Symptom experiences in hypertension: A mixed methods systematic review

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Abstract

Aim

Blood pressure guidelines have undergone multiple revisions in accordance with updated science. Understanding patients' hypertension symptoms can assist healthcare professionals' awareness of individual, cultural, and behavioural responses and improve diagnostic accuracy to optimize treatment. Therefore, the purpose of this review was to evaluate and synthesize current literature exploring symptoms experienced by patients with hypertension.

Methods

Databases searched included MEDLINE ® (PubMed ®), CINAHL ® (EBSCO), Scopus, and Web of Science[™] from January 2010 to January 2022 for studies with reported hypertension symptoms. The search followed the PRISMA guidelines. The McMaster critical review forms were used to determine quality of both qualitative and quantitative articles. Synthesis of the data was guided by the Joanna Briggs Institute Convergent Integrated Approach to Mixed Study Systematic Reviews. Results

Forty-one articles were included in the review, including nine qualitative studies and thirty-two quantitative. Quality of the articles varied. Symptoms included commonly reported symptoms and some less prevalent, including some reporting absence of symptoms. Factors that affected symptoms included culture, beliefs, psychosocial factors and knowledge. We also found that there may be a bidirectional relationship with symptoms and behaviours that may lead to selfmanagement.

Conclusion

Hypertension is common and symptoms are frequently reported. Hypertension management is related to multiple factors. Symptoms continue in a number of individuals after initial diagnosis. Evaluating symptoms after initial diagnosis may help to optimally manage and meet BP guidelines. Keywords: hypertension, symptoms, mixed methods review, systematic review

Symptom Experiences in Hypertension: A Mixed Methods Systematic Review Introduction/ Background

The management of hypertension is a global concern and multiple organisations have strived to develop guidelines for prevention and management. The British National Institute for Health & Care Excellence [1], and the World Health Organisation [2], The American Heart Association (AHA), and the European Society of Cardiology/Hypertension (ESC/ESH) Guidelines for management of primary hypertension have published recommendations for the clinical management of hypertension. Despite these guidelines, hypertension remains a worldwide concern. A recently published global cross-sectional survey [5] that assessed blood pressure in 1.2 million individuals across 80 countries reported that over a third (34.9%) of participants were hypertensive. Of those receiving pharmaceutical treatment, 46.3% remained hypertensive and therefore had higher morbidity and mortality risks [5].

In the past hypertension has been frequently referred to as asymptomatic or a "silent killer" [6–8] due to the ambiguity and late onset of symptoms and this dated perception persists in both academic and public media, despite evidence to the contrary. Diagnosis often occurs by chance during routine blood pressure measurements or health screens [3,7]. Relying solely on blood pressure measurement to diagnose HTN fails to account for the social, behavioural, dietary, physical, and other variables that may influence blood pressure [4,9]. As a result, HTN is under diagnosed or not diagnosed in a timely manner, which leaves patients at risk of associated cardiovascular complications [9].

Symptoms such as headache have been attributed to HTN since as early as 1913 [10]. Throughout the remainder of the century, early studies aimed at investigating HTN reported a high prevalence of a wide range of other symptoms including dizziness, epistaxis, tinnitus, dyspnoea, weakness, and drowsiness. [11–15]. Early observational studies explored occurrence and frequency of symptoms and attempted to characterise relationships between perceived symptoms and measured blood pressure [16–19]. These studies failed to demonstrate significant associations or correlations between symptom experiences and blood pressures measured by sphygmomanometry. A more recent study also failed to detect an association [20]. Findings from early studies suggested that symptoms were attributable to psychological/ psychosomatic components such as the awareness of a HTN diagnosis, anxiety, tension, stress and neuroticism [13,18,21]. Symptoms have also been attributed to other commonly associated co-morbidities such as diabetes mellitus, and other cardiovascular disease [4].

Conversely, findings from some early studies suggested an association between HTN and headaches [15,22]. More recently, Law et al.'s meta-analysis of 94 randomised placebo-controlled trials concluded that blood pressure lowering medication significantly reduced the number of reported headaches in patients with known HTN [23].

The exact nature of the relationship between signs and symptoms and HTN has been a consistent source of contention. It may be a misnomer to describe HTN as "asymptomatic"; many studies suggest that patients with HTN consistently report symptoms. Merely, the association between the presence or absence of these symptoms and real-time alterations in systolic or diastolic blood pressures has not been demonstrated.

Exploration of the impact and management of symptoms has not been prioritised due to the lack of agreement on the significance of perceived symptoms associated with HTN. This leaves many unanswered questions that warrant further consideration. Understanding the characteristics of perceived symptoms and associations with HTN may be important in prompting patients to seek expert medical help to gain an early diagnosis. Early recognition of patients' perceived symptoms can facilitate prompt treatment and effective self-management strategies leading to reduced blood pressure and maintenance within a target range to reduce morbidity and mortality. Law et al. estimated that a 10-mmHg reduction in BP can lead to a 41% reduction in stroke and a 22% reduction in coronary heart disease [23]. Furthermore, attention to patients' perceived symptoms is essential for effective holistic management of this long-term condition.

Purpose

Understanding patients' symptom experiences can enhance healthcare professionals' awareness of symptoms associated with HTN and improve diagnostic accuracy to begin treatment at an earlier stage. Therefore, the purpose of this review was to evaluate and synthesize current literature exploring symptoms experienced by patients with HTN.

Methods

Design

This was a mixed methods systematic review informed by Joanna Briggs Convergent Integrated Approach to Mixed Study Systematic Reviews [24]. The report is guided by the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines [25]. The research team agreed on the review aims, identified databases, key concepts, search terms, inclusion and exclusion criteria, screening tools and roles in the process. The screening process was conducted using Covidence© systematic review software.

Data sources and searches

A search strategy was developed in consultation with a health sciences librarian (AH). Searches were conducted across a selection of relevant databases specific to the question. Databases searched included MEDLINE ® (PubMed ®), Cumulative Index to Nursing and Allied Health Literature (CINAHL ®/EBSCO), Scopus ®, and Web of Science[™]. Date limits were January 2010 to January 2022. Controlled vocabulary and keywords were translated and mapped across all databases for the following concepts: patient reported symptoms, symptomology, symptomatology, HTN, blood pressure, pulse pressure, qualitative, quantitative, study, and survey. The completed searches are stored on the East Carolina University institutional repository, The ScholarShip, and are accessible at the following link: https://thescholarship.ecu.edu/handle/10342/9651. Searches were originally completed on July 20, 2020 and updated on February 5, 2022.

