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Blood pressure and childhood obstructive sleep apnea: A systematic review and meta-analysis

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ABSTRACT

Obstructive sleep apnea (OSA) is an established risk factor for high blood pressure (BP) in adults. However, it remains unclear whether the same association could be found in children and adolescents. Therefore, we conducted a systematic review and meta-analysis of observational studies to evaluate the associations between childhood OSA and BP outcomes. The review protocol was registered in PROSPERO (CRD42021225683). We performed a systematic literature search to identify relevant cross-sectional and longitudinal studies up to July 6, 2021. Of the 4902 identified articles, a total of 12 cross-sectional studies and 2 cohort studies were included in the final analyses. In the cross-sectional analyses, the mean systolic BP (SBP) were significantly higher in children with mild or moderate-to-severe OSA compared to the healthy controls, and these effects were more pronounced during the nighttime. In prospective studies, moderate-to-severe childhood OSA was associated with a risk of elevated SBP in adulthood (Mean difference = 4.02 mm Hg, 95% CI = 1.32 to 6.72). Taken together, our results suggest that moderate-to-severe childhood OSA is associated with a higher risk of adverse SBP outcomes. Early detection and treatment of OSA may promote cardiovascular health in children and adolescents and possibly in future adulthood.

1. Introduction

Sleep-disordered breathing (SDB) is a prevalent sleep disorder among children and adolescents, which can be divided into primary snoring, upper airway resistance syndrome, and obstructive sleep apnea syndrome (OSA) [1,2]. The prevalence of OSA ranges from 1.2% to 25% in children aged 5–12 years [3]. Several large-scale longitudinal studies in adults have suggested that untreated OSA is associated with an increased risk of hypertension [4–7] which is one of the most common cardiovascular diseases and the leading cause of morbidity and mortality worldwide [8,9]. As proposed by the American Academy of Pediatrics in 2017, children with OSA may confer a higher risk of developing prehypertension and/or hypertension [10]. Cross-sectional studies have suggested that childhood OSA was associated with elevated blood pressure (BP) [11–14]. Nonetheless, previous meta-analyses conducted on children and adolescents have reported inconsistent results on the contributing effects of OSA on BP outcomes. One meta-analysis did not find an association between OSA and BP outcomes in children and

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Abbreviations

ABPM	ambulatory blood pressure monitoring
AHI	apnea-hypopnea index
AXIS	The Appraisal Tool for Cross-Sectional Studies
SDB	sleep-disordered breathing
BMI	body mass index
BP	blood pressure
CI	confidence interval
DBP	diastolic blood pressure
NOS	Newcastle-Ottawa Scale
OSA	obstructive sleep apnea
PSG	polysomnography
PTT	pulse transit time
SBP	systolic blood pressure

adolescents [15], while a subsequent one suggested that childhood OSA was associated with a greater risk of hypertension [16]. Therefore, the adverse effects of childhood OSA on BP outcomes remain to be determined.

More recently, a few longitudinal studies have provided new evidence that childhood OSA may be an independent risk factor for adverse BP outcomes in late adolescence and adulthood [17–19]. Given that the existing meta-analysis has not included the most updated longitudinal cohort studies, it is timely to summarize the current evidence to confirm the association between childhood OSA and elevated BP. In particular, a separate analysis of longitudinal data was conducted to examine the association of childhood OSA with the longitudinal BP outcomes in late adolescence and adulthood.

2. Methods

Our meta-analysis was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines and Meta-analysis Of Observational Studies in Epidemiology (MOOSE) guidelines [20,21]. The detailed checklists of PRISMA and MOOSE are listed in Table S1 and S2.

3. Search strategy and selection criteria

Three databases, including Embase, Web of Science, and PubMed were searched for English-language articles published before July 6, 2021, using the following search criteria. Observational studies (e.g., cross-sectional, case-control, and longitudinal cohort studies) that investigated BP parameters (e.g., systolic/diastolic BP [SBP/DBP] during sleep or wakefulness, BP load, and non-dipping) of children (aged less than 13 years) and adolescents (age ranged from 13 to 17 years) with mild OSA or moderate-to-severe OSA. According to a previous study, mild OSA was defined as an obstructive apnea-hypopnea index (OAHI) or apnea-hypopnea index (AHI) between 1 and 5 events/hour, while moderate-to-severe childhood OSA was defined as an OAHI or AHI $\geq$5 events/hour [22]. We also searched the reference lists and review articles for additional studies that met the inclusion criteria. The detailed search strategies for each database are presented in Table S3 in the Supplementary materials.

The exclusion criteria of the present study were: 1) lack of controls (e.g., healthy controls or primary snoring); 2) no measurement of BP or BP measurements cannot be transformed to raw SBP or DBP level; 3) recruited children or adolescents had other pathological conditions (e.g., congenital heart disease); 4) BP was measured after an intervention; 5) review articles, animal studies, and articles without original data; 6) studies known to involve overlapping sample populations. To avoid data duplication, we only chose the article with the largest sample size if more than one article was reported on the same sample. Two researchers (L.Z.X and W.S.S) independently examined the titles, abstracts, and full text to identify eligible articles. In case of disagreement, a third reviewer (A.S.Z) evaluated the article in order to reach an agreement. The review protocol was registered in PROSPERO (CRD42021225683) (https://www.crd.york.ac.uk/prospero/).

4. Data extraction

We extracted the following information from each study: 1) name of the first author, 2) country (origin) of data collection, 3) year of publication, 4) sample size, 5) mean age or age range, 6) sex ratio, 7) methods of BP measurement, 8) methods of monitoring sleep at night, and 9) mean SBP/DBP and standard deviation during wakefulness or nighttime (Table S4). If raw data were not available in the text, we would look for any additional data or graphical information.

