Biomolecules and Biomedicine
ISSN: 2831-0896 (Print) | ISSN: 2831-090X (Online)
Journal Impact Factor® (2024): 2.2
CiteScore® (2024): 5.2
www.biomolbiomed.com | blog.bjbms.org

META-ANALYSIS

Hao et al: SDB and mortality in dialysis

Prognostic impact of sleep-disordered breathing on mortality and cardiovascular events in renal dialysis: A meta-analysis

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DOI: https://doi.org/10.17305/bb.2025.13100

ABSTRACT

Sleep-disordered breathing (SDB) is prevalent among patients undergoing renal dialysis, yet its prognostic implications for mortality and cardiovascular outcomes remain unclear. This meta-analysis investigates the relationship between SDB and all-cause mortality as well as major adverse cardiovascular events (MACEs) within this demographic. A systematic search of PubMed, Embase, and Web of Science was conducted from inception to May 29, 2025, focusing on longitudinal observational studies that assessed SDB in adult dialysis patients. The primary outcome analyzed was all-cause mortality, while the secondary outcome was MACEs. Pooled hazard ratios (HRs) with 95% confidence intervals (CIs) were computed using random-effects models to account for heterogeneity. A total of eleven cohort studies encompassing 656,328 dialysis patients, of which 23,725 had SDB, were included. The results indicated that SDB was significantly associated with an increased risk of all-cause mortality (HR: 1.79, 95% CI: 1.42–2.25; $I^2 = 32\%$; $p < 0.001$). Notably, the association was more pronounced in Asian studies (HR: 2.07) compared to non-Asian studies (HR: 1.35; p for subgroup difference = 0.008) and in studies employing polysomnography or pulse oximetry versus those using ICD codes (HR: 2.57 and 2.00 vs. 1.35; $p = 0.002$). Furthermore, five studies indicated that SDB was linked to an elevated risk of MACEs (HR: 2.68, 95% CI: 1.86–3.85; $I^2 = 0\%$; $p < 0.001$). In conclusion, SDB is associated with heightened mortality and cardiovascular risk in patients on renal dialysis. These findings underscore the necessity for increased awareness and management of SDB in this population. However, further interventional studies are required to ascertain whether systematic screening and treatment can enhance clinical outcomes.

Keywords: Sleep-disordered breathing, hemodialysis, peritoneal dialysis, mortality, meta-analysis.

INTRODUCTION

End-stage renal disease (ESRD) is a growing global health burden, with rising incidence driven by population aging and increasing prevalence of diabetes, hypertension, and other chronic kidney diseases (1, 2). Renal replacement therapy, primarily dialysis or kidney transplantation, is essential for sustaining life in patients with ESRD (3). Dialysis, including hemodialysis (HD) and peritoneal dialysis (PD), effectively removes uremic toxins and excess fluid, corrects electrolyte imbalances, and alleviates symptoms related to renal failure (4). Despite these benefits, patients on dialysis continue to face markedly reduced survival compared with the general population, largely due to cardiovascular disease, infections, and other complications (5, 6). Identifying novel, modifiable predictors of poor prognosis in dialysis patients is therefore crucial to enable earlier intervention and improve outcomes (7).

Sleep-disordered breathing (SDB) encompasses a spectrum of conditions characterized by abnormal respiration during sleep, including obstructive sleep apnea, central sleep apnea, and mixed apnea (8, 9). It is typically diagnosed using objective methods such as polysomnography, portable sleep monitoring, or overnight pulse oximetry, with indices such as the apnea–hypopnea index (AHI) or oxygen desaturation index (ODI) used to define severity (10, 11). Beyond its role in sleep fragmentation and hypoxemia, SDB has been linked to hypertension, obesity, diabetes, and dyslipidemia, all of which are established risk factors for cardiovascular morbidity and mortality (8, 9). These associations highlight the potential for SDB to exacerbate vascular and metabolic burden in vulnerable populations (8, 9). Recent work has also emphasized the systemic vascular implications of SDB, including alterations in retinal microvasculature (12), providing further evidence of its broad impact on cardiovascular health. In dialysis patients, SDB may contribute to adverse outcomes through intermittent hypoxia, sympathetic overactivity, endothelial dysfunction, inflammation, and metabolic disturbances, which can exacerbate cardiovascular disease and accelerate mortality (13, 14). While SDB has been extensively studied in the general population and in non-dialysis chronic kidney disease, evidence in dialysis populations is limited and inconsistent, with individual studies varying in design, sample size, diagnostic criteria, and adjustment for confounding factors (15-25). To clarify these discrepancies and provide a more precise estimate of the prognostic impact of SDB, we performed a meta-analysis of

longitudinal observational studies to evaluate the association between SDB and all-cause mortality in adult patients receiving renal dialysis, with major adverse cardiovascular events (MACEs) as a secondary outcome.

MATERIAL AND METHODS

The study was conducted in accordance with the PRISMA 2020 guidelines (26) and the Cochrane Handbook for Systematic Reviews of Interventions (27), ensuring methodological rigor in study selection, data extraction, statistical analysis, and result interpretation. The protocol was prospectively registered with PROSPERO (ID: CRD420251121897).

Literature search

A comprehensive literature search was performed in PubMed, Embase, and Web of Science, utilizing a broad set of search terms that integrated the following keywords and concepts: (1) "sleep disordered breathing" OR "sleep breathing disorders" OR "sleep apnea syndrome" OR "obstructive sleep apnea" OR "obstructive sleep apnea syndrome" OR "obstructive sleep hypopnea syndrome" OR "OSAHS" OR "OSAS" OR "sleep apnea"; (2) "dialysis" OR "hemodialysis" OR "peritoneal dialysis"; and (3) "mortality" OR "death" OR "deaths" OR "prognosis" OR "survival" OR "adverse events" OR "cardiovascular". The search was limited to human studies and included only full-text articles published in English in peer-reviewed journals. To ensure completeness, we also manually screened the reference lists of relevant original and review articles for additional eligible studies. The search covered all publications from database inception up to May 29, 2025. The detailed search strategy for each database is displayed in **Supplemental File 1**.

Study eligible criteria

We applied the PICOS framework to define the inclusion criteria.

Population (P): Adult patients (≥18 years) undergoing renal dialysis, including HD or PD, regardless of dialysis vintage, sex, or comorbidities.

Intervention/Exposure (I): Presence of SDB, including obstructive sleep apnea, central sleep apnea, or mixed apnea, identified through objective diagnostic methods consistent with the criteria used in the original studies (e.g., polysomnography, home sleep apnea testing, or clinical diagnostic criteria). In addition, validated hypoxemia

indices such as the ODI or average SaO_2 were accepted as objective surrogates for SDB in dialysis populations.

Comparison (C): Patients on renal dialysis without SDB.

Outcomes (O): The primary outcome is all-cause mortality and the secondary outcome is the composite outcome of MACEs, which generally include myocardial infarction, heart failure, stroke, and cardiovascular deaths, compared between patients with and without SDB.

Study Design (S): Observational studies with longitudinal follow-up (prospective or retrospective cohort studies) that report risk estimates (e.g., hazard ratios, relative risks, or odds ratios) for the association between SDB and outcomes of interest.

