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Pharmacological and nonpharmacological approaches to hypertension treatment among veterans: a systematic review protocol

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Abstract

Background Hypertension (HTN) is the leading cause of mortality worldwide, contributing to significant healthcare spending in both developed and developing countries. Veterans are disproportionately affected by HTN, potentially owing to exposure to active combat, a risk factor specific to this population. However, the most recent review of existing treatment approaches for HTN in this population was conducted in 2014 and addressed only behavioral interventions. We aim to examine existing pharmacological and nonpharmacological interventions to improve HTN control or blood pressure measures among veterans.

Methods This is the protocol for a systematic review that will examine existing pharmacological and nonpharmacological interventions (i.e., lifestyle modifications and psychological and psychosocial interventions) to improve HTN control or blood pressure measures among veterans. Our systematic review will follow the Joanna Briggs Institute Manual for Evidence Synthesis, searching four databases (Embase, MEDLINE, Cochrane, and PsycINFO) for eligible studies. The risk of bias will be assessed using the Mixed Methods Appraisal Tool (MMAT) version 2018, followed by content analysis with narrative synthesis to classify and describe the associated interventions and outcomes.

Discussion Although we expect to identify gaps in the literature, the findings from this review may guide further research on veteran health and help establish treatment guidelines for this population. This review is one of the few focusing on the veteran population and encompassing both pharmacological and nonpharmacological approaches to treating HTN. It is also the first review on the topic conducted in the last 10 years.

Systematic review registration: PROSPERO CRD42024579112.

Keywords Systematic review protocol, Veterans' health, Hypertension, Blood pressure control, Antihypertensive agent/therapeutic use, Health behavior

Background

Hypertension (HTN) is one of the most common chronic conditions; it is a leading cause of cerebrovascular accidents and the most recognized cause of mortality worldwide [1–3]. The estimates of HTN worldwide predict an even further increase in the population affected by this condition by 2025, increasing to 1.5 billion people [4]. The latest estimation of the global financial burden of HTN, dating back to 2001, is 370 billion USD, which is 10% of overall healthcare expenditures, amounting to considerable healthcare spending in both developed and developing countries [1, 5].

The primary care clinics of the Veterans Health Administration (VHA) in the USA provided care for up to 5.51 million veterans in 2021 [6]. Among those, up to 2.46

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million had a diagnosis of HTN, making it the most common disease in the veteran population [6]. Furthermore, with the changes in the definition of HTN as per the SPRINT trial, the number of veterans with HTN is even more significant [7]. Similarly, in Ukraine, HTN is among the most common chronic conditions in military personnel, with up to 51.8% of military personnel having HTN prior to the escalation of the war with Russia and this number continuing to rise to 83.6% among active military members as of today [8]. This rise is also consistent with studies describing the noxious effect of active combat on HTN [9]. Therefore, not only does the veteran population have a higher prevalence of cardiovascular risk factors than the general population, but they also have an additional risk factor associated with active combat, rarely seen by civilians [9–11].

Furthermore, one of the recent cohort studies noted the alarming tendency in the veteran population to have a higher incidence of HTN occurring at a young age in the population of young veterans than in the general population [12, 13]. Blood pressure (BP) control among veterans with HTN is also a strong determinant of all-cause mortality and cerebrovascular complications [14]. Considering the lifelong trajectory of HTN, this might yield a greater burden of HTN in the population of veterans than in the general population.

Many options for treating HTN are considered efficient and cost-effective in the general population [15–18]. These treatments include pharmacological interventions with different antihypertensives and nonpharmacological interventions, such as behavioral interventions, lifestyle and diet modifications, and psychosocial interventions aimed at reducing the risk factors associated with HTN [15–19]. However, most of the current reviews of HTN treatment have been conducted in general or aging populations.

The most recent literature review examining HTN treatment to improve BP and/or BP control in veterans was conducted in 2014 [19]. Additionally, this review used only one database and included only behavioral interventions. Therefore, after almost 10 years of ongoing research, it is necessary to reexamine the existing interventions to improve BP and/or BP control in veterans and to further encompass the existing pharmacological and nonpharmacological interventions to HTN treatment in this population.