5. Study quality assessment

We used the Newcastle-Ottawa Scale to assess the quality of case-control and cohort studies (NOS; http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp). This scale applies a "star system", which includes three components: the selection of the study population, the comparability of the study groups, and the ascertainment of exposure or outcome. According to the Agency for Research and Quality standards, the NOS scores were converted into "good," "fair," and "poor" quality. The Appraisal Tool for Cross-Sectional Studies (AXIS) was used to assess the quality of cross-sectional studies [23]. This tool consists of 20 questions, which need to be responded to as 'yes', 'no', or 'don't know'. Studies with a score of thirteen or more (out of 20) were considered good quality studies.

6. Statistical analysis

In the meta-analyses, we compared the mean values of SBP and DBP during wakefulness and nighttime between participants with SDB and healthy controls. To account for the potential affect of heterogeneity, the mean differences (MD) and the 95% confidence intervals (CIs) for the SBP and DBP were separately pooled by a Hartung-Knapp method random-effects model [24]. These results were presented in forest plots and overall effects were examined by Z-statistics and associated p values. Heterogeneity among studies was assessed by the Cochrane P value ($P < 0.10$ was considered significant) and the degree of heterogeneity using the I^2 statistics, with cutoff values of 25%, 50%, and 75% to represent low, medium, and high degrees of heterogeneity respectively. In order to further explore the potential sources of heterogeneity, we also used Baujat plots to identify articles that had a high contribution to the heterogeneity of this research [25]. If there was moderate to high heterogeneity, the sources of heterogeneity were explored by subgroup and sensitivity analyses in which we removed studies with low methodological quality. We constructed Contour-enhanced funnel plots as a visual representation of bias in the main analyses and used Egger's test to assess publication bias [26,27]. All statistical analyses were conducted using the "meta", "dmetar" package in R software (version 4.0.4; R Core Team, Vienna, Austria), with a 2-side test of $\alpha = 0.05$ as the significance level.

7. Results

7.1. Clinical characteristics of included studies

Fig. 1 shows the flowchart of research selection. Among the 4902 records initially retrieved, 3900 non-duplicated titles were identified. After screening for eligibility by topics and abstracts, 52 abstracts were evaluated for further full text screening. A total of 14 eligible articles were included in the meta-analysis, including 12 cross-sectional studies and two cohort studies [12,13,17,18,28–37]. All studies were classified as high quality, with a mean AXIS score of 17 for cross-sectional studies (Table S5), and a mean NOS score was 7 (Table S6). The clinical characteristics of these studies are shown in Table 1. A total of 3081 participants aged from 3 to 17 years were enrolled in these studies. The follow-up time was 10 years and 7.4 years in the two prospective cohort studies, respectively [17,18]. Of the 14 studies, five were conducted in the United States, four in China, four in Australia, and one in Greece. Eight of the studies used hospital-based samples, four studies used community samples, and two studies used hospital-based samples in the OSA group and age-sex-matched community samples in the control group. Eight studies used age- and sex-matched healthy participants as controls, five studies used primary snoring as controls, and one study used an apnea hypopnea index (AHI) of <2 as controls. For the BP measurements, five studies used 24-h ambulatory blood pressure monitoring (ABPM), five used office BP, three used finger photoplethysmography, and one used pulse transit time (PTT).

7.2. Quantitative synthesis

Fig. 2 and Fig. 3 respectively show the forest plots of awake and nighttime differences of BP between OSA participants and healthy controls based on cross-sectional data. Both awake and nighttime SBP levels were significantly higher in mild (Awake: Fig. 2A, MD = 0.98 mmHg; 95%CI = 0.73 to 1.22; nighttime: Fig. 3A, MD = 4.44 mmHg; 95%CI = 2.55 to 6.63) and moderate-to-severe OSA (Awake: Fig. 2B, MD = 4.93 mmHg; 95%CI = 1.30 to 8.57; nighttime: Fig. 3B, MD = 7.66 mmHg; 95%CI = 6.29 to 9.03) than those of health controls. Similar results were observed for awake and nighttime DBP levels in the moderate-to-severe OSA group (Awake: Fig. 2D, MD = 3.10 mmHg; 95%CI = 1.36 to 4.84; nighttime: Fig. 3D MD = 3.80 mmHg; 95%CI = 2.41 to 5.19). However, only nighttime DBP levels were significantly higher in the mild OSA group (Awake: Fig. 2C, MD = 0.98 mmHg; 95%CI = −0.08 to 2.05; nighttime: Fig. 3C, MD = 3.01 mmHg; 95%CI = 0.45 to 5.57) than those of health controls.

Fig. 4 shows the differences in awake BP between OSA participants and healthy controls in the longitudinal studies. Compared with the healthy controls, a significantly higher SBP in late adolescence or young adulthood was found in participants with moderate-to-severe childhood OSA (Fig. 4B, MD = 4.02 mmHg; 95% CI = 1.32 to 6.72), but not in those with mild childhood OSA (Fig. 4A, MD = 1.66 mmHg; 95%CI = −0.25 to 3.58). As for DBP, no significant differences with controls were found in the mild (Fig. 4C, MD = 1.09 mmHg; 95%CI = −0.24 to 2.42) and moderate-to-severe childhood OSA groups (Fig. 4D, MD = 1.37 mmHg; 95%CI = −1.56 to 4.30).

We further evaluated the awake and nighttime BP differences between participants with OSA and those with primary snoring. We found that both awake (Figure S1B, MD = 2.35 mmHg; 95%CI = 0.36 to 4.33) and nighttime SBP levels (Figure S2B, MD = 4.34 mmHg; 95%CI = 2.32 to 6.36) in the moderate-to-severe OSA group, but not in the mild OSA group, were significantly higher than those in the primary snoring group. However, there were no significant differences in the awake and nighttime DBP between the primary snoring group and both the mild and moderate-to-severe OSA groups. No significant asymmetry was found in the visual detection of the Contour-enhanced funnel plots (Figure S3, Figure S4, and Figure S5), and Egger's linear regression test (Table S7) also supported a lack of potential publication bias in the present study.

