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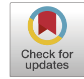

Increasing incidence and burden of obstructive sleep apnoea in the Finnish population: A cohort study from 2005 to 2019

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A R T I C L E I N F O

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A B S T R A C T

Background: Obstructive sleep apnoea (OSA) is a significant public health problem. We sought to characterize the typical features of patients with OSA and to study the burden and treatment of OSA in Finland from 2005 to 2019.

Methods: Our data included adult patients with OSA (n = 50 317) treated in 2005–2019 in secondary care in the Hospital District of Helsinki and Uusimaa (HUS). We collected diagnosis and procedure codes and healthcare contacts from HUS data lake. Word search from patient records included body mass index (BMI), smoking status, Epworth Sleepiness scale (ESS), apnoea-hypopnea-index (AHI), continuous positive airway pressure (CPAP) treatment, and Mallampati score. ResMed Airview program was used to calculate the prevalence of CPAP treatment in 2018–2022.

Findings: The annual incidence of OSA increased from 99 per 100 000 to 564 per 100 000 (+470 %) during 2005–2019. The most significant increase in healthcare contacts occurred in remote care and nurse visits from 336 to 35 959 per year (+10 602 %) and from 1051 to 23 609 per year (+2146 %), respectively. The prevalence of CPAP treatment increased from 0·74 % to 2·48 % during 2018–2022 (+235 %).

Interpretation: As the prevalence of OSA is increasing, the need for more efficient treatment protocols was seen as a shift towards telemedicine and as an increase in nurse visits. Data lake offers an efficient way to analyse large data sets of OSA patient characteristics and treatment strategies.

2. Introduction

Obstructive sleep apnoea (OSA) is an increasingly common public health problem that causes repeated upper airway collapse during sleep, leading to oxygen desaturation and sleep fragmentation [1]. The prevalence of OSA increases especially in the obese and aging population [2–5]. The current global prevalence of OSA in high-income countries is estimated to be 17 % in middle-aged males and 9 % in middle-aged females [6]. However, population-based studies have revealed a wide variation of prevalence estimates (4–77 % for mild OSA

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and up to 37 % for moderate-severe OSA) [3,6–8]. Additionally, obesity significantly increased the prevalence of OSA and affected its severity [5]. Two recent studies reported the Finnish prevalence to be 3·7–4·2 % and the annual incidence to be 600 per 100 000, although the prevalence values were considered to be underestimated [7,8]. Data on the incidence of clinically diagnosed OSA are limited.

The diagnosis of sleep apnoea is based on symptoms, clinical examination, and apnoea-hypopnoea index (AHI) examined by polysomnography (PSG) or respiratory polygraphy [9]. The main risk factors include small upper airway lumen, male sex, older age, and obesity; at least two thirds of patients with OSA are overweight or obese [1,10–12]. Comorbidities (such as cardiovascular diseases and other diseases associated with obesity), impaired quality of life, and early death are particularly associated with severe untreated OSA [1,12].

For decades, the gold standard of treating OSA has been continuous positive airway pressure (CPAP) [13]. An alternative to CPAP or a second-line treatment if CPAP is not tolerated is a mandibular advancement device (MAD) [12,14]. In some cases, surgery may also be considered for patients with appropriate anatomic features, such as craniofacial abnormalities or marked tonsil hypertrophy, or as a second-line treatment for patients intolerant to CPAP [15]. Bariatric surgery also appears to result in an improvement of OSA severity in obese patients [12].

We sought to estimate the incidence of OSA, to characterize the typical features of OSA patients treated in Hospital District of Helsinki and Uusimaa (HUS) in Finland, and to observe the change in the burden of OSA for the healthcare system in 2005–2019 using a large database (HUS data lake; HUS Tietoallas) [16]. Additionally, we hypothesized that the increasing prevalence and associated burden of OSA patients, combined with technological advancements, have underscored the growing importance of telemedicine.

3. Materials and methods

3.1. Study population and data collection

This retrospective, observational cohort study of Finnish OSA patients included all patients aged ≥18 years with a diagnosis of OSA (International codes of diseases, tenth revision, ICD-10: G47.3) or obesity hypoventilation syndrome (OHS) (ICD-10: E66.2) treated in HUS hospitals between January 1, 2005, and December 31, 2019 (HUS population base 1 685 770 in year 2019, 31 % of the Finnish population). In the HUS region, almost all patients for whom treatment for OSA is being considered are referred to secondary care for evaluation. We collected the data from the HUS Data lake, which contains electronic medical records of all patients treated in secondary care living in the HUS region. The STROBE checklist was used in reporting the study [17].

