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SYSTEMATIC REVIEWS (WITH OR WITHOUT META ANALYSES)

The prognostic value of emergency department measured hypertension: A systematic review and meta-analysis

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Abstract

Objectives: The objective was to assess the prognostic value of hypertension detected in the emergency department (ED).

Methods: The ED presents a unique opportunity to predict long-term cardiovascular disease (CVD) outcomes with its potential for high-footfall, and large-scale routine data collection applied to underserved patient populations. A systematic review and meta-analyses were conducted to assess the prognostic performance and feasibility of ED-measured hypertension as a risk factor for long-term CVD outcomes. We searched MEDLINE and Embase databases and gray literature sources. The target populations were undifferentiated ED patients. The prognostic factor of interest was hypertension. Feasibility outcomes included prevalence, reliability, and follow-up attendance. Meta-analyses were performed for feasibility using a random effect and exact likelihood.

Results: The searches identified 1072 studies after title and abstract review, 53 studies had their full text assessed for eligibility, and 26 studies were included. Significant heterogeneity was identified, likely due to the international populations and differing study design. The meta-analyses estimate of prevalence for ED-measured hypertension was 0.31 (95% confidence interval 0.25–0.37). ED hypertension was persistent outside the ED (FE estimate of 0.50). The proportion of patients attending follow-up was low with an exact likelihood estimate of 0.41. Three studies examined the prognostic performance of hypertension and demonstrated an increased risk of long-term CVD outcomes.

Conclusion: Hypertension can be measured feasibly in the ED and consequently used in a long-term cardiovascular risk prediction model. There is an opportunity to intervene in targeted individuals, using routinely collected data.

KEYWORDS
cardiovascular disease, emergency medicine, preventative medicine

BACKGROUND

Cardiovascular disease (CVD) remains the leading cause of premature death in the western world.[1] It is estimated that population-based primary prevention to reduce mean blood pressure and cholesterol by 10% would reduce the incidence of major CVD by 45%.[2] However, because important risk factors for CVD such as hypertension and dyslipidemia are usually asymptomatic, identification of at-risk individuals can be challenging unless they regularly attend primary care appointments.

While there has been a tremendous technological advance that can allow the rapid diagnosis of acute coronary syndrome (ACS) in the emergency department (ED), few examine long-term CVD. In a feasibility study evaluating use of the Manchester Acute Coronary Syndromes (MACS) decision aid in practice,[3] patients were dissatisfied with an approach that simply informed them that they "do not have ACS" and did not address future cardiovascular risk.

There were 23.4 million patient presentations to the United Kingdom's EDs in 2016, and this has been increasing by 10% each year, which is mirrored in the United States.[4,5] The increase in ED attendance represents a paradigm shift in the way patients access health care, and although this has caused many previously noted problems, it also presents opportunity. Patients who do not see their primary care practitioner frequently are more likely to attend the ED. Therefore, the ED interaction is with a portion of society underserved by primary care.[6] Preventative medicine is not a new concept to emergency medicine, and it has been previously researched and successfully implemented.[7] Patients demand and expect clinical staff in the acute care setting to have tools to inform them of their long-term cardiovascular risk.[3] This presents an excellent opportunity for emergency physicians to identify a large population of patients at high risk of future CVD, at a time when they are likely to be particularly receptive. This systematic review sought to establish the evidence base for the predictor hypertension when measured in the acute care setting, which is commonly used in long-term cardiovascular risk prediction. The objective was to determine whether hypertension detected in the ED can be used to predict long-term CVD outcomes.

METHODS

We conducted a systematic review and meta-analysis in accordance with Preferred Reporting Items for Systematic Reviews (PRISMA) and meta-analysis guidelines and have registered on PROSPERO (CRD42018110517).[8,9]

Search question

The question structure of population, prognostic factor, and outcome was used (PFO).[10] The target population was ED patients and the outcome was long-term CVD outcomes (>12 months). The prognostic factor of interest was hypertension.

Studies to be included were those that matched the PFO question, conducted in the past 20 years, were randomized controlled trials or observational studies, and were conference abstracts or published/in press studies, in English language.

The prognostic factor of interest was hypertension measured in the ED, it was envisaged that the most widely available variable would be dichotomous around the common clinically significant threshold of 140/90 mmHg. The U.K. guidelines state that to diagnose hypertension serial readings should be used alongside ambulatory measurements or home blood pressure monitoring.[11] It was not envisaged that this would be universal in the EDs but we planned to attempt sensitivity analysis of the different measurement techniques if possible, to attempt to detect any effect it may have had on measurement.[12]

Outcome measurement

We examined the feasibility of the measurement of hypertension and its prognostic characteristics for cardiovascular outcomes. Feasibility measures included study prevalence, persistence of abnormal readings, and proportion of patient attendance for follow-up. The cardiovascular outcomes included acute myocardial infarction, coronary revascularisation, coronary heart disease, angina, stroke, transient ischemic attack, cerebrovascular event, and death (all cause and CVD).

