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Authors

Cai, Yi

Tripuraneni, Priyanka

Gulati, Arushi

et al.

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Patient-Defined Goals for Obstructive Sleep Apnea Treatment

Yi Cai, MD¹, Priyanka Tripuraneni, MS¹, Arushi Gulati¹,
 Erika M. Stephens¹, Dang-Khoa Nguyen, MS²,
 Megan L. Durr, MD², and Jolie L. Chang, MD³

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Abstract

Objectives. To characterize the treatment goals and values of adult patients with obstructive sleep apnea (OSA).

Study Design. Mixed methods design based on semistructured interviews followed by cross-sectional surveys.

Setting. Academic medical center and integrated managed care consortium.

Methods. Phase 1 involved qualitative analysis of focus groups and interviews to define treatment goal categories. Phase 2 included analysis of cross-sectional surveys on most important treatment goals from patients with OSA presenting to sleep surgery clinic. Positive airway pressure (PAP) use, Epworth Sleepiness Scale score, and apnea-hypopnea index were obtained to determine influences on goal choices.

Results. During focus groups and interviews, treatment goal themes identified included improving sleep quality, reducing daytime sleepiness, snoring sound reduction, and health risk reduction. In phase 2, 536 patients were surveyed, and they reported the primary treatment goals of health risk reduction (35%), sleep quality improvement (28%), daytime sleepiness improvement (21%), and snoring sound reduction (16%). The primary treatment goal was associated with age ($P < .0001$), excessive daytime sleepiness (Epworth Sleepiness Scale score >10 , $P < .0001$), PAP use status ($P < .0001$), and OSA severity (apnea-hypopnea index, $P < .0001$). Severity of OSA was associated with increasing proportion of patients choosing health risk reduction as the main treatment goal ($P < .05$).

Conclusions. Adult OSA treatment goal choices vary with age, symptoms, PAP history, and OSA severity. Understanding patient-specific goals is the essential first step in the shared decision-making process when choosing surgical or nonsurgical treatments. Ultimately, goal-focused discussions ensure alignment of priorities and definitions of success between the patient and the provider.

Keywords

obstructive sleep apnea, treatment goals, positive airway pressure, age, apnea hypopnea index, sleep surgery, shared decision making.

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In adults with obstructive sleep apnea (OSA) who are interested in positive airway pressure (PAP) alternatives, the multiple approaches to effective therapy may present a challenge to patients and providers when selecting a preferred treatment modality. We previously demonstrated high rates of decisional conflict and the potential for decision delay or regret in this population.¹

Thus, there is a need to improve patient preparedness for decision making and decision quality through better shared decision-making (SDM) processes and tools. Key components of the patient-centered SDM process include understanding patient preferences and treatment goals to enhance patient education, promote patient engagement, and align definitions of optimal outcomes.²

One key contributor to decisional conflict is incomplete understanding of, or de-emphasis on, patient-defined goals for pursuing treatment. OSA treatment effectiveness is often measured by changes in disease severity via the apnea-hypopnea index (AHI) or symptom scores such as the Epworth Sleepiness Scale (ESS). However, focusing solely on these metrics does not capture patient-driven treatment goals or values (eg, cost, convenience, or recovery time), which affect adherence and efficacy.² Literature regarding the treatment goals of patients with OSA, especially those seeking surgical treatment, is limited. In this study, we used a mixed methods approach to identify major treatment goal categories in adult patients with OSA. We then assessed patients' the most important treatment goal and characterized the relationships between treatment goals and patient characteristics with

¹Department of Otolaryngology–Head and Neck Surgery, School of Medicine, University of California–San Francisco, San Francisco, California, USA

²Department of Head and Neck Surgery, Kaiser Permanente, Oakland, California, USA

³Surgery Service, Department of Veterans Affairs Medical Center, San Francisco, California, USA

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Corresponding Author:

Jolie L. Chang, MD, Department of Otolaryngology–Head and Neck Surgery, School of Medicine, University of California–San Francisco, 2233 Post St, Box 1225, San Francisco, CA 94115, USA.
 Email: Jolie.chang@ucsf.edu

a larger-scale cross-sectional survey. This information can be used to guide counseling and help patients select treatments that best meet their individual goals.