For this study, we used data of patients with registered primary diagnosis ICD-10 codes of G47.3 or E66.2, including all inpatient and outpatient contacts (appointments with doctors and nurses and remote care, including phone calls, treatment letters, and remote care without patient contact). The dates of outpatient contacts and inpatient visits were obtained. OSA was diagnosed using either respiratory polygraphy or polysomnography [9,18]. The majority of OSA diagnoses in the HUS area during the study period were based on respiratory polygraphy. Polysomnography's were performed only in specific cases, such as when differential diagnosis was required. The number of home-based studies has increased over the years.

Procedure codes with primary diagnosis codes of G47.3 or E66.2 included MAD (SHB00), nasal turbinate reduction (DHB50), nasal septorhinoplasty (DJD20, DLD10, DLD20), nasal polypectomy (DHB20), operations of pharynx (EMB-, ENC30), Le Fort I osteotomy (EEC05), and bilateral sagittal split osteotomy (BSSO) (EDC00, EDC05, EDC10, EDC15, EDC20, EDC25).

A word search was performed for different variables, including body mass index (BMI), smoking status, Epworth sleepiness scale (ESS), AHI, CPAP treatment, and Mallampati score. Sex and age at diagnosis were available separately from the data. Demographic and clinical characteristics were assessed at the date of OSA diagnosis.

Age, BMI, and ESS were continuous variables. Smoking status was categorised as non-smoker, former smoker, current smoker, and not known according to word search data. OSA severity was categorised as mild (AHI 5–14·9/h), moderate (AHI 15–29·9/h), or severe (AHI ≥30/h) [9,12]. Mallampati, defining a visibility of the distance from the tongue base to the roof of the mouth, was scored from one (normal) to four (very narrow) [19].

CPAP treatment was categorised according to word search as yes (in use) or no (not in use). In addition, prevalence data for CPAP treatment was applied from ResMed Airview (Resmed, San Diego, CA, USA) cloud and reported since availability of data in areas of HUS (Helsinki and Peijas from 2018 to 2022 and others from 2020 to 2022).

3.2. Defining variables in data lake

Data were obtained from HUS data lake through HUS data services. Programming languages Python version 3.11 [20]. and R version 4.3.1. (2023-6-16) [21] were used to search and limit the data. Search algorithms were modified according to the searchable parameters.

BMI was chosen as close as possible from the date of the primary AHI value. Values more than 36 months before or after the diagnosis were considered as missing values. ESS was chosen as close as possible from the date of the primary AHI value. ESS values more than 6 months before or after the diagnosis were considered as missing values. Any registered Mallampati and mention of smoking status were retrieved.

AHI value was acquired from patient records using algorithms that chose the overall AHI value or, if not available, the AHI value from sleeping position that was most present during the investigation. Individual false values were rejected by excluding AHI values > 150/h. AHI 0–4·9/h was considered as missing values, as this is supposed to indicate the residual AHI during treatment. Accuracy of the algorithms was manually validated.

Information on use of CPAP treatment and about the decision not to start CPAP treatment was found via word search. We concluded that treatment was not initiated if there was no mention of CPAP treatment in the patient records. The year when CPAP was first mentioned in the patient record was considered the initiation year of CPAP treatment.

3.3. Statistical analysis

Descriptive statistics were used to report the basic and clinical characteristics of OSA patients, including median with interquartile range (IQR), mean with standard deviation (SD), frequencies, and missing data. Missing values are shown in Table 1.

Level of significance was calculated with R using Wilcoxon rank-sum test for comparing distributions of two continuous outcomes and Fisher's exact or Chi-squared test to assess the independence of two categorical variables.

For an ordinal level outcome, a proportional-odds logit regression model was fitted. Due to the large number of missing values, a Multivariate Imputations by Chained Equations (MICE) model was used (Fig. 3). We assumed that missingness process was missing at random (MAR).

3.4. Ethical considerations

Health-related data used in this study were generated during routine clinical practice and were retrieved retrospectively from the HUS data lake and ResMed Airview cloud. Permission for the collection and processing of research data was granted from HUS in May 2021 (§15 HUS/237/2021).

The study was performed in accordance with the declaration of Helsinki and in compliance with applicable national laws. According to

Table 1
Demographics of obstructive sleep apnoea patients treated in Hospital district of Helsinki and Uusimaa (HUS) in 2005–2019.

