META-ANALYSIS

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Differences of blood pressure measured at clinic versus at home in the morning and in the evening in Europe and Asia: A systematic review and meta-analysis

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Abstract

Numerous studies have indicated that there might be great differences among different populations in Europe and Asia in terms of home morning and evening blood pressure (BP). Thus, the authors performed a systematic review to determine the quantitative differences of BP measured at clinic versus at home in the morning and in the evening in Europe and Asia. PubMed, Embase, and Scopus databases were searched up to October 2021. Studies that compared clinic BP with home morning and (or) home evening BP in European and Asian populations were included. A random effect model was applied to pool the differences between clinic BP and home morning/evening BP. Thirty-five studies, for a total of 49 432 patients, were included in this meta-analysis. Mean clinic systolic blood pressure (SBP) values were significantly higher than home morning SBP values by 3.79 mmHg (95% CI, 2.77–4.80). The differences were much larger in Europe [(6.53 mmHg (95% CI, 4.10–8.97)] than in Asia [(2.70 mmHg (95% CI, 1.74–3.66)], and the region was a significant predictor for the differences. Mean clinic SBP values were also significantly higher than home evening SBP values by 6.59 mmHg (95% CI, 4.98–8.21). The differences were much smaller in Europe [5.85 mmHg (95% CI, 3.24–8.45)] than in Asia [7.13 mmHg (95% CI, 4.92–9.35)], while age and clinic SBP might contribute to it. Our findings showed that the difference between clinic and home morning SBP was much larger in European than Asian populations, whereas the difference between clinic and home evening SBP was the opposite. The differing characteristics of the region, ethnic, age, and clinic BP might explain the diversities.

KEYWORDS
clinic blood pressure, comparison, home blood pressure

1 | INTRODUCTION

Home blood pressure (BP) measurement, as one of the out-of-office blood pressure measurement techniques, is currently recommended by most hypertension guidelines and is widely used around the world.[1,2] Unlike clinic BP, home BP provides additional information about time, which incorporates both morning and evening measurements. There are many potential factors affecting home morning and evening BP, such as gender, alcohol consumption, cardiovascular disease (CVD), sleep disorders, and use of antihypertensive medication.[3]

However, clinic BP is the golden standard for the diagnosis and management of hypertension.[1,2] As many studies and researches about hypertension are based on clinic BP, it is still the most widely used routine BP measurement technique. It is universally acknowledged that clinic BP values are always higher than corresponding home BP values, which might be largely due to the alerting reaction and white coat effect.[4] In fact, multiple factors were reported to be associated with the differences between clinic BP and home BP, like age, gender, clinic BP value, and anti-hypertensive treatment.[4]

Several hypertension guidelines in Europe and Asia have recommended 135/85 mmHg as the diagnostic threshold for hypertension when using home BP monitoring,[1,2] but the evidence that they included was mainly 10 or even 20 years ago.[5] With the development of society and changes in lifestyle, more updated evidence has been cumulated, which provokes the discussion about whether the threshold is appropriate currently. Several studies conducted in Europe have presented that home morning BP levels were almost comparable to those of home evening BP.[6-8] Conversely, in the studies conducted in Asia, home morning BP values were always higher than home evening BP,[9-11] which indicated that there might be great differences among different populations in Europe and Asia in terms of home morning and evening BP. It could be attributable to pathophysiologic mechanisms including discrepancies in salt sensitivity and activity of the sympathetic nervous system as well as differences in lifestyle.[12,13] Considering that the diagnostic threshold for hypertension by home BP monitoring is the same in Europe and Asia, we proposed the hypothesis that there might be differences between Europe and Asia while comparing clinic BP with home morning BP as well as home evening BP.

Therefore, we performed the systematic review to determine the quantitative differences of BP measured at clinic versus at home in the morning and in the evening in Europe and Asia.

2 | METHODS

2.1 | Search strategy

A systematic literature search was conducted to identify relevant studies in the PubMed, Embase, and Scopus databases up to October 2021. Only studies with the English language were included. The specific keywords and search strategies were presented in the Supplementary Appendix. In addition, we also checked the reference lists of included studies to identify relevant studies.

2.2 | Selection of studies

Two reviewers (Huanhuan Miao and Shijie Yang) assessed the eligibility of studies by screening the title, abstract and even full text of them independently, and the disagreements were settled through discussion. Studies were considered for inclusion if they met the following criteria: (1) including a comparison between clinic BP and home morning BP, and(or) a comparison between clinic BP and home evening BP at a single time point; (2) the mean values and standard deviations (SD) of clinic BP and corresponding home morning BP and(or) home evening BP were reported respectively; (3) participants aged ≥18 years; (4) European or Asian populations. In addition, the studies were excluded if they met any of the following criteria: (1) incomplete reporting data; (2) unpublished or conference data; (3) participants who were pregnant or had atrial fibrillation.

2.3 | Data extraction and collection

After identifying relevant articles, two reviewers (Huanhuan Miao and Shijie Yang) extracted the data independently and the disagreements were resolved through discussion. The following data were extracted: study characteristics (authors, year of publication, journal, country/region, study design), baseline information of participants (sample size, mean age, gender, hypertensive status, antihypertensive treatment, diabetes, and CVD comorbidities), BP measurement (methods and devices of BP measurement both at clinic and at home), mean values and SD of clinic and home morning/evening BP measurement.

2.4 | Quality assessment

Two reviewers (Huanhuan Miao and Shijie Yang) independently evaluated the quality of included studies using Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2).[14] The method assessed the risk of bias of included studies in 4 main domains (i.e., selection of patients, index test, reference standard, flow and timing) and assessed the applicability of studies in three domains (i.e., selection of patients, index test, and reference standard).[14]

2.5 | Statistical analysis

Continuous variables were presented as mean ± SD, and the categorical variables were presented as proportions. We separately analyzed the differences between: 1) clinic systolic blood pressure (SBP) and home morning SBP; 2) clinic SBP and home evening SBP; 3) clinic diastolic blood pressure (DBP) and home morning DBP; 4) clinic DBP and home evening DBP in Europe and Asia. A random-effect model was used and the results were reported as mean differences (MDs) of BP values. Heterogeneity was estimated by a Q test ($p < 0.1$) and I^2 statistic, with I^2 values of 25%, 50%, and 75% representing mild, moderate and severe heterogeneity, respectively. We performed
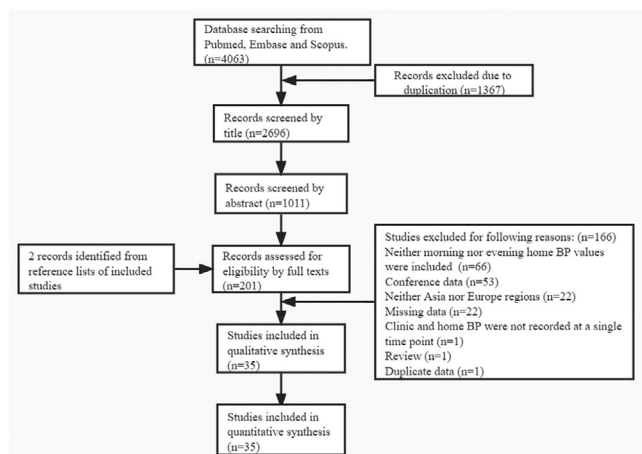
FIGURE 1 Flow chart of the study selection