Studies were excluded if they: (1) did not involve renal dialysis patients; (2) SDB diagnosed solely on patient-reported symptoms or questionnaires; (3) lacked a comparator group without SDB or fail to stratify patients based on SDB status; (4) were cross-sectional, case reports, editorials, reviews, or conference abstracts without full-text data; (5) did not report all-cause mortality or MACEs as outcomes; (6) provided insufficient data to extract or calculate effect estimates with 95% confidence intervals; or (7) were duplicate publications using the same cohort data without additional relevant information. In cases of overlapping populations, only the study with the largest sample size was retained for inclusion in the meta-analysis.

Study quality evaluation

Two reviewers independently conducted the literature search, screened studies, assessed methodological quality, and extracted data. Any discrepancies were resolved through consultation with the corresponding author. The quality of included studies was evaluated using the Newcastle–Ottawa Scale (NOS) (28), which examines study selection, control of confounding variables, and outcome assessment. The NOS assigns scores ranging from 1 to 9, with a score of 7 or above indicating high methodological quality.

Data collection

The data collected for the meta-analysis included study details (author, year, country, and design), patient characteristics (sample size, mean age, sex distribution, and type of dialysis received), exposure details (methods for the diagnosis of SDB, and number

of patients with SDB at baseline), mean follow-up durations, outcomes reported, numbers of patients who died or developed MACEs during follow-up, and covariates adjusted for in the regression models.

Statistical analysis

We used hazard ratios (HRs) and 95% confidence intervals (CIs) to assess the association between SDB and the clinical outcomes of patients on renal dialysis. HRs and their standard errors were either directly extracted or derived from reported 95% confidence intervals or p-values, followed by logarithmic transformation to stabilize variance and achieve a normal distribution (27). If multiple HRs were reported from different models, we used the one with the most complete adjustment. When HRs and 95% CIs were not directly reported, we reconstructed them from published Kaplan–Meier curves using the Parmar/Tierney approach (29). Heterogeneity was assessed using the Cochrane Q test and the I^2 statistic (30), with a p-value < 0.10 indicating significant heterogeneity and I^2 values of < 25%, 25–75%, and > 75% indicating low, moderate, and high heterogeneity, respectively. Random-effects models were applied using the DerSimonian–Laird inverse-variance method in RevMan, which provides pooled estimates incorporating between-study variance (τ^2) (27). To complement the conventional 95% CI, we also calculated 95% prediction intervals (PI), which estimate the expected range of effects in future studies (27). In addition to the DerSimonian–Laird random-effects model, we conducted sensitivity analyses using the Hartung–Knapp–Sidik–Jonkman (HKSJ) method to provide more robust confidence intervals, particularly given the moderate number of included studies (27). To assess the stability of the results, sensitivity analyses were conducted by sequentially excluding each study. For the primary outcome of all-cause mortality, predefined subgroup analyses were conducted based on study country (Asian vs. non-Asian), design (prospective vs. retrospective), type of renal dialysis (HD vs. PD), methods for the diagnosis of SDB, follow-up durations, and study quality scores. Subgroup analyses were stratified using the median values of continuous variables to ensure balanced groupings. Publication bias was evaluated through funnel plot visualization and assessed for asymmetry using Egger's regression test (31). To further evaluate small-study effects, we applied the trim-and-fill method, which estimates the number of potentially missing studies and recalculates the pooled effect after imputing them (31). All analyses were performed using RevMan (Version 5.1;

Cochrane Collaboration, Oxford, UK) and Stata (Version 12.0; Stata Corporation, College Station, TX, USA).

RESULTS

Study inclusion

The study selection process is shown in **Figure 1**. We first identified 848 records from the three databases. Following the removal of 292 duplicate records, 556 articles underwent title and abstract screening. Of these, 527 were excluded for not aligning with the objectives of the meta-analysis. The remaining 29 full-text articles were assessed independently by two reviewers, resulting in the exclusion of 18 studies for specific reasons detailed in **Figure 1**. At last, 11 studies were included in the subsequent analysis (15-25).

Summary of study characteristics

The key characteristics of the 11 studies included in this meta-analysis are presented in **Table 1**. Together, these studies involved 656,328 adult patients receiving renal dialysis. The studies were conducted across diverse geographic regions, including Italy, Korea, Hong Kong (China), Japan, the United Kingdom, the United States, Taiwan (China), and Brazil, and were published between 2002 and 2023. Eight studies used prospective cohort designs (15-20, 22, 23), while three were retrospective (21, 24, 25). Mean participant age ranged from 50.1 to 67.0 years, and the proportion of male patients ranged from 46.1% to 70.0%. Dialysis modalities included HD (16, 18-20, 22, 24, 25), PD (17, 21, 23), or both (15), with the majority focusing on HD (n = 7). Sleep apnea diagnosis was based on objective methods such as polysomnography (16, 17, 19, 20, 22, 23), overnight pulse oximetry (15, 18, 24), or with the International Classification of Disease (ICD) codes and sleep study confirmation (21, 25), with diagnostic criteria varying across studies. Accordingly, a total of 23,725 patients had SDB at baseline. The follow-up durations spanned from 23.2 to 70.0 months. The primary outcome, all-cause mortality, was reported in all studies (15-25), while five studies also assessed MACEs (15, 17, 18, 20, 24). MACEs were defined across studies as composite cardiovascular outcomes, generally including cardiovascular death, myocardial infarction, stroke or transient ischemic attack, heart failure, arrhythmia, peripheral artery disease, and other major thrombotic or revascularization events, with details provided in **Supplemental Table 1.** Most

studies (15-19, 21-25) adjusted for important confounders such as age, sex, comorbidities, and dialysis-related factors with a varying extent, and one study (20) only reported univariate results.

Study quality

Study quality was assessed using the NOS, with scores ranging from 7 to 9, indicating moderate to high methodological quality (**Table 2**). Two studies achieved the maximum score of 9, reflecting strong representativeness, robust exposure and outcome ascertainment, and adequate control for confounding (17, 23). Five studies scored 8 (15, 18, 19, 21, 24), mainly due to limited exposure ascertainment or representativeness of the exposed cohort. The remaining four studies scored 7 (16, 20, 22, 25), primarily owing to incomplete adjustment for confounders or less rigorous exposure assessment. Overall, the included studies demonstrated adequate follow-up durations and reliable outcome measurements, supporting the robustness of the pooled estimates in this meta-analysis.

Association between SDB and all-cause mortality

A total of 11 cohort studies (15-25), including one study with HR and 95% CIs from Kaplan–Meier curves (21), reported the association between SDB and all-cause mortality in patients on renal dialysis. Moderate heterogeneity was observed (p for the Cochrane Q test = 0.14; $I^2 = 32\%$; $\tau^2 = 0.04$). Pooled results from a random-effects model showed that, overall, SDB was associated with a higher risk of all-cause mortality in these patients (HR: 1.79, 95% CI: 1.42–2.25, $p < 0.001$; **Figure 2A**). The 95% PI ranged from 1.06 to 3.02, indicating that most future studies are expected to demonstrate an adverse association. Further meta-analysis using the HKSJ method yielded consistent results (HR: 1.79, 95% CI: 1.32–2.44; **Supplemental Figure 1A**), further supporting the robustness of the association.