		All (%)	Male (%)	Female (%)	p value
Population		50 317 (100)	33 735 (67)	16 582 (33)	
Age, in years	**Mean (SD)**	54·6 (12·3)	53·4 (12·4)	57·0 (11·9)	p < 0·0001
	18–64	40 166 (80)	27 702 (82)	12 464 (75)	
	65–74	8067 (16)	4893 (15)	3174 (19)	
	≥ 75	2084 (4)	1140 (3)	944 (6)	
BMI, kg/m^2	**Mean (SD)**	32·4 (7·0)	31·8 (6·4)	33·7 (7·9)	p < 0·0001
	Not known	22 381 (44)	15 262 (45)	7119 (43)	
Smoking	**Current smoker**	8204 (16)	5483 (16)	2721 (16)	
	Non-smoker	20 015 (40)	12 269 (36)	7746 (47)	
	Former smoker	1962 (4)	1422 (4)	540 (3)	
	Not known	20 136 (40)	14 561 (43)	5575 (34)	
ESS	**Mean (SD)**	8·1 (4·7)	7·8 (4·6)	8·9 (4·8)	p < 0·0001
	Not known	43 318 (86)	28 891 (86)	14 427 (87)	
AHI,/h	**Median (IQR)**	28·1 (32·6)	31·4 (35)	23·8 (26)	p < 0·0001
	5–14·9	7069 (14)	4089 (12)	2980 (18)	
	15–29·9	11 806 (23)	7417 (22)	4389 (26)	
	≥ 30	17418 (35)	12770 (38)	4648 (28)	
	Not known	14 024 (28)	9459 (28)	4565 (28)	
CPAP treatment	**Yes**	38 762 (77)	26 289 (78)	12 473 (75)	
	No	11 555 (23)	7446 (22)	4109 (25)	
Mallampati	**1**	1471 (3)	913 (3)	558 (3)	
	2	3422 (7)	2255 (7)	1167 (7)	
	3	3202 (6)	2110 (6)	1092 (7)	
	4	2427 (6)	1628 (5)	799 (5)	
	Not known	39 795 (79)	26 829 (79)	12 966 (78)	

Number of patients are presented in the table including percentages, mean values with standard deviation (SD), and median values with interquartile ranges (IQR). BMI = body mass index kg/m^2, ESS = Epworth sleepiness scale, AHI = Apnoea-hypopnoea index, CPAP = continuous positive airway pressure. Mallampati, defining a visibility of the distance from the tongue base to the roof of the mouth, scored from one (normal) to four (very narrow).

Finnish legislation, informed consent is not required for studies based on patient records. Data were pseudonymized in the data lake and no patients could be identified.

4. Results

There were 50 317 diagnosed adult OSA patients from 2005 to 2019 in the HUS district. Patients were on average obese (BMI >30) and most had severe OSA (Table 1). The different distribution of variables between male and female OSA patients is shown in Table 1.

The annual incidence of OSA in secondary care was 99 per 100 000 in 2005 and 564 per 100 000 in 2019 (+470 %). The incidence of CPAP treatment increased from 125 per 100 000 to 449 per 100 000 (+260 %), respectively. During the follow-up period, 77 % of OSA patients (male 78 % and female 75 %) used CPAP treatment. MAD treatment initiations increased in 2012 from 38 per 1000 OSA patients to the highest value of 104 per 1000 OSA patients in 2018 (+160 %) (Fig. 1). During the follow-up period, 5 % of OSA patients had MAD treatment.

The prevalence of CPAP treatment was 0·74 % in 2018 and 2·48 % in 2022 (+235 %), and the annual incidence of CPAP treatment varied between 322 per 100 000 and 542 per 100 000 in 2018–2022.

Surgical operations due to OSA or closely related as part of treatment of OSA were rare. During the follow-up period, there were <5 BSSO, 0 Le Fort Osteotomies, 0–5 nasal polypectomies, <5–24 nasal septorhinoplasties, 5–101 nasal turbinate reductions, and 0–38 operations of pharynx per year. Nasal turbinate reductions decreased from 24 per 1000 OSA patients per year in 2015 to 5 per 1000 OSA patients per year in 2019 (−380 %).

The number of healthcare outpatient visits due to OSA increased from 804 in 2005 to 8176 in 2019 (+917 %). However, remote and nurse contacts became more common and increased from 336 to 35 959 (+10 600 %) and from 1051 to 23 609 (+2146 %), respectively. Inpatient visits increased from 271 to 1116 (+312 %) (Fig. 2a). Outpatient visits due to newly diagnosed OSA (the year of OSA diagnosis and the following year) increased from 804 to 6675 (+730 %). Correspondingly, remote contacts increased from 336 to 24 964 (+7330 %), nurse contacts from 1051 to 16 200 (+1440 %), and inpatient visits from 226 to 852 (+277 %). However, in relation to the number of new patients, inpatient and outpatient visits decreased at the end of the follow-up period (Fig. 2b).

Variables associated with OSA severity were BMI ≥30, male sex, and older age (Fig. 3). Higher BMI in this population was associated with higher AHI, younger age, and female sex (Fig. 4). The proportion of elderly and female patients increased during the follow-up period (Fig. 5).

5. Discussion

Our study revealed a rapid and significant increase in the incidence and prevalence of OSA, which has challenged the healthcare system to adapt accordingly. Despite the sharp increase in OSA and CPAP incidence, the prevalence of CPAP treatment remained notably below OSA prevalence estimates. The data lake offered an efficient means to analyse large data sets of OSA patient characteristics and treatment strategies.