Methods

This study was approved by the Institutional Review Boards of the University of California–San Francisco (UCSF) and Kaiser Permanente Oakland.

Phase 1: Semistructured Focus Groups and Interviews—Qualitative Analysis

We employed a mixed methods approach,³ gathering data from semistructured interviews that were used to inform the design of our larger clinical survey. Methodology was in accordance with the Consolidated Criteria for Reporting Qualitative Research (Supplemental Table S1, available online).⁴ Focus groups and semistructured interviews were conducted by 2 members of the research team (P.T. and D.K.). Convenience sampling was used in recruiting participants.⁵ Adult patients newly diagnosed with OSA were recruited from Kaiser Permanente Oakland OSA education classes (treatment-naïve group). Eight 30-minute focus groups were held, with 2 or 3 participants per group. Patients with a history of OSA therapy were also recruited from the UCSF Sleep Surgery Clinic for semistructured interviews conducted individually in person or via telephone after the sleep surgery consultation (“history of treatment” group). Participants were compensated with gift cards. Recruitment was completed when themes discussed became repetitive (saturation).

Interview questions were based on prior studies examining barriers to OSA treatment and expert opinions from sleep medicine or surgery physicians at both institutions. The interview script focused on OSA symptoms, prior treatments, overall goals of treatment, and important factors when considering treatment options. During sessions, patients were encouraged to engage in conversation and introduce related topics. Following semistructured interviews, participants provided ESS scores, demographics, and AHI. Questionnaire and demographic data were documented with REDCap (Research Electronic Data Capture), a secure web-based software platform hosted at UCSF.^{6,7}

Patient conversations were audio recorded and transcribed. Two investigators made field notes from transcripts and coded each one to identify key themes and ideas. Using a framework method (thematic analysis), each coder created a coding set that included collective themes that were grouped.⁸ New codes were identified from ideas that emerged in conversation, and codes were consistently revised to be more inclusive of ongoing interview themes. Each transcript was independently reviewed at least twice by each coder. As the coders became more familiar with the data, overarching themes and subthemes were identified. Saturation was achieved when no further codes were identified. Coding was done independently through Dedoose (version 8.3.47; Socio-Cultural Research Consultants), and coding sets were compared to ensure that no ideas were missed and to limit the

discrepancies in coding style. A third investigator resolved discrepancies between coding sets and performed final analysis of transcripts to identify common themes (3 independent reviewers, 5 distinct reviews of each transcript).

Phase 2: Survey of Patients Presenting to Sleep Surgery Clinic

An electronic REDCap survey was administered to patients prior to their first consultation at the UCSF Sleep Surgery Clinic between January 2018 and October 2020. The survey queried OSA-related symptoms (ESS), PAP use, and treatment goals. Patients were asked to rate the degree to which OSA affected their daily function, using a visual analog scale (VAS-F) from 0 (no difficulty) to 100 (totally disabled). The importance of 4 common goals was queried, as based on literature, expert review, and the preceding qualitative analysis of semistructured interviews:

Your goal(s) for seeking sleep apnea treatment include: 1) To improve my daytime fatigue and feel less sleepy in the daytime, 2) To improve my snoring so those sleeping near me are not bothered by the sounds, 3) To reduce the health risks related to sleep apnea (such as heart disease and stroke), 4) To improve my sleep quality so I feel more refreshed when I wake up, and 5) Other.

Patients were asked to choose their most important primary treatment goal from the list with the option of writing in separate goals.

Medical records were reviewed for demographic and clinical data, including gender identity, age, body mass index, AHI, and ultimate pursuit of sleep surgery or related procedures (ie, drug-induced sleep endoscopy) at our institution.

Survey responses were analyzed in Microsoft Excel (version 14.5.3). ESS scores >10 represented excessive daytime sleepiness. OSA severity was based on AHI. Patients with sleep-disordered breathing and AHI <5 were included as a comparison group. Chi-square analysis compared the distribution of most important treatment goals among subgroups of patients. For comparison of treatment goals based on ESS, PAP use history, VAS-F scores, and ultimate decision to pursue surgery. Only $P < .05$ was used to define statistical significance.