7.3. Heterogeneity analysis

Our main analyses showed evidence of high heterogeneity in several BP comparisons (I^2>75% in some comparisons). In order to analyze the reasons for the high heterogeneity, we conducted Baujat plots and influence analyses on these results to detect which study had the greatest influence on the BP comparisons (Figure S6-S13). After excluding these outliers, the results were largely consistent with the main analyses, that is, participants with

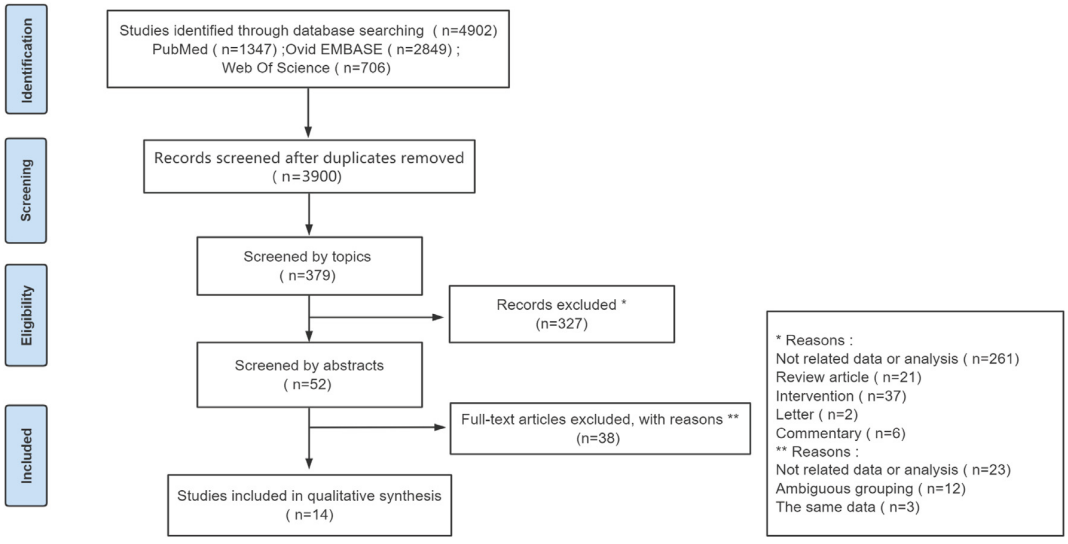

Fig. 1. Flowchart for the studies included in the meta-analysis.

Table 1
Baseline characteristics of included studies.

Study (Ref.)	Year	Country	Size/ male	Outcome	Study design (sample)	Measurement methods of BP	Control	Age (yrs)
Amin et al. [13]	2004	America	60/ 36	BP	cross-sectional study (hospital-based)	ABPM	primary snoring (AHI<1/h)	5-17 (range)
Amin et al. [28]	2008	America	125/ 71	BP	cross-sectional study (hospital-based)	ABPM	healthy control (Age- and gender matched healthy children)	7-13 (range)
Bixler et al. [29]	2008	America	700/ 336	BP/MAP	cross-sectional study (community-based)	Office BP	without SDB (AHI<1/h)	5-12 (range)
Chan et al. [17]	2020	China	243/ 143	BP	cohort study (community-based)	ABPM	healthy control (no history of snoring)	9.9 ± 1.8
Geng et al. [30]	2019	China	140/ 92	BP	cross-sectional study (hospital-based)	PTT	primary snoring (OAHI<1/h)	3-11 (range)
Fernandez-Mendoza et al. [18]	2021	America	421/ 227	BP	cohort study (community-based)	Seated (baseline and follow-up), supine (follow-up only), and standing (follow-up only)	AHI< 2	5-12 (range)
Horne et al. [31]	2011	Australia	141/ 80	MAP/HR	cross-sectional study (hospital and community)	Finger photoplethysmography	healthy control (OAHI≤1/h, no history of snoring)	7-13 (range)
Horne et al. [32]	2020	Australia	533/ 298	BP	cross-sectional study (hospital-based)	Office BP	non-snoring controls	7.2 ± 0.1
Kaditis et al. [33]	2010	Greece	95/ 51	BP/FE_{Na}	cross-sectional study (hospital-based)	Office BP	primary snoring (OAHI<1/h)	6.3 ± 2.6
Kang et al. [34]	2017	China	163/ 109	BP/MAP	cross-sectional study (hospital-based)	ABPM and office BP	primary snoring (AHI<1/h)	8.2 ± 3.3
Li et al. [12]	2008	China	306/ 199	BP	cross-sectional study (community-based)	ABPM	healthy control (obstructive apnea– hypopnoea index (AHI) < 1 and history of snoring<3 nights per week)	6-13 (range)
McConnell et al. [35]	2009	America	169/ 134	BP	cross-sectional study (hospital-based)	Finger photoplethysmography	the absence of a history of OSA and the absence of any sleep-disordered breathing or alveolar hypoventilation on PSG	7-13 (range)
O'Driscoll et al. [36]	2009	Australia	30/ 15	MAP/HR	cross-sectional study (hospital-based)	Office BP and finger photoplethysmography	primary snoring (OAHI<1/h)	9.2 ± 0.2
O'Driscoll et al. [37]	2011	Australia	96/ 59	Urinary catecholamines	cross-sectional study (hospital and community)	Office BP	non-snoring controls	3-12 (range)

Values are mean ± SEM. ABPM, ambulatory blood pressure monitoring; AHI, apnea–hypopnea index; BP, blood pressure; FE_{Na}, fractional urinary excretion of sodium; HR, heart rate; MAP, mean arterial pressure; OAHI, obstructive apnea hypopnea index; OSA, obstructive sleep apnea; PSG, polysomnography; PTT, pulse transit time; SDB, sleep-disordered breathing.

moderate-to-severe OSA were still associated with a higher BP level compared to healthy controls, both during awake and nighttime (Figure S8, Figure S10, and Figure S13). However, the nighttime DBP difference between participants with mild OSA and healthy controls was no longer significant (Figure S12).