Most patients in this study population were overweight and more than half were obese. The global prevalence of obesity continues to increase and is twice that compared with four decades ago in over 70 countries and is increasing steadily in other countries worldwide [2]. In Finland, 12 % of males and 18 % of females were obese in 1980; the corresponding values in 2023 were 27 % and 30 % [22,23]. In addition to obesity, population aging affects the increasing prevalence of OSA. In 2005, the proportion of over 65-year-old individuals in the Finnish population was 16 %; the corresponding value in 2019 was 22 % [24]. The increasing age of OSA patients and the correlation between older age and OSA severity was observed in our study.

Incidence values similar to those from our study have also been reported earlier, [7,25] and the prevalence of CPAP treatment was quite similar to what has been observed in Europe previously [26,27]. Individuals with OSA in this study resembled those that have been reported in earlier studies (male dominant, obese on average, and mean age >50 years) [11,12,28]. However, the proportion of female patients increased during follow up and may reflect the increased awareness of OSA in females [29]. Moderate and severe OSA was more common in this population compared with mild OSA, which is expected considering that the population mainly consists of OSA patients that have been referred to secondary care for treatment evaluation. Obesity was associated with higher AHI values and younger age, but the reliability of this estimate may be affected by the large number of missing BMI values. Some previous studies have shown that the association of obesity and OSA appears to weaken with increasing age [30]. Our study highlights the fact that OSA is strongly associated with obesity, and that increasing obesity in the population increases the prevalence and likely severity of

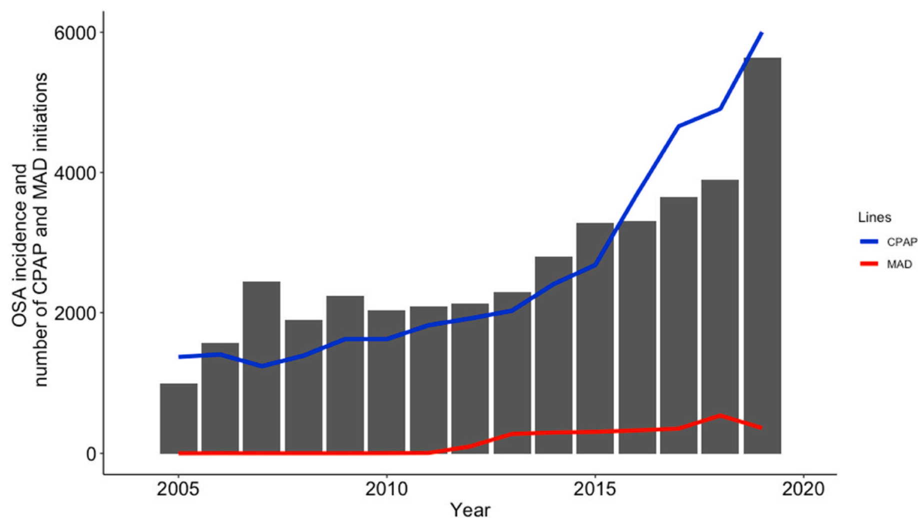

Fig. 1. The annual incidence of obstructive sleep apnoea (OSA) per 1 000 000 inhabitants (columns) and the initiations of continuous positive airway pressure (CPAP) treatment (blue line) and mandibular advancement device (MAD) treatment (red line) in secondary care in Hospital district of Helsinki and Uusimaa (HUS) in 2005–2019. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

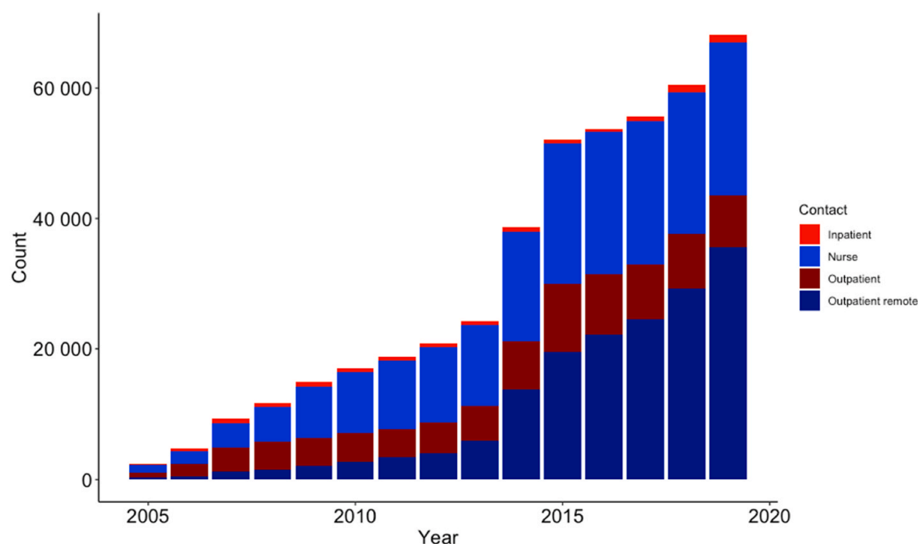

Fig. 2a. Number of annual inpatient and outpatient visits and all remote care contacts (including phone calls, treatment letters, and remote care without patient contact) due to obstructive sleep apnoea in secondary care in Hospital district of Helsinki and Uusimaa (HUS) in 2005–2019.

