An umbrella review of systematic reviews and meta-analyses of observational investigations of obstructive sleep apnea and health outcomes

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Abstract

Purpose  The previous analysis of systematic reviews and meta-analyses have illustrated that obstructive sleep apnea (OSA) is correlated with multiple health outcomes. In the present research, our main aim was to execute an umbrella review to assess the available evidence for the associations between OSA and health outcomes.

Methods  Herein, a meta-analysis of previous observational investigations that have reported associations between OSA and health outcomes in all human populations and settings was performed. We used these studies to execute an umbrella review of available meta-analyses and systematic reviews.

Results  Sixty-six articles comprising 136 unique outcomes were enrolled in this analysis. Of the 136 unique outcomes, 111 unique outcomes had significant associations \((p < 0.05)\). Only 7 outcomes (coronary revascularization after PCI, postoperative respiratory failure, steatosis, alaninetransaminase (ALT) elevation, metabolic syndrome (MS), psoriasis, and Parkinson's disease) had a high quality of evidence. Twenty-four outcomes had a moderate quality of evidence, and the remaining 80 outcomes had a weak quality of evidence. Sixty-nine outcomes exhibited significant heterogeneity. Twenty-five outcomes exhibited publication bias. Sixty-three (95%) studies showed critically low methodological quality.

Conclusion  Among the 66 meta-analyses exploring 136 unique outcomes, only 7 statistically significant outcomes were rated as high quality of evidence. OSA may correlate with an increased risk of coronary revascularization after PCI, postoperative respiratory failure, steatosis, ALT elevation, MS, psoriasis, and Parkinson’s disease.

Keywords  Obstructive sleep apnea · Health · Umbrella review · Meta-analysis

Introduction

Obstructive sleep apnea (OSA) is a prevalent but treatable chronic sleep disorder that is determined through episodes of sleep apnea and hypopnea during sleep and results in recurrent episodes of hypercapnia and hypoxemia [1–3]. OSA has a prevalence of between 5 and 20% depending on the population surveyed and the definition utilized [4, 5]. The prevalence is also increasing due to an increase in body mass index which is one of its major predisposing factors. Apart from causing uncomfortable symptoms such as headache [6] and attention deficit [7], earlier studies indicated that OSA also contributed to the advancement of several diseases including hypertension [8], cardiovascular disease [9, 10], and diabetes [11]. Recent studies have drawn consistent conclusions [12–14]. Recently, a great number of researches have explored the correlation between OSA and other diseases. Multiple investigations and meta-analyses have illustrated that OSA poses a threat to human health because it increases the risk of various diseases, including cancers [15–17], depression [18], laryngopharyngeal reflux disease [19], metabolic disease [20], Parkinson’s disease [21], and chronic kidney disease (CKD) [22].

These studies suggest a possible causal relationship between OSA and different health outcomes, indicating that OSA has a bad influence on human health. However, several factors are known to decrease the validity and strength...
of reported evidence including publication bias, protocol design flaws, or inconsistencies of studies. Currently, there have been no systematic reviews that have accurately summarized and critically appraised existing studies. In the current study, an umbrella review was executed to comprehensively evaluate published systematic reviews and meta-analyses of observational researches that reported associations between OSA and health information. This work can provide important guidance in the diagnosis and treatment of OSA.

Materials and methods

The protocol of the research was registered with PROSPERO (registration number: CRD42020220015) before the umbrella review began. A systematic exploration of the literature search was accomplished in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocols [23].

Literature search

From initiation until November 23, 2020, literature searches were performed using online databases such as Embase, PubMed, the Cochrane Database of Systematic Reviews, and the Web of Science. Literature searches were independently conducted by two researchers (CZ and LG). The search terms applied were (“obstructive sleep apnea” OR “obstructive sleep apnea–hypopnea” OR “OSA” OR “OSAH”) AND (Meta-Analysis[ptyp] OR metaanaly*[tiab] OR metaanaly*[tiab] OR Systematic review [ptyp] OR “systematic review”[tiab]). The references were manually screened to identify eligible articles to be included in the study. The article titles, abstracts, and the complete manuscripts of the identified paper were then further assessed. A discussion was used to resolve potential discrepancies; ST acted as an arbiter to deal with discrepancies that could not be resolved by discussion among the investigators.

Eligibility criteria and exclusion criteria

The eligibility of articles was based on a systematic search by the authors to identify the most pertinent studies. Only systematic reviews or meta-analyses on the basis of the epidemiological studies performed in humans were considered in the analysis. Diagnostic trials and meta-analyses of interventional trials were not performed as part of the current study. Furthermore, the abstracts of the conference on review questions were not included in the final analysis. The final systematic reviews and meta-analyses that were analyzed had to include the data of pooled summary effects (i.e., relative risks (RRs); odds ratios (ORs); hazard ratios (HRs); mean difference (MD); weighted mean difference (WMD); standard mean difference (SMD); and their 95% confidence intervals (CIs)), number of included researches, number of participants and cases, heterogeneity, and publication bias. Whenever more than one meta-analysis was executed using on the basis of the same outcome, the agreement with the main conclusions reported in the study were verified. When the reported conclusions were conflicting, the meta-analysis with the greatest number of investigations was considered.

Data extraction

For investigations to be eligible for inclusion in the meta-analysis, two researchers (WC and YL) independently extracted data from the articles. This included the first author, the number of included investigations, the year of publication, the study design, the whole numbers of cases, and participants. The reported relative summary risk evaluates (ORs, RRs, HRs, SMD, WMD, or MD) and the corresponding 95% CIs were extracted, for each eligible systematic review and meta-analysis. The values of $p$ for the total pooled effects, Cochran $Q$ measurement, Egger’s measurement, and $I^2$ were extracted. Discrepancies in the analyses were resolved by discussion among the investigators.

Assessment of methodological quality

Two investigators (WC and YL) independently assessed the quality of the methods reported in the studies. This was performed using a 16-criteria checklist included in AMSTAR 2 [24]. AMSTAR 2 is a fundamental revision of the original instrument of AMSTAR which was devised to evaluate systematic reviews that included randomized controlled experiments. The AMSTAR 2 score is categorized as high in studies that have no or one noncritical weakness, moderate in surveys with more than one noncritical weakness, low when the study has only one serious flaw without or with noncritical weaknesses, and seriously low when a study has more than one serious flaw without or with nonserious weaknesses. Discrepancies between the AMSTARS 2 scores for the articles were resolved by discussion between the investigators.

Assessment of the evidence quality

Two investigators (WC and YL) independently evaluated the quality of the evidence conforming to the parameters that have previously been applied in various fields [25–28]. Discrepancies were resolved by discussion. First, $p$ value...
for the estimate < 0.001 \([29, 30]\) and more than 1000 cases of the disease, which indicated fewer false-positive results. Second, \(I^2 < 50\%\) and \(p\) value for Cochran \(Q\) test > 0.10, which indicated consistency of results. Third, \(p\) value for Egger’s test > 0.10, which exhibited no evidence of small-study impacts. When all of the above criteria were satisfied, the strength of the epidemiologic evidence was rated as high. When 1 of the criterion was not satisfied and the \(p\) value for the estimate was < 0.001, the strength of the epidemiologic evidence was rated as moderate. Then, the rest was defined as weak (\(p < 0.05\)). The value of \(p\) for the evaluation can be assessed from the 95% confidence interval of the pooled impact estimate utilizing an established method [31] if it was not directly reported in the article.

### Data analysis

From each of the published studies, the outcome data of the available meta-analyses was extracted along with the estimated summary effect at the corresponding 95% CI. The total impacts of the pooled meta-analysis were considered significant when the \(p\)-value was < 0.05. Heterogeneity was appraised by the \(I^2\) test and \(Q\) test, publication bias was estimated by utilizing Egger’s test, and both were considered significant at \(p < 0.1\). Studies that did not have the heterogeneity or publication bias results were reanalyzed if raw data were available.

### Results

#### Characteristics of the meta-analyses

The outcomes of the systematic investigation and the selection of eligible investigations are summarized in Fig. 1. Overall, 1972 articles were searched from which 66 meta-analyses of observational investigations were identified that had 136 unique outcomes [21, 22, 32–95]. The 66 eligible non-overlapping meta-analyses had publication dates ranging from 2009 to 2020 and are summarized in Table 1. The median number of primary investigations per evidence synthesis was 7 (range 2–64). Furthermore, 1 meta-analysis [54] lacked the data of both participants and cases, and 2 meta-analyses [52, 95] lacked the data of cases. Among the meta-analyses identified in this study, the median number of cases was 900 (88–3,117,496) and the median number of participants was 2962 (170–56,746,100). An extensive

