

# Trends in Perioperative Practice and Resource Utilization in Patients With Obstructive Sleep Apnea Undergoing Joint Arthroplasty

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**BACKGROUND:** Emerging evidence associating obstructive sleep apnea (OSA) with adverse perioperative outcomes has recently heightened the level of awareness among perioperative physicians. In particular, estimates projecting the high prevalence of this condition in the surgical population highlight the necessity of the development and adherence to “best clinical practices.” In this context, a number of expert panels have generated recommendations in an effort to provide guidance for perioperative decision-making. However, given the paucity of insights into the status of the implementation of recommended practices on a national level, we sought to investigate current utilization, trends, and the penetration of OSA care-related interventions in the perioperative management of patients undergoing lower joint arthroplasties.

**METHODS:** In this population-based analysis, we identified 1,107,438 (Premier Perspective database; 2006–2013) cases of total hip and knee arthroplasties and investigated utilization and temporal trends in the perioperative use of regional anesthetic techniques, blood oxygen saturation monitoring (oximetry), supplemental oxygen administration, positive airway pressure therapy, advanced monitoring environments, and opioid prescription among patients with and without OSA.

**RESULTS:** The utilization of regional anesthetic techniques did not differ by OSA status and overall <25% and 15% received neuraxial anesthesia and peripheral nerve blocks, respectively. Trend analysis showed a significant increase in peripheral nerve block use by >50% and a concurrent decrease in opioid prescription. Interestingly, while the absolute number of patients with OSA receiving perioperative oximetry, supplemental oxygen, and positive airway pressure therapy significantly increased over time, the proportional use significantly decreased by approximately 28%, 36%, and 14%, respectively. A shift from utilization of intensive care to telemetry and stepdown units was seen.

**CONCLUSIONS:** On a population-based level, the implementation of OSA-targeted interventions seems to be limited with some of the current trends virtually in contrast to practice guidelines. Reasons for these findings need to be further elucidated, but observations of a dramatic increase in absolute utilization with a proportional decrease may suggest possible resource constraints as a contributor. (Anesth Analg 2017;125:66–77)

Obstructive sleep apnea (OSA) is a prevalent disease characterized by repeated obstruction of the upper airway during sleep and significant consequences for cardiovascular health.<sup>1</sup> While increasing awareness of this problem and its consequences has led to the development of successful long-term treatment strategies such as the use of nighttime positive airway pressure devices (PAP), the

impact of sleep apnea and its management in the perioperative setting has been less well defined. Recently, however, evidence on postoperative outcomes in patients with sleep apnea have broadened our understanding of the impact of this medical condition on utilization and outcomes.<sup>2–5</sup> This is especially important because the prevalence of OSA among surgical patients appears to exceed that of the general population with OSA suspected in approximately every fourth patient undergoing elective surgery.<sup>6</sup> In this context, numerous studies and reviews of literature have demonstrated that OSA represents an independent risk factor for adverse events, thus sparking interest in the development of clinical approaches to these patients.<sup>2–4</sup> Reflecting the heightened level of concern, the American Society of Anesthesiologists (ASA) provided guidelines in 2006 and 2014 for the perioperative management of patients with sleep apnea, including the perioperative use of PAP therapy, continuous surveillance, oxygen therapy, and increased utilization of regional anesthesia as measures of precaution.<sup>7,8</sup> However, to date there is only limited evidence to substantiate and support the efficacy of various recommended interventions.<sup>9–11</sup> Furthermore, data documenting utilization and trends of various interventions as recommended by the ASA to prevent OSA-related complications remain sparse.

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Therefore, we sought to investigate rates and trends in the perioperative utilization of anesthesia techniques and pain management, blood oxygen saturation monitoring (oximetry), supplemental oxygen administration as well as of PAP therapy and the utilization of advanced monitoring settings to provide data on clinical practice and identify whether recent findings and guideline recommendations have translated into perioperative care of this patient population. In this context, we also explored potential differences among patients with and without OSA. We specifically studied hip and knee arthroplasty recipients in the time period from 2006 to 2013, because these procedures are relatively standardized, highly suitable for regional anesthesia techniques as recommended, and because the prevalence of OSA is particularly high in orthopedic patients.<sup>4</sup> We hypothesized (1) that the utilization of resources would be significantly higher among patients with OSA than in the non-OSA population; (2) that the utilization of targeted interventions would be applied only in a minority of patients with OSA; and (3) the utilization of resources and interventions would be increasing over time.

## METHODS

### Data Source

We used pooled data from the Premier Perspective database<sup>12</sup> covering years 2006 to 2013, and extracted from claims of >20% of hospitals in the United States. Services provided were determined through the analysis of *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9) codes, *Current Procedural Terminology* codes, and standardized billing items. This study was exempt from requirements for consent by the Hospital for Special Surgery and Icahn School of Medicine at Mount Sinai institutional review boards because the data are compliant with the Health Insurance Portability and Accountability Act.

### Study Sample

Elective procedures of primary lower extremity joint arthroplasty, defined by ICD-9 codes for primary hip (81.51) and primary knee (81.54) surgeries, between 2006 and 2013 were identified. Five hundred ninety-six hospitals were identified in which these procedures were performed in the data set during the study period. Patients with OSA were identified by the following registered diagnostic ICD-9 codes: 327.20, 327.21, 327.22, 327.23, 327.24, 327.25, 327.26, 327.27, 327.29, 786.03, 780.53, 780.51, and 780.57. We excluded individuals with unknown gender (n = 69), unknown discharge status (n = 498), and multiple procedures during the index hospital admission (n = 212).

### Variables

Patients with OSA were identified using ICD-9 codes. While the ability of this approach to capture all patients with OSA in administrative databases may have limitations,<sup>13</sup> those with an ICD-9 code for OSA are very likely to have either a formal diagnosis or be at high risk for the disease, thus driving clinical decision-making for the utilization of resources and interventions. Demographic variables included age, race (white, black, Hispanic, and other), year of procedure, and comorbidity prevalence. In brief, the comorbidity burden was established by using the Deyo adaption of the Charlson

comorbidity index (Deyo Index), a score derived from identified comorbidities that correlates with risk of adverse outcomes.<sup>14</sup> Interventions of interest were: administered anesthesia technique (general, neuraxial, peripheral nerve blocks, other, or unknown), postoperative opioid prescription, oximetry, and supplemental oxygen, PAP therapy, and the utilization of advanced monitoring environments (ie, telemetry, stepdown, and intensive care units [ICUs]). Opioid prescription was defined as postoperatively prescribed opioids for in-hospital use on the day of surgery and postoperative day 1. This was converted into oral morphine equivalents calculated from use of fentanyl, hydrocodone, hydromorphone, meperidine, morphine, oxycodone, and propoxyphene (using the Lexicomp<sup>15</sup> [Lexi-Comp, Inc, Hudson, OH] "opioid agonist conversion" and the GlobalRPH<sup>16</sup> [GlobalRPh, VA Medical Center, Detroit, MI] "opioid analgesic converter").

