



## Scientific Research Report

## Knowledge and Attitude of Dentists Towards Obstructive Sleep Apnea

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## ABSTRACT

**Background:** Obstructive sleep apnoea (OSA) is the most common sleep-related breathing disorder. Dentists should play an essential role in OSA screening, referral, and management. However, few studies have investigated dentists' knowledge and attitude towards OSA.

**Objective:** This cross-sectional survey aimed to assess the level of knowledge and attitude regarding OSA amongst dentists and evaluate whether the level of knowledge affects their attitude towards OSA.

**Methods:** Using the Google Forms platform, an online questionnaire was distributed via e-mail to all Ministry of Health dentists (N = 352). The questionnaire included 3 sections: demographics, knowledge, and attitude. Participant responses were stratified by professional title (general dentists, specialists, or consultants) and practice sector (primary health care centres or hospitals). Descriptive statistics, independent t tests, one-way analyses of variance, and Pearson's correlation were used to analyse the data.

**Results:** Of the 352 dentists, 191 responded to the questionnaire (54.55%). Although 80.6% of the respondents reported having previous OSA knowledge in the self-assessment question, 65.58% scored below 12 in the total knowledge scores, and 63.35% scored below 3 in the total attitude scores based on Bloom's cutoff. The mean total knowledge score was 9.86, while the mean total attitude score was 2.08. No significant differences between the mean total knowledge and attitude scores were found based on sex, professional title, or practice sector. A positive and statistically significant correlation was found between total knowledge and attitude scores (P value = .001).

**Conclusions:** This study showed that dentists had a low OSA-related knowledge and a negative attitude towards OSA, and a positive association was seen between knowledge level and attitude. Dental practitioners with high knowledge scores tended to have a positive attitude towards OSA. These findings suggest that dentists in Jeddah require more education and clinical training in sleep medicine to maximise patient benefits and minimise adverse outcomes.

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## Introduction

Healthy individuals spend roughly one-third of their lives asleep, and adequate sleep is a vital indicator of overall body health and function.<sup>1</sup> Of the many sleep-related breathing disorders that disrupt regular sleep cycles, obstructive sleep apnoea (OSA) is the most common.<sup>2</sup> It is a clinical disorder

that induces recurrent episodes of complete or partial obstruction of the upper airway occur for more than 10 seconds despite persistent respiratory efforts.<sup>3,4</sup> In addition to loud snoring with choking or air gasping,<sup>5</sup> OSA induces frequent sleep fragmentation and repetitive arousal.<sup>6</sup> The interruption of sleep continuity leads to further consequences, included fatigue, headache, and cognitive impairment.<sup>4,7</sup> Moreover, repetitive airway obstruction can cause hypoxia and hypercapnia, thereby severely affecting the body's metabolic and cardiovascular systems.<sup>6,8</sup> Undiagnosed or untreated OSA has further been implicated as a risk factor for

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developing insulin-resistant diabetes, systemic hypertension, and acute myocardial infarction.<sup>9-11</sup>

OSA is considered a global health issue because of its high prevalence in the general population.<sup>2-15</sup> The prevalence of OSA in the United States was estimated to be 3% to 7% in males and 2% to 5% in females.<sup>10,12,16</sup> The severity of OSA is usually measured using the apnea-hypopnea index (AHI), which is defined as the number of apnoea or hypopnea events per hour of sleep.<sup>17</sup> According to the American Academy of Sleep Medicine (AASM), OSA is diagnosed when AHI exceeds 15 or falls below 5 in the presence of associated signs and symptoms.<sup>18</sup> In Saudi Arabia, the overall prevalence of OSA, as defined by the AASM, was 8.8%.<sup>19</sup>

Male patients aged  $\geq 40$  years who are obese and have a neck size of more than 18 inches are at high risk of having OSA.<sup>20</sup> The presence of various craniofacial anatomical variables reduces the upper airway patency and might contribute to the development of OSA.<sup>21,22</sup>

Implementing an appropriate screening protocol for new OSA cases, followed by a proper referral to sleep physicians for sleep studies and treatment, is usually performed by dentists.<sup>23,24</sup> Hence, the high prevalence of undiagnosed OSA is mainly due to the lack of appropriate knowledge and training amongst dentists.<sup>25,26</sup> The AASM, the American Academy of Dental Sleep Medicine (AADSM), and the American Dental Association (ADA) state that a dentist's role in OSA management is to identify cases of OSA, refer at-risk patients, and provide oral appliances such as mandibular advancement devices.<sup>27,28</sup>