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**Fig. 1** Flowchart of the selection procedure
Table 1  Associations between OSA and multiple health outcomes

| Outcomes                               | Publication                                      | Number of studies | Number of participants | Number of cases | Type of metric | Relative risk (95% CI) | P value* | P value# | I² (%) | P value※ | Whether exist publication bias |
|----------------------------------------|--------------------------------------------------|-------------------|------------------------|-----------------|----------------|------------------------|----------|----------|---------|----------|-------------------------------|
| Cardiovascular disorders               |                                                  |                   |                        |                 |                |                        |          |          |         |          |                               |
| Aortic dissection                       | Xiushi Zhou (2018)                                | 1 cohort study, 2 case-control studies | 55,911                | 16,019          | OR             | 1.60 (1.01–2.53)       | 0.04     | 0.44     | 0       | 0.58     | No                             |
| Cardiovascular disease (CVD)           | Xia Wang (2013)                                   | 11 cohort studies | 25,594                 | 2628            | RR             | 1.79 (1.47–2.18)       | <0.001   | 0.131    | 31.5    | 0.028    | Yes                            |
| Stroke                                 | Min Li (2014)                                     | 10 cohort studies | 18,609                 | 678             | RR             | 2.10 (1.50–2.93)       | <0.001   | 0.04     | 47.5    | 0.288    | No                             |
| Ischemic heart disease (IHD)           | Wuxiang Xie (2014)                               | 6 cohort studies  | 1083                   | 625             | RR             | 1.83 (1.15–2.93)       | 0.011    | 0.111    | 44.2    | 0.006    | Yes                            |
| Coronary heart disease (CHD)           | Chengjuan Xie (2017)                             | 17 cohort studies | 26,698                 | 2628            | RR             | 1.63 (1.18–2.26)       | 0.003    | 0.061    | 52.7    | 0.145    | No                             |
| Major adverse cardiac events (MACCEs)  | Chengjuan Xie (2017)                             | 16 cohort studies | 26,698                 | 2628            | RR             | 2.04 (1.56–2.66)       | <0.001   | 0.018    | 55.7    | 0.132    | No                             |
| Atrial fibrillation                    | Irini Youssef (2018)                             | 4 cross-sectional studies, 5 cohort studies | 19,837               | 12,255          | OR             | 2.12 (1.84–2.43)       | <0.001   | 0.004    | 64.4    | 0.097    | Yes                            |
| Resistant hypertension                 | Haifeng Hou (2018)                               | 6 case-control studies | 1465                 | 925             | OR             | 2.84 (1.70–3.98)       | <0.001   | 0.816    | 0       | 0.187    | No                             |
| Essential hypertension                 | Haifeng Hou (2018)                               | 2 case-control studies, 5 cohort studies | 7102                 | 4513            | OR             | 1.80 (1.54–2.06)       | <0.001   | 0.221    | 26      | 0.0526   | Yes                            |
| Atrial fibrillation recurrence after catheter ablation | Chee Yuan Ng (2011)                             | 6 observational studies | 3995                 | 958             | RR             | 1.25 (1.08–1.45)       | 0.003    | 0.008    | 49      | 0.879    | No                             |
| Stroke after PCI                       | Xiao Wang (2018)                                 | 9 observational studies | 2755                 | 1581            | RR             | 1.96 (1.36–2.81)       | <0.001   | 0.02     | 54      | 0.002    | Yes                            |
| Myocardial infarction (MI) after PCI   | Hua Qu (2018)                                    | 6 observational studies | 2342                 | 1112            | OR             | 1.59 (1.14–2.23)       | 0.007    | 0.32     | 15      | 0.655    | No                             |
| Coronary revascularization after PCI   | Hua Qu (2018)                                    | 7 observational studies | 2415                 | 1163            | OR             | 1.57 (1.23–2.01)       | <0.001   | 0.7      | 0       | 0.483    | No                             |
| Re-admission for heart failure after PCI | Hua Qu (2018)                                 | 4 observational studies | 1774                 | 793             | OR             | 1.71 (0.99–2.96)       | 0.06     | 0.86     | 0       | 0.254    | No                             |
| Left ventricular hypertrophy (LVH)     | Cesare Cuspidi (2020)                            | 9 observational studies | 3244                 | 1802            | OR             | 1.70 (1.44–2.00)       | <0.001   | <0.001   | 60      | 0.0876   | Yes                            |
| Left ventricular diastolic diameter (LVEDD) | LetYu (2019)                                | 13 observational studies | 882                  | 563             | WMD            | 1.24 (0.68, 1.80)      | <0.001   | 0.658    | 0       | 0.431    | No                             |
| Left ventricular systolic diameter (LVESD) | LetYu (2019)                                | 11 observational studies | 630                  | 396             | WMD            | 1.14 (0.47, 1.81)      | 0.001    | 0.696    | 0       | 0.722    | No                             |
| Left ventricular mass (LVM)            | LetYu (2019)                                    | 6 observational studies | 432                  | 304             | WMD            | 35.34 (20.67, 50.00)   | <0.001   | <0.001   | 79.1    | 0.914    | No                             |
| Left ventricular ejection fraction (LVEF) | LetYu (2019)                                | 15 observational studies | 1104                 | 710             | WMD            | ~3.01 (~1.90, 0.79)    | 0.001    | <0.001   | 64.7    | 0.048    | Yes                            |
| Left atrial diameter (LAD)             | LetYu (2019)                                    | 7 observational studies | 468                  | 311             | WMD            | 2.13 (1.48, 2.77)      | <0.001   | 0.408    | 2.2     | 0.072    | Yes                            |
| Left atrial diameter volume index (LAVI) | LetYu (2019)                                | 3 observational studies | 228                  | 159             | WMD            | 3.96 (3.32, 4.61)      | <0.001   | 0.445    | 0       | 0.735    | No                             |
| Right ventricular internal diameter (RVID) | Abdirashit Margiev (2017)           | 16 observational studies | 1498                 | 902             | WMD            | 2.49 (1.62, 3.37)      | <0.001   | <0.001   | 96.8    | 0.001    | Yes                            |
| Outcomes                                      | Publication                                 | Number of studies | Number of participants | Number of cases | Type of metric | Relative risk (95% CI) | $P$ value* | $P$ value# | $I^2$ (%) | $P$ value※ | Whether exist publication bias |
|----------------------------------------------|--------------------------------------------|-------------------|------------------------|-----------------|----------------|------------------------|------------|------------|-----------|-----------|-----------------------------|
| Right ventricular free wall thickness (RVWT) | Abdirashit Maripov (2017)                  | 9 observational studies | 976                    | 579             | WMD            | 0.82 (0.51, 1.33)     | <0.001     | <0.001     | 95.6      | 0.671     | No                                         |
| Right ventricular myocardial performance index (RV MPI) | Abdirashit Maripov (2017)                  | 14 observational studies | 1298                  | 864             | WMD            | 0.08 (0.06, 0.10)     | <0.001     | <0.001     | 84.1      | 0.15      | No                                         |
| Tricuspid annular systolic velocity (RV S' ) | Abdirashit Maripov (2017)                  | 14 observational studies | 1030                  | 639             | WMD            | −0.95 (−0.32, −1.59)  | 0.003      | <0.001     | 88.4      | 0.347     | No                                         |
| Tricuspid annular plane systolic excursion (TAPSE) | Abdirashit Maripov (2017)                  | 11 observational studies | 1033                  | 655             | WMD            | −1.76 (−0.78, −2.73)  | <0.001     | <0.001     | 89.3      | 0.462     | No                                         |
| Right ventricular fractional area change (RA FAC) | Abdirashit Maripov (2017)                  | 6 observational studies | 661                   | 422             | WMD            | −3.16 (−0.73, −5.60)  | 0.011      | <0.001     | 80.2      | 0.006     | Yes                                        |
| Epicardial adipose tissue (EAT) thickness   | Guang Song (2020)                          | 9 observational studies | 1178                  | 898             | WMD            | 0.95 (0.73, 1.16)     | <0.001     | <0.001     | 64.7      | 0.549     | No                                         |
| Coronary flow reserve (CFR)                 | Rui-Heng Zhang (2020)                      | 1 case-control study, 4 cross-sectional studies | 1336                  | 829             | WMD            | −0.78 (−0.32, −1.25)  | <0.001     | <0.001     | 84.4      | 0.49      | No                                         |
| Systolic blood pressure (SBP)               | De-Lei Kong (2016)                         | 2 cross-sectional studies, 3 cohort studies, 1 case-control studies | 1046                  | 534             | SMD            | 0.56 (0.40, 0.71)     | <0.001     | 0.132      | 41.03     | NA        | NA                                         |
| Cerebral and cerebrovascular disease        |                                           |                   |                        |                 |                |                        |            |            |          |           |                |
| Cerebral white matter changes               | Bo-Lin Ho (2018)                           | 10 observational studies | 1582                  | 818             | OR             | 2.06 (1.52–2.80)     | <0.001     | 0.025      | 48.5      | 0.338     | No                                         |
| Cerebrovascular (CV) disease                | Zhenhong Wu (2018)                         | 15 cohort studies   | 3,120,368             | 3,117,496       | HR             | 1.94 (1.31–2.89)     | 0.001      | <0.001     | 90.3      | > 0.05    | No                                         |
| White matter hyperintensities (WMH)         | Yuhong Huang (2019)                        | 11 cross-sectional studies, 2 case-control studies | 4412                  | 2065            | OR             | 2.23 (1.53–3.25)     | <0.001     | <0.001     | 80.3      | < 0.01   | Yes                                        |
| Silent brain infarction (SBI)               | Yuhong Huang (2019)                        | 9 cross-sectional studies, 2 case-control studies, 1 cohort study | 3353                  | 1893            | OR             | 1.54 (1.06–2.23)     | 0.023      | 0.018      | 52        | 0.605     | No                                         |
| Cerebral microbleeds (CMBs)                 | Yuhong Huang (2019)                        | 3 cross-sectional studies | 342                   | 271             | OR             | 2.17 (0.61–7.73)     | 0.234      | <0.01      | 60.2      | NA        | Unclear                                    |
| Perivascular spaces (PVS)                   | Yuhong Huang (2019)                        | 2 cross-sectional studies | 267                   | 152             | OR             | 1.56 (0.28–8.57)     | 0.623      | <0.01      | 69.5      | NA        | NA                                         |
| Asymptomatic lacunar infarction (ALI)       | Anthipa-Chokoesou-Tansakul (2019)          | 6 cross-sectional studies, 1 cohort study | 1756                  | 713             | OR             | 1.78 (1.06–3.08)     | 0.03       | 0.128g    | 41        | 0.43      | No                                         |
| Mortality                                   |                                           |                   |                        |                 |                |                        |            |            |          |           |                |
| All-cause mortality                         | Lei Pan (2016)                             | 12 cohort studies  | 34,382                 | 18,139          | HR             | 1.26 (1.09–1.43)     | 0.001      | <0.001     | 70.4      | 0.003     | Yes                                        |