7.4. Subgroup analyses

To further explore the source of heterogeneity, we performed a series of subgroup analyses to stratify the data. For the different BP measurements, ABPM showed a relative lower heterogeneity and provided consistent evidence for the BP comparisons, while other BP measurements, such as finger photoplethysmography and PTT, contributed to the considerable heterogeneity of the main analyses (Figs. 5–6, Figure S14-S15). For the study sites, studies conducted in America showed a relative higher heterogeneity for the awake BP comparisons, but most of the comparisons were not significant (Figure S16-S19). For the age, studies that included participants aged less than 9 years old showed a relatively lower heterogeneity than those of studies that included participants aged over 9 years old (Figure S20-S23). In addition, we also analyzed the influence of study population on the heterogeneity of our results, there were no significant differences between hospital and community-based samples (Figure S24-S27).

8. Discussion

In this meta-analysis, we evaluated the impact of childhood OSA on BP outcomes by using both cross-sectional and longitudinal data. Our results showed that both mild and moderate-to-severe childhood OSA were associated with elevated awake and nighttime SBP levels in cross-sectional analysis, while cohort studies provided evidence to support that only moderate-to-severe OSA was associated with future risk of elevated SBP at longitudinal follow-up. The high level of heterogeneity may partially be attributable to the various BP measurement methodologies among studies, and in this regard, ABPM provided the most consistent evidence with the least heterogeneity. Nevertheless, our subgroup and sensitivity analyses also supported that moderate-to-severe OSA was associated with a high risk of elevated BP, regardless of the BP measurement methods.

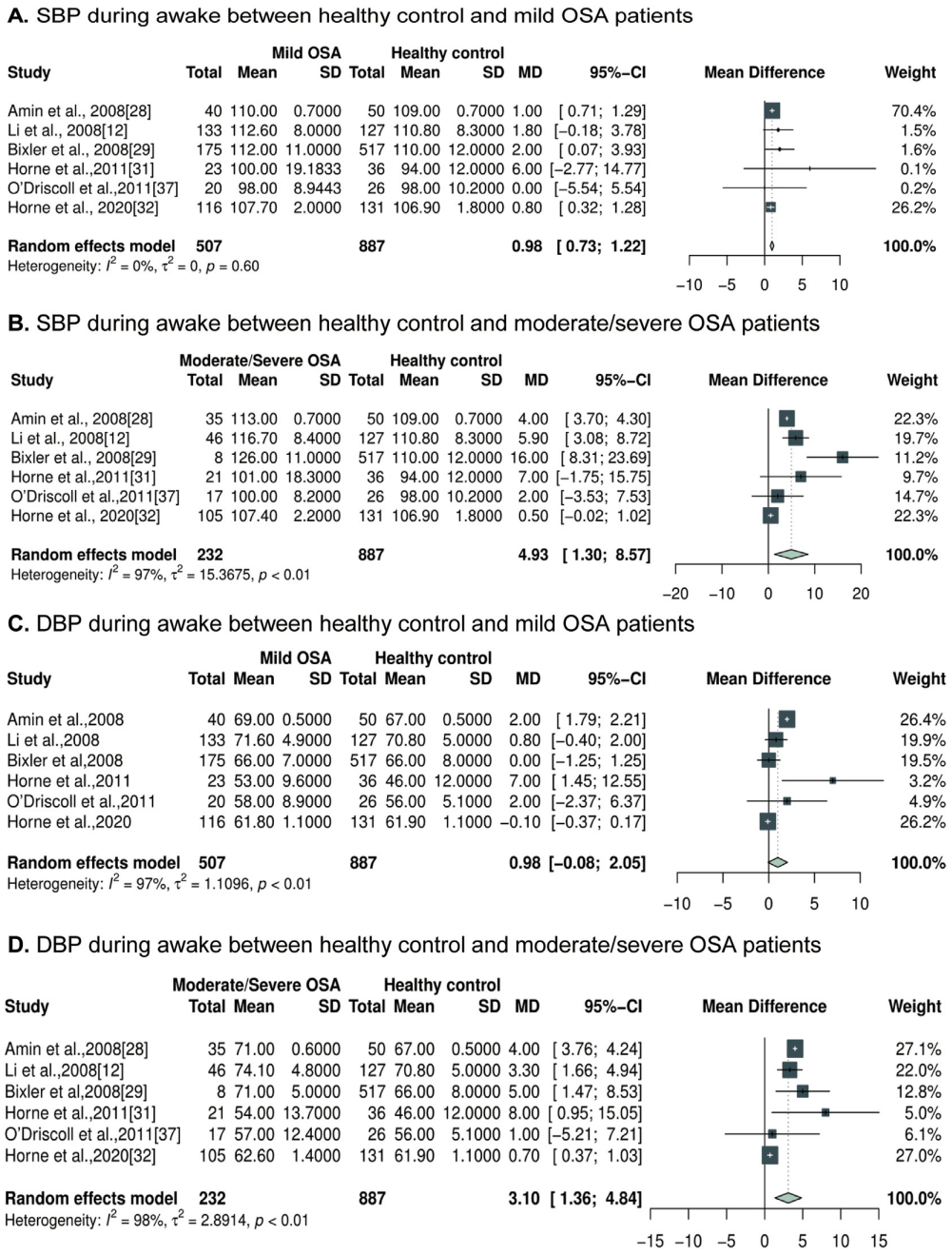

Fig. 2. Forest plots of differences in awake blood pressure at baseline compared to the healthy control group. A. SBP during the awake between healthy control and mild OSA patients. B. SBP during the awake between healthy control and moderate/severe OSA patients. C. DBP during the awake between healthy control and mild OSA patients. D. DBP during the awake between healthy control and moderate/severe OSA patients.