Results

Phase 1: Semistructured Interviews

Eight focus groups with 20 patients newly diagnosed with OSA (treatment naïve) and 8 interviews with patients who had undergone prior therapy (history of treatment) were completed (**Table 1**). Analysis of goals for OSA therapy identified 9 subthemes (**Table 2**). The most common treatment goals were improving daytime sleepiness, reducing health risk with focus on cardiovascular health, improving sleep quality (depth and restfulness), and improving snoring sounds (reduction or termination).

Table 1. Focus Group and Interview Participants.

	Treatment naïve	History of treatment
Age, years, mean (range)	52 (37-71)	50 (29-67)
Gender identity, No.		
Male	10	6
Female	10	2
Apnea Hypopnea Index, mean \pm SD	29.5 \pm 14.4	41.7 \pm 24.2
Epworth Sleepiness Scale, mean \pm SD	12.1 \pm 4.0	11.6 \pm 6.1
Current or prior PAP use, %	0	100

Abbreviation: PAP, positive airway pressure.

Table 2. Treatment Goal Themes Identified During Semistructured Interviews.^a

Goal theme	Treatment naïve	Prior treatment	Illustrative quotation
Improve daytime sleepiness	14 (70)	8 (100)	“For me, I’m just always fatigued. I can remember one time in the past two to three years where I actually got good sleep and felt refreshed the next day. I can’t concentrate and perform like I want to . . . so it’s fatigue for me.”
Reduce health risks	7 (35)	3 (37.5)	“My first concern is I don’t want to take the risk to have a heart attack.” “I expected that I would reverse the heart and blood pressure issues.”
Improve sleep quality	7 (35)	3 (37.5)	“I want full restful sleep at night. And I just want to be where I will be calm at night.” “Restful sleep. Not just light sensitive sleep but a deeper sleep.” “I can hardly drag myself out of bed these days.”
Improve snoring	5 (25)	4 (50)	“My main reason is to stop snoring. . . . I used to snore and they started recording me.” “Mainly so my spouse can sleep better, so noise; I guess my snoring.”
Improve concentration and memory	4 (20)		“I’m just out of it sometimes. Sometimes my boss would notice that I’m not putting focus on my job.” “Every time I get to work, I feel so lethargic and I can’t really focus on the work.”
Improve impact on professional life/driving	3 (15)	3 (37.5)	“I can’t concentrate and perform like I want to. Professionally, I need to get it together.” “Safety. I actually had a car accident because of my sleep apnea. . . . I fell asleep in the middle of the day and almost killed myself. . . . So it was mostly health and health safety that prompted me to do this.”
Reduce daytime headaches	2 (10)	2 (20)	“I was referred to sleep medicine for chronic migraines because sleep apnea and chronic migraines are connected. I’m hoping I will have fewer migraines when I’m sleeping normally.”
Improve nasal congestion	1 (5)		“I struggle daily with breathing out of my nose during the day so I’d love it if I didn’t have to worry about that.”
Decrease nighttime urinary frequency	1 (5)		“I didn’t even realize but frequency of urination. I’ve noticed in the past year, I’m constantly getting up throughout the night.”

^aNo. (%) of participants who mentioned each theme.

Table 3. Treatment Value Themes Identified During Semistructured Interviews.^a

Treatment value theme	Treatment naïve	Prior treatment	Illustrative quotation
Aversion to surgery	14 (70)		"I would look into any other option first. I think surgery would be the last"
Treatment efficacy	13 (65)	8 (100)	"I want what works the best. I don't want to beat around the bush if it's not gonna work"
Cost	8 (40)		"I was worried about cost. . . . I didn't know about the loaner thing so I came in today with a credit card. . . . When they said it was a loaner machine, I was like 'yes!'"
Convenience	5 (25)	5 (62.5)	"This is the next step for me after the oral device. I think it's the simplest next step. . . . But this is an easy thing to try to see if it'll alleviate the symptoms." "I'll pay anything just to be convenient . . . you don't have any mask to wear or put anything when you travel." "Going about my day and forgetting to clean it . . . having another thing on my to do list"
Comfort	3 (15)	4 (50)	"I'm just wondering about getting used to this machine because the feel I got [was] the continuous air going through your nose. That's not easy to get used to."

