SYSTEMATIC REVIEW/META ANALYSIS

Factors Predicting Treatment Adherence Among Patients with Hypertension: A Systematic Review and Meta-Analysis

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ABSTRACT

Background: Through the increased prevalence of hypertension, the notch of following the prescribed anti-hypertensive treatment among these populations is very inadequate, and the unsatisfactory disease control rate. This study systematically reviewed and identified their characteristics of the predicting factors on it and their magnitude.

Methodology: By the Joanna Briggs Institute (JBI) methodology, the included articles were critically appraised and assessed their certainty of evidence with the GRADE guidelines. Four databases (Google Scholar, ScienceDirect, PubMed, and WILEY online) and the keywords of treatment adherence" OR "compliance" AND "determinants" OR "factors" OR "predictors" OR "influences" AND "hypertension" OR "high blood pressure" were applied. The integrated effect sizes (z), 95% confidence intervals (CIs), and I^2 index were reported.

Findings: Descriptive correlational and longitudinal designs were included in total 20 studies. The significant predictors were demographic, intrapersonal, interpersonal, condition-related, and health system-related ones. Patients' self-efficacy, perception, co-morbidity and social support produced the most significant effects. Additionally, various adherence levels to treatment were reported as low to acceptable.

Conclusion: The hypertension society should strengthen their adherence practices by clear instructions and guidance, especially for multimorbid ones, by improving their self-efficacy and perception on their disease, building social support and virtuous patient-provider communication.

Keywords: Hypertension, Treatment Adherence, Factors, Systematic review, Meta-analysis

ARTICLE INFO

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Introduction

Globally hypertension prevalence is increasing around the world as 1.28 billion people aged over 30 years. However, the blood pressure control rate was still poor, reported in 80% of all diagnosed cases.[1,2] Furthermore, it stands as a significant cause of cardiovascular diseases and death according to Global Health Estimates in 2020[3] and as their preventable origin.[4] Taking anti-hypertensives and following lifestyle modifications can control blood pressure effectively.[5,6] Altogether, the patients are responsible for taking anti-hypertensive treatment precisely as directed by physicians. Hence, adherence was defined as "the extent to which a person's behavior medication, following a diet, and executing lifestyle changes, corresponds with agreed recommendations from a healthcare provider".[7] Treatment adherence in hypertension involves taking anti-hypertensive drugs and lifestyle modification instructions such as eating a low-salt diet, physical exercise, maintaining body weight, quitting tobacco, and reducing alcohol intake.[8] However, its chronic and asymptomatic nature can easily change people's behavior due to their symptom orientation.[9]

Moreover, many physical, social, and psychological impacts result from poor adherence to anti-hypertensive treatment.[10] Although both medications and lifestyle modifications treat hypertension with various guidelines, poor adherence rates were experienced globally, and serious complications were faced in this population. Following the prescribed anti-hypertensive treatment comprised of taking medications and lifestyle modifications is very critical for improving quality of life, preventing serious complications and death.[10,11] However, various studies previously explored the factors and barriers to anti-hypertensive medications,[12] blood pressure control,[13] and a single factor of social support on treatment adherence.[14] Moreover, there is still a gap in conducting systematic reviews and meta-analyses of factors predicting treatment adherence among hypertensive people. Therefore, the major predicted factors for poor treatment adherence should be explored and it is necessary to rejuvenate it because adherence to anti-hypertensive medications and lifestyle modifications cannot be separated in controlling high blood pressure. Singular studies may give the inconsistent findings, and the magnitude and comprehensive and unbiased report of the predicting factors for treatment adherence should be updated. Consequently, any healthcare personnel can understand the efficient predicting factors and their characteristics on treatment adherence by accumulated effects of statistically more stout conclusions. Then, their patients can be managed effectively by bolding their needs for good treatment adherence which will further increase disease control rates and prolong their lives. Additionally, multiple interventional adherence promotion programs could be established around the world. This review aimed 1) to systematically review the literature on the association between predicting factors and treatment adherence in patients with hypertension and 2) to identify their characteristics and magnitude.

Methodology

The methodology of the included studies was evaluated using the standardized critical appraisal instruments from the Joanna Briggs Institute (JBI) for systematic review,[15] consisting of search strategy, study selection, methodological quality assessment, data extraction, and data analysis/synthesis. Four electronic databases (PubMed, Science Direct, WILEY Online, and Google Scholar) were applied for searching the published English full-text articles with peer-review from 2013 to 2024, examining the association between predicting factors and treatment adherence by setting the inclusion criteria. The Preferred Reporting Items for Systematic Reviews and Meta-Analysis 2020 (PRISMA) guidelines were followed,[16] and the registration to PROSPERO register was performed for this review (CRD42023470364). Key terms for this review were "treatment adherence" OR "compliance" AND "determinants" OR "factors" OR "predictors" OR "influences" AND "hypertension" OR "high blood pressure" as a search strategy. Detailed search strategies are mentioned in Appendix 1. Most of the studies were cross-sectional correlational studies with one longitudinal design. The JBI critical appraisal tools were utilized to determine the methodological quality of all these studies and Grading of Recommendation, Assessment, Development and Evaluations (GRADE) guidelines were applied for evaluating the certainty of evidence.[17] The narrative synthesis presented the findings of this review with a summary table including name of authors and study design, rates of treatment adherence, the associated factors examined and their statistical values, measurement instruments for the dependent variable, setting and sample size, and finally, their Level of Certainty of evidence.

Meta-analysis and statistical method: Firstly, the effect size was calculated using 'Fisher's r-to-z transformation' for each correlation coefficient on "treatment adherence" to summarize the characteristics of factors predicting it according to Borenstein et al. (2009).[18] All the correlations (r) were converted to the Fisher's z scale using the following formula.

$$z = 0.5 \times \ln\left(\frac{1+r}{1-r}\right).$$

Other statistics with significant p values were derived to effect sizes (proportion/rate) by using the traditional equation (number of events divided by number to total),[19,20] which then converted to Fisher's z values by using $z=0.5 \cdot \ln(1-p/1+p)$. Then, all the transformed values were analyzed after calculation of standard error, $SE(z)=1/\sqrt{(n-3)}$.