8.1. Comparison with previous studies

A systematic review and meta-analysis of 5 articles by Zintzaras et al. [15] did not find any significant increase in the risk of elevated BP in childhood moderate-to-severe SDB, while Kwok et al. [16] found that childhood OSA is associated with blood pressure dysregulation. Compared with the Zintzaras [15] and Kwok [16] studies, only the study by Amin et al. [13] was included in our study, the other studies were not included in the current analysis due to the lack of OSA severity classification and/or controls [14,38–43]. There are several possible reasons for the negative results reported in the meta-analysis conducted by Zintzaras et al. [15]. First, there were only 5 studies included in this meta-analysis. The limited number of studies may have under-recognized the association between OSA and elevated BP. Moreover, the included studies in this meta-analysis were heterogeneous in terms of BP measurements. Third, the Zintzaras meta-analysis also included studies at which participants had received treatment (e.g., adenotonsillectomy) for

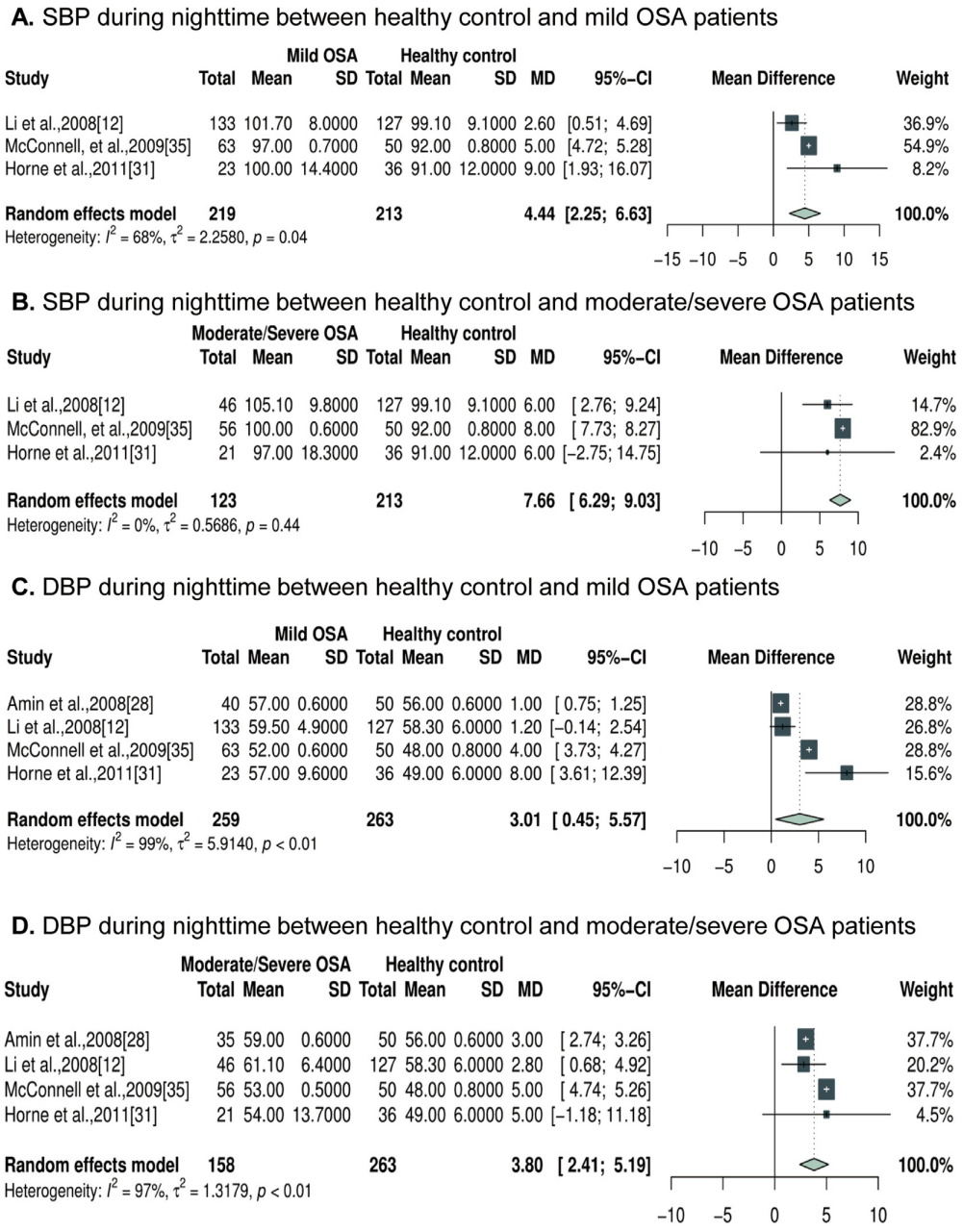

Fig. 3. Forest plots of differences in nighttime blood pressure at baseline compared to the healthy control group. A. SBP during the nighttime between healthy control and mild OSA patients. B. SBP during the nighttime between healthy control and moderate/severe OSA patients. C. DBP during the nighttime between healthy control and mild OSA patients. D. DBP during the nighttime between healthy control and moderate/severe OSA patients.

OSA, which may have affected the representativeness of the included studies. On the other hand, Kwok et al. [16] included participants with more severe OSA (AHI> 5) [43]. Moreover, the definition of outcomes in the two previous meta-analyses was different. Kwok et al. used hypertension rather than awake/sleep SBP/DBP as the main outcome [16]. These differences may account for the potential discrepancy in the results between the two meta-analyses [15,16].