a meta-regression analysis to explore whether potential variables (region, mean age, gender, mean BP values, proportion of hypertension, proportion of antihypertensive treatment, and proportion of diabetes) were associated with the outcome. Besides, we also performed a subgroup analysis by the mean levels of clinic BP. In addition, sensitivity analyses were conducted to explore the influence of individual studies on the outcome by omitting each study in turn. Further sensitivity analyses were conducted with studies that focused on hypertensive populations or performed home BP measurement at least twice each time and on at least 3 consecutive days. Publication bias was presented by Begg's funnel plot and then examined by Begg's test and Egger's test, with p values < 0.05 representing significant publication bias. All statistical analyses were performed using Stata 12 (StataCorp, College Station, Texas) and Revman 5 (The Cochrane Collaboration, The Nordic Cochrane Centre, Copenhagen, Denmark).

3 | RESULT

3.1 | Study selection and characteristics

A total of 4063 records was identified through our searching strategy from PubMed, Embase, and Scopus databases (Figure 1). After the removal of 1367 duplicates, 1685 studies were excluded by title screening and 812 studies were further excluded by abstract screening. Two records were added from reference lists of included studies. A total of 201 studies were eligible for full-text screening and 166 articles were excluded at this stage for following reasons: neither morning nor evening home BP values were included ($n = 66$); conference data ($n = 53$); neither Asia nor Europe regions ($n = 22$); missing data ($n = 22$); clinic and home BP were not recorded at a single time point ($n = 1$); review ($n = 1$) and duplicate data ($n = 1$). In total, 35 studies were included in the meta-analysis. Among the included studies, 22 studies contained both home morning and evening BP values,[6–11,15–30] whereas 13 studies contained only home morning BP values.[31–43] 10

studies were conducted in European countries.[6–8,15–19,22,25] whereas 25 studies were conducted in Asian countries[9–11,20,21,23,24,26–43] (22 in Japan).[9–11,20,21,23,24,26,27,29,31,33–43] A total of 49 432 patients were examined, and study populations varied from unselected groups to populations with hypertension, chronic kidney disease (CKD), diabetes, etc. The detailed characteristics of included studies were summarized in Table 1 and descriptions of the clinic and home BP measurement methods in each study were reported in Table S1 (see Supplementary Appendix).

Almost all of the included studies had different degrees of bias due to the lack of clarity in methods (Table S2). Twenty-seven studies did not illustrate whether they enrolled patients consecutively or randomly. Besides, the timing and blinding information of clinic and home BP measurements were also poorly reported. As for concerns regarding the applicability, several studies were unclear or at high risk of bias in index text and reference standard domains since the absence of detailed descriptions of measurements or nonstandard measurements.

3.2 | Comparison between clinic BP and home morning BP

Thirty-five studies, including a total of 49 432 patients, compared clinic BP with home morning BP, with 10 studies conducted in Europe and 25 studies in Asia. Mean clinic BP values were significantly higher than home morning BP values by 3.79 mmHg (95% CI, 2.77–4.80) for SBP (Figure 2) and 0.84 mmHg (95% CI, 0.14–1.55) for DBP (Figure 3). The differences were much larger in Europe than in Asia both for SBP [6.53 mmHg (95% CI, 4.10–8.97) in Europe vs. 2.70 mmHg (95% CI, 1.74–3.66) in Asia] and DBP [3.31 mmHg (95% CI, 2.40–4.22) in Europe vs. −0.05 mmHg (95% CI, −0.75–0.66) in Asia]. However, there were significant statistical heterogeneities between included studies ($I^2 = 94\%$, $p<0.01$ for SBP; $I^2 = 95\%$, $p<0.01$ for DBP).

To explore potential affecting factors (region, mean age, gender, mean BP values, the proportion of hypertension, the proportion of antihypertensive treatment, and proportion of diabetes) for the differences between clinic BP and home morning BP, we performed meta-regression analyses for each variable listed above, which showed that the region was a significant predictor for both SBP and DBP differences, and the clinic DBP was a significant predictor for DBP difference (Table S3).

To further determine whether clinic BP had an influence on the differences between clinic BP and home morning BP, subgroup analysis by the mean levels of clinic BP was conducted (Figure S1–S4, see Supplementary Appendix). We found that the differences between clinic SBP and home morning SBP tended to be greater with the increase of clinic SBP values in European populations, except for clinic SBP < 130 mmHg subgroup which only included one study, whereas no significant tendency was founded in Asian populations.

Finally, we examined the publication bias by Begg's funnel plots, which indicated no evidence of bias. Further Begg's test ($p>0.05$) and Egger's test ($p>0.05$) also proved it.

