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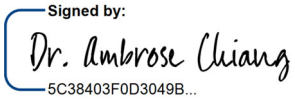
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THE IMPACT OF TECHNOLOGY IN THE MYOFUNCTIONAL THERAPY TREATMENT OF OBSTRUCTIVE SLEEP APNEA SYNDROME

By

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Submitted in partial fulfillment of the requirements for the degree of
Master of Science in Dentistry

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TABLE OF CONTENTS

ACKNOWLEDGEMENTS.....3

ABSTRACT.....4

REVIEW OF LITERATURE.....5

LITERATURE REVIEW REFERENCES.....38

STATEMENT OF THESIS..... 45

MANUSCRIPT FOR PUBLICATION.....46

MANUSCRIPT REFERENCES……60

APPENDIX FOR RESEARCH DATA….....62

IRB APPROVAL…….....78

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ABSTRACT

Introduction: The aim of this study is to compare the effects of myofunctional exercises in subjects diagnosed with OSA when delivered via a smartphone app versus a self-directed analog method. Also, we are comparing the effect on adherence to myofunctional therapy (MFT) when using the smartphone app versus a self-directed analog method. **Methods:** All patients agreed to participate and provided offline informed consent. At the initial visit, several specific variables were collected. Basic demographic data (age, sex, height, weight) were self-reported and/or calculated (BMI). Neck size and weight size at time of enrollment were assessed. Subjects were given several OSA questionnaires to assess their baseline OSA risk assessment, breathing efficiency and sleep quality. (STOP-Bang, NOSE, PROMIS Sleep Disturbance 8b Short Form, PROMIS Sleep Impairment 8a Short Form, and Epworth Daytime Sleepiness). Baseline tongue protrusion, posterior tongue elevation and buccinator strength were measured with the Iowa Oral Performance Instrument (IOPI). For those patients randomized into the smartphone app group, they were instructed to download and set-up the Airway Gym app for MFT routine. For those subjects randomized into the self-directed analog myofunctional exercises group, they were given a set of exercises where instructions to the MFT routine will be given on paper. Subjects in the analog group were given a 30-day diary to track adherence with daily exercises. Finally, subjects were fitted with a Belun Ring which recorded the subject's AHI and Oxygen Saturation. Subjects returned for monthly follow-ups for a total study duration of 3 months. At month 1, month 2 and month 3, data from Belun ring were uploaded, Tongue protrusion & posterior elevation strength and buccinator strength on both the right and left side were recorded with IOPI device and the PROMIS & Epworth questionnaires were completed. For adherence assessment, the Airway Gym app was reviewed each visit or for the analog group, the 30-day diary was collected. **Results:** The percent change (Δ) at each timepoints for all variables collected when compared between the analog group and the Airway Gym group were not statistically significant. There was no statistical difference between the decrease in AHI amongst the two groups. While both groups displayed a decrease in adherence over the course of the study, the percentage by which the Airway Gym group displayed a loss in adherence was much larger when compared to the Analog group. **Conclusion:** There is no statistical difference in the outcomes of numerous variables listed in the study when myofunctional therapy is delivered via analog or smartphone application. There appears to be a difference in compliance where patients prefer the analog format to these exercises over the use of the Airway Gym app.

Literature Review

Background

Sleep related breathing disorders (SRBDs) are conditions of abnormal and difficult respiration during sleep, including chronic snoring and sleep apnea. Some sleep-related breathing disorders have limited health impact but others can have serious consequences because of their potential effects on sleep and the balance of oxygen and carbon dioxide in the blood. These disorders include, primary snoring, upper airway resistance syndrome, OSA and other related manifestations of central sleep apnea and sleep-related hypoventilation.

Obstructive Sleep Apnea (OSA) (Behrents 2019) occurs as a function of increased collapsibility of the upper airway. This collapsibility of the upper airway is related to a reduced neuromuscular tonicity of these upper airway musculature. Respiratory work is increased by the body as a response to maintain airflow, which, according to Behrents group, results in a relative increase in serum carbon dioxide and decrease in serum oxygen. This increased effort in breathing causes arousal from sleep and raises heart rate, blood pressure and a tendency towards cardiac arrhythmias. This arousal serves to increase airflow and upper airway patency. For patients with OSA, sleeping is a constant cycle if sleep-related upper airway

collapse with arousal and then a return back to sleep. This disturbance in sleep can occur multitudes of times per hour during a patient's sleep. OSA is further complicated by the fact that its etiology is multifactorial involving multiple areas of the body including variations in neuromuscular muscle tone which may induce changes in craniofacial structures. Other related anatomical factors may also be at play, such as the fact that complexity of OSA may also be related to central respiratory control or loop gain. Patency of the airway is further affected by hormonal fluctuations, obesity, rostral fluid shifts and genetic predisposition causing anatomical factors that would increase the risk of a patient to develop OSA. Craniofacial morphologies that may predispose patients to OSA include retrognathic mandible, dolichocephalic facial types, high vaulted palates, steep mandibular plane angle, anterior open bite, maxillary midface deficiency and a lower hyoid bone position. OSA (Reuda 2020) is characterized by episodes of apnoea (the complete cessation of ventilation) or hypopnea (reduced breathing) during sleep. Untreated OSA can have numerous serious consequences and result in a general decrease in a person's quality of life. OSA is associated with an increased risk in occupational injuries, being involved in motor vehicle accidents, metabolic disease, cardiovascular diseases, and mortality. OSA increases the risk of insulin resistance,

coronary artery disease, congestive heart failure, myocardial infarctions, hypertension, stroke, cardiac arrhythmias, and sudden cardiac death. Neurocognitive impairment due to poor quality of sleep leads to decreased performance in school and in occupation. Chronic fluctuations in serum oxygen levels, increased sympathetic neural activity and associated endothelial damage and heightened inflammation are related to metabolic dysfunction and ultimately organ failure.

Estimates of overall prevalence of OSA in adults is about 14% of all men and 5% of all women in the population, with prevalence rates increased in populations with increased risk factors. Underdiagnosis and lack of understanding in self-reporting of OSA likely leads to a false reduction in the true population prevalence of the disease. Obesity is probably the most significant risk factor for OSA in adults and children (Carneiro 2018 & Andersen 2019). It is estimated that over 70% of patients with OSA are obese and the prevalence of obese people with OSA is as high as 45%. Socioeconomic status is also a potential risk factor for OSA. Coupled with obesity and access to healthcare, there are correlations between OSA and ethnic minorities (Guglielmi 2019).

Patients with OSA often report a history significant of snoring, gasping respiration, choking and witnessed pauses in breathing by a partner (apneic events) during sleep. Classic

symptoms such as snoring, unrestful sleep, or excessive daytime sleepiness are experienced mainly by men. Women's symptoms can be more unspecific; namely fatigue, tiredness, sleep onset and sleep maintenance, insomnia and/or morning headaches. Other common clinical symptoms include difficulty with attention and concentration, unstable mood shifts, and uncontrolled other medical comorbidities such as diabetes mellitus, hypertension and obesity.

Treatments Available

OSA in its severity falls on a wide spectrum. This large range in presentation leads to a variety of management approaches and differences in individual treatment response. The severity of OSA is categorized by AHI or RDI per hour. AHI is defined as the apnea-hypopnea index which is the number of apneas and hypopneas per hour that a patient experiences during sleep. RDI is defined as the respiratory disturbance index which includes the number of apneas, hypopneas, and respiratory effort-related arousals per hour that a patient experiences during sleep. If AHI/RDI is less than 5 times per hour in an adult, the patient is considered within normal limits. Mild OSA is classified as patients that have between 5 to 15 AHI/RDI. Moderate OSA is classified as 15 to 30 AHI/RDI. Severe OSA is any patient that has AHI/RDI of beyond 30.

Managements (Chang 2019) for such a condition classically includes modification of daily behavior, weight loss counseling, continuous positive airway pressure (CPAP), fabrication of oral appliances, medication, and/or surgery. For clarification, Chang classifies behavioral modifications as addressing factors that may increase the likelihood for OSA. Discontinuation of alcohol and sedatives use is strongly recommended for all OSA patients. Weight loss is known to favorably affect airway integrity by minimizing snoring and apneic events. Not sleeping in a supine position also potentially reduces the frequency of apneic events.

First line of treatment for OSA is usually continuous positive airway pressure, where the upper airway is held open by air pressure to improve airway patency during sleep. Regular use of CPAP effectively reduces symptoms of daytime sleepiness and improves quality of life measures across the board in many but not all patients with moderate to severe OSA. Patil et al 2019 states that the CPAP has a general compliance rate of 67%. However, Handan 2019 reports that rates of non-adherence, where adherence is described as 4 or more hours of use nightly for about 75% of the days in a month, ranges from 46% to 83%. Therefore, treatment alternatives to the CPAP have been widely investigated in healthcare.

Another popular modality for treatment in patients with OSA is oral appliances (OA's). Ferguson et al 1997 reports that compared to OAs, CPAP yields better polysomnography outcomes, especially in the reduction of AHI. Thus, they conclude that CPAP is more effective for improving sleep-disordered breathing. However, in terms of clinical results, OAs and CPAP achieve similar outcomes. Kushida et al 2006 states that OA is the preferred therapy for OSA when CPAP is ineffectual. OAs are not without their own downsides as well. Araie et al 2018 described that long term OA use was associated with dental changes. Significant changes in mandibular incisor inclination contributes, in some patients, to decreased overjet and overbite. They do continue to assert that while these side effects may seem substantial, they are outweighed by the potential benefits of using an OA. It is crucial and the responsibility of the provider that patients prescribed to use OAs are informed of the possible long-term side effects before beginning therapy with OAs.

