

# The efficacy of cognitive behavioral therapy-based interventions on patients with hypertension: a systematic review and meta-analysis

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# Published

2021

Journal Title

**Preventive Medicine Reports** 

# Version

Accepted Manuscript (AM)

# DOI

https://doi.org/10.1016/j.pmedr.2021.101477

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1	The efficacy of cognitive behavioral therapy-based
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3	review and meta-analysis
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#### 35 Abstract

Recently, the benefits of cognitive behavioral therapy (CBT)-based interventions for patients with hypertension have been recognized, but there has been no systematic review that has comprehensively analyzed the efficacy of CBT on health outcomes in this population. We aimed to explore the therapeutic effect of CBT-based interventions on hypertension patients through a meta-analysis.

Relevant randomized controlled trials (RCTs) were obtained by searching electronic databases. The primary outcomes were physiological indicators (blood pressure, blood lipid profile). Secondary outcomes were psychological indicators (anxiety, depression), and the quality of sleep. Stata version 15.0 software was used to analyze the results.

A total of 15 RCTs were included. The main analysis revealed that CBT-based 45 interventions reduced systolic pressure: -8.67 (95% CI: -10.67 to -6.67, P=0.000); 46 diastolic pressure: -5.82 (95% CI: -7.82 to -3.81, P=0.000); total cholesterol levels: -47 0.43 (95% CI: -0.76 to -0.10, P=0.010); depressive symptoms: -3.13 (95% CI: -4.02 to 48 -2.24, P=0.000); anxiety symptoms: -3.63 (95% CI: -4.40 to -2.87, P=0.000); and 49 50 improved quality of sleep: -2.93 (95% CI: -4.40 to -1.47, P=0.000). Additionally, the results of subgroup analysis indicated that long-term group-based CBT-based 51 interventions were particularly beneficial for blood pressure management in 52 hypertension patients. 53

54 CBT-based interventions are effective in reducing systolic pressure, diastolic pressure, 55 total cholesterol levels, anxiety symptoms, depressive symptoms, and improving 56 quality of sleep in hypertension patients.

57

Key words: hypertension, cognitive behavioral therapy, physiological indicators,
psychological indicators, quality of sleep

60

#### 61 1 Introduction

Hypertension is a chronic disease characterized by continuously elevated arterial 62 blood pressure. It is an important cause of, and a risk factor for, cardiovascular and 63 cerebrovascular diseases (Mills et al., 2016), affecting the structure and function of the 64 heart, brain, kidneys, and other important organs (Ndanuko et al., 2016). It causes 65 myocardial infarction, heart failure, chronic kidney disease, and other complications, 66 including high fatality and disability rates (Biswas et al., 2003). The latest data indicates 67 that the number of adults with hypertension will reach 1.5 billion by 2025, which is 68 about 30% of the world's population (Hu et al., 2015; Li et al., 2015). It is now a global 69 problem, and is deleterious for human physical and mental health (Liu et al., 2017b) 70 and imposes a heavy burden on the patient, their family, and society. Therefore, 71 72 effectively preventing and treating hypertension is of particular importance.

Currently, drug therapy is the main treatment for high blood pressure (Mann, 73 2011), and lifestyle changes are also highly recommended (Williams et al., 2018). 74 However, due to the long course of the disease and duration of the need for medication, 75 76 patients are prone to negative emotions such as anxiety and depression during treatment (Kretchy et al., 2014). Furthermore, these psychological problems have become an 77 important factor affecting the occurrence and development of hypertension (Jonas et 78 al., 1997; Rutledge and Hogan, 2002). Therefore, in the treatment of hypertension, 79 timely adoption of psychological interventions may be conducive to the treatment and 80 prognosis of the disease. Cognitive behavioral therapy (CBT) is a group of short-term 81 psychological therapies that aim to change unreasonable cognitions and thereby 82 eliminate dysfunctional behaviors (Creswell et al., 2010). CBT can effectively solve 83 general psychological problems and is often used to treat depression, anxiety, sleep 84 disorders, and chronic pain (McMain et al., 2015). In recent years, an increasing number 85 of studies (Abgrall-Barbry and Consoli, 2006; Liu et al., 2017a; Xue et al., 2008) have 86 applied CBT as an intervention for hypertension. Abgrall-Barbry and colleagues 87 (Abgrall-Barbry and Consoli, 2006) compared the therapeutic effects of CBT, 88 89 relaxation, meditation, and biofeedback therapy on hypertension, showing that these methods had an anti-hypertensive effect, with CBT being the most efficacious. Xue and 90

colleagues (Xue et al., 2008) conducted a five-week group cognitive behavioral self-91 management project for patients with mild-to-moderate essential hypertension to 92 evaluate its benefits for blood pressure management and found that patients' blood 93 pressure decreased significantly. Similarly, Lei Liu and colleagues (Liu et al., 2017a) 94 conducted a cohort study on hypertensive patients in the Chinese working population 95 and found that a psychological intervention based on CBT plus medication was more 96 effective in improving blood pressure compared to usual medication alone. However, 97 98 Nolan and colleagues (Nolan et al., 2018) conducted a remote intervention based on CBT for hypertension patients and found the difference in systolic blood pressure 99 reduction between the intervention group and the control group was statistically 100 significant, whereas the change in diastolic blood pressure was not. 101

102 The results of the above studies of CBT-based interventions for hypertension are inconsistent, and there are few relevant meta-analyses. To address this gap in the 103 research we undertook a systematic review of the literature to evaluate whether 104 comprehensive CBT-based interventions have a positive effect on physiological and 105 106 psychological indicators and the quality of sleep in hypertension patients. In doing so, we aimed to provide a scientific basis for CBT intervention therapy in patients with 107 hypertension and to provide references for how to design appropriate CBT-based 108 interventions efficiently. 109

110

#### 111 2 Methods

112This systematic review was conducted in accordance with the Preferred Reporting113Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher et al.,1142009). The review protocol was registered at the PROSPERO International Prospective115Register of Systematic Reviews (Registration ID: CRD42020213587 PROSPERO1162020 website: <a href="https://www.crd.york.ac.uk/prospero/#recordDetails">https://www.crd.york.ac.uk/prospero/#recordDetails</a>). Ethical approval117and patient consent were not required as this was a systematic review and meta-analysis118of previously published studies.

#### 120 **2.1 Search strategy**

Databases searched included PubMed, Embase, Cochrane Central Register of 121 Controlled Trials, Scopus, Proquest, Web of Science, CINAHL and Chinese databases 122 (WanFang, China National Knowledge Infrastructure). Key search words were 123 "hypertension" and "cognitive behavioral therapy". We searched using the form of 124 subject words + free words with Boolean operators AND/OR in the abstract, key words, 125 or title, with a language limitation of English and Chinese. In the process of retrieval, 126 the search terms were modified according to the search rules for the different databases. 127 We also searched the reference lists of the original papers to find additional relevant 128 articles. Our retrieval time was from inception to October 2020. Articles collected were 129 managed by Endnote X8 Software (Clarivate Analytics, PA, USA). Two researchers 130 conducted literature reviews separately. In case of disagreement, a third researcher was 131 consulted, and consensus reached. 132

#### 133 2.2 Study selection

Inclusion criteria were developed using the population, intervention, control,outcomes, study type (PICOS) approach:

136 (1) P: The target *population* was adults ( $\geq$ 18) with essential hypertension regardless of 137 disease stage and severity, including grade I hypertension, grade II hypertension, grade 138 III hypertension, and isolated systolic hypertension. Participants in this review were 139 diagnosed with hypertension according to established definitions or guidelines. Trials 140 that reported the recruitment of subjects with definite hypertension but without specific 141 diagnostic criteria were also included.

(2) I: *Interventions* were described as CBT or based on CBT principles. The strategies
had to be under the umbrella of CBT including cognitive therapy and behavioral therapy,
and common CBT techniques such as problem-solving, relaxation, goal-setting,
behavioral experiments, and cognitive restructuring. The interventions could be CBT
alone or CBT combined with other methods, delivered face-to-face or remotely (e.g.,
via telephone and internet) and used in individual or a group form.

(3) C: The *control* conditions included non-CBT interventions (e.g., medication,
education), or usual care or wait list. If there were multiple comparison groups, we
chose the usual care group.

151 (4) O: The primary *outcomes* were physiological indicators (blood pressure, blood lipid

profile: low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), total cholesterol). Secondary outcomes included psychological indicators (anxiety, depression), and the quality of sleep. We used the Pittsburgh Sleep Quality Index (PSQI) score to represent the quality of sleep.