| Outcomes                                      | Publication                        | Number of studies | Number of participants | Number of cases | Type of metric | Relative risk (95% CI) | P value* | P value# | I² (%) | P value※ | Whether exist publication bias |
|-----------------------------------------------|------------------------------------|-------------------|------------------------|-----------------|----------------|------------------------|----------|---------|--------|---------|-------------------------------|
| Cardiovascular mortality                      | Xiahui Ge (2013)                   | 4 cohort studies  | 5228                   | 239             | RR             | 2.21 (1.61–3.04)       | < 0.001  | 0.418   | 0      | 0.448   | No                            |
| All-cause death after PCI                     | Xiao Wang (2018)                   | 4 cohort studies  | 1919                   | 1154            | RR             | 1.70 (1.05–2.77)       | 0.03     | 0.71    | 0      | 0.176   | No                            |
| Cardiac death after PCI                       | Hao Qin (2018)                     | 7 cohort studies  | 2465                   | 1187            | OR             | 2.05 (1.15–3.65)       | 0.01     | 0.96    | 0      | 0.826   | No                            |
| Cancer mortality                              | Xiaobin Zhang (2017)               | 3 cohort studies  | 7346                   | 179             | HR             | 1.38 (0.79–2.41)       | 0.257    | 0.004   | 66.1   | 0.205   | No                            |
| Postoperative complications                   |                                    |                   |                        |                 |                |                        |          |         |        |         |                               |
| Postoperative respiratory failure             | Faizi Hai BA (2013)                | 12 cohort studies | 5611                   | 2390            | OR             | 2.42 (1.53–3.84)       | < 0.001  | 0.39    | 5      | 0.28    | No                            |
| Postoperative cardiac events                  | Faizi Hai BA (2013)                | 11 cohort studies | 3781                   | 2109            | OR             | 1.63 (1.16–2.29)       | 0.005    | 0.7     | 0      | 0.187   | No                            |
| Postoperative desaturation                    | R. Kaw (2012)                      | 11 cohort studies | 3645                   | 1764            | OR             | 2.27 (1.20–4.26)       | 0.01     | < 0.001 | 68     | 0.04    | Yes                           |
| Postoperative ICU transfer                    | R. Kaw (2012)                      | 9 cohort studies  | 5743                   | 2062            | OR             | 2.81 (1.46–5.45)       | 0.002    | 0.02    | 57     | 0.033   | Yes                           |
| Postoperative composite endpoints of postoperative cardiac or cerebrovascular complications | Ka Ting Ng (2020)                  | 12 observational studies | 2,003,694              | 126027          | OR             | 1.44 (1.17–1.78)       | < 0.001  | NA      | 89     | NA      | Unclear                       |
| Postoperative myocardial infarction           | Ka Ting Ng (2020)                  | 8 observational studies | 714,650               | NA              | OR             | 1.37 (1.19–1.59)       | < 0.001  | NA      | 36     | NA      | Unclear                       |
| Postoperative congestive cardiac failure      | Ka Ting Ng (2020)                  | 3 observational studies | 2104                  | NA              | OR             | 3.16 (1.02–9.81)       | 0.05     | NA      | 0      | NA      | Unclear                       |
| Postoperative atrial fibrillation             | Ka Ting Ng (2020)                  | 6 observational studies | 1,463,449              | NA              | OR             | 1.50 (1.30–1.73)       | < 0.001  | NA      | 87     | NA      | Unclear                       |
| Postoperative cerebrovascular accident        | Ka Ting Ng (2020)                  | 5 observational studies | 1,641,495              | NA              | OR             | 1.09 (0.75–1.60)       | 0.65     | NA      | 61     | NA      | Unclear                       |
| Postoperative composite endpoints of pulmonary complications | Ka Ting Ng (2020)                  | 8 observational studies | 1,983,748              | NA              | OR             | 2.52 (1.92–3.31)       | < 0.001  | NA      | 96     | NA      | Unclear                       |
| Postoperative pneumonia                      | Ka Ting Ng (2020)                  | 10 observational studies | 2,675,205              | NA              | OR             | 1.66 (1.17–2.35)       | 0.004    | NA      | 96     | NA      | Unclear                       |
| Postoperative reintubation                    | Ka Ting Ng (2020)                  | 9 observational studies | 2,061,288              | NA              | OR             | 2.29 (0.90–5.82)       | 0.08     | NA      | 99     | NA      | Unclear                       |
| Postoperative in-hospital mortality           | Ka Ting Ng (2020)                  | 6 observational studies | 2,497,794              | NA              | OR             | 0.86 (0.42–1.36)       | 0.68     | NA      | 94     | NA      | Unclear                       |
| Postoperative 30-day mortality               | Ka Ting Ng (2020)                  | 6 observational studies | 661,754                | NA              | OR             | 1.27 (1.03–1.57)       | 0.02     | NA      | 0      | NA      | Unclear                       |
| Postoperative acute kidney injury            | Ka Ting Ng (2020)                  | 5 observational studies | 1,724,922              | NA              | OR             | 2.41 (1.93–3.02)       | < 0.001  | NA      | 92     | NA      | Unclear                       |
| Postoperative delirium                       | Ka Ting Ng (2020)                  | 6 observational studies | 2346                  | NA              | OR             | 2.45 (1.59–4.08)       | < 0.001  | NA      | 2      | NA      | Unclear                       |
| Postoperative venoembolism                   | Ka Ting Ng (2020)                  | 10 observational studies | 2,100,013              | NA              | OR             | 1.63 (1.17–2.27)       | 0.004    | NA      | 94     | NA      | Unclear                       |
| Postoperative surgical site infection         | Ka Ting Ng (2020)                  | 5 observational studies | 2962                   | NA              | OR             | 1.30 (0.93–1.83)       | 0.13     | NA      | 0      | NA      | Unclear                       |
| Outcomes                                      | Publication                        | Number of studies | Number of participants | Number of cases | Type of metric | Relative risk (95% CI) | P value* | P value# | I² (%) | P value※ | Whether exist publication bias |
|----------------------------------------------|------------------------------------|-------------------|------------------------|-----------------|----------------|------------------------|----------|----------|--------|----------|-----------------------------|
| Postoperative bleeding                       | Ka Ting Ng (2020)                  | 3 observational   | 18.712                 | NA              | OR             | 1.10 (0.40–3.01)     | 0.85     | NA       | 63     | NA       | Unclear                     |
| Postoperative length of hospital stay        | Ka Ting Ng (2020)                  | 15 observational  | 1.569,278              | NA              | MD             | 0.09 (0.00–0.17)     | 0.04     | NA       | 96     | NA       | Unclear                     |
| Pregnancy-related disorders                  | Xing Zhang (2020)                  | 6 cohort studies  | 2,532,547              | 139,559         | RR             | 1.60 (1.21–2.12)     | 0.004    | 0.003    | 69.2   | 0.4829   | No                          |
| Gestational diabetes mellitus (GDM)         | Lina Liu (2019)                    | 3 observational   | NA                     | NA              | OR             | 1.42 (1.12–1.79)     | < 0.001  | < 0.001  | 86.5   | NA       | Unclear                     |
| C-section                                    | Lina Liu (2019)                    | 3 observational   | NA                     | NA              | OR             | 1.94 (0.88–4.28)     | 0.1      | < 0.001  | 98.6   | NA       | Unclear                     |
| Pregnancy-related prolonged hospital stay    | Lina Liu (2019)                    | 3 observational   | NA                     | NA              | OR             | 1.87 (1.56–2.24)     | < 0.001  | 0.883    | 0      | NA       | Unclear                     |
| Pregnancy-related wound complication         | Lina Liu (2019)                    | 3 observational   | NA                     | NA              | OR             | 6.35 (4.25–9.50)     | < 0.001  | 0.294    | 18.2   | NA       | Unclear                     |
| Small for gestational age                    | Lina Liu (2019)                    | 4 observational   | NA                     | NA              | OR             | 1.26 (0.80–2.01)     | 0.321    | 0.01     | 73.8   | NA       | Unclear                     |
| Stillbirth                                   | Lina Liu (2019)                    | 3 observational   | NA                     | NA              | OR             | 1.12 (0.85–1.49)     | 0.413    | 0.572    | 0      | NA       | Unclear                     |
| Poor fetal growth                           | Lina Liu (2019)                    | 4 observational   | NA                     | NA              | OR             | 1.15 (0.98–1.34)     | 0.091    | 0.266    | 24.3   | NA       | Unclear                     |
| Gestational hypertension                    | Liwen Li (2018)                    | 4 cross-sectional | 56,731,077             | 19,047           | OR             | 1.80 (1.28–2.52)     | 0.001    | 0.72     | 0      | 0.649    | No                          |
| Preclampsia                                  | Liwen Li (2018)                    | 2 cross-sectional | 56,097,993             | 19,776           | OR             | 2.63 (1.87–3.30)     | < 0.001  | < 0.01   | 78     | 0.797    | No                          |
| Preterm birth                                | Liwen Li (2018)                    | 2 cross-sectional | 56,746,100             | 18,337           | OR             | 1.75 (1.21–2.55)     | 0.003    | < 0.01   | 90     | 0.931    | No                          |
| Birth weight                                 | Liwen Li (2018)                    | 4 cohort studies  | 4311                   | 1387             | WMD            | −47.46 (−242.09, 147.16) | 0.281    | < 0.01   | 93     | NA       | No                          |
| Neonatal intensive care unit (NICU) admission| Ting Xu (2014)                     | 4 cohort studies  | 757                    | 177              | RR             | 2.65 (1.86–3.76)     | < 0.001  | 0.235    | 29.6   | 0.061    | Yes                         |
| Ophthalmologic disorders                     |                                    |                   |                        |                 |                |                       |          |          |        |          |                |
| Diabetic retinopathy (DR)                    | Zhenliu Zhu (2017)                 | 6 case-control     | 1092                   | 608              | OR             | 2.01 (1.49–2.72)     | < 0.001  | 0.062    | 52.4   | 0.112    | No                          |
| Keratoconus                                  | Marco Pellegriti (2020)            | 4 case-control     | 33,844                 | 16,922           | OR             | 1.84 (1.16–2.91)     | 0.009    | 0.003    | 74.6   | 0.07     | Yes                         |
| Glaucoma                                     | Xinhuo Wu (2015)                   | 12 observational   | 36,909                 | 11,765           | OR             | 1.65 (1.44–1.88)     | < 0.001  | 0.06     | 43     | 0.335    | No                          |
| Floppy eyelid syndrome (FES)                 | Lab-Kang Huo (2016)                | 7 cross-sectional  | 902                    | 337              | OR             | 4.70 (2.98–7.41)     | < 0.001  | 0.129    | 39.3   | 0.379    | No                          |
| Nonarteritic anterior ischemic optic neuropathy (NAION) | Yong Wu (2015) | 4 cohort studies, 1 case-control study | 5916 | 164 | OR | 6.18 (2.00–19.11) | 0.002 | 0.002 | 77 | 0.35 | No |
| Central serous choroidopathy (CSCR)          | Chris Y Wu (2018)                  | 6 case-control     | 7238                   | 1479             | OR             | 1.56 (1.16–2.10)     | 0.003    | 0.237    | 26.3   | 0.281    | No                          |

