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Orthodontic interventions as a management option for children with residual obstructive sleep apnea: a cohort study protocol

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ABSTRACT

Introduction Obstructive sleep apnoea (OSA) is a sleep-breathing disorder that seems likely to have long-term negative social and health consequences in children and adolescents. There are no established standard management approaches when the first line of therapy, the tonsillectomy and adenoidectomy (T&A), is not indicated or fails to address paediatric OSA (residual paediatric OSA). This protocol describes a prospective cohort study that aims to assess the effectiveness of orthodontic interventions for managing residual paediatric OSA in patients with concomitant craniofacial issues.

Methods and analysis Children aged 6–16 years who with an OSA diagnosis and did not benefit from previous T&A or qualified for T&A will be recruited. Orthodontic intervention(s), when adequately indicated (maxillary expansion, mandibular advancement or maxillary complex advancement with skeletal anchored headgear), and a control (orthodontic intervention declined) cohorts will be involved. A sample size of 70 participants (n=35 per cohort) is planned. Effectiveness data will be assessed through nocturnal polysomnography, a craniofacial index, sleep questionnaires and medical records. Additionally, the association of residual OSA and two comorbidities, obesity and asthma, will be investigated through assessing blood, urine and saliva metabolites. The changes on body mass index will also be investigated as a secondary outcome. Other additional outcomes, including association between residual paediatric OSA and periodic limbs movement, restless leg syndrome, insomnia, and the use of abiometric shirt to sleep monitoring purposes will also be considered. All participants will be followed up for 12 months after treatment allocation. The effectiveness of the intervention will be analysed by the assessment of sleep parameters, medical history (from medical chart reviews), questionnaire responses, craniofacial characteristics and metabolomic markers using an algorithm to be developed.

Ethics and dissemination This study was approved by the Health Research Ethics Board-Health Panel, University of Alberta, Edmonton, Canada (Pro00084763). The findings will be shared with scientific and patient content-specific social network communities to maximise their impact on clinical practice and future research in the study topic.

Strengths and limitations of this study

⇒ The study aims to approach a population in need, namely children who need alternative care for paediatric obstructive sleep apnoea (OSA) because they did not benefit from or qualify for adenotonsillectomy, the standard of care treatment.
⇒ This study will follow a prospective approach to explore the effectiveness of orthodontic interventions as a management option for residual OSA.
⇒ Reliable methods will be used for outcome evaluation, such as polysomnography exams, sleep and quality of life questionnaires, medical chart analysis and metabolites evaluation.
⇒ The cost of orthodontic treatment in Canada and the impossibility of randomisation are limitations of this study.

Trial registration number NCT03821831; Pre-results.

INTRODUCTION

Paediatric obstructive sleep apnoea (OSA) is a sleep-related breathing disorder that results in partial or complete airway airflow obstruction,[1] with a prevalence varying from 1% to 5%.[2 3] This condition is associated with multiple diseases and comorbidities such as asthma,[4] obesity[5] and cardiac abnormalities.[6] Paediatric OSA also increases healthcare utilisation by up to 40% when compared with children without OSA.[7] Children with OSA are more likely to experience poor school performance and long-lasting adverse consequences later in life, such as difficulties to find employment and a reduced monthly income.[8]

Diagnosing and managing paediatric OSA is challenging. Nocturnal polysomnography (nPSG) examination is required to properly diagnose this disorder, which is costly and difficult to obtain in many countries.[9] Similarly, tonsillectomy and adenoidectomy

(T&A), the most common management option for OSA due to the increased frequency of hypertrophic adenoids and tonsils among these cases,[9] may not be indicated or effective in improving OSA signs and symptoms. Between 19% and 49% of children with OSA may not benefit from T&A.[10 11] OSA persistence after T&A is referred to as residual OSA. This condition is more common among children with obesity and severe OSA than children with normal weight and mild to moderate OSA.[10] Additional management options have been suggested for residual OSA in children, such as pharmacological drugs, Continuous Positive Airway Pressure (CPAP) and selected orthodontic interventions (eg, maxillary expansion, mandibular advancement).[12–14]