Other variables of interest were use of mechanical ventilation, length of stay, and cost of hospitalization. The presence of obesity was also considered in the analysis. In addition to presenting continuous data, we dichotomized length of stay and opioid prescription based on the 75th percentile to present a measure of extremes. Entries above the 75th percentile were considered to represent increased length of stay or opioid utilization, respectively. Except for the use of anesthesia technique, our data generally refer to the postoperative utilization of the specified interventions of interest on the day of surgery and postoperative day 1.

## Statistical Analysis

### Utilization of Interventions of Interest Among OSA Versus Non-OSA.

Differences in the use of interventions of interest were compared between those diagnosed with OSA and non-OSA individuals. Means and percentages and the associated 95% confidence intervals were described for continuous and categorical variables, respectively. Median and interquartile ranges were used to describe opioid prescription, age, cost, and length of hospital stay, because their distributions were nonnormally distributed.  $\chi^2$  tests and Mann-Whitney *U* tests for categorical and continuous variables were used to compare differences in utilization between the 2 groups. Logistic regression analysis was performed to adjust for important baseline characteristics, including age, race, Deyo comorbidity burden, obesity, year of procedure, anesthesia type, peripheral nerve block use, any opioid administration, use of oximetry, supplemental oxygen, ventilation, PAP, ICU, stepdown, telemetry, and cost and length of stay.

### Temporal Trends of Resource Utilization Among OSA.

Among those diagnosed with OSA, temporal trends (by 1-year increments) of resource utilization were described using proportions and the associated 95% confidence intervals for binomial distributed data. The Cochran-Armitage test<sup>17</sup> was used to assess the statistical significance of temporal trends of resource utilization for all binary variables. Median regression was used to assess linear trends of opioid utilization, because there was no evidence of departures from linearity using natural cubic splines.<sup>18</sup>

All analyses were performed in Stata version 14.0 statistical software (StataCorp LP, College Station, TX).

## RESULTS

### Utilization

In this descriptive analysis, we identified 1,107,438 cases of patients having undergone total hip and knee arthroplasty between 2006 and 2013 after applying exclusion criteria (unknown gender:  $n = 69$ ; unknown discharge status:  $n = 498$ ; multiple procedures:  $n = 212$ ). Overall, 114,269 (10.0%) patients carried a diagnosis of OSA while the incidence more than doubled over the study period. Patients affected by OSA exhibited a higher comorbidity burden as measured by the Deyo Index and higher rates of obesity (17.6% vs 44.8%; Table 1).

The utilization of anesthetic techniques did not differ in clinically relevant terms by OSA status; <25.0% received neuraxial anesthesia and the rate for peripheral nerve blocks was below 15.0% regardless of the diagnosis of sleep apnea.

Differences in the postoperative utilization of resources on the day of surgery and postoperative day 1 were identified between patients with and without a diagnosis code of OSA. Although the utilization rate of oximetry was 42.0% in patients with OSA, 35.9% of the patients without sleep apnea received this mode of continuous surveillance ( $P < .001$ ). Furthermore, 53.7% of patients with OSA received supplemental oxygen compared to 49.8% in the non-OSA cohort ( $P < .001$ ). The largest absolute differences were seen in PAP use, because this was administered to 14.6% of patients with OSA, whereas only 0.5% of non-OSA patients received this intervention ( $P < .001$ ). In addition, telemetry, stepdown, and ICUs were utilized approximately twice as often in

cases involving patients with OSA compared to non-OSA encounters ( $P < .001$ ; Table 2).

While there was no clinically relevant difference in length of hospital stay between the 2 groups (median [interquartile range] = 3[3, 4] days for OSA versus non-OSA), the cost of hospitalization was slightly higher in the OSA population (median = 15,426 USD versus 15,004 USD for OSA versus non-OSA,  $P < .001$ ). Differences depicted in Tables 1 and 2 remained significant at a .01 level after adjustment for important baseline characteristics.

### Temporal Trends

Tables 3 to 5 show temporal trends in the distribution of anesthesia techniques, the utilization of resources, and pain management strategies in patients with a diagnosis of OSA.

Our data demonstrate that the prevalence of a diagnosis code for OSA more than doubled from 6.0% in 2006 to 13.4% in 2013.

While changes in the utilization of anesthetic techniques such as general and neuraxial anesthesia were mostly subtle, the use of peripheral nerve blocks increased by >50% from 9.2% in 2006 to 15.1% in 2013. The prescription of opioids as measured in oral morphine equivalents significantly decreased over this timeframe (median mg/day = 283 in 2006 to 235 in 2013, an average linear decrease of 5 mg/day per year,  $P < .001$ ).

Interestingly, the proportion of patients with OSA utilizing oximetry, supplemental oxygen, and PAP significantly decreased over time. The utilization of oximetry decreased

**Table 1. Demographic Characteristics of Individuals Receiving Elective Primary Total Hip or Knee Arthroplasty in the Premier Perspective Database, Stratified by OSA Status**

