

# **Short and long-time prognosis of hypertensive crisis**

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**Short and long-time prognosis of hypertensive crisis**

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We studied the short and long-time prognosis of hypertensive crisis (HTN-C) and the leading clinical risk factors of HTN-C related mortality.

We performed a literature search using three commonly used scientific databases including 39 original research articles for our systematic review. We performed a random effect meta-analysis to estimate the mortality rates for different subtypes of HTN-C and hazard ratios for clinical covariates with HTN-C related mortality.

The overall mortality rate was 0.06 events per person year (95% CI 0.03-0.12) after HTN-C. The short-time mortality rate may be higher compared to the long-time mortality rate. More severe forms of HTN-C may also lead to higher mortality rates. For each 10-year increase in age, we observed 1.36-fold ( $P < 0.001$ ) higher mortality. Sex and baseline systolic blood pressure were not significantly associated with mortality.

Hypertensive crisis is associated with an increased mortality rate and age is the leading clinical covariate for mortality risk.

**Keywords:** Blood pressure, Hypertension, hypertensive crisis, systematic review

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## 1 Introduction

Hypertension is a major global contributor to disability-adjusted life years (DALYs), reflecting its significant burden on public health worldwide (Stanaway et al. 2018). The ‘rule of halves’ in hypertension still stands accurate: half of all individuals with high blood pressure (BP) remain undiagnosed, half of those diagnosed are not treated, and half of those treated do not achieve adequate BP control (Zhou et al. 2021; Hooker 1999). Although hypertension is typically clinically asymptomatic contributor for mortality, in the US, 0.6% of the emergency department visits are related to hypertension (Janke et al. 2016). Approximately 1-2% of individuals with hypertension develop hypertensive crisis (HTN-C) (Gezie et al. 2023), a severe manifestation of elevated BP, associated with high mortality and target-organ dysfunction risk. Complications induced by HTN-C include heart failure, acute coronary syndrome, aortic dissection, acute renal failure, hypertensive retinopathy, cerebrovascular events, and pulmonary edema which may lead to fatal cardiovascular events (Talle et al. 2022).

Therefore, better understanding of the factors that predict HTN-C-related complications would enhance the ability of the physicians to identify high-risk individuals among those presenting with high BP in emergency services (Murray et al. 2020). Prior systematic reviews have reported, in particular, the prevalence of hypertension-mediated organ damage (HMOD) and in-hospital mortality in individuals treated in emergency departments (Siddiqi et al. 2023; Astarita et al. 2020). However, to the best of our knowledge, no review has summarized the current evidence on the short- and long-term prognosis of hypertensive crisis based on prospective data and survival analyses in representative populations.

We performed a systematic review and meta-analysis of the currently published literature aiming to uncover factors influencing the long- and short-term prognosis in HTN-C. We excluded studies that reported results solely for highly specialized patient groups. For our random-effects meta-analysis, we included all studies that reported HTN-C related mortality incidence and Cox regression results for the mortality. This approach enables the comprehensive assessment of the short- and long-term prognosis of HTN-C and the identification of key risk factors for HTN-C related mortality.

## 2 Methods

We carried out a systematic literature review and meta-analysis for original research articles reporting longitudinal results for hypertensive emergencies. We combined search terms describing different states of hypertensive crisis ("hypertensive emergency" or "hypertensive urgency" or "malignant hypertension" or "hypertensive crises" in title, abstract, Medical Subject Headings [MeSH] keywords or Emtree search terms) with search terms for long and short-term prognosis ("prognosis" or "outcome" in title, abstract, Medical Subject Headings [MeSH] keywords or Emtree search terms). We targeted the search without language or publication date restrictions to three commonly used scientific databases: PubMed, Excerpta Medica database (Embase), and Web of Science (Bramer et al. 2017). This systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines (Page et al. 2021).

We excluded preclinical studies and human studies that reported results exclusively for children or specific clinical populations such as hematological disorders and pre-eclampsia. We also excluded reviews, editorials, case reports, and meeting abstracts. Duplicate search results were automatically identified using Digital Object Identifiers. After the search, manual screening was performed using 1) titles, 2) abstracts, and 3) full manuscript text. The initial screening of all studies was performed by a single author, who also identified studies of uncertain eligibility for further evaluation. The flagged studies were subsequently reviewed by all three authors and studies receiving at least one affirmative vote progressed to the next screening stage or were included in the final review.

We performed meta-analyses to study the mortality rate after HTN-C and to identify the clinical risk factors for HTN-C related mortality. First, we performed random effects meta-analysis of study incidence rates to estimate the overall annual mortality rate for individuals with hypertensive crisis using R package meta (Balduzzi et al. 2019). We defined person time at risk using mean follow-up time multiplied by the number of study participants; we used median follow-up time to estimate mean follow-up time if mean follow-up time was not reported. We used Z-tests to compare annual mortality rates between different subtypes of HTN-C. Second, we performed random-effects meta-analysis to detect risk factors for mortality associated with HTN-C using results from Cox regression results from all available studies. However, we excluded the studies that only reported results for complex composite

endpoints. The analysis was performed using the R package metafor (Viechtbauer 2010). We estimated the heterogeneity between studies using Cochran's Q test and  $I^2$  index. We used R version 4.3.2 in all the analyses. The source code used for the analyses is publicly available at DOI:10.5281/zenodo.15172713. (Joonatan Palmu 2025)

### 3 Results

We performed the search on July 11, 2023, finding 1,637 potential research articles. We excluded 1,231 articles in title screening, 303 in abstract screening, and 64 in full-text screening for final size of 39 articles (Figure 1). We summarize the articles included in the systematic literature review in Table 2 and the articles included in the meta-analysis of the mortality risk in Table 1. To analyze the short- and long-time mortality associated with HTN-C, we defined a short follow-up as up to 1.0 years.