Inclusion and exclusion criteria and quality appraisal

Inclusion criteria were articles that were empirical studies, peer-reviewed, reported symptoms of HTN by participants, published in English and within the defined years. Excluded were studies that were dissertations, review articles, abstracts, related to HTN in pregnancy and children, animal model studies and malignant hypertensive crisis.

The McMasters Critical Review Forms were used for all studies with the quantitative form [26] and qualitative form [27] used respectively according to the method of each study. The quality of the studies was independently reviewed by five authors (CH, LS, SS, CS, LB). The team discussed the quality appraisal of all studies until consensus was achieved.

Search results

Records from database searches were collected and deduplicated using EndNote 20 by the health sciences librarian (AH). A total of 5,632 citations were retrieved in the databases, and 2,500 duplicates were removed. Deduplicated results were uploaded to Covidence© for independent review. A total of 3,132 records' titles and abstracts were screened by four authors (CH, LS, SS, CS). After title and abstracts were screened within Covidence©, conflicts regarding the eligibility of 240 records remained to be resolved. Resolution of those articles was completed independently by two authors (LB, CT). The remaining 164 articles were collected for full text review. Full text reviews were completed by six authors (CH, LS, SS, CS, LB, CT) with each article read twice by two different authors. Conflicts were resolved by a third reviewer (SM). After full text review, 41 articles [28–68] remained for synthesis (see Figure 1 for PRISMA and Table 1 for included studies).

Data Extraction and synthesis

Data extraction was completed using a developed matrix table. Extracted information included purpose, design, methods, sample, instruments, measurement, reported symptoms and study outcome(s). Data extraction was completed by the six authors (CH, LS, SS, CS, LB, CT) that reviewed the full texts. All articles in the matrix table were verified and reviewed by all members of the team for appropriateness of inclusion relevant to the research purpose.

Synthesis of the findings was completed separately for the qualitative and quantitative articles. Qualitative data were independently extracted, synthesized, and coded by two authors (LS, SS). The authors independently grouped similar codes into tentative themes. The themes were reviewed and discussed within the team until a consensus of substantive themes was achieved. Quantitative data was extracted and independently reviewed by two authors (CH, LB). Due to the heterogeneity of studies and the data generated, meta-analysis was not possible. Quantitative data were independently reviewed for quality and synthesized according to symptom outcomes [69,70]. Quantitative findings were transformed into a narrative synthesis by two authors (CH, LB) and agreed on by the research team. Finally, the qualitative and quantitative syntheses were integrated by converging the narratives into a unified synthesis of the data.

Quality rating

The quality of the articles was assessed using the Critical Review Form for qualitative studies (Version 2.0) and the Critical Review Form for quantitative studies from McMaster University [26,27]. Guidelines accompany each form. Each form contained criteria for the respective type of study. A dichotomous yes/no was associated with most responses. A response of not addressed or not sure was also available with some criteria. In order to formulate scale ratings, each criterion was assigned a score of 1 for a yes response or a 0 for a no, not sure, or not addressed response. The total possible score for quantitative studies was 15 and the total possible for qualitative studies was 24. See Table 2 for each criterion assessed with associated points for both critical review forms. No study was excluded from this review due to quality rating.

Ratings for qualitative studies ranged from 13 to 21 points. Overall, methodological quality was strong in the collection and analysis of the data, with consistent agreement between two or more researchers involved in data analysis. Some studies failed to comprehensively discuss the theoretical basis of the research and the researchers' biases and assumptions. This is not unusual in published studies due to word limits. The study conducted by Shresthra et al. reported the qualitative arm of a larger cohort study which left uncertainty regarding the influence of the cohort study on the conduct and findings of the qualitative aspect [57]. See Table 4 for qualitative study details with quality ratings.

Ratings for the quantitative studies ranged from 4 to 14 points. The methodological quality of most studies was appropriate for the purpose of the study. Three points were assigned for interventional studies. However, most studies were not interventional, which resulted in deducting three points. Most studies did not justify the sample size due to the non-interventional nature of the studies. Similarly, no studies reported drops outs. See Table 3 for quantitative study details with quality ratings.

Results

General characteristics of studies

Forty-one studies were included in this review (see Table 1). No studies in this review used a randomized control trial design. Most studies were non-randomized, cross-sectional and region-specific. Only two studies used a quasi-experimental design [35,55]. Multiple countries were represented in this review with the United States having the most representation (n=12). Most

studies reported a mixed sample that included men and women. Nine studies reported all-female samples [30,32,34,39,43–45,47,62]. One study did not report gender [55]. Most studies were community based or took place in an outpatient primary care facility. Six studies were conducted in a hospital or medical center [28,48,57,58,61,66].

Qualitative Synthesis

Nine studies were included in the qualitative synthesis [36-38,41,46,51,52]. Data collection methods used in the studies were semi-structured interviews and focus groups. Designs used by most studies included qualitative descriptive design (n = 5), phenomenology (n = 2), and grounded theory (n = 1).

Findings

Analysis resulted in two themes that were synthesised from findings. *Theme 1: The range of symptoms experienced:* this theme described a wide range of symptoms experienced by participants. Well defined physical and psychological symptoms were frequently reported. Equally, participants described more complex symptom experiences which were less well defined, variable and enmeshed within other illness experiences. Codes that constitute this theme are physical and psychological symptoms, ill-defined and indistinguishable symptoms, and understanding HTN. *Theme 2: The landscape of symptoms and behaviours:* this theme describes the complex landscape of behaviours and symptom experiences that influence a person's behaviour, and behaviours that influence the symptom experience. Codes included within this theme are medication, self-management, and reporting symptoms.

Theme 1: Range of Symptom Experiences

In the studies reviewed, participants reported symptoms that they perceived to be associated with alterations in their blood pressure and attributed to their HTN. A range of well-defined physical symptoms associated with HTN was reported. For example, all studies included in this review reported headaches and dizziness as part of participants' symptom experiences. Other symptoms included visual changes [36,39,45], flushing [31,39], neck pain [31,45], nausea, fatigue, heart palpitations, and sleep disturbances [36,39,45,58]. In two studies, participants described psychological symptoms such as anxiety [36,45] and stress [57]. These symptoms were inconsistent, intermittent, and caused varying degrees of distress for study participants.