TABLE 1 Characteristics of the included studies

Study	Journal	Country/region	Type of population	Sample size	Mean age	Male (%)	Hypertension (%)	Diabetes mellitus (%)	Antihypertensive treatment (%)	CVD comorbidities (%)
Al-Karkhi, I. et al. 2015[6]	Blood Pressure Monitoring	Sweden, Europe	General population	162	62.6 ± .5	48.8%	82.1%	n.a.	n.a.	n.a.
Asayama, K. et al. 2019[9]	Hypertension Research	Japan, Asia	Hypertensive population	308	71.8 ± 10.1	42.2%	100%	17.9%	96.4%	Nonfatal stroke and myocardial infarction 4.9%
Campo, C. et al. 2007[7]	Blood Pressure	Spain, Europe	hypertensive population	142	57.8 ± 11.3	53.1%	100%	18.9%	100%	Ischemic heart disease 5.6%
Chantrel, F. et al. 2020[15]	Blood Pressure Monitoring	France, Europe	CKD with hypertension population	225	67.0 ± 13.0	61%	100%	37%	100%	n.a.
de Heus, R. A. A. et al. 2019[16]	European Journal of Cardiovascular Nursing	Netherlands, Europe	Mild cognitive impairment/dementia population	213	73.4 ± 9.0	58.2%	n.a.	n.a.	58.2%	43.2%
Divisón, J. A. et al. 2004[17]	Blood Pressure Monitoring	Spain, Europe	General population	989	44.3 ± 16.4	49.6%	0	n.a.	0	n.a.
Jula, A. et al. 1999[18]	Hypertension	Finland, Europe	Hypertensive population	233	46.0 ± 4.9	58.4%	100%	8%	0	n.a.
Kario, K. et al. 2013[10]	Drugs in R and D	Japan, Asia	Hypertensive population	4852	64.8 ± 11.9	47.1%	100%	17.8%	45.5%	Heart disease 11.3% cerebrovascular disorder 7.4%
Kjeldsen, S. E. et al. 2002[19]	Blood Pressure	Sweden and Norway, Europe	hypertensive population	87	58.0 ± 6.0	49.0%	100%	2%	21%	n.a.
Kondo, K. et al. 2016[11]	Blood Pressure Monit	Japan, Asia	Hypertensive population	75	66.6 ± 11.8	65.3%	100%	34.7%	100%	n.a.
Mancia, G. et al. 2002[8]	Blood Pressure Monitoring	Italy, UK and the Netherlands, Europe	Hypertensive population	426	55.3 ± 9.8	64.3%	100%	16%	n.a.	Angina pectoris 5% cerebrovascular event 4%
Mori, H. et al. 2017[20]	Hypertension Research	Japan, Asia	Normotensive population	451	52.4 ± 15.7	17.4%	0	0	0	n.a.
Nakano, M. et al. 2016[21]	Journal of Clinical Hypertension	Japan, Asia	Hypertensive population	95	58.7 ± 13.4	37.9%	100%	6.3%	86.0%	Myocardial infarction 1.1%
Niiranen, T. J. et al. 2006[22]	Journal of Hypertension	Finland, Europe	General population	2051	56.4 ± 8.5	46.4%	55.2%	n.a.	22.7%	n.a.

(Continues)

TABLE 1 (Continued)

Study	Journal	Country/ region	Type of population	Sample size	Mean age	Male (%)	Hypertension (%)	Diabetes mellitus (%)	Antihypertensive treatment (%)	CVD comorbidities (%)
Ohta, Y. et al. 2014[23]	Clinical and Experimental Hypertension	Japan, Asia	Hypertensive population	208	66.0 ± 11.0	47.1%	100%	n.a.	100%	n.a.
Okada, T. et al. 2008[24]	American Journal of Nephrology	Japan, Asia	CKD population	137	64.8 ± 10.2	71.5%	n.a.	n.a.	92.7%	n.a.
Saito, I. et al. 2013[41]	Hypertension Research	Japan, Asia	Hypertensive population	21571	64.8 ± 11.9	49.4%	100%	20.4%	50.2%	Cardiovascular or cerebrovascular disease 10.5%
Stenehjem, A. E. et al. 2006[25]	Blood Pressure Monitoring	Norway, Europe	Renal transplant population	49	53.4 ± 14.2	46.9%	86%	n.a.	n.a.	n.a.
Udani, J. et al. 2015[26]	Functional Foods in Health and Disease	Japan, Asia	Hypertensive population	10	50.4 ± 8.1	80%	100%	n.a.	0	n.a.
Uno, H. et al. 2008[27]	Hypertension Research	Japan, Asia	Hypertensive population	72	59.7 ± 10.2	65.3%	100%	4.2%	43.1%	Angina pectoris 2.8% stroke 2.8%
Kadowaki, S. et al. 2021[33]	Hypertension Research	Japan, Asia	General population	1056	64.2 ± 9.8	100%	n.a.	22.2%	32.5%	n.a.
Kakio, Y. et al. 2017[34]	Blood Pressure Monitoring	Japan, Asia	Hypertensive population	84	67.7 ± 10.9	47.6%	100%	45.2%	100%	Myocardial infarction 6.0% angina pectoris 9.5% stroke 7.1%
Kamoi, K. et al. 2010[35]	Clinical and Experimental Hypertension	Japan, Asia	Diabetes population	400	65.0 ± 10.0	53.0%	71%	100%	49%	Coronary heart disease 10% cerebrovascular disease 17.5%
Kuriyama, S. et al. 2014[36]	Clinical and Experimental Nephrology	Japan, Asia	Hypertensive population	74	60.7 ± 11.6	87.8%	100%	29.7%	100%	Myocardial infarction 5.4% angina pectoris 5.4% stroke 8.1%
Miyagawa, S. et al. 2012[37]	Clinical and Experimental Hypertension	Japan, Asia	Hypertensive population	151	66.9 ± 9.5	51%	100%	19%	100%	n.a.
Mori, H. et al. 2013[38]	Hypertension Research	Japan, Asia	Hypertensive population	188	61.5 ± 11.7	57.4%	100%	n.a.	100%	n.a.

(Continues)

TABLE 1 (Continued)

Study	Journal	Country/ region	Type of population	Sample size	Mean age	Male (%)	Hypertension (%)	Diabetes mellitus (%)	Antihypertensive treatment (%)	CVD comorbidities (%)
Ohkubo, T. et al. 2004[39]	Hypertension Research	Japan, Asia	Hypertensive population	3400	66.2 ± 10.5	44.8%	100%	13.7%	100%	Cerebrovascular disease 9.1% ischemic heart disease 8.2%
Ohta, Y. et al. 2011[40]	Clinical and Experimental Hypertension	Japan, Asia	Hypertensive population	262	67.0 ± 11.0	44.0%	100%	n.a.	100%	n.a.
Satoh, A. et al. 2019[42]	Journal of Hypertension	Japan, Asia	General population	919	64.5 ± 9.6	100%	n.a.	n.a.	32.2%	10%
Suzuki, K. et al. 2011[43]	Clinical and Experimental Hypertension	Japan, Asia	Diabetes with hypertension population	34	57.5 ± 1.8	52.9%	100%	100%	11.8%	Cerebrovascular disorder 14.7% heart disease 8.8%
Yasui, D. et al. 2012[29]	Blood Pressure Monitoring	Japan, Asia	General population	2651	57.6 ± 14.1	39.0%	39.8%	9.0%	29.3%	4.7%
Asayama K. et al. 2012[31]	Hypertension Research	Japan. Asia	Hypertensive population	3518	59.6 ± 10.0	49.9%	100%	15.3%	0	3.0%
Huang, H. C. et al. 2005[32]	Journal of International Medical Research	Taiwan, Asia	Hypertensive population	85	46.9 ± 10.2	52.9%	100%	n.a.	100%	n.a.
Xu, J. et al. 2016[28]	Patient Preference and Adherence	China, Asia	New onset TIA or ischemic stroke population	2608	62.5 ± 11.1	67.6%	70.6%	28.4%	n.a.	Ischemic stroke 88.9% transient ischemic attacks 11.1%
Zhang, D. Y. et al. 2020[30]	Journal of hypertension	China, Asia	Hypertensive population	1646	55.7 ± 13.8	100%	100%	15.1%	66.8%	10.6%

Abbreviations: CKD, chronic kidney disease; CVD, cardiovascular disease; TIA, transient ischemic attack.