*Relative risk (95% CI): Estimate of the risk of the outcome associated with exposure to the factor of interest relative to the risk of the outcome for non-exposed individuals.

#P value: Statistical significance of the relative risk estimate.

※I² (%): Proportion of variance due to heterogeneity across studies.

PO: Whether exist publication bias.

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| Outcomes                                      | Publication                                | Number of studies | Number of participants | Number of cases | Type of metric | Relative risk (95% CI) | P value* | P value# | I² (%) | P value※ | Whether exist publication bias |
|-----------------------------------------------|-------------------------------------------|-------------------|------------------------|-----------------|---------------|------------------------|----------|----------|--------|----------|-----------------------------|
| Retinal nerve fiber layer (RNFL) thickness    | Cheng-Lin Sun (2016)                      | 8 case-control studies | 1237                  | 763             | WMD           | −2.92 (−4.61, −1.24)   | 0.001    | 0.017    | 59.1   | 0.929    | No                          |
| Choroidal thickness                          | Chris Y. Wu (2018)                        | 9 case-control studies | 778                   | 514             | WMD           | 25.52 (−78.79, −27.76) | 0.824    | 0.001    | 98.6   | 0.137    | No                          |
| Digestive disorders                          |                                          |                   |                        |                 |               |                        |          |          |        |          |                |
| Gastroesophageal reflux disease              | Zong-Hong Wu (2019)                       | 1 case-control study, 6 cross-sectional studies | 2699           | 1452           | OR            | 1.75 (1.18–2.59)      | 0.006    | 0.04     | 54     | 0.052    | Yes                         |
| Steatosis                                    | Shanshan Jin (2018)                       | 3 cohort studies, 1 cross-sectional study          | 1635           | 1375           | OR            | 3.19 (2.34–4.34)      | <0.001   | 0.677    | 0      | 0.89     | No                          |
| Lobular inflammation                        | Shanshan Jin (2018)                       | 3 cohort studies                         | 350            | 205            | OR            | 2.85 (1.8–4.49)       | <0.001   | 0.994    | 0      | 0.469    | No                          |
| Ballooning degeneration                      | Shanshan Jin (2018)                       | 3 cohort studies                         | 350            | 205            | OR            | 2.29 (1.36–3.84)      | 0.002    | 0.774    | 0      | 0.888    | No                          |
| NAFLD activity score (NAS)                   | Shanshan Jin (2018)                       | 3 cohort studies                         | 350            | 205            | OR            | 1.63 (0.68–3.86)      | 0.271    | 0.259    | 25.9   | 0.839    | No                          |
| NAFLD defined by liver histology             | G. Musso (2013)                           | 8 cross-sectional studies                 | 994            | 537            | OR            | 2.01 (1.36–2.97)      | <0.001   | 0.4      | 4      | 0.303<sup>6</sup> | No                          |
| NAFLD defined by radiology                   | G. Musso (2013)                           | 6 cross-sectional studies                 | 561            | 269            | OR            | 2.99 (1.79–4.49)      | <0.001   | 0.33     | 13     | 0.433<sup>6</sup> | No                          |
| NAFLD defined by AST elevation               | G. Musso (2013)                           | 11 cross-sectional studies                | 746            | 368            | OR            | 2.36 (1.46–3.82)      | <0.001   | 0.99     | 0      | 0.65<sup>6</sup> | No                          |
| NAFLD defined by ALT elevation               | G. Musso (2013)                           | 14 cross-sectional studies                | 1833           | 938            | OR            | 2.60 (1.88–3.61)      | <0.001   | 0.74     | 0      | 0.179<sup>6</sup> | No                          |
| Nonalcoholic steatohepatitis (NASH)          | G. Musso (2013)                           | 10 cross-sectional studies                | 1114           | 589            | OR            | 2.37 (1.59–3.51)      | <0.001   | 0.81     | 0      | 0.404<sup>6</sup> | No                          |
| Fibrosis                                     | G. Musso (2013)                           | 10 cross-sectional studies                | 1114           | 589            | OR            | 2.16 (1.45–3.20)      | <0.001   | 0.67     | 0      | 0.778<sup>6</sup> | No                          |
| Alanine transaminase (ALT)                   | Shanshan Jin (2018)                       | 7 cohort studies, 1 cross-sectional study    | 2059           | 1684           | SMD           | 0.21 (0.11, 0.31)     | <0.001   | 0.672    | 0      | 0.468    | No                          |
| Aspartate transaminase (AST)                 | Shanshan Jin (2018)                       | 7 cohort studies, 1 cross-sectional study    | 2059           | 1684           | SMD           | 0.07 (−0.03, 0.17)    | 0.152    | 0.918    | 0      | <0.05    | Yes                         |
| Endocrine and metabolic system disorders     |                                          |                   |                        |                 |               |                        |          |          |        |          |                |
| Type 2 diabetes (T2DM)                       | Ranran Qie (2020)                         | 16 cohort studies                   | 338,912        | 19,355         | RR            | 1.40 (1.32–1.48)      | <0.001   | 0.045    | 40.8   | 0.221<sup>6</sup> | No                          |
| Metabolic syndrome (MS)                      | Shaoyong Xu (2015)                        | 15 cross-sectional studies              | 4161           | 2457           | OR            | 2.87 (2.41–3.42)      | <0.001   | 0.23     | 20     | 0.232    | No                          |
| Fasting blood glucose (FBG)                  | De-Lei Kong (2016)                        | 3 cross-sectional studies, 5 cohort studies, 2 case-control studies | 2053           | 1296           | SMD           | 0.35 (0.18, 0.53)     | <0.001   | 0.008    | 59.6   | NA       | No<sup>5</sup>                 |
| Total cholesterol (TC)                       | Rashid Nadeem (2014)                      | 63 observational studies               | 18,111         | NA             | SMD           | 0.267 (0.146, 0.389)   | 0.001    | NA       | NA     | NA       | No<sup>5</sup>                 |
| Outcomes                                      | Publication                  | Number of studies | Number of participants | Number of cases | Type of metric | Relative risk (95% CI) | P value* | P value# | P value※ | I² (%) | Whether exist publication bias |
|-----------------------------------------------|------------------------------|-------------------|------------------------|-----------------|----------------|------------------------|----------|----------|----------|--------|-------------------------------|
| Low-density lipoprotein (LDL)                 | Rashid Nadeem (2014)        | 50 observational  | 13,894                 | NA              | SMD            | 0.296 (0.156, 0.436)   | 0.001    | NA       | NA       | No     |                               |
| High-density lipoprotein (HDL)                | Rashid Nadeem (2014)        | 64 observational  | 18,116                 | NA              | SMD            | −0.433 (−0.604, −0.262) | < 0.001  | NA       | NA       | No     |                               |
| Triglyceride (TG)                             | Rashid Nadeem (2014)        | 62 observational  | 17,831                 | NA              | SMD            | 0.603 (0.431, 0.775)   | < 0.001  | NA       | NA       | No     |                               |
| Adiponectin                                   | Li (2019)                   | 20 case-control   | 1356                   | 878             | SMD            | −0.71 (−0.92, −0.49)   | < 0.001  | < 0.01   | 73       | 0.09   | Yes                           |
| Oxidized low-density lipoprotein (Ox-LDL)     | Fadaei (2020)               | 8 case-control    | 623                    | 391             | SMD            | 0.95 (0.24, 1.67)      | 0.009    | < 0.001  | 94.1     | < 0.16 | No                            |
| Total cholesterol (TC)                        | Rashid Nadeem (2014)        | 62 observational  | 17,831                 | NA              | SMD            | 0.603 (0.431, 0.775)   | < 0.001  | NA       | NA       | No     |                               |
| Triglyceride (TG)                             | Rashid Nadeem (2014)        | 62 observational  | 17,831                 | NA              | SMD            | 0.603 (0.431, 0.775)   | < 0.001  | NA       | NA       | No     |                               |
| | | | | | | | | | | | | |
| Urological disorders                          |                             |                   |                        |                 |                |                        |          |          |          |        |                               |
| Diabetic kidney disease (DKD)                 | Bun Leong (2016)            | 7 cross-sectional | 1877                   | 1159            | OR             | 1.59 (1.16–2.18)       | 0.004    | 0.224※  | 26.8     | 0.684※ | No                            |
| Microalbuminuria                              | Liu (2020)                  | 4 cross-sectional | 667                    | 415             | RR             | 2.32 (1.48–3.62)       | < 0.001  | 0.578    | 0.55     | No     |                               |
| Chronic kidney disease (CKD)                  | Der-Hwa Hsu (2017)          | 16 cross-sectional | 7090                   | 3720            | OR             | 1.77 (1.37–2.29)       | < 0.001  | < 0.001※ 87.2※ 0.011※        | Yes     | 0.011※  | No                            |
| Serum uric acid level                         | Shi (2019)                  | 14 observational  | 5219                   | 2656            | WMD            | 50.25 (36.36–64.33)    | < 0.001  | < 0.001  | 91.2     | 0.001  | Yes                           |
| Serum cystatin C                              | Liu (2020)                  | 7 cross-sectional | 1412                   | 234             | SMD            | 0.53 (0.42,0.64)       | < 0.001  | 0.16     | 33.7     | 0.111  | No                            |
| Estimated glomerular filtration rate (GFR)    | Liu (2020)                  | 13 cross-sectional | 3344                   | 657             | SMD            | −0.19 (−0.27, −0.12)   | 0.001    | 0.057    | 33.1     | 0.516  | No                            |
| Albumin/creatinine ratio (ACR)                | Liu (2020)                  | 3 cross-sectional | 740                    | 88              | WMD            | 0.71 (0.58,0.84)       | < 0.001  | 0.003    | 69.2     | 0.574  | No                            |
| Outcomes                          | Publication                        | Number of studies | Number of participants | Number of cases | Type of metric | Relative risk (95% CI) | P value* | P value# | I² (%) | P value※ | Whether exist publication bias |
|----------------------------------|------------------------------------|-------------------|------------------------|-----------------|----------------|-----------------------|----------|----------|--------|----------|-----------------------------|
| **Diabetic neuropathy**          | Xiandong Gu (2018)                 | 11 case-control studies | 1842                  | 840              | OR             | 1.84 (1.18-2.87)      | 0.007    | <0.01   | 68.6   | 0.13     | No                          |
| **Psoriasis**                    | Tzong-Yun Ger (2020)               | 3 cohort studies  | 5,544,674              | 42,656           | RR             | 2.52 (1.89-3.36)      | <0.001   | 0.95     | 0      | 0.545    | No                          |
| **Nocturia**                     | Jiatong Zhou (2019)                | 3 cohort studies, 8 case-control studies, 2 cross-sectional studies | 9924              | 406              | RR             | 1.41 (1.26-1.59)      | <0.001   | 0.001    | 63.3   | 0.076    | Yes                         |
| **Allergic rhinitis**            | Yuan Cao (2018)                    | 1 cross-sectional study, 2 case-control studies, 1 cohort study | 1283              | 371              | OR             | 1.73 (0.94-3.20)      | 0.078    | 0.023    | 64.8   | 0.977    | No                          |
| **Parkinson's disease**          | A-Ping Sun (2020)                  | 4 cohort studies, 1 case-control study | 83,449             | 26,070           | HR             | 1.59 (1.36-1.85)      | <0.001   | 0.17     | 40     | 0.186    | No                          |
| **Erectile dysfunction**         | Luhao Liu (2015)                   | 1 cohort study, 3 case-control studies, 1 cross-sectional study | 834                | 532              | RR             | 1.82 (1.12-2.97)      | 0.016    | 0.002    | 76.5   | 0.077    | Yes                         |
| **Female sexual dysfunction**    | Luhao Liu (2015)                   | 2 case-control studies, 2 cohort studies | 438               | 149              | RR             | 2.01 (1.29-3.08)      | 0.002    | 0.194    | 36.4   | 0.327    | No                          |
| **Sexual dysfunction**           | Luhao Liu (2015)                   | 3 cohort studies, 5 case-control studies, 1 cross-sectional study | 1272              | 681              | RR             | 1.87 (1.35-2.58)      | <0.001   | 0.001    | 70.1   | 0.692    | No                          |
| **Osteoporosis**                 | Sikarin Upala (2016)               | 2 cohort studies, 2 cross-sectional studies | 113,922            | 3441             | OR             | 1.13 (0.60-2.14)      | 0.703    | <0.001   | 89.1   | 0.608★   | No                          |
| **Gout**                         | Tingting Shi (2019)                | 3 cohort studies  | 154,455               | 30,109           | HR             | 1.25 (0.91-1.70)      | 0.162    | <0.001   | 91     | 0.876    | No                          |
| **Cancer incidence**             | Ghanshyam Palamaner Shubh Shan- tha (2015) | 5 cohort studies | 112,226              | 904              | RR             | 1.40 (1.01-1.95)      | 0.04     | 0.04     | 60     | 0.069    | Yes                         |
| **Depression**                   | Cass Edwards (2020)                | 5 cohort studies  | 45,056                | 10,983           | RR             | 2.18 (1.47-2.88)      | <0.001   | 0.005    | 72.8   | 0.669★   | No                          |
| **Crash risk**                   | Stephen Tregear (2009)             | 10 observational studies | 10,846             | 214              | RR             | 2.43 (1.21-4.89)      | 0.013    | <0.001   | 89     | 0.838★   | No                          |
| **Work accidents**               | Sergio Garbarino (2016)            | 7 cross-sectional studies | 8819              | 2738             | OR             | 2.38 (1.53-3.10)      | <0.001   | 0.02     | 61     | 0.61     | No                          |
| **Carotid intima-media thickness (CIMT)** | Min Zhou (2016) | 10 case-control studies, 8 case-control studies | 1896              | 1247             | SMD            | 0.88 (0.65, 1.12)     | <0.001   | <0.001   | 81     | 0.94     | No                          |