In addition to the well-defined symptoms, participants in the studies described symptom experiences that were diffuse and nebulous. These variable individual experiences were best illustrated by a participant in De Andrade et al.'s study who used the Portuguese term 'corpu baixo,' meaning 'inferior body,' an indistinct feeling that could not be described but only experienced [36]. Other studies describe this symptom as malaise [58] or feeling uneasy [31]. The sub-theme "I can tell" in Franklin et al.'s study discussed how participants could 'feel' when their blood pressure was elevated [39]. This innate sense of knowing when their blood pressure had increased was also reflected in the accounts of participants in three other studies [31,36,45].

Participants' symptom experiences were further complicated by conflating symptoms of HTN with symptoms caused by other conditions such as diabetes mellitus, arthritis, and Human Immunodeficiency Virus [31,58,68]. Participants in Bokhour et al.'s study described how they experienced symptoms of HTN as part of their overall health condition and not as distinct symptoms [31].

Findings from included studies indicated that participants formulate their understanding of HTN as a long-term condition based on their symptom experiences. Jahan et al. noted that participants understood HTN only in terms of their symptoms and were particularly fearful of severe symptoms which may lead to detrimental consequences [45]. This finding was echoed in other

studies where participants described heart attacks, strokes, paralysis, and death as possible consequences of not controlling their symptoms and thus their HTN [31,39,45,57,68].

Theme 2: The landscape of behaviour and symptoms

The literature indicated that there is a subtle interplay between participants' symptom experiences and behaviours. The relationship is more complex than a bi-directional linear relationship and more closely resembles a landscape where symptoms and behaviours are enmeshed with individual health beliefs, social and cultural factors. The key codes arising from the studies' data related to medication concordance and self- management activities which included predominantly diet and exercise and reporting of symptoms.

Concordance with medication regimens were influenced by the presence or absence of symptoms. Participants in many of the studies reported how they adjusted doses of their antihypertensive medications in accordance with how well or unwell they felt [36,39,45]. For example, a participant in De Andrade et al.'s study described how they would take their medication only if they experienced a headache or dizziness [36]. Similarly, participants in Jahan et al.'s study reported taking medication only when they felt unwell and discontinuing their medication when they felt better [45]. Shresthra et al. cited a lack of awareness of the necessity of regular medications as a reason for poor concordance [57]. However, other studies gave examples of participants who did not think about or forgot about, taking their medications unless they experienced symptoms that they associated with HTN [31,36,45]. In two studies, financial constraints acted as a barrier to taking antihypertensive medications [45,57]. In other studies, participants who took their prescribed antihypertensives said the medications reduced their symptoms [45,66] and made them feel 'normal' [39].

Participants identified poor dietary choices, [31,36,39,45,57,66], high stress levels [31,66], and environmental and social factors [36,57,66] that adversely influenced their perceptions of symptoms. A participant in Franklin et al.'s study reported that eating a bag of chips would 'run their blood pressure up' [39] while participants in other studies described triggers, such as stressful or emotional situations, that led to increases in their blood pressure [36,57].

Five studies discussed how the presence of symptoms facilitated healthier self-management behaviours such as making healthy dietary choices, and exercising or engaging in stress reducing activities [31,39,45,57,68]. Most studies reported that participants were aware of the importance of self-management activities but also discussed barriers to consistently engage with healthy self-management activities. Examples of barriers included Bokhour et al. linking self-management to perceptions of the causes of HTN [31], lack of time and work commitments [57], and social hinderances and financial constraints [36].

Findings also suggest reluctance to discuss symptoms with medical providers. This reluctance was sometimes ascribed to cultural factors [36,66] or a distrust of the medical profession [68]. Participants in Jahan et al.'s [45] and Franklin et al.'s [39] studies reported insufficient time to thoroughly discuss symptoms with their medical providers during consultation. A participant in Tsiantou et al. reported that participants preferred to discuss their symptoms with others who also suffer from HTN because they felt more comfortable and understood [68]. Other studies indicated that people prefer to bypass their medical provider and instead get information about HTN and related symptoms from the internet, social media, the pharmacist or other people living with HTN [57,66].

Quantitative Synthesis

Due to the nature of exploring signs and symptoms in people living with HTN, we anticipated descriptive quantitative studies. In some studies, symptoms were not identified as primary study outcomes but were reported incidentally within the study findings. Overall quality of the articles was moderate. Two studies used quasi experimental non-random sampling designs [35,55]. Most of the

studies were cross sectional or longitudinal. Three longitudinal studies were secondary analyses of parent studies [37,44,46]. Established measures used in studies included the World Health Organization-Quality Of Life-BREF (WHO-QOL-BREF) [28], Centre for Epidemiological Studies Depression Scale CESD-10 [37,46], Survey of Health and Living Status of the Middle Age and Elderly [49], Symptom Representation Questionnaire [38], Kellner's Symptom Questionnaire [42] Patient Health Questionnaire (PHQ8), General Anxiety Disorder-7 (GAD-7), Baecke Physical Activity Questionnaire [50], Illness Perception Questionnaire-Revised [62], and the Present State Examination-Index Definition and Psychiatric Symptom Frequency scale [67].

Symptoms

Studies were heterogenous and symptoms varied. Symptoms that were common in the literature included headache and dizziness [28,29,33,38,40,41,53,55,56,62], as well as less common symptoms such as restless leg syndrome [59,64]. Some studies were focused on specific symptoms associated with HTN [29,34,35,37,38,41–44,49,50,52,54,55,59,64,65,67] while others were aimed at specific population outcomes [28,32,33,40,46,47,51,60–62]. In some of the studies, participants reported not having symptoms associated with HTN [33,52,53,62,63]. Overall, symptoms associated with HTN can be categorized according to absence of symptoms, body system associated symptoms or gender associated. Most symptoms had neurological (including headache, dizziness, vertigo, confusion, fingers tingling, migraine with aura) and psychological (apathy, anxiety, depression, distress, stress) associations.

Absence of Symptoms.

HTN is often associated with not having symptoms or reported as unrecognizable symptoms. We found six quantitative studies in this review that discussed HTN as asymptomatic [33,52,53,62,63] or having symptoms that may be periodically present [48]. Most of these studies associated knowledge or lifestyle behaviour with beliefs surrounding HTN. Several studies attributed participants reporting "no symptoms" as a lack of knowledge [33,53,63]. However, cultural factors were influential in three of the studies [33,52,62]. In all these studies except for two [52,63], symptoms were categorized into distinct body systems.

Neurological System Symptoms.

