Selection

Articles were considered for the meta-analysis if they met the following inclusion criteria: (1) they investigated the prevalence of hypertensive emergencies in patients presenting to the ED; (2) they reported data on HMOD or hospitalization and in-hospital mortality due to hypertensive emergency; and (3) they were published in English. Articles were excluded if they focused on hypertensive emergencies in pregnant women and if participants were treated in a department other than the ED. Case reports and editorials were not considered.

Data Extraction

Two reviewers independently retrieved data for essential baseline characteristics. The number of cases of hypertensive emergencies presenting to the ED over various periods, the total number of patients presenting to the ED in a specific period, the prevalence of subtypes of HMOD, hospitalization, and in-hospital mortality were all outcomes of interest.

Statistical Analysis

All statistical analysis was performed using OpenMetaAnalyst.[9] The frequency of hypertensive emergency cases, the total number of patients, the prevalence of hypertension-meditated organ damage, the frequency of subsequent hospitalizations, and in-hospital mortality were arcsine transformed to avoid bias and reduce the heterogeneity in estimated effect sizes. The arcsine transformation is used to stabilize the variance of the proportions and makes it easier to visually compare the results of different studies. However, concerns have been raised regarding the transformation.[10] Therefore, we present our results as a percentage with its 95% CI, in order to provide a better intuitive comprehension of the effect size and its accuracy. A random effects model was used to pool the results. The prevalence of hypertensive emergency was calculated by dividing the total cases of hypertensive emergency by the total number of ED visits. The subtypes of HMOD, hospitalizations, and in-hospital mortality were obtained by dividing the number of cases by the total number of hypertensive emergencies presenting to the ED. A meta-analysis was performed on the calculated frequencies of the outcomes of interest, and an average frequency was obtained for each outcome. I^2 was used to assess the heterogeneity between the studies, and a value of I^2=25% to 50% was considered mild, 50% to 75% as moderate, and >75% as severe.[11] A P value of <0.05 was considered significant at all times. We also conducted a subgroup analysis based on the regions of the included studies and if a particular region had 2 or more studies.

RESULTS

Literature Search and Study Characteristics

Initial search revealed a total of 236 potential articles. After the exclusion of 222 articles, 14 articles (15 studies) were included in the meta-analysis.[12–25] The Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart summarizing the study selection process is given in Figure 1. The total number of included patients with hypertensive emergency was 4370. Among the included participants, 47% (n=2055) were men and the mean age was 63.7 years. Among the included patients with hypertensive emergencies, 48% (n=2097) had preexisting hypertension. The majority of the studies (14–18, 20, 23, 24) had a diagnostic criterion of systolic BP >180 mm Hg or diastolic BP >120 mm Hg for hypertensive emergency. Eight studies (14–16, 18, 20–22, 26) had a retrospective study design, whereas 5 studies (17, 23–25, 27) had a prospective study design. Four studies were conducted in Italy, 3 in Brazil, 2 in Thailand, and 2 in Ethiopia, whereas the United States, France, Tanzania, and Burkina Faso (Africa) had 1 study each. The baseline characteristics of the included studies is summarized in Table 1.

Results of Meta-Analysis

The results of the meta-analysis are summarized in Figure 2. Detailed forest plots are provided in Figures S1 through S23. Subgroup analysis based on the region of the included studies was conducted; however, subgroup analysis for the United States was not conducted because there was only 1 study from this region. The subgroups included are Africa (Ethiopia, Burkina Faso, and Tanzania), Europe (Italy and France), South America (Brazil), and Asia (Thailand).

Prevalence of Hypertensive Emergency in the Emergency Department

Out of 15 selected studies, 14 studies reported the prevalence of hypertensive emergency among patients presenting to the ED (total patients, 1 229 111; events,

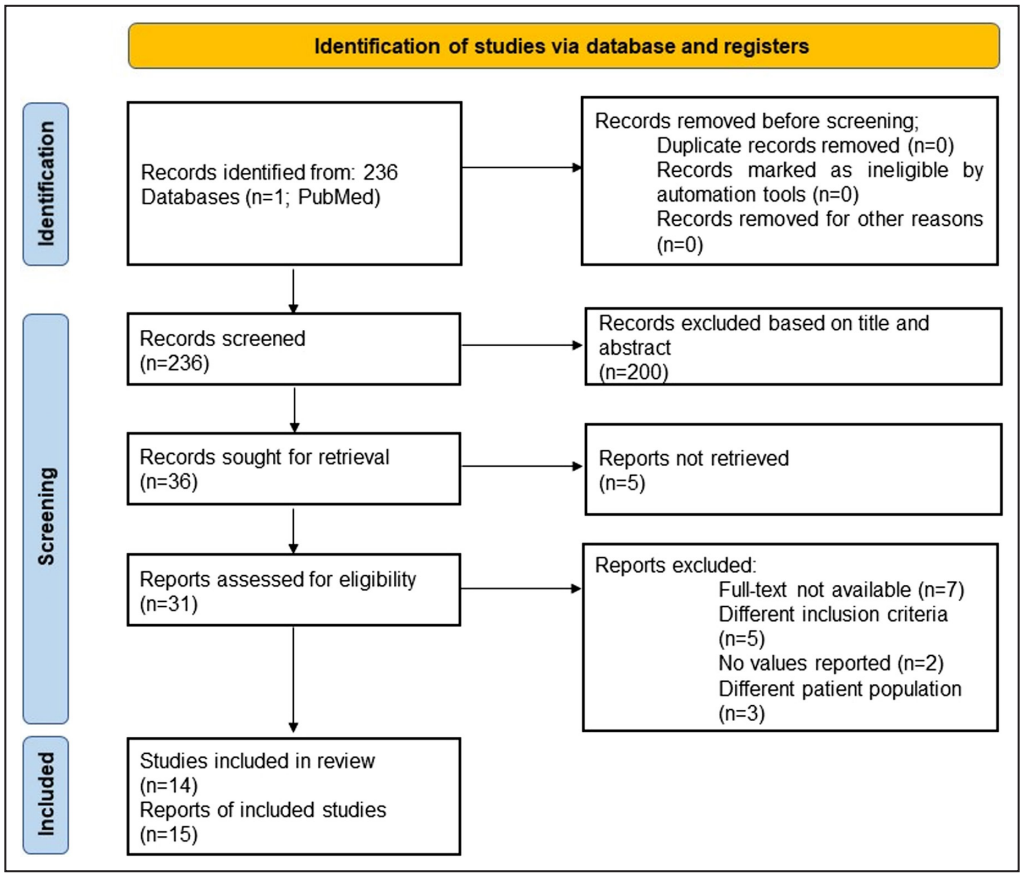

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart summarizing the study selection process.

3740). Our pooled analysis demonstrates that the mean prevalence of hypertensive emergencies presenting in ED was 0.5% (95% CI, 0.40%–0.70%; Figure S1). Subgroup analysis demonstrated that the prevalence of hypertensive emergency among patients presenting to the ED was 15.6% (95% CI, 4.5%–31.9%; Figure S2) in Africa, 4.0% (95% CI: 2.5%–5.8%; Figure S2) in Europe, 0.2% (95% CI, 0.1%–0.3%; Figure S2) in South America, and 0.2% (95% CI, 0.0%–0.8%; Figure S2) in Asia.

Prevalence of Hypertensive Emergency in Patients With Hypertensive Crisis in the Emergency Department

Out of 15 selected studies, 14 studies reported the prevalence of hypertensive emergency among patients presenting with hypertensive crisis to the ED (total patients, 17 691; events, 3740). Our pooled analysis demonstrates that the mean prevalence of hypertensive emergencies presenting to the ED was 35.9% (95% CI, 26.7%–45.5%; Figure S3). Subgroup analysis demonstrated that the prevalence of hypertensive emergency among patients presenting with hypertensive crisis to the ED was 50.0% (95% CI, 29.8%–70.2%; Figure S4) in Africa, 27.7% (95% CI, 16.6%–40.4%; Figure S4) in Europe, 40.1% (95% CI, 16.9%–65.9%; Figure S4) in South America, and 24.6% (95% CI, 5.3%–51.9%; Figure S4) in Asia.

Hypertensive-Mediated Organ Damage

Ischemic Stroke

Out of 15 selected studies, 9 studies reported ischemic stroke (total patients, 3052; events, 1115). Ischemic stroke was the most prevalent type of HMOD, and its prevalence in patients with hypertensive emergency presenting to the ED was 28.1% (95% CI, 18.7%–38.6;% Figure S5). Subgroup analysis demonstrated a prevalence of 15.3% (95% CI, 3.4%–33.6%; Figure S6) in Africa, 25.5% (95% CI, 14.4%–38.5%; Figure S6) in Europe, 30.6% (95% CI, 16.2%–47.4%; Figure S6) in South America, and 43.9% (95% CI, 31.9%–56.3%; Figure S6) in Asia.