Sensitivity analyses were performed by removing one dataset at a time, and the results remained stable (HR: 1.64–2.06, $p < 0.05$ for all comparisons; **Table 3**). Specifically, a sensitivity analysis limited to studies with multivariate analyses at least adjusting for age (15-19, 21-25) showed consistent results (HR: 1.76, 95% CI: 1.39–2.23, $p < 0.001$; $I^2 = 32\%$). In addition, a sensitivity analysis excluding the study by Prabu et al. (25) showed similar results but significantly reduced the heterogeneity (HR: 2.06, 95% CI: 1.60–2.65, $p < 0.001$; $I^2 = 0\%$).

Subsequent subgroup analysis suggested a stronger association between SDB and mortality in patients on dialysis from Asian countries as compared to non-Asian countries (HR: 2.07 vs. 1.35, *p* for subgroup difference = 0.008; **Figure 2B**). The results were not significantly different between prospective and retrospective studies (*p* for subgroup difference = 0.24; **Figure 2C**), or studies including patients on HD or PD (*p* for subgroup difference = 0.93; **Figure 3A**). A stronger association between SDB and mortality was observed in studies with SDB diagnosed with overnight pulse oximetry or polysomnography compared to that using ICD codes (HR: 2.57 and 2.00 vs. 1.35, *p* for subgroup difference = 0.002; **Figure 3B**). Finally, similar results were observed between studies with follow-up duration < or ≥ 45 months (*p* for subgroup difference = 0.52; **Figure 4A**), and between studies with different study quality scores (*p* for subgroup difference = 0.29; **Figure 4B**).

Association between SDB and MACEs

Further meta-analysis of five studies (15, 17, 18, 20, 24) showed that SDB was also associated with a higher risk of MACEs in these patients (HR: 2.68, 95% CI: 1.86–3.85, $p < 0.001$; **Figure 5**) with no significant heterogeneity (*p* for the Cochrane Q test = 0.64; $I^2 = 0\%$; $\tau^2 = 0$). The 95% prediction interval was 1.48–4.84, closely overlapping with the CI and reinforcing the robustness of the findings. Similarly, further meta-analysis with the HKSJ method confirmed the association between SDB and MACEs (HR: 2.68, 95% CI: 1.77–4.06; **Supplemental Figure 1B**). Sensitivity analyses excluding one study at a time did not materially change the results (HR: 2.49–2.88, *p* all < 0.05; **Table 3**). Specifically, sensitivity analysis limited to studies with multivariate analyses (15, 17, 18, 24) also showed consistent results (HR: 2.81, 95% CI: 1.93–4.09, $p < 0.001$; $I^2 = 0\%$).

Publication bias

Funnel plots assessing the association between SDB and clinical outcomes of patients on dialysis are shown in **Figure 6A-B**. For mortality (k = 11), visual inspection of the funnel plot suggested approximate symmetry, although interpretation is limited by the small number of studies (**Figure 6A**). Egger's test did not indicate significant asymmetry (intercept = 0.42, $p = 0.44$). A trim-and-fill analysis did not impute any additional studies, and a selection model yielded results consistent with the primary analysis, suggesting that the observed association was not driven by small-study

effects. For MACEs (k = 5), the funnel plot was not formally tested due to insufficient power, and publication bias was assessed descriptively (**Figure 6B**).

DISCUSSION

This meta-analysis provides compelling evidence that SDB is associated with an increased risk of all-cause mortality and MACEs in patients receiving renal dialysis. The association was consistent in sensitivity analyses restricted to multivariable-adjusted studies, suggesting that the observed relationship is unlikely to be explained solely by confounding. Nevertheless, the included studies varied in the extent of adjustment for covariates, and one study reported only univariate results, which limits the ability to fully confirm independence of effect across all studies. Importantly, the results also revealed that the association was more pronounced in studies from Asian countries and in those using polysomnography or pulse oximetry for diagnosis compared with those relying on administrative coding, underscoring the significance of diagnostic accuracy in estimating risk. These findings suggest that SDB is not merely a coexisting condition in dialysis patients but a clinically relevant risk factor that may contribute to their poor prognosis.

Several pathophysiological and clinical mechanisms may explain the observed association. Intermittent hypoxia, a hallmark of SDB, triggers sympathetic nervous system activation, oxidative stress, systemic inflammation, and endothelial dysfunction, all of which accelerate the progression of cardiovascular disease (32, 33). In patients with ESRD on dialysis, these effects may be compounded by uremia, anemia, chronic inflammation, and fluid overload (34). SDB can exacerbate nocturnal blood pressure surges, impair left ventricular diastolic function, and increase the risk of arrhythmias, further elevating cardiovascular risk (35). Fluid redistribution from the lower extremities to the neck during recumbency may narrow the upper airway, aggravating obstructive events in dialysis patients (36-38). Clinically, SDB often presents with non-specific symptoms such as fatigue and reduced exercise tolerance, which may be overlooked in the dialysis setting, delaying diagnosis and intervention (39).

The subgroup analyses offer additional insights. The stronger association seen in Asian cohorts may reflect differences in craniofacial structure, body composition, prevalence of certain comorbidities, and dialysis practice patterns, all of which can influence both the occurrence and severity of SDB (40, 41). However, the stronger

association between SDB and mortality observed in Asian cohorts requires careful interpretation. The Asian studies included in this meta-analysis were from Korea, Hong Kong, Taiwan, and Japan. While these countries differ in healthcare systems and dialysis delivery, they share some epidemiological and clinical features: dialysis patients often have lower BMI and a higher prevalence of hypertension and diabetes compared with Western counterparts, which may amplify the cardiovascular risks of SDB. Dialysis practice patterns also differ: peritoneal dialysis is more widely used in Asia, and all Asian cohorts in our study comprised PD patients, whereas the non-Asian studies were almost exclusively hemodialysis. This imbalance in dialysis modality likely contributed to the subgroup difference. Moreover, follow-up duration was relatively long in the PD cohorts (41–70 months), which may have increased the likelihood of capturing adverse outcomes. Taken together, these factors—population characteristics, dialysis modality, and follow-up—should be considered when interpreting the regional subgroup findings, and caution is warranted in generalizing the results to all dialysis populations. On the other hand, the more modest association in studies using ICD coding could be due to misclassification, underdiagnosis, or inclusion of milder cases (42). The diagnostic method influenced effect size, with polysomnography and oximetry yielding stronger associations than ICD coding. This likely reflects misclassification or under ascertainment in administrative data, which can dilute true associations. By prioritizing objectively measured SDB as the primary analysis, our findings more accurately capture the prognostic impact of SDB in dialysis populations. In addition, the lack of significant differences between prospective and retrospective studies and between HD and PD populations suggests that the adverse impact of SDB is broadly applicable across dialysis modalities and study designs. Sensitivity analyses excluding the very large Prabu study (25) substantially reduced heterogeneity, indicating that sample size and data source can influence pooled effect estimates, but the direction of the association remained unchanged.

