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Quality of life in children and adolescents with overweight or obesity: Impact of obstructive sleep apnea

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ABSTRACT

Objectives: To investigate the association between obstructive sleep apnea (OSA) and health related quality of life (HRQOL) in children and adolescents referred to an obesity treatment clinic. In addition, we examined the association between body mass index standard deviation score (BMI SDS) and HRQOL comparing children and adolescents with overweight or obesity without OSA with a control group of children and adolescents with normal weight without OSA.

Methods: This cross-sectional study included 130 children and adolescents with overweight or obesity (BMI SDS > 1.28) aged 7–18 years recruited from an obesity treatment clinic. The control group consisted of 28 children and adolescents with normal weight (BMI SDS ≤ 1.28) aged 7–18 years recruited from schools. Sleep examinations were performed using a type 3 portable sleep monitor, Nox T3. OSA was defined as apnea-hypopnea index (AHI) ≥ 2. HRQOL was measured by the Pediatric Quality of Life Inventory (PedsQL) 4.0 generic core scale.

Results: A total of 56 children and adolescents with overweight or obesity were diagnosed with OSA (43%). The children and adolescents with OSA were older ($p = 0.01$) and had higher BMI SDS ($p = 0.04$) than children and adolescents without OSA. In generalized linear regression analyses adjusted for age, sex, BMI SDS and pubertal development stage there was no association between OSA or AHI and HRQOL in children and adolescents with overweight or obesity. In the analysis, including children and adolescents without OSA and the normal-weight control group, the generalized linear regression adjusted for age, sex and AHI revealed an association between BMI SDS and HRQOL ($p < 0.001$).

Conclusion: We found no association between AHI or OSA and HRQOL in children and adolescents with overweight or obesity. However, we found an association between BMI SDS and HRQOL in children and adolescents without OSA.

1. Introduction

Obstructive sleep apnea (OSA) is a disorder during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction that disrupts normal ventilation during sleep [1]. OSA is a common problem in children and adolescents with overweight or obesity compared with children and adolescents with normal weight [1–3]. The prevalence rate of OSA in children and adolescents with overweight or obesity ranges between 13-59% in previous studies [4,5].

OSA in children and adolescents is associated with several serious comorbidities such as cardiovascular complications [1], neurocognitive deficits [1,6], behavioral problems and metabolic derangements [1]. Health related quality of life (HRQOL) may also be affected by the presence of OSA in children and adolescents [7,8]. Several studies have found that HRQOL improves after adenotonsillectomy [9–12], which is considered first line treatment for OSA in children [1], suggesting that

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OSA may be associated with HRQOL. Only a few studies have investigated the association between OSA and HRQOL [7,8,13,14], and most of these studies included children and adolescents recruited from sleep clinics on suspicion of OSA [8,13,14]. Three studies compared a group of children with OSA with a group of children without OSA [7,13,14], but only one study examined the association between OSA and HRQOL in a population of children and adolescents with overweight [14]. In addition, the previous findings are ambiguous. Two of the studies found an association between OSA severity and HRQOL [7,8]. On the contrary, two other studies found no association between OSA and HRQOL [13,14], but found an association between symptoms of OSA and HRQOL.

HRQOL may also be affected by other factors such as age [15–20], sex [15,16,18–21] and body mass index standard deviation score (BMI SDS) [15,17,21–26]. Given the high prevalence of OSA in children and adolescents with overweight or obesity and the ambiguous previous findings regarding the association between OSA and HRQOL more knowledge in this area is required.

We conducted a cross-sectional study investigating the association between OSA and HRQOL, measured by the Pediatric Quality of Life Inventory (PedsQL) 4.0, in children and adolescents referred to an obesity treatment clinic. We hypothesized that HRQOL was associated with the apnea-hypopnea index (AHI) or the presence of OSA in children and adolescents with overweight or obesity. Furthermore, we conducted an analysis to investigate the association between BMI SDS and HRQOL comparing children and adolescents with overweight or obesity without OSA with a control group of children and adolescents with normal weight without OSA.

2. Material and methods

2.1. Design and study population

In this cross-sectional study, children and adolescents with overweight or obesity were recruited while entering the multidisciplinary treatment program at the Children's Obesity Clinic, Department of Pediatrics, Holbæk University Hospital, Denmark, from June 2015 to July 2016. The inclusion criteria were BMI SDS > 1.28 equivalent to the 90th percentile [27] and age 7–18 years. The exclusion criteria were neuromuscular disease, craniofacial syndromes/abnormalities and laryngeal and/or tracheal malformations. The inclusion of participants has been described in detail previously [4].

A group of children and adolescents with normal weight without OSA were included in the study as control group. They were recruited from schools on Zealand, Denmark. The inclusion criteria for the normal-weight group were BMI SDS in the normal range [i.e. $-1.28 <$ BMI SDS ≤ 1.28] and age 7–18 years. The exclusion criteria were the same as for the group of children and adolescents with overweight or obesity.