Recent evidence, as presented by Camacho et al 2017, have suggested that rapid maxillary expansion is an effective treatment method for OSA in children with maxillary constriction. The expander can increase the size of the nasal cavity and substantially increase the volume of airflow through the nasal airway. It is important to note that there are several

factors to consider with rapid maxillary expansion. It often produces large unwanted tooth movements, especially as the patient is closer to skeletal maturation. As described in literature throughout the American Journal of Orthodontics and Dentofacial Orthopedics, such as Ghoneima et al 2011, RME is more effective for expansion of the anterior and inferior parts of the maxilla but less so in the posterior and superior regions due to the more rigid ossifications of the maxilla to the sphenoid bone. In mature adult patients, options are far more limited with respect to rapid maxillary expansion. In adults, expansion must be surgically assisted. These surgical procedures increase the risk of morbidity and increase treatment costs for the patients. Mini-implant assisted rapid maxillary expansion (MARME) is now a common alternative offered to adults and adolescents who are skeletally mature. Recently, studies by Kim et al 2018 and Storto et al 2019 have shown that MARME is achievable and predictable in younger adults. Beyond just providing an effective solution for maxillary transverse deficiency in patients, MARME can also reduce upper airway resistance. This further supports that MARME may be an effective treatment modality for adults with OSA.

Current studies are lacking to confirm the extent of effectiveness of maxillary skeletal expansion on OSA across a larger number of adult patients. Because of its lower costs and

fewer risks when compared to surgical expansion or surgically-assisted rapid maxillary expansion, the MARME protocol offers a great future for not only nonsurgical maxillary orthopedic expansion but also minimally invasive treatment for OSA.

The most invasive treatment options for adults with OSA would necessitate consideration for certain surgical procedures. One of the most common surgical procedures for OSA patients is the uvulopalatopharyngoplasty (UPPP), which essentially involves the resection of the tonsils, uvula, and posterior velum. As reported by Auroa et al 2010, UPPP does not consistently achieve normalization of AHI though. Thus, the American Academy of Sleep Medicine does not recommend UPPP as the sole treatment for patients with moderate to severe OSA. In fact, a meta-analysis done by Choi et al 2016 reports that only Friedman stage I classification (patients with large tonsils and relatively normal palatal position) reports surgical success and marked improvement in severe OSA symptoms.

The most effective surgical treatment reported for OSA remains Maxillomandibular advancement surgery or MMA with success rates reported between 75%-100%; Riley et al 1993. The standard MMA surgical technique is a standard Le Fort I osteotomy with a mandibular bilateral sagittal split osteotomy for bimaxillary advancement. Through this movement, the base of the tongue and the soft palate are drawn forward, which

increases upper airway space and decreases upper airway resistance. Most patients with high AHI after failing other lines of treatment for OSA are likely to benefit from MMA. Walte et al 1995 group considers MMA as the gold standard for surgical orthodontic care for OSA patients. Hsieh et al 2013 showed that MMA is an effective treatment for OSA not only because it enlarges the upper airway in the anteroposterior and lateral dimensions, but that it also raises the hyoid bone. Tracheostomy is considered as a last resort surgical procedure for patients with OSA. It involves particularly invasive surgical procedures that act to bypass upper airway obstructions which would substantially improve OSA at the sacrifice of quality of life for day-to-day activities. Thus, the ideal tracheostomy candidates are patients who have failed all other lines of treatments, who are not candidates for soft tissue surgeries, and/or have refused MMA surgery. According to Guilleminault et al, tracheostomies were the primary surgical modality for treating OSA subjects when other medical managements have failed from the late 1960s to the early 1980s.

Nowadays, surgical procedures can be staged or be delivered in phases in different combinations depending on the patient's needs. It is generally accepted that the site of upper airway obstruction varies amongst OSA patients. These sites include the soft palate, lateral pharyngeal wall, base of the tongue, or

hypopharynx. As per Li et al 1999, the first phase of surgery is based on the level of obstruction, as determined in a presurgical evaluation. In the first phase, surgery procedures can include UPPP for oropharyngeal obstructions or genioglossus advancement with hyoid myotomy, or suspension for base-of-tongue obstructions. Six months after phase I surgery, a repeat polysomnography is performed, and patients who did not achieve surgical success or cure are referred for phase II surgery. The second phase of surgery only occurs when patients fail from the first phase and consists of MMA advancement osteotomies.
Finally, the next evolution of surgical treatment of OSA is neurostimulation, specifically hypoglossal nerve stimulation. In 2014, the US FDA approved the use of hypoglossal nerve stimulation for treating OSA. Sleep surgeons implant an upper-airway stimulation device in OSA patients, which is a popular option for patients who have difficulty tolerating or adhering to CPAP usage. Neurostimulation for the stability of the upper airway during sleep was introduced as a less invasive and more effective option for these select patients. According to Wray et al 2016, the success rate of hypoglossal nerve stimulation is highest in patients who have a low body mass index, AHI’s less than 50 on average, and an anteroposterior pattern of palatal collapse.

Myofunctional Therapy

Myofunctional therapy is one of the newest treatments for sleep disordered breathing. This is an exercise therapy of the tongue and oropharyngeal muscles and aimed at correcting an "aberrant swallow" and encouraging nasal breathing; it was originally designed to help foster the development of straight teeth and improve facial growth in children. The idea behind its use in OSA therapy is that these exercises will improving the tone/strength of the upper airway muscles, thereby reducing collapsibility. Swallowing and habit correction requires three-times-a-day practice, but muscular strengthening can be achieved with once daily practice. The idea is that increased tone will stiffen the pharyngeal walls, thereby reducing airway collapsibility and reducing the severity of OSA. Myofunctional therapy and proper tongue positioning in the oral cavity have been described since 1918 to improve mandibular growth, nasal breathing, and facial appearance. A study done by Puhan et al 2005 generated a lot of excitement in this treatment modality when they showed that upper airway muscle training while awake with the use of didgeridoo playing significantly aided in reducing OSA severity and its associated symptoms. This study was inspired when a didgeridoo instructor noticed that he and his pupils experience subjective improvements in daytime sleepiness and snoring after practicing this instrument for

several months. The results of this study showed that compared to control, there was a statistically significant reduction in daytime sleepiness, AHI and their partners reported significantly less sleep disturbance.

Myofunctional therapy for OSA consists of a multi-component intervention including several combinations of oropharyngeal exercises. The patient is instructed to perform these exercises regularly three times a day for at least 3 months, with weekly sessions with a myofunctional therapist to ensure proper performance of exercises. To note, myofunctional therapy is generally associated with low adherence. Additional barriers to therapy exist, including cost and a general lack of insurance coverage for it in the USA. There are many variations and proposals by groups regarding the time frame of the treatment, the type and intensity of exercises to be included, and the delivery of the interventions. Therapies can include isotonic and isometric exercises involving several muscle groups and areas of the mouth, pharynx, and upper respiratory tract. These exercises work by asking the patients to perform functions such as speaking, breathing, blowing, sucking, chewing or swallowing. Because the dilator muscles of the upper airway play a critical role in maintaining an open airway during sleep, researchers have aimed to explore airway trainings and exercises that target the oral cavity and oropharyngeal structures as a method to

treat OSA. As asserted by Reuda 2020, myofunctional therapy aims to improve the functioning of the "upper airway dilator muscles" that are essential for maintaining the patency of the patient's upper airway; the site of obstruction for patients with OSA. These muscular endurance exercises aim to improve the tone, tension and mobility of oropharyngeal muscles and soft tissues, in order to effectively reduce airway closures during sleep. These therapies may also reduce parapharyngeal fat pads, such as tongue fat, which are increased in patients with OSA.

In the current landscape where many of the current techniques for treating snoring and OSA are invasive, surgical or involve wearing a device, a technique that can serve either as a primary treatment or as an adjunct treatment without necessitating surgery or wearing a device would be very beneficial. Tongue and oropharyngeal exercises have been shown to improve OSA in both children and adults.

The most cited study of myofunctional therapy exercises as a treatment for OSA was published by Guimaraes et al in 2009. The exercises involved the soft palate, tongue, and facial muscles performed 30 mins a day. They functioned to address stomatognathic functions also. For soft palate exercises, patients were instructed to pronounce oral vowel sounds either continuously (isometric exercises) or intermittently (isotonic exercises). Tongue exercises included moving the tongue along

the superior and lateral surfaces of the teeth, positioning the tip of the tongue against the anterior aspect of the hard palate, pressing the entire tongue against the soft and hard palate, and finally forcing the tongue onto the floor of the mouth. Facial exercises addressed the lip via contraction and relaxation of the orbicularis oris muscle, the buccinators via suction movements and applying intraoral force with finger pressure against the buccinator muscles, and jaw muscles via lateral jaw movements. Stomatognathic functions were exercised by instructing the patients to inhale nasally and exhale orally without and then with balloon inflation. Specific swallowing and chewing exercises performed three times a day and during meals were then prescribed at the end of the series by asking the patient to swallow with the teeth lightly touching, tongue positioned in the palate and without contraction of the perioral muscles, while alternating chewing sides. Anthropometric measurements, snoring frequency & intensity, Epworth daytime sleepiness and Pittsburgh sleep quality questionnaires, and a full polysomnography were performed at baseline and at study conclusion. Patients randomized to oropharyngeal exercises in this study had a significant decrease in neck circumference, snoring frequency, snoring intensity, daytime sleepiness, sleep quality score and AHI. The changes in neck circumference correlated inversely with changes in AHI. By finding

statistically significant reduction in neck circumference (39.6 +/- 3.6 vs. 38.5 +/- 4.0 cm), snoring frequency (4 [4-4] vs. 3 [1.5-3.5]), snoring intensity (3 [3-4] vs. 1 [1-2]), daytime sleepiness (14 +/- 5 vs. 8 +/- 6), sleep quality score (10.2 +/- 3.7 vs. 6.9 +/- 2.5), and OSAS severity (apnea-hypopnea index, 22.4 +/- 4.8 vs. 13.7 +/- 8.5 events/h), the group was able to conclude with statistical significance that oropharyngeal exercises significantly reduces OSA severity and its associated symptoms and asserts that myofunctional therapy is a promising treatment for moderate OSA.