	Combined Hip and Knee				Hip				Knee			
	No OSA <sup>a</sup>		OSA <sup>b</sup>		No OSA <sup>a</sup>		OSA <sup>b</sup>		No OSA <sup>a</sup>		OSA <sup>b</sup>	
	(N = 993,169 [90%])		(N = 114,269 [10%])		(N = 329,393 [92%])		(N = 29,167 [8%])		(N = 663,776 [88%])		(N = 85,102 [11%])	
	N	% (+IQR)	N	% (+IQR)	N	% (+IQR)	N	% (+IQR)	N	% (+IQR)	N	% (+IQR)
Age (y)	66	(59, 74) <sup>c</sup>	64	(57, 70) <sup>c</sup>	67	(57, 74)	63	(56, 70)	67	(59, 74)	64	(58, 70)
Race <sup>d</sup>												
White	753,949	75.91	89,801	78.59	255,011	77.42	23,088	79.16	498,938	75.17	66,713	78.39
Black	69,533	7.00	8786	7.69	22,194	6.74	2088	7.16	47,339	7.13	6698	7.87
Hispanic	13,677	1.38	918	0.80	2957	0.9	173	0.59	10,720	1.62	745	0.88
Other	156,010	15.71	14,764	12.92	49,231	14.95	3818	13.09	106,779	16.09	10,946	12.86
Deyo category <sup>d</sup>												
0	754,415	75.96	70,450	61.65	251,746	76.43	18,437	63.21	502,669	75.73	52,013	61.12
1	173,227	17.44	29,658	25.95	54,972	16.69	7071	24.24	118,255	17.82	22,587	26.54
2	45,518	4.58	8312	7.27	15,450	4.69	2049	7.03	30,068	4.53	6263	7.36
3	20,009	2.01	5849	5.12	7225	2.19	1610	5.52	12,784	1.93	4239	4.98
Obesity <sup>d</sup>	174,632	17.58	51,234	44.84	44,686	13.57	11,883	40.74	129,946	19.58	39,351	46.24
Year <sup>d,e</sup>												
2006	95,529	93.96	6146	6.04	30,892	95.43	1480	4.57	64,637	93.27	4666	6.73
2007	101,358	92.76	7912	7.24	32,453	94.61	1850	5.39	68,905	91.91	6062	8.09
2008	105,098	91.77	9421	8.23	33,364	93.81	2201	6.19	71,734	90.86	7220	9.14
2009	118,755	90.55	12,388	9.45	39,215	92.74	3070	7.26	79,540	89.51	9318	10.49
2010	130,340	89.50	15,289	10.50	42,753	91.72	3858	8.28	87,587	88.46	11,431	11.54
2011	138,282	88.65	17,705	11.35	46,104	91.17	4466	8.83	92,178	87.44	13,239	12.56
2012	148,791	87.43	21,398	12.57	51,175	89.92	5736	10.08	97,616	86.17	15,662	13.83
2013	155,016	86.59	24,010	13.41	53,437	89.15	6506	10.85	101,579	85.30	17,504	14.70

All values are column percentages unless otherwise stated.

All adjusted differences are significant at the .01 level. Demographic data presented in column percentages, proportions by year presented in row percentages.

Abbreviation: IQR, interquartile range.

<sup>a</sup>Individuals without OSA, or undiagnosed, or not coded.

<sup>b</sup>Individuals diagnosed with OSA.

<sup>c</sup>Values are median (IQR).

<sup>d</sup>Values are N (%).

<sup>e</sup>Row percentages.

**Table 2. Resource and Health Care Utilization for Individuals Receiving Elective Primary Total Hip or Knee Arthroplasty in the Premier Perspective Database, Stratified by Diagnosed OSA Status**

	Combined				Hip				Knee			
	No OSA <sup>a</sup>		OSA <sup>b</sup>		No OSA <sup>a</sup>		OSA <sup>b</sup>		No OSA <sup>a</sup>		OSA <sup>b</sup>	
	N	% (+IQR)	N	% (+IQR)	N	% (+IQR)	N	% (+IQR)	N	% (+IQR)	N	% (+IQR)
Anesthesia techniques												
Anesthesia type <sup>c</sup>												
General	587,066	59.11	67,868	59.39	200,149	60.76	17,986	61.67	386,917	58.29	49,882	58.61
Neuraxial	105,531	10.63	12,226	10.70	31,432	9.54	2,731	9.36	74,099	11.16	9,495	11.16
General + neuraxial	108,344	10.91	13,547	11.86	34,650	10.52	3,246	11.13	73,694	11.10	10,301	12.10
Other	103,828	10.45	10,745	9.40	31,302	9.50	2,444	8.38	72,526	10.93	8,301	9.75
Unknown	88,400	8.90	9,883	8.65	31,860	9.67	2,760	9.46	56,540	8.52	7,123	8.37
Peripheral nerve block	120,197	12.10	14,994	13.12	24,118	7.32	2,196	7.53	95,252	14.35	12,668	14.89
Pain management												
Prescribed any opioids <sup>c</sup>	932,501	93.89	108,117	94.62	308,616	93.69	27,571	94.53	623,885	93.99	80,546	94.65
Morphine equivalent (mg/d)	220	(127.5, 365) <sup>d</sup>	246	(148, 400) <sup>d</sup>	210	(120, 354) <sup>d</sup>	240	(139.2, 390) <sup>d</sup>	225	(131, 372) <sup>d</sup>	250	(150, 400.8)
Morphine equivalent (75th % Y) <sup>e</sup>	235,457	25.25	31,761	29.38	73,679	23.87	7,763	28.16	161,778	25.93	23,998	29.79
Oxygen delivery and monitoring												
Oximetry <sup>c</sup>	356,066	35.85	47,974	41.98	112,653	34.20	11,708	40.14	243,413	36.67	36,266	42.61
Supplemental oxygen <sup>c</sup>	494,156	49.76	61,337	53.68	153,919	46.73	14,626	50.15	340,237	51.26	46,711	54.89
Mechanical ventilation <sup>c</sup>	1623	0.16	613	0.54	635	0.19	199	0.68	988	0.15	414	0.49
PAP <sup>c</sup>	4922	0.50	16,714	14.63	1309	0.40	4056	13.91	3612	0.54	12,658	14.87
Surveillance												
ICU <sup>c</sup>	27,605	2.78	6,244	5.46	10,349	3.14	1,914	6.56	7,256	2.60	4,330	5.09
Stepdown <sup>c</sup>	20,292	2.04	4,758	4.16	6,978	2.12	1,282	4.40	13,314	2.01	3,476	4.08
Telemetry <sup>c</sup>	25,746	2.59	5,498	4.81	8,884	2.70	1,440	4.94	16,862	2.54	4,058	4.77
Healthcare resources												
Cost <sup>d</sup>	15,004	(12,347.86, 18,514.24) <sup>d</sup>	15,426	(12,711.6, 19,070.85) <sup>d</sup>	15,470	(12,759.09, 18,931.6) <sup>d</sup>	16,020	(13,154.09, 19,594.84) <sup>d</sup>	14,778	(12,169.2, 18,277.07) <sup>d</sup>	15,234	(12,579.43, 18,856.73)
LOS (d)	3	(3, 4) <sup>d</sup>	3	(3, 4) <sup>d</sup>	3	(2, 3) <sup>d</sup>	3	(2, 4) <sup>d</sup>	3	(3, 4)	3	(3, 4)
LOS (75th % Y) <sup>e</sup>	256,106	25.79	30,522	26.71	81,946	24.88	7,514	25.76	174,160	26.24	23,008	27.04

All values are column percentages unless otherwise stated.

All adjusted differences are significant at the .01 level. Y\* values are n > 75th percentile where 75th percentile is based on the entire data set.

Abbreviations: ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; PAP, positive airway pressure.

<sup>a</sup>Individuals without obstructive sleep apnea, or undiagnosed, or not coded.

<sup>b</sup>Individuals diagnosed with obstructive sleep apnea.