Compared with these two previous studies [15,16], the present study provided substantial evidence to support that moderate-to-severe childhood OSA is associated with an increased risk of elevated BP in late adolescence or adulthood. This present study has several advantages compared to previous ones. First, to our knowledge, our study is the most up-to-date study published with the largest sample size. A total of 14 studies, including 2 recent large-scale cohort studies, were included in the final analyses. The relatively large sample size substantiated our vigorous analyses and was deemed to be more powerful than the previous study with a limited number of cross-sectional studies [15]. Second, we did not include interventional studies, such as adenotonsillectomy or continuous positive pressure ventilation, to minimize the confounding effect of the treatment. Third, we conducted a

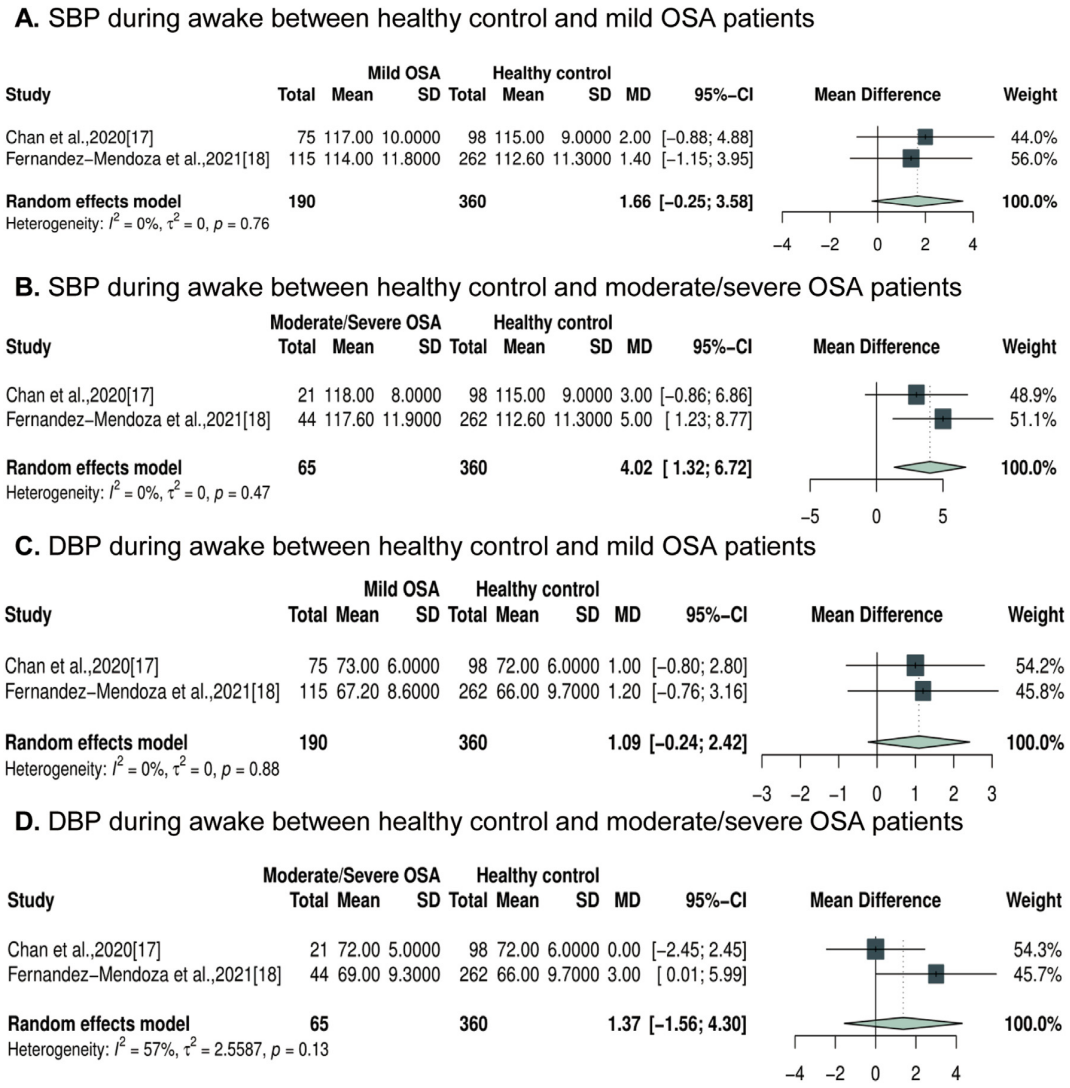

Fig. 4. Forest plots of differences in awake blood pressure at longitudinal follow-up compared to the healthy control group. A. SBP during the awake between healthy control and mild OSA patients. B. SBP during the awake between healthy control and moderate/severe OSA patients. C. DBP during the awake between healthy control and mild OSA patients. D. DBP during the awake between healthy control and moderate/severe OSA patients.

comprehensive analysis to investigate the source of heterogeneity and found that different BP measurement methods contributed to the high heterogeneity. Compared with other BP measurements, ABPM provided consistent evidence in supporting the adverse effects of moderate-to-severe OSA on BP outcomes. It has been demonstrated that 24-h ABPM provides a more accurate and comprehensive measurement of BP and diagnosis of hypertension among adults with OSA [44–46]. Several studies also indicated that ABPM is more sensitive to detecting preclinical organ damage than office BP measurements in children [47–49]. Thus, ABPM should be recommended to identify the BP abnormalities in children and adolescents with OSA.

Evidence from cross-sectional studies supported that childhood OSA was associated with a higher risk of increased BP [12,30,34,50–54], while cohort studies did not demonstrate the adverse effects of mild childhood OSA on adulthood BP outcomes [17,18] These findings may be due to the high rate of spontaneous remission of mild OSA over time along with the shrinkage of tonsils and adenoid tissues in children. It has been demonstrated that the remission rates of mild OSA and snoring ranged from 40% to 70% in children aged 6–17 years [55–58]. However, moderate-to-severe OSA was less likely to remit with growth [17]. A recent study showed that persistent childhood OSA is associated with a three-fold increased risk of future hypertension [18]. Thus, it is paramount that childhood OSA, especially for those with moderate-to-severe disease, should be diagnosed and treated as early as possible to reduce the future risk of hypertension.