Search methods for identification of studies

Information sources

The following traditional and gray information sources were searched independently by two researchers: the electronic databases MEDLINE and Embase (see Data Supplement S1 [available as supporting information in the online version of this paper, which is available at http://onlinelibrary.wiley.com/doi/10.1111/acem.14324/full] for search terms), International Committee of Medical Journal Editors, World Health Organization–International Clinical Trials Registry Platform, World Medical Association, British Library Thesis, secondary reference checking, guideline clearing house (https//www.guidelines.com), and University of Manchester library search; and the opinion of experts in the field, Professor Richard Body and Professor Tony Heagerty.

Data collection

The studies returned from the initial searches had their title and abstract screened by two independent clinical–academic reviewers. Selected papers then underwent full-text review by the same researchers; when disagreement occurred a third independent researcher reviewed the paper and agreement was met by consensus.

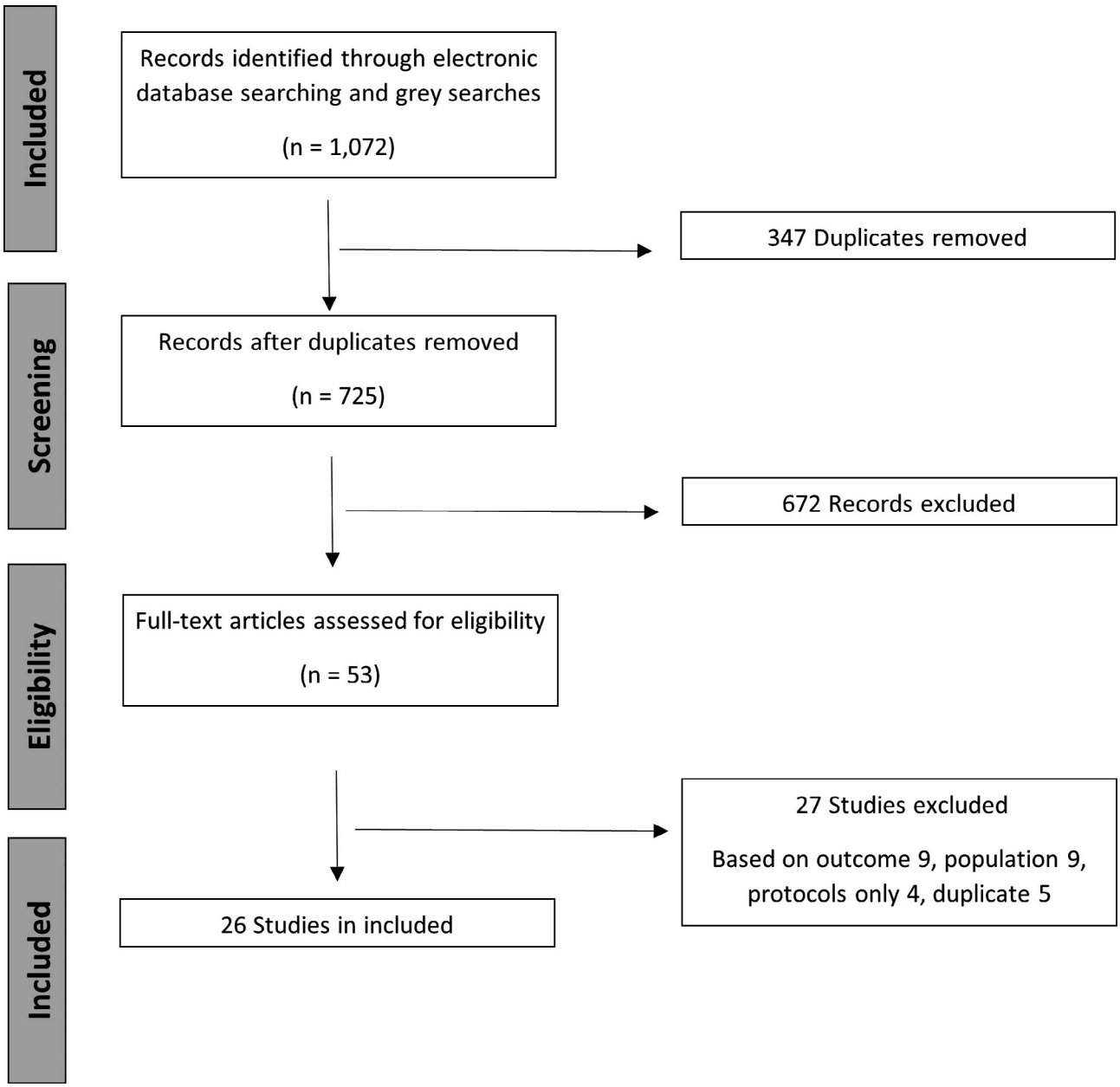

FIGURE 1 Flowchart of blood pressure study selection process

Bespoke electronic study and data collection forms were created for the purpose of the systematic review. We used the Quality In Prognosis Studies (QUIPS) tool to analyze the risk of bias in each prognostic factor study.[13]

To measure the value of the prognostic factor, we extracted data with a preference toward hazard ratio and adjusted measures. To assess heterogeneity we calculated I^2 and when a large outlier was identified examined the effect of removal.