#### 3.1 Definitions for hypertensive crisis in the studies

Hypertensive crisis (HTN-C) is defined as acute elevated systolic BP (SBP) >180 mmHg or diastolic BP (DBP) >110 mmHg with or without target organ damage (Al Bannay et al. 2015; Garadah et al. 2011; Gebresillassie and Debay 2020; Maraey et al. 2021; Nkoke et al. 2022; Wan et al. 2018; Pothuru et al. 2022). In hypertensive urgency (HTN-U) only BP is acutely severely elevated, defined as SBP >180 and DBP >100–110 without any organ damage (Shin et al. 2021; Paini et al. 2021; Guiga et al. 2017; Shao et al. 2018). In hypertensive emergency (HTN-E) the previous severe BP rise is complicated with acute or progressive target organ damage (Paini et al. 2021; Guiga et al. 2017; Shao et al. 2018; Gupta et al. 2022; Park et al. 2022; Leiba et al. 2016; Afonso et al. 2011). Some of the articles also used term acute severe hypertension (HTN-A) (Gore et al. 2010; Katz et al. 2009; Kleinschmidt et al. 2014; Peacock et al. 2011; Szczech et al. 2010; Mayer et al. 2011) and malignant hypertension (HTN-M) (Amraoui et al. 2012; Bureau et al. 2023; Gonzalez et al. 2010; Lane et al. 2009; Rubin et al. 2019; Shantsila et al. 2012) referring to various degrees of HTN-E. We will use the terminology of the authors when summarizing specific articles and favor the more clearly defined terms when summarizing multiple articles simultaneously.

#### 3.2 Short-time mortality associated with HTN-C

In short time follow-up (under one year), history of untreated hypertension and elevated BP levels were linked with higher mortality rates (Yizengaw et al. 2022; Sobrinho et al. 2007). Mortality was also increased in association with HMOD such as markedly reduced kidney function (Szczech et al. 2010; Mandi et al. 2019) (hazard ratio [HR] 2.16, 95% confidence interval [CI] 1.08-4.32, P=0.03) (Mandi et al. 2019)

, neurological impairment (1.8% mortality in HTN-A for stroke) (Mandi et al. 2019; Gore et al. 2010), and acute coronary syndrome (Gebresillassie and Debay 2020). In HTN-A, no difference was observed in the survival between discharged and admitted patients ( $P = 0.69$ ) (Kleinschmidt et al. 2014) and in patients with heart failure compared to healthy controls ( $P=0.62$ ) (Peacock et al. 2011). While individuals with chronic kidney disease (CKD) had higher mortality rates compared to healthy controls ( $P<0.001$ ) in HTN-C, no difference was observed in mortality between individuals with CKD and end-stage renal disease (ESRD;  $P=0.69$ ) (Pothuru et al. 2022). However, individuals with ESRD had a higher proportion of cardiovascular events compared to healthy controls in HTN-C (odds ratio (OR) for cardiac arrest 4.52, 95% CI 1.53–13.3,  $P = 0.01$ ) (Park et al. 2022). While type 2 myocardial infarction was an independent predictor of poor outcome in patients presenting with HTN-C, increased odds of in-hospital mortality was observed only in patients with HTN-U (OR 4.14, 95%CI 1.47–11.62) but not in patients with HTN-E (OR 0.71, 95% CI 0.26–1.97) (Maraey et al. 2021). The overall mortality up to one year was 0.6-8% in HTN-C, 1.8% in HTN-U, and 12.5% in HTN-E (Guiga et al. 2017; Shao et al. 2018).

### **3.3 Long-time mortality associated with HTN-C**

While short-term mortality in individuals with HTN-C is mainly caused by neurovascular events, the significance of neurovascular and cardiovascular events becomes similar after one year follow-up (Guiga et al. 2017). The prognosis of HTN-E may also depend on treatment advances, as one study showed a decrease in 12-month mortality from 16.7% during 1991–1995 to 3.6% in 2006–2010 (Leiba et al. 2016). The overall long-time mortality was 12.1% in HTN-U (Shin et al. 2021) and 37.2% in HTN-E (Afonso et al. 2011). Adverse renal function has been reported as an independent risk factor of long-time mortality in multiple studies (Shin et al. 2021; Amraoui et al. 2012; Lane et al. 2009; Rubin et al. 2019; Shantsila et al. 2012). Prevalent diabetes (HR 3.5, 95% CI 1.7–7.2,  $P<0.001$ ) (Al Bannay et al. 2015), coronary artery disease (HR 1.5, 95% CI, 1.0–2.1,  $P=0.03$ ) (Afonso et al. 2011) and cerebrovascular disease (HR 4.17, 95% CI 1.9–9.0,  $P < 0.001$ ) (Paini et al. 2021) have also been linked to higher mortality rates.