2.2. Health related quality of life

HRQOL of all participants was assessed through the PedsQL 4.0 generic core scale. It is a validated 23-items questionnaire assessing physical, emotional, social and school functioning [28]. The PedsQL has been shown to be able to differentiate between healthy children and children with acute and chronic diseases [29,30]. The participants were asked to complete the PedsQL upon entry in the study. The PedsQL is age-specific and is separated into the following age categories: 5–7, 8–12 and 13–18 years. The participants were asked how much of a problem each item had been for them during the past one month. The response consisted of a five-point rating scale for the 8-12 year-olds and 13-18 year-olds (0 = never, 1 = almost never, 2 = sometimes, 3 = often, 4 = almost always) and a three-point rating scale for the 5-7 year-olds (0 = not at all, 2 = sometimes, 4 = a lot). Subsequently, the scores were transformed into a scale from 0 to 100 (0 = 100, 1 = 75, 2 = 50, 3 = 25, 4 = 0). A higher score indicated a higher HRQOL. Scale scores for the categories, physical, emotional, social and school, were calculated by dividing the sum of the scores in each category by the number of questions answered in each category, thereby accounting for unanswered questions. A psychosocial scale score was calculated as a weighted mean of the emotional, social and school scale scores. A total scale score was calculated as a weighted mean of the physical, emotional, social and school scale scores. If more than 50% of the questions in one scale were not answered the scale score was not calculated and therefore not included in the total scale score or the psychosocial scale score. The participants were excluded, if they did not complete the PedsQL questionnaire at all or if they completed the PedsQL more than 10 days prior to or after the sleep examination.

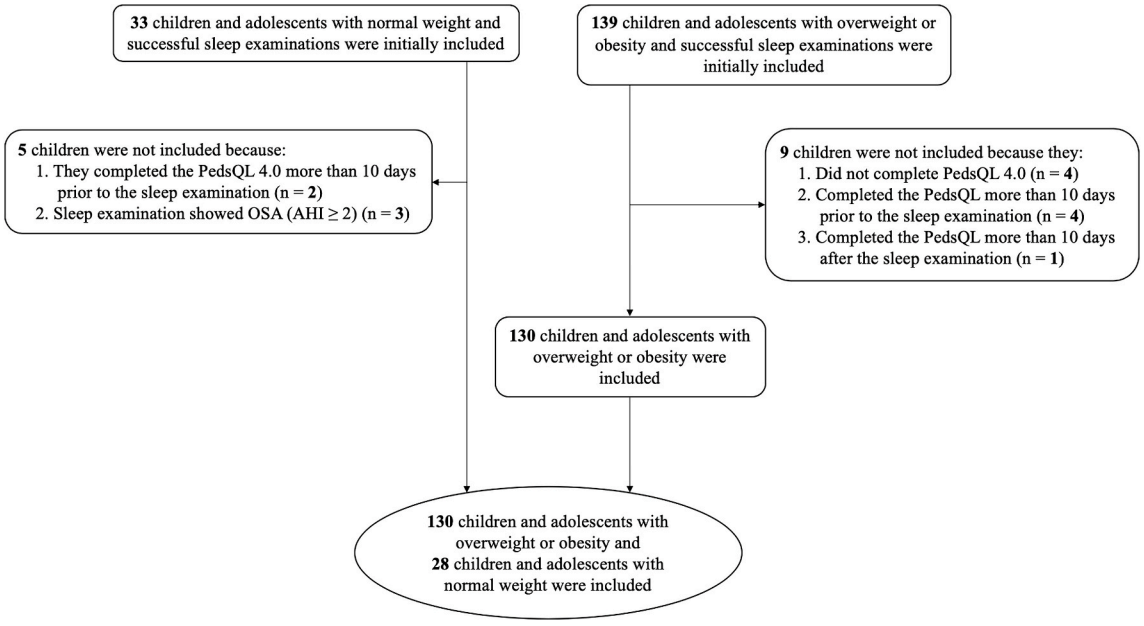

Fig. 1. Flow chart demonstrating the inclusion of children and adolescents in the study.

Table 1
Comparing children and adolescents with overweight or obesity with or without OSA.