Pulmonary Edema/Acute Heart Failure

Out of 15 selected studies, 14 studies reported pulmonary edema/acute heart failure (total patients, 3839;

Table 1. Characteristics of the Studies Included in the Meta-Analysis

Author, year, reference number	Country	Study type	Enrollment years	Inclusion criteria/ diagnostic criteria	Exclusion criteria	Patients (n)	Age (y)	Men (%)	Preexisting hypertension (N)	Risk factors	Background therapy
Desta, 2020[12]	Ethiopia	Retrospective	2018–2019	SBP>180 mm Hg or DBP>120 mm Hg and organ damage	SBP/DBP of ≤180/120 mm Hg	42	59±15	45	…	Hypertension, diabetes, MI, stroke	Antihypertensives
Gebresillassie, 2020[13]	Ethiopia	Retrospective	2013–2017	SBP>180 mm Hg or DBP>120 mm Hg and organ damage	None	86	56±18	16	69	Heart failure, CKD, dyslipidemia, CAD, diabetes, asthma, HIV, benign prostatic hyperplasia, atrial fibrillation	Antihypertensives, diuretic, CCB, BB, ACEi
Kotruchin, 2020[14]	Thailand	Retrospective	2016–2019	SBP ≥180 mm Hg or DBP ≥120 mm Hg	Pregnancy, known secondary hypertension	1308	66±14	52	833	CKD, hypertension, CAD, diabetes, COPD, malignancy	…
Mandi, 2019[15]	Africa	Prospective	2016	SBP>180 mm Hg or DBP>120 mm Hg and organ damage	Pregnant	113	49±16	66	74	Hypertension, diabetes, dyslipidemia, obesity, smoking, cocaine abuse, sedentary lifestyle	Nonsteroidal anti-inflammatory drugs
Pierin, 2019[16]	Brazil	Retrospective	2015	SBP>180 mm Hg or DBP>120 mm Hg and organ damage	None	83	63±13	21	45	Hypertension, stroke, diabetes, acute pulmonary edema, MI	ACEi, diuretics, BB, antiplatelet therapy, CCB, benzodiazepines
Shao, 2018[17]	Tanzania	Descriptive cohort	2015	SBP>180 mm Hg or DBP>110 mm Hg and organ damage	None	138	54±18	45	114	Alcohol use, smoking history, hypertension	…
Kotruchin, 2018[18]	Thailand	Retrospective	2012–2017	SBP>180 mm Hg or DBP>120 mm Hg and organ damage	Pregnancy, known secondary hypertension	172	61±13	n.a.	…	CAD, diabetes, CKD, Hyperlipidemia	…
Shah, 2017[19]	United States	Retrospective	2002–2012	High BP and organ damage	None	630	68±17	42	…	Secondary hypertension, CKD, COPD, peripheral vascular disease, diabetes	…
Guiga, 2017[20]	France	Retrospective	2015	SBP>180 mm Hg or DBP>110 mm Hg and organ damage	Pregnancy, acute kidney injury	385	76±18	47	295	…	CCB, diuretic, BB, ACEi/ARBs
Salvetti, 2015[21]	Italy	Prospective	2015	SBP>180 mm Hg or DBP>120 mm Hg and organ damage	Pregnancy, resuscitated cardiac arrest	187	73±13	55	83	Hypertension, diabetes	…

(*Continued*)

Table 1. Continued

Author, year, reference number	Country	Study type	Enrollment years	Inclusion criteria/ diagnostic criteria	Exclusion criteria	Patients (n)	Age (y)	Men (%)	Preexisting hypertension (N)	Risk factors	Background therapy
Pinna, 2014[22]	Italy	Prospective	2009	SBP>220 mm Hg or DBP>120 mm Hg and organ damage	Pregnancy	391	70±14	53	309	Smoking history, hypertension	BB, CCBs, diuretics, ACEi/ARBs
Vilela-Martin, 2011[23]	Brazil	Prospective	2006	DBP>120 mm Hg with organ damage	Pregnancy; pseudocrisis	231	63±13	51	197	Hypertension, sedentary lifestyle, Smoking history	Antihypertensives
Salvetti, 2008[21]	Italy	Prospective	2008	SBP>180 mm Hg or DBP>120 mm Hg and organ damage	Pregnancy, resuscitated cardiac arrest	317	71±14	54	78	Hypertension, diabetes	…
Vilela-Martin, 2004[24]	Brazil	Retrospective	2020	DBP>120 mm Hg with organ damage	None	179	60±15	55	…	Diabetes, smoking history	…
Zampaglione, 1996[25]	Italy	Prospective	1992–1993	DBP>120 mm Hg with organ damage	None	108	67±16	49	…	…	…

ACEi/ARB indicates angiotensin-converting enzyme inhibitor/angiotensin receptor blocker; BB, beta blocker; CAD, coronary artery disease; CCB, calcium channel blocker; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DBP, diastolic blood pressure; and SBP, systolic blood pressure.

events, 969). Pulmonary edema/acute heart failure was the second most frequent type of HMOD, and its prevalence in patients with hypertensive emergency presenting to the ED was 24.1% (95% CI, 19.0%–29.7%; Figure S7). Subgroup analysis demonstrated a prevalence of 12.0% (95% CI, 5.0%–21.4%; Figure S8) in Africa, 34.7% (95% CI, 32.1%–37.4%; Figure S8) in Europe, 27.5% (95% CI, 23.4%–31.7%; Figure S8) in South America, and 19.6% (95% CI, 17.6%–21.7%; Figure S8) in Asia.

Hemorrhagic Stroke

Out of 15 selected studies, 7 studies reported hemorrhagic stroke (total patients, 2579; events, 343). The prevalence of hemorrhagic stroke in patients with hypertensive emergency presenting to the ED was 14.6% (95% CI, 9.9%–20.0%; Figure S9). Subgroup analysis demonstrated a prevalence of 7.1% (95% CI, 5.2%–9.3%; Figure S10) in Europe, 13.8% (95% CI, 8.8%–19.5%; Figure S10) in South America, and 14.9% (95% CI, 10.7%–19.5%; Figure S10) in Asia.

Acute Coronary Syndrome

Out of 15 selected studies, 14 studies reported acute coronary syndrome (total patients, 3839; events, 442). The prevalence of acute coronary syndrome in patients with hypertensive emergency presenting to the ED was 10.8% (95% CI, 7.3%–14.8%; Figure S11). Subgroup analysis demonstrated a prevalence of 3.9% (95% CI, 2.4%–5.9%; Figure S12) in Africa, 18.7% (95% CI, 13.8%–24.0%; Figure S12) in Europe, 10.8% (95% CI, 7.5%–14.5%; Figure S12) in South America, and 8.8% (95% CI, 4.1%–15.0%; Figure S12) in Asia.

Renal Failure

Out of 15 selected studies, 8 studies reported renal failure (total patients, 2580; events, 134). The prevalence of renal failure in patients with hypertensive emergency presenting to the ED was 8.0% (95% CI, 2.9%–15.5%; Figure S13). Subgroup analysis demonstrated a prevalence of 18.7% (95% CI, 6.8%–34.7%; Figure S14) in Africa, and 1.4% (95% CI, 0.9%–2.1%; Figure S14) in Asia.

Subarachnoid Hemorrhage

Out of 15 selected studies, 6 studies reported subarachnoid hemorrhage (total patients, 2297; events, 171). The prevalence of subarachnoid hemorrhage in patients with hypertensive emergency presenting to the ED was 6.9% (95% CI, 3.9%–10.7%; Figure S15). Subgroup analysis demonstrated a prevalence of 8.0% (95% CI, 2.6%–16.0%; Figure S16) in Europe, and 2.9% (95% CI, 1.5%–4.7%; Figure S16) in South America.

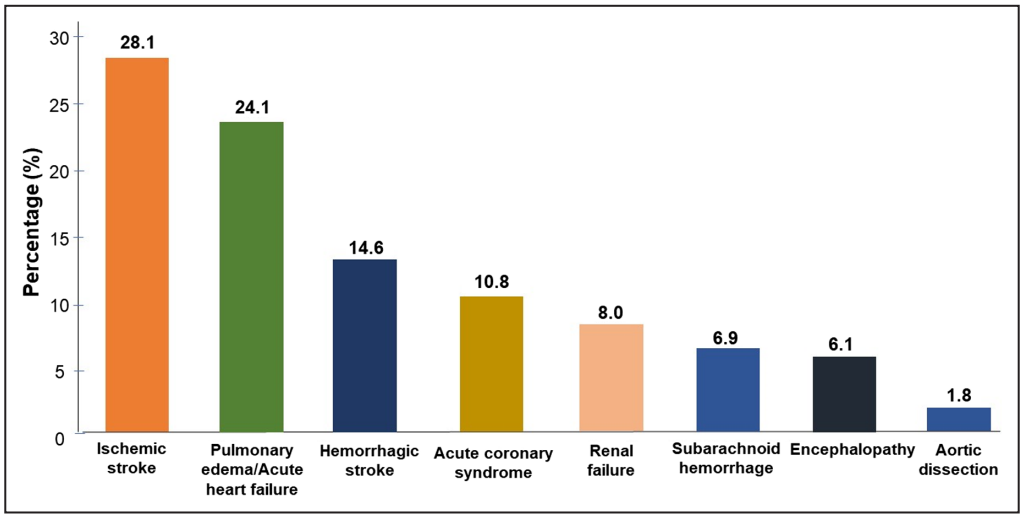

Figure 2. Summary of forest plots of the prevalence of hypertension-mediated organ damage, hospitalization, and in-hospital mortality among patients with hypertensive emergency presenting to the emergency department.

Encephalopathy

Out of 15 selected studies, 6 studies reported encephalopathy (total patients, 1101; events, 66). The prevalence of encephalopathy in patients with hypertensive emergency presenting to the ED was 6.1% (95% CI, 1.9%–12.4%; Figure S17). Subgroup analysis demonstrated a prevalence of 9.7% (95% CI, 0.2%–39.5%; Figure S18) in Africa, and 9.7% (95% CI, 1.5%–23.9%; Figure S18) in Europe.

Aortic Dissection

Out of 15 selected studies, 6 studies reported aortic dissection (total patients, 2477; events, 53). Aortic dissection was the least prevalent HMOD, and its prevalence in patients with hypertensive emergency presenting to the ED was 1.8% (95% CI, 1.1%–2.8%; Figure S19). Subgroup analysis demonstrated a prevalence of 2.2% (95% CI, 0.4%–5.2%; Figure S20) in Europe, and 2.8% (95% CI, 1.8%–3.9%; Figure S20) in Asia.

Hospitalization

Out of 15 selected studies, 2 reported results on hospitalization (total patients, 581; events, 489). Our pooled analysis demonstrates that the prevalence of hospitalization among patients with hypertensive emergency presenting to the ED was 84.1% (95% CI, 80.5%–87.3%; Figure S21).