Data synthesis

If fewer than three studies reported the estimate of interest, a narrative review is given. Otherwise, a meta-analysis is performed, using a random effect and exact likelihood for binomial distribution described by Hamza et al.[14] to accommodate the heterogeneity between studies. We used the statistical software R, including packages metaphor and ggplot2.[15-17]

RESULTS

Search results

All searches were conducted on the October 27, 2020. We identified 1,072 studies, of which 725 were unique. After title and abstract review, 53 studies had their full text assessed for eligibility, and 26 studies were included (Figure 1): 17 were from the United States;

TABLE 1 Characteristics of the included studies examining hypertension

Author, Country, Year	Study design	N	Measurement of BP	Recruitment period	Follow-up	Outcome measure	Risk of bias
Adhikari, United States, 2016[35]	R	179	ED	2011	N/A	BP advice	M
Backer, United States, 2003[36]	P	407	3 × ED	2000	6 months	F/U BP	M
Baumann, United States, 2007[23]	P	991	3 × Researcher	2004	N/A	Descriptive	M
Baumann, United States, 2009[26]	R	4,245	ED	2005–2006	N/A	Repeat ED BP	M
Cienki, United States, 2013[34]	R	1,000	ED	2005–2010	N/A	BP advice	M
Cline, United States, 2006[39]	R	1,391	EPR	2003–2004	3 months	Secondary care F/U	M
Collins, UK, 2008[22]	P	765	2 x Researcher	2005–2006	6 months	Primary care F/U	M
Dolatabadi, Iran, 2014[28]	P	346	2 x ED	2009 – 2010	30 day	Prevalence	M
Fleming, UK, 2005[19]	P	991	2 x Researcher	2004	30 days	Sustained HTN	M
Goldberg, United States, 2017[31]	P	151	3 x Researcher	2014–2017	2 weeks	Sustained HTN	M
Julliard, United States, 2012[30]	R	662	EPR	2009	3 months	Primary care F/U	M
Karras, United States, 2005[20]	P	7,238	1 X ED	2002	30 day	Primary care F/U	M
Lee, South Korea, 2018 [42]	R	262.927	EPR	2002–2013	10 years	MACE	M
Masood, Canada, 2016[43]	R	206,147	EPR	2002–2012	2 years	All-cause mortality	M
McNaughton, United States, 2015[18]	R	701,952,422	EPR	2006–2012	N/A	Descriptive	M
Meurer, United States, 2019[41]	P	201	1 x ED 1 x self reported	2014–2015	3 months	Sustained HTN	M
Oras, Sweden, 2020[32]	R	300,193	EPR	2010–2016	6 years	MACE	M
Shah, United States, 2011[27]	R	601	EPR	2009–2010	N/A	F/U	M
Shiber-Ofer, Israel, 2015[38]	P	195	ED	2009–2010	5 years	F/U BP	L
Souffront, United States, 2016[33]	R	2,367	EPR	2014–2015	N/A	N/A	M
Svenson, United States, 2008[24]	R	2,821	EPR	2006	1 year	Descriptive	M
Tan, Australia, 2013[29]	P	534	1 x Researcher	2010–2011	5 weeks	Descriptive	M
Tanabe, United States, 2008[37]	P	175	2 x ED	2005–2006	1 week	Sustained HTN	L
Tilman, United States, 2007[21]	R	1,574	EPR	2004	N/A	BP advice	M
Tsoi, Hong Kong, 2012[40]	P	245	2 x ED	2010	2 weeks	Primary care F/U	M
Umscheid, United States, 2008[25]	R	2,061	EPR	2005	N/A	Descriptive	M

Abbreviations: R = retrospective; P = prospective; EPR = electronic patient record; N/A = not applicable; F/U = follow-up; HTN = hypertension; BP = blood pressure; MACE = major adverse cardiac events; H = high risk of bias; M = moderate risk of bias; L = low risk of bias.