	OSA (AHI ≥ 2) (n = 56)	*Non-OSA (AHI < 2) (n = 74)*	p-value
Sex (n (%))			
Boys	24 (42.9)	30 (40.5)	0.7
Girls	32 (57.1)	44 (59.5)	
Age (mean (SD))	13.1 (2.7)	11.8 (2.7)	**0.01**
BMI SDS (mean (SD))	3.0 (0.6)	2.8 (0.5)	**0.04**
Pubertal development (n (%))			
Pre-pubertal	15 (26.8)	27 (36.5)	0.2
Pubertal or post-pubertal	41 (73.2)	47 (63.5)	
Tonsillectomy[a]			0.4
No	49 (87.5)	68 (93.2)	
Yes	7 (12.5)	5 (6.8)	
Adenoidectomy[b]			0.1
No	45 (80.4)	66 (91.7)	
Yes	11 (19.6)	6 (8.3)	
Sleep parameters:			
AHI (median [IQR])	3.4 [2.7, 5.4]	0.8 [0.4, 1.3]	**<0.001**
OAI (median [IQR])	0.2 [0.1, 0.7]	0.0 [0.0, 0.1]	**<0.001**
HI (median [IQR])	2.9 [2.2, 4.7]	0.8 [0.4, 1.3]	**<0.001**
MAI (median [IQR])	0.0 [0.0, 0.1]	0.0 [0.0, 0.0]	**<0.001**
CAI (median [IQR])	0.8 [0.5, 1.5]	0.7 [0.3, 1.3]	0.2
ODI (median [IQR])	2.3 [1.7, 3.7]	1.1 [0.7, 1.7]	**<0.001**
SPO_2 (median [IQR])	94.9 [93.9, 95.8]	95.6 [95.1, 96.5]	**0.001**
SPO_2 nadir (median [IQR])	86.0 [82.0, 89.0]	88.0 [82.3, 91.0]	0.1
Sleep time (median [IQR])	7.6 [5.5, 8.4]	7.6 [6.3, 8.5]	0.4
HRQOL:			
Physical scale score (median [IQR])	75.0 [62.5, 84.4]	79.7 [68.8, 87.5]	0.1
Emotional scale score (median [IQR])	65.0 [50.0, 80.0]	70.0 [50.0, 80.0]	0.5
Social scale score (median [IQR])	75.0 [65.0, 90.0]	80.0 [65.0, 95.0]	0.2
School scale score (mean (SD))	59.1 (19.7)	59.4 (19.1)	0.7
Psychosocial scale score (mean (SD))	65.4 (18.0)	67.7 (15.3)	0.3
Total scale score (mean (SD))	67.3 (16.9)	70.9 (13.7)	0.1

For continuous normal distributed variables mean and standard deviation are reported.
For continuous non-normal distributed variables median and interquartile range are reported.
Age: Years, Sleep time: Hours.
Bold values indicate $p < 0.05$.
BMI SDS: Body mass index standard deviation score, HRQOL: Health related quality of life, AHI: Apnea-hypopnea index, OAI: Obstructive apnea index, HI: Hypopnea index, MAI: Mixed apnea index, CAI: Central apnea index, ODI: Oxygen desaturation index, SPO_2: Oxygen saturation.
[a] One did not know the answer.
[b] Two did not know the answer.

2.3. Consultation and anthropometry

Characteristics regarding sex, height, weight and pubertal development were recorded during the clinical consultation. Height was measured to the nearest millimeter using a stadiometer. Weight was measured to the nearest 100 grams with the child wearing light indoor clothes and without shoes. BMI was calculated as the weight in kilograms divided by the square of the height in meters (kg/m2). The BMI SDS was estimated using the LMS method [31] based on Danish references [27]. Pubertal development was assessed according to Tanner stages [32,33]. Testicular size was measured by Prader's orchidometer. Tanner stage was only obtained in children and adolescents with overweight or obesity. The medical history was registered, including self-reported adenotonsillar surgery. The children and their parents were instructed in the use of the portable sleep monitor. The clinical consultations were performed by the same physician throughout the study period.

2.4. Sleep examinations

Sleep examinations were performed for one night using the type 3 portable sleep monitor Nox T3 (Nox Medical Inc., Reykjavik, Iceland). Children and adolescents with overweight or obesity slept with the device in the obesity clinic while children and adolescents with normal weight slept with the device at home. The Nox T3 device monitors airflow via a nasal cannula, respiratory effort via chest and abdominal belts, body position and activity via an integrated accelerometer and pulse and oxygen saturation via an oximeter. One registered polysomnographic technologist analyzed the sleep examinations according to the pediatric respiratory rules defined by the American Academy of Sleep Medicine [34].

Apneas were identified by a ≥ 90% drop in air flow for the duration of at least two breaths. Obstructive apneas were defined as apneas associated with respiratory effort throughout the entire period of the event. Mixed apneas were defined as apneas without respiratory effort during one part of the event and presence of respiratory effort in another part of the event. Central apneas were defined as apneas without respiratory effort throughout the entire period of the event. Hypopneas were identified by a ≥ 30% drop in airflow for the duration of at least two breaths accompanied by a ≥ 3% oxygen desaturation. The AHI was defined as the average number of obstructive apneas, mixed apneas, and hypopneas per hour of sleep [i.e., the sum of the Obstructive Apnea Index (OAI), the Mixed Apnea Index (MAI), and the Hypopnea Index (HI)] [35]. The Central Apnea Index (CAI) was not included in the AHI [35]. The Oxygen Desaturation Index (ODI) was defined as the average number of oxygen desaturations ≥ 4% per hour of sleep. Sleep time was estimated as the total recording time minus the episodes of signal artefacts and time spent in an upright position. Sleep examinations containing < 3.75 hours of sleep or with a signal quality < 90% were considered ineligible for analysis. OSA was defined as AHI ≥ 2. Mild OSA was defined as 2 ≤ AHI < 5, moderate OSA was defined as 5 ≤ AHI < 10 and severe OSA was defined as AHI ≥ 10. The oxygen saturation