* p value of significance level
# p value for Q test
★ p value for Egger’s test
The publication bias was assessed using funnel plot
The result was reanalyzed
range of data were reported such as cardiovascular disorders \((n = 31)\), cerebral and cerebrovascular disease \((n = 7)\), mortality \((n = 5)\), postoperative complications \((n = 20)\), pregnancy-related disorders \((n = 13)\), ophthalmic disorders \((n = 8)\), digestive disorders \((n = 13)\), endocrine and metabolic system disorders \((n = 17)\), urological disorders \((n = 7)\), and other data \((n = 15)\) (Fig. 2).

**Summary effect size**

A brief explanation of the effects of the included meta-analysis is given in Table 1. Overall, 111 (82%) of the 136 data reported significant summary outcomes \((p < 0.05)\). These associations relate to the outcomes of the following different systems: 29 meta-analyses in cardiovascular disorders, 5 in cerebral and cerebrovascular disease, 4 in mortality, 14 in postoperative complications, 8 in pregnancy-related disorders, 7 in ophthalmic disorders, 11 in digestive disorders, 14 in endocrine and metabolic system, 7 in urological disorders, and 12 in other outcomes. Therefore, it can be concluded that OSA can enhance the risk of disease and have adverse effects on human health.

**Heterogeneity and publication bias**

For heterogeneity, 5 results in 5 articles were reanalyzed owing to that they did not exhibit the outcomes of heterogeneity \([22, 36, 46, 59, 64]\). Among the 136 outcomes including the reanalyzed articles, 47 outcomes showed no heterogeneity between researches \((p \geq 0.1 \text{ of } Q \text{ test})\), whereas 69 indicated significant heterogeneity \((p < 0.1 \text{ of } Q \text{ test})\). However, there were still 20 results in 2 articles that could not be reanalyzed due to the lack of raw data \([52, 95]\), so we could not evaluate their heterogeneity. For publication bias, 76 outcomes demonstrated no statistical evidence on publication bias \((p \geq 0.1 \text{ of } \text{Egger’s test})\), whereas 25 outcomes presented publication bias \((p < 0.1 \text{ of } \text{Egger’s test})\). There were still 35 results in 9 articles that could not be reanalyzed due to the lack of raw data \([45, 52, 54, 55, 87, 92–95]\), so we could not evaluate their publication bias.

**AMSTAR 2 and summary of evidence**

The results for the evaluation of the methodological qualities of the 66 included articles are shown in Table 2. Only 3 (5%) studies were determined to be low; the remaining 63 (95%) studies were determined to be critically low (Fig. 3). Based on the AMSTAR 2 criteria, none of the investigations were graded as moderate or high quality.

The outcomes of the evidence measurement are shown in Table 3. When a study did not present the result of heterogeneity and publication bias, the corresponding criteria were considered to be not satisfied. Among the 111 statistically significant outcomes, 7 (6%) showed high epidemiologic evidence, 24 (22%) showed moderate epidemiologic evidence, and the remaining 80 (72%) were rated as weak (Fig. 4).