We aim to answer the question of what pharmacological and nonpharmacological interventions are associated with enhancing BP control among the veteran population. In our systematic review, we aim to describe the existing research concerning pharmacological and nonpharmacological interventions to improve BP and/or BP control in the veteran population.

Methods

This protocol is reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses–Protocols (PRISMA-P) guidelines, the checklist of which can be found in the Supplementary material 1 [20]. We will conduct a systematic review following the Joanna Briggs Institute Manual for Evidence Synthesis [21]. It will be reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [22]. This review is registered on the PROSPERO platform (CRD42024579112).

Eligibility criteria

We established our eligibility criteria following the framework Population, Intervention/Exposure, Comparison, and Outcomes (PICO) [23].

Population

We will include studies of veterans (active or nonactive military members) with HTN, regardless of sex, ethnicity, religion, or geographic area. Studies reporting findings for adults who are not veterans and studies of the veterans' population with prehypertension will be excluded. In cases of mixed populations (veterans and nonveterans), the study will be included if the results for veterans are reported separately.

Intervention

We will include studies describing any intervention to enhance BP or BP control. These interventions may include pharmacological treatments (any medication used with the goal of BP control or management) and non-pharmacological treatments (i.e., lifestyle modifications and psychological or psychosocial interventions).

Comparison

We will consider studies with and without controls. The control groups might include participants who were not exposed to the intervention or participants before the beginning of the intervention.

Outcomes of interest

The outcomes of interest are systolic and/or diastolic BP, BP control, as reported by the authors, and changes in BP with the intervention. The secondary outcomes of interest are the side effects and discomfort associated with the intervention.

Study setting

Studies from any setting will be included.

Types of design and materials

We will consider mixed, qualitative, and quantitative observational (e.g., cohort, cross-sectional, case–control) or experimental peer-reviewed studies. We will also consider clinical trials whose results have been reported on clinical trial registration platforms without peer-reviewed publication. We will exclude systematic and scoping reviews, but the studies included in such reviews will be considered for inclusion if relevant. We will also exclude case studies, commentaries, letters to the editor, and others, conference abstracts, and theses.

We will not apply any restrictions on the language or year of publication.

Information sources and search strategies

The search strategy is being developed under the leadership of an information specialist, and the latest search results can be found in the Supplementary material 2. The search will be conducted in Embase, MEDLINE (via PubMed), PsycINFO, and the Cochrane Library. An initial search will be developed for MEDLINE and then adapted to match the syntax of Embase, the Cochrane Library, and PsycINFO. A mix of controlled (e.g., "Veterans" [Mesh], "Hypertension/therapy" [Mesh]) and free vocabulary (e.g., Veteran [TIAB]), veterans [TIAB], and hypertension therapy [TIAB]) will be used to search for the main concepts. No review of gray literature is planned. However, we perform a reference search to supplement our search strategy.

Selection, extraction, and management of data

Selection process

We will conduct a pilot screening with randomly chosen studies to verify comprehension of the eligibility criteria for each selection stage. Afterward, pairs of independent reviewers will screen titles and abstracts, followed by full-text screening. We will resolve disagreements via discussions between reviewers until a consensus is reached.

Data collection process

Pairs of independent reviewers will conduct data extraction using standardized extraction forms. The pilot phase will verify the understanding of the extraction forms prior to the start of the data extraction. Extracted information will include (1) study identification information (e.g., title, authors, year of publication and journal); (2) study characteristics (e.g., country, study design, and sample size); (3) demographics of the study population (e.g., age, sex, gender when available, ethnic background, and other chronic conditions if any); (4) intervention description (treatment methods, modalities and duration); and (5) outcomes (HTN control, BP or changes to BP, and treatment side effects and associated discomfort if any), their definitions, and tools used for measurements.