Altered craniofacial anatomical features have been linked to paediatric OSA. The mandibular advancement devices, rapid maxillary expansion (RME) and maxillary complex advancement approaches are promising orthodontic interventions to address residual OSA in children.[15] These interventions have been found to reduce some OSA symptoms in children with craniofacial problems or anomalies associated with an orthodontic indication, at least temporarily.[12 16] It is hypothesised these interventions may increase upper airway space (naso- and oropharynx) and reduce airflow resistance, improving sleep breathing.[15] However, few clinical studies with a significant risk of bias have investigated orthodontic-based management options for children with OSA and their consequences to quality of life and associated comorbidities.[15 17] Based on them, these orthodontic interventions may represent a potential option to manage residual OSA in children, but its effectiveness remains to be elucidated.

In addition, the impact of OSA-related comorbidities on the management of this disorder is not well understood. Among those, obesity and asthma have been linked to paediatric OSA with a negative consequence on sleep quality and quality of life.[18 19] Additionally, other sleep breathing disorders, including insomnia, periodic limb movement disorder (PLMD) and restless legs syndrome (RLS), can share symptoms and comorbidities with OSA[20] and may contribute to an increased OSA severity.[21–23] OSA management's impact on these comorbidities needs to be further investigated, considering the multifactorial nature of OSA disorder and its long-term health consequences.

Difficulties accessing nPSG also affect the OSA management in children.[24] Adjunctive tools have been proposed to screen for risk factors and symptoms of OSA[25–27] as a possible option to identify children at high-risk for OSA and better support a referral for nPSG. Sleep monitoring through biometric shirts was found beneficial for screening purposes in adults but has not been evaluated in children yet.[28 29] Identifying new validated screening methods will likely reduce healthcare costs, decrease diagnosis time and improve the follow-up of children with OSA.[30]

In summary, paediatric OSA is a complex disorder associated with multiple risk factors and the available consensus-based guidelines have not provided a clear management protocol for residual OSA, including the role that alternative management options can play in managing this condition.[9 31] This highlights the need to understand residual OSA screening and management better, so that provided alternatives are more effective and feasible. For a residual OSA subgroup with a specific craniofacial phenotype, orthodontic treatment alternatives may be a helpful management alternative.[16 32] Hence, the primary aim of this prospective cohort study is to assess the effectiveness of orthodontic management, when adequately justified, in residual OSA symptoms and quality of sleep and life in children with this condition. In addition, we will also investigate the changes in severity and symptoms of PLMD, insomnia, obesity and asthma across the management and control arms; and the use of a biometric shirt as an alternative to nPSG for sleep monitoring in children with residual OSA.

METHODS AND ANALYSIS

Study design

A prospective cohort study is planned to evaluate the effectiveness of selective orthodontic interventions on sleep parameters and quality of life in children with residual OSA or children with OSA and without an indication for T&A who have craniofacial disturbances. Each participant will choose between properly indicated orthodontic intervention or no intervention. An observational design was chosen as randomisation was not possible due to the lack of clearly established clinical management indications and the fact that selective orthodontic interventions have a high cost for families in our setting. This study is part of a major project investigating the effectiveness of CPAP in children with residual OSA in an independent cohort from this study. The study's start date was in December 2021 and the planned end date will be in December 2026.

The Strengthening the Reporting of Observational Studies in Epidemiology statement was considering during the designing and reporting of this protocol (online supplemental data).[33]

Sample definition and eligibility criteria

The participants must be 6–16 years of age. Children with an established OSA diagnosis who present persistent OSA after surgical removal of the tonsils and adenoid tissue will be considered for inclusion, and those who did not qualify for this first management option. For simplicity, we adopted the term residual OSA to refer to children who presented both persistence of OSA after T&A surgery or that were diagnosed to OSA and were not eligible to T&A surgery for any reason (eg, absence of adenotonsillar hypertrophy). The persistence of OSA was defined after a postsurgery assessment of the child by a sleep specialist, in which any level of OSA detected was considered as persistence of the disorder, following the American Academy of Sleep Medicine guidelines for

paediatric OSA diagnosis.[34] Children of any sex will be eligible.