### 3.4 Meta-analysis

The annual mortality rate with individuals with HTN-C is 0.06 events per person year (95% CI 0.03-0.12; Figure 2), HTN-U 0.02 events per person year (95% CI 0.00-0.16; Figure 3), and HTN-E 0.34 events per person year (95% CI 0.15-0.35; Figure 4). We did not observe statistically significant difference between the mortality rate of HTN-C and HTN-E ( $P=0.68$ ) or between HTN-U and HTN-E ( $P=0.84$ ). Dividing the HTN-C data into two groups based on follow-up duration, the short-time mortality rate was 0.19 events per person year (95% CI 0.12–0.32) and long-time rate 0.03 events per person year (95% CI 0.02–0.07); however, the observed difference was not statistically significant ( $P=0.94$ ). We observed high heterogeneity ( $I^2>90\%$ ) between incidence rates between all the studies.

We identified five studies (Table 1) that reported Cox regression results using consistent mortality endpoints (Shin et al. 2021; Reis et al. 2020; Lane et al. 2009; Yizengaw et al. 2022; Afonso et al. 2011). Using information from journal articles, supplementary materials, and private communications with the authors, we obtained required summary statistics for age, sex, and SBP. Our meta-analysis showed that in individuals with HTN-C, each 10-year increase in age was associated with a 1.36-fold higher risk of mortality (95% CI 1.19–1.54,  $P < 0.001$ ; Figure 5A). However, no significant association was observed for male sex (HR 1.17, 95% CI 0.84–1.65,  $P = 0.35$ ; Figure 5B) or SBP (HR 1.14, 95% CI 0.95–1.37,  $P = 0.15$ ; Figure 5C). We detected substantial between-study variance in the results for SBP (Cochran's Q test  $P<0.001$ ,  $I^2=94.3\%$ ) while the heterogeneity for sex (Cochran's Q test  $P=0.17$ ,  $I^2=45.3\%$ ) and age (Cochran's Q test  $P=0.26$ ,  $I^2=38.5\%$ ) was low. Higher heterogeneity supports the choice of random effect meta-analysis.

## 4 Discussion

In this systematic review and meta-analysis, we assessed the long and short-term prognosis of HTN-C and the main risk factors for the HTN-C related mortality. We observed that included studies reported generally consistent findings for HTN-C and the related HMOD. In our meta-analysis, the overall mortality rate in individuals with HTN-C was 0.06 events per person year (95% CI 0.03-0.12). HTN-E (0.34 events per person year) may predict a higher mortality rate compared to HTN-U (0.02 events per person year) but the difference was not statistically significant. The short-time mortality rate was higher (0.19 events per person year) compared to long-time mortality rate (0.03 events per person year) but the difference was not statistically significant. A 10-year increase in individual's age was associated with 1.36-fold (95% CI 1.19–1.54;  $P < 0.001$ ) higher mortality risk while baseline systolic BP and sex were not significantly associated to mortality.

We observed considerable heterogeneity in the reported mortality rates between studies which can be at least partially attributed to differences in study populations and study designs. While the low number of studies reporting mortality rates for HNT-U, HNT-E, and short-time HTN-C reduced the statistical power of our Z-tests, the raw mortality rates reflected the expected trends. Sex and baseline systolic BP were not statistically significant risk factors for mortality. However, the total number of individuals in the meta-analyses was only 868 due to the low number of studies reporting Cox regression results; we also were limited to analyze the three clinical covariates that were reported in more than one article. We observed a potentially harmful trend with the higher systolic BP values with mortality, but for the sex the results are indistinguishable. However, the sex-differentiated cardiovascular risk factors are also age-related, with the protective role of estrogen in particular diminishing after menopause (Vaura et al. 2022).

Although our study is grounded in strong methodological approach, our results must be interpreted in the context of their limitations. Due to the large number of publications available, we had to limit the scope of the current study to just mortality. However, the small number of studies reporting mortality rates or Cox regression results limited the scope and power of our meta-analyses. Varying terminology, use of composite endpoints, and the

heterogeneity in the study designs reduced our ability to directly compare results across different studies in our analyses.

In conclusion, HTN-C increases both short- and long-time mortality rates and older individuals have higher risk of mortality compared to younger individuals. Different studies reported generally consistent findings for HTN-C and the related HMOD while we observed high heterogeneity between incidence rates and HR that can be contributed to differences in study populations and designs. Our knowledge about HTN-C and HMOD could be improved by performing large population-based cohort studies conducted in diverse study populations.

## 5 Author contributions

All three authors participated in developing the subject of the review. Ville Paavonsalo is accountable for the search terms in the databases with the help of information specialist of University of Turku. When search results were compiled VP reviewed the articles in three stages: 1) by title, 2) by abstract, and 3) by full-text. When there was uncertainty about whether an article should be included all three authors voted. Joonatan Palmu participated in conduction of the meta-analysis. The writing process of the article was carried out by VP under supervision of JP and MV. VP prepared the table summarizing the articles included in the review.