<sup>c</sup>Values are N (%).

<sup>d</sup>Values are median (IQR).

**Table 3. Temporal Trends of Resource and Health Care Utilization for Patients With OSA Receiving Elective Primary Total Hip or Knee Arthroplasty in the Premier Perspective Database**

Primary Total Hip or Knee Replacement in the PROMETHEUS Cooperative Database																	
Anesthesia Technique																	
General						Neuraxial				General + Neuraxial				Block			
Year	N	n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
2006	6146	4482	72.9%	71.8%	74.0%	708	11.5%	10.7%	12.3%	780	12.7%	11.9%	13.5%	566	9.2%	8.5%	10.0%
2007	7912	5731	72.4%	71.4%	73.4%	918	11.6%	10.9%	12.3%	966	12.2%	11.5%	13.0%	721	9.1%	8.5%	9.8%
2008	9421	6606	70.1%	69.2%	71.0%	1144	12.1%	11.5%	12.8%	1141	12.1%	11.5%	12.8%	841	8.9%	8.4%	9.5%
2009	12,388	8913	71.9%	71.1%	72.7%	1387	11.2%	10.6%	11.8%	1632	13.2%	12.6%	13.8%	1264	10.2%	9.7%	10.7%
2010	15,289	10,811	70.7%	70.0%	71.4%	1747	11.4%	10.9%	11.9%	2162	14.1%	13.6%	14.7%	1980	13.0%	12.4%	13.5%
2011	17,705	12,120	68.5%	67.8%	69.1%	1993	11.3%	10.8%	11.7%	2212	12.5%	12.0%	13.0%	2623	14.8%	14.3%	15.3%
2012	21,398	15,201	71.0%	70.4%	71.6%	2021	9.4%	9.1%	9.8%	2164	10.1%	9.7%	10.5%	3372	15.8%	15.3%	16.3%
2013	24,010	17,551	73.1%	72.5%	73.7%	2308	9.6%	9.2%	10.0%	2490	10.4%	10.0%	10.8%	3627	15.1%	14.7%	15.6%
Oxygen Delivery and Monitoring																	
Oximetry						Supplemental Oxygen				PAP							
Year	N	n	%	95% CI		n	%	95% CI		n	%	95% CI					
2006	6146	2915	47.4%	46.2%	48.7%	4017	65.4%	64.2%	66.5%	980	15.9%	15.0%	16.9%				
2007	7912	3678	46.5%	45.4%	47.6%	5101	64.5%	63.4%	65.5%	1181	14.9%	14.1%	15.7%				
2008	9421	4266	45.3%	44.3%	46.3%	5896	62.6%	61.6%	63.6%	1439	15.3%	14.6%	16.0%				
2009	12,388	5422	43.8%	42.9%	44.6%	7369	59.5%	58.6%	60.4%	1811	14.6%	14.0%	15.3%				
2010	15,289	7198	47.1%	46.3%	47.9%	8832	57.8%	57.0%	58.6%	2430	15.9%	15.3%	16.5%				
2011	17,705	7834	44.2%	43.5%	45.0%	9789	55.3%	54.6%	56.0%	2632	14.9%	14.3%	15.4%				
2012	21,398	8522	39.8%	39.2%	40.5%	10,322	48.2%	47.6%	48.9%	2945	13.8%	13.3%	14.2%				
2013	24,010	8139	33.9%	33.3%	34.5%	10,011	41.7%	41.1%	42.3%	3296	13.7%	13.3%	14.2%				
Surveillance and Pain Management																	
ICU						Stepdown				Telemetry				Morphine Equivalent <sup>a</sup>			
Year	N	N	%	95% CI		n	%	95% CI		n	%	95% CI		Median	95% CI		
2006	6146	472	7.7%	7.0%	8.4%	204	3.3%	2.9%	3.8%	202	3.3%	2.9%	3.8%	283	275	288	
2007	7912	571	7.2%	6.7%	7.8%	303	3.8%	3.4%	4.3%	259	3.3%	2.9%	3.7%	265	260	270	
2008	9421	699	7.4%	6.9%	8.0%	473	5.0%	4.6%	5.5%	396	4.2%	3.8%	4.6%	257	255	263	
2009	12,388	746	6.0%	5.6%	6.5%	709	5.7%	5.3%	6.1%	570	4.6%	4.2%	5.0%	255	253	260	
2010	15,289	852	5.6%	5.2%	5.9%	764	5.0%	4.7%	5.4%	728	4.8%	4.4%	5.1%	245	240	250	
2011	17,705	962	5.4%	5.1%	5.8%	780	4.4%	4.1%	4.7%	907	5.1%	4.8%	5.5%	241	240	245	
2012	21,398	1034	4.8%	4.5%	5.1%	739	3.5%	3.2%	3.7%	1146	5.4%	5.1%	5.7%	244	240	246	
2013	24,010	908	3.8%	3.5%	4.0%	786	3.3%	3.1%	3.5%	1290	5.4%	5.1%	5.7%	235	230	236	

All trends, measured by the Cochran-Armitage trend test were statistically significant at the .001 level.

Abbreviations: CI, confidence interval; ICU, intensive care unit; OSA, obstructive sleep apnea; PAP, positive airway pressure.

<sup>a</sup>Trend measured by linear quintile regression was statistically significant at the .001 level and decreasing by a median 5 mg/d per year increase.

from 47.4% in 2006 to 33.9% in 2013. Supplemental oxygen use declined from 65.4% in 2006 to 41.7% in 2013. However, this trend was less pronounced in the utilization of PAP, which dropped from 15.9% in 2006 to 13.7% in 2013. It must be noted, however, that our data show a significant discrepancy between changes in relative and absolute use with the latter in fact increasing. Furthermore, we found that although there was a slight increase in the use of telemetry from 3.3% in 2006 to 5.4% in 2013, admissions to ICUs decreased from 7.7% in 2006 to 3.8% in 2013.

## DISCUSSION

### Prevalence of OSA

In this retrospective review of population-based data from >500 hospitals across the United States, we describe prevalence and trends in the utilization of interventions and resources relevant to the care of patients with OSA from 2006 to 2013. Data on 1,047,438 patients undergoing total hip and knee arthroplasty were obtained from the Premier Perspective database.