Meta-analysis was performed by using RevMan (5.4) to calculate the integrated effect sizes (z) as the main index, standard errors, and 95% confidence intervals (CIs) for the demographic, intrapersonal, interpersonal, condition-related, and health system-related factors. I^2 index was applied to assess the heterogeneity and τ^2 (tau-squared) statistic to estimate the amount of true heterogeneity or variability between the effect sizes of the included studies ($p< 0.1$ and $I^2>$ 75% mean significant heterogeneity and $p> 0.1$, and I^2 values close to 0% with small heterogeneity, τ^2 is the lower the variability between studies when closer to zero). The random effect model was used because of the expected heterogeneity. A funnel plot was assessed to evaluate the publication bias according to Light & Pillemar (1984).[21] Then, the final z value was converted to r again by using the following formula by Borenstein et al. (2009): [19]

$$r = \frac{e^{2z} - 1}{e^{2z} + 1}.$$

Study selection and data collection: Two independent authors performed the eligibility assessment. Twenty articles with full text were selected to assess their study quality. For any disagreement or conflict between the two authors during study selection, the third author resolved the conflicts between reviewers to reach a consensus by determining whether a study meets the eligibility criteria. After the discussion, the third author confirmed the final decision. Then, the reasons for the exclusion of the studies were recorded.

Eligibility criteria: Inclusion criteria were: 1) Studies exploring the treatment adherence of patients with hypertension among adults aged over 18 years, 2) studies reporting the predicting factors of TA, 3) studies written in the English language, online accessible, peer review and full-text articles, and 4) studies within the period of 1st Dec 2013 to 31st Dec 2024. Exclusion criteria were the studies written in languages other than English and published before Nov 2013, at Conference abstracts, protocol registrations, thesis, books, and other reviews.

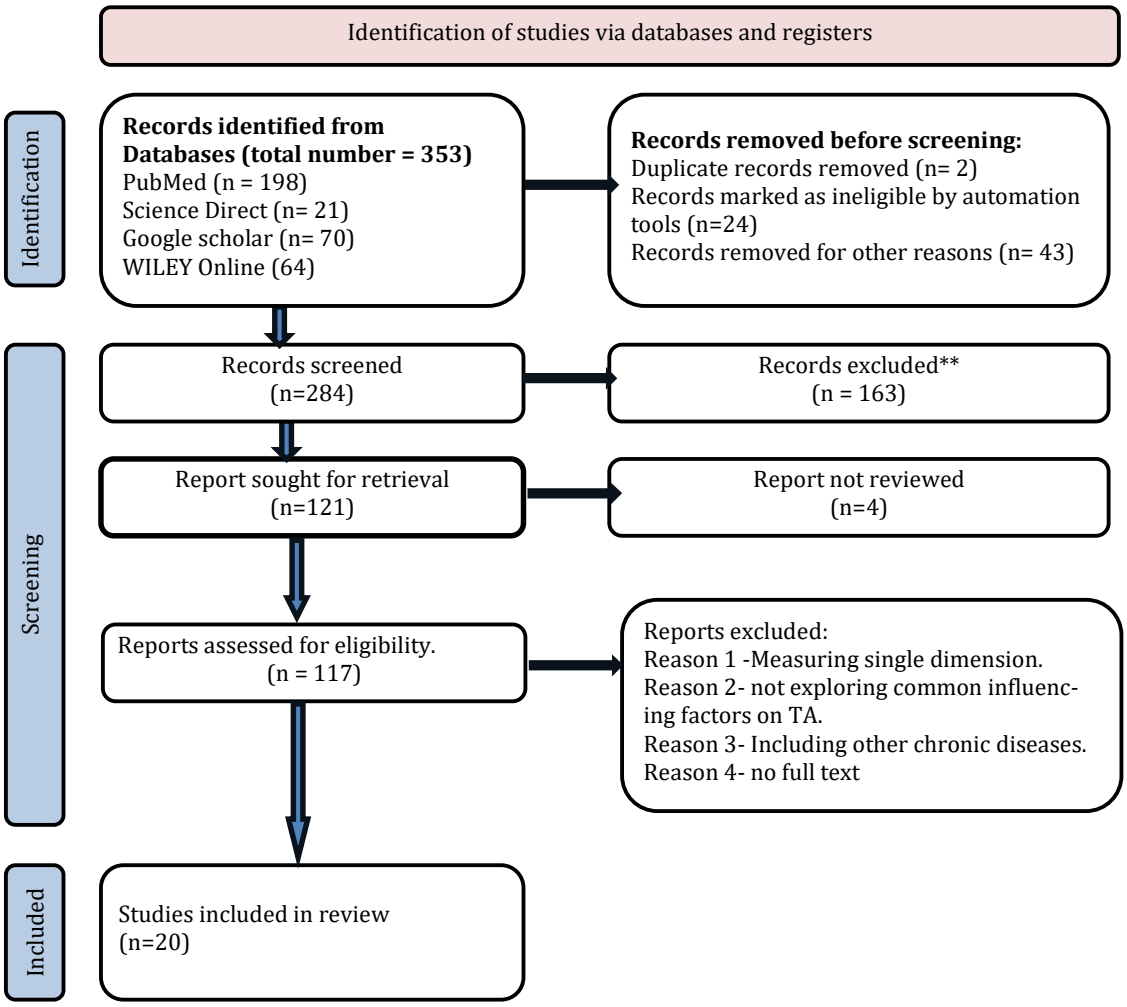


Fig 1: PRISMA flow diagram (2020)

(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)

RESULTS

General information: Of 353 articles, only 117 were retained for further assessment, and finally, 20 articles met the inclusion criteria. This systematic review consisted of only cross-sectional correlational studies and one longitudinal study. Then, all included analyses were run to evaluate their methodological quality and the certainty of evidence guided by the JBI critical appraisal tools and GRADE guidelines. Over half of the quality scores (50%) were obtained for all included studies with the evidence level from moderate to high.

Total participants of this systematic review were 7,377 patients with hypertension. The various settings included: one study from Jordan,[22] three studies from China,[23,24,25] two from Thailand,[26,27] two from Poland,[28,29] one from Boston,[30] one from Vietnam,[31] one from Palestine,[32] one from Slovakia,[33] one from Los Angeles,[34] one from Malaysia,[35] one from Algeria,[36] one from Nepal,[37] one from Iran,[38] and one from New York, United States of America,[39] one from Egypt,[40] and one from South Africa.[41] The participants from different parts of the world produced high generalizability in the findings of this review.