In-Hospital Mortality

Out of 15 selected studies, 5 studies reported in-hospital mortality (total patients, 130664; events, 736). Our pooled analysis demonstrates that in-hospital mortality among patients with hypertensive emergency presenting to the ED was 9.9% (95% CI, 1.4%–24.6%; Figure S22). Subgroup analysis demonstrated a prevalence of 14.6% (95% CI, 5.1%–28.0%; Figure S23) in Africa.

DISCUSSION

To our knowledge, this is one of the largest systematic review and meta-analysis of patients with hypertensive emergency presenting to the ED and their clinical outcomes. Our study demonstrated that incidence of hypertensive emergency among patients presenting to ED was 0.5%, whereas 35.9% of patients presenting with hypertensive crisis in the ED were categorized as hypertensive emergency. Moreover, the most common complications of hypertensive emergencies are ischemic stroke and pulmonary edema/acute heart failure. Lastly, almost 10% of patients with hypertensive emergencies died during the hospitalization period.

According to our pooled analysis of 15 studies, which included 4370 patients with hypertensive emergency, the prevalence of hypertensive emergency was 0.5%, which is similar to the prevalence of hypertensive emergencies found in a smaller meta-analysis that included 8 studies with 1970 patients with hypertensive emergency and indicated a prevalence of 0.3% among patients presenting to the ED.[26] Moreover, our analysis demonstrates that prevalence of hypertensive emergency among patients with hypertensive crisis in ED was 35.9%. Previous meta-analysis corroborates these findings, as hypertensive urgency was considered to

be significantly higher than hypertensive emergency (odds ratio, 2.5 [1.4%–4.3%]) in patients presenting to ED.[26] Our findings are similarly consistent with the STAT (Studying the Treatment of Acute Hypertension) registry, the largest database of patients with hypertensive emergency in the United States, which reported a 0.2% prevalence of hypertensive emergencies.[27] Loss of hypertension control is a major issue that can influence prevalence of hypertensive emergency. In a study to analyze the trend of hypertension between 2 study periods, analysis demonstrated that hypertension control rates increased from 2009 to 2014; however, after a temporary stationary period, a significant decline was observed from 2015 to 2018.[28] Further analysis demonstrated that a significant reduction in initiation of antihypertensive therapy, from 75.3% to 70.7%, can be linked to declining hypertension control rates.[28] Moreover, the impact of COVID-19 on hypertension control has been undesirable. Analysis shows reduced outpatient visits for myocardial infarction, stroke, and heart failure, with a 20% elevated incidence of mortality during COVID-19 compared with before the pandemic.[29]

In our study, the most common HMOD among the included participants was ischemic stroke (28.1%), as opposed to a previously published meta-analysis, which found that acute pulmonary edema was the most common condition.[26] Studies with patients presenting with ischemic stroke and additional comorbidities, such as obesity or diabetes, were included in our analysis. This corroborates the current evidence, as Anderson et al. have suggested that the presentation of ischemic stroke is more common in patients with comorbidities but has shown less association with sex or age.[30] Ischemic stroke may present with seizures, epilepsy, recurrent stroke, delirium, and other neurological complications. According to a previous meta-analysis evaluating the common symptoms of patients with hypertensive emergency presenting to the ED, it was concluded that the most common symptoms included a presentation of neurological complications.[26] However, it is possible that the observed HMOD may have been influenced by other factors, in addition to severe hypertension, such as the presence of coronary artery disease, pulmonary edema, or atrial fibrillation (Table 1), and hence, warrants further evaluation.

Our research also reflects on hypertension-related in-hospital mortality, and our analysis demonstrates that in-hospital mortality was 9.9%. Our results corroborate the current evidence, such as the STAT registry, which reports that mortality in patients with hypertensive emergency is 11%.[27] Among our included studies, Zhou et al conducted a prospective cohort study and found that hypertension is the leading cause of all-cause mortality and cardiovascular disease mortality.[31] Because our analysis demonstrated ischemic stroke as the most common HMOD, previous analysis has demonstrated that presentation of neurological complications may increase the incidence of mortality up to 24%.[27] Our analysis also demonstrated an 84% incidence of hospitalization. Treatment guidelines for hypertensive emergencies are complex. In order to avoid causing organ ischemia, BP is typically reduced slowly over the span of 24 hours, with a goal to reduce BP no more than 25% from baseline.[32] Subsequent to lowering of BP, if the patient appears symptom free, it may be safe to discharge these patients with oral antihypertension medications and make plans for a follow-up appointment in an outpatient facility within 24 hours, continued with maintaining prevention strategies.[33] These prevention strategies include multidrug regimen therapy for hypertension to patients who were noncompliant to drugs that triggered hypertensive emergency. Moreover, in patients with end-stage kidney disease, maintenance dialysis and volume regulation are required to achieve hypertension control and may require visits to dialysis centers to support BP control along with antihypertensive medications.[32]

Our study has potential clinical implications. Patients who are discharged after adequate control of BP in the emergency setting may be considered “stable,” but clearly these patients continue to carry a substantial risk of subsequent hospitalization. Thus, multidisciplinary evaluation before discharge and close follow-up thereafter are essential. There is a need to develop treatment protocols that can allow not just management of severe hypertension in the acute phase but also ameliorate hypertension and organ damage in the chronic phase.

A potential limitation of our study is that specific clinical outcomes, such as cardiovascular disease mortality or all-cause mortality, were not evaluated due to a lack of studies providing such data. Similarly, any racial or ethnic minority groups were also not evaluated. This restricts our capacity to quantitatively assess the frequency of hypertensive emergencies and their clinical consequences in these populations quantitatively. Moreover, 1 study was from patients in the United States. It is necessary to conduct more studies in high-risk patients and create a link between trends in the loss of hypertension control in these patients and hypertensive emergency. Moreover, the impact of COVID-19 on the prevalence of hypertensive emergencies and HMOD could not be evaluated and warrants further exploration. Different assessment methodologies for subtypes of HMOD, as well as variance in the established criteria that categorize an individual as a patient with a hypertensive emergency, might explain the discrepancy across the included studies. Additional retrospective and prospective studies in patients with hypertensive emergency are required to ascertain other subtypes of organ damage, such as papilledema or hypotension, which were not included in the current

analysis due to a lack of studies. The data on subsequent hospitalization were limited and obtained from patients surviving an acute severe hypertension event; however, time after discharge was not published in our included studies. Therefore, studies evaluating the incidence of hospitalization among various predefined durations such as 30 days, 3 months, 6 months, and 1 year are required to understand the risk factors of hospitalization.

Our analysis included single-arm retrospective or prospective studies. These studies are not designed to establish a cause-and-effect relationship between variables, such as the relationship between severe hypertension and HMOD, due to the lack of a comparison group. To establish cause-and-effect relationships, controlled studies are optimal as they include a comparison group. However, for patients with hypertensive emergency, there is a lack of controlled studies. In the case of severe hypertension and HMOD, controlled studies are warranted that would compare the incidence of organ damage between patients with severe hypertension and prescribed a particular treatment, and a control group of patients with severe hypertension who received a different treatment or no treatment at all. Additionally, controlled studies should also use rigorous analysis to adjust for confounding factors such as age, sex, comorbidities, or any other variables that may influence HMOD. Furthermore, controlled studies should also evaluate and reduce bias due to conditions that can lead to certain organ damage in low BP conditions, such as aortic dissection. Controlled studies should also evaluate, and reduce bias, due to conditions that can lead to certain organ-damage in low BP conditions, such as aortic dissection. Future studies should also provide analysis regarding the impact of conditions such as connective tissue disorders, congenital abnormalities of the aorta, or the trauma on incidence of hypertensive emergency, in order to reduce the heterogeneity in prevalence of hypertensive emergency. In addition to this, a lack of data in the existing literature limited our ability to conduct an analysis on the impact of severe hypertension with or without particular risk factors. Therefore, large-scale, high-powered controlled studies with comparators are crucial to assess the impact of coexistence of various comorbidities that can influence organ damage in patients with severe hypertension. Such studies also help in developing personalized treatment strategies that address multiple risk factors and improve hypertension control. Furthermore, data are limited regarding patients with hypertensive emergency who were admitted after presenting to the ED, with only 2 studies reporting this outcome. One study belonged to France (Europe), and another study was from Tanzania (Africa). Hence, more studies with rigorous analysis are warranted to further evaluate the reasons for not admitting patients with hypertensive emergency, such as differences in severity of condition, variation in health care systems and practices, and comorbidities or other factors that could make hospitalization challenging. Lastly, the included studies may have missed some patients with severe BP elevations but not quite high enough for inclusion BP thresholds who had new or worsening target-organ injury that was likely attributable to their BP.

CONCLUSIONS

Our findings show that ischemic stroke and pulmonary edema/acute heart failure are the most commonly reported organ damage caused by hypertensive emergency. According to our findings, there is a substantial incidence of in-hospital mortality (nearly 10%) among patients with hypertensive emergency who present to the ED. More studies are required to discover the incidence, interval, and secondary causes of subsequent hospitalization and to evaluate additional causes and complications associated with mortality in patients with hypertensive emergency.