Similar to other reports utilizing administrative databases, we identified a substantial increase in OSA prevalence from 2006 to 2013.<sup>5</sup> Whether this demonstrates a true increase in prevalence or at least in part reflects the growing attention for OSA in the perioperative setting is debatable.<sup>19</sup>

### Utilization of Anesthesia Techniques

Despite recommendations by the ASA to adequately adjust anesthetic techniques and medications for patients with OSA,<sup>7,8</sup> we found no significant distinction in anesthetic choice among patients with and without OSA. Moreover, similar to previous reports in the general orthopedic population,<sup>20</sup> approximately 70% of joint arthroplasty cases among patients with OSA were conducted under general anesthesia and <25% received neuraxial anesthesia (with or without general anesthesia). The high utilization of general anesthesia and relative underutilization of neuraxial anesthesia in this population are interesting not only given current evidence indicating improved perioperative outcomes related to regional anesthesia,<sup>21</sup> but also considering the existence of specific guidelines. Although not without controversy, population-based data suggest that in peripheral procedures, the utilization of neuraxial anesthesia and peripheral nerve blocks, rather than general anesthesia, may be associated with a reduction in adverse outcome.<sup>22</sup> Similarly, the avoidance of airway instrumentation and reduction in the need for centrally acting medication may be beneficial to the physiology of the upper airway and pulmonary system.<sup>7</sup> Moreover, recent guidelines by the ASA recommend the use of major conductance anesthesia including

**Table 4. Temporal Trends of Resource and Health Care Utilization for Patients With OSA Receiving Elective Primary Total Hip Arthroplasty in the Premier Perspective Database**

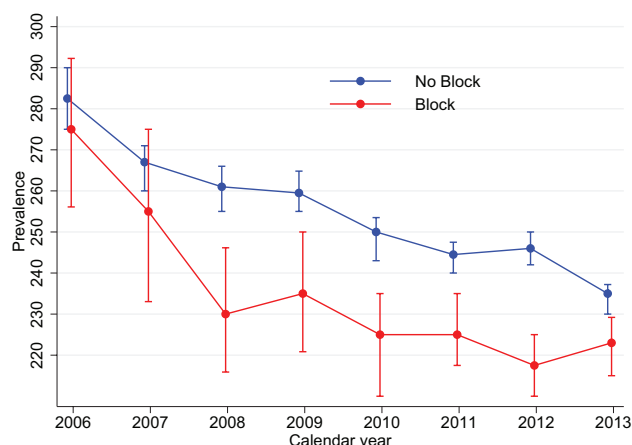
Year	Anesthesia Technique										Block		
	General			Neuraxial			General + Neuraxial				%		95% CI
	N	n	%	n	%	95% CI	n	%	n	%	n	%	
2006	1480	1088	73.51%	151	10.2%	8.7%	172	11.62%	10.03%	13.36%	91	6.15%	4.98%
2007	1850	1382	74.70%	163	8.8%	7.6%	217	11.73%	10.30%	13.28%	107	5.78%	4.76%
2008	2201	1545	70.20%	224	10.2%	8.9%	248	11.27%	9.98%	12.66%	127	5.77%	4.83%
2009	3070	2209	71.95%	308	10.0%	9.0%	391	12.74%	11.58%	13.97%	179	5.83%	5.03%
2010	3858	2739	71.00%	442	11.5%	10.5%	513	13.30%	12.24%	14.41%	252	6.53%	5.77%
2011	4466	3153	70.60%	423	9.5%	8.6%	514	11.51%	10.59%	12.48%	330	7.39%	6.64%
2012	5736	4180	72.87%	488	8.5%	7.8%	546	9.52%	8.77%	10.31%	533	9.29%	8.55%
2013	6506	4936	75.87%	532	8.2%	7.5%	645	9.91%	9.20%	10.67%	582	8.95%	8.26%
Oxygen Delivery and Monitoring													
Year	Oximetry			Supplemental Oxygen			PAP						95% CI
	N	n	%	n	%	95% CI	n	%	n	%	n	%	
2006	1480	692	46.76%	906	61.22%	58.68%	224	15.14%	13.35%	17.06%			
2007	1850	847	45.78%	1158	62.59%	60.34%	271	14.65%	13.07%	16.34%			
2008	2201	966	43.89%	1310	59.52%	57.43%	314	14.27%	12.83%	15.80%			
2009	3070	1273	41.47%	1683	54.82%	53.04%	426	13.88%	12.67%	15.15%			
2010	3858	1772	45.93%	2075	53.78%	52.20%	578	14.98%	13.87%	16.15%			
2011	4466	1886	42.23%	2339	52.37%	50.90%	644	14.42%	13.40%	15.48%			
2012	5736	2203	38.41%	2585	45.07%	43.77%	774	13.49%	12.62%	14.41%			
2013	6506	2069	31.80%	2570	39.50%	38.31%	825	12.68%	11.88%	13.51%			
Surveillance and Pain Management													
Year	ICU			Stepdown			Telemetry			Morphine Equivalent			95% CI
	N	n	%	n	%	95% CI	n	%	n	%	n	%	
2006	1480	132	8.92%	57	3.85%	2.93%	61	4.12%	3.17%	5.26%	265.75	255.00	280
2007	1850	159	8.59%	83	4.49%	3.59%	54	2.92%	2.20%	3.79%	255.00	240.00	265
2008	2201	187	8.50%	110	5.00%	4.13%	102	4.63%	3.79%	5.60%	245.00	235.59	255
2009	3070	245	7.98%	180	5.86%	5.06%	140	4.56%	3.85%	5.36%	245.00	237.44	255
2010	3858	266	6.89%	232	6.01%	5.28%	174	4.51%	3.88%	5.21%	235.00	228.00	240
2011	4466	312	6.99%	194	4.34%	3.76%	230	5.15%	4.52%	5.84%	232.50	225.00	240
2012	5736	335	5.84%	221	3.85%	3.37%	316	5.51%	4.93%	6.13%	240.00	234.00	244
2013	6506	278	4.27%	205	3.15%	2.74%	363	5.58%	5.03%	6.17%	230.00	223.05	235

Abbreviations: CI, confidence interval; ICU, intensive care unit; OSA, obstructive sleep apnea; PAP positive airway pressure.