Study or Subgroup	clinic SBP Mean	SD	Total	home morning SBP Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Europe								
Al-Karkhi, I. et.al.2015	130.1	18	162	131.2	17	162	2.4%	-1.10 [-4.91, 2.71]
Campo, C. et.al.2000	140.4	13.7	142	134.8	20.2	142	2.4%	5.60 [1.59, 9.61]
Chantrel, F. et.al.2020	154	19	225	146	18	225	2.6%	8.00 [4.58, 11.42]
de Heus, R. A. A. et.al.2019	156.1	23.3	213	139.8	17.6	213	2.4%	16.30 [12.38, 20.22]
Divisón, J. A. et.al.2004	123.8	20.2	989	116.5	21.5	989	3.3%	7.30 [5.46, 9.14]
Jula, A. et.al.1999	144.5	12.6	233	137.1	13.7	233	3.1%	7.40 [5.01, 9.79]
Kjeldsen, S. E. et.al.2002	148.2	17	87	143.5	14.8	87	2.1%	4.70 [-0.04, 9.44]
Mancia, G. et.al.2002	158.6	13.9	426	149.2	16.4	426	3.2%	9.40 [7.36, 11.44]
Niiranen, T. J. et.al.2006	137.4	20.2	2051	128.1	19.7	2051	3.5%	9.30 [8.08, 10.52]
Stenehjem, A. E. et.al.2006	133.1	16.3	49	144.4	23.3	49	1.1%	-11.30 [-19.26, -3.34]
Subtotal (95% CI)			4577			4577	26.2%	6.53 [4.10, 8.97]
1.1.2 Asia								
Asayama, K. et.al.2019	139.3	16.9	308	128	9.4	308	3.2%	11.30 [9.14, 13.46]
Asayama K. et al.2012	154.2	17.5	3518	151.6	12.4	3518	3.6%	2.60 [1.89, 3.31]
Huang, H. C. et.al.2005	133.8	13.7	85	124.8	13	85	2.4%	9.00 [4.99, 13.01]
Kadowaki, S. et.al.2021	136.5	19.2	1056	137.2	18.5	1056	3.4%	-0.70 [-2.31, 0.91]
Kakio, Y. et.al.2017	150.3	14.7	84	141.4	15.7	84	2.1%	8.90 [4.30, 13.50]
Kamoi, K. et.al.2010	143.9	23	400	141.3	22.6	400	2.7%	2.60 [-0.56, 5.76]
Kario, K.et.al.2013	157.5	18.7	4852	156.9	16.4	4852	3.7%	0.60 [-0.10, 1.30]
Kondo, K.et.al.2016	154.3	11.5	75	154.2	11.1	75	2.5%	0.10 [-3.52, 3.72]
Kuriyama, S. et.al.2014	164.5	17.8	74	166.5	17.6	74	1.7%	-2.00 [-7.70, 3.70]
Miyagawa, S. et.al.2012	158	9	151	153	11	151	3.1%	5.00 [2.73, 7.27]
Mori, H. et.al.2013	158.7	17.7	188	156.5	16.2	188	2.6%	2.20 [-1.23, 5.63]
Mori, H. et.al.2017	115.2	12.4	451	116.3	12.8	451	3.4%	-1.10 [-2.74, 0.54]
Nakano, M. et.al.2016	135.5	12.9	95	134	9.9	95	2.7%	1.50 [-1.77, 4.77]
Ohkubo, T. et.al.2004	143	14	3400	140	14	3400	3.7%	3.00 [2.33, 3.67]
Ohta, Y. et.al.2011	133	12	262	132	11	262	3.3%	1.00 [-0.97, 2.97]
Ohta, Y. et.al.2014	137	12	208	132	8	208	3.3%	5.00 [3.04, 6.96]
Okada, T. et.al.2014	132	18.2	137	137	14.9	137	2.4%	-5.00 [-8.94, -1.06]
Saito, I. et al. 2013	153.6	19	21571	151.6	16.4	21571	3.7%	2.00 [1.67, 2.33]
Satoh, A. et.al.2019	136.8	19	919	137.2	18.5	919	3.4%	-0.40 [-2.11, 1.31]
Suzuki, K. et.al.2011	147	2.1	34	147	2.6	34	3.6%	0.00 [-1.12, 1.12]
Udani, J. et.al.2015	149.2	8.3	10	143.7	13.1	10	0.9%	5.50 [-4.11, 15.11]
Uno, H. et.al.2008	160.4	17	72	154.9	16.9	72	1.8%	5.50 [-0.04, 11.04]
Xu, J. et.al.2016	136.9	13.9	2608	134.5	12.7	2608	3.6%	2.40 [1.68, 3.12]
Yasui,D. et.al.2012	130.6	18	2651	123.7	15.2	2651	3.6%	6.90 [6.00, 7.80]
Zhang, D. Y. et.al.2020	140.3	16.5	1646	135.5	14	1646	3.6%	4.80 [3.75, 5.85]
Subtotal (95% CI)			44855			44855	73.8%	2.70 [1.74, 3.66]
Total (95% CI)			49432			49432	100.0%	3.79 [2.77, 4.80]

Europe — Heterogeneity: Tau² = 12.13; Chi² = 71.77, df = 9 (P < 0.00001); I² = 87%. Test for overall effect: Z = 5.26 (P < 0.00001)

Asia — Heterogeneity: Tau² = 4.31; Chi² = 327.08, df = 24 (P < 0.00001); I² = 93%. Test for overall effect: Z = 5.53 (P < 0.00001)

Total — Heterogeneity: Tau² = 7.28; Chi² = 601.26, df = 34 (P < 0.00001); I² = 94%. Test for overall effect: Z = 7.28 (P < 0.00001). Test for subgroup differences: Chi² = 8.27, df = 1 (P = 0.004), I² = 87.9%