The neurological symptom of headache was the most commonly reported across all quantitative studies [28,29,33,38,41,53,56,62]. Dizziness was the second most commonly reported symptom [28,38,41,55,56,62]. Other symptoms reported were vertigo and confusion [29], tingling fingers [38], and migraine [40]. In the cross-sectional study conducted by Gardener et al., authors studied migraines and HTN symptoms relevant to ethnicity [40]. The reported odds ratios were stronger for the relationship between HTN and migraine with aura than migraine without aura and was more prevalent in African Americans.

Psychological Symptoms.

Studies showing relationships between HTN and psychological symptoms have increasingly been published within the last twelve years. In some studies, it is unclear whether the psychological symptoms started prior to the HTN diagnosis or as a result of the chronic condition of HTN. In eight studies, depression was the most prevalent psychological symptom reported with HTN [35,37,42,43,48,49,60,61]. In addition, two studies reported clinically significant depression as the outcome [50,54]. Maatouk et al. studied associations between HTN and depression and generalized anxiety in an elderly population whose ages ranged from 57-84 years [50]. Participants with clinically significant depression had greater odds of having a diagnosis of HTN. It was unclear if participants

were depressed prior to being diagnosed with HTN. However, Rantanen et al. found that participants who were normotensive or those unaware of being hypertensive had lower risk for depression compared to participants who were aware of being diagnosed with HTN [54]. Participants in Rantanen's study were younger, $M = 58 \pm 7$ years, compared to those in Maatouk's study.

Anxiety [42,43,48] and distress/stress [42,53,65] were commonly reported in the literature. Uncommon symptoms included insomnia [37], nervousness [41], fear [48], well-being [60,65], hostility [61], apathy [51], and affective symptoms [67]. Guidi *et. al.* conducted a cross-sectional study with a gender and age matched sample comparing allostatic overload using the clinimetric criteria in participants with and without HTN [42]. Using this criterion enabled the authors to estimate psychological distress above normal coping. Participants with HTN had higher allostatic overload, greater psychological distress, reduced well-being, and lower quality of life. Additionally, cardiovascular risk was significantly increased among participants with HTN [42]. Thus, increasing psychological factors was positively related to increased cardiovascular risk.

General Symptoms.

A number of general symptoms were found in the studies. Fatigue was the most commonly reported general symptom [28,29,55,56,62]. Schmieder measured commonly reported symptoms in hypertensive adults prior to achieving BP control with medication [56]. Participants were reassessed after the target BP was achieved. All participants reported symptom improvement with antihypertensive therapy. Similarly, Roales-Nieto et al. found that modification of false beliefs about HTN and knowledge of HTN symptoms was associated with adherence to antihypertensive therapy [55].

Anjum [29] and Stallings and Schneider [62] investigated symptoms associated with HTN in specific populations. Anjum's study was aimed at exploring correlations of systolic and diastolic BP with symptoms across age and gender groups [29]. In the study, males were more likely to have HTN if they were tall, smoked, had vision changes, dyspnea, and palpitations. However, females were more likely to have HTN if they were above 40 years of age, tall, experienced severe headaches, sleep apnea, and palpitations. Stallings and Schneider studied perceptions of symptoms associated with HTN in a cohort of Black women [62]. More than 50% of the sample reported no symptoms of HTN and more than 40% reported one to six symptoms. Commonly reported symptoms included headache and dizziness (neurological), breathlessness (pulmonary), and fatigue (general symptom) [62].

Cardiac, Pulmonary and General Fatigue.

Cardiac symptomology is often associated with a diagnosis of HTN. Seven studies reported cardiac related symptoms, including palpitations, tachycardia, chest tightness, irregular heartbeat and a pounding heart [29,33,41,53,55,56,62]. Several of these studies also reported pulmonary symptoms [29,53,56,62]. Pulmonary related symptoms were described as breathlessness, cough, dyspnea or shortness of breath. Interestingly, fatigue was associated with cardiac and/or pulmonary symptoms. Several studies reported the three symptoms of fatigue, cardiac, and pulmonary together [29,56,62].

Women's Symptoms.

Six quantitative studies were specifically aimed at investigating symptoms in females [32,34,43,44,47,62]. Stallings and Schneider [62] explored perceptions of general symptoms related to HTN in Black women. Chung *et. al.* examined the effects of menstrual symptoms associated with HTN in a sample of mid-20-year-old women [34]. In their study, women who reported heavy and irregular menstruation had an increased risk for chronic HTN.

Brown et al. [32], Kagitani et al. [47] and Jackson et al. [44] studied the association between hot flashes and HTN in a cohort of middle-aged females. Brown et al. measured women's BP within 10 minutes of having a hot flash to estimate effect [32]. Women's BP increased with hot flashes but there was little effect on long term increases in BP. In larger samples, both Kangatani et al. [47] and Jackson et al. [44] investigated hot flashes in women whose mean ages were 45 to 46 years old. Both studies found higher BPs in participants who had hot flashes. In the Kangatani study, the effect was especially prevalent among smokers [47]. Furthermore, Jackson et al. found a correlation between hot flashes and developing HTN over time in women [44]. These studies suggest that hot flashes in women may be an important factor for medical providers to assess during health screenings.

Convergence of findings

Symptoms of HTN have been studied for many years. This article reported findings from a systematic review of reported symptoms associated with HTN and was limited to studies published in the last 12 years. We developed a conceptual model (see Figure 2) which was facilitated by converging data from qualitative and quantitative studies. All studies reported ranges of symptoms that were comparable across quantitative and qualitative research and also including absence of symptoms. The presence or absence of symptoms appears to influence behaviours such as medication concordance, self-management, and reporting of these symptoms to providers. We found that symptom experiences were affected by complex combinations of knowledge, beliefs, overall health, gender, and culture. The exact nature of the relationship between symptoms and behaviours is not clear from the data. However, study findings suggest that symptom experiences and HTN are related in a conditional process. Most quantitative studies described the range, frequency, and scope of a varied number of symptoms associated with HTN. Symptoms specifically among women were discussed only in quantitative data. Elevated blood pressure and an awareness of it also influenced the presence of perceived symptoms and behaviours.

To a lesser extent, it is evident that behaviours may also influence the occurrence of symptoms. Psychological symptoms were clearly related to HTN but the nature and direction of the relationship is not clear. Specifically, it is difficult to determine if HTN leads to psychological distress or psychological distress effects HTN. Although symptoms are presented as a list, participants experienced these more fluidly within the context of managing chronic HTN in tandem with multiple related factors that appear to worsen or improve the condition.