In the systematic review and meta-analysis done by Camacho et al in 2015 reviewing nine adult and two pediatric studies evaluating the effect of myofunctional therapy on OSA, they were able to draw five main conclusions overall. First, myofunctional therapy provided an overall reduction in AHI in approximately 50% of adult subjects and 62% of child subjects. The pre- and post-myofunctional AHI for adults decreased from 24.5/h to 12.3/h. For pediatric patients, the pre- and post-myofunctional therapy AHI decreased from 4.87/h to 1.84/h. In studies with control groups, there was little to no improvement in AHI for the control groups when compared to the groups that had received intervention with myofunctional therapy. They also saw clear improvement in lowest oxygen saturation by approximately 3-4%. Second, myofunctional therapy decreases snoring both

subjectively and objectively. End of study polysomnography demonstrated a 72.4% reduction in snoring pre- versus post-myofunctional therapy with a snoring rate of 14.05% pre-intervention reduced to 3.87% after-intervention. In subjective metrics, studies quantifying outcomes reported that during the post-myofunctional therapy review, there was a reported decrease in snoring to either light snoring, or that the sound changed to something similar to normal breathing amongst study subjects. Third, subjective sleepiness also improved post-myofunctional therapy as demonstrated by a significant reduction in Epworth Sleepiness Scale for subjects in which this particular questionnaire was administered. There was a reduction from an total average score of 14.8 pre- to 8.2 post-. At that particular post treatment level, the subjects reached a ESS score that is below the threshold for hypersomnia. Fourth, despite the heterogeneity in the prescribed oral and oropharyngeal exercises amongst all the studies in the meta-analysis, there were overall improvements in polysomnographic outcomes and sleepiness across the board. Myofunctional therapy was recorded to be performed as little as 5 mins a session, twice daily, 4 days a week for 2 months to as many as 10 mins, three to five times daily for 3 months. The longest published follow-up timeline for myofunctional therapy for adult OSA was that with the Guimaraes group, which was 6 months of follow up.

The fifth and final conclusion drawn from the Camacho meta analysis was that future research is still needed to help explain the mechanism of action and patho-physiology of myofunctional therapy as treatment for OSA. It was hypothesized that the exercises improve oral and oropharyngeal muscle tone and that they may also serve to decrease the amount of fatty deposition of tongue, but this has not been currently proven in today's literature. The heterogeneity of the prescribed oral and oropharyngeal exercises are also a problem. It is recommended by this group that future researchers consider standardizing the prescribed exercises . It was stated by the Guimaraes group that because myofunctional therapy is based on an integrative approach with a series of exercises, it is not possible to determine the effects of specific exercises to determine which one contributes the most to improvements in each and every outcome. The group recommends that future research is needed in exploring the individualistic contributions of each specific exercise to the muscle groups that each exercise is working.

In a systematic review done by Rueda et al in 2020 where they reviewed nine RCT studying the benefits and harms of myofunctional therapy for the treatment of OSA, they were able to reach several important conclusions. In these nine RCT's, myofunctional therapy was compared against various control groups such as sham therapy or no intervention, the CPAP, other

active intervention, and combination therapy with iterations alternating between CPAP, sham therapy and myofunctional therapy.

This review concluded that compared to sham therapy or no therapy, myofunctional therapy probably reduces daytime sleepiness, increases sleep quality, and may result in a large reduction in Apnoea-Hypopnoea Index. Compared to sham therapy, there may be little to no effect in the reduction of snoring frequency but the evidence is described as very uncertain and probably reduces subjective snoring intensity slightly.

Similar to the CPAP, myofunctional therapy exhibits improvements in daytime sleepiness, may reduce AHI and may result change in snoring frequency and snoring intensity. This conclusion highlights the possible strong role that myofunctional therapy can play in improving key metrics in patients with OSA. Myofunctional therapy is shown to be comparable in several outcomes with the CPAP, which is the gold standard in therapy in patients with OSA.

Compared to certain respiratory exercises prescribed by the group plus nasal dilator strip, myofunctional therapy may result in little to no difference in daytime sleepiness, probably increases sleep quality slightly and may result in little to no difference in AHI.

Finally compared to standard medical treatment for OSA, Reuda et al found that myofunctional therapy may reduce daytime sleepiness, may increase sleep quality and may reduce snoring frequency slightly and may reduce snoring intensity. In the pediatric population, adding myofunctional therapy may result in little to no difference in AHI.

All the studies reviewed by the Rueda group were deemed to suffer from small sample size. The length of the interventions and follow-up periods of the studies reviewed were also short, which was defined as less than four months in total study duration. Therefore, they were unable to state that the potential beneficial effects of myofunctional therapy will endure in the medium to long term and cannot also speak on whether compliance with the treatment will persist.

Exercise and its Effect on Muscle Hypertrophy and Tonicity

It is well established that a regimented resistance exercise can promote significant increase in muscle strength and hypertrophy, which improvements in outcome measures are seen irrespective of age and or gender. According to Zou et al 2011, exercise-induced muscular adaptations are at least in part attributed to a phenomenon called mechanotransduction where sarcolemmal-bound mechanosensors, such as integrins and focal adhesins, convert mechanical energy into chemical signals that

mediate myocellular anabolic and catabolic pathways. When skeletal muscles are placed under mechanical overload, the upregulated anabolic processes results in a net increase of muscle protein synthesis, thus resulting in an enlargement of muscle fibers

A meta-analysis was done by Schoenfeld et al 2017 to compare the changes in strength and hypertrophy of skeletal muscle between low- versus high-load resistance training protocols. Current literature at that time in resistance training guidelines assert that loads must be in excess of 70% of one repetition maximum (RM) in order to maximize progression in muscular strength and hypertrophy. RM is defined as the highest resistance that can be applied to a muscle group in order for a participant to do one repetition of exercise. It was debatable as to whether lighter load training where loading is <60% of 1RM, as such in calisthenics (of which myofunctional therapy falls under this class) is capable of recruiting enough motor units to build skeletal muscle in a given set of repetitions.

According to the study however, both heavy and light loads showed a large effect for 1RM increases, in which light loads increased 1RM by 28%. The meta-analysis showed that lighter loads promoted significant increase in isotonic strength. In isometric strength, low loading exercises produced an increase by 20.5% in outcomes. In terms of overall muscle hypertrophy,

there was an overall 7.0% increase in muscle mass in low loading exercises, which is no statistically significant difference when compared to higher loading exercises. The study asserts that the findings indicate that light loads can be effective in promoting muscle growth and muscle strength provided that training is carried out with a high level of effort and/or compliance.

Smartphone in Healthcare and its Effect on Compliance

The use of smartphone applications have been prevalent in many fields in healthcare as an adjunct tool for treatment and patient management strategies. Across many disciplines, literature has shown that patient behavioral patterns can be altered and important health outcomes can be affected with the implementation of smartphone technologies.

Carter et al 2013 investigated in a clinical trial adherence to a smartphone application for weight loss compared to a paper diary and a website. The clinical trial revealed that the smartphone application is a feasible and acceptable weight loss intervention. The group found that adherence to the use of the smartphone application was statistically significantly higher in the smartphone group when compared to that of the website and paper diary group. It is important to note however that adherence in all 3 groups declined over time by the 6 months mark. At the 6 month mark, only 16% of the smartphone

application users continued to use the app. This is still in contrast to the website and paper diary group where the adherence dropped to 0% altogether.

Similarly, Stephens et al 2013 conducted a systematic review to determine the effectiveness of smartphone applications to promote weight reduction and physical activity. The review revealed that smartphone applications are well accepted amongst all subjects and provide beneficial effects on increasing physical activity and modifying other behaviors, such as decreasing sugar-sweetened beverage intake, decreasing screen time, and encouraging healthier eating patterns. In health outcomes, smartphone applications also succeeded in reducing body weight, decreasing waist circumference, decreasing BMI and decreasing fat mass.

Montes et al 2012 conducted a RCT investigating the impact of a smartphone based strategy to increase adherence to self-administering PO medication schedule. Results showed that the use of smartphones for daily feedback was efficacious in the enhancement of adherence to administering oral medication on time, especially in patients with historically suboptimal adherence. Improvement in adherence amongst patients remained significantly greater than routine clinical care even after the 6 months of follow-up. Interestingly, there was also a significant improvement in attitude towards the medication

amongst patients who had the intervention of the smartphone application. It was shown to be very useful in increasing adherence among patients who simply forget to take their medication but was still rejected by those patients that had previously rejected the medication. In contrast, there was not an increase in awareness generated in the illness being treated by the medication in either group even when adherence increased. Patients may feel better after treatment, but it does not necessarily imply an increased acknowledgement of the underlying illness.

Finally, in regards to myofunctional therapy, O'Connor-Reina et al 2020 showed that adherence was relatively high because of the ease of contact with a provider and that the app delivered instantaneous acoustic and visual feedback about the patient's performance after every exercise. O'Connor-Reina's group found that in their study, subjects adhered to the Airway Gym program at a rate of 64% on average, while the national average for adherence to myofunctional therapy has historically been around 10%.