OSA, as shown previously [5,31].

Some differences in patient characteristics were noticeable between sexes. Female patients were older than male patients, had higher BMI, and had lower AHI. Despite milder OSA, females suffered from sleepiness more than males. These findings are consistent with results from previous studies [29]. Overall, ESS did not increase with higher AHI values in this data. However, this conclusion is limited by the substantial proportion of missing data.

CPAP treatment initiation largely increased parallel with the incidence of OSA. The proportion of patients with OSA receiving CPAP remained quite constant during the follow-up period regardless of the change in type of physician contacts. The population consisted mainly of patients with moderate-to-severe OSA, and it can be assumed that CPAP treatment was started in accordance with generally accepted indications [12].

There was a sharp increase in initiation of MAD treatment between 2012 and 2018. Overall, the role of MAD treatment is small compared with CPAP treatment in Finnish OSA patients, as only 5 % of patients had MAD treatment compared with 77 % for CPAP treatment. The clinical guidelines of the American Academy of Sleep Medicine and Dental Sleep Medicine recommend that MAD should be prescribed, rather than no therapy, for OSA patients who are intolerant to CPAP or who prefer alternative therapy [32]. According to current practice in the HUS region, MAD treatment is offered in secondary care to patients with moderate-to-severe OSA who have failed CPAP treatment and are not obese (BMI ≤30). The matter is considered individually for professional drivers.

In our data, surgery played only a minor role as a treatment option for OSA during follow up. Operation volumes remained rather stable, but a small reduction in some surgical operations was observed, especially in nasal turbinate reductions. Although there is no strong evidence to support the role of nasal surgery in reducing OSA severity, some studies have revealed a reduction in symptoms after surgery [12]. CPAP is the best primary treatment option given the lack of good evidence for surgery as a primary modality to treat OSA. In selected cases, surgery is considered a second-line treatment for patients who fail CPAP [12,15].

To address the increase in incidence of OSA and the number of patients left for follow up, the treatment and follow-up procedures were

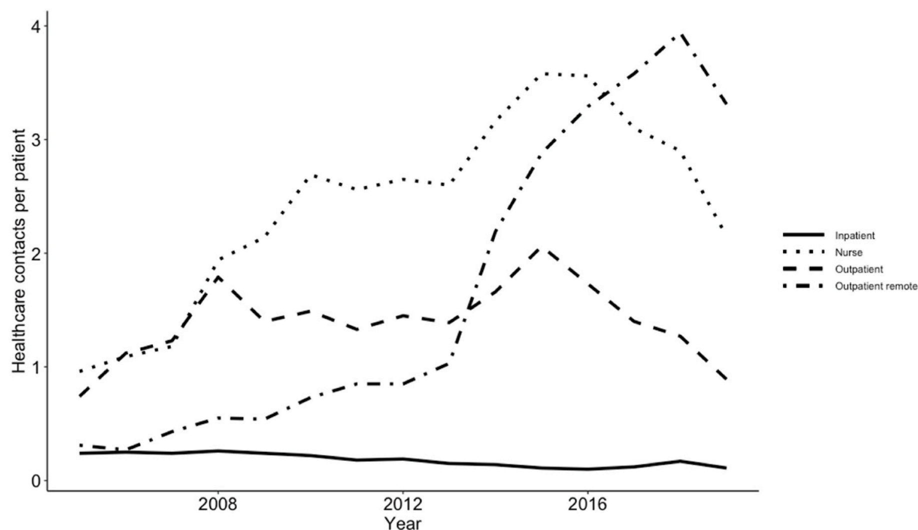

Fig. 2b. Annual number of healthcare contacts due to obstructive sleep apnoea (OSA) during the year of OSA diagnosis and the following year per diagnosed OSA patient. Healthcare contacts include inpatient and outpatient visits and remote care contacts (including phone calls, treatment letters, and remote care without patient contact) in secondary care in Hospital district of Helsinki and Uusimaa (HUS) in 2005–2019.