**Table 5. Temporal Trends of Resource and Health Care Utilization for Patients With OSA Receiving Elective Primary Total Knee Arthroplasty in the Premier Perspective Database**

Year	N	General				Neuraxial				General + Neuraxial				Block			
		n	%	95% CI		n	%	95% CI		n	%	95% CI		n	%	95% CI	
2006	4666	3394	72.74%	71.44%	74.01%	557	11.9%	11.0%	12.9%	608	13.03%	12.08%	14.03%	475	10.18%	9.33%	11.08%
2007	6062	4349	71.74%	70.59%	72.87%	755	12.5%	11.6%	13.3%	749	12.36%	11.54%	13.21%	614	10.13%	9.38%	10.92%
2008	7220	5061	70.10%	69.03%	71.15%	920	12.7%	12.0%	13.5%	893	12.37%	11.62%	13.15%	714	9.89%	9.21%	10.60%
2009	9318	6704	71.95%	71.02%	72.86%	1,079	11.6%	10.9%	12.2%	1241	13.32%	12.63%	14.03%	1085	11.64%	11.00%	12.31%
2010	11,431	8072	70.61%	69.77%	71.45%	1,305	11.4%	10.8%	12.0%	1649	14.43%	13.79%	15.08%	1728	15.12%	14.46%	15.79%
2011	13,239	8967	67.73%	66.93%	68.53%	1,570	11.9%	11.3%	12.4%	1698	12.83%	12.26%	13.41%	2293	17.32%	16.68%	17.98%
2012	15,662	11,021	70.37%	69.65%	71.08%	1,533	9.8%	9.3%	10.3%	1618	10.33%	9.86%	10.82%	2839	18.13%	17.53%	18.74%
2013	17,504	12,615	72.07%	71.40%	72.73%	1,776	10.1%	9.7%	10.6%	1845	10.54%	10.09%	11.00%	3045	17.40%	16.84%	17.97%
Oxygen Delivery and Monitoring																	
Year	N	Oximetry				Supplemental Oxygen				PAP							
		n	%	95% CI		n	%	95% CI		n	%	95% CI					
2006	4666	2223	47.64%	46.20%	49.09%	3111	66.67%	65.30%	68.03%	756	16.20%	15.16%	17.29%				
2007	6062	2831	46.70%	45.44%	47.97%	3943	65.04%	63.83%	66.25%	910	15.01%	14.12%	15.94%				
2008	7220	3300	45.71%	44.55%	46.86%	4586	63.52%	62.40%	64.63%	1125	15.58%	14.75%	16.44%				
2009	9318	4149	44.53%	43.51%	45.54%	5686	61.02%	60.02%	62.01%	1385	14.86%	14.15%	15.60%				
2010	11,431	5426	47.47%	46.55%	48.39%	6757	59.11%	58.20%	60.01%	1852	16.20%	15.53%	16.89%				
2011	13,239	5948	44.93%	44.08%	45.78%	7450	56.27%	55.42%	57.12%	1988	15.02%	14.41%	15.64%				
2012	15,662	6319	40.35%	39.58%	41.12%	7737	49.40%	48.61%	50.19%	2171	13.86%	13.32%	14.41%				
2013	17,504	6070	34.68%	33.97%	35.39%	7441	42.51%	41.78%	43.25%	2471	14.12%	13.60%	14.64%				
Surveillance and Pain Management																	
Year	N	ICU				Stepdown				Telemetry				Morphine Equivalent			
		n	%	95% CI		n	%	95% CI		n	%	95% CI		Median	95% CI		
2006	4666	340	7.29%	6.56%	8.07%	147	3.15%	2.67%	3.69%	141	3.02%	2.55%	3.55%	286.38	279.93	295	
2007	6062	412	6.80%	6.18%	7.46%	220	3.63%	3.17%	4.13%	205	3.38%	2.94%	3.87%	270.00	261.00	275	
2008	7220	512	7.09%	6.51%	7.71%	363	5.03%	4.53%	5.56%	294	4.07%	3.63%	4.55%	262.00	255.00	267	
2009	9318	501	5.38%	4.93%	5.85%	529	5.68%	5.22%	6.17%	430	4.61%	4.20%	5.06%	260.00	255.00	265	
2010	11,431	586	5.13%	4.73%	5.55%	532	4.65%	4.28%	5.06%	554	4.85%	4.46%	5.26%	250.00	243.64	254	
2011	13,239	650	4.91%	4.55%	5.29%	586	4.43%	4.08%	4.79%	677	5.11%	4.74%	5.50%	245.00	240.00	248	
2012	15,662	699	4.46%	4.14%	4.80%	518	3.31%	3.03%	3.60%	830	5.30%	4.95%	5.66%	245.00	240.54	250	
2013	17,504	630	3.60%	3.33%	3.89%	581	3.32%	3.06%	3.60%	927	5.30%	4.97%	5.64%	235.00	232.50	238	

Abbreviations: CI, confidence interval; ICU, intensive care unit; OSA, obstructive sleep apnea; PAP, positive airway pressure.



**Figure 1.** Trends of perioperative pain management, median (95% confidence intervals) of morphine equivalent stratified by block use over calendar time for patients with OSA undergoing elective primary total hip or knee arthroplasty in the Premier Perspective database 2006–2013. OSA indicates obstructive sleep apnea.

spinal and epidural anesthesia, for peripheral procedures, in light of the higher propensity of patients with OSA to postoperative respiratory compromise after systemic use of anesthetics, sedatives, and opioids.<sup>8</sup>

While reasons for these observations remain speculative, mechanistic evidence on how regional techniques can prevent complications and improve outcomes is still lacking, and some studies have failed to confirm improved outcomes with regional versus general anesthesia.<sup>23,24</sup> Furthermore, it is known that evolution from evidence to best practice, although possible, is associated with a lengthy and comprehensive process.<sup>25</sup> Consistently, our data demonstrate the sustained predominance of general anesthesia along with a slight decrease in neuraxial anesthesia over the study period.

### Perioperative Pain Management

Similar to previous data in orthopedic patients, we found that the use of peripheral nerve blocks significantly increased by approximately 50% during the observation period.<sup>26</sup> We also found a concurrent decrease in the utilization of opioids, which are known to attenuate ventilatory response to hypoxia and hypercarbia and potentially aggravate sleep apnea symptoms.<sup>27</sup> Because peripheral nerve blocks have been shown to reduce opioid requirements, it is conceivable that these trends might be causally related to some extent, particularly because decreased opioid utilization was even more pronounced in patients who received a peripheral nerve block compared to patients without this intervention (Figure 1). However, this notion is not verifiable in this retrospective analysis, in part because preoperative and postdischarge opioid use as well as chronic pain could not be investigated. In this context, the recent rise in the use of local anesthesia infiltration should also be mentioned as a potential driver of reduced opioid utilization, although not traceable in our data.<sup>28</sup> Considering the complexity of pain control particularly in this patient population, these observations might be indicating the transition toward multimodal analgesia, because combining analgesic strategies to achieve additive and synergistic effects while

minimizing opioid side effects<sup>29</sup> is of particular importance in OSA.

### Oximetry and Supplemental Oxygen

We found that although initially approximately half of the OSA population was postoperatively monitored by oximetry, the use of this intervention significantly dropped to approximately one third of the population in 2013. In absolute terms, however, as the OSA prevalence increased, the annual number of monitored patients significantly increased. Similarly, the administration of supplemental oxygen significantly decreased by approximately 36%, however again, with an increase in absolute use.<sup>7</sup> These findings are interesting given recent recommendations that patients with OSA should undergo postoperative continuous pulse oximetry monitoring and receive supplemental oxygen postoperatively until baseline oxygen saturation is achieved on room air.<sup>8</sup>

There may be multiple explanations for these observations.