^aNo. (%) of participants who mentioned each theme.

All of the "history of treatment" group and 70% of the treatment-naïve group cited improving daytime sleepiness and fatigue as a major treatment goal. Effects of daytime sleepiness included impact on professional life, work performance, and safety while driving.

Improved health was another common treatment goal between the groups. Patients were most concerned about the cardiovascular effects of untreated OSA ("I don't want to . . . have a heart attack"). Important sleep quality considerations included achieving more restful sleep ("not just light, sensitive sleep"), waking up feeling refreshed ("I can hardly drag myself out of bed"), and improving daytime headaches.

One-third of participants wished to reduce snoring associated with OSA, with some individuals describing this as their most important goal. Some wanted to unburden their bed partners or noted negative social pressures.

When factors or values important in treatment decisions were discussed, 5 major themes arose in both groups: efficacy, cost, convenience, comfort, and aversion to surgery (**Table 3**). Cost considerations were important to 50% of the treatment-naïve cohort but not mentioned by patients with history of treatment". Convenience was a motivator ("I'll pay anything . . . [so] you don't have any mask to wear"). Many patients perceived PAP as burdensome ("another thing on my to do list everyday"). Treatment-naïve patients had concerns about PAP comfort ("wondering about getting used to this machine"). In the "history of treatment" group, patients shared experiences with discomfort related to PAP and oral appliance use ("very uncomfortable for my jaw and my teeth"). The majority of patients in the treatment-naïve group expressed an aversion to surgery and a desire to start with PAP therapy. However, no patients who had prior treatment shared this concern.

Phase 2: Survey of Patients Prior to Consultation for PAP Alternatives

A preconsultation survey was administered to 536 adult patients with a mean age of 52 years and mean AHI of 30.4 (**Table 4**). Among 503 patients who had a sleep study prior to their consultation, 90.1% had an AHI ≥ 5 . Of patients with an AHI ≥ 5 , 40% were current PAP users and 38% were previous users. When participants were asked to select any treatment goals that were important to them, 83% of respondents chose sleep quality improvement ($n = 450$) and OSA-related health risk reduction ($n = 446$). The majority also identified improvement in daytime sleepiness (73%) and reduction in snoring (65%) as important goals.

When the most important primary treatment goal was queried, health risk reduction (35%) and improving sleep quality (28%) were most frequently chosen amongst patients who completed this portion of the survey (**Table 4**). Primary treatment goal distributions differed by age <50 or ≥ 50 years ($P < .0001$), PAP use status ($P < .0001$), ESS scores ($P < .0001$), AHI level ($P < .0001$), and VAS-F scores <60 or ≥ 60 ($P < .0001$; **Table 5**). A higher proportion of patients with ESS scores >10 selected reduction in daytime sleepiness as their primary treatment goal than did patients with ESS scores ≤ 10 ($P < .0001$). Furthermore, a higher proportion of patients aged ≥ 50 years cited OSA-related health risk reduction as a primary goal than did patients aged <50 years ($P = .01$). Primary treatment goal distributions did not differ by gender or decision to pursue drug-induced sleep endoscopy or sleep surgery.

Post hoc comparisons of the most important treatment goal selections were performed based on OSA severity defined by AHI groups <5 , 5 to <15 (mild), 15 to <30 (moderate), and

Table 4. Patient Characteristics for Survey Respondents.