The review included treatment-adherence patient-reported outcome measures, as presented in Table 1. The Hill-Bone Compliance Scale (HBCS) in nine studies,[22,25,29,32,33,35,37,39,41] self-structured questionnaires for measuring treatment adherence,[28,30,36,40] Hypertensive Adherence to Therapeutic Regimens Scale (HATRS),[26,27] the therapeutic adherence scale for hypertensive patients (TASHP) questionnaire,[24] Hypertensive Treatment Adherence Scale (HTAS),[38] Treatment Adherence questionnaire of patients with hypertension (TAQPH),[23] combination of 8-item Morisky Medication Adherence Scale (MMAS-8) and non-pharmacological adherence guidelines from Ministry of Health,[31] and blood pressure self-care scale.[34] The scoring system of most instruments is that a higher score means better adherence and lower indicates better compliance on the HBCS. Overall, treatment adherence rates in patients with hypertension ranged from 14.7% in the study conducted by Sadeghi & Ahmadipour (2019)[38] to 82.8% by Aldaken & Eshah (2017).[22] The specific adherence rate to medication was from 11.7% by the report of Thuong et al. (2022)[31] to 77.17% by Mohamed et al. (2015),[40] and to lifestyle modifications was from 15.5% by Adinkrah et al. (2020)[33] to 81.4% by Thuong et al. (2022).[31]

Moreover, the significant dimensions of the treatment adherence were adherence to antihypertensives and lifestyle modifications. All studies covered medication adherence, but different subdomains for lifestyle modifications were studied. Based on the measurements, adherence sub-domains of lifestyle modifications for hypertension differed, such as diet and appointment keeping in HBCS, nonsmoking, limiting alcohol, follow-up visits, and salt reduction in most measurements. However, studies reported only studying single dimensions of TA were excluded, such as medication adherence or adherence to lifestyle modifications, exploring the association of factors with only one of them, associations to blood pressure outcomes, no statement of common influencing factors, and some including other chronic diseases.

Major findings: Factors predicting treatment adherence among hypertensive patients: This review had various factors predicting adherence to anti-hypertensive treatment. Those factors were demographic, intrapersonal, interpersonal, condition-related, and health system-related; the exact relationships between the subjects and the treatment adherence are outlined in Appendix 2.

Demographic Factors

Demographic factors were related to the structure of the population. These factors included age,[28,32,35,38] gender,[24,25,28,35] education,[23,29,35,38] working status,[39] and residence.[24]

Forest Plots and Funnel Plots of Demographic Factors: Age, gender, and education were involved in the meta-analysis of demographic factors obtained from seven studies (Fig 2.1, 2.2 and 2.3). As a result, gender had the most significant effect on treatment adherence based on the analysis (Total Effect Size (z)= 0.39, 95% CI: 0.15-0.63, I^2= 96%, τ^2= 0.06, p=0.001). Then, it was followed by education (Total Effect Size (z)= 0.35, 95% CI: 0.24-0.46, I^2= 81%, τ^2= 0.01, p<0.00001). The age produced the third effect on treatment adherence (Total Effect Size (z)= 0.27, 95% CI: 0.08-0.47, I^2= 92%, τ^2= 0.03, p=0.007). No publication bias was reported by the symmetrical funnel plot among studies involved in this domain (Fig 2.4).

Fig 2.1) Age to Treatment Adherence

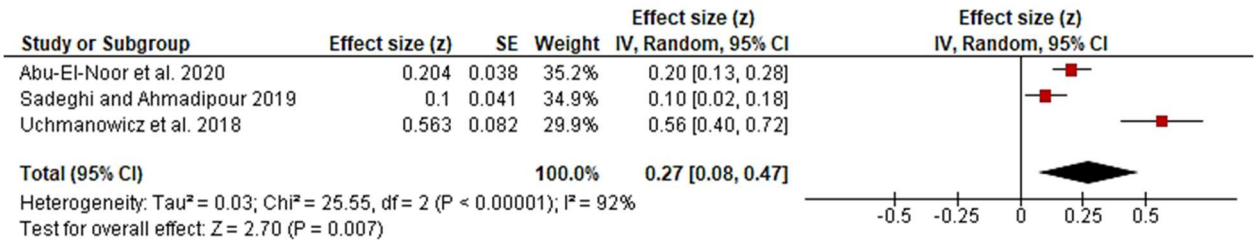


Fig 2.2) Gender to Treatment Adherence

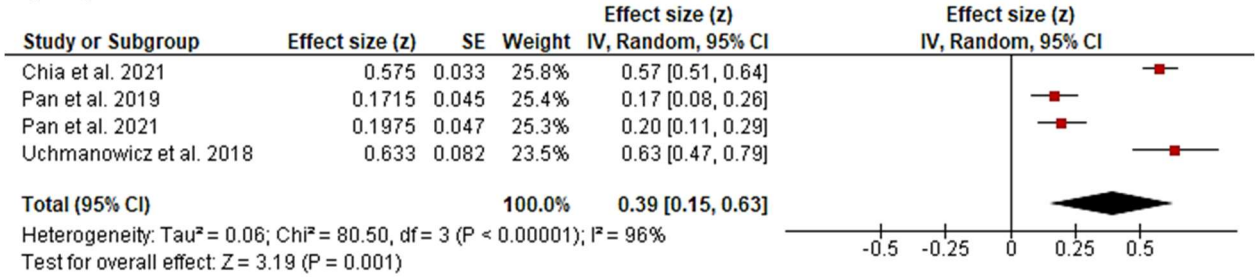
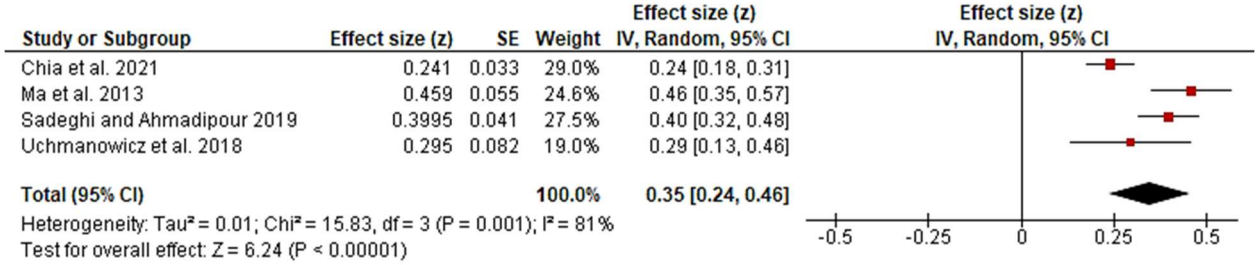