Discussion

Symptom experiences in persons with HTN are prominent in the literature but directionality in relationships between reported symptoms and blood pressure values are hard to establish. Failure to demonstrate these directional associations between HTN and reported symptoms may be partially explained by the fact that HTN is sometimes reported as symptomless. However, considering the prevalence of reported symptoms in patients with HTN, additional research is warranted to test the significance of these relationships. For example, some people with HTN fail to report headaches while the presence of headaches appears to be a barometer for HTN in others. Moreover, despite a list of symptoms associated with hypertension-related organ damage published by the ESC/ESH (Carolyn, do you have a link to the guideline?), there was no evidence in the literature that healthcare providers address symptoms associated with HTN above and beyond pharmacological management aimed at improving sphygmomanometry readings. Likewise, the AHA does not address reassessment of symptoms after the initial clinical evaluation to establish the diagnosis of HTN. Providers may need to consider capturing relevant data and symptoms associated with HTN beyond the initial assessment that establishes diagnosis. Reassessment and management of reoccurring symptoms can assist with pharmacologic management and may prevent further morbidity, such as stroke.

Converging the data, it showed that there are many factors that contribute to HTN symptoms, including beliefs about HTN, cultural factors, gender, knowledge and psychosocial factors. There seems to be a bidirectional flow between symptoms and behaviours of the individual. Health-related behaviours affect self-management, medication concordance and symptom reporting. Medical personnel are constantly striving for the person to self-manage their conditions. However, the literature reviewed suggests that engagement with self-management is determined by the symptoms experienced. For example, individuals would take their antihypertensive medication dependent on whether symptoms were present or not present. On-going symptom evaluation may assist in improvement of medication concordance and self-management.

Most systematic reviews related to HTN have not explored qualitative and quantitative data separately. This mixed methods systematic review has done this and converged the data to support a model that shows how symptoms with hypertension are bidirectional and may continue to affect the individual after initial diagnosis. As seen, there may be a need for on-going symptom evaluation after treatment of HTN.

Limitations

Symptoms were often a secondary outcome measure and therefore buried in other data. It is possible that some studies that reported symptoms of HTN were not identified during our search. The grey literature and studies not published in the English language were excluded from this study. Therefore, relevant studies may have been excluded. There was variance in the way symptoms were reported with some using established symptom surveys and others self-reporting the symptoms. In studies using a list of symptoms, it may have omitted individual symptoms that the participant may have experienced.

Conclusion

Our systematic review found varied symptoms and behaviour among participants in the studies. Due to the complexity of symptoms related to HTN, the approach of a mixed methods review allowed us to identify a range of relevant studies and synthesize the findings. The benefit of broadening the conceptualization to include both qualitative and quantitative studies assist in methodological inclusivity and facilitating a comprehensive and well-rounded understanding of the evidence. Our integration of studies provides quantitatively measurable data along with an understanding of the qualitative experiences of persons living with HTN. This approach is useful in understanding the complexity of symptoms associated with HTN. Findings from our examination of relevant and reliable research can improve knowledge in the public sphere and among healthcare professionals caring for these patients.

HTN affects people around the globe. The World Health Organization [2] has prioritized HTN, since less than half of those that have it have been diagnosed. Multiple countries and almost all continents are represented in this review. After appraising the literature and synthesizing findings from 41 studies, we conclude that HTN is associated with common symptom experiences in people across multiple countries. It is vitally important to improve our understanding of HTN and related symptomology in order to treat and stabilize this condition.

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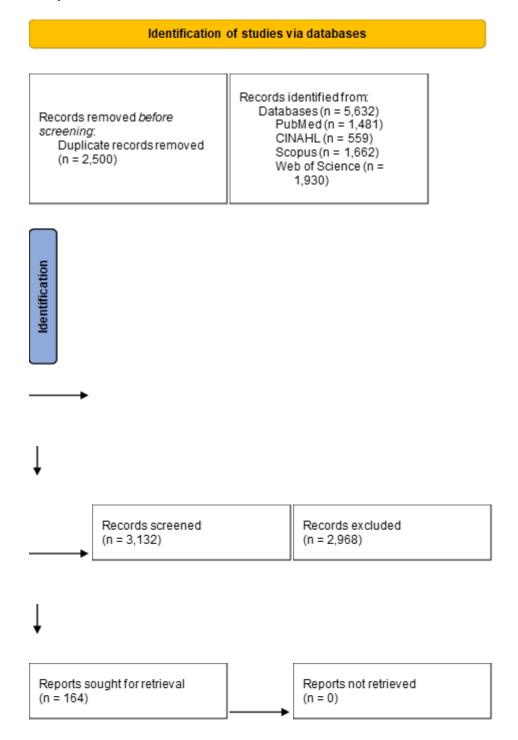
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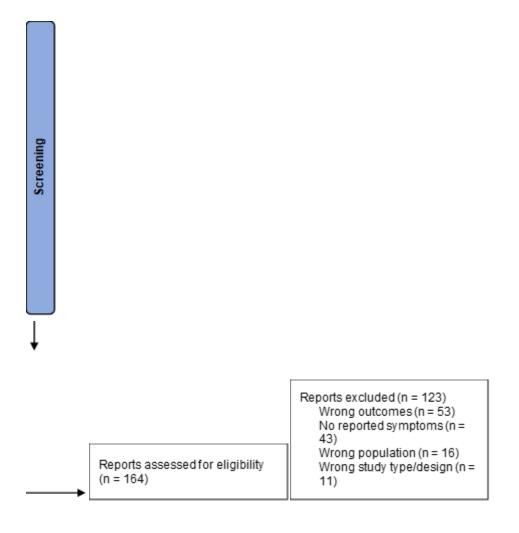
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PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only





Studies included in review (n = 41)