ARTICLE INFORMATION

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Affiliations

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Disclosures

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Supplemental Material

Table S1
Figures S1–S23

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Supplemental Material

Table S1: Search string used for data extraction from inception till November, 2021

(("hypertense"[All Fields] OR "hypertension"[MeSH Terms] OR "hypertension"[All Fields] OR "hypertension s"[All Fields] OR "hypertensions"[All Fields] OR "hypertensive"[All Fields] OR "hypertensive s"[All Fields] OR "hypertensives"[All Fields]) AND ("emerge"[All Fields] OR "emerged"[All Fields] OR "emergence"[All Fields] OR "emergences"[All Fields] OR "emergencies"[MeSH Terms] OR "emergencies"[All Fields] OR "emergency"[All Fields] OR "emergent"[All Fields] OR "emergently"[All Fields] OR "emergents"[All Fields] OR "emerges"[All Fields] OR "emerging"[All Fields]) AND ("emergency service, hospital"[MeSH Terms] OR ("emergency"[All Fields] AND "service"[All Fields] AND "hospital"[All Fields]) OR "hospital emergency service"[All Fields] OR ("emergency"[All Fields] AND "department"[All Fields]) OR "emergency department"[All Fields]) AND (("organ"[All Fields] OR "organ s"[All Fields] OR "organism"[All Fields] OR "organism s"[All Fields] OR "organisms"[All Fields] OR "organs"[All Fields]) AND ("damage"[All Fields] OR "damaged"[All Fields] OR "damages"[All Fields] OR "damaging"[All Fields])))

Figure S1: Prevalence of Hypertensive emergency in patients presenting to the emergency department

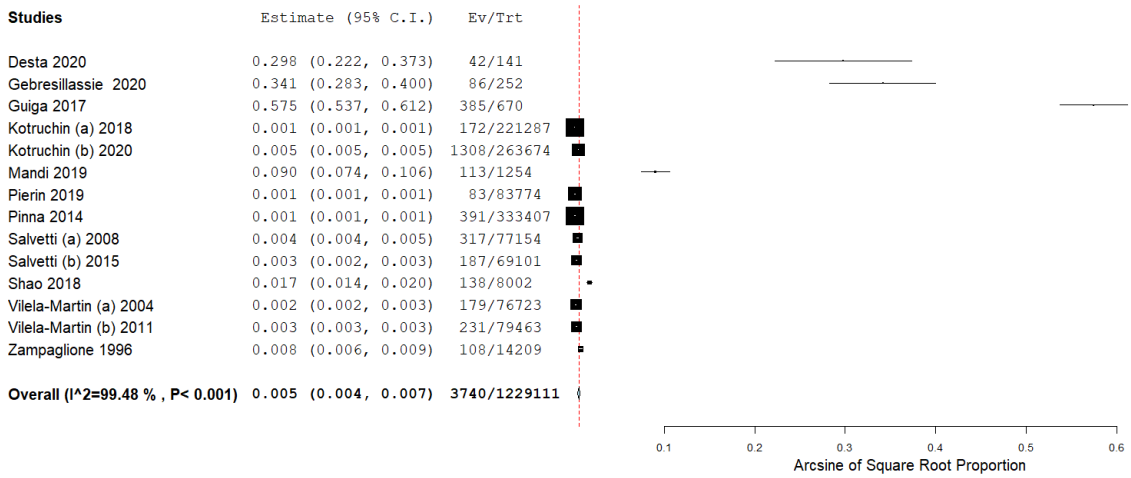
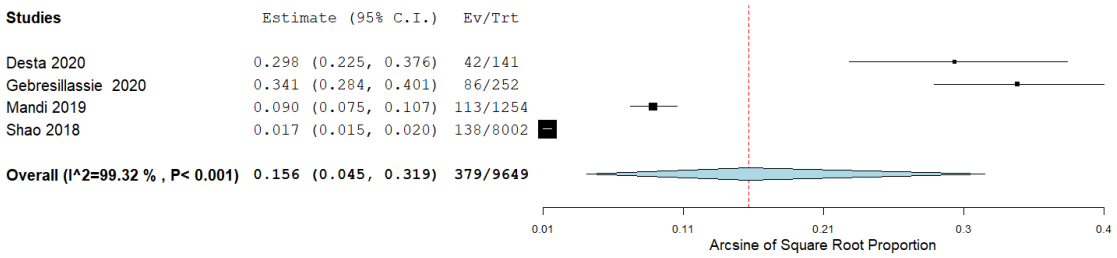
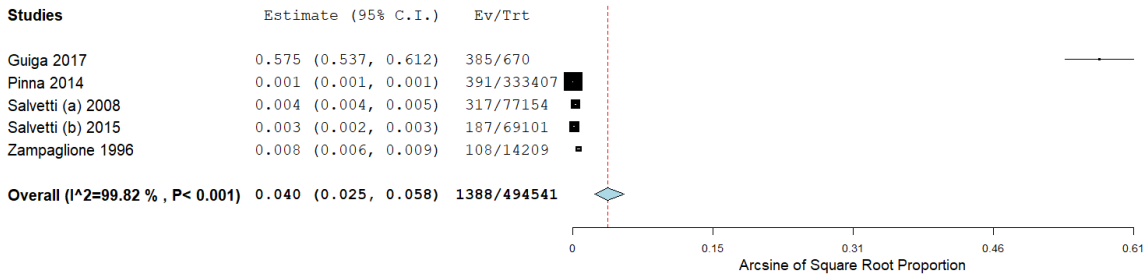


Figure S2: Prevalence of Hypertensive emergency in patients presenting to the emergency department, divided by regions

AFRICA



EUROPE



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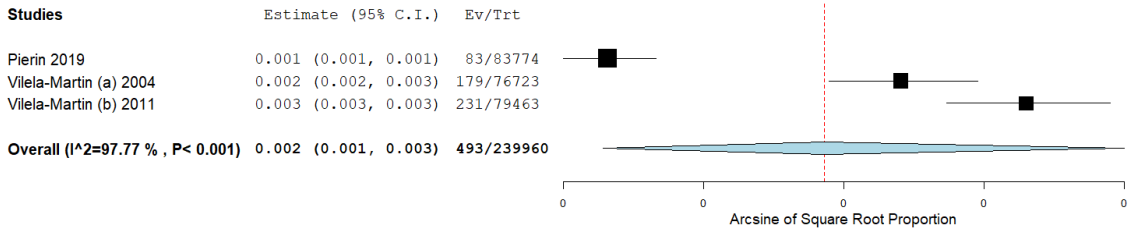

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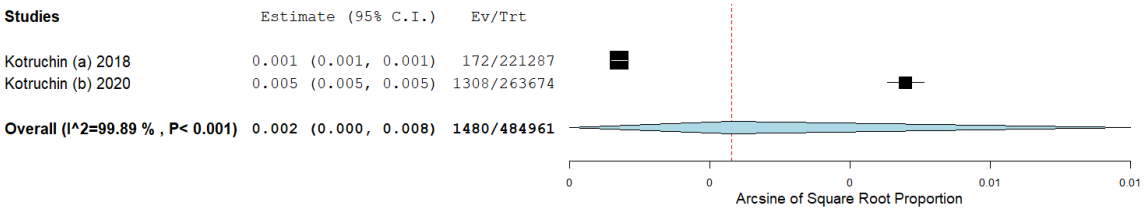


Figure S3: Prevalence of Hypertensive emergency in patients with complaint of hypertension presenting to emergency department

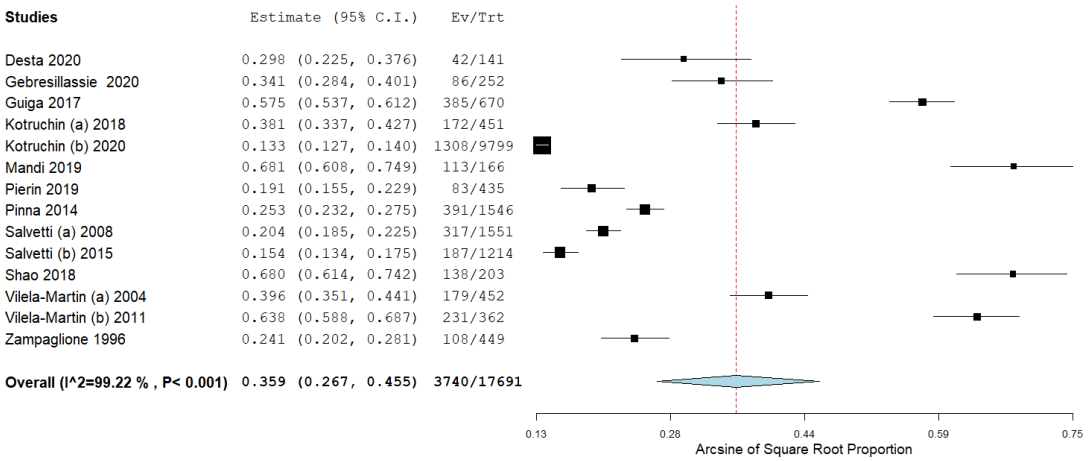


Figure S4: Prevalence of Hypertensive emergency in patients with hypertension presenting to emergency department, divided by regions