## 6 Tables

Table 1 The characteristics of studies included in the meta-analysis of the mortality risk.

| Study             | Study population          | Age               | Male   | N  | N event | Outcome                       | Follow-up                      |
|-------------------|---------------------------|-------------------|--------|--|---------|-------------------------------|--------------------------------|
| Shin et al 2021   | Gyeonggi-do, Korea        | 59.0±17.3 years   | 49.0%  | 4488 individuals with hypertensive urgency in emergency department   | 612     | All-cause mortality           | 5.2 years                      |
| Reis et al 2020   | Mwanza, Tanzania          | 62 years          | 32.7%  | 150 individuals with hypertensive urgency in outpatient clinic       | 53      | Hospitalization and mortality | December 2018 to February 2020 |
| Lane et al 2009   | Birmingham, UK            | 48.2 years        | 63.2 % | 365 individuals with malignant hypertension attending study hospital | 203     | All-cause mortality           | 8.7 years                      |
| Yizengaw et al    | Jimma, Ethiopia           | 52.8 ± 13.6 years | 77.1%  | 140 individuals with hypertensive emergency attending study hospital | 16      | All-cause mortality           | 8.5±3.6 days                   |
| Afonso et al 2011 | Detroit and Michigan, USA | 57.6 years        | 46.7%  | 567 individuals with hypertensive emergency admitted to hospital     | 211     | All-cause mortality           | 3.1 years,                     |

Table 2. The summary of studies included in the systematic review.

| Study               | Study population  | Follow-up                     | Main findings   |
|---------------------|---|-------------------------------|---|
| Guiga et al 2017    | N=670: HTN-E=385, HTN-U=285                             | 12 months                     | 12-month mortality differed between HTN-E and HTN-U groups (P=0.001) and the in-hospital mortality was statistically significantly higher for HTN-E than for HTN-U.   |
| Afonso et al. 2011  | HTN-E=567 with 381 individuals with elevated troponin T | 3.1 years                     | Age, coronary artery disease, and blood urea nitrogen level predicted mortality in HTN-E. Troponin elevation did not predict mortality in multivariate analysis.  |
| Rubin et al 2018    | HTN-M=153, multi-organ damage hypertension N=15         | 4 years                       | Out of 153 individuals with HTN-M, 6% died during follow-up. Worsening renal function in follow-up was documented in 22 patients (14%)  |
| Merlo et al 2012    | HTN-E=15, HTN-U=50, asymptomatic BP elevation=99        | 1 year                        | No difference between occurrence of cardiovascular events in asymptomatic patients and HTN-U/HTN-E. Seven patients died during follow-up, mostly because of congestive heart failure.                           |
| González et al 2010 | HTN-M=227   | 7.8±7.3 years                 | Of the 227 patients with HTN-M, 4.0% died during initial admission and 2.6% during follow-up. Smoking and SBP at presentation were factors that predicted cardiovascular events.                                |
| Amraoui et al 2012  | HTN-M=120   | 5.6 years (IQR 2.3-9.0 years) | Out of 120 patients, 15% died during follow-up. Initial serum creatinine $\geq 175$ $\mu\text{mol/L}$ and uncontrolled hypertension (BP $\geq 140/90$ mmHg) during follow-up were main predictors of mortality. |

|                      |   |  |  |
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| Leiba et al 2016     | HTN-E=142   | 1 year   | The average one-year mortality was 12.9%. Mortality decreased significantly between the compared periods 1991–1995 and 2006–2010.  |
| Paini et al 2021     | HTN-E 158, HTN-U=737  | 1±0.4 years  | During the follow-up, 28 fatal cardiovascular events occurred. Hypertensive emergency, age, diabetes and a history of a cerebrovascular disease, but not sex, were predictors of fatal event.  |
| Al Bannay et al 2015 | 145 diabetic individuals and 152 nondiabetic individuals with HTN-C | 2.5 (0.1–2.7) years for nondiabetic individuals and 2.0 (0–2.3) years for diabetic individuals | Out of 297 patients, 12.5% died during follow-up. Mortality between diabetic individuals and non-diabetic individual groups differed statistically significantly ( $p=0.001$ ). Also, non-fatal events were more common in diabetic individuals. |
| Preston et al 2019   | N=156 with SBP $\geq$ 220 mmHg or DBP $\geq$ 120 mmHg               | 2 years  | The hypertensive cohort discovered 99 new hypertensive target organ events. 4 deaths ear follow-up.  |
| Gupta et al 2022     | HTN-E=205   | 1-4 days   | Elevated cTnI group had 10.8% mortality while no deaths were observed in controls ( $P<0.002$ ).   |
| Vlcek et al 2007     | HTN-U=384, CG=295   | 4.2 years (IQR 2.9–5.7 years)  | No significant differences in fatal cardiovascular events between HTN-U (n=6) and hypertensive control group (n = 7)   |