Fig 2.3) Education to Treatment Adherence



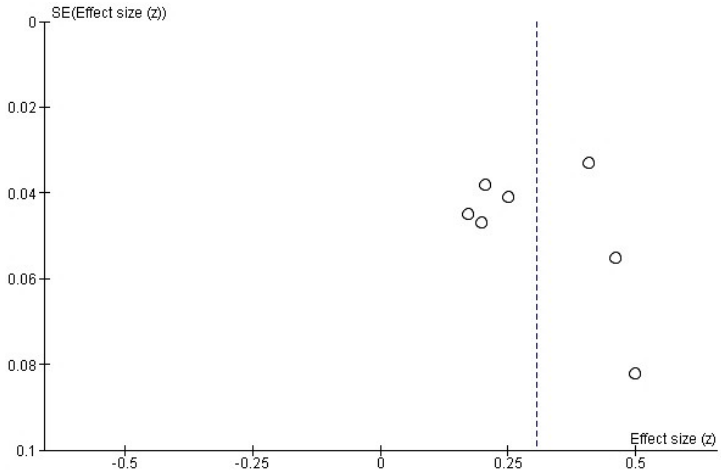


Fig 2.4 Funnel plot of seven studies involved in demographic factors

Fig 3.1) Knowledge to Treatment Adherence

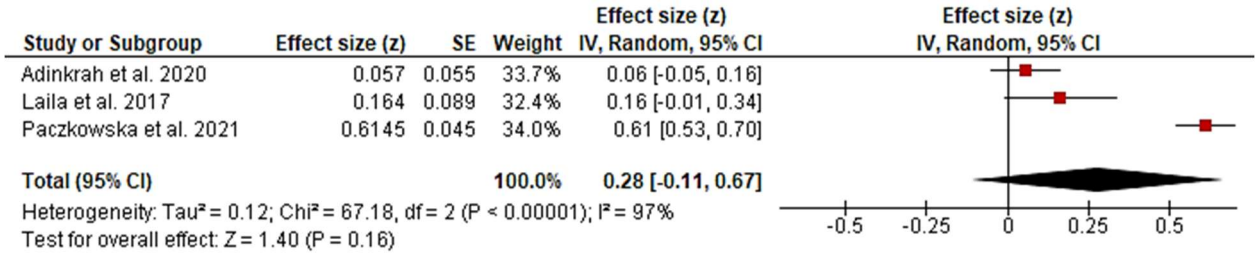


Fig 3.2) Self-efficacy to Treatment Adherence

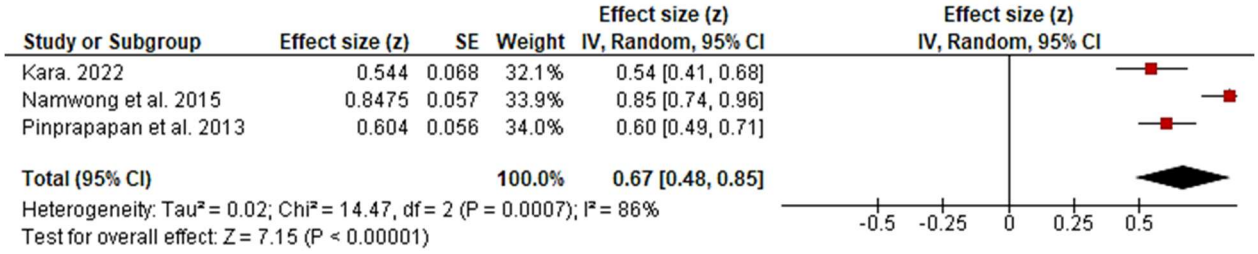
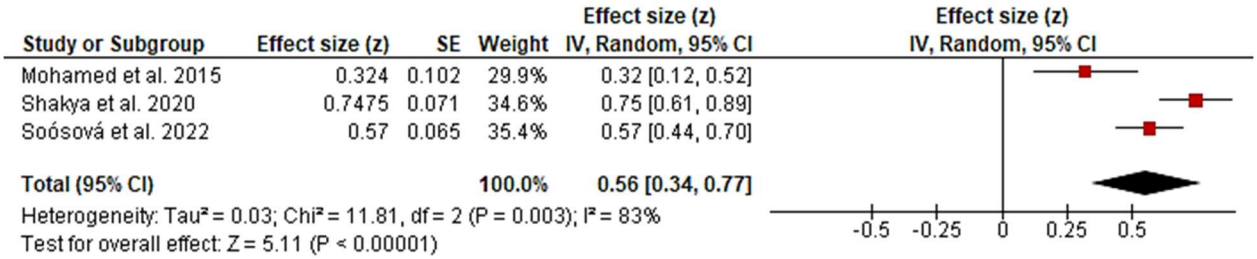


Fig 3.3) Perception to Treatment Adherence



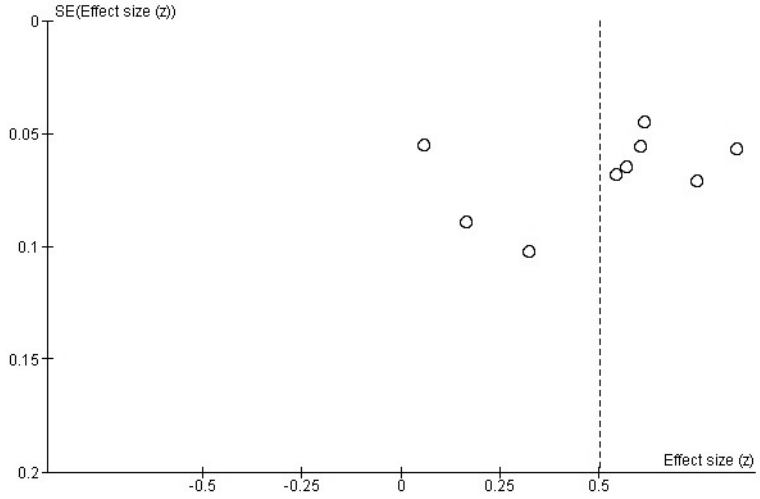
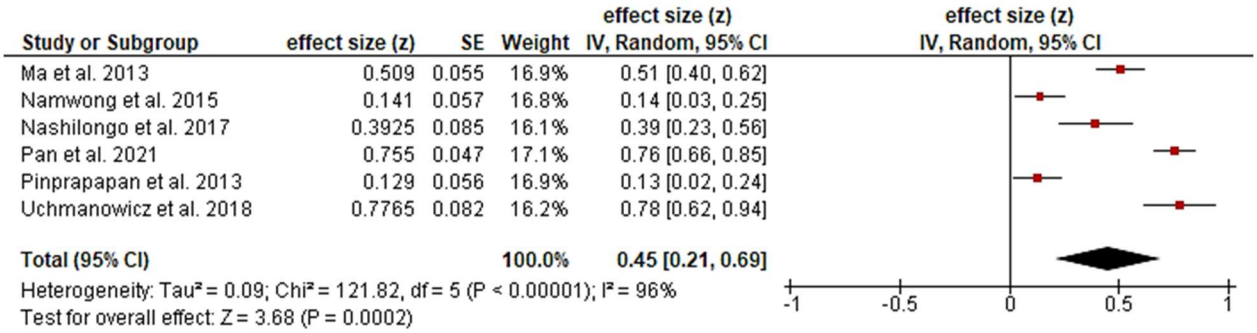