- 156 Articles reporting one or more of the above outcomes were included.
- 157 (5) Studies had to involve a randomized controlled trial (RCT) design, with no
  158 restrictions on the length of follow-up.
- 159 (6) Articles written in English or Chinese.
- 160 (7) Accessibility of full-text publication.
- 161 The study exclusion criteria were:
- 162 (1) Participants with cognitive impairment or substance abuse.
- 163 (2) Solely cognitive or behavioral interventions as opposed to a comprehensive,
- 164 integrated CBT approach;
- 165 (3) Lacking quantitative analysis;
- 166 (4) Literature reviews or protocols, incomplete in terms of data used or inconsistent
- 167 statistical methods;
- 168 (5) Duplicate publications;
- 169 (6) Judged to be of low quality on the PEDro tool (Verhagen et al., 1998);
- 170 (7) Not peer-reviewed journal articles.
- 171 **2.3 Data extraction**

The following information was extracted: (a) Basic information, including first author, year of publication, country; (b) Study design, including information on participants (number, age, gender, diseases), drop-out rates, frequency/length of followup, intervention method, comparison group, outcomes. Data were extracted independently by two researchers. Where data was incomplete the corresponding author was contacted to obtain the data. The primary outcome variables were physiological indicators (blood pressure, blood lipid profile: LDL-C, HDL-C, TG, total
cholesterol). Secondary outcomes included psychological indicators (anxiety,
depression), and the quality of sleep.

#### 181 **2.4 Quality assessment**

Two reviewers independently read the full texts of the included articles and 182 assessed their methodological quality using the PEDro tool (Verhagen et al., 1998). 183 PEDro includes ten items: random allocation of subjects into groups, concealed 184 185 randomization, similarity of baseline information between groups, blinding to subjects, blinding to assessors and researchers, attrition rate, use of "intention to treat" analysis, 186 use of variability measures, and use of between-group comparison methods. Based on 187 these ten items, PEDro categorizes the quality of studies into three levels: high quality 188 (8 or more points), moderate quality (4–7 points), and lower quality (3 points or less). 189 If there were disagreements in rating the quality of the included studies, they were 190 resolved through consultation with a third researcher. 191

#### 192 **2.5 Statistical analysis**

193 Stata version 15.0 software (Harris et al., 2008) was used for analysis, and a pvalue <0.05 was considered to be statistically significant. A separate meta-analysis was 194 performed for each outcome variable. The pooled mean difference (MD), with a 95% 195 confidence interval (CI) was used for continuous outcome variables. Standardized 196 197 mean difference (SMD) and 95% CI were used to measure the effect size of continuous outcome variables. When the SMD was between 0.2 and 0.5, the effect size was small; 198 between 0.5 and 0.7, this was medium; and more than 0.7, this was large. The 199 significance level was set as 0.05 (two-sided). 200

The Chi-square test and I<sup>2</sup> were used for heterogeneity testing among the included articles. If I<sup>2</sup><50% or P>0.05, the level of homogeneity was considered good and if I<sup>2</sup>>50%, it was considered to be heterogeneous. The random-effect model was adopted no matter the heterogeneity. We conducted sensitivity analysis by removing each individual study at a time from the meta-analysis to evaluate the stability of the pooled results and investigate the potential source of the heterogeneity if it was significant. To explore the heterogeneity, we performed subgroup analysis based on the country

(developed country vs. developing country); intervention type (CBT combined with 208 other interventions vs. CBT alone); treatment form (group vs. individual); treatment 209 course ( $\geq$ 12 weeks vs. <12 weeks); duration of session ( $\geq$ 50min vs. <50 min); number 210 of session ( $\geq 10$  vs. <10); mode of delivery (remote vs. face-to-face); use of a 211 hypertension-specific manual (yes vs. no); drop-out rate ( $\geq 20\%$  vs. < 20%); patients 212 with comorbid mood symptoms (yes vs. no); and treatment used specific components 213 of CBT (yes vs. no). The definition of using components for CBT was based on the 214 Comprehensive Psycho-therapeutic Intervention Rating Scale and previous studies 215 (Koelen et al., 2014; Liu et al., 2019; Trijsburg et al., 2002; Yang et al., 2020). The 216 following components of CBT were included in the subgroup analysis: 217 psychoeducation, behavioral strategies, cognitive strategies, affective strategies, 218 interpersonal strategies, exposure, body-directed strategies, behavior experiments, 219 220 mindfulness and attention, homework assignments, goal-setting and planning, problemsolving, stress management, dietary interventions, and physical activity. These 221 components were identified as "yes" (mentioned as an important technique), or "no" 222 223 (not mentioned and not a core technique).

Publication bias was evaluated using the Egger test. A p-value of less than 0.05 represented statistically significant publication bias. If the number of meta-analysis studies was 10 or above, a funnel plot was used to analyze whether there was a publication bias.

228

229 **3 Results** 

#### 230 **3.1 Literature search**

A total of 1781 articles were included, including 1780 articles from literature retrieval and one article from references of a relevant review and meta-analysis. After removing duplicate articles, 1376 articles were screened for titles and abstracts. From these, 1304 publications were identified and discarded, including those that clearly did not fulfill the inclusion criteria. Finally, 72 articles were retrieved for full-text screening. During this assessment, two researchers read the full text of the article independently, screened and excluded all articles strictly according to the inclusion rules, and carefully

recorded the reasons for the exclusion. In the case of any disagreement, a third 238 researcher was invited to review the article until consensus was reached. Through full-239 text screening, 57 articles were excluded for the following reasons: protocol or review; 240 non-English or Chinese; unrelated subjects; non-CBT-based intervention; no control 241 group; non-RCT; PEDro≤3; no access to the full article, or insufficient data. The 242 specific process of identifying relevant articles for inclusion in the systematic review 243 and meta-analysis is described in Figure 1. This resulted in 15 studies being included 244 in the meta-analysis. 245

#### 246

#### [Insert Figure 1]

#### 247 **3.2 Study characteristics**

Full details of the included studies are displayed in Table 1. A total of 2195 248 participants were included in the 15 RCTs. Among these, 1102 participants were in 249 intervention groups and 1093 in control groups. The mean age of those in the 250 intervention groups was 55.40 and 55.23 in control groups. The mean proportions of 251 females were 48.92% and 47.38% in the intervention and control groups, respectively. 252 253 Twelve studies were undertaken in developing countries (Birashk et al., 2018; Hualei et al., 2013; Jing, 2020; Mingming, 2017; Qing et al., 2019; Qingmei, 2010; Weiwei et 254 al., 2015; Xinju et al., 2017; Youyou, 2013; Yu et al., 2018; Yuanyuan, 2017; Yurong 255 et al., 2012) and three in developed countries (Clemow et al., 2018; Mensorio et al., 256 2019; Sung et al., 2012). 257

Regarding interventions, a single CBT method was used in three studies (Clemow 258 et al., 2018; Sung et al., 2012; Yuanyuan, 2017), and CBT combined with drug therapy 259 or treatment as usual was used in the remaining 12 studies (Birashk et al., 2018; Hualei 260 et al., 2013; Jing, 2020; Mensorio et al., 2019; Mingming, 2017; Qing et al., 2019; 261 Qingmei, 2010; Weiwei et al., 2015; Xinju et al., 2017; Youyou, 2013; Yu et al., 2018; 262 Yurong et al., 2012). Additionally, control groups that adopted drug therapy or usual 263 interventions were described in 14 articles (Birashk et al., 2018; Clemow et al., 2018; 264 265 Hualei et al., 2013; Jing, 2020; Mensorio et al., 2019; Mingming, 2017; Qing et al., 2019; Qingmei, 2010; Sung et al., 2012; Weiwei et al., 2015; Xinju et al., 2017; Youyou, 266 2013; Yu et al., 2018; Yurong et al., 2012). A wait list control group was used in only 267