Included

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

For more information, visit: <u>http://www.prisma-statement.org/</u>

1 st Author Last Name∕Year	Country	Design						Reported Sympt	oms			
			Absent Symptoms	Cardiac	ENT	General	GI	GU/Reproduct	ive Neurological	Psychological	Pulmonary	Women's Symptoms
Adedapo (2015) [28]	Nigeria	Prospective cross-sectional				Fatigue			HA, Dizziness		Breathlessne	SS
Anjum (2018) [29]	Pakistan	Cross-sectional single cohort		Palpitation		Fatigue Sleep Apnea		Urinary Frequency	HA, Vertigo Confusion		Dyspnea	
Bokhour (2012) [30]	US	Qualitative grounded theory	No Symptoms						HA Dizziness			
Boitchi (2021) [31]	Bangladesh	Qualitative narrative		Chest discomfort		Neck pain, Fatigue			Dizziness, Light- headedness, Migraine		Breathing problems	
Brown (2011) [32]	US	Cross-sectional										Hot Flashes
Chimberengwa (2016) [33]	Zimbabwe	Cross-sectional	Asymptomatio	c Palpitation	S				HA			
Chung (2021) [34]	Australia	Longitudinal cohort										Dysmenorrhea Menorrhagia, irregular periods
Daviri (2016) [35]	Greece	Quasi- experimental								Depression		
DeAndrade (2018) [36]	US	Qualitative	Hard to explain		Vision Changes	Malaise			НА	Anxiety		
Dong (2019)		Longitudinal								Depression		
[37] Franklin (2013) [38]	US	Cross-sectional			Vision changes	Flushing			HA Dizziness	Insomnia		

Franklin (2016) US Qualitative Feeling Vision **Turning Red** HA [39] heart beat changes Swelling Fatigue phenomenology Dizziness Hearing/feeling blood rush to head Gardener (2016) US Migraine with Cross-sectional [40] cohort aura Guidi (2020) Bologna **Cross Sectional** Anxiety, Depression, [41] Distress HA Granados-Spain Longitudinal Tachycardia Flushing Nervousness Gameza (2015) descriptive Dizziness [42] Depression, Jackson, CA Australia Longitudinal (2016) [43] Anxiety US Longitudinal Jackson, EA Hot flashes (2016) [44] Jahan (2020) Bangladesh Qualitative Chest HA Vomiting [45] discomfort Dizziness, Vertigo Longitudinal Jin (2019) China Depression [46] Kagitani (2014) Japan Hot flashes Cross-sectional [47] Kressin (2019) US Cross-sectional Symptoms Anxiety, [48] Depression, come and go Fear Kuo (2011) Longitudinal Taiwan Depression [49]

Fingers tingling

Maatouka (2016)Germany [50]	Cohort					Clinically significant depression	
Moonen (2015) Netherlands [51]	Cohort					Apathy	
Pierin (2016) Brazil [52]	Cross sectional No symptom	S					
Qvist (2014) Denmark [53]	Cross-sectional No symptom	s Palpitations	Nosebleed		НА		Shortness of breath
Rantanen (2018) Finland [54]	Cross-sectional					Clinically significant depression	
Roales-Nieto Spain (2014) [55]	Quasi- experimental	Tachycardia	Head & neck pain, Fatigue		Dizziness		
Schmieder Austria/Germar (2017) [56]	ny Observational	Chest tightness Irregular heart beat, Pounding heart	Fatigue, Head pressure, Cold hands or feet, Drowsiness, Sweating hands or feet, Restlessness, Swollen ankles, Tiredness, Sleep disturbance		HA Dizziness		Shortness of breath
Shamsi (2017) Iran [57]	Qualitative		Flushing, Fatigue	Sexual problems	HA Dizziness	Anxiety, Insomnia Spiritual problems	
Shrestha (2018) Nepal [58]	Qualitative No symptom	S			HA Dizziness	Anger	
Sieminski (2016) Finland [59]	Cohort- retrospective		Restless leg syndrome				

Spruill (2012) [60]	US	Cross-sectional						Depression	
Spruill (2016) [61]	US	Cross-sectional						Depression Hostility	
Stallings (2017) [62]	US	Cross-sectional No symptoms	5 Fast heart rate	Fatigue Pain Flushed Sleep difficultie Loss of strength	s	Loss of libido	HA Dizziness		Breathlessness
Steiner (2011) [63]	Austria	Cross-sectional No symptoms	5						
Sunwoo (2019) [64]	Korea	Cross-sectional		Restless leg syndrome					
Taft (2018) [65]	Sweden	Cohort						Stress, Well- being	
Taylor (2012) [66]	Nigeria	Qualitative phenomenology		Fatigue, Weakness			HA Dizziness		
Tikhonoff (2016 [67]	5) United Kingdom	Longitudinal						Affective symptoms	
Tsiantou (2016) [68]	Greece	Qualitative		Feeling strange			HA	Anxiety	

Criteria-Quantitative	Points	Criteria-Qualitative	Points
Clear Purpose	1	Clear Purpose	1
Background literature	1	Background literature	1
Design	1	Design	1
Sample description	1	Theoretical perspective	1
Sample size justified	1	Methods used	1
Dropouts reported	1	Sampling	1
Outcomes appropriate	1	Saturation/Redundancy	1
Outcome measures valid	1	Informed consent	1
Intervention described	1	Clear site description	1
Contamination of intervention avoided	1	Participant description	1
Cointervention avoided	1	Researcher relationship identified	1
	1	Researcher assumption & biases	1
		Procedural Rigor	1
Statistical statistics reported Analysis appropriate Clinical importance	1	Inductive analyses	1
Conclusions/Implications	1	Consistent & reflective findings	1
	1	Decision trail	1
		Detailed analysis of data described	1
		Meaningful picture of phenomenon emerge	1
		Credibility	1
		Transferability	1
		Dependability	1
		Confirmability	1
		Conclusion appropriate	1
		Finding contribute to theory	1
			_

Total possible points	15	Total possible points	24

Study	Purpose/Aim	Study Descriptors (<i>N,</i> Age, Gender)	Outcome	Quality Score*
Adedapo et al (2015) [28]	Compare health related quality of life, effect of BP control and medication use with hypertension.	f <i>N = 713</i> Mean age 57 <u>+</u> 13 M 45.9%, F 54.1%	HTN and antihypertensive medication reduced health related quality of life. Lower symptoms count and income improve quality of life.	10
Anjum et al (2018) [29]	Determine correlation of systolic and diastolic BP, sign and symptoms with age and gender.	Mean age 48.61 <u>+</u> 12.54	Gender difference apparent in symptoms of HTN.	10
Brown et al (2011) [32]	Examine BP 10 minutes prior and during hot flashes.	N = 202 Mean age 50.6 <u>+</u> 3.0 F 100%	After hot flashes, a transient increase in BP occurs, but was not found to be causal.	10
Chimberengwa et al (2016) [33]	Determine HTN knowledge, practices and attitudes in Zimbabwe province.	N = 304 Mean age 59 M 35.5, F 64.5	Decreased knowledge and shortages of antihypertensive medication were factors in poor HTN control.	9
Chung et al (2021) [34]	Examine effects of menstrual symptoms association with risk of HTN.	N = 7729 w/ Chronic HTN f Mean age 24.6 <u>+</u> 1.4 F 100%	Women experiencing irregular and heavy periods are at increased risk of chronic HTN.	10
Daviri et al (2016) [35]	Determine if a stress management and health promotion program have an effect on BP.	N = 548 Mean age 52.9 <u>+</u> 8.6 (test group) 52.4 <u>+</u> 8 (control) M 61%, F 39% (test) M 36%, F 64%	Intervention with medium effect on BP. Systolic BP reduction related to Body Mass Index change. Diastolic BP reduction related to change in depression.	14
Dong et al (2019) [37]	Determine if increased insomnia symptoms have an effect on HTN and depression over time.		Insomnia is a predictor and can contribute to incident HTN and depression in the older adult	8

