Supplementary digital content 8: Detailed report of sensitivity analyses

Healthy user effect

The possibility of a healthy user effect among patients with obstructive sleep apnea (OSA) compared to non-OSA controls was tested. Such an effect would entail that diagnosed OSA and undiagnosed OSA patients experienced improved outcomes by seeking other health promoting behaviors in addition to diagnosis and treatment of OSA[1]. This would imply that comorbidities in undiagnosed OSA and diagnosed OSA patients would more likely represent milder and better managed disease with a less significant effect on postoperative outcomes than in control patients. However, no significant interactions between the comorbidities in the final multivariate models (Table 3 of the manuscript) and undiagnosed OSA, diagnosed OSA or OSA overall were found, thus failing to support the existence of a significant healthy user effect.

Changes in the care of OSA patients in the later years of data

The effect of possible changes in perioperative care of OSA patients in the later years of data was also tested. Changing rates of admission after minor surgery were used as a potential indicator. The relative odds of admission after minor surgery in OSA patients versus matched non-OSA controls were determined for each calendar year of available data. For both undiagnosed and diagnosed OSA subgroups, rates of admission significantly increased ($p < 0.01$) after December 31, 2004 compared to before, in both univariate and multivariate analyses. However, when the date of surgery (before versus after December 31, 2004) was added to the multivariate models in Table 3 of the manuscript, no significant interactions between OSA status and date of surgery were

[1] Shrank WH, Patrick AR, Brookhart MA: Healthy user and related biases in observational studies of preventive interventions: A primer for physicians. J Gen Intern Med 2011; 26: 546-50

found ($p > 0.2$ for both outcomes). This implies that if changing practice patterns for OSA patients did occur in the later years of this study, they did not significantly influence the risk of respiratory or cardiovascular complications.

It is also possible that due to changes in management leading to earlier detection of milder forms of the outcomes of interest, that diagnosis rates would increase despite reduced mortality. In order to address this hypothesis, we compared the first 11 years of data collection to the last 11 years using January 1, 1998 as a cut date. We found non-significant decreases in the later years of the data for the crude incidence of both respiratory ($p = 0.09$) and cardiovascular ($p = 0.63$) complications: 0.66% to 0.46% and 0.91% to 0.83%, respectively. Among patients who had cardiovascular complications, the crude death rate increased from 14.8% to 18.5% in the later years of the data ($p = 0.78$). Among patients who had respiratory complications, the crude death rate decreased from 35.0% to 22.4% ($p = 0.37$). When surgery after January 1, 1998 is entered into the final models presented in Table 3, it is not a significant predictor of increased complications, for either respiratory or cardiovascular complications. Thus, we do not find evidence for significant increases in diagnosis of complications nor significant decreases in mortality from better management, or earlier detection of milder forms of the complications.

Complication rates in excluded surgeries

Complication rates among excluded surgeries were high: 37.0% of tracheostomies had respiratory complications and cardiovascular complications occurred in 24.9% of excluded cardiovascular surgeries.

Other sensitivity analyses

For the remaining sensitivity analyses, the results as presented in Table 3 of the manuscript were considered robust if the sensitivity analysis did not result in a change in the significance of an OSA related predictor variable (i.e. results were robust if significant OSA subgroups remained significant and non significant OSA subgroups remained non significant).

Both analyses (respiratory and cardiovascular complications) remained robust to the removal of OSA patients who were also diagnosed with central sleep apnea or obesity hypoventilation syndrome. (Their matched controls were also removed.) These patients with complex sleep disorders may have been substantially different from the rest of the OSA patients.

Both analyses also remained robust to the removal of the Charlson comorbidity index from the models and its replacement with those individual comorbidities that reached statistical significance. These models included the 1128 surgeries at free standing surgical centres that were exlcluded from the models as presented in Table 3 because the Charlson comorbidity score could not be calculated. The model estimates for this sensitivity analysis can be found in the Table at the end of this document.

It is possible that by forcing OSA into every model, OSA may have acted as a confounder, obscuring potential significant effects of individual comorbidities on the outcomes. In order to address this issue we built models using all the relevant predictor variables, except OSA. For statistical efficiency, we removed variables that were not significant ($p > 0.05$), using stepwise backwards regression. When only significant variables remained in the model, we added OSA status variables back to the model. The findings of both analyses remained robust in these models. In fact, once comorbidities

which were no longer statistically significant were removed from these models, they were identical to the ones presented in Table 3 of the manuscript.