Quality assessment

Due to the inclusion of various study designs, we plan to use the MMAT for bias and quality assessment [24]. This tool is applicable to a wide range of studies, including both quantitative and qualitative analyses, which will facilitate the comparability of the bias assessment [24]. This assessment will be conducted independently by pairs of reviewers. In cases of discrepancies, the reviewers will discuss them to reach a consensus.

Data management

EndNote 20 (Clarivate) will be used to store references, whereas Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia, www.covidence.org) will be the main tool in the article selection and extraction process. The statistics will be calculated separately and confirmed between the calculations and the Covidence statistics. We will use EndNote 20 to highlight duplicates before they are removed after the confirmation of a reviewer.

Data synthesis and analysis

We will conduct descriptive statistics (e.g., means, ranges) to describe the characteristics of the included studies. We plan to examine existing interventions to improve BP and its control in veteran populations, as well as their potential effects and side effects. We will use content analysis to classify these interventions (pharmacological and nonpharmacological with potential further classification as per the included studies).

We will also use content analysis and narrative synthesis to describe the definitions of the outcomes and measurement methods and to compare the impacts of interventions. Owing to the anticipated heterogeneity of studies, we will not perform a meta-analysis. However, subgroup analysis of interventions to compare behavioral, psychosocial, pharmacological, and lifestyle modification interventions will be conducted when possible. The pharmacological interventions will be analyzed according to the class of the medication as applicable. We will also analyze the effectiveness of interventions on the basis of the gender and sex of participants as reported and the presence of comorbidities. We will conduct a sensitivity analysis separating the studies without control groups to verify the potential changes in the results.

Patient and public involvement

We will discuss preliminary results with veteran patients and clinicians involved in their care to improve interpretation and understanding of possible implications. The results will be distributed among direct and indirect stakeholders and disseminated via scientific conferences, research webinars, and publications in peer-reviewed journals.

Ethics and dissemination

No ethical approval is necessary for the systematic review, as neither human nor animal subjects are involved.

Discussion

There are numerous BP and BP control intervention studies. Nevertheless, there seems to be a lack of reviews concerning such interventions in the veteran population. As the most recent review on this topic was conducted almost 10 years ago by Zullig, LL et al., there is a need to reexamine the existing interventions aiming to affect BP and/or BP control once more [19]. This systematic review has the potential to provide updates from the most recent review and expand it, including a wide variety of pharmacological and nonpharmacological interventions to improve BP and BP control. With side effects as the secondary outcome, we will also be able to provide a fuller understanding of the treatment options and their impacts on the lives of veterans. We will summarize the knowledge concerning BP control interventions and describe the gaps in evidence for HTN treatment in the veteran population.

This systematic review contributes to the existing knowledge and helps establish further research goals for HTN treatment among veterans. Furthermore, the evidence will guide clinicians' participation in the healthcare of veterans in terms of the particularities of HTN treatment in this population. The results may also guide governmental policies in veterans' health, especially in terms of the secondary prevention of cardiovascular health, such as myocardial infarction, stroke, and mortality associated with cardiovascular diseases.

The existing limitations of our systematic review need to be discussed. Despite the search of four databases and the inclusion of clinical trial result reports, we will not include gray literature in the search strategy. Thus, publication bias might impact the results of the proposed review by overestimating the interventions' effectiveness. However, our search strategy includes four different databases containing interdisciplinary literature sources. Furthermore, owing to the potential heterogeneity in the interventions, no meta-analysis is planned. Nevertheless, subgroup analyses, as feasible, will be conducted, aiding in the description of interventions for different populations.

Some of the strengths of this systematic review include the lack of restrictions by language or country. In the case of studies written in languages not spoken by our team, we will use existing programs to translate and analyze associated data.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13643-025-02900-5.

Supplementary Material 1: PRISMA-P 2015 Checklist.

Supplementary Material 2: Strategy.

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Authors' contributions

Conceptualization: OS. Methodology developments OS, ON. Search strategy development: OS, ON. PROSPERO submission: OS. Database searches: OS, ON. Writing initial draft: OS, ON.

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Data availability

The search strategy and other materials are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors have no competing interests to declare.