The present study has several notable strengths. First, it represents the most comprehensive and up-to-date synthesis of longitudinal cohort studies examining SDB and prognosis in dialysis patients. Second, the inclusion of only studies with longitudinal follow-up strengthens the temporal relationship between SDB and subsequent adverse outcomes. Third, the analysis incorporated extensive subgroup and sensitivity analyses, which enhance confidence in the stability and

generalizability of the results. Finally, study quality was generally high, with all studies scoring ≥ 7 on the NOS, ensuring reasonable methodological rigor. However, some limitations warrant consideration. There was marked heterogeneity in the methods and criteria used to diagnose SDB across studies, ranging from gold-standard polysomnography to overnight pulse oximetry and administrative coding. Although diagnostic criteria varied somewhat (AHI vs ODI or SaO_2 thresholds), all studies relied on objective measures of disordered breathing or hypoxemia. This variability precluded subgrouping strictly by diagnostic index, but the consistent associations across definitions suggest that the prognostic impact of SDB is robust. Second, dialysis-specific design features varied across studies. Some defined time origin as dialysis initiation, whereas others enrolled patients after variable periods on dialysis, thereby mixing incident and prevalent populations. This inconsistency may contribute to survivor bias and could affect hazard estimates. Because individual participant-level data were not available, we were unable to perform sensitivity analyses restricted to incident dialysis cohorts. Third, although most studies adjusted for major confounders such as age, sex, comorbidities, and dialysis-related factors, residual confounding from unmeasured variables (e.g., SDB severity, treatment adherence, socioeconomic status) is likely. While most studies adjusted for demographic factors and major comorbidities, important variables such as dialysis adequacy (e.g., Kt/V, ultrafiltration), inflammatory status, nutritional indices, and socioeconomic factors were not consistently accounted for. These unmeasured or variably adjusted confounders could bias the observed associations, either attenuating or exaggerating the true effect of SDB on mortality and cardiovascular outcomes. This limitation underscores the need for future prospective studies with more comprehensive adjustment. Fourth, because all included studies were observational, causality cannot be established. Moreover, data on the timing of SDB diagnosis relative to dialysis initiation, the impact of SDB treatment, and cause-specific mortality were limited, precluding more detailed mechanistic exploration. In addition, the MACE definition was not fully standardized across studies, and key analytic details—such as whether only first events were counted or how kidney transplantation was handled (censoring vs competing risk)—were generally not reported. This variability limits interpretability of the pooled secondary outcome and should be considered when applying our findings. Furthermore, although we searched three major databases (PubMed, Embase, Web of Science), Scopus was not included. Given the overlap in

coverage, the risk of missing eligible studies is small but cannot be entirely excluded. Finally, the small number of studies reporting MACEs limited the statistical power to detect heterogeneity or publication bias for this outcome. Although no evidence of publication bias was detected for mortality, the number of included studies was modest, limiting statistical power. Therefore, funnel plot symmetry should be interpreted with caution. For MACEs, with only five studies, publication bias assessment remained descriptive.

From a clinical perspective, the findings highlight the importance of recognizing and addressing SDB as part of the comprehensive care of dialysis patients. Given its high prevalence in this population and its strong association with poor outcomes, routine screening for SDB could allow for earlier identification and intervention. Portable sleep monitoring and validated questionnaires could be integrated into dialysis units to facilitate case finding, followed by confirmatory polysomnography when indicated. Treatment of SDB, particularly obstructive sleep apnea, with continuous positive airway pressure (CPAP) has the potential to improve patient outcomes. Notably, a recent observational study in Japanese dialysis patients with SDB demonstrated that CPAP use was associated with a nearly 50% reduction in all-cause mortality compared with non-use, even after adjustment for age, sex, comorbidities, and AHI (43). These findings suggest that targeted intervention may mitigate some of the excess risk associated with SDB. However, these findings must be interpreted cautiously, as observational designs are subject to residual confounding and cannot establish causality. Pragmatic randomized or stepped-wedge trials are needed to determine whether systematic screening and treatment of SDB truly improve survival and cardiovascular outcomes in this population. Further research should also explore the optimal timing of screening (before versus after dialysis initiation), the role of individualized treatment approaches, and the impact of adherence to CPAP or alternative therapies. Investigating the mechanistic interplay between SDB, fluid status, cardiovascular function, and dialysis parameters could yield valuable insights into patient-specific risk modification strategies.

CONCLUSION

In conclusion, this meta-analysis demonstrates that SDB is associated with increased risks of all-cause mortality and major adverse cardiovascular events in patients receiving dialysis. While causality cannot be inferred from observational evidence,

the consistency of findings suggests that SDB may represent a potentially modifiable risk factor in this vulnerable population. Emerging observational data also indicate that treatment with continuous positive airway pressure could be linked to lower mortality, but randomized trials are needed to confirm this effect. These results support systematic screening for SDB in dialysis units and highlight the need for pragmatic interventional studies, including randomized or stepped-wedge designs, to determine whether early detection and management of SDB can improve patient outcomes.

Conflicts of interest: Authors declare no conflicts of interest.

Funding: Authors received no specific funding for this work.

Data availability: All data generated or analyzed during this study are included in this published article.

Submitted: August 8, 2025

Accepted: September 16, 2025

Published online: October 10, 2025

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TABLES AND FIGURES WITH LEGENDS

Table 1. Characteristics of the included studies

Study	Country	Design	No. of patients	Mean age (years)	Men (%)	Dialysis type	Diagnosis of SDB	No. of patients with SDB	Follow-up duration (months)	Outcomes reported	No. of patients died	No. of patients with MACEs	Variables adjusted
Zoccali 2002	Italy	PC	50	50.1	62	Mixed (HD: 40; PD: 10)	Nocturnal pulse oximetry (average SaO_2 <95%)	9	32	Mortality and MACEs	13	19	Age, cholesterol, LVMI, BP, smoking, dialysis vintage
Jung 2010	Korea	PC	30	55.8	70	HD	PSG (Sleep time SaO2< 90%)	25	48	Mortality	14	NA	Age
Tang 2010	Hong Kong,	PC	93	55.3	51.6	PD	PSG (AHI ≥	51	41	Mortality and	30	53	Age, sex, diabetes,

	China						15)			MACEs			dialysis vintage, residual renal function, minimal nocturnal SaO_2
Masuda 2011	Japan	PC	94	64.4	53.2	HD	Pulse oximetry (3% ODI ≥5 events/hour)	44	55	Mortality and MACEs	25	40	Age, sex, diabetes, serum albumin, cardiothoracic ratio
Sivalingam 2013	UK	PC	91	60.2	66	HD	Limited sleep study (PSG AHI ≥15 + ODI ≥15 or	40	44	Mortality	25	NA	Age, BMI, CRP, cancer status