Table. Multivariate models of postoperative respiratory and cardiovascular complications that include all patient surgeries by excluding the Charlson comorbidity index as a predictor variable.

Variable[i]	**Respiratory complications** *Odds ratio [95% confidence limits]*	*P*	**Cardiovascular complications**[ii] *Odds ratio [95% confidence limits]*	*P*
Obstructive sleep apnea[iii]				
Overall				
Mild	1.65 [0.75-3.63]	0.21	-	-
Moderate	1.49 [0.63-3.50]	0.36	-	-
Severe	2.73 [1.61-4.63]	< 0.001	-	-
Undiagnosed				
Mild	-	-	1.23 [0.28-5.32]	0.78
Moderate	-	-	1.57 [0.48-5.12]	0.46
Severe	-	-	2.58 [1.26-5.29]	0.01
Diagnosed				
Mild	-	-	0.73 [0.29-1.82]	0.5
Moderate	-	-	0.67 [0.24-1.88]	0.45
Severe	-	-	0.73 [0.35-1.53]	0.41
Comorbidities at the time of surgery				
Age (years)	1.04 [1.02-1.06]	< 0.001	1.04 [1.02-1.05]	< 0.001
Chronic obstructive pulmonary disease	1.90 [1.25-2.87]	0.002	-	
Renal disease	1.96 [1.16-3.30]	0.01	-	0.01
Congestive heart failure	-	-	1.54 [1.01-2.35]	0.05
In an intensive care unit	2.56 [1.20-5.43]	0.01	6.22 [2.72-14.22]	< 0.001
Revised cardiac risk index score[iv]				
0	-		1 [Reference]	
1	-		5.39 [1.84-15.78]	0.002
2	-		7.83 [2.56-23.91]	< 0.001
≥3	-		11.92 [3.69-38.49]	< 0.001
Type of surgery				
Emergency surgery	3.49 [2.23-5.47]	< 0.001	2.30 [1.59-3.32]	< 0.001
Major surgery	3.75 [2.25-6.27]	< 0.001	2.57 [1.68-3.95]	< 0.001
Respiratory failure surgery[v]	2.93 [1.87-4.60]	< 0.001	2.22 [1.57-3.15]	< 0.001

[i]Cells with dashes indicate the variable was not included in the multivariate model for that complication.

[ii]The reference group for undiagnosed obstructive sleep apnea (OSA) patient surgeries is matched *undiagnosed* OSA controls and the reference group for diagnosed OSA patient surgeries is matched *diagnosed* OSA controls. The estimated reduction in risk for mild diagnosed OSA compared to mild undiagnosed OSA was 0.59 [0.11-3.34], p = 0.55. The estimated reduction in risk for moderate diagnosed OSA compared to moderate undiagnosed OSA was 0.43 [0.09-2.02], p = 0.28. The estimated reduction in risk for severe diagnosed OSA compared to severe undiagnosed OSA was 0.28 [0.10-0.78], p = 0.01.

[iii]There was no significant difference in outcomes between undiagnosed obstructive sleep apnea (OSA) and diagnosed OSA patients for respiratory complications. The risk of cardiovascular complications was significantly reduced in undiagnosed OSA patients (0.35 [0.16-0.77], p = 0.01). There were significant trends to increased risk with increasing OSA severity for respiratory complications in OSA overall (diagnosed and undiagnosed OSA combined, p = 0.01) and for cardiovascular complications in undiagnosed OSA patients only (p = 0.04).

[iv]The revised cardiac risk index score assigns one point each for the presence of diabetes mellitus, ischemic heart disease, congestive heart failure, history of cerebrovascular disease, parenchymal renal disease and high risk surgery (in this study defined as major surgery). Increasing scores are associated with increased risk of cardiac complications

including myocardial infarction, pulmonary edema, ventricular fibrillation, cardiac arrest and complete heart block.

[v]Surgery associated with a high risk of respiratory failure, as defined in Arozullah AM, Daley J, Henderson WG, Khuri SF: Multifactorial risk index for predicting postoperative respiratory failure in men after major noncardiac surgery. The National Veterans Administration Surgical Quality Improvement Program. Ann Surg 2000; 232: 242-53