M 41%, F 59%

Franklin et al (2015) [38]	Describe meaning and emotions of HTN symptoms	N = 26 Mean age 53.2 <u>+</u> 9.1 M 58% F 42%	Symptoms caused by HTN and not medication for control. HTN symptoms can be controlled. Beliefs of those with HTN are different than providers. The person will manage HTN based on their beliefs.	10
Gardener et al (2016) [40]	Investigate association with HTN and migraines.	N = 1338 Mean age 68.1 <u>+</u> 9.6 M 37% F 63%	Migraine is associated with HTN of duration greater than 9 years whether controlled or uncontrolled with and without aura.	7
Granados-Gameza et al (2015) [41]	Explore beliefs about symptoms of HTN and change over time.	N = 171 Mean age 53.27 <u>+</u> 10.65 M 33%, F 67%	Increase of beliefs in symptoms over time with noted significance between groups.	7
Guidi et al (2020) [42]	Determine allostatic load by clinimetric criteria, comparing hypertensive and normotensive persons.	N = 160 Mean ages 62.18 <u>+</u> 8.59 hypertensive group, 61.09 <u>+</u> 8.33 control M 33%, F 67%	Hypertensive participants had a greater level of allostatic load and psychological distress than the control group.	10
Jackson, CA et al (2016) [43]	Explore if depression and anxiety are associated with incident HTN in women		Depression and anxiety increase odds of HTN in middle aged women without adjusting of other variables. Adjusting for obesity, depression was no longer associated. Anxiety is not associated when adjusted for depression.	7
Jackson, EA et al (2016) [44]	See if there is an association with hot flashes and BP and to see if HTN develops over time.	N = 2839 Mean age 46.2 <u>+</u> 0.1 to 47.2 <u>+</u> 0.2 in 3 groups F 100%	Frequent hot flashes increase the risk of incident pre-HTN and HTN.	6
Jin et al (2019) [46]	Examine the effect of diagnosed HTN on depressive symptoms and socioeconomics.		HTN diagnosis is a stressor that increases depression in lower socioeconomic individuals.	11

Kagitani et al (2014) [47]	Probe association between hot flashes and BP among mid-aged Japanese women.	N = 1058 Mean age 45.2 <u>+</u> (4.3) F 100 %	Increased SBP and DBP were related to experiencing hot flashes. Increased pulse pressure was related to hot flashes in tobacco smokers.	6
Kressin et al (2019) [48]	Investigate how beliefs related to BP, and contextual life factors affect BP control beyond the effect of adherence to pharmacological treatment regimens.	N = 103 Age ≥ 65, 47.6% M 96.1% 3.9F %	Counseling participants about their beliefs related to BP significantly predicted BP control after controlling for medication adherence, sociodemographics, and race/ethnicity.	10
Kuo et al (2011) [49]	Test the effect of depression on mortality in elderly people with self-reported HTN.	N = 3736 Mean age 68.2 M 57.3% F 42.7%	Depression was a significant contributor to mortality in persons with HTN.	11
Maatouka et al (2016) [50]	Examine associations between HTN and depression and generalized anxiety symptomology in elderly people.	N = 3124 57-64y 24.8% 65-74y 76.5% 75-84y 23.5% M 47.4% F 52.6%	Participants with clinically significant symptoms of depression on PHQ-8 had higher odds of HTN. Generalized anxiety was not associated with HTN.	10
Moonen et al (2015) [51]	Cross-sectional exploration of relationships between SBP, DBP and MAP across varying depressive symptoms in depressed older persons.	N = 270 Mean age 70.4 <u>+</u> (7.3) M 36.3% F 63.7%	Higher SBP, DBP, and MAP were associated with higher scores on the Apathy Scale. Higher SBP was associated with higher mood subscale scores on the IDS-SR instrument.	10
Pierin et al (2016) [52]	Investigate associations between blood pressure and independent variables including bio-social and lifestyle characteristics, and factors related to HTN management.	Mean age 6th decade of life	Controlled BP was associated with being White, female, primary/secondary education, abstinence from alcohol, higher income, and regular physical activity. Hinderances to BP control were associated with personal beliefs that HTN is without symptoms and requires lifelong treatment.	11

Qvist et al (2014) [53]	Test differences in knowledge about BP and HTN between participants with self-reported HTN compared to those without self-reported HTN.	M 53.8% F 46.2%	Participants knowledge of symptoms associated with HTN included nosebleeds, headache, shortness of breath, and palpitations. Thirty percent of participants believed HTN; does not cause symptoms.	8
Rantanen et al (2018) [54]	Explore relationship between and predisposing factors associated with HTN awareness and depression symptomology.	l <i>N</i> = 2676 Mean age 58 <u>+</u> (7) M 44.3% F 55.7%	Participants who were normotensive and those who were unaware of being hypertensive had lower risk for depression. Being female, harmful alcohol use, and obesity were predictors for depressive symptomology in participants who were aware of being hypertensive.	9
Roales-Nieto et al (2014 [55]	I) Test a procedure aimed at modifying false beliefs about symptomology in HTN by identifying attributed symptoms, estimated BP, and feedback based on measured BP.	<i>N</i> = 60 d	Modification of false beliefs about HTN was associated with improved DBP, pharmacological treatment adherence, diet, exercise, and emotional control. SBP did not significantly improve.	11
Schmieder et al (2017) [56]	Investigate differences in perceptions of living with refractory HTN and the impact of antihypertensive therapy	N = 5831 Mean age 63.5 <u>+</u> (11.8) M 53% F 47%	Improvement in quality of life, perceived emotional burden associated with HTN, and symptom experiences including limitation in activity and anxiety improved during antihypertensive treatment. Improvement was more likely when target BP was achieved.	9
Sieminski et al (2016) [59]	Test the association between RLS and nocturnal BP.		RLS was associated with higher incident of nocturnal and sleep-time SBP compared to control. No appreciable nocturnal SBP dipping in participants with RLS.	9