							ESS >10)						
Kerns 2018	USA	PC	558	56	56	HD	Clinically diagnosed SDB according to medical records involving PSG	66	23.2	Mortality	104	NA	Age, sex, ethnicity, BMI, CCI, atrial fibrillation, left ventricular mass index, and average intradialytic weight change
Huang 2018	Taiwan, China	RC	9987	53.7	46.1	PD	ICD-9 codes sleep study	70	44.6	Mortality	NR	NA	Age, sex, CAD, diabetes, stroke,

							confirmation for OSA						hyperlipidemia, COPD, hypertension, CHF, obesity
Harmon 2018	Brazil	PC	55	50.9	49	HD	PSG (AHI ≥ 5)	40	45	Mortality and MACEs	9	9	None
Kang 2021	Korea	PC	103	56	67	PD	PSG (AHI ≥ 15)	57	70	Mortality	19	NA	Age, sex, BMI, diabetes, CVD, neck/abdominal circumference, fat tissue index, ECW, hemoglob

													in, serum albumin
Mochida 2023	Japan	RC	134	67	64.2	HD	Overnight pulse oximetry (3% ODI)	12	37	Mortality and MACEs	60	71	Age, sex, BMI, HD duration, diabetes, CRP
Prabu 2023	USA	RC	645133	54.3	56.4	HD	ICD-9 codes + sleep study confirmation for OSA	23311	70	Mortality	421474	NA	Age, sex, race, ethnicity, access type, ESRD etiology, tobacco/alcohol use, hypertension, diabetes, heart

													failure, arrhythmias, CVD

Note: Event counts represent first events per patient, where applicable, as reported in the original studies. For Huang 2018, only the peritoneal dialysis (PD) subgroup was used in the analysis. Abbreviations: PC: Prospective cohort; RC: Retrospective cohort; HD: Hemodialysis; PD: Peritoneal dialysis; PSG: Polysomnography; SaO_2: Arterial oxygen saturation; AHI: Apnea-hypopnea index; ODI: Oxygen desaturation index; ESS: Epworth sleepiness scale; MACEs: Major adverse cardiovascular events; LVMI: Left ventricular mass index; BP: Blood pressure; BMI: Body mass index; CRP: C-reactive protein; CCI: Charlson comorbidity index; CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; CHF: Congestive heart failure; CVD: Cardiovascular disease; ECW: Extracellular water; ESRD: End-stage renal disease; NR: Not reported; NA: Not applicable; ICD-9: International classification of diseases, ninth revision.

Table 2. Study quality evaluation via the Newcastle-Ottawa Scale

Cohort Study	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Outcome not present at baseline	Control for age	Control for other confounding factors	Assessment of outcome	Enough long follow-up duration	Adequacy of follow-up of cohorts	Total
Zoccali 2002	1	1	0	1	1	1	1	1	1	8
Jung 2010	1	1	0	1	1	0	1	1	1	7
Tang 2010	1	1	1	1	1	1	1	1	1	9
Masuda 2011	1	1	0	1	1	1	1	1	1	8
Sivalingam 2013	1	1	0	1	1	1	1	1	1	8
Kerns 2018	1	1	0	1	1	1	1	0	1	7
Huang 2018	0	1	1	1	1	1	1	1	1	8
Harmon 2018	1	1	1	1	0	0	1	1	1	7
Kang 2021	1	1	1	1	1	1	1	1	1	9
Mochida 2023	0	1	1	1	1	1	1	1	1	8
Prabu 2023	0	1	0	1	1	1	1	1	1	7

Note: NOS domains were judged as follows:

Representativeness of the exposed cohort: prospective, consecutive, or random enrollment (all studies recruited consecutive or incident dialysis patients).

Selection of the non-exposed cohort: contemporaneous dialysis patients without SDB drawn from the same base population.

Ascertainment of exposure: all studies used objective diagnostic methods (polysomnography, overnight oximetry, or validated ICD codes confirmed by sleep studies), yes if diagnostic criteria clearly stated.

Outcome not present at baseline: studies excluded patients with prior cardiovascular outcomes when analyzing incident events

Control for age: all multivariable models included age.

Control for other confounding factors: most studies additionally adjusted for sex, diabetes, BMI, cardiovascular comorbidity, or dialysis vintage.

Assessment of outcome: outcomes were obtained from adjudicated medical records, registry linkage, or standardized criteria.

Sufficient follow-up duration: all had ≥24 months of median/mean follow-up (range ~32–70 months).

Adequacy of follow-up of cohorts: ≥90% complete follow-up was achieved in each study.

Table 3. Sensitivity analyses results by excluding one study at a time

Mortality				
Study excluded	HR (95% CI)	I^2	*p* for Cochrane Q test	*p* for effect
Zoccali 2002	1.81 [1.42, 2.31]	38%	0.11	< 0.001
Jung 2010	1.77 [1.39, 2.25]	32%	0.15	< 0.001
Tang 2010	1.85 [1.42, 2.41]	35%	0.13	< 0.001
Masuda 2011	1.71 [1.37, 2.14]	28%	0.19	< 0.001
Sivalingam 2013	1.78 [1.40, 2.26]	34%	0.14	< 0.001
Kerns 2018	1.80 [1.40, 2.31]	33%	0.13	< 0.001
Huang 2018	1.86 [1.44, 2.38]	39%	0.10	< 0.001
Harmon 2018	1.76 [1.39, 2.23]	32%	0.15	< 0.001
Kang 2021	1.68 [1.37, 2.06]	24%	0.23	< 0.001
Mochida 2023	1.64 [1.34, 2.02]	20%	0.25	< 0.001
Prabu 2023	2.06 [1.60, 2.65]	0%	0.93	< 0.001
MACEs				
Study excluded	HR (95% CI)	I^2	*p* for Cochrane Q test	*p* for effect
Zoccali 2002	2.49 [1.70, 3.66]	0%	0.74	< 0.001
Tang 2010	2.65 [1.67, 4.20]	0%	0.47	< 0.001
Masuda 2011	2.58 [1.72, 3.87]	0%	0.49	< 0.001
Harmon 2018	2.81 [1.93, 4.09]	0%	0.67	< 0.001

Mochida 2023	2.88 [1.88, 4.40]	0%	0.55	< 0.001

Abbreviations: HR: Hazard ratio; CI: Confidence interval.