**Discussion**

In the current umbrella review, we identified 66 meta-analyses of observational studies and evaluated the current evidence supporting an association between OSA and various health outcomes. Also, we provide an extensive overview of the available evidence and critically evaluate the methodological quality of the meta-analyses and the quality of evidence for all the reported associations. OSA increased the risk of 111 health outcomes, including

![Map of achievements related to OSA](image-url)
### Table 2 Assessments of AMSTAR 2 scores

| Reference                  | AMSTAR 2 checklist |
|----------------------------|--------------------|
|                            | No. 1 | No. 2 | No. 3 | No. 4 | No. 5 | No. 6 | No. 7 | No. 8 | No. 9 | No. 10 | No. 11 | No. 12 | No. 13 | No. 14 | No. 15 | No. 16 | Overall assessment quality |
| Xiushi Zhou (2018)         | Yes    | No    | Yes   | Partial yes | No   | No   | Partial yes | Partial yes | Yes   | No    | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    | Critically low |
| Xia Wang (2013)            | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Partial yes | Yes    | Yes    | No    | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    | Yes    | Critically low |
| Min Li (2014)              | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Partial yes | Yes    | No    | Yes   | No    | No    | No    | No    | No    | No    | No    | Critically low |
| Wuxiang Xie (2014)         | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | No | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Chengjuan Xie (2017)       | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Irini Youssef (2018)       | Yes    | No    | No    | Partial yes | No   | No   | Yes | No | Yes | No | Yes | No | No | No | No | No | No | No | Critically low |
| Haifeng Hou (2018)         | Yes    | Yes   | Partial yes | Yes | Yes | Yes | Yes | No | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Chee Yuan Ng (2011)        | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Xiao Wang (2018)           | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Hua Qu (2018)              | Yes    | No    | Yes   | Partial yes | Yes  | Partial yes | Yes | No | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Cesare Cuspidi (2020)      | Yes    | No    | No    | Partial yes | Yes  | Partial yes | Yes | No | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Bo-Lin Ho (2018)           | Yes    | No    | No    | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Zesheng Wu (2018)          | Yes    | No    | Yes   | Partial yes | Yes  | Partial yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Yuhong Huang (2019)        | Yes    | No    | Yes   | Partial yes | Yes  | Partial yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Anthipa Chokesuvattanaskul (2019) | Yes | No | Yes | Partial yes | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Lei Pan (2016)             | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Xiaohui Ge (2013)          | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Xiaobin Zhang (2017)       | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Faizi Hai BA (2013)        | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| R. Kaw (2012)              | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Ka Ting Ng (2020)          | Yes    | Yes   | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Xinge Zhang (2020)         | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Lina Liu (2019)            | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Liwen Li (2018)            | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Ting Xu (2014)             | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Marco Pellegrini (2020)    | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Xinhuaw Wu (2015)          | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Leh-Kiong Huon (2016)      | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Yong Wu (2015)             | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Chris Y. Wu (2018)         | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Ranran Que (2020)          | Yes    | No    | Yes   | Partial yes | No   | No   | Yes | No | Yes | No | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Xiandong Gu (2018)         | Yes    | No    | Yes   | Partial yes | No   | No   | Yes | No | Yes | No | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Wen Bun Leong (2016)       | Yes    | Yes   | Yes   | Yes | Yes | Yes | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Low |
| Zhenliu Zhu (2017)         | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically low |
| Zeng-Hong Wu (2019)        | Yes    | No    | Yes   | Partial yes | Yes  | Yes  | Yes | No | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Critically低 |

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| Reference                                   | AMSTAR 2 checklist | Overall assessment quality |
|--------------------------------------------|--------------------|----------------------------|
| Shanshan Jin (2018)                        | Yes No No Partial yes Yes Yes Partial yes Yes No No Yes Yes Yes Yes Yes Yes Yes Critically low |
| G. Musso (2013)                            | Yes No Yes Partial yes Yes Yes Partial yes Partial yes Yes No No Yes Yes Yes Yes Yes Yes Critically low |
| Twong-Yun Ger (2020)                       | Yes Yes Yes Partial yes Yes Yes Partial yes Partial yes Yes No No Yes Yes Yes Yes Yes Yes Critically low |
| Jiatong Zhou (2019)                        | Yes No Yes Partial yes Yes Yes Partial yes Partial yes No No Yes No Yes Yes Yes Yes Yes Yes Critically low |
| Yuan Cao (2018)                            | Yes No Yes Partial yes Yes Yes Partial yes Yes No No No No Yes Yes Yes Yes Yes Yes Critically low |
| A-Ping Sun (2020)                          | Yes No Yes Partial yes Yes Yes Partial yes Partial yes No No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Luhao Liu (2015)                           | Yes No Yes Partial yes Yes Yes No Yes No No No No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Sikarin Upala (2016)                       | Yes Yes Yes Partial yes Yes Yes Partial yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Low |
| Tingting Shi (2019)                        | Yes No Yes Partial yes Yes Yes Partial yes Yes No Yes No No No No Yes Yes Yes Yes Yes Yes Critically low |
| Tongtong Liu (2020)                        | Yes No Yes Partial yes Yes Yes Partial yes Yes No No No No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Tzong-Yun Ger (2020)                       | Yes No No Partial yes Yes Yes Partial yes Partial yes No No Yes No Yes Yes Yes Yes Yes Yes Critically low |
| Yuan Cao (2018)                            | Yes No Yes Partial yes Yes Yes Partial yes Yes No No No No Yes Yes Yes Yes Yes Yes Critically low |
| A-Ping Sun (2020)                          | Yes No Yes Partial yes Yes Yes Partial yes Partial yes No No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Luhao Liu (2015)                           | Yes No Yes Partial yes Yes Yes No Yes No No No No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Sikarin Upala (2016)                       | Yes Yes Yes Partial yes Yes Yes Partial yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Low |
| Tingting Shi (2019)                        | Yes No Yes Partial yes Yes Yes Partial yes Yes No Yes No No No No Yes Yes Yes Yes Yes Yes Critically low |
| Tongtong Liu (2020)                        | Yes No Yes Partial yes Yes Yes Partial yes Yes No No No No Yes Yes Yes Yes Yes Yes Yes Critically low |
| De-Wei Hwu (2017)                          | Yes Yes Yes Partial yes Yes Yes Partial yes Yes Yes Yes No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Ghanshyam Palamane Subash Shantha (2015)   | Yes No No Partial yes Yes Yes Partial yes Partial yes No No Yes No Yes Yes Yes Yes Yes Yes Critically low |
| Shao Yong Xu (2015)                        | Yes No Yes Partial yes Yes Yes Partial yes Yes No Yes Yes Yes Yes Yes Yes Yes Yes Yes Critically low |
| Cass Edwards (2020)                        | Yes No Yes Partial yes Yes Yes Partial yes Yes No Yes Yes Yes Yes Yes Yes Yes Yes Yes Critically low |
| Stephen Tregear (2009)                     | Yes No No Yes Yes Yes Partial yes Partial yes No No Yes No Yes Yes Yes Yes Yes Yes Critically low |
| Sergio Garbarino (2016)                    | Yes No Yes Partial yes Yes Yes Partial yes Partial yes Yes No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Cheng-Lin Sun (2016)                       | Yes No Yes Partial yes Yes Yes Partial yes Yes No No Yes Yes Yes Yes Yes Yes Yes Yes Critically low |
| Min Zhou (2016)                            | Yes No Yes Partial yes Yes Yes Partial yes Partial yes Yes No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Guang Song (2020)                          | Yes No Yes Partial yes Yes Yes Partial yes Partial yes No No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Lei Yu (2019)                              | Yes No No Partial yes Yes Yes Partial yes Partial yes No No Yes No No Yes Yes Yes Yes Yes Yes Critically low |
| Abdirashid Maripov (2017)                  | Yes No No Partial yes Yes Yes Partial yes Partial yes No No Yes No No Yes Yes Yes Yes Yes Yes Critically low |
| Rui-Heng Zhang (2020)                      | Yes No No Partial yes Yes Yes Partial yes Yes No No Yes No No Yes Yes Yes Yes Yes Yes Critically low |
| De-Lei Kong (2016)                         | Yes No Yes Partial yes Yes Yes Partial yes Partial yes Yes No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Rashid Nadeem (2014)                       | Yes No Yes Partial yes Yes Yes Partial yes No No Yes Yes Yes Yes Yes Yes Yes Yes Yes Yes Critically low |
| Mi Lu (2019)                               | Yes No Yes Partial yes Yes Yes Partial yes Partial yes Yes No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Reza Fadaei (2020)                         | Yes No No Partial yes Yes Yes Partial yes Partial yes No No Yes No No Yes Yes Yes Yes Yes Yes Critically low |
| Fang Lu (2019)                             | Yes No Yes Partial yes Yes Yes Partial yes Partial yes Yes No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Kun Li (2017)                              | Yes No No Partial yes Yes Yes Partial yes Partial yes Yes No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Xingyu Wu (2018)                           | Yes No No Partial yes Yes Yes Partial yes Partial yes No No Yes No No Yes Yes Yes Yes Yes Yes Critically low |
| Ze-Ning Jin (2016)                         | Yes No No Partial yes Yes Yes Partial yes Yes No No No No Yes Yes Yes Yes Yes Yes Yes Critically low |
| Xiao Yan Li (2020)                         | Yes Yes Yes Partial yes Yes Yes Partial yes Partial yes Yes No Yes Yes Yes Yes Yes Yes Yes Low |
cardiovascular disorders, cerebral and cerebrovascular disease, mortality, postoperative complications, pregnancy-related disorders, ophthalmic disorders, digestive disorders, endocrine and metabolic system disorders, urological disorders, and other outcomes. The evidence quality was graded as high only for coronary revascularization after PCI, postoperative respiratory failure, steatosis, ALT elevation, MS, psoriasis, and Parkinson’s disease. The evidence quality was either moderate or low for the other associations. Furthermore, this umbrella review showed there were no considerable associations between OSA and 25 health outcomes.