Relevant Materials Pertinent to the Study

Airway Gym

A pilot randomized trial was created in 2020 by O'Connor-Reina et al to evaluate and study the effects of Airway Gym app

on the adherence to myofunctional therapy and on the AHI in patients diagnosed with severe OSA, which is categorized by a baseline AHI of >30. They also attempted to evaluate the oxygen desaturation index, used the Iowa Oral Performance Instrument to evaluate the effects of the app on the tone of the genioglossus and buccinator muscles, and used the Epworth Sleepiness Scale and the Pittsburgh Sleep Quality Index questionnaires to evaluate subjective daytime sleepiness and sleep quality. In the result, the research group was able to show that the Airway Gym app helped improve the AHI and upper airway muscle tone in patients. Over the course of the study, the group found no significant change in neck circumference, which suggests that the increase in muscle tone measured by the IOPI instead of a reduction in neck circumference as described by Guimaraes et al, helped improve the patients' AHI. The group attributes the success of the app to the fact that the myofunctional therapy was based on proprioceptive training which serves to benefit the sensorimotor deficit in the upper airway muscles of the patients. As literature has shown, the main disadvantage of myofunctional therapy is the poor adherence to the therapy and the absence of objective feedback. This study showed that adherence was relatively high because of the ease of contact with a provider and that the app delivered instantaneous acoustic and visual feedback about the patient's performance

after every exercise. Monthly visits for the measurement of IOPI scores also provided them with an objective way to evaluate patient progress and to promote adherence to the therapy. They do note that the efficacy of myofunctional therapy can be limited in patients with restricted tongue movements, permanently deviated septums, or temporomandibular joint disorder.

Iowa Oral Performance Instrument

Franciotti et al 2022 performed a meta-analysis on reliability of the Iowa Oral Performance Instrument or IOPI. They investigated whether IOPI was a reliable tool to distinguish healthy controls from patients with swallowing disorder; whether IOPI was reliable across all age groups; and whether IOPI was able to measure changes in swallowing performances following traditional treatments and tongue training exercises. They determined that the meta-analysis showed the usefulness of IOPI as a quantitative measure of swallowing performance. The tool was able to show that maximum tongue pressure was higher in healthy controls compared to affected populations.However, IOPI is not reliable for evaluating tongue endurance. Furthermore, no clear pattern could be deduced from the meta-analysis and a wide dissimilarity amongst all of the results leads to the conclusion that tongue

endurance cannot be considered as a reliable variable to distinguish healthy and diseased subjects in general. The meta-analysis showed that children had higher values for maximum tongue pressure than adults. Children with pathological conditions showed a worse tongue weakness than adults with pathological conditions. Therefore, the difference between healthy controls and patients seems to be larger in children, not only because diseased children show a weaker tongue but also that aging in itself is an ongoing change for tongue pressure. Data analysis of the intervention studies showed a greater improvement in patients after experimental tongue training exercises, especially when a worse maximum tongue pressure value was found at baseline.

Suzuki et al 2020 also observed significantly increased tongue pressures measured with the Iowa Oral Performance Instrument after myofunctional therapy, consisting of various exercises aimed at functionally obtaining the appropriate positioning of the tongue in OSA patients. They also showed a significantly decreased AHI.

STOP-Bang Questionnaire

The STOP-Bang Questionnaire was first developed in 2008. It is a simple, easy to remember, and self-reportable screening tool, which includes four subjective (STOP: Snoring, Tiredness, Observed apnea and high blood Pressure) and for demographics

items (Bang: BMI, age, neck circumference, gender). The scoring guide for the questionnaire is that 0-2 is low risk for OSA, 3-4 is intermediate risk, and 5-8 is high risk for OSA. This questionnaire is much more effective at screening for moderate to severe OSA and it is generally fails to identify clinically significant mild OSA subjects.

Nagappa et all 2015 performed a meta-analysis on validating the STOP-Bang questionnaire as a screening tool for moderate to severe OSA amongst different populations. The group found that a score greater than or equal to 3 is the cut-off for the questionnaire consistently demonstrating a high sensitivity to detect moderate to severe OSA in across different patient populations. When scores are higher than 3, the questionnaire detected OSA in 94% of moderate-to-severe OSA in sleep clinic patients and 91% in surgical patients. Chung et al 2008 wrote that overall, the STOP-Bang questionnaire is a short, practical and straightforward test that can be completed within 1-2 mins with a very high response rate of 90-100%. There is also high negative predictive value to the questionnaire because a low score has a strong correlation that the patient does not have moderate-to-severe OSA. Nagappa concludes that the STOP-Bang questionnaire is an useful clinical tool to identify patients at high risk of OSA and can facilitate the diagnosis and treatment of unrecognized OSA.

NOSE Scale Questionnaire

The Nasal Obstruction Symptom Evaluation (NOSE) scale was developed by Stewart et al in 2004. Stewart et al validated the scale as a quality of life instrument which quantifies nasal obstruction accurately. The NOSE scale questionnaire is composed of five questions. Each question is graded on a scale from 0 to 4 and the final summed score of the five questions is multiplied by 5 so that the total score ranges from 0 to 100. A score of 0 equals no obstruction and a score of 100 equals total obstruction.

Stewart et al states that the questionnaire was designed to be brief and easy to complete with minimal respondent burden. The scores remained consistent when the underlying patient's status did not change, the scores reported on what it was supposed to measure and the scores did change when the patient's status changed.

Epworth Sleepiness Scale

Sleepiness is defined as a measure of a subject's tendency at a particular time to doze or fall asleep. As one of the most used scales in the field of sleep medicine, the Epworth Sleepiness Scale is a short and quick measure that has demonstrated good reliability and validity by groups such as Kendzerska et al 2014 and Lapin et al 2018. Kendzerska et al

2014 was a systematic review evaluating the measurement properties of the Epworth Sleepiness Scale. The group found that while ESS is widely used in sleep research and clinical settings, overall it only has modest measurement properties and there is a lack of high quality evidence on its psychometric properties. Because of the level of internal consistency, the recommendation is that this instrument is used for group level comparisons but we are cautioned against using the ESS for individual level comparison. ESS had larger correlations with other measurements of daytime sleepiness but are less closely related to OSA and general health measures. Thus, ESS may be an adequate measure of OSA symptoms but should not be used to screen for OSA in patients.

PROMIS Sleep Disturbance and Sleep-Related Impairment Forms

PROMIS sleep disturbance and sleep-related impairment item banks were developed to improve self-report regarding the sleep-wake functions in adults. As per Buysse et al 2010, the group defines sleep as a reversible recurrent state of reduced awareness of and interaction with the environment, while wakefulness is an active engagement with the environment. The PROMIS Sleep Disturbance questionnaire is used to measure self-reported perceptions of sleep quality, depth, and restoration within the past seven days. This includes perceived difficulties

falling asleep and staying asleep, as well as sleep satisfaction. The PROMIS Sleep-Related Impairment questionnaire measures self-reported alertness, sleepiness, tiredness, and functional impairments associated with sleep problems within the past seven days. Higher scores on both scales indicates greater sleep/wake disturbances. Buysse et al 2010 found that there are significant differences in the PROMIS Sleep scores between individuals with and without self-reported sleep disorders and between those with treated and untreated sleep disorders. These findings supported the reliability and validity of the PROMIS scales. The group states that this scale is useful because of the ability to measure a wide range of sleep disturbance. It can readily discriminate between patient and control groups but may have limited capabilities differentiating amongst specific sleep disorders, such as chronic insomnia versus obstructive sleep apnea.

Belun Ring

Gu et al 2020 conducted a study to validate the performance of the Belun Ring Platform, a novel home sleep apnea testing system with a patented pulse oximeter sensor and a proprietary cloud-based neural networks algorithm.

The Belun Ring Platform consists of 3 components, a ring pulse oximeter, a charging cradle and a cloud based software.

Respiratory events are detected by changes in the plethysmography (pulse ox) signal that occur with sympathetic surges during termination of these events. The group found a good correlation between the ring's respiratory event index and a polysomnography's AHI report. A good correlation is also seen in the reported total sleep time between the ring and a PSG. They report that the ring exhibits a tendency to overestimate AHI in individuals with AHI under 15 and underestimate AHI in those patients with AHI over 15. This observed discrepancy is observed and reported in other sleep devices as well. It is also important to note that the ring is unable to capture central apneas. Overall, however, the Belun Ring demonstrated an acceptable accuracy in predicting AHI and total sleep time in patients.

SnoreLab Smartphone Application

The use of smartphone applications has long been prevalent as an adjunct tool for assessing healthcare outomes. Downloadable smartphone applications to assess snoring are proven to be promising tools to provide some objevtive measures of sleep disordered breathing at the consumer level. While there are many apps with high ratings and multiple functionalities, Shiao et al 2024 validated SnoreLab as a smartphone application that can provide additional confirmed data for clinicians and

patients to support their continuous daily follow-up for their snoring.

The Snore Score of SnoreLab considers the duration and loudness of detected snoring events to provide a measurement of snoring intensity. The Snore Score and Time Snoring readings of SnoreLab showed a positive correlation with a patient's AHI. Snorelab showed a significant sensitivity and specificity in recording a patient's snoring activity, offering a comprehensive overview of the user's sleep patterns and potential OSA symptoms. Based on the data collected by Shiao, it is noteworthy to conclude that the severity of snoring can be used to predict the severity of AHI. The study reports however that there is a solid cutoff value for predictability of OSA which was that the AHI of patient's were to be greater than 15. This is to say that the SnoreLab application is most reliable in patients with moderate to severe OSA.

As per my review of the literature, myofunctional exercises are now available as application in smartphones, claiming to help increase adherence, and achieve better results than analog methods. As MFT have been shown previously to have certain positive effects on various health outcomes of patients with OSA, further investigation would be beneficial in contribute to how MFT can be best prescribed to the patient population. There

are no studies at this point comparing the myofunctional therapy through an app versus analog methods.

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STATEMENT OF THESIS:

Objective:

- #1. Compare the effects of myofunctional exercises in subjects diagnosed with OSA when delivered via a smartphone app versus a self-directed analog method.
- #2. Compare the effect on adherence to myofunctional exercises in subjects when using the smartphone app versus a self-directed analog method.