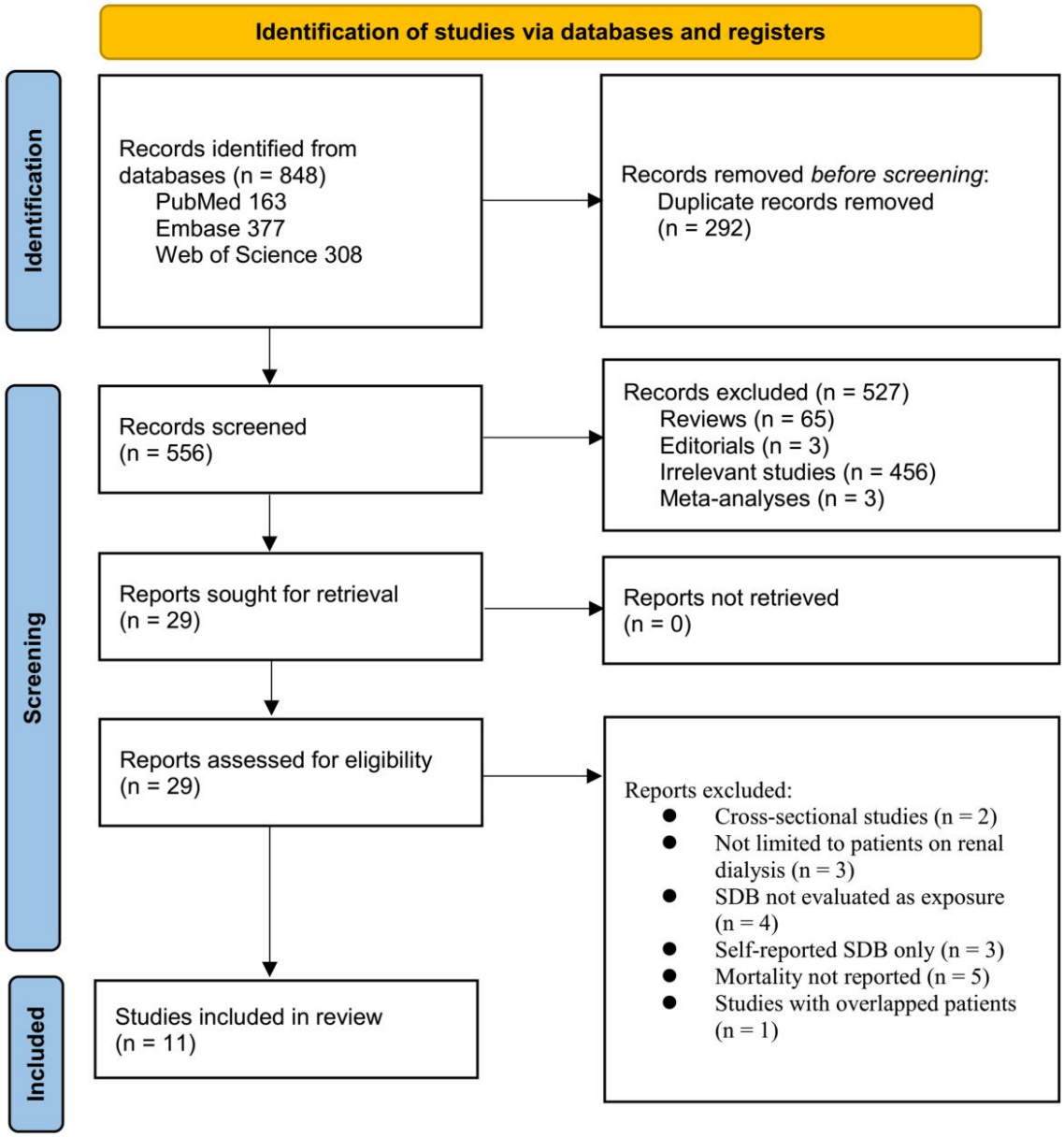

Figure 1. Flowchart of database search and study inclusion.

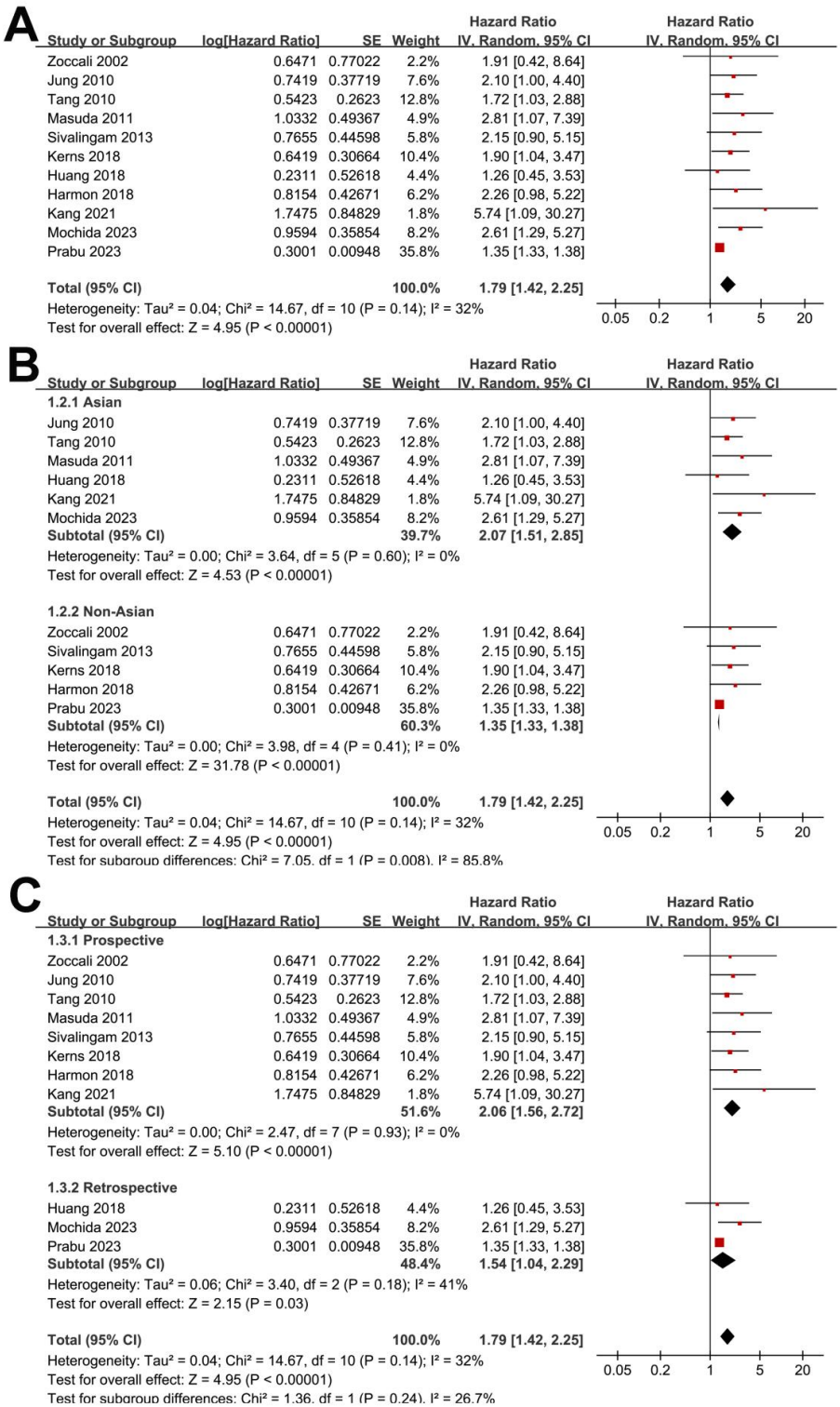

Figure 2. Association between SDB and all-cause mortality in patients on renal dialysis. (A) Forest plot of the pooled HR for all-cause mortality in 11 cohort studies. (B) Subgroup analysis stratified by geographic region (Asian vs. non-Asian populations). (C) Subgroup analysis stratified by study design (prospective vs. retrospective studies). The pooled random-effects model demonstrated that SDB was

associated with a significantly increased risk of all-cause mortality (HR: 1.79, 95% CI: 1.42–2.25, $p < 0.001$), with moderate heterogeneity ($I^2 = 32\%$). Abbreviations: SDB: Sleep-disordered breathing; HR: Hazard ratio; CI: Confidence interval; SE: Standard error; IV: Inverse variance; df: Degrees of freedom.