	Mean ± SD or No. (%)
Age, y	52.5 ± 15.0
Gender identity	
Male	395 (74)
Female	141 (26)
AHI	
<5	50 (9.9)
5 to <15	106 (21)
15 to <30	148 (29)
≥30	199 (40)
PAP use, current or prior ^a	344 (78)
Body mass index	29.0 ± 5.7
ESS score	10.0 ± 5.3
Most important treatment goal choice	
OSA-related health risk reduction	166 (35)
Sleep quality improvement	134 (28)
Daytime fatigue improvement	99 (21)
Snoring sound reduction	74 (16)

Abbreviations: AHI, apnea-hypopnea index; PAP, positive airway pressure; ESS, Epworth Sleepiness Scale; OSA, obstructive sleep apnea.

^aAmong respondents with an AHI ≥5.

≥30 (severe). Primary treatment goal distributions differed significantly among AHI groups ($P < .00001$; **Figure 1**). Choice of health risk reduction as a primary treatment goal was selected at higher rates in those with severe OSA when compared to those with mild OSA and an AHI <5. All OSA groups chose health risk reduction at higher rates than the

group with an AHI <5 (10%): mild OSA, 25% ($P = .043$); moderate OSA, 36% ($P = .001$); and severe OSA, 46% ($P < .0001$).

In comparison, a higher proportion of the group with an AHI <5 chose snoring reduction as a primary treatment goal (38%) than patients with moderate OSA (12%, $P = .0002$) and severe OSA (7%, $P < .00001$). Similarly, a higher proportion of patients with mild OSA (24%) selected snoring reduction as most important versus patients with moderate OSA ($P = .028$) and severe OSA ($P = .0001$). No differences were found by AHI group in those who chose sleep quality or daytime sleepiness improvement as the primary goal.

A comparison of the most important treatment goal was performed by history of PAP therapy. More patients without prior PAP use selected improving sleep quality (34%), while patients who had previously used but were not currently using PAP chose reducing health risk (45%). Patients using PAP were equally interested in sleep quality improvement (36%) and health risk reduction (37%; **Table 5**). On analysis of patients using PAP with an AHI ≥5 ($n = 118$), primary treatment goals differed among the mild, moderate, and severe OSA groups ($P = .0007$). Of current PAP users, health risk reduction was selected as the primary treatment goal by 44% of patients with severe OSA, whereas improving sleep quality was selected by 44% of patients with moderate OSA.

Discussion

Use of SDM for patients undergoing elective surgery has been associated with reduced decisional conflict, greater patient knowledge, and improved decision quality.^{9,10} Improved decision quality has been linked to increased treatment

Table 5. Primary Treatment Goal Distributions by Participant Subgroups.

	No.	Primary goal, No. (%)				χ^2 (df)	P value
		Reduce daytime sleepiness	Snoring reduction	Health risk reduction	Improve sleep quality		
Age, y						21.18 (3, n = 473)	<.001 ^a
<50	272	58 (29)	39 (19)	58 (29)	46 (23)		
≥50	201	41 (15)	35 (13)	108 (40)	88 (32)		
Gender identity						4.04 (3, n = 470)	.26
Women	125	32 (26)	15 (12)	46 (37)	32 (26)		
Men	345	66 (19)	59 (17)	118 (34)	102 (30)		
PAP use status						28.00 (6, n = 389)	<.001 ^a
Current user	146	24 (16)	15 (10)	54 (37)	53 (36)		
Not using	157	39 (25)	12 (8)	71 (45)	35 (22)		
Never user	86	14 (16)	21 (24)	22 (26)	29 (34)		
ESS score ^b						25.24 (3, n = 317)	<.001 ^a
>10	157	52 (33)	16 (10)	55 (35)	34 (22)		
≤10	219	28 (13)	42 (19)	83 (38)	66 (30)		
VAS-F score ^c						23.43 (3, n = 363)	<.001 ^a
<60	173	19 (11)	25 (14)	82 (47)	47 (27)		
≥60	190	55 (29)	22 (12)	55 (29)	58 (31)		

Abbreviations: PAP, positive airway pressure; ESS, Epworth Sleepiness Scale; OSA, obstructive sleep apnea; VAS-F, visual analog scale–function.

^a $P < .05$.

^bSleepiness level.

^cImpact of OSA on global function (score, 0-100).