two from the United Kingdom; and one each from Australia, Canada, South Korea, Israel, Iran, Sweden, and Hong Kong (Table 1). There were 11 prospective studies with the majority being retrospective. There was a large range in population size; McNaughton et al.[18] had by far the most participants at nearly 702 million, the implications of which are discussed later. Fifteen of the studies reported an estimate of prevalence[18–32] and the persistence of hypertension in eight studies within the ED[20,23,26,31,33–36] and 12 outside of ED.[19,20,22,28,30,31,36–41] Follow-up attendance was reported in eight studies[20,22,29,30,33,36,39,40] and three reported the prognostic performance of hypertension for CVD.[32,42,43]

Risk of bias within studies

The QUIPS tool was used to analyze the risk of bias; none were found to have a high risk of bias. Only two studies, Tanabe et al.[37] and Shiber-Ofer et al.,[38] were found to have a low risk of bias with the remainder being rated moderate. Most demonstrated a moderate risk in the study participation domain for inclusion criteria. Some studies accounted for the potential confounders of fear and anxiety.[19,35–37] They all demonstrated a persistence of hypertensive readings despite the presence of these factors. The failure to account for these potential confounders was deemed to be a moderate risk of bias for this domain.

Prevalence of hypertensive readings

The prevalence of a single hypertensive reading (≥140/90 mmHg) ranged from 0.16 to 0.62[21,31] and there was significant heterogeneity with the percentage of variation across studies estimated at 99.7% (I^2). This is possibly due to the variety of populations included and different trial designs. Meta-analysis resulted in an estimated pooled study prevalence of 0.31 (95% confidence interval [CI] = 0.25 to 0.37). The largest study, McNaughton et al.,[18] was removed in a sensitivity analysis and the resulting estimate was 0.31 (95% CI = 0.25 to 0.39; Figure 2).

TABLE 2 Risk of bias in studies examining hypertension

Author, Year	Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Domain 6	Overall
Adhikari, 2016 [35]	Moderate	Low	Moderate	N/A	Moderate	Low	Moderate
Backer, 2003[36]	Moderate	Low	Low	Low	Moderate	Low	Moderate
Baumann, 2007[23]	Low	Low	Low	Low	Low	Moderate	Moderate
Baumann, 2009[26]	Moderate	Low	Moderate	N/A	Moderate	Moderate	Moderate
Cienki, 2013[34]	Low	Low	Moderate	Moderate	Moderate	Moderate	Moderate
Cline, 2006[39]	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate	Moderate
Collins, 2008[22]	Moderate	Low	Low	Low	Low	Moderate	Moderate
Dolatabadi, 2014[28]	Low	Moderate	Low	Low	Low	Moderate	Moderate
Fleming, 2005[19]	Low	Moderate	Low	Low	Low	Low	Moderate
Goldberg, 2017[31]	Low	Low	Low	Low	Moderate	Low	Moderate
Julliard, 2012[30]	Moderate	Moderate	Low	Moderate	Moderate	Low	Moderate
Karras, 2005[20]	Low	Low	Moderate	Moderate	Moderate	Moderate	Moderate
Lee, 2018[42]	Moderate	Moderate	Moderate	Low	Moderate	Low	Moderate
Masood, 2016[43]	Moderate	Moderate	Moderate	Moderate	Moderate	Low	Moderate
McNaughton, 2015[18]	Moderate	Moderate	Moderate	N/A	Moderate	Moderate	Moderate
Meurer, 2019[41]	Low	Moderate	Moderate	Low	Low	Low	Moderate
Oras, 2020[32]	Low	Low	Moderate	Moderate	Moderate	Low	Moderate
Shah, 2011[27]	Moderate	Low	Moderate	Moderate	Moderate	Moderate	Moderate
Shiber-Ofer, 2015[38]	Low	Low	Low	Low	Low	Low	Low
Souffront, 2016[33]	Moderate	Low	Low	Moderate	Low	Moderate	Moderate
Svenson, 2007[24]	Moderate	Moderate	Low	Low	Moderate	Low	Moderate
Tan, 2013[29]	Low	Low	Low	Low	Low	Moderate	Moderate
Tanabe, 2008[37]	Low	Low	Low	Low	Low	Low	Low
Tilman, 2006[21]	Low	Low	Low	Low	Moderate	Low	Moderate
Tsoi, 2012[40]	Low	Low	Low	Low	Low	Moderate	Moderate
Umscheid, 2008[25]	Moderate	Low	Low	Moderate	Low	Low	Moderate

Note: This was conducted using the QUIPs tool.[20] Domain 1 = study participation; domain 2 = study attrition; domain 3 = prognostic factor measurement; domain 4 = outcome measurement; domain 5 = study confounding; domain 6 = statistical analysis and reporting.

Persistence of hypertensive readings

The persistence of hypertensive readings within the ED ranged from 0.44 to 0.71,[31,35] an I^2 of 0.84 demonstrating moderate heterogeneity. The pooled estimate of ED persistence was 0.62 (95% CI = 0.56 to 0.68; see Figure 3).