one study (Yuanyuan, 2017). Two studies used remote interventions, including 268 interventions over the internet (Mensorio et al., 2019; Xinju et al., 2017), and 13 studies 269 used traditional face-to-face interventions (Birashk et al., 2018; Clemow et al., 2018; 270 Hualei et al., 2013; Jing, 2020; Mingming, 2017; Qing et al., 2019; Qingmei, 2010; 271 Sung et al., 2012; Weiwei et al., 2015; Youyou, 2013; Yu et al., 2018; Yuanyuan, 2017; 272 Yurong et al., 2012). Four studies used an individual CBT intervention (Mensorio et 273 al., 2019; Qing et al., 2019; Xinju et al., 2017; Yurong et al., 2012), five studies used a 274 group-based CBT intervention (Birashk et al., 2018; Clemow et al., 2018; Hualei et al., 275 2013; Sung et al., 2012; Yuanyuan, 2017), while six did not report the treatment form 276 (Jing, 2020; Mingming, 2017; Qingmei, 2010; Weiwei et al., 2015; Youyou, 2013; Yu 277 et al., 2018). Only three studies reported using an intervention manual (Birashk et al., 278 2018; Clemow et al., 2018; Yuanyuan, 2017). The specific settings of the interventions 279 were as follows: the mean number of sessions was 9.91, the mean duration of sessions 280 was 64.75 min, and the mean duration of treatment was 10.04 weeks. Four types of 281 outcome measures were included in this analysis: physiological indicators, 282 283 psychological indicators, quality of life, and quality of sleep. Thirteen studies reported physiological indicators (Birashk et al., 2018; Clemow et al., 2018; Hualei et al., 2013; 284 Jing, 2020; Mensorio et al., 2019; Mingming, 2017; Qingmei, 2010; Sung et al., 2012; 285 Weiwei et al., 2015; Xinju et al., 2017; Youyou, 2013; Yu et al., 2018; Yurong et al., 286 2012), 11 psychological indicators (Clemow et al., 2018; Hualei et al., 2013; Mensorio 287 et al., 2019; Mingming, 2017; Qing et al., 2019; Qingmei, 2010; Weiwei et al., 2015; 288 Xinju et al., 2017; Youyou, 2013; Yuanyuan, 2017; Yurong et al., 2012), three quality 289 of life (Mensorio et al., 2019; Qing et al., 2019; Sung et al., 2012), and two reported 290 quality of sleep (Jing, 2020; Mensorio et al., 2019; Xinju et al., 2017; Yu et al., 2018). 291 The mean drop-out rates were 14.57% and 12.13% in the intervention and control 292 groups. respectively. Detailed characteristics of the intervention methods and control 293 group activities are in Table 1. 294

295

#### 296 **3.3 Pre to post-treatment effects of CBT-based interventions**

#### 297 **3.3.1 Effects on physiological indicators**

Nine studies (Hualei et al., 2013; Jing, 2020; Mingming, 2017; Sung et al., 2012; 298 Weiwei et al., 2015; Xinju et al., 2017; Youyou, 2013; Yu et al., 2018; Yurong et al., 299 2012), with a total sample of 1377 participants, analyzed the effect of CBT-based 300 interventions on blood pressure. The number of people in the intervention and control 301 groups were 701 and 676, respectively. CBT-based interventions were more beneficial 302 303 in reducing systolic pressure compared to the control conditions, with a mean reduction of systolic pressure of -8.67 (95% CI: -10.67 to -6.67, P=0.000), and a large effect size 304 (SMD -0.87 (95% CI: -1.18 to -0.55, P=0.000)). The heterogeneity was statistically 305 significant (I<sup>2</sup>=58.50%, P=0.013) (Table 2). The forest plot of the effect is presented in 306 Figure 2A. 307

308 Subgroup analysis was performed to examine the effect of CBT-based 309 interventions with different characteristics on improving systolic pressure. The results 310 demonstrated that CBT-based interventions with the following characteristics had a 311 better effect on systolic pressure: when they involved group treatment, patients did not 312 have comorbid mood symptoms (**Table 3**).

Similarly, CBT-based interventions significantly reduced diastolic pressure, with a reduced pooled mean across these studies of -5.82 (95% CI: -7.82 to -3.81, P=0.000) with a large effect size (SMD -0.77 (-1.07 to -0.47, P=0.000)). Statistically significant heterogeneity was observed (I<sup>2</sup>=80.20%, P=0.000). The forest plot of the effect is presented in **Figure 2B**.

318

#### [Insert Figure 2]

As shown in **Table 4**, CBT-based interventions statistically reduced diastolic pressure when the CBT intervention format involved a group-based intervention, and when more than 10 sessions were given.

Two studies (Hualei et al., 2013; Youyou, 2013) with a total sample of 679 participants analyzed the effect of CBT-based interventions on total cholesterol, TG, and LDL-C. The numbers of people in the intervention and control groups were 342 and 337, respectively. Meta-analysis showed a significant reduction in total cholesterol,

with mean reduction of -0.43 (95% CI: -0.76 to -0.10, P=0.010), and a medium effect 326 size of SMD -0.49 (95% CI: -0.64 to -0.33, P=0.000). The heterogeneity was 327 statistically significant ( $I^2=74.60\%$ , P=0.047) (Table 2). The forest plot of the effect is 328 presented in Figure 3A. The meta-analysis did not show a significant reduction in either 329 TG (0.00, 95% CI: -0.07 to 0.07, P=0.978) or LDL-C (0.10, 95% CI: -0.15 to 0.34, 330 P=0.441). The heterogeneity was not statistically significant for TG ( $I^2=0.00\%$ , 331 P=0.419) or LDL-C (I<sup>2</sup>=0.00%, P=0.401) (Table 2). The forest plot of the effect is 332 presented in Figure 3B and 3C. 333

334

#### [Insert Figure 3]

#### 335 **3.3.2 Effects on psychological indicators**

The effect on depressive symptoms was analyzed in nine studies (Clemow et al., 336 2018; Hualei et al., 2013; Mensorio et al., 2019; Mingming, 2017; Qing et al., 2019; 337 Qingmei, 2010; Weiwei et al., 2015; Xinju et al., 2017; Youyou, 2013) with a total 338 sample of 1620 participants. The number of people in the intervention and control 339 groups was 810 and 810, respectively. CBT-based interventions were more beneficial 340 341 for treating depressive symptoms than the control condition, with a mean reduction of depression of -3.13 (95% CI: -4.02 to -2.24, P=0.000) and a large effect size (SMD -342 1.07 (95% CI: -1.82 to -0.31, P = 0.005)). The heterogeneity was statistically significant 343 (I<sup>2</sup>=99.10%, P=0.000) (Table 2). The forest plot of the effect is presented in Figure 344 **4A**. 345

Subgroup analysis was performed to examine the effect of CBT-based 346 interventions with different characteristics on improving depressive symptoms. As 347 shown in Table 5, the results demonstrated that CBT-based interventions with the 348 349 following characteristics had a better effect on depressive symptoms: face-to-face treatment delivery, greater than 10 sessions, and in participants with comorbid mood 350 symptoms. The subgroup analysis also examined the effects of CBT-based 351 interventions with different components on improving depressive symptoms. CBT-352 based interventions showed a better effect when they used physical activity as the core 353 technique, and when they did not use behavioral strategies, homework assignment 354 strategies, or problem-solving strategies as core techniques. 355

The effect on anxiety symptoms was analyzed in 10 studies (Hualei et al., 2013; 356 Mensorio et al., 2019; Mingming, 2017; Qing et al., 2019; Qingmei, 2010; Weiwei et 357 al., 2015; Xinju et al., 2017; Youyou, 2013; Yuanyuan, 2017; Yurong et al., 2012) with 358 a total sample of 1673 participants. The number of people in the intervention and 359 control groups was 836 and 837, respectively. CBT-based interventions were more 360 beneficial for anxiety symptoms than the control interventions, with a mean reduction 361 of anxiety of -3.63 (95% CI: -4.40 to -2.87, P=0.000), and a large effect size, with SMD 362 -1.27 (95% CI: -1.68 to -0.86, P=0.000). The heterogeneity was statistically significant 363 (I<sup>2</sup>=98.50%, P=0.000) (Table 2). The forest plot of the effect is presented in Figure 364 **4B**. 365

366

#### [Insert Figure 4]

367 Subgroup analysis was performed to examine the effect of CBT-based 368 interventions with different characteristics on improving anxiety symptoms. As shown 369 in **Table 6**, CBT-based interventions statistically reduced anxiety symptoms and were 370 more effective as an individual treatment and when it emphasized cognitive strategies 371 as the core technique.

## **372 3.3.3 Effects on quality of sleep**

Two studies (Xinju et al., 2017; Yu et al., 2018), with a total sample of 290 373 participants, analyzed the effect of CBT-based interventions on sleep quality. The 374 number of people in the intervention group and the control group was 155 and 135, 375 respectively. CBT-based interventions were more beneficial in improving the quality 376 of sleep than the control condition, with a mean reduction of the PSIQ score of -2.93 377 (95% CI: -4.40 to -1.47, P=0.000), and large effect size of SMD -0.94 (95% CI: -1.29 378 to -0.59, P=0.000). The heterogeneity was statistically significant (I<sup>2</sup>=73.20%, P=0.050) 379 (Table 2). The forest plot of the effect is presented in Figure 3D. 380

**381 3.3.4 Effects on health-related behaviors** 

One study (Jing, 2020), with 100 participants, analyzed the effect of the CBTbased intervention on health-related behaviors and found that the intervention group's health behavior scores, including medication compliance, quitting smoking and drinking, reasonable diet, and exercise, were relatively higher than the control group.