At the beginning of the study, after the potential participant is considered eligible according to the sleep and medical criteria, the craniofacial anatomical disturbances will be assessed by an orthodontist. A full clinical examination will be performed focused on the analysis of malocclusions. If applicable, radiological exams (eg, cephalometric radiograph, panoramic radiograph, cone-beam CT) and intra-oral pictures will be collected. To be eligible for orthodontic management, the child must have craniofacial anatomical disturbances, such as a high arched palate, retrusive mandible or dental crowding, which will justify the need for one of the orthodontic interventions part of this study (RME, mandibular advancement or class III midface advancement with skeletal anchored headgear).

Children presenting the following diagnosed syndromes will be excluded: autism spectrum, due to sensory concerns and inability to tolerate nPSG or dental examination; Down syndrome, cystic fibrosis and pulmonary hypertension, because of problems (eg, difficulties to sleep outside home, fear and anxiety related to multiple sensors used in these exams, sensory sensitivities) affecting the ability to tolerate nPSG. Also, children with persistence of paediatric OSA after T&A surgery without craniofacial abnormalities that justify orthodontic interventions proposed by the study. Children with clear need for immediate intervention to assess severe sagittal, transversal or vertical malocclusions will not be included

Recruitment and sample size rationale

Sleep specialists and nurse practitioners will recruit participants in the Pulmonary and Sleep Medicine Division at the Stollery Children's Hospital (Edmonton, AB, Canada). Potential participants will be identified during virtual or in-person clinical appointments depending on COVID-19 restrictions. The nurse practitioners of the Pulmonary and Sleep Medicine Division will ask patients who meet the inclusion criteria and are interested in participating in the study whether they consent to be contacted by the research team. The research team will then contact the child's family to provide additional information about the study. Full written consent/assent to participate will be obtained in the hospital site or through an online form. In both in-person or remote consent options, the research team will be available to explain the study and

Table 1 Description of cohorts and interventions

Intervention	Description
Orthodontic management	
	According to each case, the rapid maxillary expansion (RME), mandibular advancement or maxillary complex advancement with skeletal anchored headgear will be presented as options after a clinical evaluation performed by an orthodontist. In all three situations, the patient should have an indication for treatment despite their sleep problem. An orthodontist will perform the clinical steps in each group. RME The maxillary expansion appliance will be made in the orthodontic dental lab (Orthodontic Clinic in Kaye Edmonton Clinic, Edmonton, Canada), consisting in an expansion screw (Dentaurum), stainless steel wire and acrylic. The appliance will be banded on the maxillary permanent first molars and first premolars. The expansion screw will be activated twice a day, 0.25 mm per turn, (0.50 mm per day) until 20% overcorrection will be achieved. After correction achieved, the appliance was left passively for 6 months as a retention period. No additional action care will be required at home. Mandibular advancement device The mandibular advancement devices will be made from stainless steel wire and acrylic in our in the orthodontic dental lab (Orthodontic Clinic in Kaye Edmonton Clinic, Edmonton, Canada). The appliances will be activated stepwise (2–3 mm every 3 months). The appliances will be removed when 20% overcorrection will be achieved, until maxillary and mandibular anterior teeth are in an edge-to-edge relationship. No additional action care will be required at home. Class III mid face advancement with skeletal anchored headgear The class III mid face advancement device is manufactured by Ormco (Protraction Face Mask, Part # 716-0001) and the rest of the device will be made from stainless steel wire and acrylic in the dental lab (Orthodontic Clinic in Kaye Edmonton Clinic, Edmonton, Canada). The patients will be instructed to wear the face mask at least 16 hours/day. The protraction elastics were applied from the vestibular hooks banded in the maxillary permanent first molars to the to the support bar of the face mask in a 30–40 downward and forward direction from the occlusal plane, to achieve orthopaedic force levels up to 400–500 g per side. A monthly clinical follow-up will be performed in all patients. The appliance will be removed when overjet of 3 mm and more and overcorrection until maxillary and mandibular anterior teeth are in an edge-to-edge relationship. Recommendations to patient The child and their families will receive hygiene instructions and they may call the orthodontic clinic in case of pain, discomfort or broken appliances.
Control	No intervention will be performed. This cohort will be followed up for 12 months.

clarify any questions the family might have before signing the consent/assent forms.