Although the mechanisms underlying the association between hypertension and childhood OSA remain unclear, there is evidence that endothelial dysfunction, impaired autonomic reflexes, activation of the hypothalamic-pituitary-adrenal axis, and proinflammatory responses may be involved in the pathways linking childhood OSA to the occurrence of hypertension [59–66]. Vascular endothelium which is related to the regulation of vascular tension, platelet activity, leukocyte adhesion, and angiogenesis plays an important role in the development of cardiovascular diseases

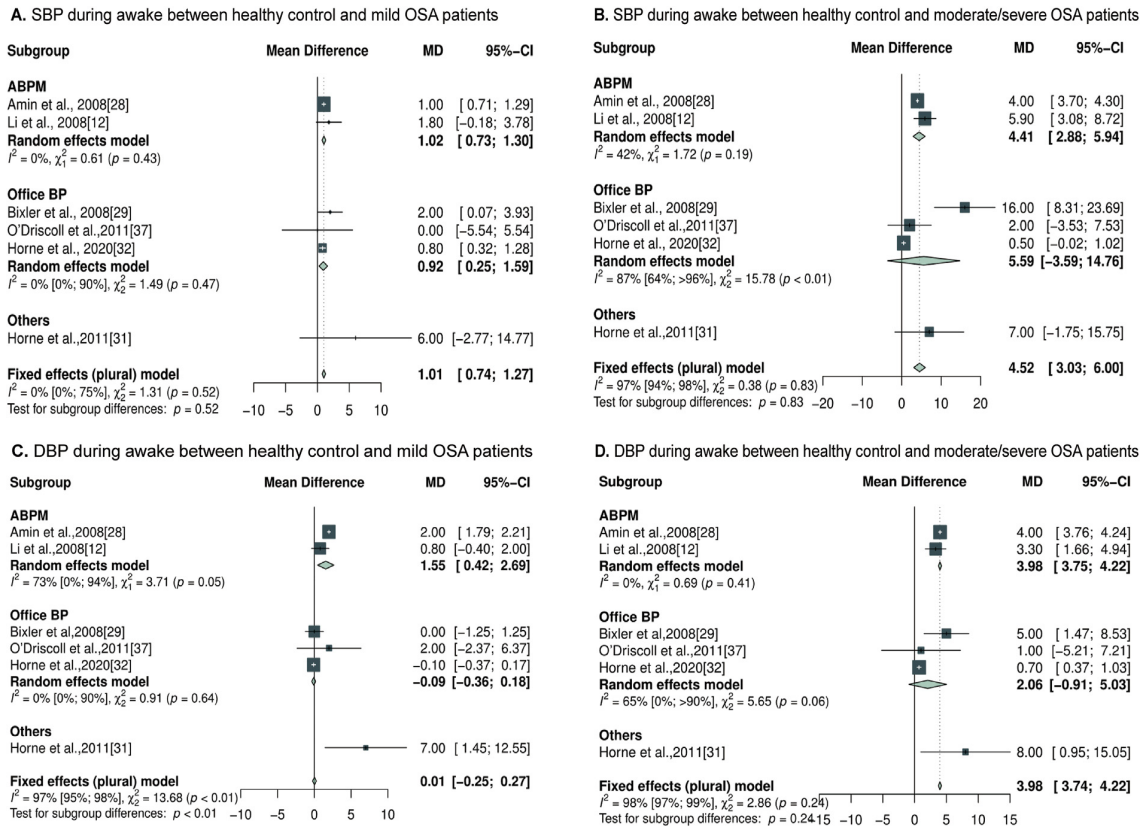

Fig. 5. Subgroup analyses of baseline awake blood pressure measurement compared to the healthy control group. A. SBP during the awake between healthy control and mild OSA patients. B. SBP during the awake between healthy control and moderate/severe OSA patients. C. DBP during the awake between healthy control and mild OSA patients. D. DBP during the awake between healthy control and moderate/severe OSA patients.

[62,67]. Previous studies have suggested that childhood OSA is associated with endothelial dysfunction [68–70], and treatment of childhood OSA appears to have a beneficial effect on endothelial function [71,72]. In addition, inflammatory cells are shown to be associated with the severity of endothelial dysfunction and BP outcomes measured by PTT [73]. A preclinical study suggested that intermittent hypoxia activates the NF-κB pathway, causing endothelial inflammatory expression and dysfunction [74].

8.2. Strengths and limitations

The main strength of this study is that the diagnosis of OSA in all studies was ascertained by the gold standard diagnostic test, namely polysomnography, which may reduce the potential bias caused by inaccurate diagnosis through self-reported questionnaires. In addition, the relatively large sample size and the comprehensive analysis conducted in this study supported our robust results. We compared the awake and nighttime BP outcomes between healthy controls and individuals across the SDB spectrum. This meta-analysis may provide a better understanding of the impact of childhood OSA on elevated BP outcomes.

Several limitations should be taken into consideration. First, we did not assess the relationship between OSA and other cardiovascular-related variables and did not evaluate the effects of other covariates, such as sex, BMI, ethnicity, family history of hypertension, and daytime activities. Previous studies showed that obesity is a risk factor for childhood OSA, while it is also recognized as a contributor to elevated BP [75–78]. It is possible that the relationship between elevated BP and moderate-severe OSA was confounded by obesity. However, we were unable to adjust for these covariates in the meta-regression due to the lack of individual data. A previous study has shown that the responsiveness of BP in black children is significantly higher than that of white children [79]. Moreover, teens with a family history of hypertension are more likely to have essential hypertension [80]. However, none of our included studies reported relevant data on ethnicity, family history, and only one study reported activity levels [28]. Therefore, we cannot rule out the potential moderating effects of these demographic covariates on the current study outcomes. Second, the classification criteria for the severity of OSA may vary between children and adolescents, which may bias the results. In addition, most of the cross-sectional studies in our meta-analysis were focused on the association between OSA and blood pressure in childhood [12,13,28–37], and only one study was conducted in adolescents [13]. Third, the inclusion of primary snoring as controls may underestimate the association between OSA and elevated BP, as our previous study showed that children with primary snoring have elevated BP compared to non-snoring control children [81]. Therefore, we only included healthy non-snoring participants as controls in the main analyses, which may minimize the potential bias. Fourth, the majority of the studies included in the final analyses were cross-sectional studies, which made it difficult to determine the temporal relationship between childhood OSA and elevated BP. More longitudinal studies are needed to ascertain the relationship between childhood OSA and future BP outcomes, especially in adulthood.