#### 387 3.4 Risk of bias and quality assessment

We used the PEDro tool to assess the quality of the included studies. All were of medium quality and the score was 5.13 on average. Specifically, three studies scored 4 (Birashk et al., 2018; Yu et al., 2018; Yurong et al., 2012), nine studies scored 5 (Hualei et al., 2013; Jing, 2020; Mingming, 2017; Qing et al., 2019; Qingmei, 2010; Sung et al., 2012; Weiwei et al., 2015; Youyou, 2013; Yuanyuan, 2017), one study scored 6 (Xinju et al., 2017), and two studies (Clemow et al., 2018; Mensorio et al., 2019) scored 7.

#### 395 **3.5 Publication bias**

Since only two studies were included to analyze the effect of CBT-based 396 interventions on total cholesterol, HDL-C and the quality of sleep, no T or p-value of 397 the Egger analysis was available for these variables. As can be seen in Table 7, we 398 found minimal publication bias on the following outcome variables: systolic pressure 399 (P=0.487), diastolic pressure (P=0.958) and depressive symptoms (P=0.076). However, 400 there was significant publication bias for anxiety symptoms (P=0.008). The one-study-401 402 removed method was used to assess sensitivity, and it was found that removing one study at a time did not change the overall results for all outcome variables. 403

404

#### 405 **4 Discussion**

In this paper we have presented the results of a meta-analysis of the efficacy of CBT-based interventions for hypertension patients. The results indicated that CBTbased interventions were superior to control interventions, significantly reducing systolic pressure, diastolic pressure, total cholesterol levels, depressive symptoms and anxiety symptoms, as well as improving the quality of sleep.

#### 411 4.1 Pre to post-treatment effects of CBT-based interventions

412 **4.1.1 Effects on physiological indicators** 

413 Consistent with previous research (Clemow et al., 2018; Shapiro et al., 1997), we 414 found that CBT-based interventions significantly reduced systolic and diastolic blood 415 pressure in patients with hypertension. It has been reported that high blood pressure 416 control using the recommended guidelines (Hypertension, 2013; James et al., 2014) is

the most effective way to reduce cardiovascular mortality in hypertension patients 417 (Burnier, 2017). However, studies have shown that 50% of people with hypertension 418 receiving "usual treatment" had uncontrolled blood pressure (Conn et al., 2015), 419 primarily due to inadequate medication adherence (Burnier, 2014; De Geest et al., 420 2014). In this context CBT-based interventions could improve medication compliance 421 by correcting patients' misconceptions about medication usage, thereby reducing blood 422 pressure. Another possible explanation for the effectiveness of CBT is that patients' 423 424 health-related behaviors improved. Previous research indicates that CBT interventions can result in increased physical activity (Xue et al., 2008), modifications to unhealthy 425 eating patterns (Mensorio et al., 2019), and promote quitting smoking and drinking 426 alcohol (Jing, 2020) in hypertension patients, thereby improving their blood pressure 427 control. 428

Further subgroup analysis showed that the use of a CBT group-based approach and an intervention lasting longer than 10 sessions is more effective in reducing systolic blood pressure and diastolic blood pressure compared with individual treatment and interventions of less than 10 sessions. This may be because group-based interventions facilitate social support among patients, reinforcing the effects of the intervention (Wolgensinger, 2015), and longer intervention times are required to change the maladaptive cognitions and behavior of patients with hypertension.

We found that the total cholesterol levels of patients in the intervention groups was 436 reduced by a greater amount compared to that of patients in the control groups. Patients 437 438 with high blood pressure are more prone to negative emotions, such as depression and anxiety, causing increased sympathetic nervous activity, which results in a series of 439 440 physiological and pathological changes, including excessive secretion of catecholamines, disordered lipid metabolism, and increased heart rate (Chen and Huang, 441 2006; Lehto et al., 2008). Through the CBT intervention, negative emotions can be 442 alleviated, and the sympathetic excitability of the patients reduced, thereby promoting 443 stability in lipid metabolism. Similarly, studies by Mao (Youyou, 2013) found that 444 CBT-based interventions significantly reduced total cholesterol in patients with 445 hypertension. As only two studies reported TG and low-density lipoprotein results, we 446

did not find a significant reduction in these. We should therefore be cautious in drawingconclusions in this area and need to include more studies to confirm our findings.

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#### 4.1.2 Effects on psychological indicators

We found that CBT-based interventions had a larger effect on depressive and anxiety symptoms in hypertension patients compared to the control interventions. This study is the first meta-analysis on the effect of comprehensive CBT-based intervention on negative emotions in patients with hypertension, and the tentative conclusion is that such interventions have a significant impact on anxiety and depressive symptoms in these patients.

Subgroup analysis on depression and anxiety found that face-to-face and 456 individualized, rather than group-based, treatment had a more significant effect on the 457 improvement of depressive and anxiety symptoms in hypertension patients, in 458 agreement with Liu and colleagues' previous study (Liu et al., 2019). We also found 459 hypertension patients benefited more in relation to their depression and anxiety when 460 the intervention emphasized a cognitive strategy as the core technique. Previous studies 461 462 have also suggested that CBT-based intervention using this strategy are more effective in reducing depression and anxiety symptoms in hypertension patients (Qing et al., 463 2019; Qingmei, 2010). In addition, the number of sessions offered during the 464 intervention was important. Interventions involving greater than 10 sessions were more 465 effective in improving depressive symptoms, possibly because cognitive reconstruction 466 of dysfunctional thoughts takes time (Liu et al., 2019). 467

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#### 4.1.3 Effects on quality of sleep

Two studies reporting sleep quality were included in our meta-analysis, and the results showed that CBT-based interventions were able to significantly reduce the PSQI score and improve sleep quality in patients with hypertension. Similarly, a review by Takaesu and colleagues (Takaesu and Inoue, 2012) found that CBT-based interventions can relieve symptoms of insomnia in patients with metabolic syndrome comorbidities, while also preventing the recurrence of insomnia. The proposed mechanism for this is that offering sleep hygiene education, stimulation control and relaxation therapy helps patients to gradually establish an improved sleep-wake biological rhythm, thusimproving their sleep quality.

#### 478 **4.2 Strengths and limitations of the study**

We undertook a systematic review and meta-analysis on the efficacy of CBT-479 based interventions for patients with hypertension using a reasonable number of RCTs 480 481 with a moderate quality study design and minimal publication bias. Despite the findings of this systematic review, there are several limitations that need to be acknowledged. 482 483 Firstly, this meta-analysis showed high heterogeneity. The possible reason is that as yet there is no standardized procedure for CBT-based interventions for hypertension, so 484 there have been notable differences in study design, treatment form, duration of 485 treatment, number of sessions, duration of sessions, intervention composition, and the 486 professional background of therapists, including nurses, general practitioners or 487 psychologists. Further, the studies were from different types of institution, including 10 488 from hospitals (Birashk et al., 2018; Jing, 2020; Mensorio et al., 2019; Mingming, 2017; 489 Qing et al., 2019; Qingmei, 2010; Weiwei et al., 2015; Xinju et al., 2017; Youyou, 2013; 490 491 Yurong et al., 2012), two from medical centers (Clemow et al., 2018; Sung et al., 2012), two from community health service centers (Hualei et al., 2013; Yu et al., 2018), and 492 one from a nursing home (Yuanyuan, 2017). Secondly, only the results before and after 493 the intervention were compared and analyzed, and long-term follow-up results were not 494 discussed due to insufficient data. Therefore, the long-term effect of CBT-based 495 interventions on patients with hypertension was unclear. Thirdly, only two studies 496 (Clemow et al., 2018; Mensorio et al., 2019) used concealed randomization and one 497 (Mensorio et al., 2019) had assessors who were blind to participants' group allocation, 498 499 while none of the others achieved the corresponding blinding methods, leading to the 500 overall quality of evidence being relatively low due to a high risk of bias. Fourth, two articles (Sung et al., 2012; Yu et al., 2018) did not fully realize randomized grouping. 501 We conducted a strict quality evaluation on these two papers and after finding that they 502 met the remaining inclusion conditions, we decided to include them in the analysis. Last 503 but not the least, medication (Ferdinand and Nasser, 2017), psychological factors 504 (Hamer et al., 2010; Liu et al., 2017b), including stress, distress, as well as lifestyle 505

factors (Beilin et al., 1999; Huntgeburth et al., 2005; Omboni, 2020; Samadian et al.,
2016), including smoking, alcohol, have not been included in the meta-analysis due to
insufficient data, but also due to the fact that they have an influence on blood pressure
management. More research is needed to explore these relationships.

#### 510 4.3 Implications

An increasing number of studies have applied CBT-based interventions in the 511 management of chronic pain, diabetes, coronary heart disease, and other chronic 512 513 diseases, and found a positive effect. At present, relatively few RCTs have applied CBT interventions in patients with hypertension. However, this meta-analysis found a 514 positive effect of CBT-based interventions on blood pressure management. Given other 515 researchers (Shapiro et al., 1997) have found that CBT offered as an adjunctive 516 treatment was twice as effective as the control treatment in reducing drug requirements, 517 future studies could examine its impact in terms of decreasing the costs and side effects 518 of antihypertensive medications. This will have a profound impact on the prevention 519 and management of hypertension. 520

#### 521 4.4 Conclusion

The findings of this systematic review and meta-analysis suggest that CBT-based interventions are efficacious in reducing systolic pressure, diastolic pressure, total cholesterol level, anxiety symptoms, depressive symptoms, and improving quality of sleep in patients with hypertension. In addition, CBT maybe more effective for blood pressure management in these patients when it is offered long term and in group-based settings.