This is an exploratory study in the field that evaluates the efficacy of a management options to OSA. Balancing the need to answer the clinical question proposed by our study and its feasibility, the sample size was not defined based on power analysis or statistical level of significance. Our sample size justification is based on expert observation. According to the clinical team of the Pulmonary and Sleep Medicine Division, 2–3 potential participants, on average, can be identified per week. Considering the cost and commitment to an orthodontic intervention option for young children and a typical trial dropout rate, we anticipate 50% of participants would be eligible for orthodontic intervention. Thus, approximately two participants per month will be included in our study, either in the intervention or no intervention cohort arm. We plan to recruit 7 participants per cohort each year over 5 years (70 participants in total). Once a management arm has 35 participants, it will be closed to additional participants. Each participant will be followed for 1 year after enrolment. This sample size is assumed to be statistically relevant to determine the effectiveness of the target treatments.

Management and control cohort

The two options (orthodontic intervention or no intervention) will be presented to the child and their guardians. They will choose to engage in one of the two cohorts based on their inclusion criteria.

In both cohorts, the participants will be followed-up for 12 months. Parameters related to sleep quality, quality of life, craniofacial features, medical history and sleep monitoring will be collected to assess both primary and secondary outcomes. Among participants who choose to engage in an orthodontic management option, three possibilities might be available: RME, mandibular advancement or maxillary complex advancement with skeletal anchored headgear. These three options were included in this study due to previous literature associating these approaches to an improvement in paediatric OSA signs and symptoms among children in selected cases.[15] An orthodontist will assess the eligibility for these management options at the beginning of the study and will provide with the intervention, if applicable.

Table 1 describes the protocol for intervention and follow-up in each cohort from this study.

Primary outcome

The primary outcome of this study is the effectiveness of orthodontic management on OSA symptom reduction and quality of sleep and life. To evaluate these outcomes, data will be collected through nPSG, a craniofacial index,[35] multiple sleep questionnaires[36–41] and medical records at baseline and 12 months after enrolment (table 2).

Secondary outcome

Our secondary outcome is the evaluation of changes in baseline body mass index (BMI) at 12 months. The BMI data will be collected from the medical charts.

Other outcomes

As part of our study, we also would like to explore three additional outcomes: effectiveness of a biometric shirt as a tool for sleep monitoring, the relationships between residual OSA and specific sleep-related disorders, as well as their relationship to asthma and obesity.

Table 2 Parameters assessed in the primary outcome

Parameters	Methods of assessment
Sleep parameters and quality of life	nPSG exam The PSG will be conducted at baseline and after 12 months in each cohort. The following information will be collected: date, AHI (obstructive and central) index, low and mean oxygen saturations, CO_2 (transcutaneous and end-tidal).
	Questionnaires Five questionnaires will be evaluated during baseline and after 12 months Paediatric Sleep Questionnaire Paediatric Daytime Sleepiness Scale The validated Nasal Obstruction Symptom Evaluation scale Children's Sleep Habits Questionnaire Paediatric Quality of Life Inventory 4.0 (child-self report and parent proxy responses) Health Screening Questionnaire
Craniofacial parameters	A craniofacial index focused on the most common orthodontic problems observed among children with OSA will be assessed at baseline and after 12 months.
Demographic and clinical variables	Medical charts Data from the first sleep consult (reason for appointment, date of sleep referral and nPSG), anthropometric data (blood pressure, growth percentiles for height and weight (preintervention and postintervention), Mallampati score and tonsil size), additional diagnosis and past surgeries, family history, age at the time of sleep consult and postal code.