Spruill et al (2012) [60]	Appraise differences in relationships between HTN labeling and health-related quality of life and depression across White and Black participants.	N = 308 Mean age 58.4 <u>+</u> (10.7) M 38.6% F 61.4%	Black and White participants labeled as hypertensive reported comparably poorer physical health compared to unlabeled participants. Labeling was associated with poorer mental health and increased depression symptomology unexplained by differences in socioeconomic status.	10
Spruill et al (2016) [61]	Identify psychosocial variables associated with BP dipping in African Americans.	N = 668 Mean age 58.4 <u>+</u> (10.7) M 31.4% F 68.6%	Nondipping occurred in 64% of participants and was associated with lower perceived social support, increased hostility, and depression. Perceived support was the only covariate associated with BP dipping.	11
Stallings & Schneider (2017) [62]	Secondary analysis to explore perceptions of symptoms associated with HTN among Blacl women.	, , ,	One to six symptoms were reported by 41.3% of 1 participants and attributed to HTN. Most frequently reported symptoms included headache, dizziness, fatigue, breathlessness, fast heart rate, and pain.	7
Steiner et al (2011) [63]	Reassess longitudinal trends related to knowledge of health risks related to HTN in Austria.	N = 1005 15-29y 22% 30-49y 39% 50+y 39% M 48% F 52%	Participants had good understanding of risks associated with HTN but had misconceptions related to BP symptomology and low rates of BP checks.	4
Sunwoo et al (2019) [64]	Test relationships between RLS and HTN in Korean adults.	N = 2740 Mean age 44.5 <u>+</u> (33-81) M 49.9%, F 50.1%	Self-reported HTN was associated with RLS symptoms occurring at least once a week, increased age, being overweight, lower education level, diabetes mellitus, and short sleep duration.	10
Taft et al (2018) [65]	Investigate relationships between self-monitored blood pressure and self-reported coincident pharmacological therapy, well- being, stress, physical activity, an symptomology.	Mean age 59.5 (33-81) M 52%, F 48%	Pharmacologic therapy, improved well-being, lower stress and increased physical activity were associated with lower same-day SBP and DBP. Symptoms including dizziness, headache, restlessness, fatigue and palpitations were not associated with BP.	10

Tikhonoff et al (2016) [67]	Explore associations between affective symptoms and awareness of HTN diagnoses across repeated measures of affective symptoms.	N = 1683 M 47.6%, F 52.4%	Participants who were diagnosed with HTN and "labeled" as hypertensive were more likely to report affective symptoms controlling for antihypertensive therapy and affective symptoms at time of diagnosis. No associations were seen in participants with measured HTN but who were not diagnosed or labeled as hypertensive.	10
Study	Purpose/ Aim	Study Descriptors (N, Age, Gender)	Outcomes	Quality Score*
Boitchi et al (2021) [30]	Examine women's understanding of HTN, experiences of symptoms and complications with modification, medication adherence, management and barriers		HTN symptoms, risk factors and treatment not perceived through a biomedical lens. HTN management impacted by socioeconomic status.	20
Bokhour et al., (2012) [31]	Explore how the experience of hypertension and social context relate to daily self -management.	N = 48 Mean age 60 + 10.31 M 92% F 8%	Perceptions of the cause and course of HTN, experiences of HTN symptoms, and beliefs about the treatment were related to different HTN self-management behaviours; lifestyle choices influenced optimal HTN management.	18
DeAndrade et al (2018) [36]	To characterize patient understanding and management of HTN in a Cape Verdean immigrant community	N = 20 Median age 57.5 M = 35%, F 65%	Believed HTN to be symptomatic, with headache being the most common symptom; some took medication only when they felt symptoms; poor understanding of hypertension and language barriers in order to communicate with providers.	18
Franklin et al (2016) [39] Describe the experiences of women with HTN self-managing their perceived BP changes	N = 13 Mean 50.53 + 9.62 F 100%	Primary theme, "getting to normal," described the need of the women to get their BP to normal. The women felt they could tell when their BP changed based on symptoms and would act to get it down, especially if distressful symptoms were experienced.	18

Jahan et al (2020) [45]	experiences of HTN among rural	N = 74 Mean 52.2 F 100%	3 Primary themes: Perception of HTN based on experiences, barriers to knowledge of management of HTN, and barriers to management of HTN. Group only knew HTN by symptoms from acquaintances and feared the consequences. In this country, BP check at home was not available, so they could only rely on symptoms.	19
Shamsi et al (2017) [57]	-	N = 27 Mean age 52.6 + 1.1 M 55.6 F 44.4	3 Primary Themes: Disease shadow, dual understanding of the effect of drug therapy with perceived benefits and negative outcome, facing the disease. HTN causes problems in physical, social, psychological and spiritual aspects. Control is within the context of cultural beliefs and values.	21
Shresthra et al., (2018) [58]	Explore barriers and facilitators in controlling HTN among those with a new diagnose		Limited knowledge and misbeliefs were prevalent. Barriers included absence of symptoms, reluctance to take medicine, low perceived seriousness of the disease, challenges in behaviour change and lack of communication and trust with provider. Facilitating factors were fear of consequences of the disease, and family support in controlling diet and adhering to treatment.	16
Taylor et al (2012) [66]	symptoms and treatment of HTN in a primary care practice in	N = 70 Average age M = 59.4, F = 53.0 M 41% F 59%	4 themes of HTN: perceptions of hypertension, consequences, effect on daily life, and perception of treatment. Social and cultural factors affect beliefs and behaviours of managing. Varying views on treatment and long-term management. Men felt stressors outside home and women felt family stressors contributed to HTN.	17
Tsiantou et al (2010) [68]	Investigate factors of HTN and antihypertensive medication adherence in Greece	N = 43	HTN was considered serious and the person would listen to the provider as opposed to others. Some patients discontinued treatment when they believed that they had	13

Mean age Group A	controlled their blood pressure. Younger people may have
(semistructured interviews)	greater difficulty accepting diagnosis and treatment.
63.7	Communication with provider important.
Group B (Focus groups) 44.6	
Group A M = 48%, F = 52%	
Group B M =50%, F = 50%	