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|----------------------|--|------------------------|---|
| Pothuru et al. 2023  | HTN-C=37,214                           | 1 year                 | Overall, in-hospital mortality, 30-day, and 1-year mortality were 0.6%, 2.3%, and 21.8%, respectively. 30-day mortality risk factors were age, female sex, black race and a history of stroke. Additional risk factors for 1-year mortality were diabetes, heart failure and peripheral vascular disease. |
| Pacheco et al 2013   | HTN-E=412, HTN-U=126                   | No follow-up           | The mortality rate was 4.6% in HTN-E and 0.8% in HTN-U.   |
| Park et al 2022      | ESRD=3,177 and CG=3,177 with HTN-E     | No follow-up           | No difference in the in-hospital mortality of HTN-E patients with and without ESRD (P=0.86). Individuals with ESRD had higher odds of cardiac arrest and acute pulmonary edema.   |
| Maraey et al 2021    | HTN-E=37,742, HTN-U=59,590             | 0.2 years              | Out of 101,211 patients, 0.002% died during hospitalization. This study showed that T2MI increases odds of in-hospital mortality in patients with HTN-U but not statistically in patients with HTN-E.   |
| Shantsila et al 2012 | N=365 with HTN-M                       | 7 years (1.5–14.8) IQR | Out of 341 patients with HTN-M, 56% died during follow-up. Predictors of death or dialysis were in multivariate analysis: age, smoking, proteinuria and creatinine level.   |
| Bureau et al 2023    | HTN-M=114                              | 3 years (IQR 1–7)      | During follow-up, only 1 death was observed, while 13% of patients were lost during follow-up.  |
| Sobrinho et al 2007  | HTN-C=57, hypertensive pseudocrisis=53 | 0.4±0.1 years          | All deaths were in the HTN-C group (P=0.0004). Patients who died had higher BP levels and more target organ damage.   |

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| Garadah et al 2011       | HTN-C=241, HTN-E=62, HTN-U=176 | Not reported                                | In the HTN-E group, five patients died, four had intra-cerebral bleeding and one went into severe pulmonary congestion and cardiac arrest. No deaths occurred in the HTN-U group.                               |
| Gokdemir et al 2018      | HTN-E=48, HTN-U=48             | Not reported                                | Out of 48 patients with HTN-E, 16.7% had a cardiac arrest within 24 h of hospital admission.  |
| Roubsanthisuk et al 2010 | HTN-E=184                      | 1.2 ±1.1 years, other group 4.3 ±0.3 years  | Out of 184 patients with HTN-E, hospital mortality was 15 % and total mortality 35.3 %. Infections and stroke with its complications were most common reasons of death.   |
| Yizengaw et al 2022      | HTN-E=140                      | Follow-up from admission to discharge/death | Out of 140 patients, 11.4% died during follow-up with average time to death of 2.88±2.47 days. Age, regular physical exercise and history of untreated hypertension were associated with in-hospital mortality. |
| Nkoike et al 2022        | HTN-E=56, HTN-U=39             | Not reported                                | Out of 95 patients, 6.3% died during follow-up. Death was more likely in HTN-E group than HTN-U group. In bivariate analysis cerebral infarction predicted death.   |
| Mandi et al 2019         | HTN-E=113, HTN-U=53            | 0.1 years                                   | Out of 166 patients, 21.7% died during follow-up. History of HTN, acute brain-related damage and renal dysfunction were linked with the risk of mortality.  |

|                           |  |  |  |
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| Gebresillassie et al 2020 | HTN-E=86, HTN-U=166                      | Not reported                                   | Out of 252 patients with HTN-E, 3.9% died during hospitalization. Cause of death were acute renal failure (n=4), intracranial hemorrhage (n=4), and acute myocardial infraction (n=2).   |
| Kolo et al 2012           | N=735 hypertension-related complications | Not reported                                   | Out of 735 patients with HTN-E, 16.7% died during follow-up. There was no difference in the deaths between men (n=59) and women (n=64).  |
| Lane et al 2009           | HTN-M=446                                | Median follow-up 8.6 (2.6–20.9) years.         | Out of 446 patients with HTN-M, 55.6% died during follow-up. In multivariate analyses age, decade of diagnosis, baseline serum creatinine, and follow-up SBP were independent risk factors for death.                                      |
| Shao et al 2018           | N=203, HTN-E=138, HTN-U=65               | Not reported                                   | Out of 203 patients, 19.2% died during hospitalization. In-hospital mortality was higher in HTN-E (n=37) compared to HTN-U (n=2) with $P < 0.0001$ .   |
| Shin et al 2021           | HTN-U=4,488                              | Median follow-up 3.1 years (IR; 2.0–4.1 years) | Out of 4,488 patients, 13.6% died during the follow-up. In the multivariate adjusted analyses, age $\geq 60$ years, male sex, history of chronic kidney disease and proteinuria were independent predictors of 3-year all-cause mortality. |