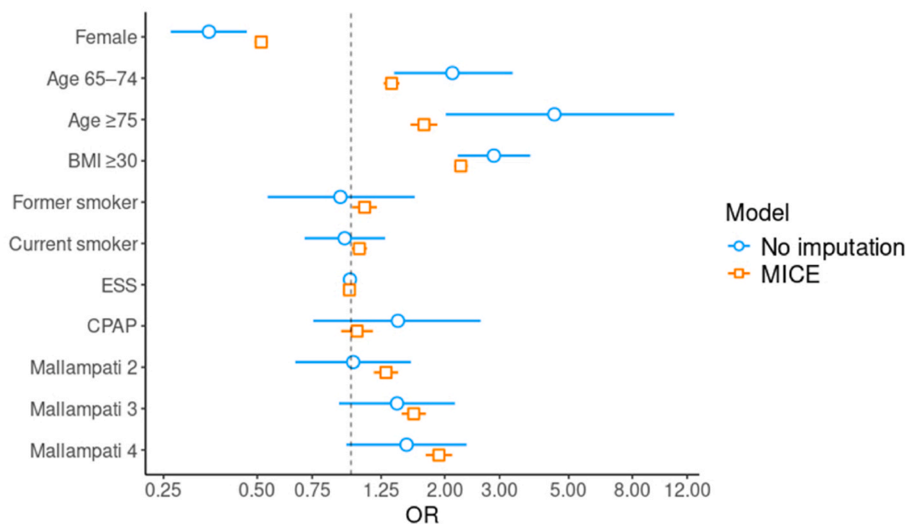

Fig. 3. The association of different variables and the severity of obstructive sleep apnoea (OSA)
Proportional odds ratios (OR) with 95 % confidence intervals (CI) for the severity of OSA calculated with no imputations and using a Multivariate Imputations by Chained Equations (MICE) model. The severity of OSA is defined as mild with apnoea-hypopnoea index (AHI) 5–14·9/h, moderate with AHI 15–29·9/h, and severe with AHI ≥30/h. References for predictors are male sex, age 18–64 years, BMI <30 kg/m^2, non-smoker, no CPAP treatment, and Mallampati score 1. Epworth sleepiness scale (ESS) is calculated as a continuous variable.

streamlined and standardized due to reduced opportunities for physician contacts [25]. Results from our data confirmed the assumption that the increasing prevalence of OSA has mainly contributed to the increase in remote care and nurse visits rather than outpatient visits to the physician. A similar change in use of telemedicine in diagnostics, treatment, and follow up has become more common and also occurred elsewhere in Europe [33].

Comprehensive assessment is important in examining patients with OSA, as sleep-disordered breathing is only one cause for excessive daytime sleepiness (EDS). The role of treating or preventing comorbidities of OSA with CPAP is mostly unclear [13] and in some situations, patients would likely benefit from a more thorough assessment of treatment options [34].

Treating and preventing obesity in addition to other treatments is vital for reducing the incidence of OSA and other obesity-related comorbidities [35]. Given that OSA treatment primarily occurs in secondary care settings in Finland, the focus in treatment tends to centre around the initiation of CPAP treatment. It is still evident that solely treating OSA within the broader context of obesity-related health issues will not resolve this public health challenge. Improving involvement of primary care in OSA treatment may be beneficial in addressing this problem more comprehensively.

One of our aims in this study was also to evaluate the usability of Finnish data lake data for the OSA population in the HUS region. It seems that data lake technology allows efficient analysis of a large population with a multitude of variables. Some clinical studies utilizing data lake technology in Finnish subpopulations have been performed in recent years to analyse different morbidities. Data lake technology is still not commonly used and routine use is still developing. We faced some problems with sampling and limiting the data at the beginning of this study.