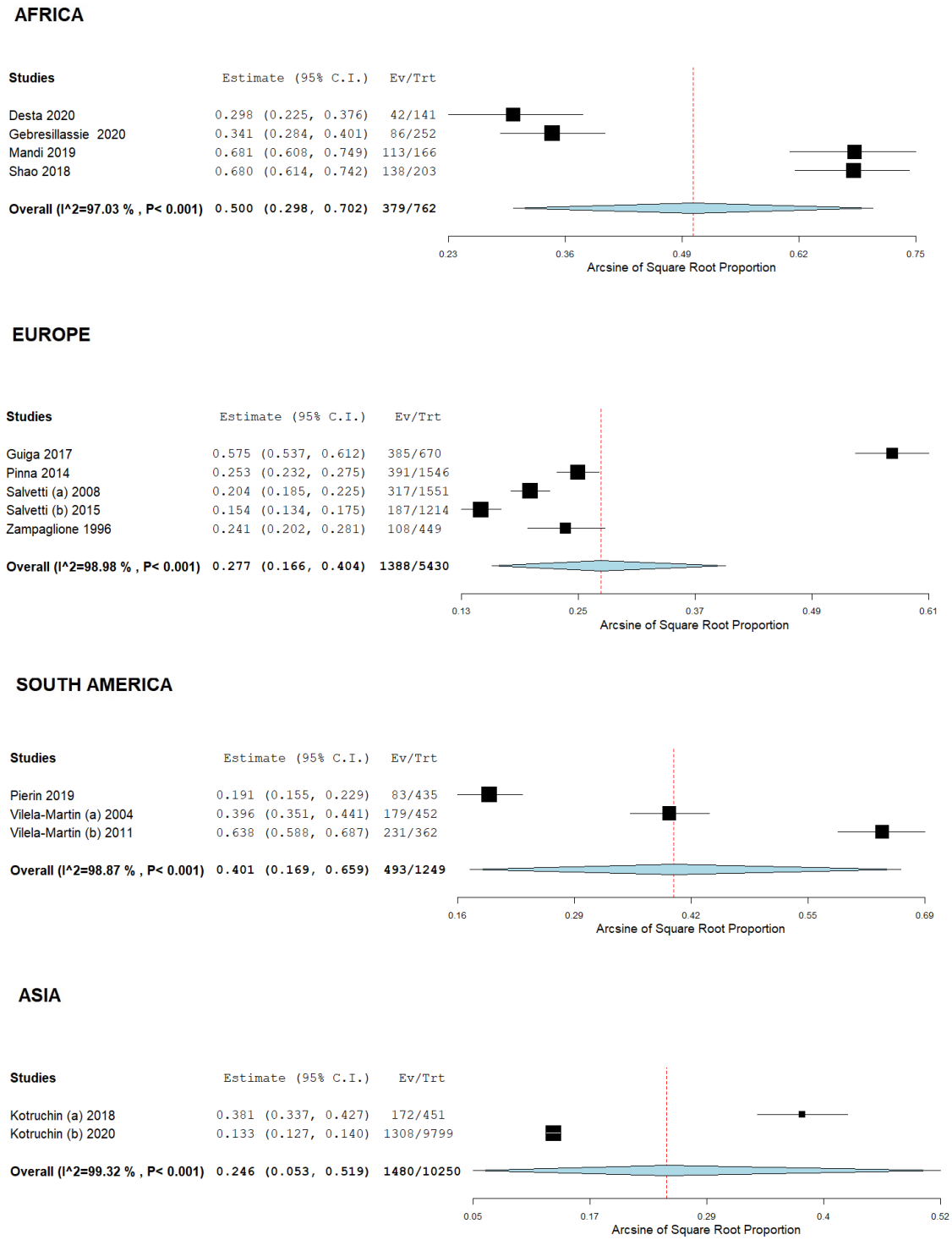


Figure S5: Prevalence of ischemic stroke

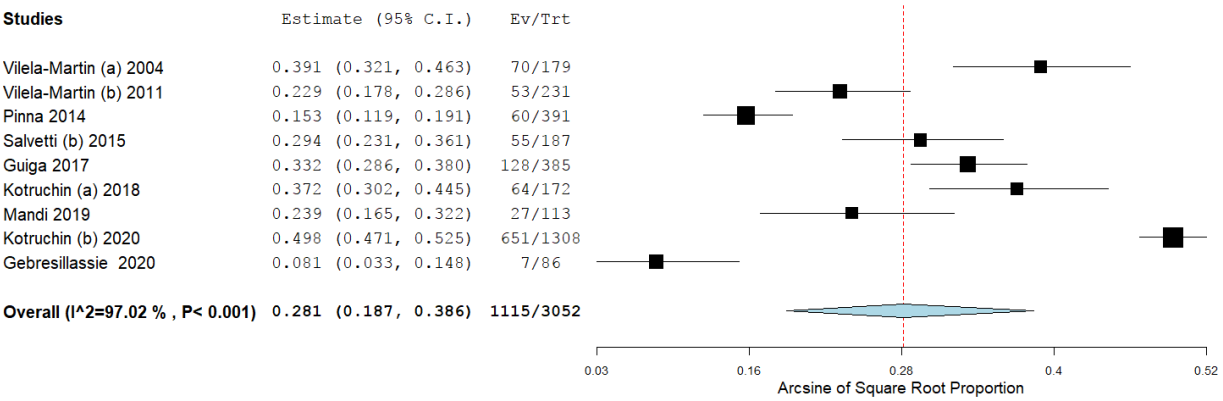
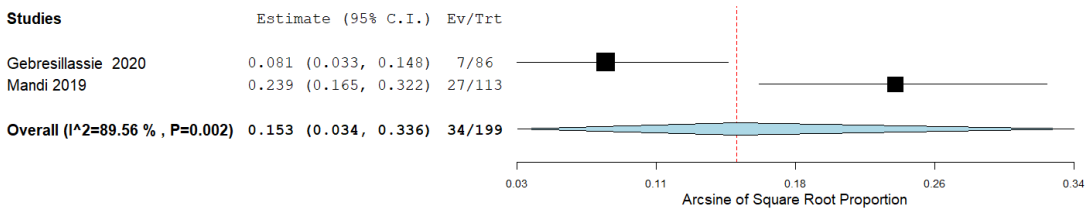


Figure S6: Prevalence of ischemic stroke, divided by regions

AFRICA



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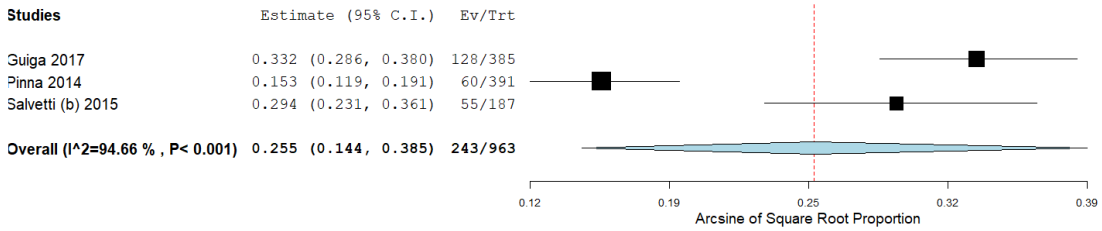

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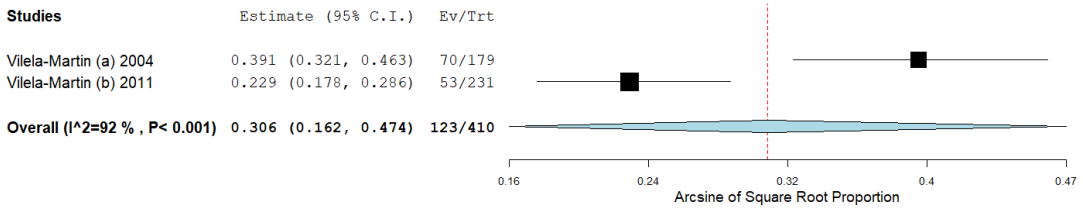

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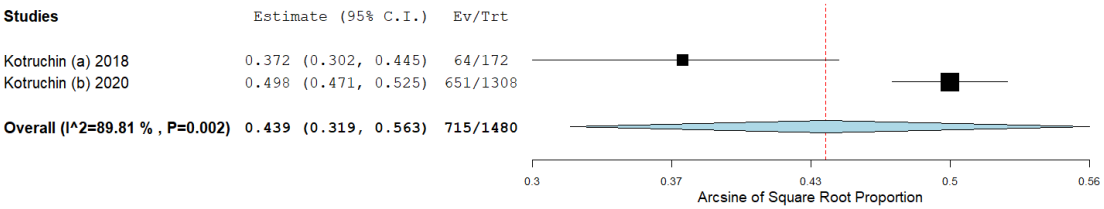


Figure S7: Prevalence of pulmonary edema/acute heart failure

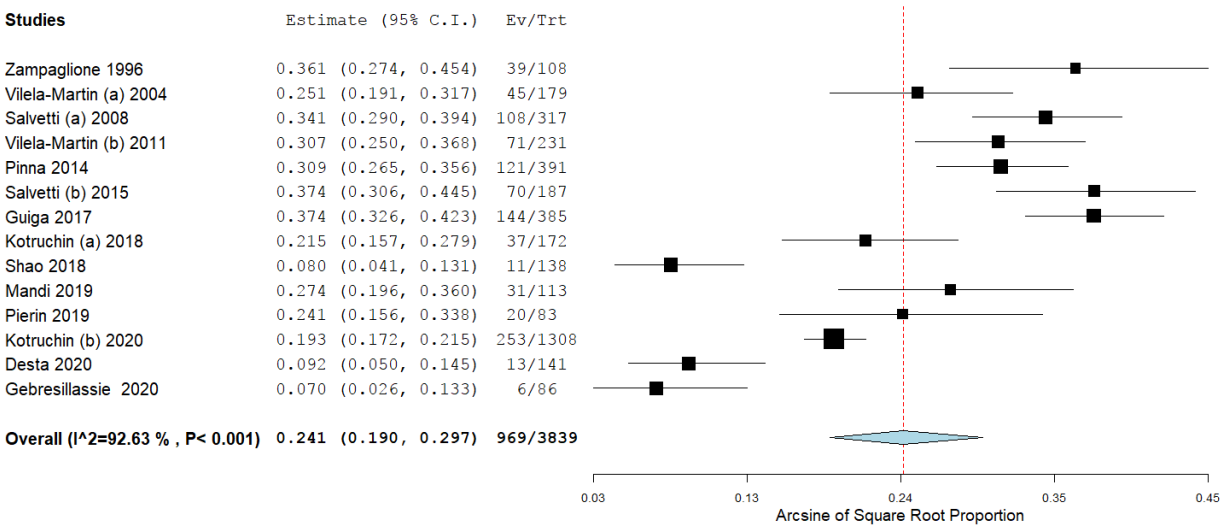
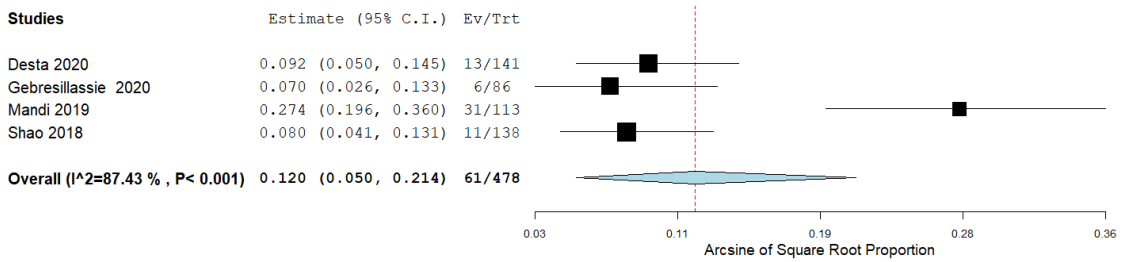