Most previous OSA studies were performed in medical fields other than dentistry, and very few have been performed by dental researchers.<sup>29-38</sup> The latter found knowledge and clinical training concerning sleep disorders in dental schools to be lacking. One study investigated the extent of the knowledge about OSA amongst dental students, interns, practitioners, and faculty members in Riyadh, Saudi Arabia, and found that of the 450 participants, 20% did not know what OSA meant.<sup>34</sup> However, the level of knowledge and the attitude of dental practitioners at the Ministry of Health concerning OSA remains unclear.

This cross-sectional survey aimed to assess the knowledge and attitudes of the Ministry of Health-affiliated dentists regarding OSA in primary health care (PHC) centres and hospitals in Jeddah, Saudi Arabia. Additionally, this survey evaluated the relationship between their level of knowledge and attitude towards OSA.

## Methods

### Study population

This cross-sectional survey included all general dentists (having a bachelor's degree), specialists (having specialty training with a master's degree), and consultants (having specialty training with board certification or a doctorate degree) who were employed in 2020 at the Ministry of Health in Jeddah, Saudi Arabia. The study protocol was approved by the General Directorate of Research & Studies, Jeddah Health Affairs, Ministry of Health, Saudi Arabia (Reference number: A00849).

A list of all dental employees in 6 hospitals and 43 PHC centres was obtained. There were 352 licensed dental practitioners, including 186 general dentists, 67 specialists, and 99 consultants; 261 individuals of this sample worked at hospitals and 91 at PHC centres. The required total sample size was calculated using the Raosoft sample size calculator. By setting a 50% response rate, a 5% margin of error, and a 95% confidence interval, the minimum required total sample size was 184.

### Study instrument

Adapted from OSA's relevant literature and dental guidelines,<sup>24,27,28,30,31</sup> the questionnaire was delivered via an e-mail that was administered in the English language and prepared using the Google Forms platform.

The questionnaire was initiated with an invitation message, followed by a consent agreement for participation. The questionnaire included 3 sections that queried the respondents' demographic information, knowledge concerning OSA, and attitude towards OSA. Demographic characteristics included sex (male or female), professional title (general dentist, specialist, or consultant), and practice sector (PHC or hospital).

The knowledge section began with a yes-or-no self-assessment question as follows "Do you have a previous knowledge of obstructive sleep apnea (OSA)?," followed by asking the source of the responder's knowledge. If "yes" was selected in the self-assessment question, 20 knowledge statements would be presented to evaluate the dentist's exact extent of knowledge concerning OSA: specifically prevalence, symptoms, diagnosis, risk factors, treatment, and the dentist's role in its management. Possible responses included "true," "false," and "do not know." The total knowledge scores (range 0-20) for each respondent were calculated, with 1 point awarded for a correct answer and none for an incorrect one. The "do not know" option was included to minimise the guessing effect and was scored as incorrect. The total knowledge scores were categorised into 3 levels based on Bloom's cutoff: high level, moderate level, and low level (Table 1).<sup>39</sup> The mean total knowledge score was also determined. If "no" was selected in the self-assessment knowledge question, the Google form immediately redirected the participants to the attitude section.

The attitude section consisted of 5 questions; 2 questions were related to the importance subscale, which assessed the importance of knowing OSA in dentistry and screening all

**Table 1 – Bloom's cutoff categories for the total knowledge and attitude scores.**

	Category	Scores (%)	n	%
<b>Knowledge</b>	High level	16-20 (80%-100%)	8	5.2%
	Moderate level	12-15 (60%-79%)	45	29.22%
	Low level	<12 (<60%)	101	65.58%
<b>Total</b>			154	100%
<b>Attitude</b>	Positive Attitude	4-5 (80%-100%)	20	10.47%
	Neutral Attitude	3 (60%-79%)	50	26.18%
	Negative Attitude	<3 (<60%)	121	63.35%
<b>Total</b>			191	100%

dental patients for possible OSA. The other 3 questions comprised the confidence subscale, which evaluated a dentist's confidence to use screening tools to identify at-risk patients, their ability to fabricate oral appliances, and their knowledge of the referral system to sleep physicians in their practice. Response scales in the attitude section included "yes" (1 point awarded, indicating positive attitude) or "no" or "do not know" (no points awarded, indicating negative attitude). The total attitude scores were calculated for each respondent and categorised into 3 levels based on Bloom's cutoff: positive attitude, neutral attitude, and negative attitude (Table 1).<sup>39</sup> The total attitude and subscales means were also computed.