Among the 111 outcomes, 54 outcomes had serious heterogeneity between studies. These possible confounding parameters (e.g., sex, body mass index, age, method of assessing OSA, OSA severity, smoking, alcohol drinking, the region of study, and follow-up period) may be the cause of heterogeneity. Substantial heterogeneity led to unreliable results. Of the 111 health outcomes, 23 outcomes possessed a remarkable publication bias, demonstrating that some negative achievements were not presented. Several reasons were leading to publication bias. First, when people start a study, they tend to assume that a positive result may ensure their work complies with the hypothesis during publication. Second, positive results have a higher probability of being published compared to negative results. Third, the study population is only a small fraction of the actual population with the disease. According to AMSTAR 2 criteria, 95% of the studies included in this umbrella analysis had “critically low” methodological quality. The critical flaws considered the absence of a registered protocol, the absence of the risk of bias in the considered investigations, and the absence of consideration of the risk of bias in the included investigations when interpreting or discussing the achieved outcomes of each study. Moreover, none of the meta-analyses in this study explained details of the funding source that had supported the work. The majority of the evaluated meta-analyses had considerable heterogeneity and small-study impacts; these were the main reasons for the evidence rating downgrade.

An umbrella review is a more beneficial method compared to a normal systematic review or meta-analysis due to it representing an overall illustration of achievements for phenomena or special questions [96]. To our knowledge, we are the first to use this method to present a comprehensive critical literature appraisal on published associations between OSA and diverse health information. Also, our two authors systematically searched four scientific databases using a strong search strategy with clearly defined eligibility criteria and data extraction parameters. The quality of included systematic reviews was also evaluated through AMSTAR 2. This is a benchmark methodological quality measurement that is utilized to assessing the quality of the methods utilized for meta-analyses. Furthermore, we graded the epidemiologic evidence conforming to established, prespecified criteria. Its criteria included an assessment of heterogeneity, publication bias, and precision of the estimate, which is more objective than the GRADE system criteria.

There are some limitations in our umbrella review. First, in this analysis, we explained associations evaluated through the meta-analyses of observational investigations. In doing so, we may have missed other health outcomes that have not yet been investigated by meta-analyses. Second, this umbrella analysis included systematic reviews and meta-analyses that were only published in English. The potential missing information in other languages could influence the assessment outcomes. Third, the majority of the meta-analyses had heterogeneity; observational researches are susceptible to uncertainty and confounding bias.

Conclusions

The associations between OSA and an extensive range of health information have been broadly reported in many meta-analyses. Based on our umbrella review, 66 meta-analyses explored 136 unique outcomes, only 7 outcomes showed a high level of epidemiologic evidence with statistical significance. OSA could be associated with the enhanced risk of coronary revascularization after PCI, postoperative respiratory failure, steatosis,
Table 3  Detail of results for evidence quality assessing

| Outcomes                              | Reference                          | Precision of the estimate | Consistency of results | No evidence of small-study effects | Grade |
|---------------------------------------|------------------------------------|---------------------------|------------------------|------------------------------------|-------|
|                                       |                                    |                           |                        |                                    |       |
|                                       | Grade                              |                           |                        |                                    |       |
|                                       |                                    |                           |                        |                                    |       |
| Cardiovascular disorders              |                                    |                           |                        |                                    |       |
| Aortic dissection                     | Xiushi Zhou (2018)                 | Yes                       | No                     | Yes                                | Weak  |
| Cardiovascular disease (CVD)          | Xia Wang (2013)                    | Yes                       | Yes                    | Yes                                | Moderate |
| Stroke                                | Min Li (2014)                      | No                        | Yes                    | No                                 | Weak  |
| Ischemic heart disease (IHD)          | Wuxiang Xie (2014)                 | No                        | No                     | Yes                                | Weak  |
| Coronary heart disease (CHD)          | Chengjian Xie (2017)               | Yes                       | No                     | No                                 | Weak  |
| Major adverse cardiac events (MACEs)  | Chengjian Xie (2017)               | Yes                       | Yes                    | No                                 | Weak  |
| Atrial fibrillation                   | Irini Youssef (2018)               | Yes                       | Yes                    | No                                 | Weak  |
| Resistant hypertension                | Haifeng Hou (2018)                 | No                        | Yes                    | Yes                                | Moderate |
| Essential hypertension                | Haifeng Hou (2018)                 | Yes                       | Yes                    | Yes                                | Moderate |
| Atrial fibrillation recurrence after catheter ablation | Chee Yuan Ng (2011) | No | No | No | Weak |
| Major adverse cardiovascular event (MACE) after PCI | Xiao Wang (2018) | Yes | Yes | No | Weak |
| Myocardial infarction(MI) after PCI   | Hua Qu (2018)                      | Yes                       | No                     | Yes                                | Weak  |
| Coronary revascularization after PCI  | Hua Qu (2018)                      | Yes                       | Yes                    | Yes                                | Weak  |
| Left ventricular hypertrophy (LVH)    | Cesare Cuspidi (2020)              | Yes                       | No                     | No                                 | Weak  |
| Left ventricular diastolic diameter (LVEDD) | LeiYu (2019)                     | No                        | Yes                    | Yes                                | Moderate |
| Left ventricular systolic diameter (LVESD) | LeiYu (2019)                     | No                        | No                     | Yes                                | Weak  |
| Left ventricular mass (LVM)           | LeiYu (2019)                       | No                        | Yes                    | No                                 | Weak  |
| Left ventricular ejection fraction (LVEF) | LeiYu (2019)                     | No                        | No                     | No                                 | Weak  |
| Left atrial diameter (LAD)            | LeiYu (2019)                       | No                        | Yes                    | Yes                                | Weak  |
| Left atrial diameter volume index (LAVI) | LeiYu (2019)                   | No                        | Yes                    | Yes                                | Weak  |
| Right ventricular internal diameter (RVID) | Abdirashit Maripov (2017)                | No                        | Yes                    | No                                 | Weak  |
| Right ventricular free wall thickness (RVWT) | Abdirashit Maripov (2017)                | No                        | Yes                    | No                                 | Weak  |
| Right ventricular myocardial performance index (RV MPI) | Abdirashit Maripov (2017)                | No                        | Yes                    | No                                 | Weak  |
| Tricuspid annular systolic velocity (RV S') | Abdirashit Maripov (2017)                | No                        | No                     | No                                 | Weak  |
| Tricuspid annular plane systolic excursion (TAPSE) | Abdirashit Maripov (2017)                | No                        | Yes                    | No                                 | Weak  |
| Right ventricular fractional area change (RA FAC) | Abdirashit Maripov (2017)                | No                        | No                     | No                                 | Weak  |
| Epicardial adipose tissue (EAT) thickness | Guang Song (2020)                  | No                        | Yes                    | No                                 | Weak  |
| Coronary flow reserve (CFR)           | Rui-Heng Zhang (2020)              | No                        | Yes                    | No                                 | Weak  |
| Systolic blood pressure (SBP)         | De-Lei Kong (2016)                 | No                        | Yes                    | No                                 | Weak  |
| Cerebral and cerebrovascular disease  |                                    |                           |                        |                                    |       |
| Cerebral white matter changes         | Bo-Lin Ho (2018)                   | No                        | Yes                    | No                                 | Weak  |
| Cerebrovascular (CV) disease          | Zesheng Wu (2018)                  | Yes                       | No                     | No                                 | Weak  |
| White matter hyperintensities (WMH)   | Yuhong Huang (2019)                | Yes                       | Yes                    | No                                 | Weak  |
| Silent brain infarction (SBI)         | Yuhong Huang (2019)                | Yes                       | No                     | Yes                                | Weak  |
| Outcomes                                                                 | Reference                                      | Precision of the estimate | Consistency of results | No evidence of small-study effects | Grade   |
|--------------------------------------------------------------------------|-----------------------------------------------|----------------------------|------------------------|-----------------------------------|---------|
| Asymptomatic lacunar infarction (ALI)                                    | Anthipa Chokesuwattanaskul (2019)             | No                         | No                     | Yes                               | Weak    |
| Mortality                                                               |                                               |                            |                        |                                   |         |
| All-cause mortality                                                      | Lei Pan (2016)                                | Yes                        | No                     | Yes                               | Weak    |
| Cardiovascular mortality                                                | Xiaohui Ge (2013)                             | No                         | Yes                    | Yes                               | Moderate|
| All-cause death after PCI                                               | Xiao Wang (2018)                              | Yes                        | No                     | Yes                               | Weak    |
| Cardiac death after PCI                                                 | Hua Qu (2018)                                 | Yes                        | No                     | Yes                               | Weak    |
| Postoperative complications                                             |                                               |                            |                        |                                   |         |
| Postoperative respiratory failure                                        | Faizi Hai BA (2013)                           | Yes                        | Yes                    | Yes                               | High    |
| Postoperative cardiac events                                            | Faizi Hai BA (2013)                           | Yes                        | No                     | Yes                               | Weak    |
| Postoperative desaturation                                              | R. Kaw (2012)                                 | Yes                        | No                     | No                                | Weak    |
| Postoperative ICU transfer                                              | R. Kaw (2012)                                 | Yes                        | No                     | No                                | Weak    |
| Postoperative composite endpoints of postoperative cardiac or cerebrovascular complications | Ka Ting Ng (2020)                             | Yes                        | Yes                    | No                                | NA      |
| Postoperative myocardial infarction                                      | Ka Ting Ng (2020)                             | NA                         | Yes                    | Yes                               | NA      |
| Postoperative atrial fibrillation                                       | Ka Ting Ng (2020)                             | NA                         | Yes                    | No                                | NA      |
| Postoperative composite endpoints of pulmonary complications             | Ka Ting Ng (2020)                             | NA                         | Yes                    | No                                | NA      |
| Postoperative pneumonia                                                 | Ka Ting Ng (2020)                             | NA                         | No                     | No                                | NA      |
| Postoperative 30-day mortality                                          | Ka Ting Ng (2020)                             | NA                         | No                     | Yes                               | NA      |
| Postoperative acute kidney injury                                       | Ka Ting Ng (2020)                             | NA                         | Yes                    | No                                | NA      |
| Postoperative delirium                                                  | Ka Ting Ng (2020)                             | NA                         | Yes                    | Yes                               | NA      |
| Postoperative venoembolism                                              | Ka Ting Ng (2020)                             | NA                         | No                     | No                                | NA      |
| Postoperative length of hospital stay (days)                            | Ka Ting Ng (2020)                             | NA                         | No                     | No                                | NA      |
| Pregnancy-related disorders                                             |                                               |                            |                        |                                   |         |
| Gestational diabetes mellitus (GDM)                                     | Xinge Zhang (2020)                            | Yes                        | No                     | No                                | Yes     |
| C-section                                                                | Lina Liu (2019)                               | NA                         | Yes                    | No                                | NA      |
| Pregnancy-related wound complication                                    | Lina Liu (2019)                               | NA                         | Yes                    | Yes                               | NA      |
| Pregnancy-related pulmonary edema                                       | Lina Liu (2019)                               | NA                         | Yes                    | Yes                               | NA      |
| Gestational hypertension                                                | Liwen Li (2018)                               | Yes                        | No                     | Yes                               | Yes     |
| Preeclampsia                                                            | Liwen Li (2018)                               | Yes                        | Yes                    | No                                | Yes     |
| Preterm birth                                                           | Liwen Li (2018)                               | Yes                        | No                     | No                                | Yes     |
| Neonatal intensive care unit (NICU) admission                            | Ting Xu (2014)                                | No                         | Yes                    | No                                | No      |