Figure S8: Prevalence of pulmonary edema/acute heart failure, divided by regions

AFRICA



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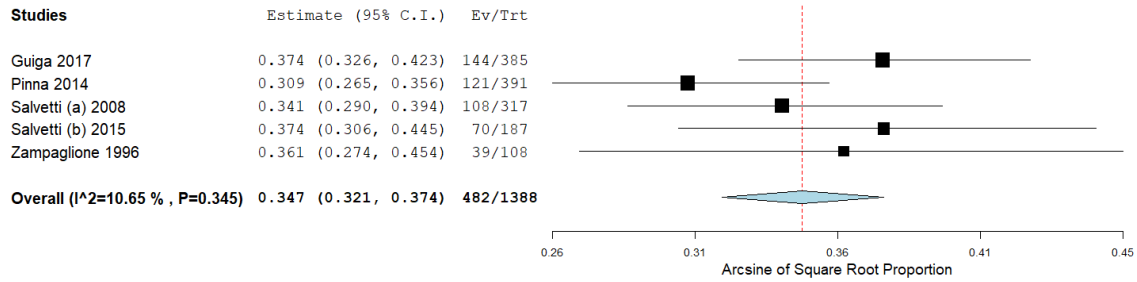

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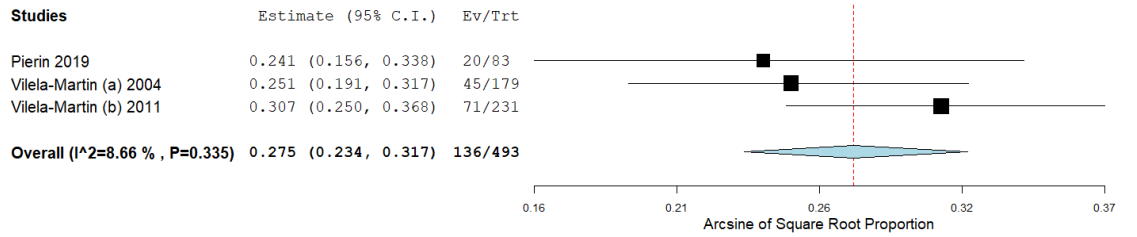

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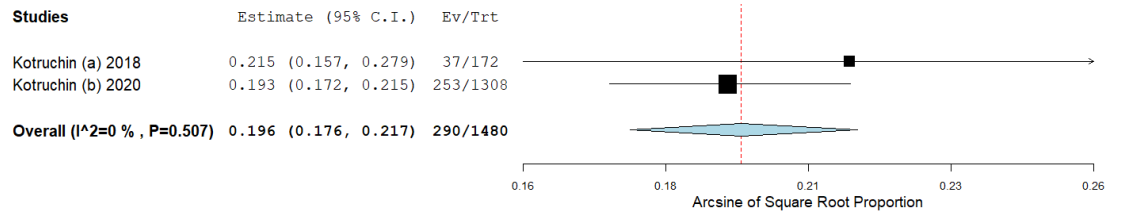


Figure S9: Prevalence of hemorrhagic stroke

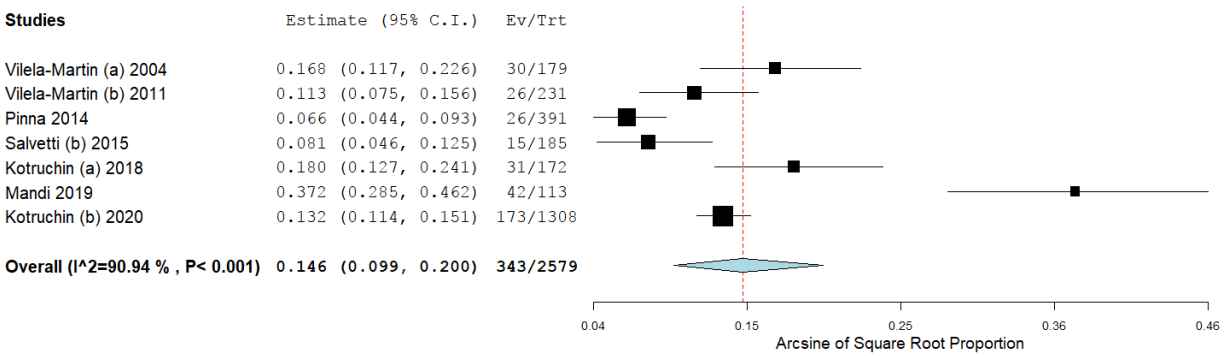
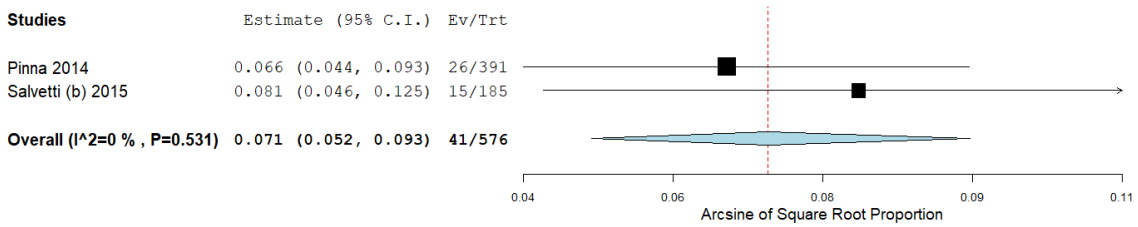


Figure S10: Prevalence of hemorrhagic stroke, divided by regions

EUROPE



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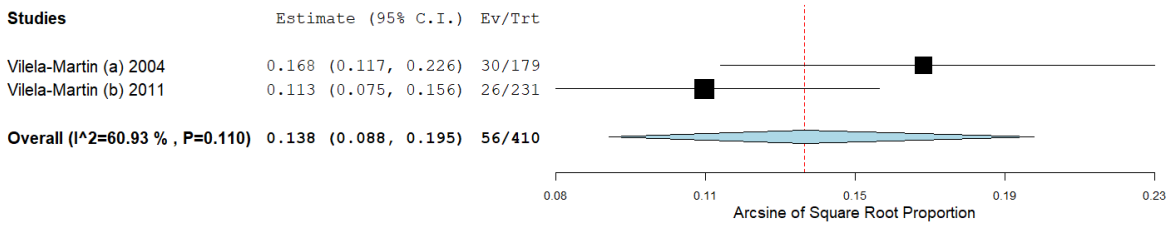

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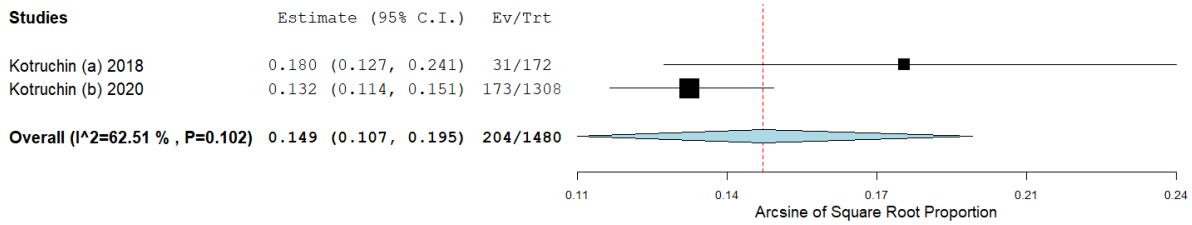


Figure S11: Prevalence of acute coronary syndrome

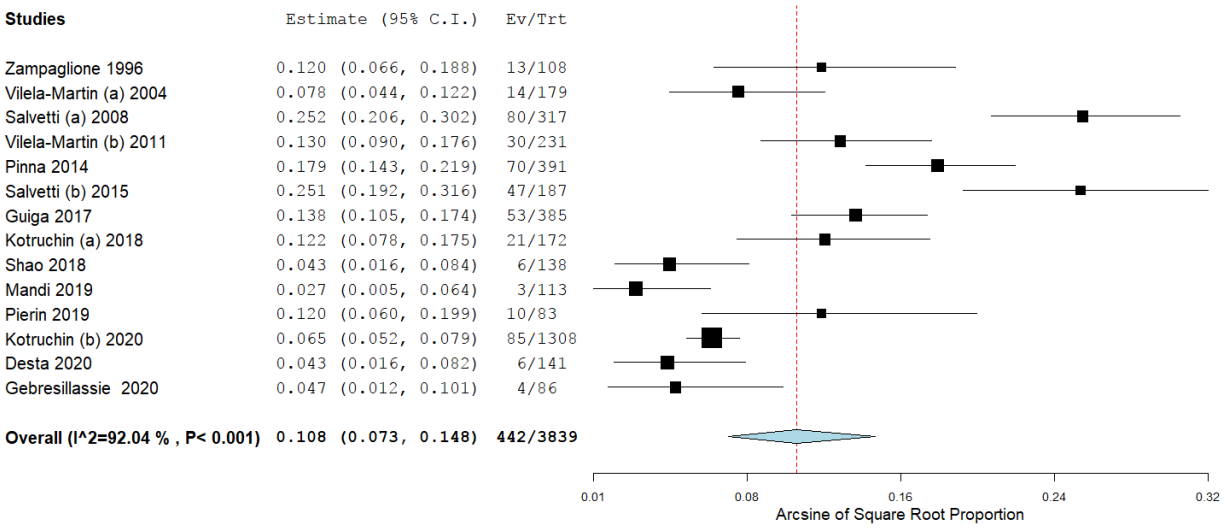
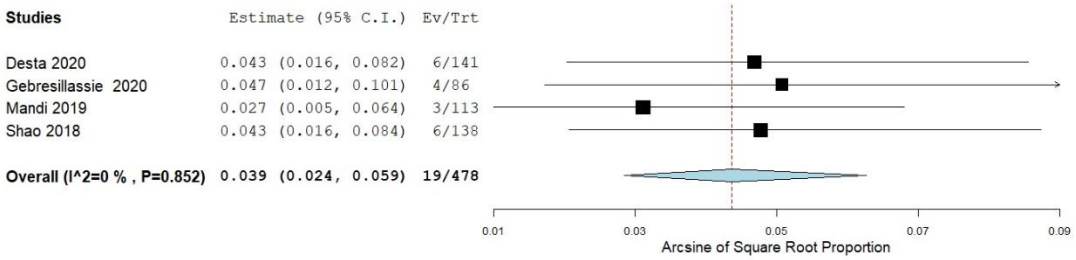