The strengths of this study include a substantial real-life patient

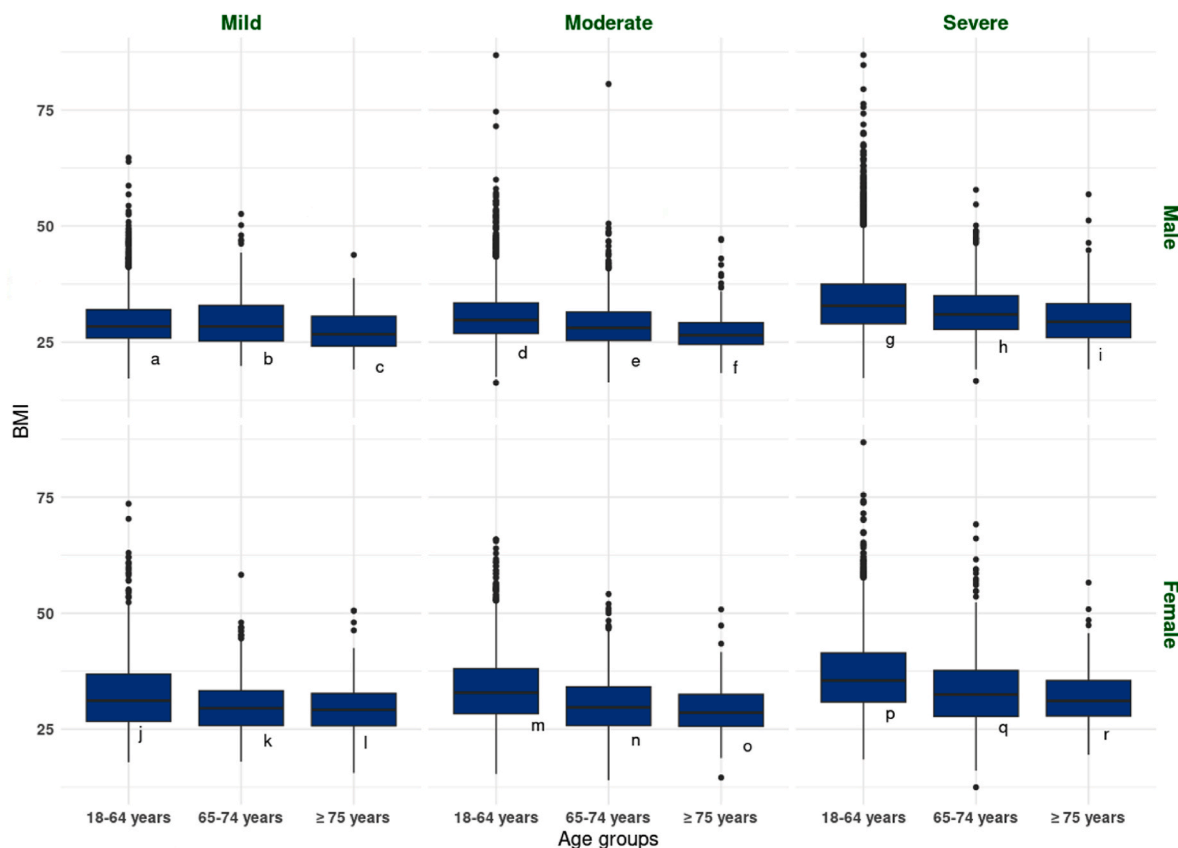

Fig. 4. Association of body mass index (BMI) with obstructive sleep apnoea (OSA) severity in different age groups and sex.
The severity of OSA is defined as mild with apnoea-hypopnoea index (AHI) 5–14·9/h, moderate with AHI 15–29·9/h, and severe with AHI ≥30/h. BMI distribution in different age groups (18–64, 65–74, and ≥ 75 years) in relation to OSA severity in male and female patients, a-r. Median BMI with interquartile range (IQR): a) 28·4 kg/m^2, 6·1 kg/m^2; b) 28·7 kg/m^2, 7·6 kg/m^2; c) 26·2 kg/m^2, 6·4 kg/m^2; d) 29·8 kg/m^2, 6·6 kg/m^2; e) 28·1 kg/m^2, 6·2 kg/m^2; f) 27·0 kg/m^2, 4·8 kg/m^2; g) 32·8 kg/m^2, 8·5 kg/m^2; h) 31·1 kg/m^2, 7·2 kg/m^2; i) 29·6 kg/m^2, 7·4 kg/m^2; j) 30·2 kg/m^2, 10·2 kg/m2; k) 29·4 kg/m2, 7·6 kg/m2; l) 29·3 kg/m2, 6·9 kg/m2; m) 32·9 kg/m2, 9·7 kg/m2; n) 29·7 kg/m2, 8·3 kg/m2; o) 28·8 kg/m2, 7·4 kg/m2; p) 35·5 kg/m2, 10·6 kg/m2; q) 32·6 kg/m2, 10·0 kg/m^2; r) 31·1 kg/m^2, 7·9 kg/m^2.

population and an extensive dataset where almost every OSA patient with a visit in secondary care in the HUS area was included in our study.

A weakness of this study is that the data on CPAP initiations was partly inaccurate at the beginning of follow up, especially in 2005 and 2006 due to left truncation of the cohort. After 2006, CPAP treatment initiations were registered concurrently with OSA diagnosis date (±1 year) in 81–91 % of cases. Additionally, in the open cohort setting, the follow-up period varied among patients depending on the date of OSA diagnosis registered in database. The duration of follow-up time was not analysed. Other weaknesses in our study include the lack of information on OSA patients who have not visited secondary care, namely patients who were diagnosed with OSA but were not significantly symptomatic and were not evaluated for specific treatment (CPAP or MAD). We assumed that the diagnosis of OSA was made based on the relevant criteria in effect at the time. However, more detailed information on the diagnostic methods was not available in this data. There was a moderately large amount of data on different variables that was missing due to missing information in patient records, which may affect the reliable interpretation of the results. Structural recording of patient documents would reduce this problem. General concerns associated with retrospective, mostly register-based epidemiological studies were also relevant to this, such as absence of reliable information on alcohol consumption. Additionally, information on socioeconomic status was not available.