The persistence of hypertensive readings in the outpatient setting ranged from 0.26 to 0.88;[20,30] however, significant heterogeneity was detected with an I^2 of 90.2%. The pooled estimate for persistence of hypertensive reading in the outpatient setting was found to be 0.50 (95% CI = 0.38 to 0.61; see Figure 4).

Proportion of attendance at follow-up

The proportion of attendance at follow-up ranged from 0.02 to 0.65[33,36] and demonstrated significant heterogeneity with an of I^2 97.3%. The estimated pooled proportion was 0.41 (95% CI = 0.23 to 0.62; see Figure 5).

Prognostic value

Masood et al.,[32] Lee et al.,[42] and Oras et al.[43] were the only studies that reported on the prognostic value of hypertensive readings for long-term cardiovascular outcomes. All were large retrospective population registry studies from Canada, South Korea, and Sweden, respectively. Among 206,147 Canadian ED patients with a coded diagnosis of hypertension, mortality at 2 years for discharged patients was 3.59% (95% CI = 3.51 to 3.68), and complications of hypertension were 9.3%.[43] The South Korean database contained 262,927 noncritical first ED attendances[42] from which Lee et al.[42] explored the association between ED-coded hypertension and major adverse cardiac events (MACE). The outcome of MACE at 0 to 3 years resulted in an estimated hazard ratio of 4.25 (95% CI = 3.83 to 4.71), for MACE at 4 to 6 years the estimated hazard ratio was 3.65 (95% CI = 3.14 to 4.24), and at 7 to 10 years 3.20 (95% CI = 2.50 to 4.11) for an ED-coded hypertension. The Swedish retrospective study included 300,193 patients and examined hazard ratios for the outcome incident atherosclerotic CVD, which was very similar to Lee et al.'s definition of

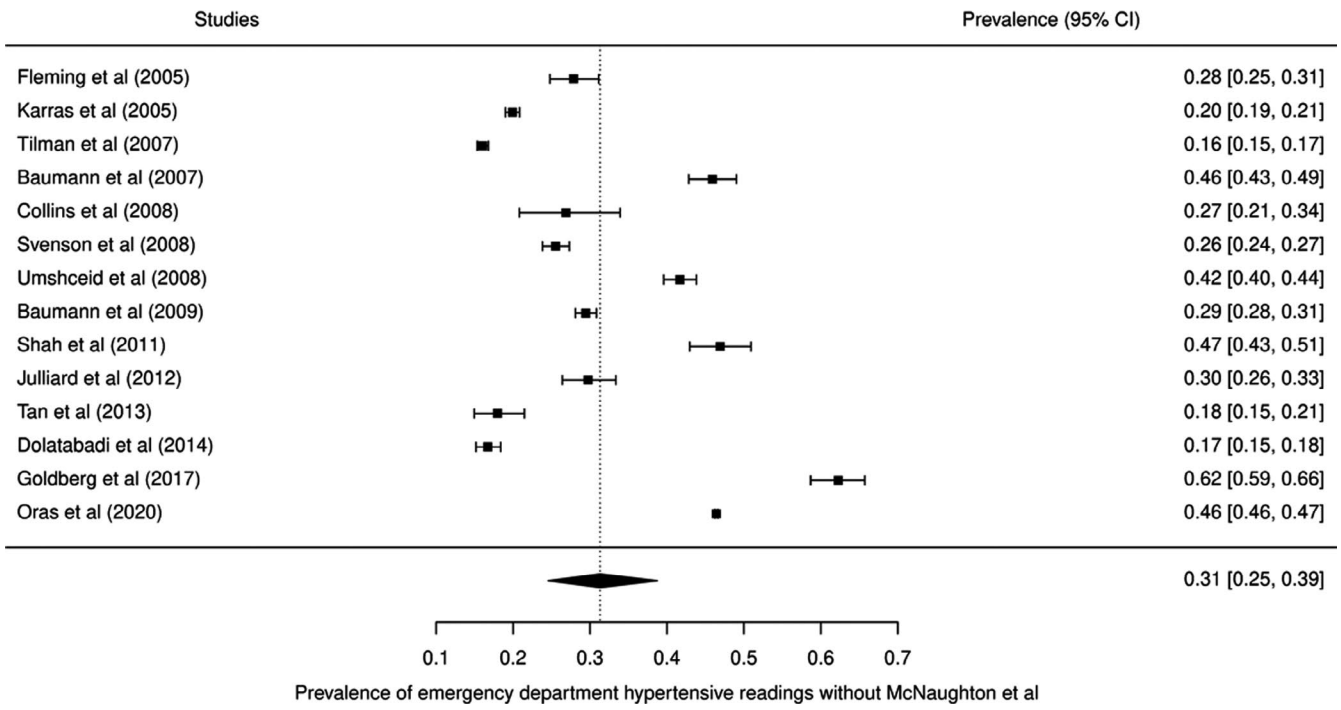

FIGURE 2 Meta-analysis forest plot of the prevalence of hypertensive readings in the ED without McNaughton et al. Exact likelihood estimation[19–32]