The questionnaire's validity was evaluated by 4 OSA experts at our university. The experts reviewed the relevance, readability, clarity, and comprehensiveness of the knowledge and attitude items. The questionnaire was then piloted by 15 general dentists and 10 consultants at our university to determine whether the questionnaire's items were clear and understandable. The study team reviewed the participants' responses, performed the necessary modifications, and concluded the final survey.

### Study design

An invitation e-mail with a survey link was sent to all dentists (N = 352). Nonrespondents were contacted 3 times over 8 weeks. One week after the initial e-mail, the first e-mail reminder was sent to nonrespondents with a link. This was followed by a second reminder 2 weeks later. The last e-mail reminder was sent 3 weeks after the second one.

### Statistical analysis

All statistical analyses were performed using the IBM SPSS Statistics for Macintosh v26 (IBM). The data were normally distributed based on the Shapiro-Wilk test (P value = .089). Descriptive statistics, the independent t test, and the one-way analyses of variance (ANOVA) were used, when appropriate, to analyse the results. Pearson's correlation analysis was used to assess the relationship amongst the total knowledge, attitude scores, and attitude importance and confidence

subscales. A P value of less than .05 was considered to indicate statistical significance.

### Results

Of the 352 dental practitioners who received the online questionnaire, 191 responded (54.55%). Most of the respondents were female (56.55%) or general dentists (51.83%). Specialists and consultants accounted for 18.84% and 29.31% of the respondents, respectively. The majority of the respondents practiced in hospitals (73.29%; Table 2).

In the self-assessment of previous knowledge concerning OSA, 80.63% (n = 154) of the respondents selected "yes." The reported sources of the OSA-related knowledge were dental school (39.8%), self-taught (28.8%), postgraduate training (22%), and conferences (18.8%).

In the knowledge section, 65.58% of the respondents earned a total knowledge score of below 12 (<60%), which indicated a low level of OSA-related knowledge (Table 1). Four respondents earned the lowest total knowledge scores (2), while 2 (1 consultant and 1 general dentist) received the highest scores (19). The mean total knowledge score amongst the 154 respondents was 9.86 (SD ± 3.57). The most correct responses (92.9%) were in response to question 5. The lowest percentage of correct responses (11%) was observed in response to question 10. In addition, more than 60% of the respondents supplied the correct answer only to 6 of the 20 questions in the knowledge section (Table 3).

A low level of knowledge was observed in terms of dentists' roles regarding OSA diagnosis and treatment based on Bloom's cutoff. About 44.8% of respondents acknowledged that dentists could not diagnose OSA, and 53.2% were aware that dentists could provide oral appliances to treat mild and moderate OSA as per sleep physicians prescription. However, a high level of knowledge was noted for dentists' roles in OSA referral. Around 84.4% of respondents knew that the dentists' roles included the referral of potential at-risk patients to sleep physicians (Table 3).

The mean total knowledge scores were 9.72 amongst the 88 female respondents and 10.06 amongst the 66 male respondents, with no statistically significant differences between the men and women (P value = .55). In addition, the

**Table 2 – Demographic characteristics of study respondents.**

Demographics	n	%	Total knowledge scores		Total attitude scores	
			Mean ± SD	P value	Mean ± SD	P value
Sex	Female			0.555		0.204
	Male	108	56.5%	9.72 ± 3.33		1.99 ± 1.09
Professional title		83	43.5%	10.06 ± 3.88		2.20 ± 1.22
	General dentist				0.354	0.209
	Specialist	99	51.8%	9.40 ± 3.79		1.95 ± 1.22
Practice sector	Consultant	36	18.8%	10.15 ± 3.25		2.14 ± 1.05
	Primary health care hospital	56	29.3%	10.28 ± 3.45		2.28 ± 1.07
Practice sector				0.247		0.146
	Primary health care hospital	51	26.7%	9.27 ± 3.73		1.88 ± 1.21
Total		140	73.3%	10.05 ± 3.51		2.15 ± 1.12
		191	100%			

Data are presented as mean ± SD or n (%), appropriately.