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#### 537 Funding

- 538 The first author was sponsored by Griffith University via Griffith University
- 539 International Postgraduate Research Scholarship (GUIPRS).
- 540 **Conflict of interest**
- 541 No conflict of interest has been declared by the authors.
- 542 Clinical trial registration
- 543 N/A.
- 544 **Declaration of interest**
- 545 None.

#### 546 **Contributor's statements**

- 547 Y.N Li: Data collection, Software, Writing- Original draft preparation.
- 548 Nicholas Buys: Data collection, Writing- Reviewing and Editing.
- 549 Z.J Li: Writing- Reviewing and Editing.
- Jing Sun: Conceptualization, Methodology, Software, Writing- Reviewing and Editing.
- 551 Li Li: Writing- Reviewing and Editing.
- 552 Qifa Song: Writing- Reviewing and Editing.
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Author	Country	Setting	Sample size (intervention/ control)	/ Gender: female,n(%)	Age(Mean±SD)	Hypertension diagnosis	Intervention	Format	Manual	Control group	Outcome measure	1	Quality of article
Birashk et al. (2018) (Birashk et al., 2018)	Iran	health center and hospital	60 (20/20/20) <sup>1</sup>	NR	NR	essential hypertension	CBT+drug therapy	group	yes	MBSR; drug therapy	1	I: 25.00 C1: 25.00 C2: 20.00	
Chao et al. (2019) (Qing et al., 2019)	China	hospital	400 (200/200)	· · · ·	I: 50.94±6.84 C: 51.48±6.83	WHO diagnostic criteria for hypertension	CBT+TAU	individua	l no	TAU	23	NR	5(mode rate)
Clemow et al. (2018) (Clemow et al., 2018)	USA	urban medical center	92 (46/46)	· · · ·	I: 48.40±8.40 C: 48.70±9.00	SBP: 140-180mm Hg DBP: 90-110 mm Hg	CBT	group	yes	TAU	12	I: 13.04 C: 10.87	7(mode rate)
Fu (2010) (Qingmei, 2010)	China	hospital	80 (40/40)		I: 43.12±6.45 C: 43.28±6.25	WHO diagnostic criteria for hypertension	CBT+drug therapy	NR	no	drug therapy	12	NR	5(mode rate)
Huang et al.(2013) (Hualei et al., 2013)	China	community health service center	599 (302/297)	I: 187(61.92) C: 181(60.94)	I: 47.41±8.09 C: 47.96±7.94	mild hypertension SBP: 140-159mm Hg DBP: 90-99 mm Hg	CBT+drug therapy	group	no	drug therapy	12	NR	5(mode rate)
Li (2017) (Mingming 2017)	' China	hospital	120 (60/60)		I: 60.83±10.66 C: 59.05±11.12	Chinese guidelines for hypertension prevention and treatment	r CBT+drug therapy	NR	no	drug therapy	12	NR	5(mode rate)
Liu (2017) (Yuanyuan, 2017)	China	nursing home	80 (40/40)		I: 70.94±3.62 C: 70.24±3.58	WHO diagnostic criteria	CBT	group	yes	wait-list	2	I: 20.00 C: 17.50	5(mode rate)
Liu et al. (2018) (Yu et al., 2018)	China	community health service center	184 (102/82)	· · · · ·	I: 70.98±4.13 C: 72.16±4.36	Chinese guidelines for hypertension prevention and treatment 2010	r CBT+TAU	NR	no	TAU	14	NR	4(mode rate)
Mao (2013) (Youyou 2013)	' China	hospital	80 (40/40)	· · · · ·	I: 55.35±6.37 C: 54.80±5.98	WHO diagnostic criteria	CBT+TAU	NR	no	TAU	12	NR	5(mode rate)
Mensorio et al. (2019 (Mensorio et al., 2019)	) Spain	public hospital	106 (55/51)	47 (44.34)	53.00±8.90	NR	SII based on CBT+UMC	individua	l no	UMC	123	I: 21.82 C: 5.88	7(mode rate)

## TABLE 1 | Characteristics of randomized controlled trials included in this meta-analysis.

Shen et al. (2012) (Yurong et al., 2012) China	hospital	80 (40/40)	32 (40.00)	50.00±3.70	essential hypertensior	CBT+drug therapy	individu	al no	drug therapy	12	NR	4(mode rate)
Su (2020) (Jing, 2020) China	hospital	100 (50/50)	I: 23(46.00) C: 22(44.00)	I: 59.86±2.75 C: 59.82±2.71	essential hypertension	n CBT+TAU	NR	no	TAU	1	NR	5(mode rate)
Sung et al. (2012) (Sung et al., 2012) Korea	local health center	56 (28/28)	I: 20(72.00) C: 14(50.00)	I: 66.00±7.00 C: 63.00±11.00	SBP: 140-159mm Hg DBP: 90-99 mm Hg	Forest Therapy based on CBT	group	no	self- monito ing	r (1)(3)	I: 0.00 C: 0.00	5(mode rate)
Tian et al. (2015) (Weiwei et al., 2015) China	hospital	52 (26/26)	I: 0(0.00) C: 0(0.00)	I: 42.60±9.60 C: 43.20±9.80	Chinese guidelines fo hypertension prevention and treatment 2010	r CBT+TAU	NR	no	TAU	12	NR	5(mode rate)
Yang et al. (2017) (Xinju et al., 2017) China	hospital	106 (53/53)	I: 33(62.26) C: 34(64.15)	I: 56.16±9.70 C: 56.48±11.16	JNC-8 Diagnostic criteria for hypertension	iCBT+TAU	individu	al no	TAU	124	I: 7.55 C: 5.66	6(mode rate)

1: I=CBT+drug therapy; C1= drug therapy; C2=MBSR; MBSR=mindfulness - based stress reduction; TAU=treat as usual; UMC=usual medical care; SII=self-administered Internet-based intervention

Outcome measure: ①physiological indicator=blood pressure, blood glucose, blood lipid profile (LDL - C, HDL - C, TG, total cholesterol), heart rate, BMI, waist, hip perimeter, oxidative stress, interleukin 6; ②psychological indicators=depression, anxiety stress; ③QOL; ④quality of sleep

**TABLE 2** | Total effect of CBT - based interventions on blood pressure, total cholesterol, triglyceride, LDL - C, depressive symptom, anxiety symptom, and the quality of sleep.

T. J	Outcomes: post-to pre - treatment effect									
Index	Studies,r	n Participants	s I <sup>2</sup> % (P)	Q-test ]	MD (95%,CI)	Р	SMD (95%,CI)	Р		
Systolic pressure	9	1377	58.50 (0.013)	19.27	-8.67 (-10.67, -6.67)***	0.000	-0.87 (-1.18, -0.55)***	0.000		
Diastolic pressure	9	1377	80.20 (0.000)	40.45	-5.82 (-7.82, -3.81)***	0.000	-0.77 (-1.07, -0.47)***	0.000		
Total cholesterol	2	679	74.60 (0.047)	3.94	-0.43 (-0.76, -0.10)*	0.010	-0.49 (-0.64, -0.33)***	0.000		
Triglyceride	2	679	0.00 (0.419)	0.65	0.00 (-0.07, 0.07)	0.978	0.05 (-0.10, 0.20)	0.502		
LDL	2	679	0.00 (0.401)	0.71	0.10 (-0.15, 0.34)	0.441	-0.00 (-0.21, 0.20)	0.971		
Depression	9	1620	99.10 (0.000)	870.24	-3.13 (-4.02, -2.24)***	0.000	-1.07 (-1.82, -0.31)**	0.005		
Anxiety	10	1673	98.50 (0.000)	600.01	-3.63 (-4.40, -2.87)***	0.000	-1.27 (-1.68, -0.86)***	0.000		
The quality of sleep	2	290	73.20 (0.050)	3.74	-2.93 (-4.40, -1.47)***	0.000	-0.94 (-1.29, -0.59)***	0.000		

MD=Mean difference; SMD=Standard mean difference

TABLE 3 | Subgroup analysis on the effect of CBT - based interventions on systolic pressure.