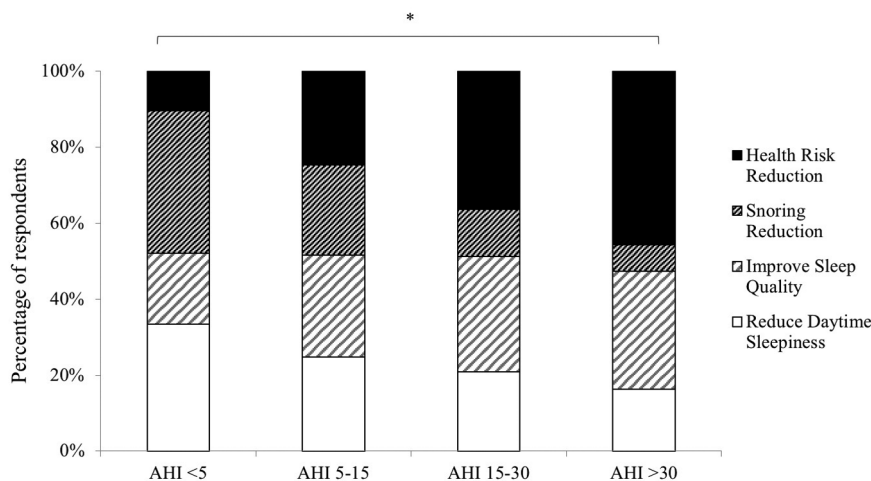


Figure 1. Primary treatment goal distributions by apnea-hypopnea index (AHI). Obstructive sleep apnea severity was associated with more patients choosing health risk reduction as their primary goal and fewer choosing snoring sound reduction. * $P < .05$.

compliance, reduced regret, and fewer appointment or surgery cancellations.¹¹ These aspects of SDM are especially pertinent to patients presenting for sleep surgery consultation, many of whom feel that they lack adequate understanding about treatment options and have a high prevalence of decisional conflict.¹ Despite the importance of SDM in adult OSA treatment planning, few data exist regarding treatment preferences and values in this population, especially for patients considering surgery. Alignment of patient-specific treatment goals to therapeutic options and expectations is essential in conversations about treatment recommendations. Therefore, characterizing the most important OSA treatment goals for patients is the first step in the SDM process.¹²

In this study, we assessed patient goals and values for OSA treatment in a qualitative analysis of patients who were newly diagnosed and who had tried OSA therapies. We identified 4 main themes for treatment goals: (1) mitigation of OSA-associated health risks, (2) reduction in daytime sleepiness and fatigue, (3) improvement in sleep quality and restfulness, and (4) reduction or termination of snoring. These findings are consistent with a prior qualitative study of PAP and oral appliance users.¹³

Our study then used goal themes to examine the most important treatment goal choice in various patient subgroups. Age (<50 or ≥ 50 years), PAP use, excessive daytime sleepiness (ESS score), degree of OSA impact on global function (VAS-F score), and OSA severity level were associated with differences in primary treatment goal. Notably, patients ≥ 50 years old were more concerned with reducing health risks than their <50-year-old counterparts, though studies on long-term effects of OSA have shown an association between age <50 years and increased all-cause mortality risk.^{14,15} Thus, patients aged <50 years may benefit from increased education on the health outcome implications of untreated OSA. Age may also influence perceptions of mortality.¹⁶

Meanwhile, patients with severe OSA and prior (noncurrent) PAP therapy were more likely to select health risk reduction as primary goal, matching the general understanding that

patients with severe and untreated OSA are at higher risk of cardiovascular morbidity than those with mild and treated OSA.¹⁷ Conversely, more patients who had never tried PAP cited improving sleep quality as a primary goal.

Analysis of a subset of patients who pursued drug-induced sleep endoscopy or sleep surgery did not demonstrate an association between primary treatment goals and ultimate decision to pursue these procedures. This finding has been shown in other surgical fields and is expected, as treatment goals and values may change over time and identification of patient treatment goals and values is just one component of the decision-making process.¹⁸

The findings of this study can be utilized in 3 ways. First, understanding treatment goal categories aids in patient counseling. Advantages and disadvantages of treatment options should be based on the abilities of each modality to achieve or not achieve patient-specific treatment goals. This core discussion is the basis of SDM and defines treatment success that is specific and personalized.