**Table 3 – Frequencies and percentages of respondents' OSA total knowledge.**

Questions	True n (%)	False n (%)	Don't know n (%)
In Saudi Arabia, the overall prevalence of OSA as defined by the American Academy of Sleep Medicine was 8.8%.	34 (22.1%)	3 (1.9%)	117 (76%)
OSA is described as frequent episodes of partial or complete obstruction of the upper airway for at least 60 seconds with accompanied respiratory efforts.	116 (75.3%)	24 (15.6%)	14 (9.1%)
OSA is more common in women than men.	20 (13%)	94 (61%)	40 (26%)
OSA leads to sleep fragmentation and hyperoxia.	102 (66.2%)	35 (22.7%)	17 (11%)
Bed partners usually complain of loud snoring and/or breathing interruption during sleep (observed apnoea).	143 (92.9%)	4 (2.6%)	7 (4.5%)
Type 2 diabetes mellitus may be linked to OSA.	59 (38.3%)	18 (11.7%)	77 (50%)
The gold standard of OSA diagnosing is polysomnography.	69 (44.8%)	6 (3.9%)	79 (51.3%)
Some OSA patients complain of fatigue, daytime sleepiness, morning headaches and/or wake with breath-holding, choking, or gasping.	137 (89%)	5 (3.2%)	12 (7.8%)
OSA is more common in people with low body mass index.	6 (3.9%)	113 (73.4%)	35 (22.7%)
Maxillofacial abnormalities that increase the risk of having OSA are retrognathia, micro-glossia, tonsillar hypertrophy, or uvular elongation.	119 (77.3%)	17 (11%)	18 (11.7%)
Dentists are responsible for OSA cases diagnosis.	52 (33.8%)	69 (44.8%)	33 (21.4%)
OSA is common in people with a neck circumference of less than 18 inches.	25 (16.2%)	31 (20.1%)	98 (63.6%)
Some orofacial pain and bruxism are linked to OSA.	61 (39.6%)	31 (20.1%)	62 (40.3%)
The dentist's role is to refer potential patients who are at high risk of OSA to a sleep physician.	130 (84.4%)	6 (3.9%)	18 (11.7%)
Untreated or undiagnosed OSA could predispose patients to systemic hypertension.	76 (49.4%)	14 (9.1%)	64 (41.6%)
Dentists could prescribe oral appliances to treat mild and moderate OSA patients without referral to sleep physicians.	44 (28.6%)	82 (53.2%)	28 (18.2%)
Untreated OSA is associated with an increased risk of mortality (heart attack or stroke).	107 (69.5%)	6 (3.9%)	41 (26.6%)
OSA is seen more in people younger than 40.	9 (5.8%)	85 (55.2%)	60 (39%)
Continuous positive airway pressure (CPAP) is the first line of treatment for mild, moderate, and severe obstructive sleep apnea.	75 (48.7%)	20 (13%)	59 (38.3%)
Untreated OSA put the patients at high risk of automobile accidents.	78 (50.6%)	22 (14.3%)	54 (35.1%)

Highlighted areas indicate the correct answers. Data are presented as n (%).  
OSA, obstructive sleep apnoea.

mean total knowledge scores did not significantly differ between respondents who were practicing at hospitals (10.05) and those practicing at PHC centres (9.27) ( $P$  value = .247). The one-way ANOVA analysis found no significant differences in total knowledge scores amongst general dentists (9.4), specialists (10.15), and consultants (10.28) ( $P$  value = .354) (Table 2).

The total attitude scores for most respondents (63.35%) were below 3, indicating a negative attitude (Table 1). In the importance subscale of the attitude section, 86.9% of the respondents acknowledged the importance of OSA

knowledge in dentistry (positive attitude), but only 45% believed that dentists' screening of all patients for possible OSA is important (negative attitude). In the confidence subscale (all negative attitude), 28.8% of respondents were confident in using screening tools to identify patients at risk for OSA, 33.5% were confident in providing oral appliances, and 14% knew the referral protocol to the sleep medicine department in their workplace (Table 4).