Given the dramatic increase in the number of patients with OSA presenting for surgery, the reduced rate of oximetry could in part be representative of the straining of resources. An evaluation of this possibility is necessary given that absolute utilization increased by approximately a 3-fold although proportional use decreased.

While resource availability may or may not be a factor in terms of decreases in supplemental oxygen administration, it should be noted that routine administration of oxygen in patients with OSA has been criticized by some, because it may prolong the time to detection of respiratory depression as a patient's oxygen saturation may remain high even during episodes of prolonged and significant hypoventilation.<sup>30</sup>

Furthermore, sustained administration of continuous pulse oximetry is associated with challenges, because this may not always be available in the nonacute postoperative period.<sup>31</sup> Difficulties might also arise from managing continuous pulse oximetry on general hospital floors or other sites, because the technology is prone to gaps and artifacts and frequent alarms from repeated desaturations or artifacts can pose a burden to caregivers and patients.<sup>31</sup>

Another potential driver regarding the utilization of interventions as a precaution to prevent complications could be the severity of OSA. However, our database does not allow judgments about the degree of OSA. Considering the significant increase in prevalence coupled with evidence indicating potential aggravation of apnea/hypopnea and desaturation on the third postoperative night,<sup>32</sup> advocates point to the development of strategies to stratify OSA patients with a high likelihood of postoperative complications to maximize safety and optimize resource allocation.<sup>33</sup> In this context, Gali et al<sup>33</sup> were able to predict patients at risk for desaturation or apneic events after discharge from postanesthesia care units (PACUs) by using preoperative OSA screening and postoperative monitoring of respiratory events in the PACU.

However, scientific literature to provide evidence-based guidance on the appropriate duration and impact of postoperative respiratory monitoring and supplemental oxygen administration is currently insufficient and therefore the lack of clinical consensus among anesthesiologists in this regard is not surprising.<sup>34,35</sup>

## Utilization of Positive Airway Pressure

While the perioperative use of PAP therapy, particularly in patients with OSA with prior familiarization, is clearly recommended,<sup>7,8</sup> our data show that PAP therapy was only utilized in approximately 15% of patients with OSA. As the absolute utilization increased by approximately 3-fold—stabilizing in the latter years—and outpaced the growth of OSA prevalence, proportional administration even decreased by approximately 14%. This finding too raises the question of lack of sufficient resources as a possible explanation. In particular, not all hospitals might be equipped with sufficient PAP devices to supply the increasing number of patients with OSA and the general lack of protocols might further represent an obstacle to patients providing their own device during hospitalization.

Interestingly, in the non-OSA population, the utilization rate for PAP was 0.5%. With estimates claiming that up to 90% of OSA patients are undiagnosed,<sup>36</sup> these cases may to some extent represent undetected individuals requiring postoperative PAP therapy but could feasibly also represent use for the treatment of pulmonary compromise.

For >3 decades now, PAP treatment has been widely established as the gold standard of OSA care capable of diminishing symptoms of sleep apnea and improving long-term health.<sup>37</sup> However, poor compliance to PAP therapy is well known with studies reporting an adherence rate <50% in the perioperative period.<sup>38,39</sup>

Further reasons for the relatively low utilization of recommended interventions may relate to the paucity of studies evaluating its efficacy and impact in the perioperative setting. Some evidence, however, exists that preoperative PAP therapy may be associated with lower rates of postoperative complications and reduced resource utilization.<sup>9</sup> As such, PAP may potentially reduce airway inflammation and increase upper airway volume.<sup>40</sup> Nevertheless, not all have been able to demonstrate significant differences between continuous PAP and noncontinuous PAP treatment.<sup>11,41</sup> Although clearly more research is needed to establish that PAP therapy can reduce perioperative adverse events in OSA,<sup>10</sup> randomization of patients in this context may be viewed as unethical, which further complicates matters.

Current ASA guidelines suggest that PAP should be initiated preoperatively in severe OSA and postoperatively utilized in previously compliant patients.<sup>7</sup> To what degree the low utilization of postoperative PAP in our study represents low preoperative PAP adherence, intolerance to postoperative application, shortages in hospital resources, or possibly a low rate of preoperative PAP prescription by providers remains to be studied and cannot be answered at this point. Interestingly, a study by Liao et al<sup>42</sup> indicates that perioperative factors may be responsible to a certain extent. The authors suggest that guidelines are not routinely observed because only 63% of the patients with sleep apnea in their study, who used home PAP therapy, received this intervention postoperatively.<sup>42</sup> However, despite limited evidence on the benefits of PAP therapy in the perioperative setting,<sup>10,11,42</sup> it seems reasonable to at least continue PAP treatment postoperatively in preoperatively accustomed patients.

## Surveillance in Advanced Care Settings

The utilization of ICUs, stepdown, and telemetry units was twice as high in patients with OSA compared to non-OSA patients. This is consistent with previous studies that additionally report longer stays of patients with OSA in ICU and PACU settings.<sup>43</sup> Interestingly, we found that in our OSA population, the utilization of ICUs decreased by 50% over time, whereas that of telemetries significantly increased in the same time period. Telemetry and stepdown units might be emerging as more cost-effective substitutes for routine surveillance of patients with OSA.

Continuous monitoring has been demanded by experts for patients with OSA,<sup>7</sup> because severe cardiorespiratory events and mortality during the postoperative period have been reported in sleep apnea,<sup>33</sup> and complications have increasingly led to malpractice lawsuits.<sup>44,45</sup>

Interestingly, Chia et al<sup>46</sup> discovered a novel association between high preoperative STOP-BANG scores and postoperative admissions to critical care units. The authors concluded that this screening tool might be helpful in planning scheduled postoperative critical care admissions. Identifying which patients will benefit from which level of surveillance will be a major challenge in terms of balancing safety and adequate resource allocation. In this context, severity of OSA and surgical procedure are likely significant factors for future targeted precautions.

Furthermore, although length of hospital stay was similar among patients with and without OSA, overall cost was slightly higher in patients carrying a diagnosis of OSA. This is consistent with reports from revision joint arthroplasties,<sup>47</sup> in which OSA was associated with increased postoperative charges as well, confirming the economic challenge of this condition, which may be due to higher resource utilization as well as increased complications.