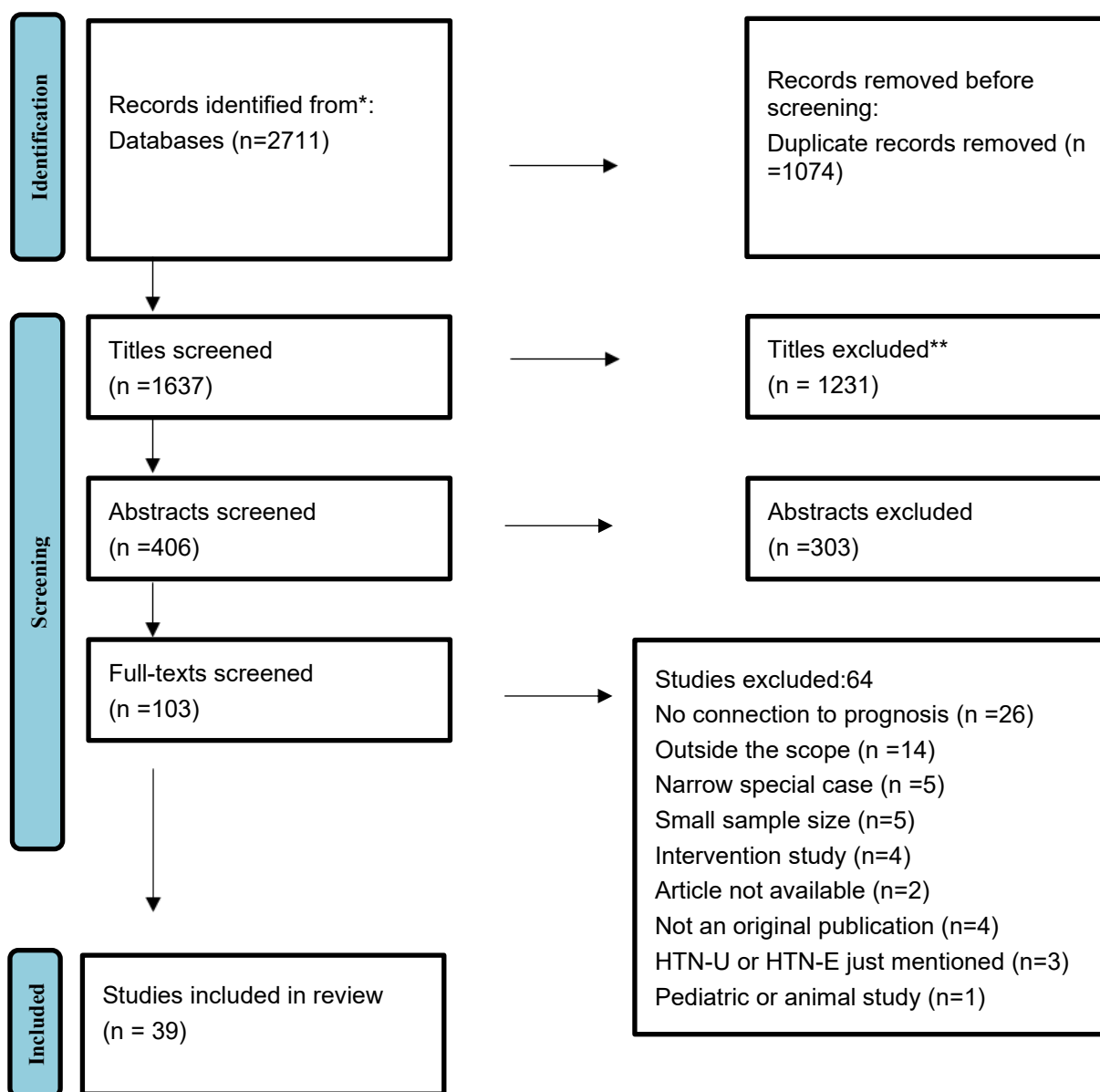
|                         |   |                |   |
|-------------------------|---|----------------|---|
| Pothuru et al 2022      | Emergency visits about HTN-C: Non-CKD=557,413, CKD 77,971, ESRD=44,948. | No follow-up   | Out of 680,332 emergency department visits about HTN-C, 0.11% resulted in death during hospitalization. The mortality was higher in individuals with CKD compared to healthy controls ( $P<0.0001$ ) while no difference was observed comparing individuals with CKD and ESRD ( $P=0.69$ ). |
| Wan et al 2018          | HTN-C=50  | 7.5–16.5 years | Development of AKI was not associated with increased mortality ( $P=0.78$ ). Individuals with underlying CKD had 6.0 odds to develop AKI ( $P=0.02$ ).  |
| Gore et al 2010         | HTN-A=1,009   | 0.5 years      | Out of 1,009 patients with HTN-A, 1.8% died during follow-up. Causes of death included stroke and cardiovascular diseases   |
| Katz et al 2009         | HTN-A=1,588   | 0.2 years      | Out of 1,588 patients with HTN-A, 6.9% died during hospitalization and 11% during follow-up. Fifth of patient that died at hospital suffered from intracranial hemorrhage.  |
| Kleinschmidt et al 2014 | HTN-A=1,053   | 0.5 years      | No difference in mortality between discharged (3.3%) and admitted patients (2.9%) with $P=0.69$ . The 90-day readmission rate was greater for admitted versus discharged patients ( $P=0.04$ ).   |