Table 2
Generalized linear regression analyses including children and adolescents with overweight or obesity. Tested for the physical, psychosocial and total scale score using the PedsQL questionnaire.

Physical scale score	Estimate (β)	95% CI	p-value
AHI	0.0	[-0.7, 0.7]	1.0
Sex	−4.9	[-10.4, 1.1]	0.1
Age	−2.2	[-3.6, −2.9]	**0.01**
BMI SDS	−4.7	[-9.8, 0.3]	0.1
Pubertal development stage	7.0	[-1.6, 15.6]	0.1
Psychosocial scale score	Estimate (β)	95% CI	p-value
AHI	0.1	[-0.6, 0.8]	0.7
Sex	−2.4	[-8.5, 3.6]	0.4
Age	−1.7	[-3.1, 0.0]	**0.05**
BMI SDS	−3.4	[-8.7, 1.9]	0.2
Pubertal development stage	4.5	[-4.5, 13.5]	0.3
Total scale score	Estimate (β)	95% CI	p-value
AHI	0.1	[-0.6, 0.7]	0.8
Sex	−3.2	[-8.7, 2.3]	0.3
Age	−1.7	[-3.1, −0.4]	**0.02**
BMI SDS	−3.9	[-8.7, 0.9]	0.1
Pubertal development stage	5.2	[-2.9, 13.4]	0.2

Age: Years, Sex: Boys (reference variable), Pubertal development stage: Pre-pubertal (reference variable).
95% CI: 95% confidence interval.
Bold values indicate $p < 0.05$.
BMI SDS: Body mass index standard deviation score, AHI: Apnea-hypopnea index, PedsQL: Pediatric Quality of Life Inventory.

(SPO_2) nadir was defined as the lowest measured SPO_2 during the sleep examination. SPO_2 mean was defined as the mean of SPO_2 during the sleep examination.

2.5. Informed consent and ethical approvals

Informed consent was obtained from all individual participants included in the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This article does not contain any studies with animals performed by any of the authors. The study was approved by the Regional Danish Ethics Committee (Protocol ID: SJ-404) and by the Danish Data Protection Agency (ID no.: REG-111-2014). The study was registered in Clinicaltrials.gov (ID no.: NCT02463201).

2.6. Statistics

Statistics were performed using R statistical software (version 3.5.1). Data were examined for normality by histograms and Shapiro-Wilk test. Descriptive characteristics between groups were compared by Fisher's exact test or Chi squared test for categorical variables and Mann Whitney *U* test or Student's T test for continues variables. A generalized linear regression was performed to describe the association between AHI or OSA and HRQOL, adjusted for BMI SDS, sex, age and pubertal development stage. OSA was dichotomized as AHI ≥ 2 being OSA and AHI < 2 being non-OSA. Residuals of the generalized linear regression models were examined for normality by histograms and QQ-plots, and the distribution of the residuals were found to be normal or close to normal distribution. The AHI was not log transformed since log transformation did not change the overall distribution of the residuals. HRQOL scores were not transformed due to negative skewness. Tanner stage was dichotomized as 1 being pre-pubertal and 2–5 being pubertal or post-pubertal. Cronbach's alpha was calculated to assess the internal consistency of PedsQL in this study. A Cronbach's alpha of 0.7 or greater is recommended when comparing patient groups [30]. The p-values reported are two-tailed and alpha was set at 0.05.

3. Results

Initially, 139 children and adolescents with overweight or obesity were included in the study. In total, nine children and adolescents fulfilled one of the exclusion criteria (Fig. 1). A total of 130 children and adolescents with overweight or obesity and with a median age of 12 years [range 7.0–17.9] were included in the final analysis. Initially, 33 children and adolescents with normal weight were included in the study as control group. However, five children and adolescents fulfilled one of the exclusion criteria (Fig. 1). Thus, a total of 28 children and adolescents with normal weight and a median age of 12 years [range 7.1–16.5] were included. The excluded children and adolescents did not differ with regard to age, sex, BMI SDS or AHI compared with the included children and adolescents. None of the children and adolescents in any of the groups reported known sleeping disorders at the time of inclusion in the study. In total, three participants left more than 50% of the questions unanswered in one or more of the scales in the PedsQL. To assess the internal consistency of the PedsQL in this study Cronbach's alpha was calculated. Cronbach's alpha for the total scale was 0.9.