THE IMPACT OF TECHNOLOGY IN THE MYOFUNCTIONAL THERAPY TREATMENT OF OBSTRUCTIVE SLEEP APNEA SYNDROME

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Introduction

Obstructive Sleep Apnea (OSA) occurs as a function of increased collapsibility of the upper airway [1]. This collapsibility of the upper airway is related to a reduced neuromuscular tonicity of these upper airway musculature [2]. Respiratory work is increased by the body as a response to maintain airflow, which may have serious consequences to the balance of oxygen and carbon dioxide in the bloodstream. This increased effort in breathing causes arousal from sleep and raises heart rate, blood pressure and a tendency towards cardiac arrhythmias. For patients with OSA, sleeping is a constant cycle if sleep-related upper airway collapse with arousal and then a return back to sleep. OSA is further complicated by the fact that its etiology is multifactorial involving multiple areas of the body including variations in craniofacial structures, obesity, neuromuscular tone and physiological factors related to central respiratory control (loop gain) [3]. Estimates of overall prevalence of OSA in adults is about 14% of all men and 5% of all women in the population, with prevalence rates increased in populations with increased risk factors [4-5]. Underdiagnosis and lack of understanding in self-reporting of OSA likely leads to a false reduction in the true population prevalence of the disease [5].

Managements for such a condition [6-10] classically include continuous positive airway pressure or CPAP, modification of daily behavior, weight loss counseling, fabrication of oral appliances, medication, and/or surgery. Myofunctional therapy (MFT) is one of the newest treatments for sleep disordered breathing [11]. As OSA originates from suboptimal functioning of the upper airway muscles, daily exercises are prescribed; working oropharyngeal muscles in an attempt to strengthen them and to

facilitate opening of the airway. Patients traditionally are instructed to perform exercises three times a day and to follow-up with a myofunctional therapist at least once a week for feedback [12]. MFT works to increase the tone of the intrinsic and extrinsic muscles of the tongue (genioglossus, hyoglossus, styloglossus and palatoglossus) and certain muscles of the face and the airway (pharyngeal constrictors and stylopharyngeus) [1].

However, the main limitations to MFT are the poor adherence to the therapy and the absence of live objective feedback. The national average for adherence to myofunctional therapy has historically been around 10% [13].

The use of smartphone applications has been prevalent in many fields in healthcare as an adjunct tool for treatment and patient management strategies. Across many disciplines, literature has shown that patient behavioral patterns can be altered and important health outcomes can be affected with the implementation of smartphone technologies. Previous trials [14] studied adherence to a smartphone application for weight loss compared to a paper diary and a website. The clinical trial revealed that the smartphone application is a feasible and acceptable weight loss intervention. The group found that adherence to the use of the smartphone application was statistically significantly higher in the smartphone group when compared to that of the website and paper diary group. A systematic review conducted [15] revealed that smartphone applications are well accepted amongst all subjects and provide beneficial effects on increasing physical activity and modifying other behaviors, such as decreasing sugar-sweetened beverage intake, decreasing screen time, and encouraging healthier eating patterns. In health outcomes, smartphone applications also succeeded in reducing body weight, decreasing waist circumference, decreasing BMI and decreasing fat mass.

Finally, a RCT [16] investigating the impact of a smartphone based strategy to increase adherence to self-administering PO medication schedule showed that the use of smartphones for daily feedback was efficacious in the enhancement of adherence to administering oral medication on time, especially in patients with historically suboptimal adherence.

Myofunctional exercises are now available as application in smartphones, claiming to help increase adherence, and achieve better results than analog methods. As MFT have been shown previously to have certain positive effects on various health outcomes of patients with OSA, further investigation would be beneficial in contribute to how MFT can be best prescribed to the patient population. This feasibility study aims to compare the effects of myofunctional exercises in subjects diagnosed with OSA when delivered via a smartphone app versus a self-directed analog method. Also, we are comparing the effect on adherence to MFT when using the smartphone app versus a self-directed analog method. This will help us determine if the use of smartphone apps can achieve better health outcomes while simultaneously addressing the biggest problem with the MFT treatment modality for OSA, which is adherence and accessibility. With our conclusions, it will allow us to make more informed recommendations to patients who are seeking treatment alternatives for OSA.

Materials and Methods

This was a non sponsored study coordinated by the orthodontic department of Case Western Reserve University School of Dental Medicine, Cleveland, Ohio. The protocol was designed and written by the author and was approved by the CWRU

School of Dental Medicine Institutional Review Board (STUDY20231615). All patients provided informed consent. The author vouches for the accuracy and completeness of the data reported and for the fidelity of the study to the protocol.

This was a prospective randomized controlled clinical study in patients diagnosed with OSA; multi-visit and non-blinded.

Patients with newly diagnosed OSA (<1 year on most recent Polysomnography (PSG) with measures of AHI and oxygen saturation) were recruited in person in the CWRU Orthodontics clinic. All sleep studies were interpreted by a sleep technician according to the standard criteria of the American Academy of Sleep Medicine Manual for the Scoring of Sleep and Associated Events, and all interpretations were reviewed by certified physicians.

All patient were recruited based on the inclusion criteria shown in Table 1. In the scope of our study, exclusion criteria is simply the opposite of inclusion criteria.

Randomization was done by block randomization to ensure a generally equal number of subjects in each group; the two blocks being the smartphone application group and the other being the analog group. Subjects were then assigned to each treatment group in the order they were recruited and enrolled.

All patients agreed to participate and provided offline informed consent. At the initial visit, several specific variables were collected. Basic demographic data (age, sex, height, weight) were self-reported and/or calculated (BMI). Please note that no patients were excluded for having a change in BMI of greater than 5% throughout the duration of the study. Neck size and weight size at time of enrollment were assessed. Subjects were given several OSA questionnaires to assess their baseline OSA risk assessment,

nasal patency, sleep quality, and daytime symptoms. (STOP-Bang, NOSE, PROMIS Sleep Disturbance 8b Short Form, PROMIS Sleep Impairment 8a Short Form, and Epworth Daytime Sleepiness). Baseline tongue protrusion, posterior tongue elevation and buccinator strength were measured with the Iowa Oral Performance Instrument (IOPI). The instrument is able to accomplish this by measuring the maximum pressure that an individual can produce in a standard-sized air-filled bulb by pressing the bulb against various parts of the roof of the mouth with the tongue or against the teeth with the teeth. Patient was asked to perform each measurement three times and the maximum pressure out of the three repetitions was recorded. Figure 1 illustrates the three different placements of the bulb for measurements taken.

For those patients randomized into the smartphone app group, they were instructed to download and set-up the Airway Gym app for MFT routine. For those subjects randomized into the self-directed analog myofunctional exercises group, they were given a set of exercises where instructions to the MFT routine will be given on paper. Subjects in the analog group were given a 30-day diary to track adherence with daily exercises. Finally, subjects were fitted with a Belun Ring which recorded the subject's AHI and Oxygen Saturation. Patients were asked to record their sleep data with the Belun Ring 3 nights prior to each follow-up appointment.

Subjects in the smartphone application group were introduced to the app and were instructed to perform the prescribed MFT routine once per day. Subjects in the analog group were given the same exercise routine as presented by the Airway Gym app but printed on paper. They were instructed to perform the exercises once a day and record on the 30-day diary if they were able to complete the routine for each day in the

follow-up cycle.

Subjects returned for monthly follow-ups for a total study duration of 3 months. At month 1 and month 2 follow-up appointments, data from Belun ring were uploaded, Tongue protrusion & posterior elevation strength and buccinator strength on both the right and left side were recorded with IOPI device and the PROMIS & Epworth questionnaires were completed. For adherence assessment, the Airway Gym app was reviewed each visit or for the analog group, the 30-day diary was collected. Adherence was calculated as a percentage of how many days out of a 30-day period did the subject perform the exercises prescribed. At the month 3 follow-up appointment, this visit was also the study's close-out visit. All previously listed procedures associated with follow-up were completed, with several additional outcomes measured as part of the final visit. Final age, height and weight were obtained and final BMI was calculated. Final neck size and waist size were also assessed.

For reference, Table 2 consists of the variables collected for the study and their associated devices.

The Airway Gym app and analog routine included 9 exercises based on myofunctional therapy that are aimed at improving the tonicity of various muscles involved in the pathogenesis of OSA. In the smartphone application group, before every exercise, an animated demonstration and a video would show the subject how to perform each exercise. After each exercise, the subject receives visual, acoustic, and tactile feedback about the success of their performance as a point score. When the subject finishes the exercises, the results are saved on an online cloud storage where the researcher can then externally evaluate the subject's performance and adherence to

the exercise routine. Subjects using the app can follow the progress of their daily activity over time. A chat function is available through which the patient can contact the researcher directly. In the analog group, subjects were given the exercises printed on paper and the researcher reviewed the exercises with the subjects at the initial appointment. Any clarifications that the subjects required about the exercises were given during follow-up appointments but no formal verification was done to ensure that the exercises were being performed as intended at home.

The main objective of these exercises was to increase the tone of the intrinsic and extrinsic muscles of the tongue (genioglossus, hyoglossus, styloglossus and palatoglossus) and certain muscles of the face and the airway (pharyngeal constrictors and stylopharyngeus).

Power sample calculation using G* Power was completed for this study and was determined that ultimately a sample size of at least n=32 was needed for statistical significance. As this is a study for feasibility, the author recognizes that the outcomes from this study is under-powered for analysis of statistical significance. This minimal sample size, however, should provide enough data to assess feasibility of the protocol and experimental design of a research study and allow us to make comments on trends that appear in various outcomes.

Data was collected and aggregated using Microsoft Excel. Given that the study enrolled patients with a wide array of baseline measures, effectiveness of the interventions were measured using percentage changes, between baseline and each follow-up timepoint, as the primary outcome measure. Outcomes that were assessed for statistical significance include IOPI readings on posterior tongue elevation, tongue

protrusion, and buccinator strength, Epworth Sleepiness score, Sleep Disturbance short form 8b t-score, Sleep Impairment short form 8a t-score, AHI, SpO2 Nadir, T90%, and adherence.

