| **First Author, Year** | **Did the study have differential attrition or overall high attrition raising concern for bias?** | **Were outcome measurements equal, valid and reliable?** | **Were outcome assessors masked?** | **Was the duration of followup adequate to assess the outcome?** | **Did the analysis control for baseline differences between groups?** | **Does the analysis control for potential confounders? (or are confounders addressed via restriction, matching, or stratification)** | **Does the analysis account for differences in treatment received by the groups?** | **Are the statistical methods used to assess the outcomes appropriate?** | **Quality Rating** | **Comments** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Blackwell, 2015290  MrOS | No (missing outcome data for 4.5% of the 2,760 who were cognitively intact at baseline and had baseline PSG) | Yes (although unclear whether using the top decile of change for Trails B is a valid way to determine clinically significant decline) | NR | Unknown (mean 3.4 years) | Yes (except perhaps caffeine use) | Yes | Yes, they removed the 197 men using CPAP or oxygen in additional analyses (results were similar) | Yes | Fair | Controlled for a large number of potential cofounders; did not control for caffeine or cholesterol (but controlled for number of comorbid medical conditions); risk of residual confounding; multiple comparisons performed and some findings may be due to chance |
| Ensrud, 2012220  MrOS | No (missing vital status for just 1%; 7% of those who were eligible and had PSG at baseline were excluded from analyses, but were known to be living) | Yes | NR | Yes | Unclear (baseline data reported by frailty status, not by AHI categories) | Yes\* | Yes, they excluded those who started treatment | Yes | Fair | Controlled for a large number of potential cofounders, but did not control for cardiovascular disease, diabetes, hypertension, cholesterol (but controlled for number of comorbid medical conditions); risk of residual confounding† |
| Gooneratne, 2011223 | No | Yes | NRǂ | Yes | Unclear (baseline data NR by AHI categories; reported by EDS vs. not) | Yes | No | Yes | Fair |  |
| Gottlieb, 2010224  SHHS | No§ | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Good | Regarding measures, they were valid and reliable measures for CHD; some variation in how they were assessed because it depended on the parent cohort (but it does not seem to differ by AHI, and adjudication methods were similar). For HF, adjudication methods differed across cohorts (but some reassurance from statistical analyses that it didn’t matter) |
| Marin, 200550 | No | Uncertain; single physician assessed all patients at baseline and during followup | NR (seems unlikely given that a single physician assessed all patients at baseline and during followup) | Yes | Yes | Yes‖ | Yes | Yes | Fair |  |
| Marshall, 2014229  Marshall, 2008228  Busselton Health Study | No | Yes for all-cause mortality; no or uncertain for other outcomes (e.g., no independent adjudication of stroke outcomes; relied on hospital codes) | NR | Yes | Yes | Yes, for all-cause mortality; some limitations for other outcomes (e.g., lacking some cancer risk factors) | No (although they indicate that they think that none were treated) | Yes | Fair for all-cause mortalityPoor for other out-comes | Lack of masking outcome assessors of lesser importance when using death index to determine mortality; very wide CIs; lack of precision; only 18 people with moderate to severe OSA; 1 town in Western Australia. High risk of measurement bias and confounding for outcomes other than all-cause mortality |
| Nieto, 2012221  WSCS | No | Yes | NR | Yes | Yes | Yes, but small number of events (cancer deaths) yielded imprecise results (7 total cancer deaths in the severe SDB group and 5 in the moderate SDB group) | Yes (included analyses that removed those treated; and the effects increased slightly) | Yes | Fair for cancer mortality | Moderate risk of residual confounding; lack of precise information for Some cancer risk factors (e.g., smoking was current, past, or never, rather than pack-years) |
| Punjabi, 2009227  SHHS | No | Yes | Probably¶ | Yes | Yes | Yes | Yes, excluded those who reported treatment with PAP (n 147) | Yes | Good |  |
| Redline, 2010225  SHHS | No | Yes | Probably¶ | Yes | Yes | Yes | Yes, excluded those who reported CPAP use | Yes | Good |  |
| Yaffe, 2011222 | Yes, overall 35% (163/461 who had PSG were not included in analyses because of death, not completing outcome assessment, or other reasons); differential attrition NR | Yes | Yes (clinical cognitive status was adjudicated by panel of experts blinded to sleep-disordered breathing status) | Yes | Yes | Yes# | NR | Statistical analyses used appropriate methods, although nothing was done to handle missing data | Fair | Some strengths in controlling for a large number of potential confounders, masked expert panel adjudicating cognitive status, and strength of association increased when controlling for baseline cognitive status. Moderate risk of bias due to high attrition (and differential attrition was NR); no handling of missing data; longer followup than 5 years might be needed to better estimate the relationship between OSA and cognitive impairment. Possible applicability limitations |
| Young, 2008226  WSCS | No | Yes | NR | Yes | Yes | Yes | Yes (included analyses that removed those treated; and the effect increased) | Yes | Good |  |

\* Age, race, site, health status, body mass index, education, social support, alcohol intake, smoking, antidepressant, benzodiazepine, non-benzodiazepine sedative hypnotic use, number of comorbid medical conditions, cognitive function, and baseline frailty status

† The ORs they report are 1.74 or 1.88 and just barely reach significance and additional adjustment could alter findings. Possible that the effect could increase over longer followup though (this had shorter followup than some other studies)

ǂ But minimal concern for risk of bias from this with this type of mortality outcome assessment

§ No followup data or missing covariates for about 10% (476/4422)

‖ Used matching for age and BMI to select healthy community participants; long list of potential confounders considered in forward stepwise Cox model

¶ Unclear if masked, but seems likely that some/all/most were given the reliance on the physician review and the parent cohorts that these come from

# Adjusted for age, race, BMI, education, smoking status, diabetes, hypertension, antidepressant use, benzodiazepine use, and use of non-benzodiazepine anxiolytics; additional models adjusted for baseline cognitive test scores

**Abbreviations:** AHI=apnea-hypopnea index; CHD=coronary heart disease; EDS=excessive daytime sleepiness; HF=heart failure; HRs=hazard ratios; MrOS=; NR=not reported; OSA=obstructive sleep apnea; PAP=positive airway pressure; PSG=polysomnography; SDB=Sleep Disordered Breathing; SHHS=Sleep Heart Health Study; vs.=versus; WSCS=Wisconsin Sleep Cohort Study.