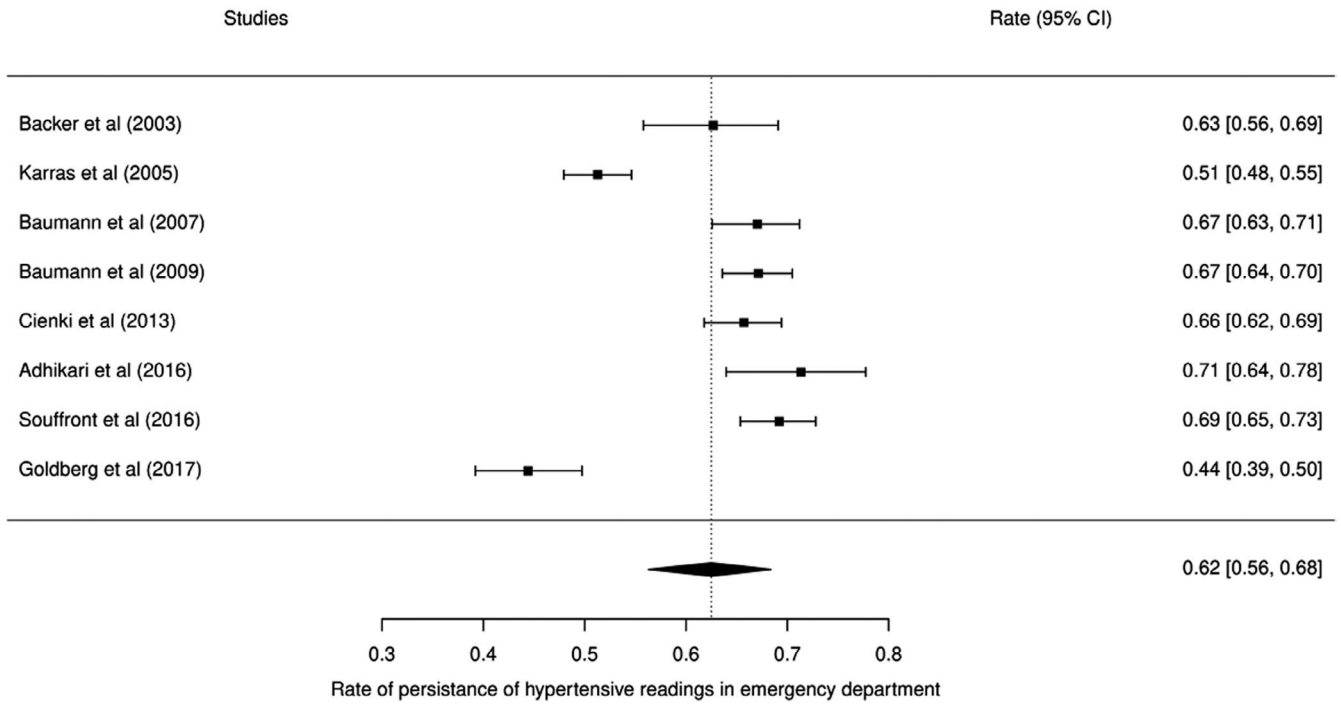

FIGURE 3 Meta-analysis forest plot of the persistence of hypertensive readings the ED. Exact likelihood estimation[20,23,26,31,33–36]

MACE.[32] This study reported adjusted hazard ratios stratified by grade of hypertension and it demonstrated a exposure–response relationship. A systolic blood pressure (SBP) of 140 to 159 mm Hg had a hazard ratio of 1.24 (95% CI = 1.09 to 1.41), sBP 160 to 179 mm Hg had a HR of 1.62 (95% CI = 1.42 to 1.85), and an SBP greater than 180 mm Hg demonstrated a HR of 2.02 (95% CI = 1.75 to 2.33).