Data was tested for normality using Kolmogorov-Smirnov test and Shapiro-Wilk test. Those data sets that were normally distributed were compared using two-tailed paired t-tests. Pearson correlational analysis was used to assess the associations between the changes in the AHI and changes in our other measured variables, including IOPI readings and compliance. Intra-operator reliability was assessed for data collected with IOPI. A P-value of <0.05 was considered to be significant. However, due to the fact that a sample size of n=32 is needed for statistical power, it is important to state that the study is underpowered and there is an increased risk for Type 1 and Type 2 error in our analysis. Therefore, no definitive statements of statistical significance will be made in the scope of this study.

Results

Patients

Eighteen patients were enrolled and randomized from August 2024 to September 2024. Five patients were lost to follow-up or opted to drop out of the study. The data for thirteen patients were included in the study. The full research flow chart can be visualized on Figure 2.

The baseline demographic and sleep characteristics are presented for the two groups in Table 3. There were no significant differences in any characteristics, including age, BMI, neck and waist circumferences. Also, at baseline, AHI and other sleep quality

assessments did not significantly differ.

Intervention

There appears to be no difference in the rate of the percent change (∆) at each timepoints for all variables collected when compared between the analog group and the Airway Gym group (Table 4a-c). While the data analyzed in Table 5 does not specifically address our research objectives, it does provide context to the effects of our study's intervention. Our intervention appeared to induce changes in tongue protrusion, posterior tongue elevation and AHI in both groups after 3 months of exercises.

Clinical and IOPI Measurements

Graphs 1-8 plots our IOPI data collected for tongue protrusion, posterior tongue elevation and buccinator pressure at each timepoint for individual subjects in both groups. The average value for tongue protrusion, posterior tongue elevation and buccinator pressure was calculated at each timepoint and plotted as a line to mark their change across timepoints. IOPI measurements were assessed for significant changes between baseline and final month three follow-up. In the analog group, tongue protrusion changes (p value= 0.05) and posterior tongue elevation (p value= 0.005) were noted. Right and left side buccinator changes were not seen. In the Airway Gym group, tongue protrusion changes (p value=0.039) and posterior tongue elevation changes (p value=0.036) were noted. Right and left side buccinator changes were not seen.

On average when compared to baseline readings, the AHI in the analog group (See Graph 15) decreased by 26.7% (std: 20.4) by month one, by 50.4% by month two (std: 26.9), and 62.1% (std: 23.6) by month three. On average when compared to

baseline readings, the AHI in the Airway Gym group (See Graph 16) decreased by 54% (std: 16.8) by month one, 66.1% (std: 16.9) by month 2 and 78% (std: 14) by month three. There does not be a difference in the rate of change between the decrease in AHI amongst the two groups. The change in AHI in the analog group appear to have a trend with tongue protrusion (R=0.49) as measured by IOPI. The change in AHI in the Airway Gym group appeared to trend with mean increase in tongue protrusion (R = 0.63) and posterior tongue elevation (R=0.58) as measured by IOPI.

Questionnaires

There was no trend observed between how patients' responses to their Epworth Sleepiness Scale, Sleep Disturbance Short Form 8b, or Sleep Impairment Short Form 8a changed between baseline and each follow-up timepoint. See Graph 9-14 for each individual subject's response in both groups and the change in response across all timepoints.

Compliance

Compliance data is listed in Table 6. Compliance is also plotted for individual subjects at each timepoint. The averaged number of days of compliance per month was calculated and plotted to mark change between timepoints. See graphs 17-18. For the analog group, adherence to the daily myofunctional exercises were on average 65% (std: 13.8) in month one, 63.9% (std: 15.3) in month two, 61.8% (16) in month 3, over the span of 30 days. For the Airway Gym group, adherence to the daily myofunctional exercises were on average 62.8% (std: 26.6) in month one, 50% (std: 24.6) in month

two, 35.3% (31.8) in month 3, over the span of 30 days. While both groups displayed a decrease in adherence over the course of the study, the percentage by which the Airway Gym group displayed a loss in adherence was much larger when compared to the Analog group. Between month 1 and month 2, there was 9% decrease in adherence in the analog group versus a 23% decrease in the Airway Gym group. Between month 1 and month 3, there was a 23.9% decrease in adherence in the analog group versus a 40.7% decrease in adherence in the Airway Gym group.

Discussion

This prospective study is the first report in the literature to assess if there are possible differences between different modalities of delivery for myofunctional therapeutic exercises; self-directed analog method versus the mHealth Airway Gym app.

As per the clinical trial completed by Guimaraes et al [13], they reported that a significant reduction in neck circumference was correlated with an improvement in AHI. However, similar to the pilot study done by O'Connor-Reina [11], our results suggest that increasing muscle tone, as measured by the IOPI, helped to improve the AHI in our research subjects. Both groups showed significant change in muscle tone independently, but there did not appear to be a difference in the rate of change between the two groups. There also did not appear to be a trend in the amount of reduction in AHI between the two groups. Because the improvements in AHI were not coupled by improvements in responses to our questionnaires utilized, it appears that the subjective

responses of subjects via questionnaires does not necessarily correlate with changes in objective biological assessments such as AHI.

We believe that the lack of difference in both groups amongst many metrics, including changes in muscle tone, AHI, and questionnaires, suggest that both modalities may be effective methods to deliver myofunctional exercises to patients. Therefore, the difference may lie in the rate of adherence amongst the two modalities. According to O'Connor-Reina [11], the average rate of adherence for myofunctional therapy is around 10%. In our study, adherence was similar to what was seen by the group (~64% on average) in month one. However, there was a larger drop-off in adherence in the Airway Gym group as compared to the analog group. In the first month, adherence rate in analog group was 65% and in the app group it was 62.8%. By the final month, adherence rate in the analog group was 61.7% but adherence dipped to 43.3% in the app group. Our sample suggests that adherence may be worse when using the Airway Gym application. According to the useability survey given to subjects at the end of studies, it was suggested that subjects had trouble integrating exercises on the smartphone into their daily lives or maybe that the Airway Gym app wasn't successful at delivering a smooth experience.

Despite our findings, we note several limitations to our study. First, the number of participants was small which increases our risk for alpha and beta errors when we attempt to interpret our dataset. Second, OSA is a multi-factorial disease and our study only assessed a limited number of variables. There exists a possibility that the true benefits of MFT were not investigated by this study. Finally, the patient population was

limited to the Case Western Reserve Orthodontics clinic. The patient demographic that is admitted to this clinic might not be representative of the entire population.

Next step is to increase sample size for the study to increase power to support our preliminary findings. Furthermore, future studies in myofunctional therapy are needed to identify the proper phenotypes of OSA that is suited for myofunctional therapy, the possible role that gender or other demographic data plays in myofunctional therapy response and if other outcomes, such as snoring is affected by myofunctional therapy. There is need for long-term follow-up of the subjects who participated in MFT research. Finally, no protocol currently exists for the maintenance of subjects who have achieved improvements in health outcomes via MFT.

Conclusion

Our study did not have adequate sample size to draw conclusions about statistical significance. However, there appears to be no difference in response in the outcomes of numerous variables listed in the study when myofunctional therapy is delivered via analog or smartphone application. There does appear to be a difference in compliance where patients prefer the analog format to these exercises over the use of the Airway Gym app.

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Appendix:

Table 1: Inclusion Criteria for enrollment of subjects in study

1.	Age range: from 18 to 75
2.	Recent PSG available
3.	BMI < 40
4.	No history of alcohol or drug abuse
5.	No history of A-fib, pacemaker, CHF, and or strokes
6.	No history of neuromuscular disease
7.	No chronic use of hypnotics
8.	No restrictions in tongue movement that would prevent the subject to touch the roof of their mouth at any amount of mouth opening
9.	No blockage in nasal passage
10.	No diagnosed temporomandibular joint disorder
11.	Must be able to present for follow up at all directed time points as per the protocol
12.	No excessive changes (>= 5%) in body weight during the duration of the study

a. Listed criteria reviewed at baseline appointment to confirm eligibility in study

Table 2: Variables collected with corresponding methodology listed

Variable	Collected via:
Age	Self-reported
Sex	Self-reported
Height	Measured On-Site
Weight	Measured On-Site
Neck Size	Measured On-Site
Waist	Measured On-Site
BMI	Calculated with Height and Weight

Tongue Protrusion Strength	IOPI device
Posterior Tongue Elevation Strength	IOPI device
Lip Strength	IOPI device
OSA Risk Assessment	STOP-Bang Questionnaire
Nasal Breathing Efficiency	NOSE Questionnaire
Sleep Quality	PROMIS Sleep Disturbance Short Form 8b
Sleep Impairment	PROMIS Sleep Impairment Short Form 8a
Daytime Sleepiness	Epworth Sleepiness Scale Questionnaire
AHI	Belun Ring Platform
Oxygen Desaturation	Belun Ring Platform

a. Demographics variables were collected at baseline and at final appointment. Research variables were collected at baseline and at each subsequent follow-up appointment

Table 3: Baseline Demographics for Study Subjects

Variable	**Analog (n=6)**	**Airway Gym (n=7)**	***P* value**
Age (yr), median (IQR)	66.5 (55.3-71.8)	60 (50.8-68.5)	0.6
Male	5	3	
Female	1	4	
Neck Circumference (in.), median (IQR)	16 (14.7-17.4)	16 (14.1-17.5)	0.57
Waist Circumference (in.), median (IQR)	43.8 (40.6-49.1)	41.5 (36.3-46.6)	0.27
BMI, median (IQR)	28.4 (26.9-32.5)	28.4 (26.6-30.2)	0.44
AHI, median (IQR)	31.3 (18.9-43.1)	32.3 (17.0-39.1)	0.89
IOPI T Protrusion (kPa), median (IQR)	47.5 (41-51.8)	34 (30.5-44.3)	0.16
IOPI T Elevation (kPa), median (IQR)	35.5 (33.5-36)	39 (20-46.3)	0.92
IOPI Cheek (kPa), median (IQR)	22.5 (20.5-29)	22 (17.8-23.3)	0.30
ESS, median (IQR)	8 (5-12.8)	7 (4.5-13.5)	0.97

S Disturbance, median (IQR)	54.8 (47.6-60.2)	56.3 (47.1-58.9)	0.92
S Impairment, median (IQR)	54.5 (48.5-60.6)	51.6 (42.4-60)	0.64

a. No significant differences in any characteristics, including age, BMI, neck and waist circumferences. AHI and other sleep quality assessments did not significantly differ as well.