3.1. Clinical characteristics and HRQOL in children and adolescents with overweight or obesity

Clinical characteristics of children and adolescents with overweight or obesity are presented in Table 1. The sleep examination diagnosed 56 children and adolescents with OSA and 74 without. In total, 40 children and adolescents had mild OSA, 10 had moderate OSA and six had severe OSA. Comparing children and adolescents with and without OSA, the groups differed significantly in age and BMI SDS. The children and adolescents with OSA were older ($p = 0.01$) and had higher BMI SDS ($p = 0.04$). The groups did not differ in regard to history of adenotonsillar surgery. By design, the sleep parameters differed significantly between the groups, except CAI and SPO_2 nadir. There were no statistically significant differences in any of the HRQOL scale scores between the groups (Table 1).

3.2. Association between AHI or OSA and HRQOL in children and adolescents with overweight or obesity

There was no association between AHI and HRQOL in any of the scales adjusted for age, sex, BMI SDS and pubertal development stage. A similar result was found using OSA as a categorical variable. Table 2 shows the results of the generalized linear regressions regarding physical, psychosocial and total scale scores. As seen, age was associated with HRQOL in all three scales. Looking at the individual scales, BMI SDS was associated with the social scale ($p = 0.04$), meaning that an increase in BMI SDS decreased HRQOL. Sex and pubertal development were not associated with HRQOL.

3.3. Comparing children and adolescents with overweight or obesity without OSA with a normal-weight control group without OSA

Table 3 compares the group of children and adolescents with overweight or obesity without OSA with the normal-weight control group of the children and adolescents without OSA.

By design, the groups differed in BMI SDS. Moreover, they differed significantly in AHI ($p = 0.001$), HI ($p = 0.001$) and sleep time ($p = 0.03$). Children and adolescents with overweight or obesity had higher AHI and HI and had shorter sleep time than children and adolescents with normal weight. The children and adolescents with normal weight had significantly higher HRQOL ($p = 0.001$) in all scales in the bivariate

Table 3
Comparing children and adolescents with overweight or obesity without OSA with children and adolescents with normal weight without OSA.

	Children with normal weight (n = 28)	*Children with overweight or obesity (n = 74)*	p-value
Sex (n (%))			
Boys	10 (35.7)	30 (40.5)	0.6
Girls	18 (64.3)	44 (59.5)	
Age (mean (SD))	11.8 (2.2)	11.8 (2.7)	0.6
BMI SDS (median [IQR])	0.5 [-0.1, 0.7]	2.8 [2.4, 3.2]	**<0.001**
Tonsillectomy[a]			0.3
No	28 (100)	68 (93.2)	
Yes	0 (0)	5 (6.8)	
Adenoidectomy[b]			0.7
No	27 (96.4)	66 (91.7)	
Yes	1 (3.6)	6 (8.3)	
Sleep parameters:			
AHI (median [IQR])	0.4 [0.2, 0.6]	0.8 [0.4, 1.3]	**0.001**
OAI (median [IQR])	0.0 [0.0, 0.0]	0.0 [0.0, 0.1]	0.6
HI (median [IQR])	0.3 [0.1, 0.6]	0.8 [0.4, 1.3]	**0.001**
MAI (median [IQR])	0.0 [0.0, 0.0]	0.0 [0.0, 0.0]	0.1
CAI (median [IQR])	0.5 [0.4, 0.8]	0.7 [0.3, 1.3]	0.1
ODI (median [IQR])	0.9 [0.5, 1.4]	1.1 [0.7, 1.7]	0.1
SPO_2 (median [IQR])	96.0 [95.3, 96.7]	95.9 [95.1, 96.5]	0.2
SPO_2 nadir (median [IQR])	89.0 [83.0, 92.0]	88.0 [82.3, 91.0]	0.3
Sleep time (median [IQR])	8.5 [7.2, 9.1]	7.6 [6.3, 8.5]	**0.03**
HRQOL:			
Physical scale score (median [IQR])	87.5 [84.4, 93.8]	79.7 [68.8, 87.5]	**0.001**
Emotional scale score (median [IQR])	77.5 [70.0, 95.0]	70.0 [50.0, 80.0]	**0.001**
Social scale score (median [IQR])	95.0 [90.0, 100.0]	80.0 [65.0, 95.0]	**<0.001**
School scale score (median [IQR])	80.0 [68.8, 82.2]	60.0 [40.0, 75.0]	**<0.001**
Psychosocial scale score (median [IQR])	85.8 [77.5, 90.4]	68.3 [57.1, 80.0]	**<0.001**
Total scale score (median [IQR])	85.3 [79.1, 90.2]	71.2 [61.1, 81.3]	**<0.001**

For continuous normal distributed variables mean and standard deviation are reported.
For continuous non normal distributed variables median and interquartile range are reported.
Age: Years, Sleep time: Hours.
Bold values indicate $p < 0.05$.
BMI SDS: Body mass index standard deviation score, HRQOL: Health related quality of life, AHI: Apnea-hypopnea index, OAI: Obstructive apnea index, HI: Hypopnea index, MAI: Mixed apnea index, CAI: Central apnea index, ODI: Oxygen desaturation index, SPO_2: Oxygen saturation.
[a] One did not know the answer.
[b] Two did not know the answer.

analyses.