AHI, Apnoea-Hypopnoea Index; nPSG, nocturnal polysomnography; OSA, obstructive sleep apnoea.

Sleep monitoring

To evaluate an alternative sleep monitoring method, all the participants in this study will wear a biometric shirt (Hexoskin, model HX1, Carre Technologies, Montreal, Canada) during both the baseline and 12-month follow-up nPSG exams. Additionally, participants enrolled in orthodontic management and control cohorts will be offered the shirt to take home for additional measures during the 12 months (two nights in a row, every month). Sleep parameters measured by the biometric shirt will be compared with those obtained by the nPSG (eg, total sleep time, sleep efficiency, wake after sleep onset, sleep latency and time in non-Rapid Eye Movement (n-REM) sleep) to determine if the body movements and breathing rates obtained through the biometric shirt correlate with the same parameters obtained from the nPSG.[42]

Sleep-related disorders and residual OSA

The changes in severity and symptoms of RLS, PLMD and paediatric insomnia across the three cohorts will be examined. The Paediatric RLS Severity Scale and the nPSG exam will be used to assess RLS and PLMD, respectively. The assessment of paediatric insomnia will be performed using history and physical examinations and the Children's Sleep Habits Questionnaire. All three conditions will be assessed at baseline and after 12 months.

Existing comorbidities and residual OSA

To examine possible asthma and obesity metabolomic markers (eg, alanine, glucose, uric acid)[43 44] associated with intervention's effectiveness, blood, urine and saliva samples will be collected and assessed at baseline and after 12 months. The information regarding existing comorbidities and/or previous health conditions related to OSA will be collected from medical records. A panel of 140 metabolites will be screened at The Metabolomics Innovation Centre (TMIC, University of Alberta), including amino acids, organic acids, monosaccharides, glycerophospholipids and carboxylic acid previously associated with obesity and asthma in children.[43 44] The blood, urine and saliva collection procedure will follow the TMIC protocol.[45–47] Metabolite concentrations from the control cohort will be used to establish normal metabolite concentrations that will be used to determine any differences between cohorts. A sevenfold cross-validation will be adopted to evaluate the differences between metabolite concentrations across cohorts.[48 49]

Data analysis plan

The effectiveness of the intervention will be determined through sleep parameters, medical history (from medical chart reviews), questionnaire responses, craniofacial characteristics and metabolomic markers at baseline and 12 months after enrollment. Results will be compared with changes or lack thereof in the control cohort.

For the data analysis, we will develop an algorithm called SmiLe (Statistical, Mathematical, Intelligence Learning E-algorithm), which is based on a combination of three scientific branches—statistics, mathematics and deep learning in artificial intelligence. The SmiLe algorithm will determine the evidence for each aim of this study. Furthermore, as subroutines of the algorithm, OSA severity by nPSG will be validated by the severity determined by (1) questionnaires and craniofacial index, (2) data obtained from the biometric device, (3) combined both (1) and (2) data sets.

Types of data, in general, can be differentiated into structured or unstructured data. For example, upper-airway shape and nPSG time series are considered unstructured, while the rest of the data sets described in our study are considered structured. There are two different approaches to analysing unstructured data. The first approach is to explore it alone using advanced techniques, such as persistent homology[50] from computational topology and/or convolutional and recurrent networks[51 52] from deep learning. This approach is advantageous because it will likely discern signals from noise in the data. However, a disadvantage is that it is not easy to incorporate its analysis with structured data. The second approach is to transform unstructured to structured (U2S) data; classical analytical methods in statistics and machine learning make a joint analysis of the combined structured and U2S data possible. However, a disadvantage of U2S might be that it is less likely to detect essential features from unstructured data than the first approach. In this project, we will use both techniques.