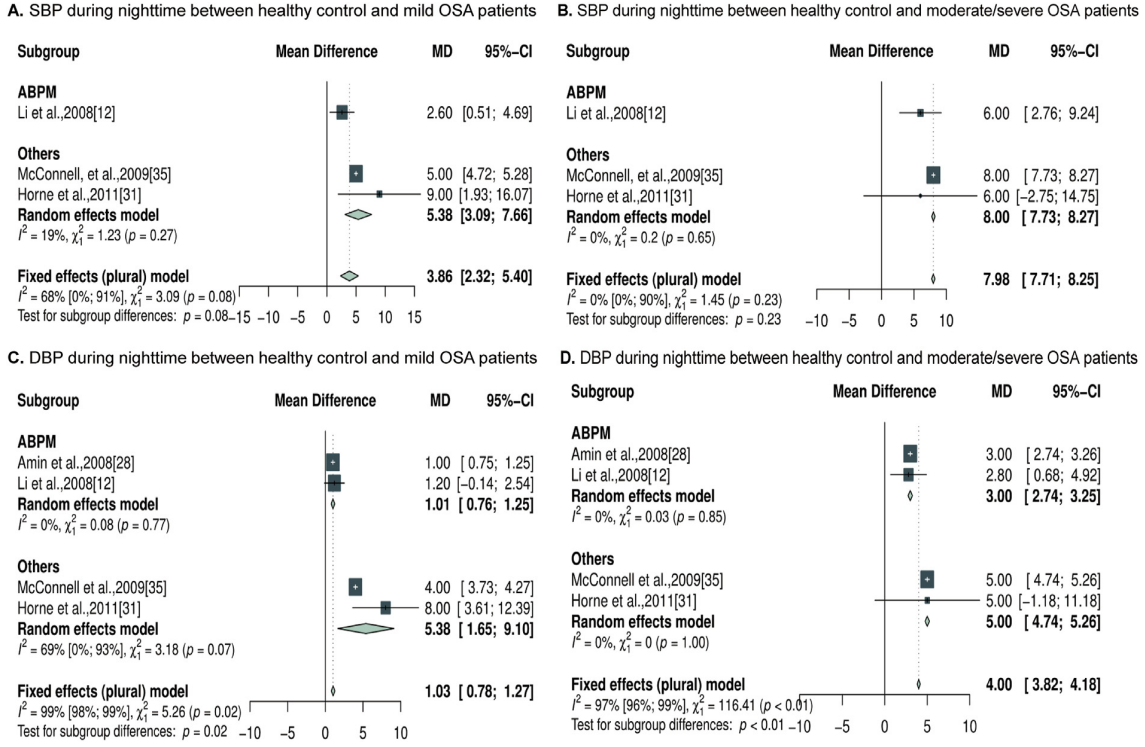

Fig. 6. Subgroup analyses of baseline nighttime blood pressure measurement compared to the healthy control group. A. SBP during the nighttime between healthy control and mild OSA patients. B. SBP during the nighttime between healthy control and moderate/severe OSA patients. C. DBP during the nighttime between healthy control and mild OSA patients. D. DBP during the nighttime between healthy control and moderate/severe OSA patients.

9. Conclusion

Both mild and moderate-to-severe childhood OSA were cross-sectionally associated with elevated SBP outcomes, while meta-analysis of longitudinal studies demonstrated that only moderate-to-severe childhood OSA was associated with a higher risk of elevated SBP in adulthood. Our findings suggest that moderate-to-severe childhood OSA is a risk factor for future adverse SBP outcomes. Early detection and intervention of childhood OSA may reduce future cardiovascular risk.

Practice points

1. Moderate-to-severe childhood obstructive sleep apnea is a consistent risk factor for elevated blood pressure in children and adolescents as well as in their future adulthood.
2. Blood pressure measurement methods may contribute to the high heterogeneity of the analyses.
3. Ambulatory blood pressure monitoring should be preferably used as a standard measurement of blood pressure in children and adolescents with obstructive sleep apnea.

Research agenda

1. Further research should focus more on standardized blood pressure monitoring to reduce the measurement bias.
2. Future longitudinal studies with more large-scale data are needed to better characterize the association between childhood obstructive sleep apnea and future hypertension in adulthood.
3. Future interventional studies of childhood sleep apnea will be needed to determine the reversibility of hypertension risk in adulthood.

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Authors' contributions

Prof. Yun-Kwok Wing, Dr. Kate Ching-ching Chan and Dr. Sizhi Ai conceived the study. Drs. Sijing Chen and Sizhi Ai helped to develop search strategies. Drs. Zhexi Li and Shanshan Wang searched the databases and checked them according to the eligibility criteria and exclusion criteria. Drs. Zhexi Li and Shanshan Wang did the data extraction, and quality assessment. Drs. Sizhi Ai and Zhexi Li analyzed the data. Drs. Jihui Zhang, Joey WY Chan, Kate Ching-ching Chan, Chun Ting Au, Prof. Albert Martin Li, and Prof. Yanping Bao gave substantial advice on meta-analysis methodology and interpretation. Drs. Sizhi Ai and Zhexi Li wrote the initial draft of the paper. All authors contributed to reviewing or revising the paper. Prof. Yun-Kwok Wing and Dr. Kate Chan are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Declaration of competing interest

Prof. Yun-Kwok Wing reported personal fees for delivering a lecture-Eisai Co. Ltd and personal fees from Sponsorship from Lundbeck HK Ltd, outside the submitted work. Joey WY Chan received a personal fee from Eisai. Co., Ltd for joining an expert panel, outside the submitted work. The other authors declared that there is no conflict of interest.

Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.smrv.2022.101663.

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