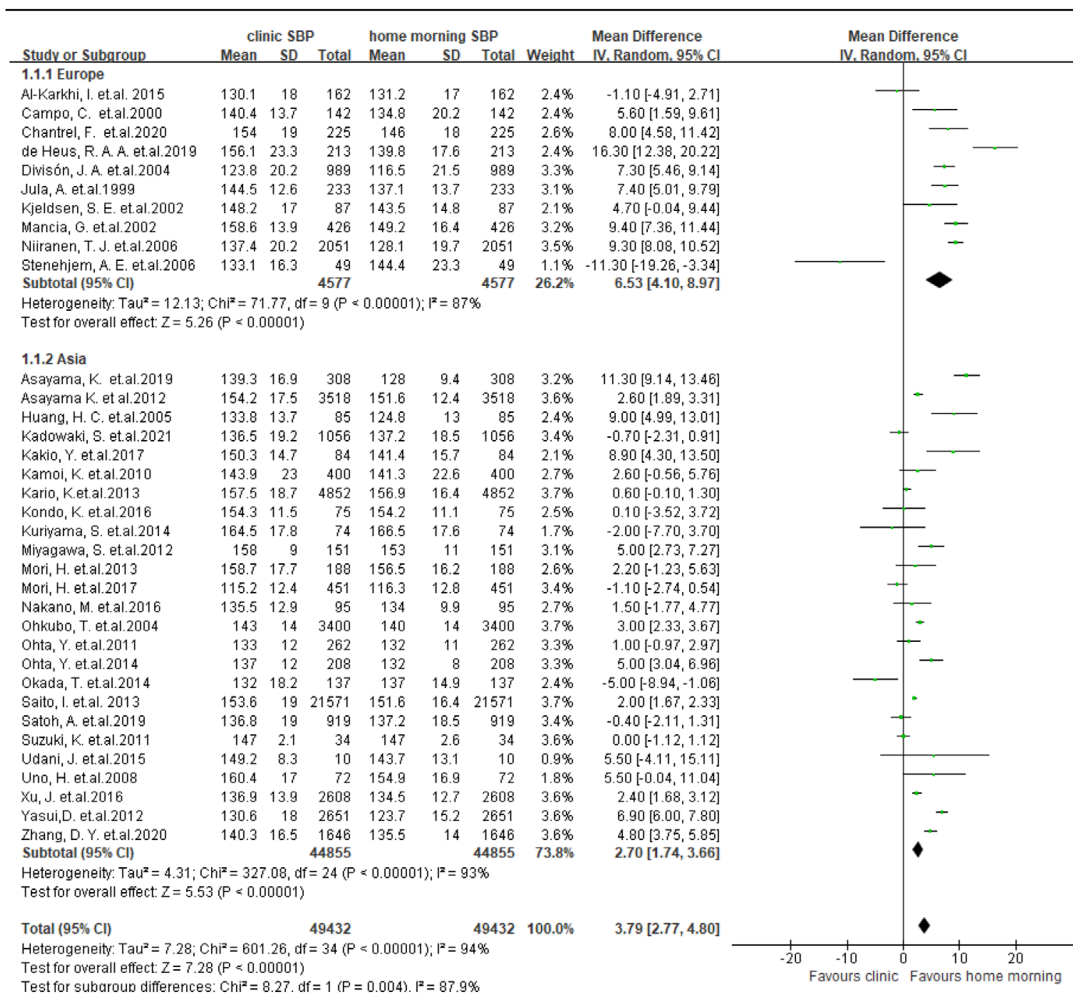Favours clinic Favours home morning (-20, -10, 0, 10, 20)

FIGURE 2 Forest plot of studies that comparing SBP difference between clinic BP and home morning BP

3.3 | Comparison between clinic BP and home evening BP

Twenty-two studies, including a total of 17 634 patients, compared clinic BP with home evening BP, with 10 studies conducted in Europe and 12 studies in Asia. Mean clinic BP values were significantly higher than home evening BP values by 6.59 mmHg (95% CI, 4.98–8.21) for SBP (Figure 4) and 3.37 mmHg (95% CI, 2.41–4.33) for DBP (Figure 5). The differences were much smaller in Europe than in Asia for SBP [5.85 mmHg (95% CI, 3.24–8.45) in Europe vs. 7.13 mmHg (95% CI, 4.92-9.35) in Asia], whereas the result was opposite for DBP [3.81 mmHg (95% CI, 2.41–5.22) in Europe vs. 2.96 mmHg (95% CI, 1.72–4.20) in Asia]. The statistical heterogeneities were also significant ($I^2 = 95\%$, $p<0.01$ for SBP; $I^2 = 93\%$, $p<0.01$ for DBP).

We also performed meta-regression analyses for the above variables, which showed that age and clinic SBP were significant predictors for SBP difference (Table S4).

To further explore the influence of clinic BP, a subgroup analysis by the mean levels of clinic BP was conducted (Figure S5–S8). Similarly, the differences between clinic SBP and home evening SBP in European populations tended to be greater with the increase of clinic SBP values except for clinic SBP < 130 mmHg subgroup, whereas no significant tendency was founded in Asian populations or for DBP differences.

All of Begg's funnel plots, Begg's test ($p>0.05$) and Egger's test ($p>0.05$) showed no evidence of publication bias.

3.4 | Sensitivity analysis

Among studies in which home BP was measured at least twice each time and on at least three consecutive days, the difference between clinic SBP and home morning SBP was 6.95 mmHg (95% CI, 4.89–9.02), whereas the difference between clinic SBP and home evening SBP was 8.42 mmHg (95% CI, 5.86–10.99) (Figure S9–S10).

Among studies in which only hypertensive populations were included, the difference between clinic SBP and home morning SBP was 4.21 mmHg (95% CI, 3.18–5.23), whereas the difference between clinic SBP and home evening SBP was 8.17 mmHg (95% CI, 6.43–9.91) (Figure S11–S12).