DISCUSSION

Among the 26 included studies, study prevalence of hypertensive readings was the most reported and consisted of mainly moderately biased studies (Table 2). The prevalence of ED hypertension was frequently adjusted for pain and we estimated the pooled prevalence of

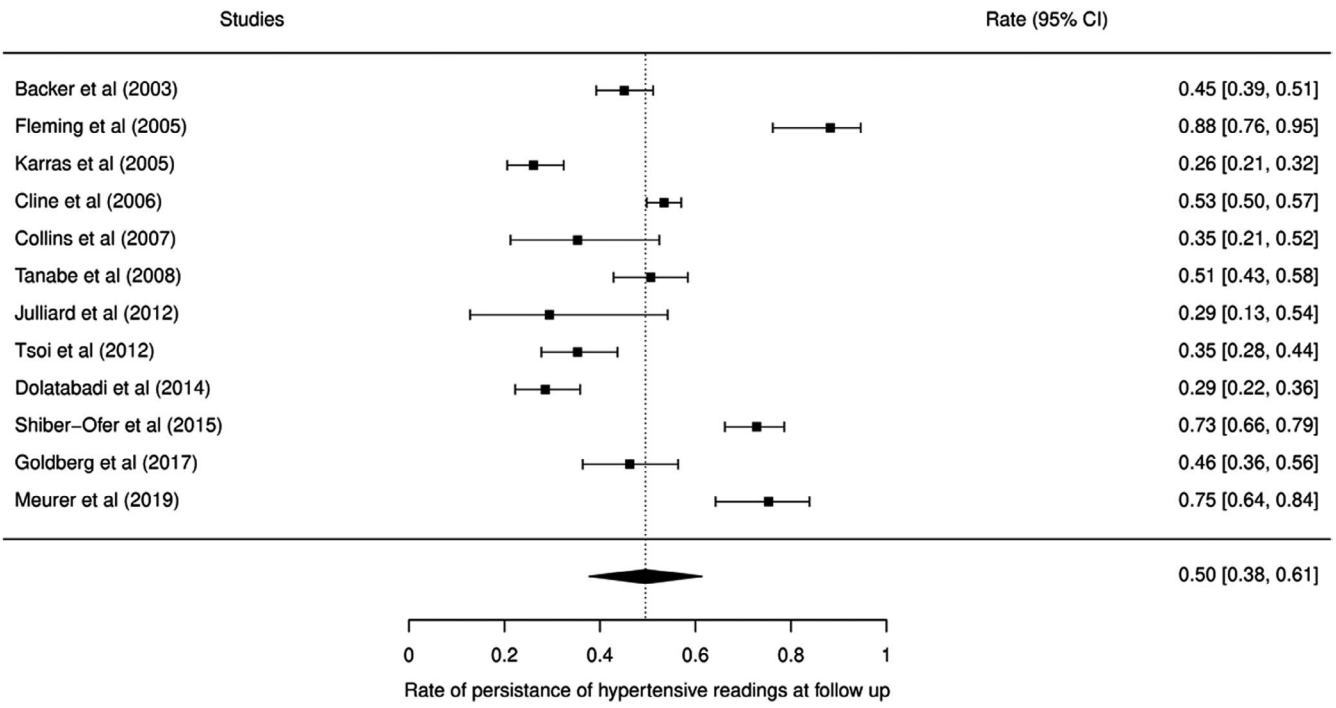

FIGURE 4 Meta-analysis forest plot of the persistence of hypertensive readings at follow-up. Exact likelihood estimation[19,20,22,28,30,31,36–41]