|                     |  |           |   |
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| Mayer et al 2011    | 432 neurological patients and 1,134 non-neurological controls with HTN-A | 0.2 years | Higher mortality was observed in neurologic (24%) compared to non-neurologic patients (6%) with HTN-A ( $P<0.001$ ). Among neurologic patients non-BP-related risk factors for 90-day mortality were older age, history of cardiac disease, and lower admission GCS scores. |
| Peacock et al 2010  | 302 heart failure patients and 897 controls with HTN-A                   | 0.2 years | Death rates at hospital ( $P=0.62$ ) and during follow up ( $P=0.60$ ) were similar between heart failure patients with HTN-A and controls with HTN-A.  |
| Szczzech et al 2010 | HTN-A=1566   | 0.5 years | Severity of AKI increased probability of in-hospital death ( $P<0.001$ ). Higher age, male gender, white versus black race and poorer baseline kidney function were predictors of death during follow-up.   |
| Reis et al 2020     | HTN-U=150  | 1 year    | 35% of individuals with HTN-A were hospitalized or died within 1 year follow-up. The strongest predictor for the study outcome was self-reported medication adherence   |

N indicates sample size; HTN-A, acute severe hypertension; HTN-E, hypertensive emergency; HTN-U, hypertensive urgency; HTN-M, malignant hypertension; HTN-C, hypertensive crises; CG, control group; ESRD, end stage renal disease; CKD, chronic kidney disease; AKI, acute kidney injury

## 7 Figures

Figure 1 Prisma plot



From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ* 2021;372:n71. doi: 10.1136/bmj.n71

Figure 2. Meta-analysis for the annual mortality in individuals with hypertensive crisis.

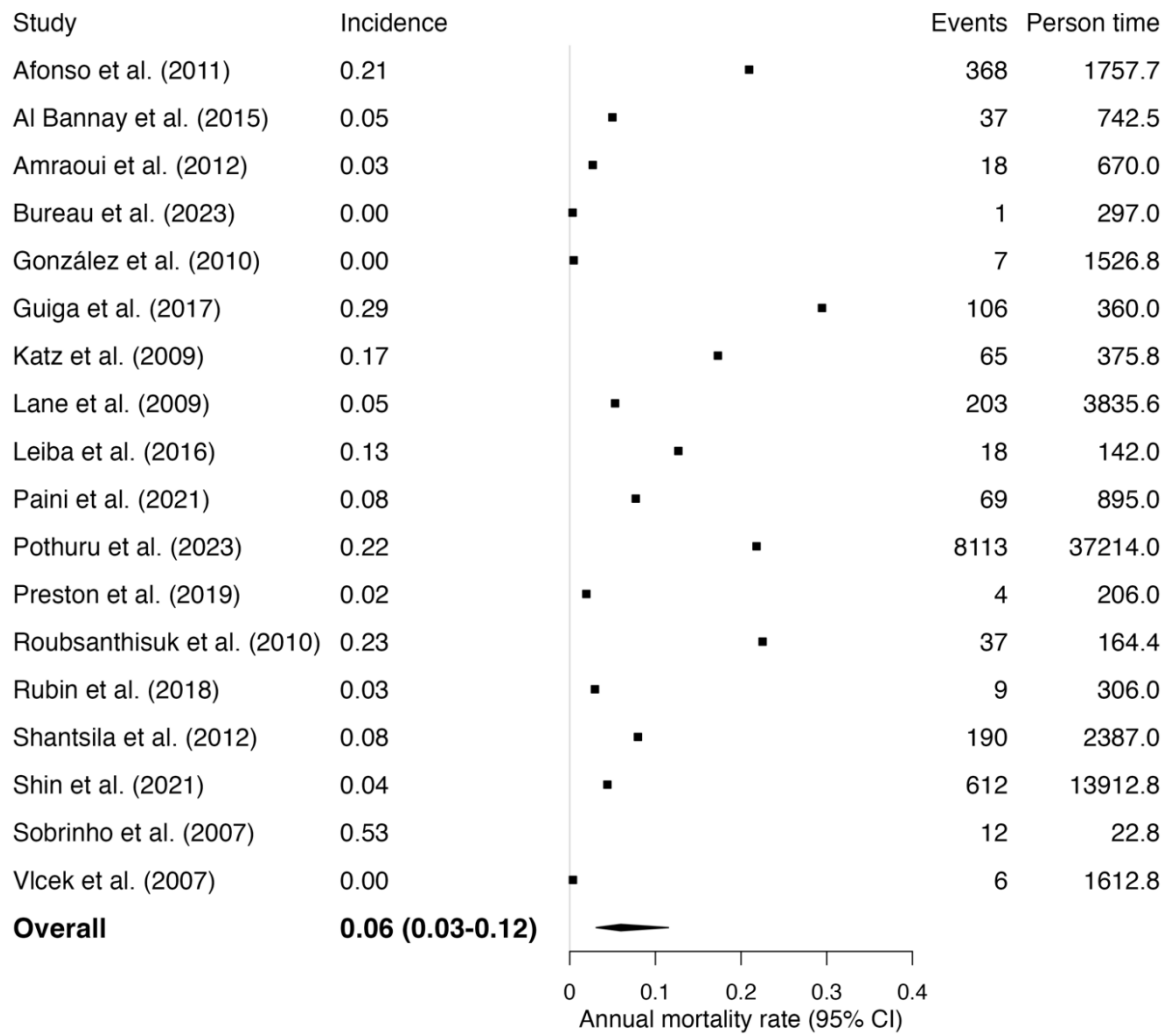


Figure 3. Meta-analysis for the annual mortality in individuals with hypertensive urgency.