Fig 3.4Funnel plot of nine studies involved in intrapersonal factors

Fig 4.1) Interpersonal factors (social support level) to treatment adherence



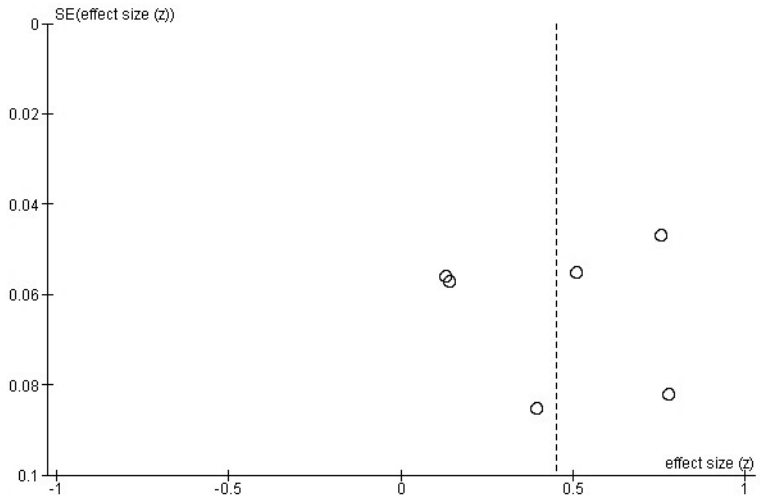


Fig 4.2 Funnel plot of six studies involved in interpersonal factors

Fig 5.1) Disease duration to Treatment Adherence

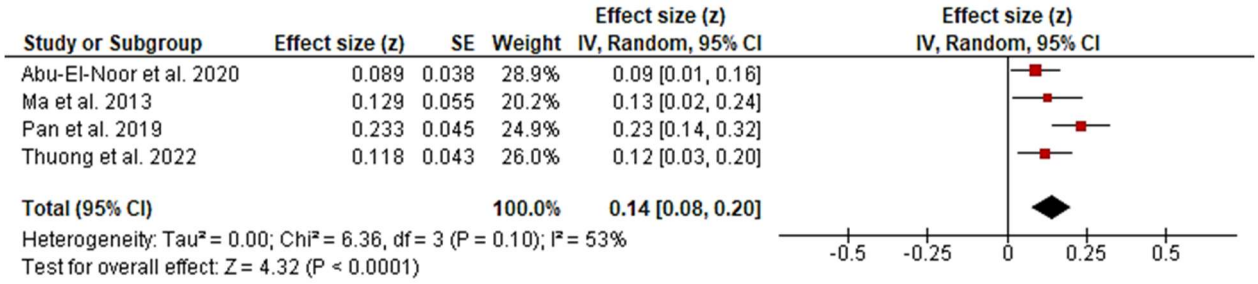
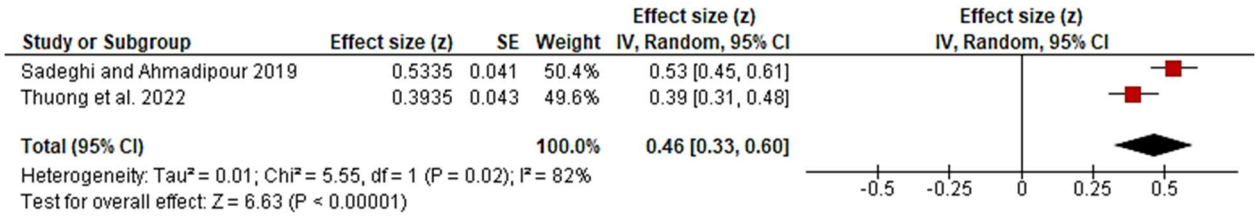


Fig 5.2) Co-morbidity to Treatment Adherence



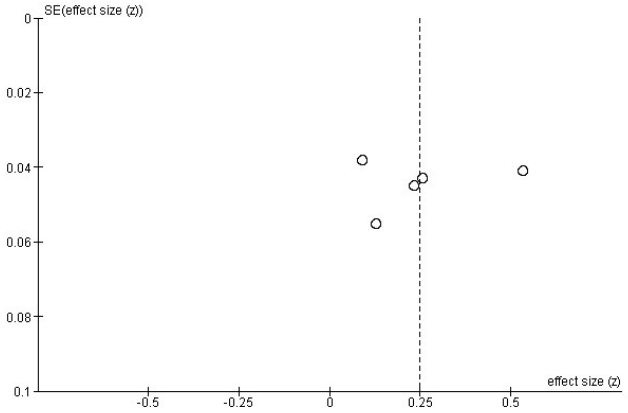
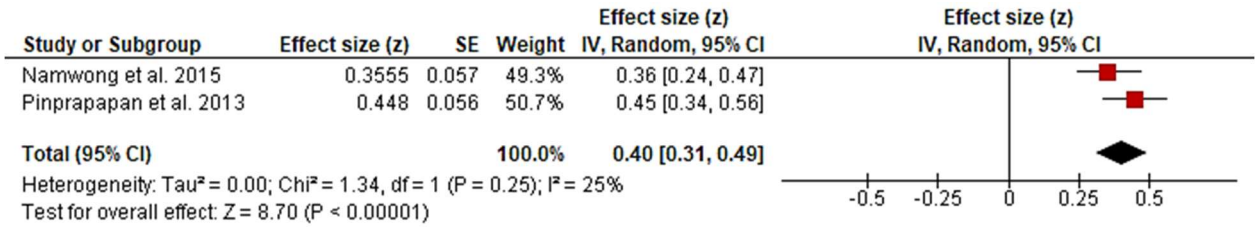