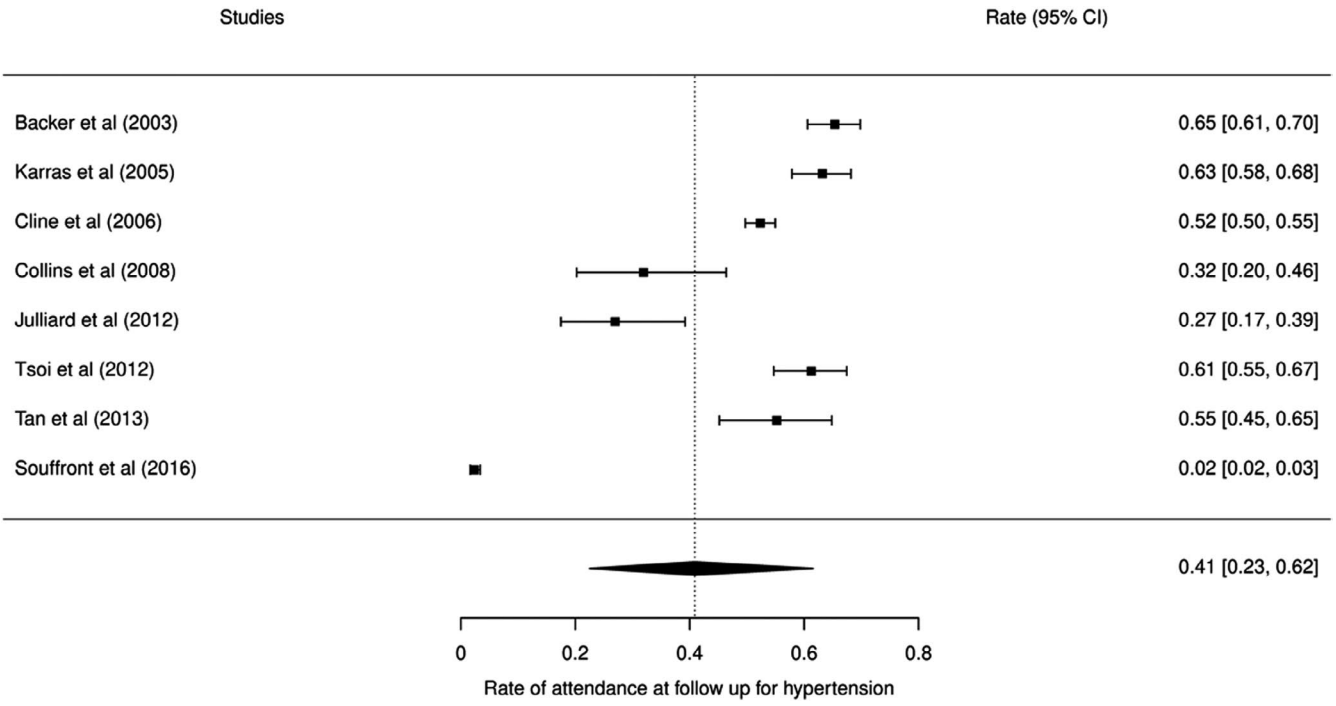

FIGURE 5 Meta-analysis forest plot of the proportion of attendance at follow-up for hypertension. Exact likelihood estimation[20,22,29,30,33,36,39,40]

ED hypertension as 0.31 (95% CI = 0.25 to 0.37). Hypertension was found to be persistent within ED multiple readings (62% remained hypertensive) and at follow-up (50%). This suggests that observing hypertension within the ED can not only be indicative of persistent hypertension but there was evidence that hypertensive ED readings were associated with an increased risk of long-term CVD outcomes.[42,43] Inviting the patient back to an outpatient clinic for confirmatory testing could be the obvious and classical approach.

However, given our pooled estimates of 41% attendance at follow-up this might fail to capture a significant proportion of patients and indicate that a different model is needed. Consequently, acting within the ED visit could be beneficial, avoiding this loss to follow-up. Bowen et al.[44] described outcomes of interest for feasibility; in keeping with this review, we have shown the likely demand for such a service in the prevalence and persistence estimates, and the success or failure of execution via the rate of attendance at follow-up. This supports the hypothesis that ED hypertension could be feasibly acted upon and utilized for long-term CVD prediction tools within the ED setting.

There are recent studies demonstrating no benefit when treating hypertension identified in admitted patients; however, these focus on relatively short-term CVD outcomes (<3 years).[45] CVD is a disease with outcome time scales classically over decades; therefore, this short-term reassurance appears to be masking a long-term problem. As the ED can feasibly detect hypertension and it has been shown to be predictive of long-term outcomes, we may have a duty to intervene in some capacity.

LIMITATIONS

Significant heterogeneity was identified; it appeared to be primarily due to differing practices in prognostic factor measurement, difference in acuity, country, and type of study. Furthermore, we included a variety of study types and, therefore, the estimates of prevalence should be generalized with caution. The prevalence and persistence are still substantial even when the lower bounds of the CIs are assumed to be correct. This would indicate that despite the significant heterogeneity, ED hypertensive readings are still, likely, of prognostic value. This systematic review included international studies. While this added new studies and evidence it also limits the precision of the estimations when generalized to a specific population and system.

CONCLUSIONS

We have found that ED hypertension was prevalent, persistent, and predictive of long-term cardiovascular outcomes. These findings must be interpreted in the context of the large heterogeneity encountered in our review, which was likely due to the diverse populations included.

The American College of Emergency Physicians already recommends that hypertensive readings are acted upon either by outpatient follow-up or immediate therapy.[46] In the context of this review this advice appears sensible and should be heeded internationally. This could be through a targeted intervention with a clinical prediction model. However, careful thought is required prior to any service implementation as follow-up attendance was low. Even with this potential shortcoming, this represents an enormous opportunity for well-designed screening and intervention care pathways in a high-risk population. Current research is ongoing examining the long-term prognostic ability of routinely collected data and the practicalities of implementation of a care pathway through qualitative studies.[47]

CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

Charles Reynard, Richard Body, Patricia Van den Berg, and Govind Oliver—review design; Charles Reynard, Patricia Van den Berg, and Richard Body—searches, screening, risk of bias assessment, and data extraction; Charles Reynard, Camilla Sammut-Powell, Richard Body, Brian McMillan, Anthony Heagerty, Patricia Van den Berg, Govind Oliver, and Mina Peter Naguib—analysis; Charles Reynard, Richard Body, Brian McMillan, Anthony Heagerty, Camilla Sammut-Powell, Patricia Van den Berg, Govind Oliver, and Mina Peter Naguib—manuscript writing.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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