The mean total attitude score was 2.08 (SD  $\pm$  1.15) amongst the 191 respondents, while the importance and confidence subscales were 1.32 (SD  $\pm$  0.68) and 0.76 (SD  $\pm$  0.81), respectively.

**Table 4 – Frequencies, percentages, means, and SD of attitude questions.**

Subscales	Questions	Yes n(%)	No n(%)	Don't know n(%)	Mean $\pm$ SD
Importance	In your opinion, is it important for dentists to have knowledge of OSA as a clinical disorder?	166 (86.9%)	10 (5.2%)	15 (7.9%)	1.32 $\pm$ 0.68
	In your opinion, should dentists screen all patients for possible OSA?	86 (45%)	77 (40.3%)	28 (14.7%)	2.08 $\pm$ 1.15
Confidence	Are you confident to use any of the OSA screening tools to identify patients at risk?	55 (28.8%)	87 (45.5%)	49 (25.7%)	0.76 $\pm$ 0.81
	If a sleep physician referred a mild or moderate OSA case to your clinic, are you confident to fabricate an oral appliance?	64 (33.5%)	81 (42.4%)	46 (24.1%)	
	Does your workplace have a distinct referral protocol to collaborate with the sleep medicine department?	27 (14.1%)	101 (52.9%)	63 (33.1%)	

Data are presented as mean  $\pm$  SD or n (%).

**Table 5 – Pearson's correlations coefficient amongst attitude subscales, total knowledge, and total attitude scores.**

	1	2	3	4
Importance subscale	1			
Confidence subscale	0.173*	1		
Total attitude scores	0.717**	0.810**	1	
Total knowledge scores	0.158	0.213**	0.255**	1

\* P value &lt; .05.

\*\* P value &lt; .01.

The mean total attitude scores did not differ between the 83 male and 108 female respondents (2.20 vs 1.99;  $P$  value = .204). Moreover, there were no significant differences in the mean total attitude scores between the 140 respondents who practiced at hospitals (2.15) and 51 respondents who practiced at PHC centres (1.88) ( $P$  value = .146). The one-way ANOVA did not reveal a significant difference in the total attitude scores ( $P$  value = .209) between different professional titles.

Moreover, Pearson's correlation coefficient demonstrated a weakly positive and statistically significant correlation between total knowledge and attitude scores ( $r = 0.255$ ,  $P$  value = .001). A significant positive association was also found between the attitude importance and confidence subscales ( $r = 0.173$ ,  $P$  value = .017), and between total knowledge score and confidence subscale ( $r = 0.213$ ,  $P$  value = .008). However, total knowledge did not show positive correlation with the importance subscale (Table 5).

## Discussion

Dentists are often the first-contact health care providers who assist in detecting, referring, and managing numerous undiagnosed OSA cases.<sup>26</sup> A patient's routine dental visits and the dentist's accessibility to examine the upper airway facilitate screening patients for OSA. Thus, dentists' suboptimal education in dental school regarding OSA may contribute to the increased number of undiagnosed cases and associated risks.<sup>14,15</sup> This cross-sectional survey provides baseline information and elucidates the relationship between the knowledge and attitudes of different dental professionals towards OSA in two practice settings under the Ministry of Health, Jeddah, Saudi Arabia.

The online self-administered questionnaire was emailed to all dentists ( $N = 352$ ), followed by 3 reminders that were emailed to the nonrespondents over 8 weeks. The response rate was 54.55%, which is similar to the average response rate for online surveys (50.5%) observed in other studies.<sup>40</sup>

Most respondents (80.6%) indicated that they had previous knowledge of OSA in the self-assessment question. In the total knowledge assessment part of the questionnaire, 65.58% of respondents scored less than 60%, and the mean total knowledge score (9.86) was below the cutoff of 12, indicating a low level of OSA-related knowledge amongst the respondents. The low scores on fundamental OSA knowledge were incongruent with the high rate of self-affirmed knowledge, which might suggest the presence of acquiescence or desirability bias. On the other hand, most respondents knew common OSA signs and symptoms and could answer pertinent questions correctly and, hence, knowledge of the signs and

symptoms of OSA might contribute to the high percentage of respondents who reported being knowledgeable of OSA.