Fig 5.3 Funnel plot of five studies involved in condition-related factors

Fig 6.1) Patient-provider communication to Treatment Adherence



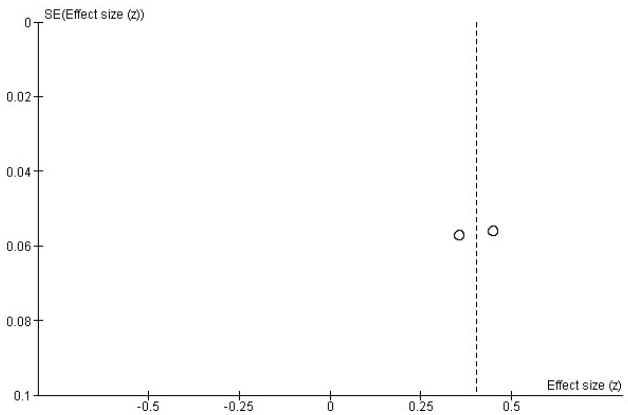


Fig 6.2 Funnel plot of two studies involved in health system-related factors

Intrapersonal Factors

Intrapersonal factors were taking place or existing within the minds of individuals. It included individuals' knowledge and skills, individual beliefs and perceptions, and physical status of a person. Specifically, factors related to an individual's knowledge and skills involve a level of knowledge,[22,28,34] and self-efficacy.[26,27,36] Those concerning individual's beliefs and perceptions consist of persons' belief about treatment[34] and patients' illness perception.[33,37,40] In physical status, the physical function of participants[26] and their nutritional status[31] were included.

Forest Plots and Funnel Plot of Intrapersonal Factors: Knowledge, self-efficacy, and perception were involved in a meta-analysis of the intrapersonal factors obtained from nine studies (Fig 3.1, 3.2 and 3.3). Self-efficacy was found to have the highest effect on treatment adherence for people with hypertension (Total Effect Size (z)= 0.67, 95% CI: 0.48-0.85, τ^2= 0.02, I^2= 86%, p< 0.00001), consequently with perception (Total Effect Size (z)= 0.56, 95% CI: 0.34-0.77, I^2 = 83%, τ^2= 0.03, p<0.00001) but not significant effect by the knowledge. No publication bias was reported by the symmetrical funnel plot with two outliers (Fig 3.4).

Interpersonal Factors

Interpersonal factors were relationships or communication among people. These factors were accounted for by social support.[23,25,26,27,29,41]

Forest Plots and Funnel Plot of Interpersonal factors (social support level): According to six studies, social support is mainly involved in interpersonal factors (Fig 4.1). The analysis showed that social support was found to have a significant effect on TA with statistical significance (Total Effect Size (z)= 0.45, 95% CI: 0.21-0.69, τ^2= 0.09, I^2= 96%, p= 0.0002). No publication bias was reported by the symmetrical funnel plot without an outlier (Fig 4.2).

Condition-related Factors

Condition-related factors are described as patients' clinical conditions. Patients' disease duration,[23,24,31,32] duration of anti-hypertensive drugs used,[25] number of anti-hypertensive medications used,[25] regular visit to physician,[22] the year with the same health care provider,[39] co-morbidities,[31,38] and stress levels[30] were involved in condition-related factors.

Forest Plots and Funnel Plot of Condition-related Factors: The disease duration and co-morbidity were involved in the meta-analysis of condition-related factors from five studies (Fig 5.1 and 5.2). Analysis reported that the co-morbidity had the significant and most remarkable effect on TA (Total Effect Size (z)= 0.46, 95% CI: 0.33-0.60, τ^2= 0.01, I^2= 82%, p<0.0001). Disease duration produced the second highest effect (Total Effect Size (z)= 0.14, 95% CI: 0.08-0.20, I^2= 53%, τ^2= 0.00, p<0.0001). No publication bias was reported by the symmetrical funnel plot with one outlier (fig 5.3).

Health-System related factors

Factors affecting the health system include how all health services are delivered. These elements were elaborated as provider-patient communication[26] and health insurance.[31]

Forest Plots and Funnel Plots of Health System-related Factors: Patient-provider communication was mainly involved in the meta-analysis of health system-related factors obtained from two studies (Fig 6.1). A meta-analysis using a randomized effect model reported that the patient-provider communication had a significant effect on patients' adherence (Total Effect Size (z)= 0.40, 95% CI: 0.31-0.49, τ^2= 0.00, I^2= 25%, p<0.00001). The symmetrical funnel plot reported no publication bias (Fig 6.2).

Discussion

All the studies included in this review applied quantitative methods, and the sampling techniques were mainly convenient sampling methods conducted in hospitals, primary health centers, and the community. Therefore, the participants from various settings can represent all hypertensive patients widely. Two studies[30,39] performed a secondary data analysis, and the second conducted his investigation. Based on the findings of this systematic review, the factors predicting TA among patients with hypertension were demographic, intrapersonal, interpersonal, condition-related, and health-system-related.

Firstly, for the demographic data, getting older (β= −0.05, 95% CI= −0.07-−0.03, p< .001) was found to have a positive relationship with TA[35] and (r= 0.1, p= .006).[38] Each subsequent year of life raises the average 0.2 points of the total scores (R^2= 0.2, p= .01).[29] Still, getting age has a positive association with adherence (r= -0.201, p= .0001).[32] That was supported by the report of a systematic review by Eicher et al. (2019) in which old patients were likely to show poor TA in chronic inflammatory disease.[42]

Similarly, gender was also imported as a debatable relationship with adherence as age. Females were found to be better adherent to anti-hypertensive treatment (β= −0.72, 95% CI = −1.30, −0.15, p= .014),[35] and males were less likely to comply to adherence (OR= 2.184, 95% CI= 1.097-4.350, p= .026)[24] and (p= .008).[25] Uchmanowicz et al. (2018) discovered that males had higher levels of adherence than females (R^2= 1.34, p= .04),[29] which is corroborated by the findings of Atan and Karabulutlu (2017) with the adherence to anti-hypertensive medications.[43] According to Eicher et al. (2019), being male was more likely to result in poor adherence.[42]