6. Conclusion

OSA is a common public health disease that causes an increasing burden to the Finnish healthcare system. During the follow-up period, the efficiency in treating OSA patients in Finland has increased. Future studies should clarify how this change in treatment protocol has affected treatment results, quality of life, and prognosis of OSA patients. Data lake technology is an efficient tool to analyse a large patient population but only partially avoids the weaknesses associated with register-based studies.

CRediT authorship contribution statement

Peik Peuranheimo: Writing – original draft, Visualization, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Hanna-Riikka Kreivi:** Writing – review & editing, Methodology, Funding acquisition, Conceptualization. **Jukka Ollgren:** Visualization, Methodology, Formal analysis, Conceptualization. **Satu Strausz:** Validation, Data curation, Conceptualization. **Tuula Vasankari:** Writing – review & editing, Methodology, Conceptualization. **Toni Ruoranen:** Validation, Data curation, Conceptualization. **Hanna M. Ollila:** Validation, Data curation, Conceptualization. **Anne Hillamaa:** Validation, Conceptualization. **Sanna Toppila-Salmi:** Validation, Conceptualization. **Tiina Mattila:** Writing – review & editing, Project administration, Methodology, Funding acquisition, Conceptualization.

Data sharing statement

The individual-level data analysed in this study are not directly available to others. Anyone may apply for a study permit and access to the data from HUS data lake. Other related documents, including memos

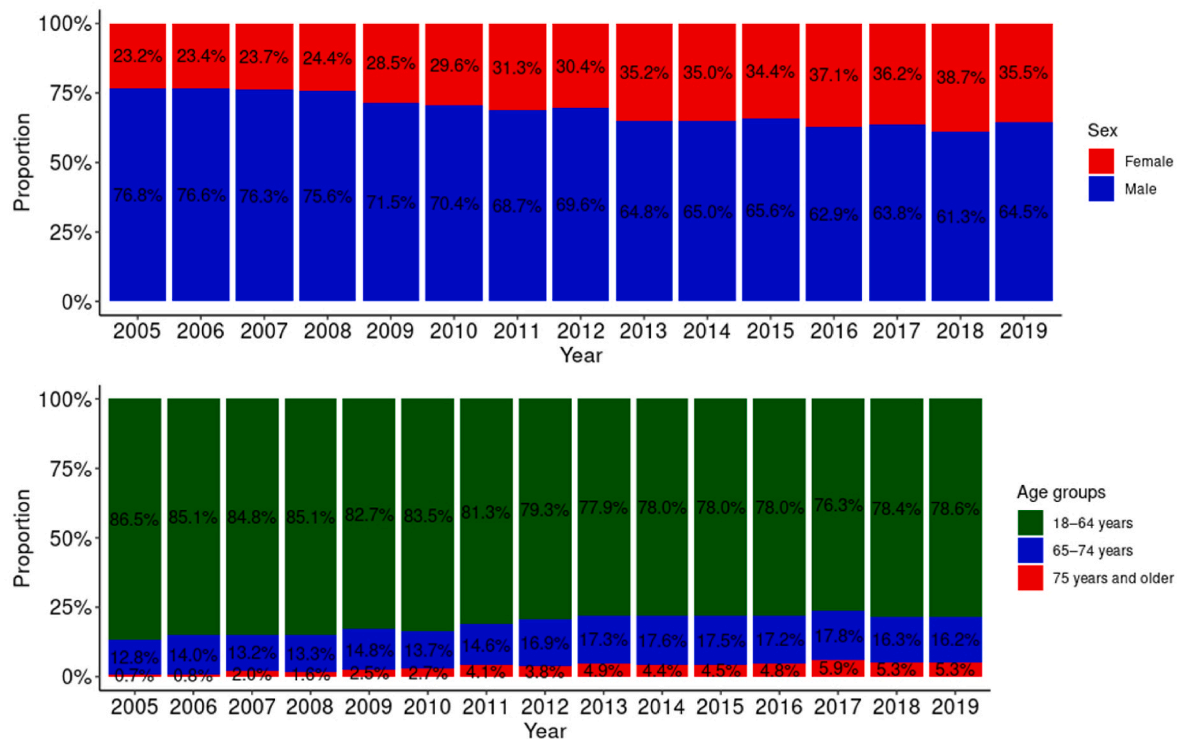

Fig. 5. The proportions of different sexes and age groups of obstructive sleep apnoea patients in secondary care in Hospital district of Helsinki and Uusimaa (HUS) in 2005–2019.

and plans for this study (mainly in Finnish), will be available for researchers 2 years after publication upon reasonable request.

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Contributions

SS and TR processed and harmonized the raw data. JO and PP collected and analysed most of the data. PP outlined the first version of the manuscript. All authors interpreted the data, contributed to the writing process, and have read and agreed to the published version of the manuscript.

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