Table 4a. Percent Change between Baseline and 1 month after exercises

	Analog	Airway Gym	
Variable	%Δ(Month 1 – Baseline)	%Δ(Month 1 – Baseline)	P-Value
IOPI Tongue Protrusion (mean, STD)	2.2, 24.0	14.7, 38.6	0.51
IOPI Tongue Elevation (mean, STD)	11.8, 18.5	22.0, 29.6	0.48
IOPI Buccinator Right (mean, STD)	2.8, 26.8	4.4, 34.7	0.93
IOPI Buccinator Left (mean, STD)	0.7, 23.6	18.6, 41.8	0.38
Epworth Sleepiness Score (mean, STD)	-19.8, 26.2	1.5, 20.9	0.132
Sleep Disturbance t-score (mean, STD)	1.4, 7.0	-1.8, 8.3	0.52
Sleep Impairment t-score (mean, STD)	-2.3, 8.0	-1.5, 7.4	0.77
AHI (mean, STD)	-26.7, 22.4	-56.7, 21.3	0.05
SpO2 Nadir (mean, STD)	Not assessed between Baseline and Month 1	Not assessed between Baseline and Month 1	N/A
T90% (mean, STD)	Not assessed between Baseline and Month 1	Not assessed between Baseline and Month 1	N/A
Compliance (mean, STD)	65.0, 13.8	62.8, 26.6	0.36

a. Comparisons were drawn between percent change of each group because of large standard deviation of each subject's baseline statistics as subjects of all baseline severities of OSA were recruited.

Table 4b. Percent Change between Baseline and 2 months after exercises

	Analog	Airway Gym	
Variable	%Δ(Month 2 – Baseline)	%Δ(Month 2 – Baseline)	P-Value
IOPI Tongue Protrusion (mean, STD)	20.0, 21.6	4.0, 16.6	0.23
IOPI Tongue Elevation (mean, STD)	24.2, 25.5	12.5, 22.4	0.46
IOPI Buccinator Right (mean, STD)	6.2, 14.3	-6.8, 16.11	0.22
IOPI Buccinator Left (mean, STD)	1.3, 7.5	15.6, 34.7	0.40
Epworth Sleepiness Score (mean, STD)	-2.9, 34.9	-19.6, 21.1	0.46
Sleep Disturbance t-score (mean, STD)	-1.9, 7.8	-4.4, 7.3	0.69
Sleep Impairment t-score (mean, STD)	-3.4, 10.1	5.0, 6.3	0.45
AHI (mean, STD)	-50.4, 29.5	-67.1, 22.2	0.32
SpO2 Nadir (mean, STD)	-0.26, 5.6	-2.03, 3.9	0.52
T90% (mean, STD)	16.4, 95.1	-43.3, 38,4	0.27
Compliance (mean, STD)	63.9, 15.3	50.0, 24.6	0.13

a. Comparisons were drawn between percent change of each group because of large standard deviation of each subject's raw statistics as subjects of all baseline severities of OSA were recruited.

Table 4c. Percent Change between Baseline and 3 months after exercises

	Analog	Airway Gym	
Variable	%Δ(Month 3 – Baseline)	%Δ(Month 3 – Baseline)	P-Value
IOPI Tongue Protrusion (mean, STD)	18.7, 17.2	35.8, 45.2	0.74

IOPI Tongue Elevation (mean, STD)	38.3, 24.4	45.4, 38.2	0.81
IOPI Buccinator Right (mean, STD)	12.7, 21.4	-14.11, 17.9	0.13
IOPI Buccinator Left (mean, STD)	9.5, 23.8	22.0, 30.1	0.22
Epworth Sleepiness Score (mean, STD)	-22.2, 20.8	-13.2, 25.8	0.44
Sleep Disturbance t-score (mean, STD)	-4.9, 10.0	-8.0, 9.0	0.87
Sleep Impairment t-score (mean, STD)	-9.3, 11.5	-6.9, 2.3	0.47
AHI (mean, STD)	-56.4, 27.5	-73.2, 17.1	0.27
SpO2 Nadir (mean, STD)	2.4, 13.0	-2.3, 4.7	0.47
T90% (mean, STD)	46.1, 150.5	-3.01, 56.9	0.62
Compliance (mean, STD)	50, 13.6	43.3, 31.8	0.69

a. Comparisons were drawn between percent change of each group because of large standard deviation of each subject's raw statistics as subjects of all baseline severities of OSA were recruited.

Table 5. Comparing Baseline variables and 3 months after exercises

	Analog		Airway Gym	
Variable	(Baseline – Month 3)	P-Value	(Baseline – Month 3)	P-Value
IOPI Tongue Protrusion (mean, STD)	47.3 (6.2) – 55.7 (6.7)	*0.049	38.9 (12.6) – 52.2 (6.1)	*0.039
IOPI Tongue Elevation (mean, STD)	34.8 (1.6) – 48.2 (8.8)	**0.004	34.3 (12.2) – 50.0 (11.4)	*0.036
IOPI Buccinator Right (mean, STD)	24.5 (7.3) – 26.7 (4.9)	0.56	25.0 (6.7) – 23.4 (6.0)	0.68
IOPI Buccinator	24.2 (4.9) – 26.2 (5.9)	0.54	21.9 (4.9) – 25.8 (5.7)	0.20

Left (mean, STD)				
Epworth Sleepiness Score (mean, STD)	8.8 (5.4) – 7.8 (5.4)	0.75	8.7 (5.1) – 7.9 (4.8)	0.75
Sleep Disturbance t-score (mean, STD)	54.4 (6.3) – 52.3 (7.1)	0.61	54.8 (7.6) – 51.8 (6.9)	0.46
Sleep Impairment t-score (mean, STD)	54.5 (5.8) – 44.8 (17.2)	0.22	52.3 (9.7) – 51.6 (8.1)	0.89
AHI (mean, STD)	32.6 (18.0) – 14.6 (16.1)	*0.049	32.5 (12.2) – 8.5 (6.8)	**0.001
SpO2 Nadir (mean, STD)	78.3 (5.4) – 72.8 (16.8)	0.47	82.3 (5.9) – 81.0 (5.2)	0.68
T90% (mean, STD)	7.4 (5.9) – 14.2 (12.5)	0.26	6.1 (9.0) – 8.3 (8.9)	0.66

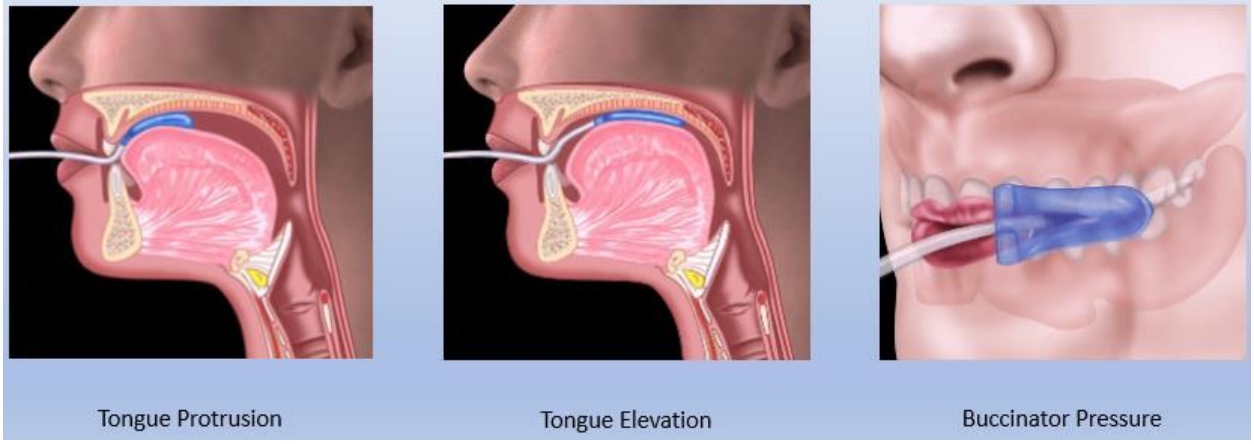
a. Intervention appeared to induce changes in tongue protrusion, posterior tongue elevation and AHI in both groups after 3 months of exercises.