Figure S12: Prevalence of acute coronary syndrome, divided by regions

AFRICA



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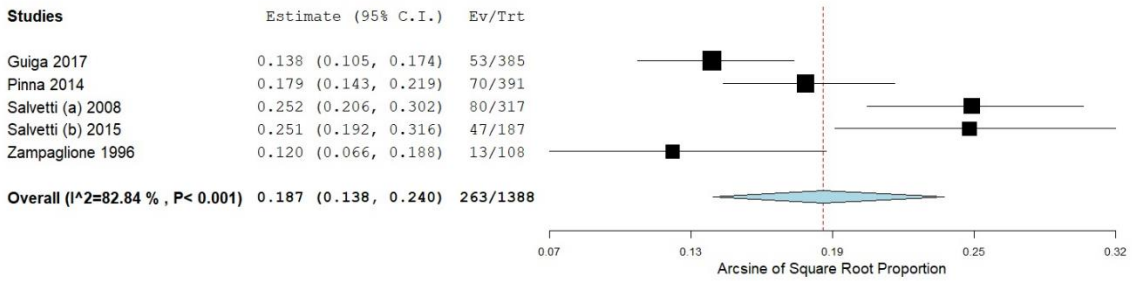

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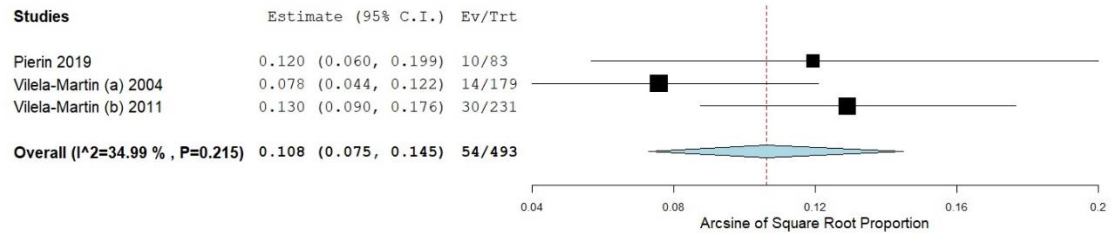

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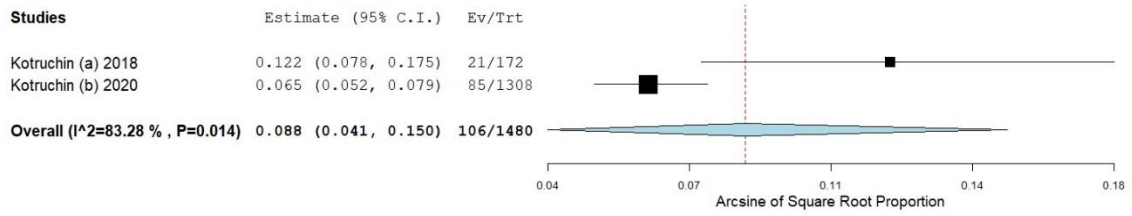


Figure S13: Prevalence of renal failure

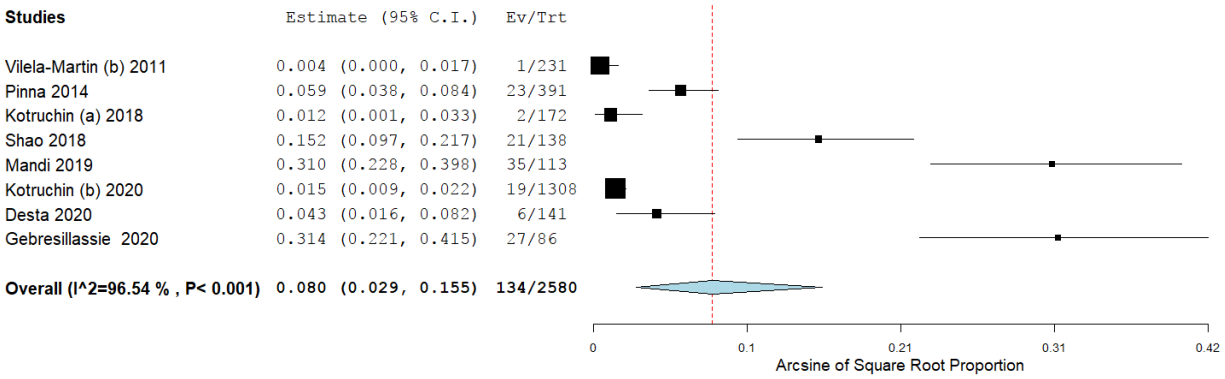
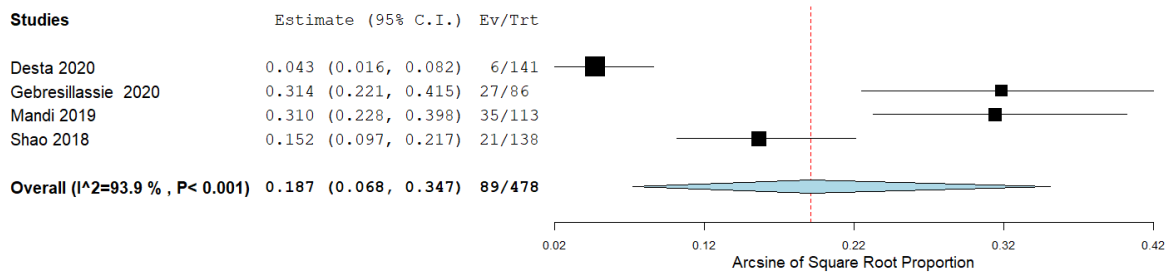


Figure S14: Prevalence of renal failure, divided by regions

AFRICA



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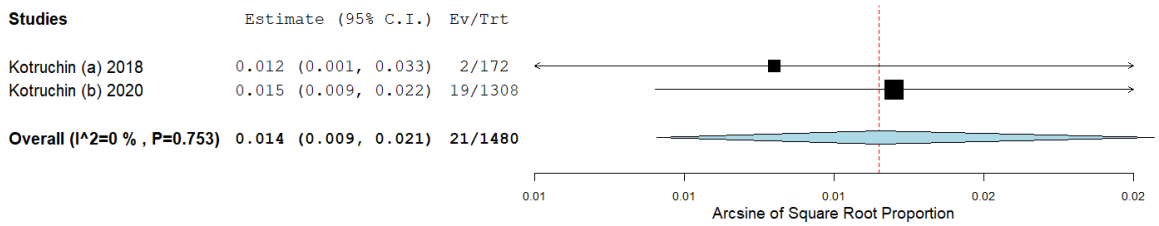


Figure S15: Prevalence of subarachnoid hemorrhage

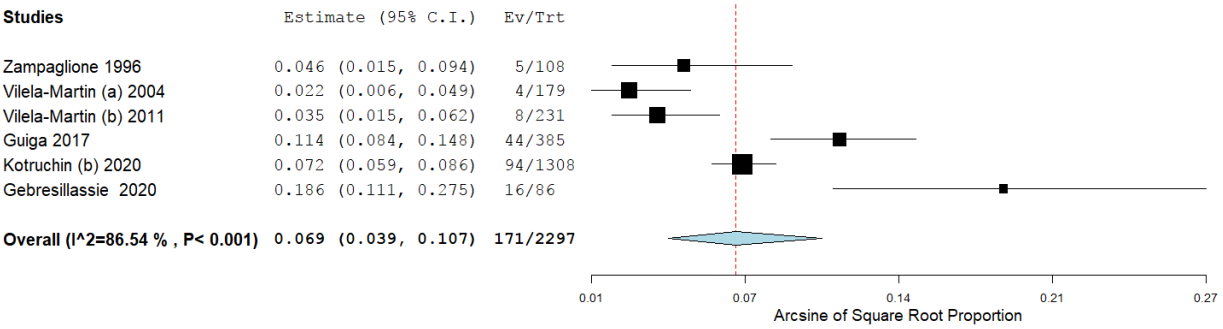
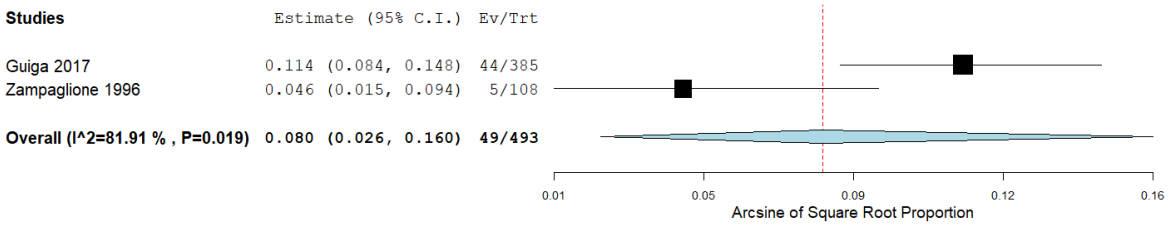