## Limitations

Due to the nature of this observational analysis, our study is subject to numerous limitations. First, we obtained retrospective data that were primarily recorded for administrative purposes, potentially constituting a source of input bias. Indeed, the use of ICD-9 coding has recently been criticized by a Canadian study reporting suboptimal diagnostic accuracy of OSA in their database.<sup>13</sup> However, these findings cannot be extrapolated to other data sets without further validation and do not negate previous findings, but rather call for more validation attempts.<sup>48</sup> Despite data validation performed by Premier Perspective, we cannot exclude input data error or coding errors. Nevertheless, we assume that these errors would be evenly distributed among study groups and therefore would result in limited differential bias. Furthermore, no causal conclusions can be drawn from database studies and associations can only be observed and interpreted in the wider context. For example, we cannot discern if the admission of a patient with OSA to an ICU was for elective surveillance purposes or as a result of complications. The same applies to the use of PAP therapy. With regard to opioid prescription, the database, derived from hospital billing information, does not allow the clear determination of actual opioid consumption or the controlling for pain levels and preoperative or postdischarge opioid use

due to a lack of this type of information. In addition, our data source does not offer information regarding the location of services provided, but rather time and date, which was considered in our analysis. However, the utilization of prescription data has been accepted as useful among public health researchers.<sup>49,50</sup> Furthermore, we acknowledge that perioperative and anesthetic practices evolve over time and not all clinical pathway changes are captured by administrative data.

As such, the **intervention of periarticular local anesthetic infiltration**, for example, which may potentially influence the use of peripheral nerve blockade and opioid utilization, is **not coded in our database**. Additionally, data used here are captured for the timeframe from 2006 to 2013, the latest year available at the time of analysis. Thus, further trends may have occurred since then. However, the timeframe studied overlaps with the publication of a number of guidelines and studies suggesting specialized care for patients with OSA and identifying it as a perioperative risk factor, thus making it a relevant period for study. Furthermore, patients in our database are identified as patients with OSA by ICD-9 coding, implying no standardized mode of diagnostic criteria. As such, we cannot determine if, for example, patients were either diagnosed by polysomnography or designated as patients with OSA by screening questionnaires. In addition, the severity of OSA, a potential driver for resource utilization, cannot be determined. Moreover, as a result of the high prevalence of undiagnosed OSA, it is likely that a proportion of our patients declared as non-OSA patients could be affected by the disease. However, our analysis primarily relates to clinical perioperative care in patients who have a diagnosis code for OSA, which is relevant for treatment decisions by providers. Because trend analysis is confined to this group, bias due to the exclusion of some patients may be limited.

Unfortunately, when it comes to cost analysis, no direct attribution to specific interventions or events can be made using our data source because only overall hospitalization cost is available. In this context, no anesthesia-specific interventions can be itemized. However, because there seem to be only modest differences in anesthesia techniques used between OSA and non-OSA patients, this information would be of limited value in the current context.

Finally, we would like to mention that, while the analysis of the impact of interventions on postoperative outcomes is of significant interest, this requires a separate analysis and is beyond the scope of the current study.

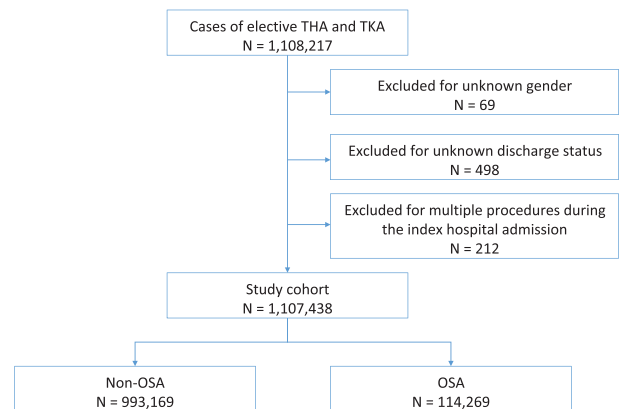
## CONCLUSIONS

We found that interventions recommended for the perioperative treatment and surveillance of patients with OSA have not been widely implemented. In fact, some of the current trends stand in contrast to practices suggested in guidelines. Although it is undisputable that further research is needed to strengthen recommendations, our data suggest that resource constraints might be a contributing factor.<sup>51</sup> In fact, the absolute rate increase in utilization of interventions and resources has outpaced the increase in OSA prevalence; however, smaller proportions are beneficiaries of these practices. Importantly, new guidelines on preoperative screening and assessment of patients with OSA have just recently been published.<sup>51</sup> These recommendations provide

a more evidence-based approach and specified instructions relating to OSA and comorbidity status in contrast to other rather broadly positioned guidelines. Although the possibility of resource shortages needs to be examined, potential health care system-related factors as well as the broadness of recommendations, largely irrespective of OSA severity and the clinical feasibility of measures of precaution, need to be kept in mind as possibly impeding the implementation of suggested practices. The limited effect of clinical practice guidelines on changing physicians' behavior is well documented,<sup>52</sup> and transition from evidence to best practice, although possible, requires comprehensive approaches specifically shaped for target groups.<sup>25</sup> Reported barriers in this matter include lack of awareness, agreement, and outcome expectancy.<sup>52</sup> Therefore, our data re-emphasize further discussion regarding the clinical feasibility of provided guidelines and point out the **need for further evidence regarding** the efficacy of recommended interventions in the context of risk-benefit stratification to define best clinical practices. ■■

## Appendix

### Study Flowchart.



## DISCLOSURES

**Name:** Crispiana Cozowicz, MD.

**Contribution:** This author helped conduct the study, analyze the data, and write the manuscript.

**Conflicts of Interest:** None.

**Name:** Jashvant Poeran, MD, PhD.

**Contribution:** This author helped conduct the study, analyze the data, and write the manuscript.

**Conflicts of Interest:** None.

**Name:** Ashley Olson, MA.

**Contribution:** This author helped conduct the study, analyze the data, and write the manuscript.

**Conflicts of Interest:** None.

**Name:** Madhu Mazumdar, PhD.

**Contribution:** This author helped conduct the study, analyze the data, and write the manuscript.

**Conflicts of Interest:** None.

**Name:** Eva E. Mörwald, MD.

**Contribution:** This author helped conduct the study, analyze the data, and write the manuscript.

**Conflicts of Interest:** None.

**Name:** Stavros G. Memtsoudis, MD, PhD.

**Contribution:** This author helped design the study, conduct the study, analyze the data, and write the manuscript.

**Conflicts of Interest:** Stavros G. Memtsoudis is a nonpaid consultant for B. Braun. Stavros G. Memtsoudis is funded by the Anna Maria and Stephen Kellen Career Development Award, New York.

**This manuscript was handled by:** Tong J. Gan, MD.

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