			Syst	olic pre	ssure: post- to pre - treatmen	nt effect	
Subgroups	Studies (n)	s Participants (n)	I <sup>2</sup> % (P)	Q-test MD (95%,CI)		SMD (95%,CI)	P (between)
Behavioral strategies							0.210
Important	2	136	44.90 (0.178)	1.81	-12.54 (-19.15, -5.93)***	-0.86 (-1.38, -0.35)**	
Not important	7	1241	57.20 (0.030)	14.01	-8.09 (-10.07, -6.12)***	-0.87 (-1.25, -0.49)***	
Cognitive strategies							0.940
Important	5	917	75.20 (0.003)	16.11	-8.59 (-12.09, -5.10)***	-0.81 (-1.23, -0.40)***	
Not important	4	460	0.00 (0.405)	2.91	-8.73 (-10.25, -7.21)***	-0.93 (-1.51, -0.35)**	
Body directed strategies							0.730
Important	6	993	67.40 (0.009)	15.36	-8.93 (-11.45, -6.41)***	-1.03 (-1.55, -0.50)***	
Not important	3	384	42.60 (0.175)	3.48	-8.10 (-12.13, -4.07)***	-0.63 (-0.83, -0.42)***	
Mindfulness and attention	L						0.090
Important	2	162	15.90 (0.275)	1.19	-5.11 (-9.39, -0.83)*	-0.43 (-0.74, -0.11)**	
Not important	7	1215	57.60 (0.028)	14.15	-9.27 (-11.34, -7.20)***	-0.99 (-1.38, -0.59)***	
Homework assignment							0.650
Important	2	719	69.30 (0.071)	3.26	-11.33 (-22.50, -0.16)*	-0.48 (-0.63, -0.33)***	
Not important	7	658	60.60 (0.019)	15.22	-8.72 (-11.04, -6.41)***	-1.00 (-1.44, -0.56)***	
Dietary intervention							0.480
Important	3	364	0.00 (0.510)	1.35	-8.33 (-9.81, -6.84)***	-1.06(-1.82, -0.29)**	
Not important	6	1013	72.00 (0.003)	17.85	-9.77 (-13.48, -6.06) ***	-0.76 (-1.10, -0.41)***	
Physical activity							0.720
Important	4	484	25.30 (0.260)	4.02	-8.35 (-10.38, -6.32)***	-0.92 (-1.48, -0.36)**	
Not important	5	893	73.80 (0.004)	15.26	-9.11 (-12.81, -5.42)***	-0.82 (-1.25, -0.39)***	
Treatment form							0.710
Group	2	655	0.00 (0.697)	0.15	-7.22 (-9.54, -4.91)***	-0.48 (-0.63, -0.32)***	
Individual	2	186	89.60 (0.002)	9.57	-9.42 (-20.90, 2.06)	-0.71 (-1.47, 0.04)	
Number of session							0.340
≥10	2	679	0.00 (0.715)	0.13	-6.87 (-9.02, -4.72)***	-0.48 (-0.63, -0.33)***	
<10	3	238	84.40 (0.002)	12.82	-10.21 (-16.71, -3.72)**	-1.09 (-1.94, -0.24)*	
Treatment course							0.150
≥12w	2	679	0.00 (0.715)	0.13	-6.87 (-9.02, -4.72)***	-0.48 (-0.63, -0.33)***	
<12w	5	414	73.10 (0.005)	14.87	-10.82 (-15.82, -5.82)***	-0.85 (-1.32, -0.39)***	
Patients with comorbid mood symptoms							0.700

Yes	2	200	71.30 (0.062) 3.48	-11.13 (-23.43, 1.18)	-0.55 (-0.83, -0.27)***
No	7	1177	61.60 (0.016) 15.64	-8.69 (-10.79, -6.59)***	-0.97 (-1.38, -0.56)***

MD=Mean difference; SMD=Standard mean difference

TABLE 4	Subgroup analysis or	the effect of CBT - based in	nterventions on diastolic pressure.
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			Diast	olic pre	ssure: post- to pre - treatme	ent effect	
Subgroups	Studies (n)	Participants (n)	I <sup>2</sup> % (P)	Q-test	MD (95%,CI)	SMD (95%,CI)	P (between)
Behavioral strategies							0.920
Important	2	136	85.10 (0.010)	6.69	-6.08 (-14.58, 2.43)	-0.74 (-1.93, 0.45)	
Not important	7	1241	80.90 (0.000)	31.37	-5.63 (-7.73, -3.52)***	-0.77 (-1.09, -0.46)***	:
Cognitive strategies							0.300
Important	5	917	84.50 (0.000)	25.80	-5.05 (-7.95, -2.16)**	-0.71 (-1.15, -0.28)**	
Not important	4	460	60.40 (0.056)	7.57	-7.07 (-9.52, -4.61)***	-0.86 (-1.26, -0.45)***	:
Body directed strategies							0.360
Important	6	993	82.10 (0.000)	27.99	-5.17 (-7.65, -2.68)***	-0.75 (-1.18, -0.32)**	
Not important	3	384	73.80 (0.022)	7.64	-7.15 (-10.64, -3.66)***	-0.84 (-1.19, -0.48)***	:
Mindfulness and attention							< 0.001
Important	2	162	0.00 (0.615)	0.25	-0.08 (-2.57, 2.41)	-0.02 (-0.33, 0.29)	
Not important	7	1215	65.80 (0.007)	17.55	-6.97 (-8.59, -5.35)***	-0.96 (-1.24, -0.68)***	:
Homework assignment							0.710
Important	2	719	66.30 (0.085)	2.97	-6.35 (-9.57, -3.13)***	-0.66 (-0.89, -0.42)***	:
Not important	7	658	83.90 (0.000)	37.24	-5.55 (-8.30, -2.79)***	-0.80 (-1.24, -0.36)***	:
Dietary intervention							0.590
Important	3	364	73.60 (0.023)	7.57	-6.54 (-9.41, -3.67)***	-0.95 (-1.37, -0.53)***	:
Not important	6	1013	83.30 (0.000)	29.90	-5.43 (-8.27, -2.58)***	-0.68 (-1.07, -0.30)***	
Physical activity							0.290
Important	4	484	63.80 (0.040)	8.28	-6.95 (-9.25, -4.66)***	-0.93 (-1.23, -0.63)***	:
Not important	5	893	85.00 (0.000)	26.59	-4.85 (-8.03, -1.66)**	-0.66 (-1.13, -0.19)**	
Treatment form							0.910
Group	2	655	33.10 (0.221)	1.49	-4.32 (-7.22, -1.42)**	-0.42 (-0.84, -0.01)*	
Individual	2	186	95.50 (0.000)		-4.90 (-15.02, 5.23)	-0.65 (-1.20, 0.70)	
Number of session			· · · ·				0.810
≥10	2	679	0.00 (0.406)	0.69	-4.83 (-6.13, -3.54)***	-0.56 (-0.72, -0.41)***	:
<10	3	238	92.00 (0.000)		-5.58 (-11.52, 0.36)	-0.89 (-1.90, 0.12)	
Treatment course			· · · ·				0.770
≥12w	2	679	0.00 (0.406)	0.69	-4.83 (-6.13, -3.54)***	-0.56 (-0.72, -0.41)***	
_ <12w	5	414	86.60 (0.000)		-5.47 (-9.60, -1.34)**	-0.72 (-1.30, -0.15)*	
Patients with comorbid mood symptoms			、 ,				0.950
Yes	2	200	74.40 (0.048)	3.90	-5.95 (-10.76, -1.14)*	-0.68 (-1.04, -0.32)***	:
No	7	1177	83.60 (0.000)		-5.77 (-8.13, -3.41)***	-0.81 (-1.18, -0.43)***	

\*P<0.05, \*\*P<0.01, \*\*\*P<0.001

MD=Mean difference; SMD=Standard mean difference

 TABLE 5 | Subgroup analysis on the effect of CBT - based interventions on depressive symptom.