The influence of individual studies on the outcomes was evaluated by omitting each study in turn, which showed no significant alternation of the outcomes, suggesting that no one study had tremendous influence on the outcomes.
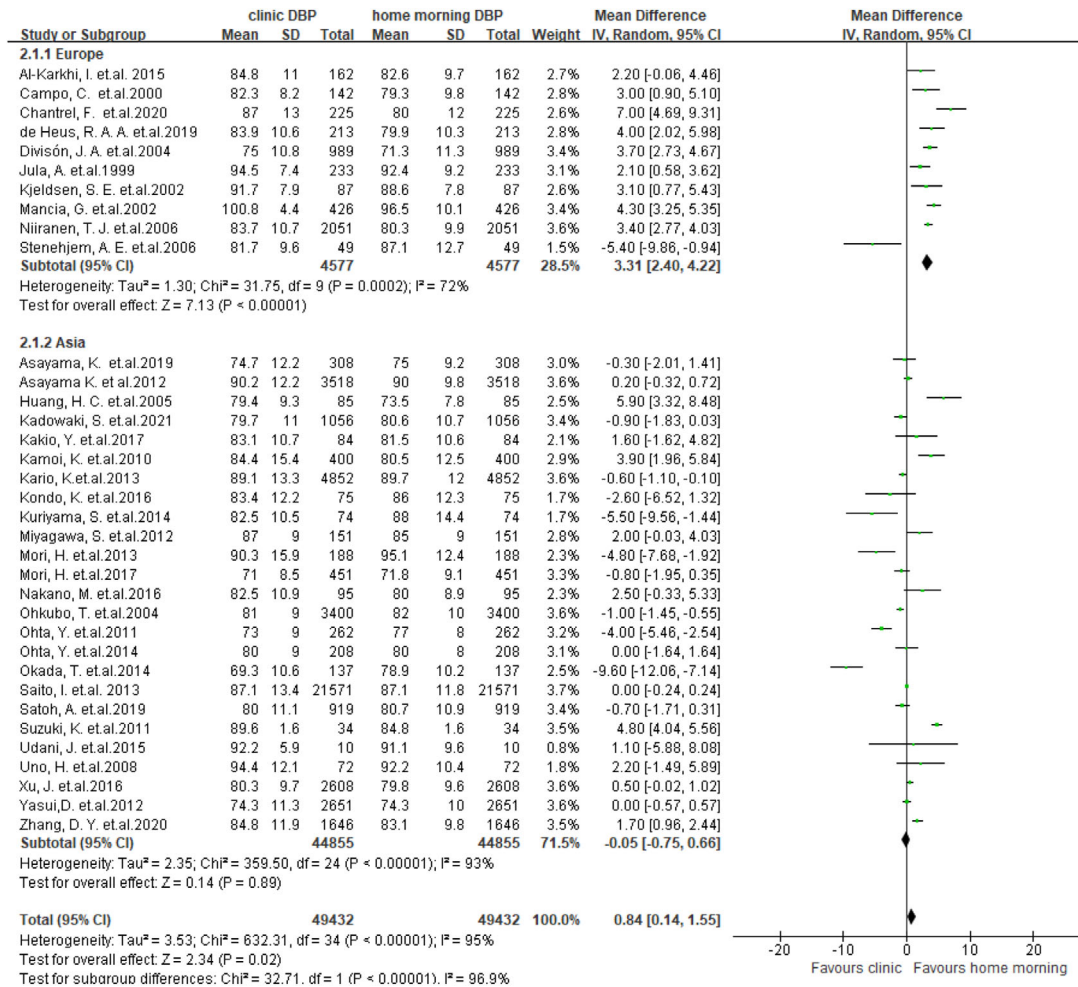
Study or Subgroup	clinic DBP Mean	SD	Total	home morning DBP Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
2.1.1 Europe									
Al-Karkhi, I. et.al.2015	84.8	11	162	82.6	9.7	162	2.7%	2.20 [-0.06, 4.46]	
Campo, C. et.al.2000	82.3	8.2	142	79.3	9.8	142	2.8%	3.00 [0.90, 5.10]	
Chantrel, F. et.al.2020	87	13	225	80	12	225	2.6%	7.00 [4.69, 9.31]	
de Heus, R. A. A. et.al.2019	83.9	10.6	213	79.9	10.3	213	2.8%	4.00 [2.02, 5.98]	
Divisón, J. A. et.al.2004	75	10.8	989	71.3	11.3	989	3.4%	3.70 [2.73, 4.67]	
Jula, A. et.al.1999	94.5	7.4	233	92.4	9.2	233	3.1%	2.10 [0.58, 3.62]	
Kjeldsen, S. E. et.al.2002	91.7	7.9	87	88.6	7.8	87	2.6%	3.10 [0.77, 5.43]	
Mancia, G. et.al.2002	100.8	4.4	426	96.5	10.1	426	3.4%	4.30 [3.25, 5.35]	
Niiranen, T. J. et.al.2006	83.7	10.7	2051	80.3	9.9	2051	3.6%	3.40 [2.77, 4.03]	
Stenehjem, A. E. et.al.2006	81.7	9.6	49	87.1	12.7	49	1.5%	-5.40 [-9.86, -0.94]	
Subtotal (95% CI)			**4577**			**4577**	**28.5%**	**3.31 [2.40, 4.22]**	
Heterogeneity: Tau² = 1.30; Chi² = 31.75, df = 9 (P = 0.0002); I² = 72%									
Test for overall effect: Z = 7.13 (P < 0.00001)									
2.1.2 Asia									
Asayama, K. et.al.2019	74.7	12.2	308	75	9.2	308	3.0%	-0.30 [-2.01, 1.41]	
Asayama K. et al.2012	90.2	12.2	3518	90	9.8	3518	3.6%	0.20 [-0.32, 0.72]	
Huang, H. C. et.al.2005	79.4	9.3	85	73.5	7.8	85	2.5%	5.90 [3.32, 8.48]	
Kadowaki, S. et.al.2021	79.7	11	1056	80.6	10.7	1056	3.4%	-0.90 [-1.83, 0.03]	
Kakio, Y. et.al.2017	83.1	10.7	84	81.5	10.6	84	2.1%	1.60 [-1.62, 4.82]	
Kamoi, K. et.al.2010	84.4	15.4	400	80.5	12.5	400	2.9%	3.90 [1.96, 5.84]	
Kario, K.et.al.2013	89.1	13.3	4852	89.7	12	4852	3.6%	-0.60 [-1.10, -0.10]	
Kondo, K. et.al.2016	83.4	12.2	75	86	12.3	75	1.7%	-2.60 [-6.52, 1.32]	
Kuriyama, S. et.al.2014	82.5	10.5	74	88	14.4	74	1.7%	-5.50 [-9.56, -1.44]	
Miyagawa, S. et.al.2012	87	9	151	85	9	151	2.8%	2.00 [-0.03, 4.03]	
Mori, H. et.al.2013	90.3	15.9	188	95.1	12.4	188	2.3%	-4.80 [-7.68, -1.92]	
Mori, H. et.al.2017	71	8.5	451	71.8	9.1	451	3.3%	-0.80 [-1.95, 0.35]	
Nakano, M. et.al.2016	82.5	10.9	95	80	8.9	95	2.3%	2.50 [-0.33, 5.33]	
Ohkubo, T. et.al.2004	81	9	3400	82	10	3400	3.6%	-1.00 [-1.45, -0.55]	
Ohta, Y. et.al.2011	73	9	262	77	8	262	3.2%	-4.00 [-5.46, -2.54]	
Ohta, Y. et.al.2014	80	9	208	80	8	208	3.1%	0.00 [-1.64, 1.64]	
Okada, T. et.al.2014	69.3	10.6	137	78.9	10.2	137	2.5%	-9.60 [-12.06, -7.14]	
Saito, I. et.al. 2013	87.1	13.4	21571	87.1	11.8	21571	3.7%	0.00 [-0.24, 0.24]	
Satoh, A. et.al.2019	80	11.1	919	80.7	10.9	919	3.4%	-0.70 [-1.71, 0.31]	
Suzuki, K. et.al.2011	89.6	1.6	34	84.8	1.6	34	3.5%	4.80 [4.04, 5.56]	
Udani, J. et.al.2015	92.2	5.9	10	91.1	9.6	10	0.8%	1.10 [-5.88, 8.08]	
Uno, H. et.al.2008	94.4	12.1	72	92.2	10.4	72	1.8%	2.20 [-1.49, 5.89]	
Xu, J. et.al.2016	80.3	9.7	2608	79.8	9.6	2608	3.6%	0.50 [-0.02, 1.02]	
Yasui,D. et.al.2012	74.3	11.3	2651	74.3	10	2651	3.6%	0.00 [-0.57, 0.57]	
Zhang, D. Y. et.al.2020	84.8	11.9	1646	83.1	9.8	1646	3.5%	1.70 [0.96, 2.44]	
Subtotal (95% CI)			**44855**			**44855**	**71.5%**	**-0.05 [-0.75, 0.66]**	
Heterogeneity: Tau² = 2.35; Chi² = 359.50, df = 24 (P < 0.00001); I² = 93%									
Test for overall effect: Z = 0.14 (P = 0.89)									
Total (95% CI)			**49432**			**49432**	**100.0%**	**0.84 [0.14, 1.55]**	
Heterogeneity: Tau² = 3.53; Chi² = 632.31, df = 34 (P < 0.00001); I² = 95%									
Test for overall effect: Z = 2.34 (P = 0.02)									
Test for subgroup differences: Chi² = 32.71. df = 1 (P < 0.00001). I² = 96.9%									