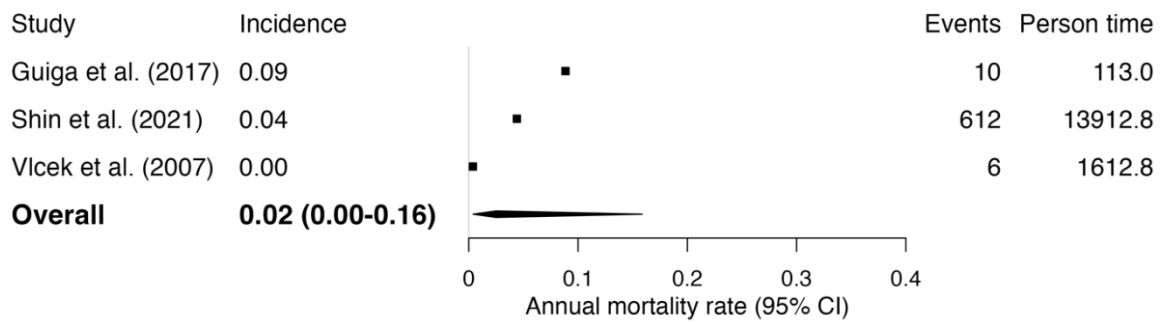


Figure 4. Meta-analysis for the annual mortality in individuals with hypertensive emergency.

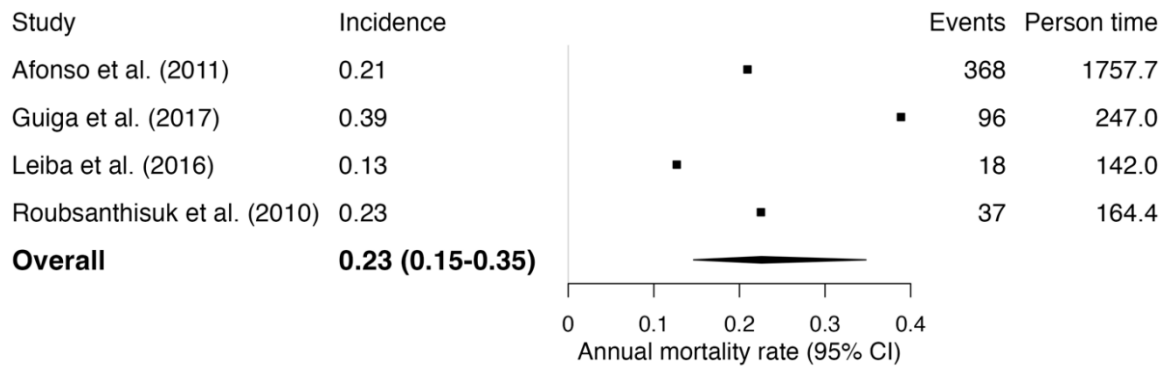
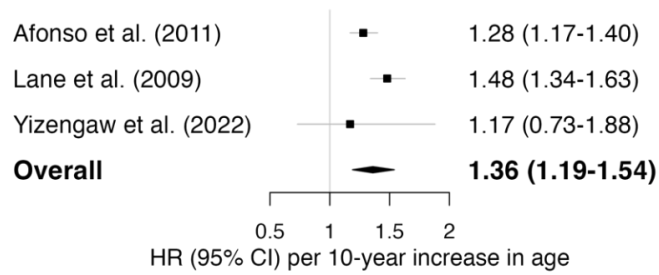
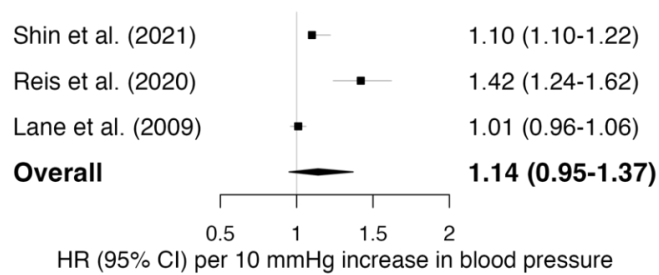
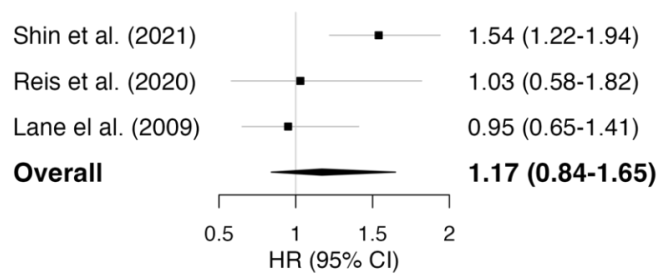


Figure 5. Meta-analysis for the risk of mortality in individuals with hypertensive emergency.

**A. Age****B. Systolic blood pressure****C. Male sex**

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