		Depressive symptom: post- to pre - treatment effect							
Subgroups	Studies Participants $I^{2\%}(P)$ (n) (n)	Q-test MD (95%,CI)	SMD (95%,CI)	P (between)					
Behavioral strategies				0.003					

Important	2	183	0.00 (0.909) 0.01	-1.06 (-2.39, 0.26)	-0.21 (-0.50, 0.08)	
Not important	7	1437	99.30 (0.000) 868.70	-3.53 (-4.50, -2.56)***	-1.31 (-2.25, -0.37)**	
Cognitive strategies						< 0.001
Important	7	1409	99.30 (0.000) 863.37	-3.88 (-4.93, -2.84)***	-1.24 (-2.21, -0.28)*	
Not important	2	211	0.00 (0.673) 0.18	-0.80 (-1.24, -0.36)***	-0.47 (-0.76, -0.19)**	
Body directed strategies						0.110
Important	6	1329	99.30 (0.000) 721.97	-2.80 (-3.79, -1.81)***	-1.01 (-2.03, 0.01)	
Not important	3	291	98.50 (0.000) 133.60	-8.46 (-15.37, -1.55)*	-1.18 (-2.38, 0.03)	
Homework assignment						0.005
Important	3	810	82.10 (0.004) 11.14	-0.48 (-1.13, 0.18)	-0.31 (-0.63, 0.02)	
Not important	6	810	99.40 (0.000) 833.99	-6.56 (-10.76, -2.35)**	-1.44 (-2.48,-0.40)**	
Problem solving						0.003
Important	2	183	0.00 (0.909) 0.01	-1.06 (-2.39, 0.26)	-0.21 (-0.50, 0.08)	
Not important	7	1437	99.30 (0.000) 868.70	-3.53 (-4.50, -2.56)***	-1.31 (-2.25, -0.37)**	
Dietary intervention						0.006
Important	4	651	99.30 (0.000) 424.61	-9.96 (-16.87, -3.06)**	-1.78 (-2.96, -0.61)**	
Not important	5	969	77.10 (0.002) 17.46	-0.24 (-0.44, -0.04)*	-0.44 (-0.84, -0.04)*	
Physical activity						0.002
Important	5	771	99.30 (0.000) 611.22	-7.93 (-12.77, -3.10)**	-1.55 (-2.59, -0.50)**	
Not important	4	849	71.30 (0.015) 10.47	-0.15 (-0.32, 0.02)	-0.41 (-0.88, 0.07)	
Country						0.003
Developed country	2	183	0.00 (0.909) 0.01	-1.06 (-2.39, 0.26)	-0.21 (-0.50, 0.08)	
Developing country	7	1437	99.30 (0.000) 868.70	-3.53 (-4.50, -2.56)***	-1.31 (-2.25, -0.37)**	
Treatment form						0.290
Group	2	691	0.00 (0.589) 0.29	-0.05 (-0.14, 0.03)	-0.10 (-0.25, 0.05)	
Individual	3	597	99.30 (0.000) 287.73	-4.63 (-13.10, 3.83)	-1.02 (-2.78, 0.74)	
Treatment delivery way						< 0.001
Remote	2	197	0.00 (0.482) 0.50	-0.71 (-1.70, 0.27)	-0.20 (-0.48, 0.08)	
Face to face	7	1423	99.30 (0.000) 868.82	-3.79 (-4.80, -2.79)***	-1.31 (-2.26, -0.37)**	
Number of session						0.510
≥10	4	851	98.40 (0.000) 186.67	-5.90 (-9.23, -2.58)**	-1.08 (-2.11, -0.04)*	
<10	4	649	99.50 (0.000) 661.83	-3.53 (-9.69, 2.63)	-1.17 (-2.56, 0.23)	
Treatment course						0.040
≥12w	4	1170	99.60 (0.000) 824.84	-9.45 (-17.33, -1.57)*	-1.42 (-2.93, 0.09)	
<12w	5	450	90.30 (0.000) 41.25	-0.93 (-1.77, -0.10)*	-0.76 (-1.34, -0.18)*	
Patients with comorbid mood symptoms						0.001
Yes	4	680	99.50 (0.000) 605.03	-9.72 (-15.45, -3.99)**	-1.85 (-2.94, -0.77)**	
No	5	940	66.90 (0.017) 12.09	-0.17 (-0.34, 0.01)	-0.37 (-0.75, 0.00)	
*P<0.05 **P<0.01 ***	*P<0.00	01				

MD=Mean difference; SMD=Standard mean difference

TABLE 6	Subgroup analysis	s on the effect of CBT	<ul> <li>based interventions or</li> </ul>	anxiety symptom.

	Anxiety symptom: post- to pre - treatment effect							
Subgroups	Studi (n)	es Participa (n)	ants I <sup>2</sup> % (P)	Q-test	MD (95%,CI)	SMD (95%,CI)	P (between)	
Behavioral strategies							0.250	
Important	3	236	96.20 (0.000)	52.80	-5.77 (-10.42, -1.13)*	-1.40 (-2.31, -0.49)**		
Not important	7	1437	98.70 (0.000)	479.63	-3.01 (-3.82, -2.20)***	-1.22 (-1.72, -0.73)***		
Cognitive strategies							0.002	
Important	8	1462	98.80 (0.000)	591.31	-4.43 (-5.33, -3.53)***	-1.45 (-1.94, -0.97)***		

Not important	2	211	86.70 (0.006) 7.49	-1.26 (-3.01, 0.49)	-0.58 (-0.85, -0.30)***
Body directed strategies					0.200
Important	7	1382	98.30 (0.000) 344.	35 -2.85 (-3.60, -2.10)***	-1.18 (-1.57, -0.79)***
Not important	3	291	99.20 (0.000) 244.	55 -7.72 (-15.17, -0.27)*	-1.56 (-3.06, -0.05)*
Homework assignment					0.070
Important	4	875	97.10 (0.000) 102.	06 -2.72 (-4.09, -1.35)***	-1.04 (-1.59, -0.48)***
Not important	6	798	99.00 (0.000) 497.	94 -5.82 (-8.85, -2.80)***	-1.43 (-2.03, -0.83)***
Dietary intervention					0.010
Important	4	651	98.90 (0.000) 279.	55 -7.41 (-12.27, -2.55)**	-1.60 (-2.48, -0.72)***
Not important	6	1022	96.20 (0.000) 130.	71 -1.32 (-1.85, -0.79)***	-1.05 (-1.44, -0.65)***
Physical activity					0.020
Important	5	771	99.00 (0.000) 389.	78 -5.88 (-9.24, -2.52)**	-1.36 (-2.12, -0.60)***
Not important	5	902	96.90 (0.000) 130.	35 -1.69 (-2.33, -1.05)***	-1.18 (-1.66, -0.71)***
Treatment form					0.730
Group	2	664	98.90 (0.000) 93.3	-6.14 (-17.54, 5.25)	-1.59 (-3.25, 0.07)
Individual	4	677	90.60 (0.000) 31.9	-4.11 (-6.24, -1.99)***	-1.04 (-1.50, -0.57)***
Treatment delivery way					0.650
Remote	2	197	62.90 (0.101) 2.69	-3.16 (-5.39, -0.94)**	-0.72 (-1.01, -0.43)***
Face to face	8	1476	98.80 (0.000) 580.	57 -3.71 (-4.54, -2.89)***	-1.42 (-1.92, -0.93)***
Number of session					0.400
≥10	3	759	99.20 (0.000) 250.4	48 -6.93 (-11.08, -2.78)**	-1.65 (-2.92, -0.38)*
<10	6	794	98.60 (0.000) 349.	26 -4.68 (-7.80, -1.57)**	-1.26 (-1.70, -0.82)***
Duration of session					0.340
≥50min	5	876	98.90 (0.000) 352.	57 -3.45 (-4.36, -2.54)***	-1.71 (-2.60, -0.82)***
<50min	2	480	91.50 (0.001) 11.8	3 -4.84 (-7.56, -2.13)***	-1.36 (-1.80, -0.93)***
Treatment course					0.080
≥12w	4	1170	99.30 (0.000) 459.	21 -7.23 (-12.16, -2.30)**	-1.58 (-2.33, -0.83)***
<12w	6	503	96.30 (0.000) 134.	03 -2.77 (-3.94, -1.60)***	-1.06 (-1.54, -0.59)***
Patients with comorbid mood symptoms					0.000
Yes	5	745	99.10 (0.000) 462.	8 -7.86 (-11.71, -4.01)***	-1.71 (-2.56, -0.86)***
No	5	928	91.20 (0.000) 45.3	6 -0.77 (-1.16, -0.38)***	-0.81 (-0.95, -0.68)***

MD=Mean difference; SMD=Standard mean difference

TABLE 7   Egger's regression analysis on publication bias.	TABLE 7	Egger's	regression	analysis	on pub	lication	bias.
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	-	-	
Variables	Т	Р	95%, CI
Systolic pressure	-0.73	0.487	(-3.55, 1.87)
Diastolic pressure	-0.05	0.958	(-5.47, 5.22)
Total cholesterol	_		
Triglycerides		_	
LDL - L	_		
Depression	-2.08	0.076	(-16.15, 1.01)
Anxiety	-3.54	0.008	(-12.44, -2.62)
The quality of sleep		_	

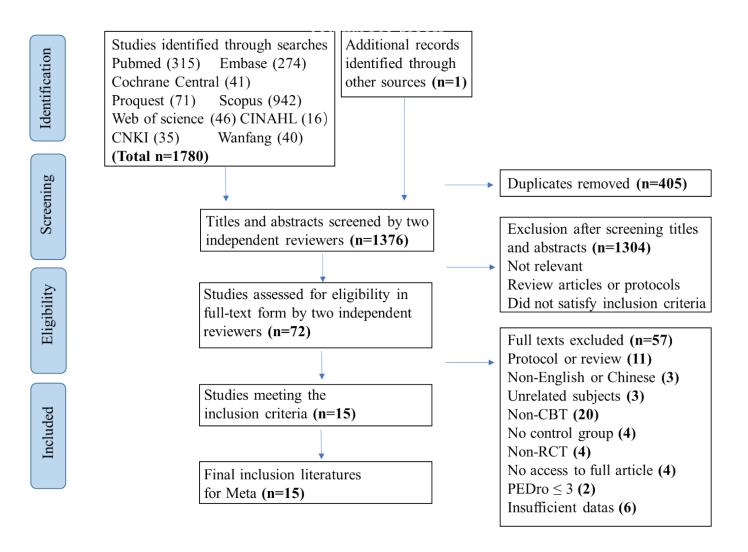


FIGURE 1 | PRISMA flow diagram.