Second, our findings identify gaps in knowledge and research needs. Comparative work is needed to understand each treatment modality's ability to not only improve AHI but also achieve common patient treatment goals of reducing daytime sleepiness, snoring sound, and cardiovascular health risk and improving sleep quality. There is limited long-term comparative objective analysis on the ability of PAP versus oral appliances versus surgery types in reducing or terminating snoring sounds.¹⁹⁻²² Similarly, data on health risk reduction with treatment are controversial. Prospective cohort studies have shown significant risks for cardiovascular morbidity and mortality in patients with OSA and risk reduction with PAP therapy.^{17,23-25} However, randomized controlled trials have not demonstrated measurable benefits of PAP in reducing cardiovascular risks, though duration of nightly PAP use was low in these studies.^{26,27} In terms of surgical outcomes, a retrospective review of >54,000 patients with OSA found that soft tissue surgery was associated with lower rates of cardiovascular, neurologic, and endocrine complications as compared with PAP; yet, no prospective controlled studies have

examined surgical outcomes.²⁸ Further studies of OSA treatment outcomes should align with the major patient-defined goals and expectations to allow clinicians to counsel according to factors that matter most to patients.

Third, characterization of common treatment goals is the first step in designing decision tools to help with the education and decision-making process. Treatment goals for adult OSA are often considered only in the context of objective metrics such as AHI, symptom inventories (ie, ESS), and impact on associated comorbidities.²⁹ As recently noted by Malhotra et al, the chief complaint of the patient with OSA may too often be overlooked.³⁰ Prior studies have demonstrated that patient and provider goals in recommending or selecting an optimal treatment frequently conflict.¹⁸ Thus, it is important to respect patient perspectives in consideration of treatment outcomes and incorporate these into development of SDM tools (ie, decision aids). Patient-defined treatment goals may also be used to define treatment success and, when not achieved, to serve as an impetus to consider other treatment modalities in a comprehensive approach.

This study has a few limitations. It was conducted with patients recruited from two sites within the San Francisco Bay Area. Thus, differences in findings between the treatment-naïve and “history of treatment” groups may be influenced by the disparate populations based on location. Regional and socioeconomic effects on the findings were not analyzed, limiting generalizability of the results. In addition, our survey focused on the four most commonly cited treatment goals from semistructured interviews with patients with OSA, and patients may have primary treatment goals beyond these. Future studies are needed to evaluate treatment goals specific to patients who undergo sleep surgery and to understand roles of multiple goals in surgical decision making. Future work should also investigate the influence of prior patient education and research on treatment goals and decision making.¹

Conclusions

Adult patients with OSA most commonly report treatment goals that can be categorized into reducing OSA-related health risks, improving sleep quality, reducing daytime sleepiness, and improving snoring. Primary treatment goal choices were associated with OSA severity, age, levels of daytime sleepiness, PAP use history, and impact of OSA on global function. Understanding and querying patient-specific goals are essential first steps in the SDM process where the conversation focuses on the ways that different treatments may or may not meet personalized goals. Ultimately, goal-focused discussions ensure alignment of priorities and definitions of success between the patient and the provider.

Authors' Note

Jolie L. Chang is now affiliated to Surgery Service, Department of Veterans Affairs Medical Center, San Francisco, California, USA.

Author Contributions

Yi Cai, data collection, data analysis and interpretation of results, manuscript preparation; **Priyanka Tripuraneni**, data collection, data analysis and interpretation of results, manuscript preparation; **Arushi Gulati**, data collection, data analysis and interpretation of results, manuscript preparation; **Erika M. Stephens**, data collection, data analysis and interpretation of results; **Dang-Khoa Nguyen**, data collection, data analysis and interpretation of results; **Megan L. Durr**, study design and supervision, manuscript preparation; **Jolie L. Chang**, study design, data collection and interpretation, supervision, manuscript preparation.

Disclosures

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Supplemental Material

Additional supporting information is available in the online version of the article.

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