

Appendix 3 (as supplied by the authors): Results of sensitivity analyses

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eTable 3A: Association between obstructive sleep apnea-related predictors and incident cancer after adjustment for the lag time between sleep apnea and cancer diagnosis (on dataset no. 3*). HR (95% CI).

OSA related predictors	All cancers (N total = 9629, n events = 627)	One year lag time (N total = 9476, n events =545)	Two years lag time (N total = 9344, n events = 493)
AHI as a categorical variable, univariate association			
AHI total, events/hour, categories: >30 vs. <5	2.02 (1.61-2.54) p<0.0001	2.08 (1.63-2.64) p<0.0001	2.00 (1.55-2.60) p<0.0001
Model 1: AHI as a continuous variable + risk factors (sex, age, body mass index and smoking status)			
AHI, total, events/hour, per 10 events	1.01 (0.98-1.04) p=0.6209	1.00 (0.97-1.04) p=0.8680	1.00 (0.96-1.03) p=0.8228
Model 2: AHI as a categorical variable + risk factors			
AHI total, events/hour, categories: >30 vs. <5	1.02 (0.80-1.30) p= 0.8841	1.04 (0.80-1.36) p=0.7507	0.99 (0.75-1.31) p=0.9514
Model 3: AHI as a categorical variable + risk factors			
AHI total, events/hour, categories: >43 vs. <18.7†	1.03 (0.83-1.27) p=0.8143	1.04 (0.82-1.31) p=0.7356	1.00 (0.78-1.27) p=0.9685
Model 4: SaO₂ as a continuous variable + risk factors			
time spent with SaO ₂ less than 90%, min, per 10 min	1.00 (0.99-1.02) p= 0.6034	1.00 (0.98-1.01) 0.8555	1.00 (0.98-1.01) p=0.722
Model 5: SaO₂ as a categorical variable + risk factors			
time spent with SaO ₂ <90%, %, categories: >12% vs. <1.2% †	1.12 (0.89-1.41) p=0.3412	1.14 (0.89-1.46) p=0.3069	1.10 (0.85-1.43) p=0.4638

Note: AHI = apnea–hypopnea index; CI = confidence interval; HR = hazard ratio; OSA = obstructive sleep apnea; SaO₂ = oxygen saturation.

*For a unified presentation of results from subgroup analyses, the findings shown are for a single imputed dataset no. 3. Pooled CIs across imputations for OSA-related variables were at most 2% wider than those presented.

†To attempt to replicate the results of only one clinic-based study that evaluated an association between OSA and incident cancer,(1) we used their categories for AHI (<18.7; 18.7–43; >43) and % of time spent with SaO₂ <90% (<1.2%; 1.2%–12%; >12%). HR (AHI >43 vs. <18.7) = 1.17, 95% CI 0.84–1.65; HR (% of sleep time spent with SaO₂ <90%, categories >12% vs. <1.2%) = 2.33, 95% CI 1.57–3.46.(1)

eTable 3B: Association between obstructive sleep apnea-related predictors and different subgroups of incident cancer after controlling for sex, age, body mass index and smoking status (on dataset no. 3*), N total = 9629. HR (95% CI).

OSA-related predictors	All cancers (n events = 627)	Smoking-related (n events =156)	Hormone-related (n events = 217)	Detectable by screening (n events = 269)	Not detectable by screening (n events = 358)
AHI as a categorical variable, univariate association					
AHI total, events/hour, categories: >30 vs. <5	2.02 (1.61-2.54) p<0.0001	2.30 (1.46-3.62) p=0.0003	1.32 (0.90-1.93) p=0.1525	1.61 (1.15-2.27) p=0.0061	2.36 (1.74-3.22) p<0.0001
Model 1: AHI as a continuous variable + risk factors					
AHI, total, events/hour, per 10 events	1.01 (0.98-1.04) p=0.6209	1.02 (0.96-1.09) p=0.4900	0.97 (0.91-1.03) p=0.2946	1.00 (0.95-1.05) p=0.9784	1.03 (0.99-1.07) p=0.1731
Model 2: AHI as a categorical variable + risk factors					
AHI total, events/hour, categories: >30 vs. <5	1.02 (0.80-1.30) p= 0.8841	1.11 (0.69-1.79) p=0.6613	0.72 (0.48-1.07) p=0.1042	0.90 (0.62-1.28) p=0.5499	1.27 (0.92-1.76) p=0.1422
Model 3: AHI as a categorical variable + risk factors					
AHI total, events/hour, categories: >43 vs. <18.7†	1.03 (0.83-1.27) p=0.8143	0.95 (0.62-1.46) p=0.8147	0.78 (0.53-1.15) p=0.2034	1.05 (0.76-1.46) p=0.7620	1.12 (0.85-1.47) p=0.4313
Model 4: SaO₂ as a continuous variable + risk factors					
time spent with SaO ₂ less than 90%, min, per 10 min	1.00 (0.99-1.02) p= 0.6034	1.03 (1.01-1.05) p=0.0108	0.98 (0.95-1.01) p=0.1444	0.98 (0.96-1.01) p=0.25	1.02 (1.00-1.03) p=0.0707
Model 5: SaO₂ as a categorical variable + risk factors					
time spent with SaO ₂ <90%, %, categories: >12% vs. <1.2% †	1.12 (0.89-1.41) p=0.3412	1.75 (1.13-2.69) p=0.0116	0.78 (0.51-1.20) p=0.2556	0.94 (0.65-1.37) p=0.7664	1.33 (1.00-1.79) p=0.0531

Note: AHI = apnea-hypopnea index; CI = confidence interval; HR = hazard ratio; OSA = obstructive sleep apnea; SaO₂ = oxygen saturation

*For a unified presentation of results from subgroup analyses, the findings shown are for a single imputed dataset no. 3. Pooled CIs across imputations for OSA-related variables were at most 2% wider than those presented.

†To attempt to replicate the results of only one clinic-based study that evaluated an association between OSA and incident cancer,(1) we used their categories for AHI (<18.7; 18.7–43; >43) and % of time spent with SaO₂ <90% (<1.2%; 1.2%–12%; >12%). HR (AHI >43 vs. <18.7) = 1.17, 95% CI 0.84–1.65; HR (% of sleep time spent with SaO₂ <90%, categories >12% vs. <1.2%) = 2.33, 95% CI 1.57–3.46. (1)

Reference

1. Campos-Rodriguez F, Martinez-Garcia MA, Martinez M, et al. Association between obstructive sleep apnea and cancer incidence in a large multicenter Spanish cohort. *Am J Respir Crit Care Med* 2013;187:99-105.