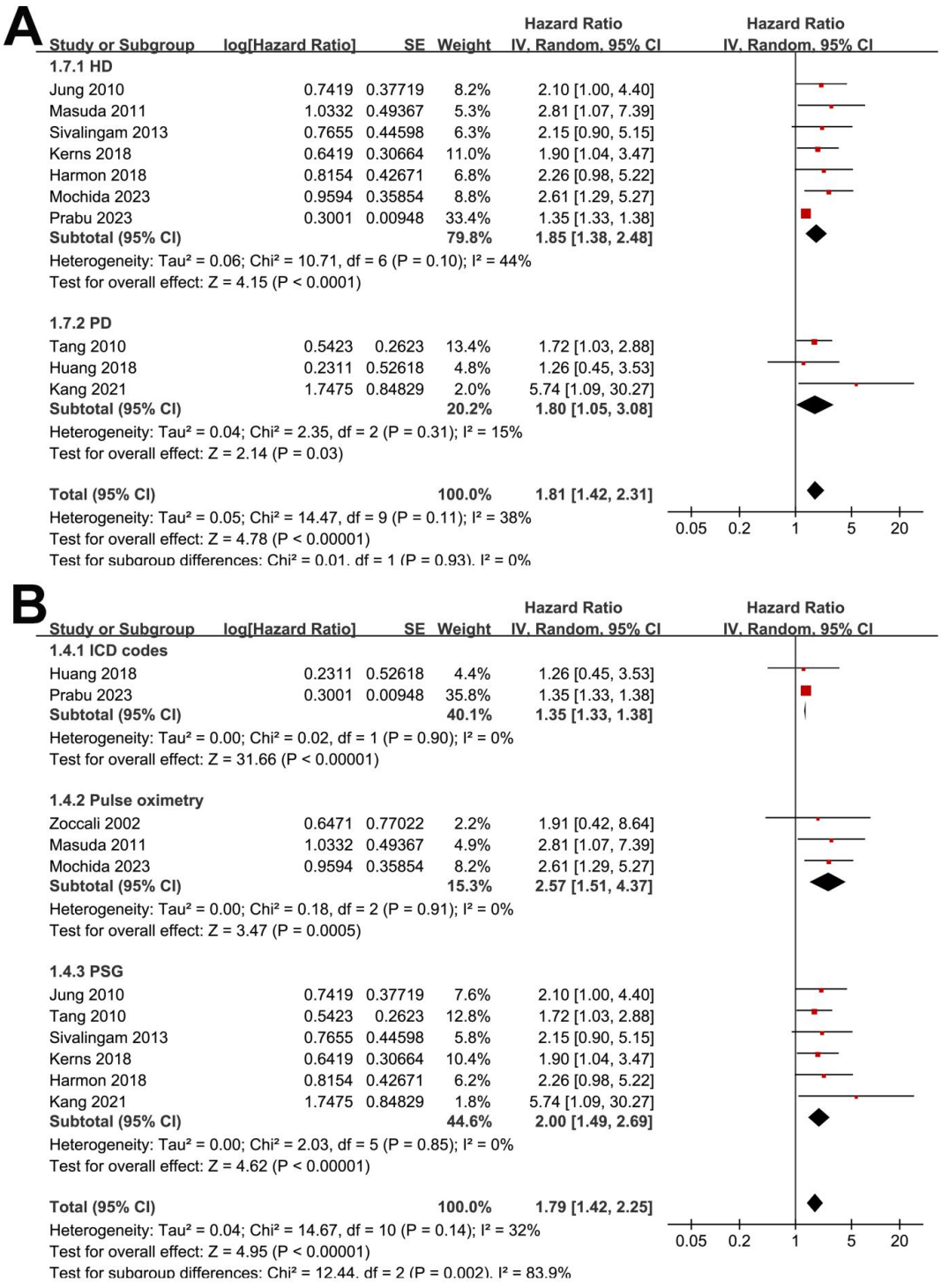

Figure 3. Subgroup analyses of the association between SDB and all-cause mortality in patients on renal dialysis. (A) Subgroup analysis stratified by dialysis modality (HD vs. PD) showed no significant difference between groups (*p* for subgroup difference = 0.93). (B) Subgroup analysis stratified by diagnostic method demonstrated a stronger association when SDB was diagnosed using overnight pulse oximetry or PSG, compared to ICD codes (*p* for subgroup difference = 0.002).

Abbreviations: SDB: Sleep-disordered breathing; HD: Hemodialysis; PD: Peritoneal dialysis; HR: Hazard ratio; CI: Confidence interval; SE: Standard error; IV: Inverse variance; df: Degrees of freedom; ICD: International classification of diseases; PSG: Polysomnography.

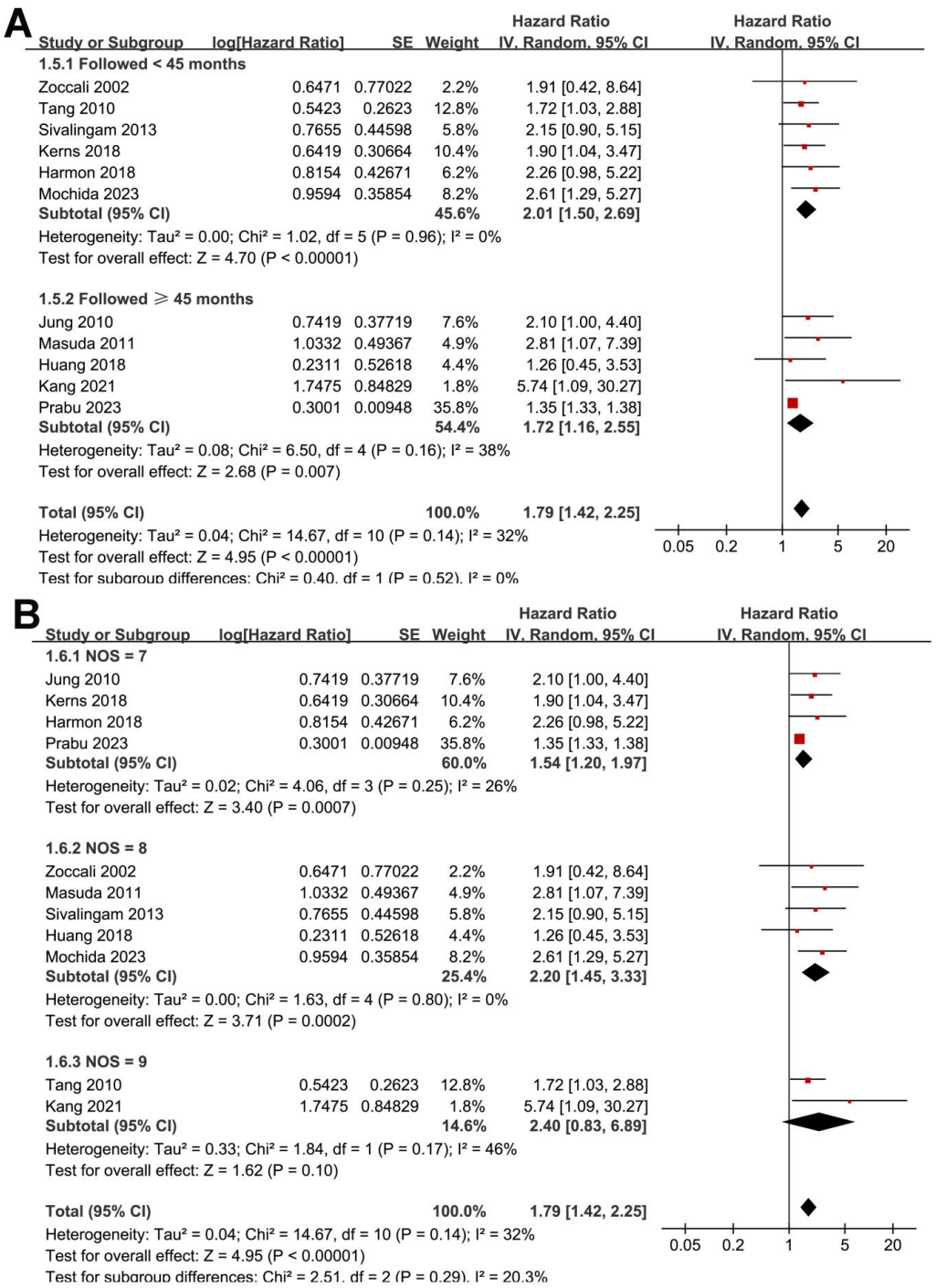

Figure 4. Subgroup analyses of the association between SDB and all-cause mortality in patients on renal dialysis. (A) Subgroup analysis stratified by follow-up duration (< 45 months vs. ≥ 45 months) showed consistent results, with no significant difference between groups (*p* for subgroup difference = 0.52). (B) Subgroup analysis stratified by study quality scores also showed similar results, without significant subgroup differences (*p* for subgroup difference = 0.29).