OSA is an independent risk factor for cardiovascular diseases and diabetes mellitus.<sup>9-11</sup> Despite practicing in a country with diabetes mellitus and hypertension epidemics, 61.7% of the respondents were unaware of the connection between OSA and diabetes, while 50.6% did not know about the connection between OSA and hypertension. Comparable results were found by Alansari et al., who showed that Saudi dental interns had insufficient knowledge of the association between OSA and diabetes (66% answered incorrectly) and hypertension (58% answered incorrectly).<sup>32</sup> Dentists' awareness of the consequences of OSA, if left undiagnosed or untreated, would maximise OSA screening, help in its early diagnosis, avoid delayed referral, and minimise the associated economic and health burden.

The mean total knowledge score did not significantly differ between the respondents according to sex, practice sectors, or professional titles. Unexpectedly, we found similar knowledge levels concerning OSA amongst specialists and consultants with advanced educational backgrounds and general dentists. This result agrees with those of Jokubauskas et al., who found no difference in OSA-related knowledge between general dentists and specialists; they attributed the findings to the small number of responding specialists and their age.<sup>31</sup> In contrast, Vuorjoki-Ranta et al. showed that dental specialists knew more about OSA because of their advanced educational levels.<sup>30</sup> The lack of significance in the present study could be due to more rigorous incorporation of dental sleep medicine topics in the pregraduate programme curriculum, raising OSA awareness amongst contemporary general dentists.

The ADA and AADSM published clinical practice guidelines on dentists' roles in OSA treatment.<sup>24,27,28</sup> Respondents in the current investigation exhibited disparate knowledge levels regarding dentists' roles. The dentists had a low level of knowledge regarding their roles in OSA diagnosis and treatment, but a higher level of knowledge regarding their roles in OSA referral. Insufficient knowledge of dentists' roles could be deduced from their desire to refer patients to specialised sleep physicians to avoid the liability risk. Therefore, raising awareness regarding their role and educating them about OSA management could improve support given to OSA patients seeking health care.

Our results revealed an overall negative attitude of respondents (63.35%) towards OSA. Most respondents believed that screening all patients for possible OSA is unnecessary because they were not confident in using screening tools, treating with oral appliances, and referring to the sleep medicine department. Only one question showed a positive attitude of respondents in the attitude section regarding the importance of OSA knowledge for dentists. Appreciating the importance of OSA knowledge indicates the respondents' willingness to learn more about OSA. Knowledge deficits lead to a lack of dentists' confidence in OSA diagnosis and management, leading to the respondents' defeatist attitude, impeding appropriate patient care. A greater emphasis on dentists' education regarding this matter can boost their confidence levels in OSA management.

All respondents expressed the same negative attitude towards OSA across the different demographics. The

similarity in the respondents' opinions, beliefs, and confidence in OSA management could be due to the lack of proper OSA-related education and clinical training in dental schools. Dentists are encouraged to enhance sleep medicine education after graduation through continuous education courses or conferences or reading related articles to enable confidence, better practice, and enhanced patient care.

Although weak, a positive and significant relationship was found between the total knowledge and attitude scores towards OSA, specifically the confidence subscale. Dentists with high knowledge scores tend to have a positive attitude towards OSA and greater confidence in OSA diagnosis and treatment. Moreover, a positive and significant association was found between importance and confidence subscales, indicating that respondents who appreciate the importance of OSA as a clinical disorder had greater confidence in screening and treating patients with OSA. Therefore, raising the dentists' knowledge level towards OSA would improve their attitudes and confidence levels.

The present study is subject to limitations. First, this survey was conducted in Jeddah city. Therefore, the present findings cannot be generalised to all dental practitioners in other Saudi regions. Hence, further studies are needed to investigate whether dental practitioners in other Saudi cities have similar levels of knowledge concerning OSA. Second, the questionnaire was constructed for our specific population. A thorough review of the literature revealed no validated questionnaires.

In conclusion, this cross-sectional study showed that the Ministry of Health dentists in Jeddah had a low level of OSA-related knowledge and a negative attitude towards OSA management as well as a weak positive relationship between total knowledge and attitude scores. As the majority of dentists acknowledged the importance of OSA-related topics in dentistry but had lower confidence in OSA screening and management, an educational alerting initiative, which focuses on educating and training all dentists to screen their dental patients, is needed to reduce the risk of OSA and improve health-related quality of life amongst patients with OSA. Urgent intervention is also required to educate dental practitioners about existing referral protocols.

### Conflict of interest

None disclosed.

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