-20 -10 0 10 20
Favours clinic Favours home morning

FIGURE 3 Forest plot of studies that comparing DBP difference between clinic BP and home morning BP

4 | DISCUSSION

The main findings of the present meta-analysis were that: (1) the MD between clinic and home morning SBP was 3.79 mmHg (95% CI, 2.77–4.80), which was much larger in the European subgroup than in the Asian subgroup; (2) the MD between clinic and home evening SBP was 6.59 mmHg (95% CI, 4.98–8.21), which was much smaller in European subgroup than in Asian subgroup. To our knowledge, the present study is the first meta-analysis that compares clinic BP with home morning and home evening BP in the European and the Asian regions.

Home morning BP is usually measured within one hour after waking up, before breakfast and drug intake.[2,44] According to normal circadian BP rhythm, BP turns to surge in the morning,[45] which might be attributable to the activation of the sympathetic nervous system and release of renin and angiotensin II at that time.[46] A previous study showed a higher morning BP surge in Japanese than in European hypertensive populations.[47] The possible mechanisms have not been elucidated yet. Increased activation of sympathetic nervous system and high salt sensitivity in Asian populations might be potential contributing factors.[12] In addition to morning BP surge, sustained nocturnal hypertension is another subtype of morning hypertension.[48] It is reported that Asian populations had a smaller nocturnal BP fall than European populations and isolated nocturnal hypertension was more prevalent in Asia.[49] This discrepancy appears to be partly due to higher salt sensitivity and excessive salt intake in Asian populations.[12,49] In the present study, we found that the difference between clinic and home morning SBP was much larger in the European subgroup than in the Asian subgroup. Meta-regression analyses showed that region was a significant predictor of the difference. Based on the above evidence, home morning BP is always higher in Asian populations, which might result in a smaller difference between clinic and home morning SBP in Asian populations than in European populations.

In the Japan Morning Surge–Home Blood Pressure (J-HOP) study, compared with patients whose home morning SBP was lower than 135 mmHg, patients with higher morning BP had a higher risk of stroke (Hazard ratio [HR], 2.45. 2.80, 3.58, and 6.52 for morning SBP 135–144, 145–154, 155–164, and ≥165 mmHg groups, respectively).[50] Morning hypertension is closely related to CVD (particularly stroke) and thus more attention should be paid to morning BP to prevent stroke, especially in Asia.
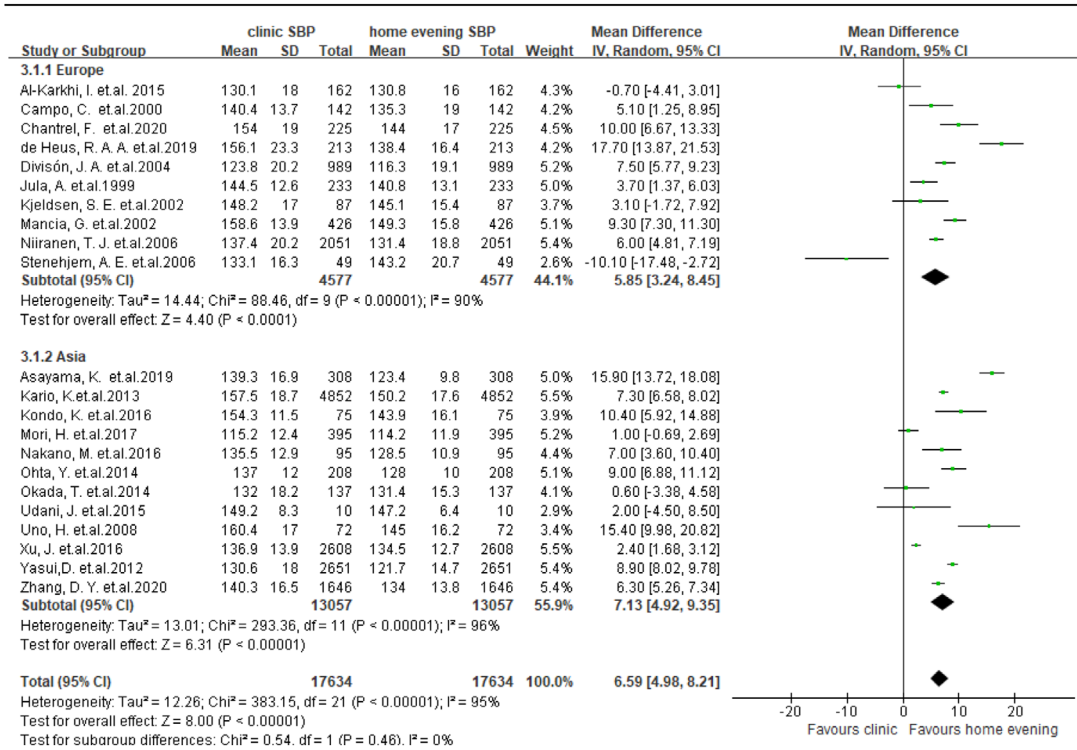
FIGURE 4 Forest plot of studies that comparing SBP difference between clinic BP and home evening BP
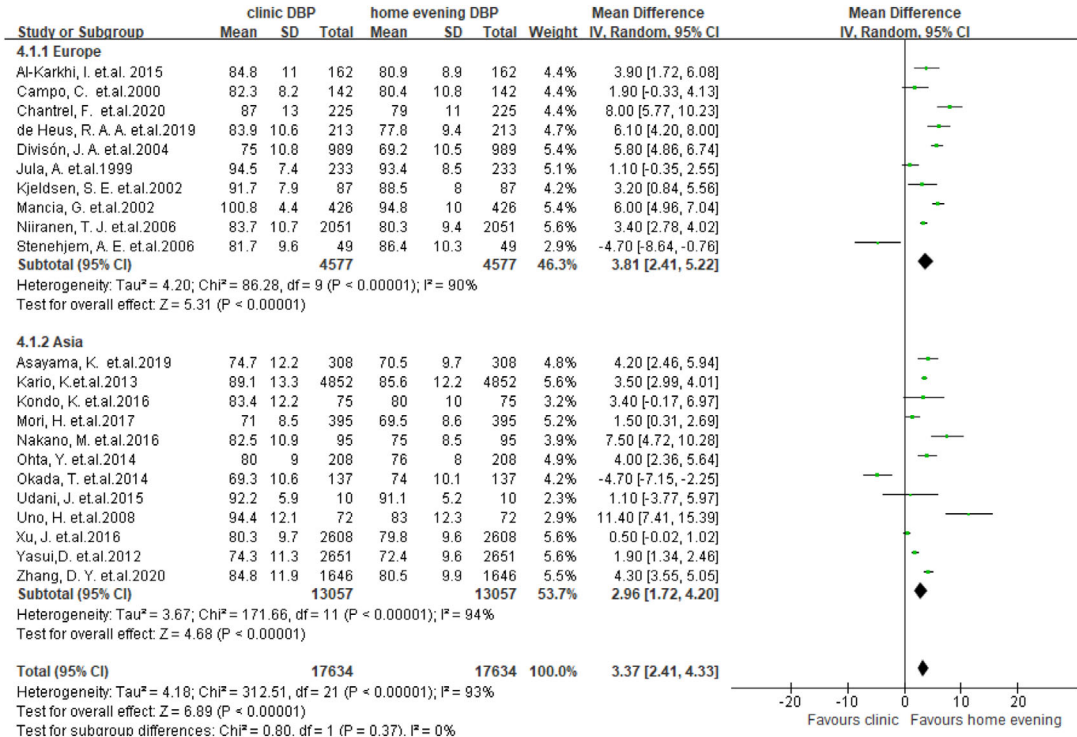