3.4. Association between BMI SDS and HRQOL in children and adolescents without OSA

In generalized linear regression analyses including children and adolescents with overweight or obesity without OSA and the normal-weight control group without OSA BMI SDS was associated with HRQOL in all scales adjusted for age, sex and AHI ($p < 0.001$) (Table 4), meaning that an increase in BMI SDS decreased HRQOL. Sex was associated with HRQOL in the physical ($p = 0.02$) and the emotional scale ($p = 0.03$), meaning that female sex decreased HRQOL. Age was not associated with HRQOL.

3.5. Sensitivity analyses regarding time difference between PedsQL completion and the sleep examination

Seven children and adolescents were excluded from the analyses due to not timely completion of PedsQL. A total of 39 children and adolescents would have been excluded with a cut-off of more than 0 days between PedsQL completion and sleep examination. Therefore, we conducted a sensitivity analysis comparing a cut off of more than 10 days with a cut-off of more than 0 days between PedsQL completion and the sleep examination. The estimates of the generalized linear regressions did not change between the two cut offs when compared to the scale of HRQOL ranging from 0 to 100. (Tables 5 and 6).

Table 4
Generalized linear regression analyses including children and adolescents with overweight or obesity without OSA and children and adolescents with normal weight without OSA. Tested for the physical, psychosocial and total scale score using the PedsQL questionnaire.

Physical scale score	Estimate (β)	95% CI	p-value
BMI SDS	−3.9	[-6.0, −1.8]	**<0.001**
Age	0.4	[-1.4, 0.7]	0.5
Sex	−6.2	[-11.4, −0.9]	**0.02**
AHI	−4.5	[-9.4, 0.5]	0.1
Psychosocial scale score	Estimate (β)	95% CI	p-value
BMI SDS	−5.7	[-7.9, −3.5]	**<0.001**
Age	−0.3	[-1.3, 0.8]	0.6
Sex	−2.0	[-7.5, 3.5]	0.5
AHI	−2.8	[-8.0, 2.4)	0.3
Total scale score	Estimate (β)	95% CI	p-value
BMI SDS	−5.0	[-7.0, −3.1]	**<0.001**
Age	−0.3	[-1.3, 0.7]	0.5
Sex	−3.4	[-8.3, 1.5]	0.2
AHI	−3.4	[-8.0, 1.3]	0.2

Age: Years, Sex: Boys (reference variable), Pubertal development: Pre-pubertal (reference variable).
95% CI: 95% confidence interval.
Bold values indicate $p < 0.05$.
BMI SDS: Body mass index standard deviation score, AHI: Apnea-hypopnea index, PedsQL: Pediatric Quality of Life Inventory.

Table 5
Sensitivity analysis. Children and adolescents with overweight or obesity. Generalized linear regression analyses adjusted for age, sex, BMI SDS and pubertal development stage. Model A (Reference): Exclusion criteria: Completion of PedsQL more than 10 days prior to or after sleep examination, 130 children and adolescents included in the analysis. Model B: Exclusion criteria: Completion of PedsQL more than 0 days prior to or after sleep examination, 100 children and adolescents included in the analysis.

	Estimate (β)	95% CI	p-value	Change (%)
Physical scale score				
Model A. AHI	0.00	[-0.66, 0.66]	1.0	
Model B. AHI	0.03	[-0.67, 0.72]	0.9	0.03%
Emotional scale score				
Model A. AHI	0.19	[-0.61, 0.99]	0.7	
Model B. AHI	0.24	[-0.64, 1.12]	0.6	0.05%
Social scale score				
Model A. AHI	−0.13	[-1.04, 0.79]	0.8	
Model B. AHI	−0.11	[-1.02, 0.80]	0.8	0.02%
School scale score				
Model A. AHI	0.32	[-0.47, 1.12]	0.4	
Model B. AHI	0.17	[-0.68, 1.03]	0.7	0.15%
Psychosocial scale score				
Model A. AHI	0.12	[-0.57, 0.81]	0.7	
Model B. AHI	0.09	[-0.66, 0.84]	0.8	0.03%
Total scale score				
Model A. AHI	0.07	[-0.56, 0.69]	0.8	
Model B. AHI	0.05	[-0.63, 0.73]	0.9	0.02%

Estimate: Estimates for AHI.
95% CI: 95% confidence interval.
Change (%): Percentage change between Model A (reference) and Model B compared to the scale of HRQOL (100).
AHI: Apnea-hypopnea index.