Analysis 1

Questionnaires, metabolic concentrates, BMI and medical data will be analysed using Bayesian networks.[53] Bayesian models of all questionnaire responses will determine whether the OSA symptoms and quality of life have improved after the intervention. Analysis of metabolite concentrations modelled by Bayesian networks might detect an association between OSA and other diseases. We will also compare the Apnoea-Hypopnoea Index (AHI) before and after the intervention to quantify OSA improvement.

Analysis 2

We will concentrate on predicting sleep states. The five sleep states that will be considered are wake, 1–3 n-REM and REM, as recommended by the American Academy of Sleep Medicine. Time series is an example of unstructured data. We will analyse the nPSG time series using advanced methods in computational topology and deep learning.[53 54] We will apply Hidden Markov models to obtain the most plausible sleep states using EEG, EOG, ECG and EMG for children with OSA. We use a probabilistic graphical structure in the Hidden Markov model where sleep states are unknown and observed time-series signals. The optimal sleep states will be calculated using the EM and Baum-Welch algorithms.[54 55] The same analysis will be repeated using heart rate, breathing rate and one-channel ECG. The reason for this is to compare sleep states between nPSG and biometric shirt data. Biometric

shirts can measure heart rate, one-channel ECG, breathing rate and movements (acceleration, activity level 1 Hz, step counting, cadence and energy expenditure estimate). Still, none of the measures are on other functional parts of the body. To make accurate comparisons between nPSG tests and the biometric shirt, the participants will wear biometric shirts during their nPSG tests. Biometric devices can only determine sleep states of wake, n-REM and REM.[42] The main objective of analysis 2 is to determine any relationship between sleep stages and severity of paediatric OSA. The second objective of analysis 2 is to see whether sleep stages determined by PSG and biometric devices are well matched.

Analysis 3

We will analyse all the nPSG time series to estimate AHI by using recurrent neural networks in deep learning. The estimated AHI will be compared with AHI scored by sleep specialists. We will also calculate AHI for biometric device outputs, including heart rate, breathing rate and ECG channel. Finally, AHI from nPSG will be compared with the estimated AHI from the Biometric shirt.

Patient and public involvement

Prior to initiate developing this study, families of paediatric patients with OSA were interviewed to understand their views about management and their journey in health services whiles seeking for care in a qualitative description study. The clinical team who screens patients target in our study was consulted prior to the design of this protocol. Participants will be asked to assess the burden of intervention (if applicable to their cohort) and time requires to participate in the study. Future discussions with participants will seek feedback on the relevance of findings and guide research dissemination and communication to wider groups.

ETHICS AND DISSEMINATION

This project was approved by the Health Research Ethics Board (Pro00084763, Health Research Ethics Board-Health Panel, University of Alberta, Edmonton, Canada).

Study findings will be disseminated in both sleep medicine and orthodontics disciplines through peer-reviewed journals and conference presentations. These findings will be shared with the Sleep division of the Stollery Children's hospital to inform clinical practice. Summaries of our findings will be made accessible to laypeople, such as parents and caregivers of children with OSA, in formats (eg, hospital's magazine, hand-outs shared to parents during visits to sleep clinic) that facilitate their understanding. These summaries will be posted on our website and shared in social media venues targeted to our participants' population.

DISCUSSION

The management protocol for residual OSA in children, when T&A is not an option or is unsuccessful, is not clearly defined. Considering the chronic nature of OSA and the long-term health consequences of this condition, investigating the effectiveness of alternative management options is urgent. This study will evaluate the effectiveness of orthodontic interventions compared with a control cohort. Outcome data will be collected at baseline and 12 months after enrolment.