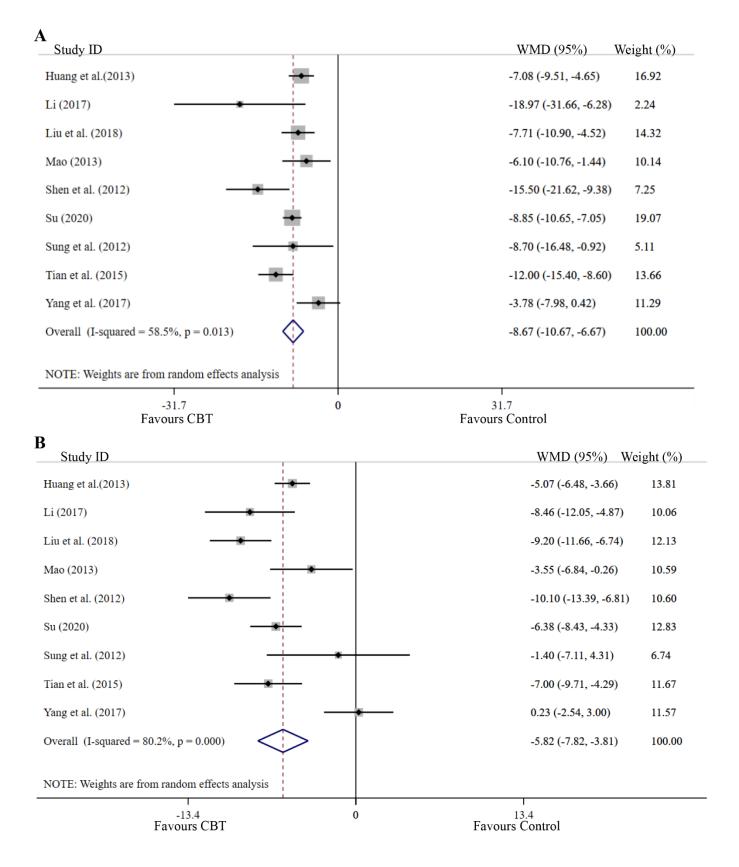
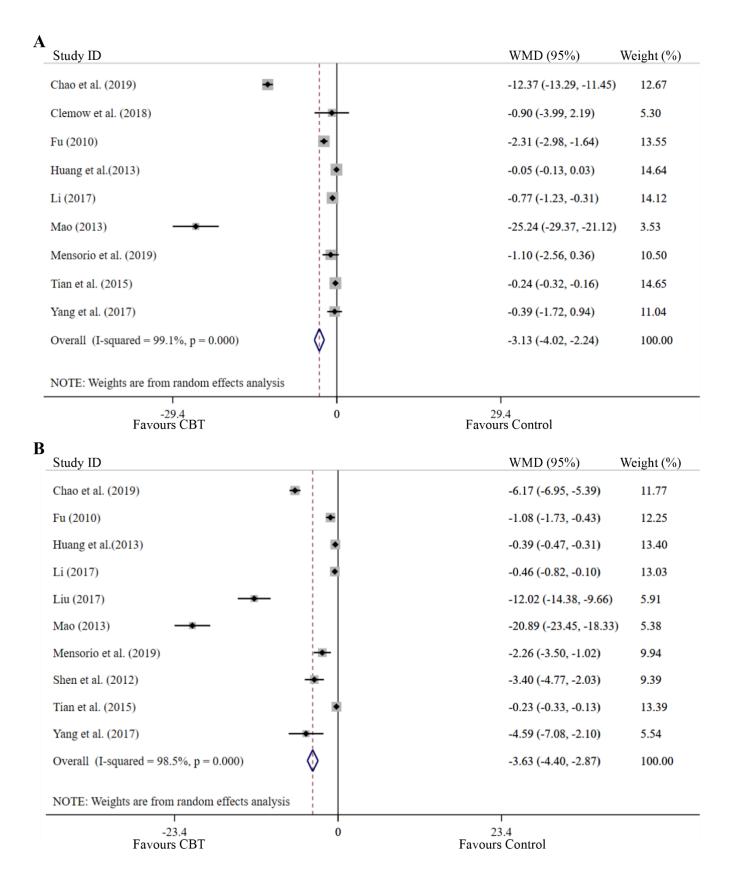
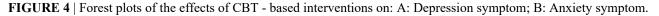


FIGURE 2 | Forest plots of the effects of CBT - based interventions on blood pressure. A: Systolic blood pressure; B: Diastolic blood pressure.

#### А Study ID WMD (95%CI) Weight(%) Huang et al.(2013) -0.58 (-0.77, -0.39) 54.53 Mao (2013) -0.24 (-0.52, 0.03) 45.47 Overall (I-squared = 74.6%, p = 0.047) -0.43 (-0.75, -0.10) 100.00 NOTE: Weights are from random effects analysis -.768 0 .768 Favours CBT Favours Control B Study ID WMD (95%CI) Weight(%) Huang et al.(2013) 0.10 (-0.15, 0.35) 7.46 Mao (2013) -0.01 (-0.08, 0.06) 92.54 Overall (I-squared = 0.0%, p = 0.419) 0.00 (-0.07, 0.07) 100.00 NOTE: Weights are from random effects analysis -.35 Favours CBT .35 Favours Control 0 С Study ID WMD (95%CI) Weight(%) Huang et al.(2013) -0.35 (-1.42, 0.72) 5.24 Mao (2013) 0.12 (-0.13, 0.37) 94.76 Overall (I-squared = 0.0%, p = 0.401) 0.10 (-0.15, 0.34) 100.00 NOTE: Weights are from random effects analysis 1.42 Favours Control 0 -1.42 Favours CBT D Study ID WMD (95%CI) Weight(%) Liu et al. (2018) -2.25 (-3.13, -1.37) 54.50 Yang et al. (2017) -3.75 (-4.99, -2.51) 45.50 Overall (I-squared = 73.2%, p = 0.053) -2.93 (-4.40, -1.47) 100.00 NOTE: Weights are from random effects analysis -4.99 Favours CBT 4.99 Favours Control 0

FIGURE 3 | Forest plots of the effects of CBT - based interventions on: A: Total cholesterol; B: Triglyceride; C: LDL - C. D: Quality of sleep.





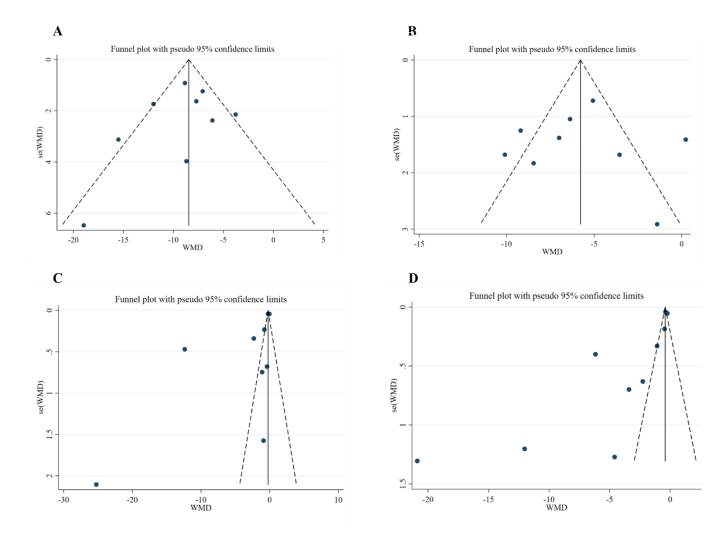


FIGURE 5 | Funnel plots for: A: Systolic blood pressure; B: Diastolic blood pressure; C: Depression symptom; D: Anxiety symptom.

# Highlights

- 1. CBT-based intervention has a positive effect on health outcomes in patients with hypertension.
- 2. CBT-based intervention might be more effective for blood pressure management in hypertension patients when it is group-based, long term, and cognitive therapy based.
- 3. CBT-based intervention might be used as an adjunctive treatment for hypertension patients to reduce drug requirements.