Figure S16: Prevalence of subarachnoid hemorrhage, divided by regions

EUROPE



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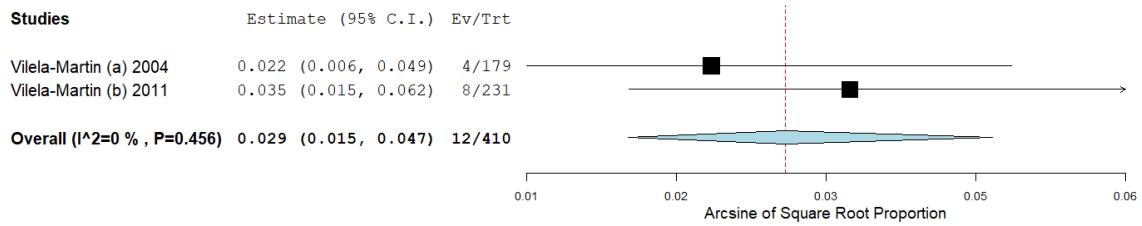


Figure S17: Prevalence of encephalopathy

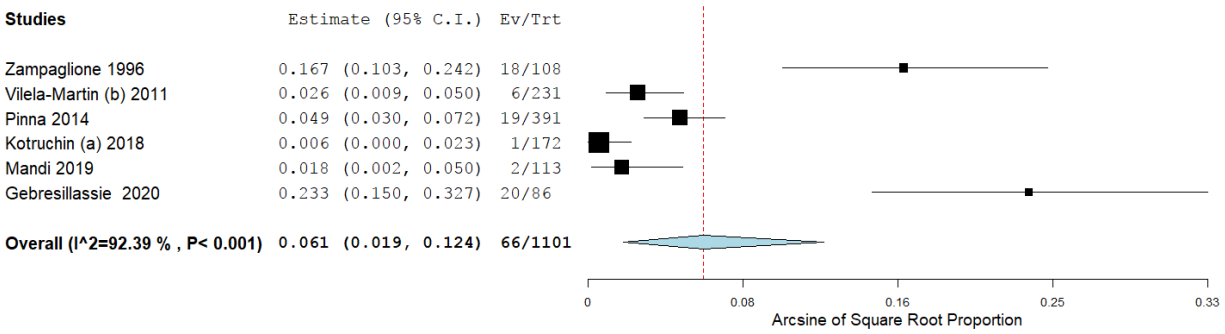
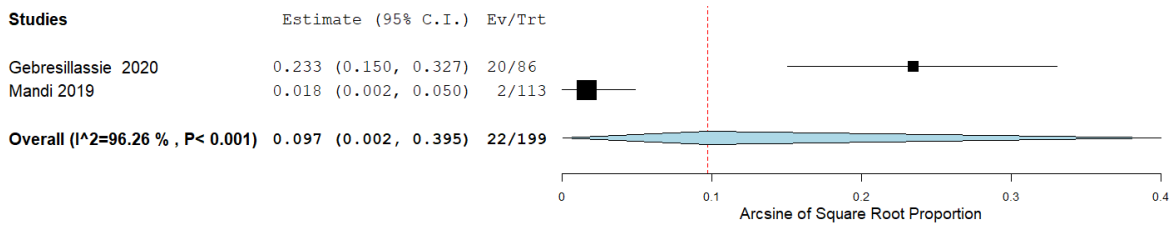


Figure S18: Prevalence of encephalopathy, divided by regions

AFRICA



EUROPE

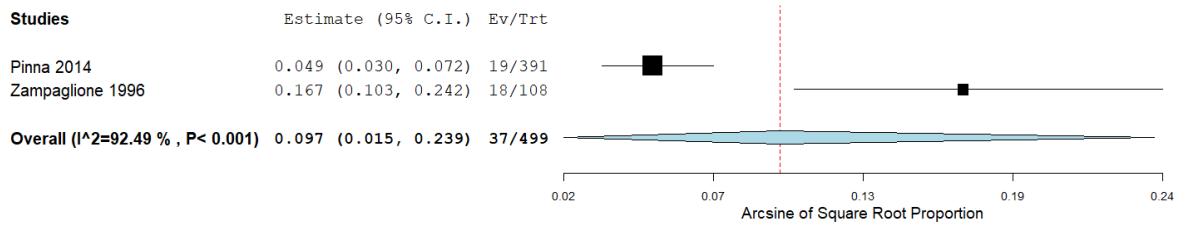


Figure S19: Prevalence of aortic dissection

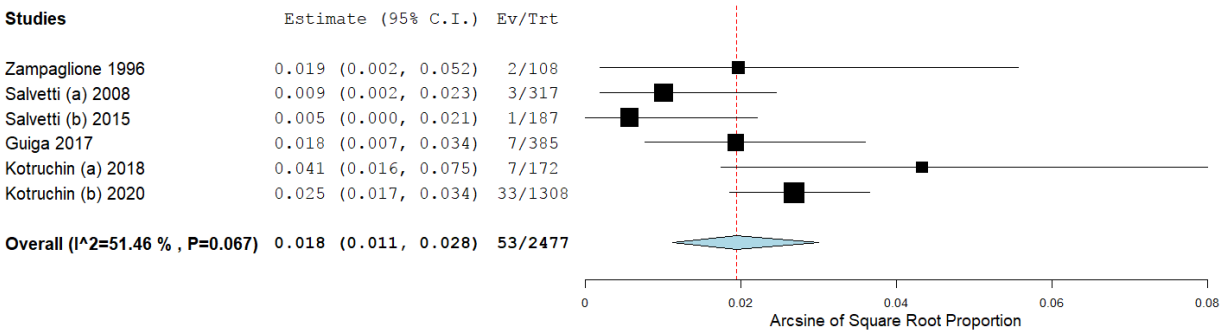
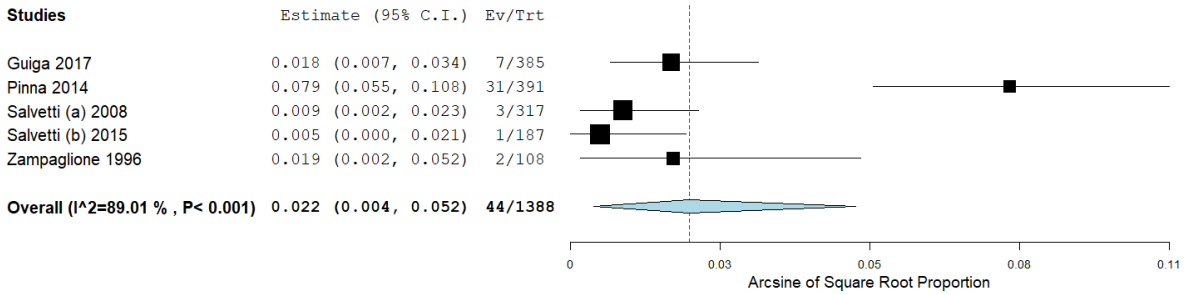


Figure S20: Prevalence of aortic dissection, divided by regions

EUROPE



ASIA

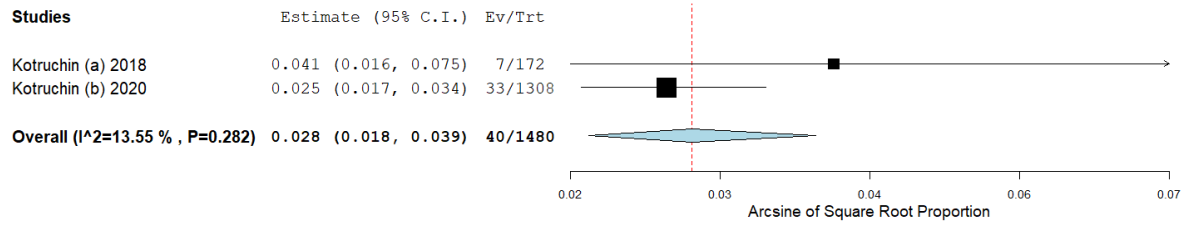


Figure S21: Hospitalization

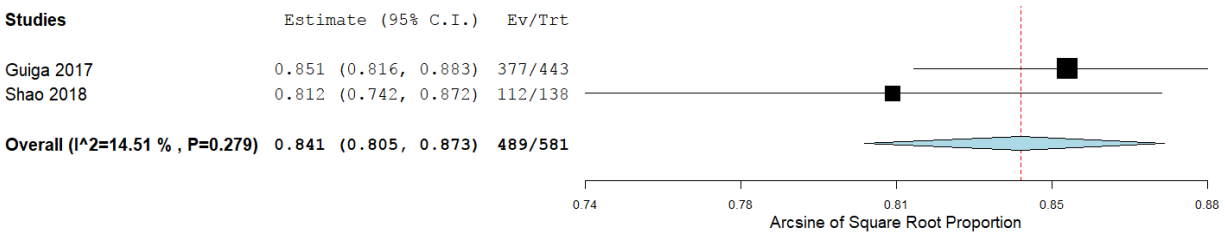


Figure S22: In-hospital mortality

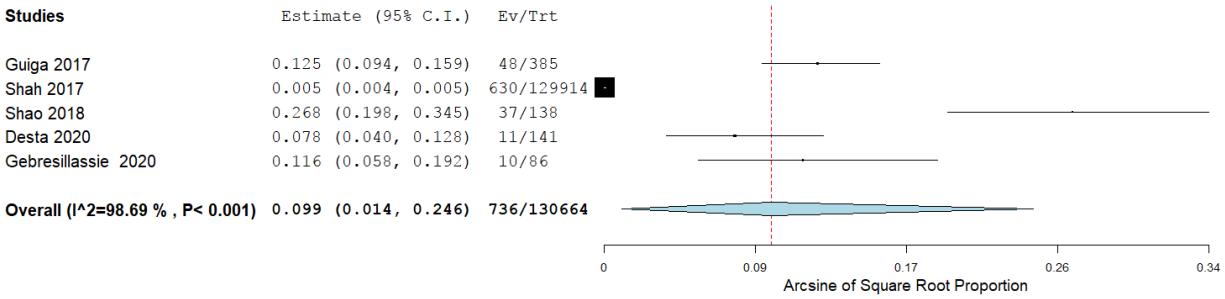


Figure S23: In-hospital mortality, divided by regions

AFRICA