For the working status, being retired had better adherence (p= .013) in the study by Madu et al. (2019).[39] This finding was supported by Aljofan et al. (2023) for addressing the influence of occupation on medication adherence in a systematic review.[44] And

then, education levels had arguable relationships with adherence in which patients with primary education level and below (β= −0.91, 95% CI= −1.59,−0.23, p= .009) had better adherence.[35] But higher professional education led to higher treatment compliance (R^2=1.75, p= .02) by Uchmanowicz et al. (2018),[29] (p= .03) by Sadeghi and Ahmadipour (2019)[38] and (β= 0.19, p= .05) by Ma et al. (2013)[23] which were supported by Atan and Karabulutlu (2017).[43] Moreover, urban residents were more adherent to their treatment plan (OR= 0.145, 95% CI= 0.022–0.971, p= .047) (Pan et al., 2019)[24] that was congruent with the findings by Nezenega et al. (2020)[45] and by Eicher et al. (2019) as a reason for distance to the clinic.[42]

Secondly, regarding the intrapersonal factors, participants who have higher levels of hypertension knowledge (β= .135, p= .008) got better TA [34] and (β= .143, p< .02) [22] with similar findings in tuberculosis patients.[45] Patients' self-efficacy had a direct effect on adherence to therapeutic regimens (path coefficient = .69, p< .01).[26] Those who perceived high self-efficacy had better adherence scores (r (214)= .496, p= .01)[36] and (path coefficient = .54, p< .01).[27] Náfrádi (2017) supported this finding by a strong and favorable relationship between self-efficacy and adherence.[46] Furthermore, having fewer negative beliefs (β= .202, p= .000) and fewer concerns (β= -0.143, p= .007) about treatment lead to people getting higher adherence in hypertension.[34] Similarly, found that negative beliefs concerning treatments and illness, unrealistic expectations and doubts were predetermined patients' adherence levels.[42,44]

Illness perception had a positive significant relation with TA of hypertensive patients (ρ= .282, p< .01) by Shakya et al. (2020).[37] Soósová et al. (2022) explored the specific dimensions of illness perception as treatment control to diet adherence (β= 0.196, p< .01), timeline to drug adherence (β= .155, p< .05), as understanding to diet adherence (β= 0.359, p< .001), to appointment keeping (β= 0.192, p< .01) and medication adherence (β= 0.184, p< .01).[33] Specific perception including disease severity (r= .461, p= .001) and (r= .599, p= .000), benefit (r= .372, p= .008), and (r= .285, p= .045), barrier (r= -.637, p= .000), and (r=-.413, p= .003), and internal factors (r= .613, p= .000) and (r= .759, p= .000) showed a significant relation with adherence in two university hospitals in Egypt.[40] The relevant evidence was shown in a study by Nezenega et al. (2020) in which beliefs and perceptions about disease and treatment as influencing factors for non-adherence to TB medication.[45]

Subsequently, physical function (path coefficient = 0.94, p< .05) had a direct effect on adherence to therapeutic regimens.[26] Aljofan et al. (2023) provided a similar finding by a relationship between the level of physical disability and TA.[44] Another positive association was with nutritional status, such as average or high body weight (OR= 1.50, 95%CI= 1.21–1.87, p< .001).[31] This result is congruent with the finding that nutritional support significantly improved TA from a systematic review among TB patients.[47]

Thirdly, for interpersonal factors, increased social support (β= 0.27, p= .05.) will result in a higher adherence level.[23] There was a positive association between social support and TA in adults (OR= 0.752, 95% CI= 0.678–0.833, p< .001) by Pan et al. (2021), [25] (OR= 5.4, 95% CI 1.687–27.6, p = .045) by Nashilongo et al. (2017)[41] and (path coefficient = 0.13, p< .01) by Pinprapapan et al. (2013)[27] and in older adults (path coefficient = 0.14, p< .01) by Namwong et al. (2015).[26] Hence, social support significantly improves TA in both adults and older age groups. Similarly, patients living alone showed a lower TA rate than those living with family support, especially for the elderly.[29] Likewise, social factors play a major role in improving TA in chronic inflammatory skin disease[42] and in Tuberculosis.[45]

Fourthly, condition-related factors, patients' adherence rates declined in longer duration of hypertension.[23,32] Also, patients with a longer hypertension duration decreased their adherence level, especially to medication, by 0.66 times every five years of illness (Thuong et al., 2022)[31] and (p< .001) by Pan et al. (2019).[24] This finding was consistent with the systematic review conducted by Eicher et al. (2019)[42] and chronicity of disease can influence patients' adherence status by Aljofan et al. (2023).[44] In this review, a longer duration of taking anti-hypertensive drugs (p= .021) and a greater number of pills (p= .008) produced better TA.[25] Additionally, regular visits to a physician made the adherence rate higher (β= 0.410, p< .001) by Al-daken and Eshah.[22] Moreover, a longer duration of treatment with the same provider was related to adherence (p= .048).[39]

In addition, stress levels were significantly associated with non-adherence, especially for non-pharmacological treatment (p= .042) by Kang et al. (2018).[30] The presence of other medical diseases (p= .007) had a significant association with better TA,[38] and having co-morbidities helps to increase TA significantly to rise 2.21 times (OR- 2.21, 95%CI: 1.28–3.83) in the study by Thuong et al. (2022).[31] It was contrasting to the finding of Nezenega et al. (2020), where more than one co-morbidity led to non-adherence.[45] However, people with psychological disorders (p= .01) harmed TA in this review.[38] Supportive findings were described by Eicher et al. (2019) whereas the impact of psychiatric illnesses such as depression and anxiety on patients' adherence in chronic skin diseases.[42]

In the fifth one, health-system-related factors, provider-patient communication (path coefficient = 0.34, p< .01) had a direct effect on adherence to therapeutic regimens by Namwong et al. (2015)[26] and (path coefficient = 0.42, p< .01) by Pinprapapan et al. (2013).[27] As a similar result to this review, the role of physician-patient communication was crucial in enhancing patients' adherence in asthma patients[48] and in Tuberculosis.[45] Next, having health insurance was

associated with TA, especially for medication (OR= 5.67, 95%CI= 2.05–15.67, p< .001)[31] that was congruent with the financial impact on TA.[42,44]

In sum, different aspects of predicting factors to TA were reported regarding education and gender in this review, and the rest were significantly positive associations.