4. Discussion

In this cross-sectional study, we found no association between AHI or OSA and HRQOL in any of the scales adjusted for age, sex, BMI SDS and pubertal development stage in children and adolescents with overweight or obesity.

This is in line with two previous studies by Carno et al. [14] and Crabtree et al. [13]. Interestingly, these studies found no association between OSA and HRQOL but found an association between symptoms of OSA and HRQOL, indicating that symptoms might have a higher predictable value than standard sleep parameters. However, the association between symptoms of OSA and HRQOL was not possible to investigate in our study, due to no Danish validated symptom questionnaires in children and adolescents. In contrast to our findings both Rosen et al. [7] and Bergeron et al. [8] found an association between OSA severity and HRQOL.

However, a direct comparison of the previous studies to our findings is challenging due to differences in inclusion criteria, the presence of a control group, the method of measurement of HRQOL and the definition of OSA. We defined OSA as AHI $\geq$ 2 because this is a commonly used definition [36]. However, the cut-off for defining OSA is arbitrary and varies between studies [36]. Additionally, we chose to asses HRQOL through the PedsQL due to the wide age range, the availability of a linguistically validated Danish version and the thorough validation studies [29,30,37–39]. We chose a generic questionnaire instead of a disease-specific questionnaire to assess the overall well-being of children and adolescents.

Carno et al. [14], Crabtree et al. [13] and Bergeron et al. [8] included children and adolescents referred to sleep clinics on suspicion of OSA and the sleep examinations revealed a high proportion of moderate to severe OSA. In our study none of the included children and adolescents were referred to sleep clinics on suspicion of OSA at the time of the inclusion and most of the children and adolescents had mild OSA (71.4%, n = 40). This might indicate that children and adolescents in our study were not affected by the presence of OSA to the same extent as children and adolescents in the previous studies. Furthermore, the low proportion of severe OSA in our study may contribute to our finding of no association between OSA and HRQOL.

In the bivariate analysis, we found that children and adolescents with OSA had higher BMI SDS than children and adolescents without OSA. This is in line with previous findings [1,3,4,40–43], but the mechanisms leading to the increased risk of OSA in children and adolescents with overweight or obesity are not fully understood. Obesity may lead to fat deposition in the pharyngeal region narrowing the upper airway and may affect the upper airway collapsibility, both factors leading to increased risk of OSA [44]. Interestingly, we found that children and adolescents with OSA were older than children and adolescents without OSA. The reason for this finding is not clear. A possible explanation is the developmental changes in the upper airway. The upper airway neuromuscular tone is reported to decrease with age [45] possibly exerting influence on the collapsibility of the upper airway during sleep.

In the generalized linear regression analyses, we found that age was associated with HRQOL in the physical, psychosocial and total scale, meaning that an increase in age decreased HRQOL. An association between age and HRQOL is consistent with previous findings [15–20], and may be caused by problems in coping with the physical and psychosocial changes during adolescence [46]. Despite age being associated with HRQOL, we found no association between the pubertal development stage and HRQOL in this study. This is also consistent with previous findings by Carno et al. [14] and Mollerup et al. [22]. In our study, sex

Table 6
Sensitivity analysis. Children and adolescents with overweight or obesity without OSA and children and adolescents with normal weight without OSA. Generalized linear regression analyses adjusted for age, sex and AHI. Model A1 (Reference): Exclusion criteria: Completion of PedsQL more than 10 days prior to or after sleep examination, 102 children and adolescents included in the analysis. Model B1: Exclusion criteria: Completion of PedsQL more than 0 days prior to or after sleep examination, 86 children and adolescents included in the analysis.

	Estimate (β)	95% CI	p-value	Change (%)
Physical scale score				
Model A1. BMI SDS	−3.90	[-5.98, −1.81]	**<0.001**	
Model B1. BMI SDS	−3.85	[-5.97, −1.73]	**0.001**	0.04%
Emotional scale score				
Model A1. BMI SDS	−5.45	[-8.20, −2.70]	**<0.001**	
Model B1. BMI SDS	−4.94	[-7.69, −2.18]	**0.001**	0.52%
Social scale score				
Model A1. BMI SDS	−6.39	[-8.91, −3.87]	**<0.001**	
Model B1. BMI SDS	−5.97	[-8.40, −3.55]	**<0.001**	0.42%
School scale score				
Model A1. BMI SDS	−5.08	[-7.94, −2.22]	**0.001**	
Model B1. BMI SDS	−4.05	[-6.95, −1.15]	**0.008**	0.13%
Psychosocial scale score				
Model A1. BMI SDS	−5.68	[-7.86, −3.49]	**<0.001**	
Model B1. BMI SDS	−5.02	[-7.26, −2.77]	**<0.001**	0.66%
Total scale score				
Model A1. BMI SDS	−5.04	[-6.99, −3.09]	**<0.001**	
Model B1. BMI SDS	−4.60	[-6.61, −2.58]	**<0.001**	0.44%