*Table 3 (continued)*)
Table 3 (continued)

| Outcomes                                           | Reference                      | Precision of the estimate | Consistency of results | No evidence of small-study effects | Grade |
|----------------------------------------------------|--------------------------------|---------------------------|------------------------|------------------------------------|-------|
|                                                    |                                |                           |                        |                                    |       |
| Ophthalmic disorders                               |                                |                           |                        |                                    |       |
| Diabetic retinopathy (DR)                          | Zhenliu Zhu (2017)             | No                        | Yes                    | No                                 | Weak  |
| Keratoconus                                        | Marco Pellegrini (2020)        | Yes                       | No                     | Yes                                | Weak  |
| Glaucoma                                           | Xinhua Wu (2015)               | Yes                       | Yes                    | No                                 | Moderate |
| Floppy eyelid syndrome (FES)                       | Leh-Kiong Huon (2016)          | No                        | Yes                    | Yes                                | Moderate |
| Nonarteritic anterior ischemic optic neuropathy (NAION) | Yong Wu (2015)              | No                        | No                     | No                                 | Weak  |
| Central serous chorioretinopathy (CSCR)           | Chris Y.Wu (2018)             | Yes                       | No                     | Yes                                | Weak  |
| Retinal nerve fiber layer (RNFL) thickness         | Cheng-Lin Sun (2016)          | No                        | No                     | Yes                                | Weak  |
| Digestive disorders                                |                                |                           |                        |                                    |       |
| Gastroesophageal reflux disease                    | Zeng-Hong Wu (2019)           | Yes                       | No                     | No                                 | Weak  |
| Steatosis                                          | Shanshan Jin (2018)           | Yes                       | Yes                    | Yes                                | High  |
| Lobular inflammation                               | Shanshan Jin (2018)           | No                        | Yes                    | Yes                                | Moderate |
| Ballooning degeneration                            | Shanshan Jin (2018)           | No                        | No                     | Yes                                | Weak  |
| NAFLD defined by liver histology                   | G. Musso (2013)               | No                        | Yes                    | Yes                                | Moderate |
| NAFLD defined by radiology                         | G. Musso (2013)               | No                        | Yes                    | Yes                                | Moderate |
| NAFLD defined by AST elevation                     | G. Musso (2013)               | No                        | Yes                    | Yes                                | Moderate |
| NAFLD defined by ALT elevation                     | G. Musso (2013)               | No                        | Yes                    | Yes                                | Moderate |
| Nonalcoholic steatohepatitis (NASH)                | G. Musso (2013)               | No                        | Yes                    | Yes                                | Moderate |
| Fibrosis                                           | G. Musso (2013)               | No                        | Yes                    | Yes                                | Moderate |
| Alanine transaminase (ALT)                         | Shanshan Jin (2018)           | Yes                       | Yes                    | Yes                                | High  |
| Endocrine and metabolic system disorders           |                                |                           |                        |                                    |       |
| Type 2 diabetes (T2DM)                             | Rannan Qie (2020)             | Yes                       | Yes                    | No                                 | Moderate |
| Metabolic syndrome (MS)                            | Shaoyang Xu (2015)            | Yes                       | Yes                    | Yes                                | High  |
| Fasting blood glucose (FBG)                        | De-Lei Kong (2016)            | Yes                       | Yes                    | No                                 | Weak  |
| Total cholesterol (TC)                             | Rashid Nadeem (2014)          | NA                        | No                     | NA                                 | Weak  |
| Low-density lipoprotein (LDL)                      | Rashid Nadeem (2014)          | NA                        | No                     | NA                                 | Weak  |
| High-density lipoprotein (HDL)                     | Rashid Nadeem (2014)          | NA                        | Yes                    | NA                                 | Weak  |
| Triglyceride (TG)                                  | Rashid Nadeem (2014)          | NA                        | Yes                    | NA                                 | Weak  |
| Adiponectin                                        | Mi Lu (2019)                  | No                        | Yes                    | No                                 | Weak  |
| Oxidized low-density lipoprotein (Ox-LDL)          | Reza Fadaei (2020)            | No                        | No                     | No                                 | Weak  |
| Fibrinogen                                         | Fang Lu (2019)                | Yes                       | Yes                    | No                                 | Weak  |
| Homocysteine                                       | Kun Li (2017)                 | No                        | No                     | No                                 | Weak  |
| Advanced glycation end products (AGEs)             | Xingyu Wu (2018)              | No                        | Yes                    | No                                 | Weak  |
| Outcomes                                                      | Reference                                      | Precision of the estimate | Consistency of results | No evidence of small-study effects | Grade |
|---------------------------------------------------------------|-----------------------------------------------|---------------------------|------------------------|-------------------------------------|-------|
| Angiotensin II (AngII)                                        | Ze-Ning Jin (2016)                            | No                        | Yes                    | No                                  | Yes   |
| Serum vitamin D                                               | Xiaoyan Li (2020)                             | Yes                       | Yes                    | No                                  | NA    |
| Urological disorders                                          |                                               |                           |                        |                                     |       |
| Diabetic kidney disease (DKD)                                 | Wen Bun Leong (2016)                          | Yes                       | No                     | Yes                                 | Yes   |
| Microalbuminuria                                              | Tongtong Liu (2020)                           | No                        | Yes                    | Yes                                 | Yes   |
| Chronic kidney disease (CKD)                                  | Der-Wei Hwu (2017)                            | Yes                       | Yes                    | No                                  | No    |
| Serum uric acid level                                        | Tingting Shi (2019)                           | Yes                       | Yes                    | No                                  | No    |
| Serum cystatin C                                              | Tongtong Liu (2020)                           | No                        | Yes                    | Yes                                 | Yes   |
| Estimated glomerular filtration rate (eGFR)                  | Tongtong Liu (2020)                           | No                        | No                     | No                                  | Yes   |
| Albumin/creatinine ratio (ACR)                                | Tongtong Liu (2020)                           | No                        | Yes                    | No                                  | Yes   |
| Other outcomes                                                |                                               |                           |                        |                                     |       |
| Diabetic neuropathy                                           | Xiandong Gu (2018)                            | No                        | No                     | No                                  | Yes   |
| Psoriasis                                                    | Tzong-Yun Ger (2020)                          | Yes                       | Yes                    | Yes                                 | Yes   |
| Nocturia                                                      | Jiatong Zhou (2019)                           | No                        | Yes                    | No                                  | No    |
| Parkinson’s disease                                           | A-Ping Sun (2020)                             | Yes                       | Yes                    | Yes                                 | Yes   |
| Erectile dysfunction                                          | Luhao Liu (2015)                              | No                        | No                     | No                                  | No    |
| Female sexual dysfunction                                    | Luhao Liu (2015)                              | No                        | No                     | Yes                                 | Yes   |
| Sexual dysfunction                                            | Luhao Liu (2015)                              | No                        | No                     | Yes                                 | Yes   |
| Cancer incidence                                              | Ghanshyam Palamaner Subash Shantha (2015)     | No                        | No                     | No                                  | No    |
| Depression                                                    | Cass Edwards (2020)                           | Yes                       | Yes                    | No                                  | Yes   |
| Crash risk                                                    | Stephen Tegear (2009)                         | Yes                       | No                     | No                                  | Yes   |
| Work accidents                                                | Sergio Garbarino (2016)                       | Yes                       | Yes                    | No                                  | Yes   |
| Carotid intima-media thickness (CIMT)                         | Min Zhou (2016)                               | Yes                       | Yes                    | No                                  | Yes   |
ALT elevation, MS, psoriasis, and Parkinson’s disease. Overall, OSA is harmful to human health but will need further exploration on this topic with high-quality prospective studies.

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Data availability The data used to support the findings of this study are included within the article. The primary data used to support the findings of this study are available from the corresponding author upon request.

Declarations

Ethics approval All analyses were based on published studies and no ethical approval was required.

Conflict of interest The authors declare no competing interests.

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