FIGURE 5 Forest plot of studies that comparing DBP difference between clinic BP and home evening BP

In terms of home evening BP, the recommended timing of measurement is inconsistent in Europe and Asia. The European Society of Hypertension guideline for home BP monitoring (2008) recommended that home evening BP should be measured before dinner.[44] whereas in Asia, the Japanese Society of Hypertension guideline for the management of hypertension (2019) suggested that evening BP should be measured at bedtime.[2] Home evening BP is affected by daytime activities and the lifestyle of individuals, like the time of dinner, alcohol consumption, and bathing. Fujiwara T et al.[13] found that BP measured at bedtime was significantly lower than before dinner in a Japanese population, which might be attributable to bathing and alcohol consumption. Most Japanese bathe every day in bathtubs, and this habit has been proven to have a significant depressor effect on BP.[51] Our study showed that the difference between clinic and home evening SBP was much larger in the Asian subgroup than in the European subgroup. The different characteristics of the timing of measurement and lifestyle might explain the diversity. Furthermore, we also elucidated that the difference between clinic and home evening SBP was significantly associated with age and clinic BP. Similarly, a previous meta-analysis about home BP measurement also reported that the difference between clinic and home SBP tended to be greater with the increase of age and clinic BP values.[4] To obtain more reliable results, we conducted a sensitivity analysis by choosing studies that measured home BP at least twice each time and on at least 3 consecutive days, which showed that the differences between clinic and home morning/evening SBP were much larger than the primary analysis. This was consistent with our knowledge that fewer measurements might lead to unstable and higher home BP records.[44] Additionally, we also chose hypertensive populations to perform a sensitivity analysis, and the results were comparable to the primary analysis.

4.1 | Clinical implications and recommendations for future research

As discussed above, home morning and home evening BP might be different not only in specific values but also in clinical implications. However, in clinical practice, some patients merely measure home morning or home evening BP when monitoring home BP due to insufficient patient education or inertia. Recently, multiple studies focused on home morning BP.[38,39] Thus, an important issue that should be considered in clinical practice is that the cut-off values of hypertension could be set separately for home morning and home evening BP. Given the differences between European and Asian populations in comparisons between clinic BP and home morning/evening BP, normalcy levels for home morning/evening BP should be defined separately among different populations.[52] To determine the proper cut-off values of clinical significance, further studies will be needed to investigate the differences between clinic BP and home morning/evening BP in different populations. Besides, further prospective randomized trials are also needed to explore the relationship between different target values of home morning and clinical outcomes in different populations for better management of hypertensive patients.

4.2 | Limitations

There are some limitations in our study. Firstly, our pooling estimates were based on some heterogeneities across the included studies. However, we attempted to explore the reasons for heterogeneities by subgroup analysis according to region and clinic BP levels, meta-regression analyses about several variables, and sensitivity analyses. And we finally observed some factors that affected the outcome such as region, age and clinic BP, which might explain a part of the heterogeneity. Besides, due to the lack of description of the detailed methods among included studies, most of them had unclear or even high risk of bias in some domains of QUADAS-2. Furthermore, in the Asian subgroup, the study populations were mainly from Japan. For that home BP monitoring is more common and prevalent in Japan than in other areas in Asia, relevant studies were abundant here. Thus, the data in our study might be less representative of the whole Asian populations. Lastly, we only reviewed literature in the English language, which might lead to language bias. However, the main strength of our study is that this is the first meta-analysis comparing clinic BP with home morning and home evening BP in Europe and Asia.

5 | CONCLUSIONS

In conclusion, the clinic BP is significantly higher than home morning and home evening BP in Europe and Asia, with the gap larger between the clinic and home evening BP. The MD between clinic and home morning SBP was much larger in European populations than in Asian populations, whereas the difference between clinic and home evening SBP much larger in Asian populations. The different characteristics of the region, ethnicity, age, and clinic BP might explain the diversities. Further studies will be needed to investigate the differences between clinic and home morning/evening BP in European and Asian regions, and explore potential affecting factors of them.

CONFLICTS OF INTEREST
There are no conflicts of interest.

AUTHOR CONTRIBUTIONS
Huanhuan Miao: Designed the analysis, collected the data, performed the analysis and wrote the manuscript. Shijie Yang: Collected the data, designed the tables and contributed the analysis tools. Yuqing Zhang: Conceived and designed the analysis, revised the manuscript.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.