Estimate: Estimates for BMI SDS.
95% CI: 95% confidence interval.
Change (%): Percentage change between Model A1 (reference) and Model B1 compared to the scale of HRQOL (100).
Bold values indicate $p < 0.05$.
BMI SDS: Body mass index standard deviation score.

was not associated with HRQOL. Several studies have found that female sex decreases HRQOL [15,16,18–21]. On the contrary, other studies found no difference in HRQOL between boys and girls [24,25]. In our primary analysis, BMI SDS was associated with HRQOL in the social scale, meaning that an increase in BMI SDS decreased HRQOL. Several studies have found an association between BMI SDS and HRQOL in both the total scale and subscales of HRQOL [15,17,21–26]. A higher BMI SDS is associated with lower HRQOL and may be due to bullying and impaired self-perception, social acceptance and physical well-being in children and adolescents with overweight or obesity [15,47].

A cut-off defining impaired HRQOL has been suggested by Varni et al. [30] based on over 10.000 families in California, USA [30]. In our study, children and adolescents with overweight or obesity demonstrated low HRQOL scores regarding total and school scale compared with the cut-off values. To investigate the impact of BMI SDS on HRQOL, we compared children and adolescents with overweight or obesity without OSA with a normal-weight group of children and adolescents without OSA. We found that children and adolescents with normal weight had significantly higher HRQOL ($p < 0.001$) in all scales in the bivariate analyses and the generalized linear regression analyses adjusted for sex, age and AHI confirmed the result. Thus, overweight and obesity increased the risk of low HRQOL, which is consistent with previous studies [15,17,21–26].

Overall, our findings indicate that children and adolescents with overweight or obesity have increased risk of low HRQOL. However, the presence of mild OSA, which we mainly found in our study, does not further impair HRQOL in children and adolescents with overweight or obesity.

4.1. Strengths and limitations

We chose to use the Nox T3 device. A portable sleep monitor is often the practical first choice due to the high cost and inaccessibility of polysomnography (PSG). Cairns et al. [48] found good measurement agreement when comparing the Nox T3 device with PSG in adults. Similar type 3 sleep monitors have been validated in children and Certal et al. [49] concluded that type 3 devices generally are valid tools for predicting both the presence and the severity of OSA in children.

In this study we chose not to exclude participants based on history of adenotonsillar surgery, as it was not considered a confounder. Excluding participants due to history of adenotonsillar surgery would reduce the number of participants further and thereby reducing the power of the study. Moreover, the groups did not differ in regard to history of adenotonsillar surgery in the bivariate analyses.

We did not obtain socioeconomic status (SES) of the participants. SES has been shown to impact HRQOL [17,24] and thus, it would be relevant to adjust for SES in our analyses. Moreover, our analyses were not adjusted for history of recent life events such as death of a family member, parents' divorce or moving to a new city or school. These life events might affect HRQOL. Also, the generalizability of the overweight group may be questioned, because HRQOL may be lower in children and adolescents, who seek treatment compared with children and adolescents, who do not seek treatment [50]. Additionally, the generalizability of the normal-weight group to the general pediatric population may be questioned as well because children and adolescents, who agree to participate in a study may have additional resources and higher HRQOL than children and adolescents, who do not participate. This might have induced selection bias and may explain why BMI SDS was only associated to HRQOL in the social scale in the primary analysis including children and adolescents with overweight or obesity in contrast to an association in all scales of HRQOL in the analysis including children and adolescents without OSA.

However, the strength of this study is that we included children and adolescents both with and without OSA. Furthermore, we focused on children and adolescents referred to an obesity treatment clinic and not on children and adolescents referred to sleep clinics for suspected OSA.

5. Conclusion

In conclusion, we did not find an association between OSA or AHI and HRQOL in a group of children and adolescents recruited from an obesity treatment clinic. However, we found an association between BMI SDS and HRQOL in children and adolescents without OSA. Our findings indicate that overweight and obesity lead to impaired HRQOL in children and adolescents, but despite an increased risk of OSA in children and adolescents with overweight or obesity [1,3,4,40–43], the presence of OSA does not lead to further impaired HRQOL. However, we still emphasize the importance of treatment of OSA in children and adolescents as OSA may lead to several other comorbidities in childhood [1].

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Author contributions

The study was designed by KNF, IGA, LAH, JCH and PH. IGA and LAH collected the data. KNF analyzed the data and drafted the manuscript. PH, JCH, LAH and IGA critically revised and approved the manuscript.

Declaration of competing interest

Author KNF declares she has no conflict of interest. Author IGA received a study related grant from ResMed Maribo, Denmark. Author LAH declares she has no conflict of interest. Author JCH declares he has no conflict of interest. Author PH declares he has no conflict of interest.

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