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References

1. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020;16(4):223–37.
2. Collaborators GBDCoD. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1736–88.
3. Collaborators GBDRF. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet. 2018;392(10159):1923–94.
4. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. Lancet. 2005;365(9455):217–23.

5. Gaziano TA, Bitton A, Anand S, Weinstein MC, International Society of H. The global cost of nonoptimal blood pressure. J Hypertens. 2009;27(7):1472–7.
6. Carrico M, Frosch C, Craig K, Carter M, Falk J, Guerrero S, et al. Implementation of Video Blood Pressure Visits in the Veterans Health Administration. Telemed J E Health. 2024;30(4):1006–12.
7. Yamada M, Wachsmuth J, Sambharia M, Griffin BR, Swee ML, Reisinger HS, et al. The prevalence and treatment of hypertension in Veterans Health Administration, assessing the impact of the updated clinical guidelines. J Hypertens. 2023;41(6):995–1002.
8. Belyi D, Nastina O, Sydorenko G, Kursina N, Bazyka O, Kovaliov O, et al. State of cardiovascular system in militaries of Ukraine Armed Forces under the war with Russia. Probl Radiac Med Radiobiol. 2023;28:254–66.
9. Howard JT, Stewart IJ, Kolaja CA, Sosnov JA, Rull RP, Torres I, et al. Hypertension in military veterans is associated with combat exposure and combat injury. J Hypertens. 2020;38(7):1293–301.
10. Assari S. Veterans and risk of heart disease in the United States: a cohort with 20 years of follow up. Int J Prev Med. 2014;5(6):703–9.
11. Baygi F, Herttua K, Jensen OC, Djalalinia S, Mahdavi Ghorabi A, Asayesh H, et al. Global prevalence of cardiometabolic risk factors in the military population: a systematic review and meta-analysis. BMC Endocr Disord. 2020;20(1):8.
12. Burg MM, Brandt C, Buta E, Schwartz J, Bathulapalli H, Dziura J, et al. Risk for incident hypertension associated with posttraumatic stress disorder in military veterans and the effect of posttraumatic stress disorder treatment. Psychosom Med. 2017;79(2):181–8.
13. Pizarro J, Silver RC, Prause J. Physical and mental health costs of traumatic war experiences among Civil War veterans. Arch Gen Psychiatry. 2006;63(2):193–200.
14. Doumas M, Tsioufis C, Fletcher R, Amdur R, Faselis C, Papademetriou V. Time in therapeutic range, as a determinant of all-cause mortality in patients with hypertension. J Am Heart Assoc. 2017;6(11).
15. Maniero C, Lopuszko A, Papalois KB, Gupta A, Kapil V, Khanji MY. Non-pharmacological factors for hypertension management: a systematic review of international guidelines. Eur J Prev Cardiol. 2023;30(1):17–33.
16. Carey RM, Wright JT Jr, Taler SJ, Whelton PK. Guideline-driven management of hypertension: an evidence-based update. Circ Res. 2021;128(7):827–46.
17. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc. 2013;2(1): e004473.
18. Theodoridis X, Chourdakis M, Chrysoula L, Chroni V, Tirodimos I, Dipla K, et al. Adherence to the DASH diet and risk of hypertension: a systematic review and meta-analysis. Nutrients. 2023;15(14).
19. Zullig LL, Bosworth HB. Behavioral interventions to improve hypertension control in the Veterans Affairs healthcare system. J Clin Hypertens (Greenwich). 2014;16(11):827–37.
20. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1.
21. Aromataris E, Munn Z. JBI Manual for Evidence Synthesis2020. Available from: https://synthesismanual.jbi.global.
22. 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.
23. Amir-Behghadami M, Janati A. Population, Intervention, Comparison, Outcomes and Study (PICOS) design as a framework to formulate eligibility criteria in systematic reviews. Emerg Med J. 2020;37(6):387.
24. Hong QN, Pluye P, Fàbregues S, Bartlett G, Boardman F, Cargo M, et al. Mixed Methods Appraisal Tool (MMAT). In: Office CIP, editor. Industry Canada Canada 2018.

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