Abbreviations: SDB: Sleep-disordered breathing; HR: Hazard ratio; CI: Confidence interval; SE: Standard error; IV: Inverse variance; df: Degrees of freedom; NOS: Newcastle–Ottawa scale.

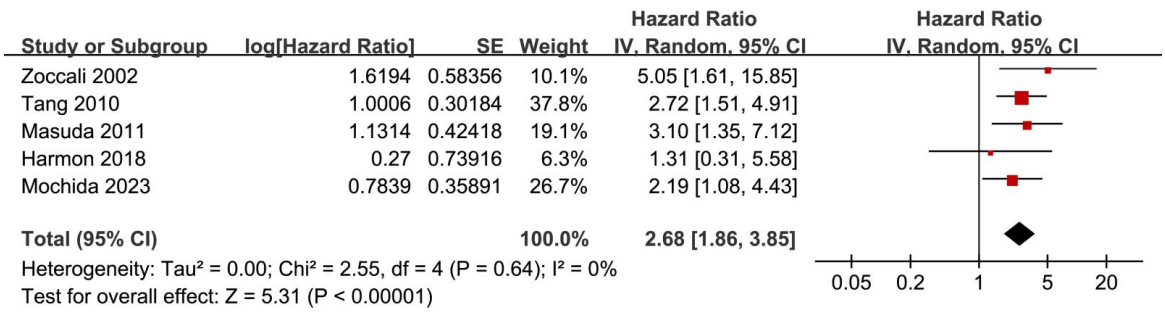

Figure 5. Association between SDB and MACEs in patients on renal dialysis. Meta-analysis of five studies demonstrated that SDB was associated with a significantly higher risk of MACEs (HR: 2.68, 95% CI: 1.86–3.85, $p < 0.001$), with no significant heterogeneity ($I^2 = 0\%$, $p = 0.64$). Abbreviations: SDB: Sleep-disordered breathing; MACEs: Major adverse cardiovascular events; HR: Hazard ratio; CI: Confidence interval; SE: Standard error; IV: Inverse variance; df: Degrees of freedom.

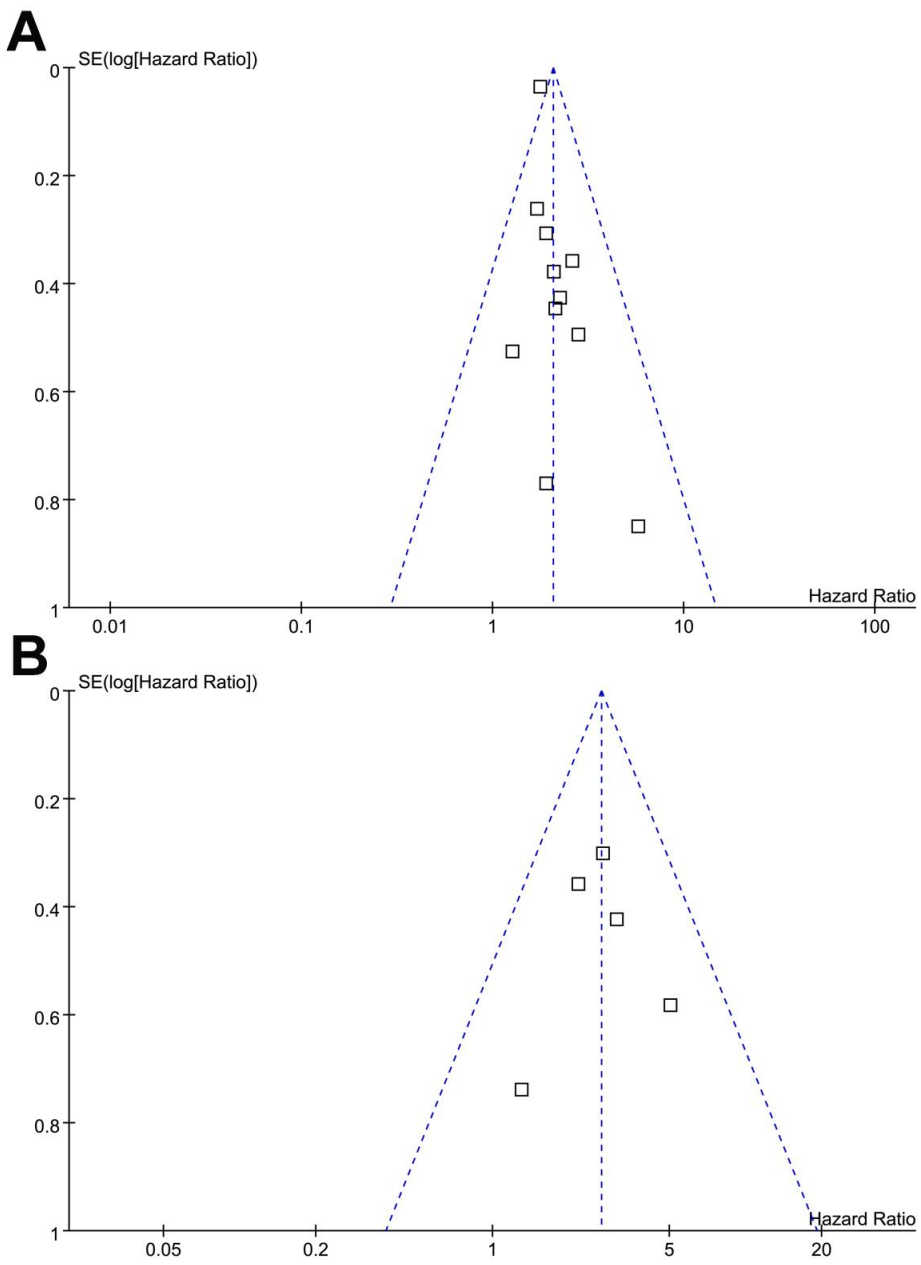

Figure 6. Funnel plots for estimating the potential publication biases underlying the meta-analyses of the association between SDB and clinical outcomes of patients on renal dialysis. (A) Funnel plots for the meta-analysis of the association between SDB and all-cause mortality; (B) funnel plots for the meta-analysis of the association between SDB and MACEs. Abbreviations: SDB: Sleep-disordered breathing; MACEs: Major adverse cardiovascular events.

SUPPLEMENTAL DATA

Supplemental data are available at the following link:

https://www.bjbms.org/ojs/index.php/bjbms/article/view/13100/4020