Some orthodontic interventions (eg, RME and mandibular advancement) have been shown to improve the AHI index and OSA signs and symptoms in children.[16 31 56] The difference between this proposed cohort study and previous related attempts lies in focusing on a sample of residual OSA children. These children were unresponsive to T&A or T&A was not indicated. This follows the currently known management pathway for paediatric OSA. This study will provide a detailed assessment of several physiological responses when orthodontic management is indicated and followed up, lacking in the existing literature. Most previous related studies relied only on the AHI index as an outcome measurement.[57] It has been suggested that the adoption of this metric only, without considering other sleep evaluation features (eg, event duration, arousal intensity, flow limitations and obstructive hypoventilation) may limit the understanding of paediatric OSA management results.[58]

Nevertheless, evidence on the effectiveness of orthodontic management in children with OSA is limited and inconclusive. A reduction in the AHI index and daytime sleepiness have been reported. However, these findings are based on either short-term or uncontrolled studies.[33 56] A broader analysis of the effectiveness of orthodontic management for residual OSA in comparison to other options is required to establish whether orthodontic interventions may be able to address residual OSA in children with selected craniofacial abnormalities. The primary outcome of this study is to evaluate the effectiveness of orthodontic interventions as a management option for residual OSA. Assessment includes the analysis of sleep parameters, craniofacial parameters, quality of life and lifestyle changes.

In addition to assessing treatment effectiveness, we aim to analyse how other sleep-related disorders, including insomnia, PLMD and RLS, relate to residual OSA and the adopted management options. Along with OSA, insomnia, PLMD and RLS figure as primary sleep disorders.[11 42] In adults, it has been suggested that sleep-related movement disorders and insomnia were more frequent in individuals with OSA compared with healthy subjects.[20 21] However, there is a lack of evidence exploring the association of both conditions in children with OSA.

A secondary outcome in our project will be the association of two comorbidities, obesity and asthma, with residual OSA. Obesity is recognised as a risk factor for paediatric OSA, and it was associated with poor outcomes for some OSA management options.[57 59] Also, children with asthma are more likely to develop chronic snoring and OSA.[4] A relationship between both of these comorbidities and paediatric OSA has been suggested.[19] This

study will evaluate this association from the metabolomics perspective, showing higher accuracy in diagnosis, prediction and therapeutic targets for diseases.[60] Among the multiple medical conditions associated with OSA, the investigation of obesity and asthma metabolites may represent a source to improve paediatric OSA understanding and future screening approaches. This technique may clarify the influence of both asthma and obesity in managing residual OSA in children.

We will assess the suitability of a biometric shirt as an adjunct screening option for identifying children with OSA. Biometric shirts have been used and previously validated in adults for sleep screening purposes.[42 50] However, no studies have investigated these wearable devices in children to date. These devices monitor movements, heart and breathing rates, and sleep parameters with more accurate sensors than actigraphy and nocturnal oximetry.[42]

Collectively, we aim to understand the effectiveness of orthodontic approaches for residual OSA management and screening from a comprehensive perspective. Along with the effectiveness of the target interventions on disorder management and quality of sleep and life, we will examine associations between residual OSA and obesity comorbidities and other sleep disorders. In addition, other potential screening options for paediatric OSA will be assessed to enhance monitoring and identification of this condition.

As an exploratory study, this project presents some limitations. First, the absence of randomisation when assigning participants to each cohort can result in a selection bias that cannot be avoided. For example, uneven proportions of children with different OSA severity or BMI across cohorts. However, adequate statistical techniques will be used to control these covariates if needed. In addition, the reduced number of in-person interactions due to the COVID-19 restrictions might prolong the recruitment of participants for the study.

After the orthodontic intervention, we expect children to improve their OSA symptoms and quality of life. This project will determine if metabolite changes in management cohorts will differ from those in the untreated control cohort. Metabolomics biomarkers may represent an effective tool in finding (and possibly predicting) comorbidities associated with paediatric OSA. To date, no research has been conducted on residual paediatric OSA and its association with other diseases based on metabolomics.

The target population for our study is children for whom T&A was not successful in managing OSA. Our study will provide evidence on whether orthodontic management improves, at least temporarily, OSA symptoms and the quality of life of these individuals. This evidence is important for the practice of orthodontics. Unfortunately, research on this potential benefit for children that responded unsuccessfully to T&A is limited.

Contributors GH and CF-M conceptualised the study. NCFF developed the first draft of the manuscript. CF-M, AP-G, DG and GH contributed to the development of the study protocol and approved the final draft of the manuscript.

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Competing interests None declared.

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