Based on the meta-analysis results, all these factors were positively related to overall adherence to antihypertensive treatment except knowledge from intrapersonal factors. Random effect models analyzed the results due to moderate-high heterogeneity across studies. Self-efficacy had the most significant effect on TA among all these factors (Total Effect Size (z)= 0.67 (r=0.585), 95% CI: 0.48-0.85, τ^2= 0.02, I^2= 86%, p< .00001) which was supported by the studies conducted in chronic diseases[49] and heart failure patients.[50] Precisely it was followed by perception as intrapersonal factors (Total Effect Size (z)= 0.56 (r=0.508), 95% CI: 0.34-0.77, τ^2= 0.03, I^2= 83%, p< .00001), co-morbidity as condition-related factors (Total Effect Size (z)= 0.46 (r=0.43), 95% CI: 0.33-0.60, τ^2= 0.01, I^2= 82%, p< .00001), social support (Total Effect Size (z)= 0.45 (r=0.422), 95% CI: 0.21-0.69, τ^2= 0.09, I^2= 96%, p= .0002) as interpersonal ones and patient-provider communication as health system related (Total Effect Size (z)= 0.40 (r=0.38), 95% CI: 0.31-0.49, τ^2= 0.00, I^2= 25%, p< .00001). The least total effect size was found in disease duration of condition-related factors (Total Effect Size (z)= 0.14 (r=0.139), 95% CI: 0.08-0.20, I^2= 83%, τ^2= 0.01, p< .00001) after gender, education, and age of demographic factors. I^2 values were reported by more than 75% except patient-provider communication the pooled effect might not equally reflect across all studies. These may be due to the different samples, study area of different cultures and possibility of using different measurements across the studies. Moreover, most studies reported very few outliers in the funnel plots for the publication bias assessment.

The second highest effect by perception was supported by Oliveira et al. (2023),[51] in which illness perception plays a significant role in TA of patients with hemodialysis and the belief of patients stood in the highest influential positions on TA in stroke patients by Rohmah and Fadjri (2023).[52] For co-morbidity, it was not consistent with the report of Smaje et al. (2018), in which higher levels of co-morbidity produced poorer adherence.[53] Then, interpersonal factors of this review were supported by the findings reported by Magrin et al. (2015),[14] in which similar reports of a significant influence of social support especially functional support on overall adherence in hypertension (Cohen's d= .18 [95 % CI: .05-.31, p<.01], I^2= 84.23). It was also supported in chronic diseases conducted by Rohmah et al. (2023) as well.[52] Moreover, social support can accomplish performance of physical activity[54] and following a healthy diet, especially in obese adults,[55] middle and older people.[56,57] The influence of health system-related factors on TA was congruent with the findings conducted by Al-Hajje et al. (2015) whereas TA in chronic diseases was significantly influenced by physician-patient communication.[58] In this study, age had a significant impact on treatment adherence (Total Effect Size (z)= 0.27, 95% CI: 0.08-0.47, I^2= 92%, τ^2= 0.03, p=0.007) that was supported by Kokenge and Ruppar (2024) in which getting older made a better adherence to medications in hypertensive people (r = 0.08, p < .01; k = 26 studies) and (r = 0.11, p = .01; k = 15) respectively.[59]

Furthermore, patients' self-efficacy, and perception as intrapersonal, and social support as interpersonal factors can be highly modified in creating effective TA programs compared to other factors such as age, gender, and education. Moreover, a better environment of patient-provider communication as health system-related factors can be established as a supportive way of improving adherence. Additionally, the co-morbidity condition of the patients as condition-related factors can be monitored without worsening, and these can subsequently maintain blood pressure control and prevent complications effectively. Healthcare providers can facilitate their communications by building patients' better self-efficacy and belief with the help of social support and emphasizing the importance of TA.

Limitations

All the studies in this review were selected by online accessible and English language. This review has some degree of global generalizability of the findings. Another limitation was the high heterogeneity in the evaluation of TA by using different scales. Additionally, this review cannot report on the mediator effects due to high heterogeneity, although the risk of bias due to confounding factors was already assessed using the JBI appraisal tools. All outcomes were assessed using a self-reported questionnaire, which may have resulted in recollections or social desirability biases. This review acknowledged the potential bias caused by the exclusion of non-English studies. In addition, the convenient sampling method was commonly used across the included study, which may lead to participant selection bias and affect the findings' precision. This review only had all the articles accessible online, which may result in publication bias due to the selective publication of research findings. Moreover, future review and meta-analyses should involve more longitudinal ones to ensure any changes because adherence behavior can change over time. Furthermore, this study included only the correlational cross-sectional studies which can reflect the association of significant predicting factors with treatment adherence in hypertensive population and cannot make a causal interpretation.

Although the outcomes were assessed by various treatment adherence questionnaires covering antihypertensive medications and lifestyle modification, some scales only measure the specific and different

subdomains of lifestyle behaviors, such as appointment keeping and reduced sodium intake in HBCS. Therefore, this review reported the general predicting factors on treatment adherence despite slight variations in the sub-domains of lifestyle activities.

Conclusion

TA is essential for getting blood pressure control, preventing serious complications, and preventing sudden death in hypertension.[60,61] The reported factors regarding TA can be helpful for health care providers to monitor the adequacy of patients' compliance, consider adherence promotion programs, facilitate their efforts, and improve the health and well-being of the total population. The researchers and the stakeholders can implement interventional programs to boost adherence to medication and lifestyle behaviors by using the updated findings. The demographic, intrapersonal, interpersonal, condition-related and health system-related factors from multiple studies of different areas can be analyzed in this study. Accordingly, self-efficacy and illness perception as intrapersonal factors, social support as an interpersonal factor, and patient-provider communication as health system related factors were observed as the ones with the highest effect on TA, and these have more handling effects used in interventional studies than the rest.

Moreover, TA promotion programs may be more cost-effective and more beneficial in controlling blood pressure than the medication adherence program alone. By performing well-established adherence promotion interventions, the hypertension population can establish better blood pressure numbers, get healthy lifestyle behaviors, prevent serious complications, and improve quality of life. For the stakeholders of a health system, they can design the adherence promotion programs such as behavioral coaching and skill building programs, behavioral cognitive therapy, and family and peer support programs. In addition, universal healthcare coverage and improvement of the providers' communication skills should be provided. For future research, implementation research can be performed by using significant influencing factors such as enhancing patients' self-efficacy and health education to correct their misperception, strengthening effective patient-provider communication, integration of social support, especially to comorbid patients.

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