Table 6. Compliance with Daily Exercise Routine

	Analog	Airway Gym	P-Value
Month 1, mean (STD)	65 (13.8)	62.8 (26.6)	0.50
Month 2, mean (STD)	63.9 (15.3)	50 (24.6)	0.19
Month 3, mean (STD)	61.8 (16)	43.3 (34.8)	0.22

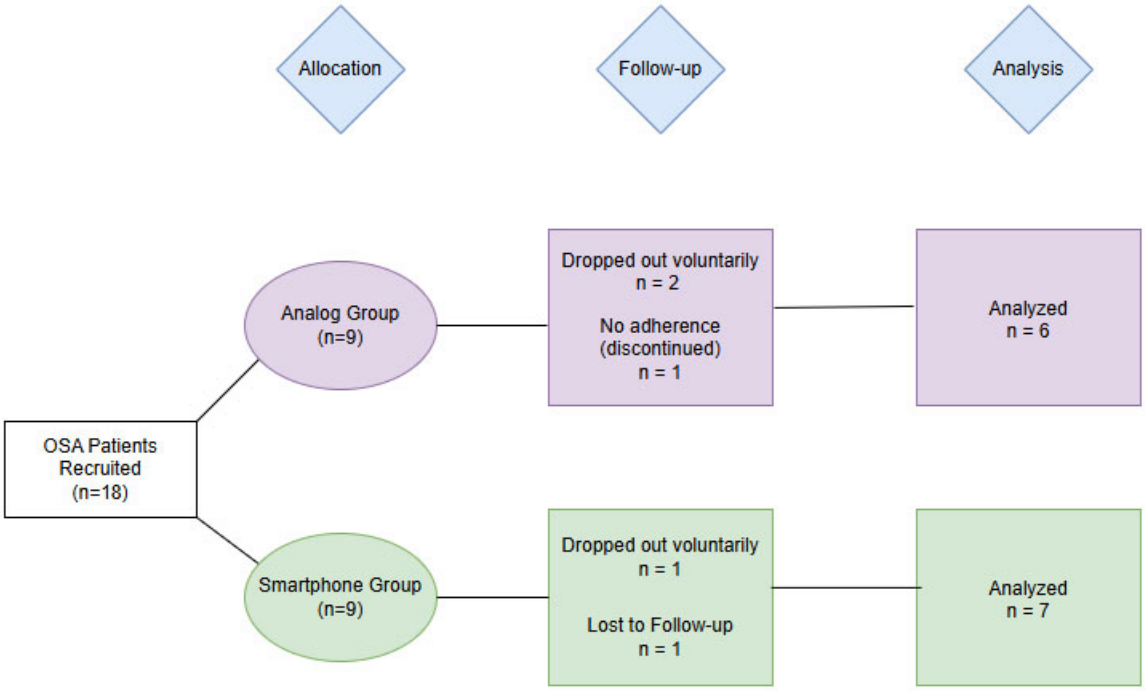
a. Compliance is expressed as a percentage out of 30 days, for the days the subjects fully completed the exercise routine. Non-compliance is defined as no exercises performed for the day or exercise routine only partially completed.

Figure 1: IOPI Measurement Locations



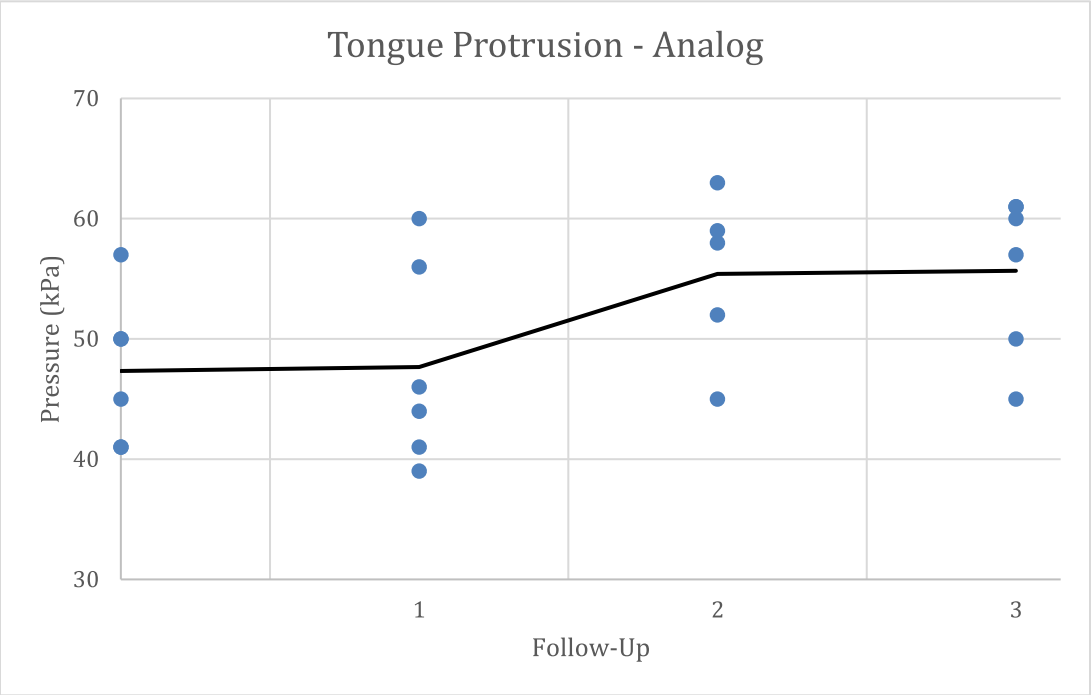
a. Bulb placed at midline of tongue at anterior palate and posterior palate. Buccinator pressure was measured by placing bulb in between teeth and cheek in the canine area on both sides

Figure 2: Research Flowchart



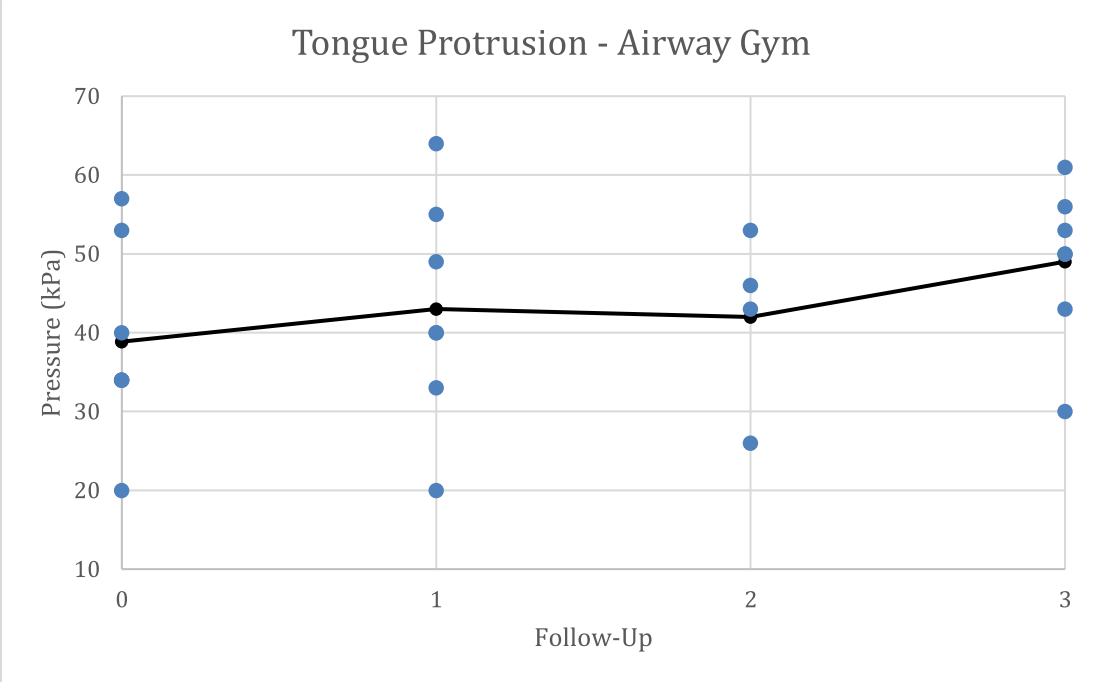
a. In analog group, 2 dropped out voluntarily and 1 removed due to non-compliance. In app group, 1 dropped out voluntarily and 1 was lost to follow up.

Graph 1. IOPI Tongue Protrusion Measurement – Analog Group



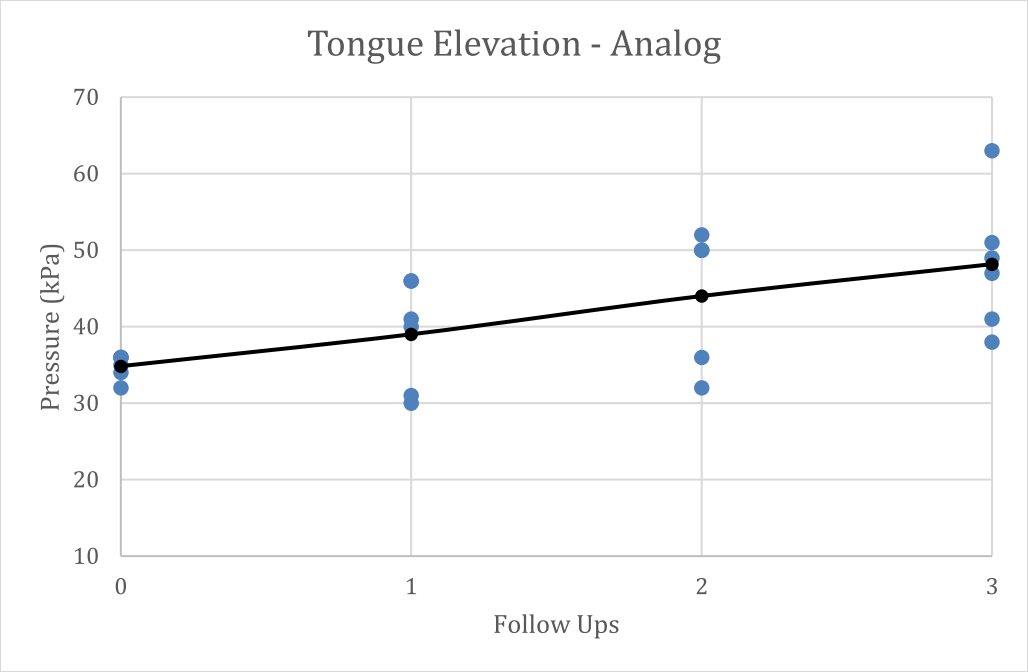
a. Blue dots plot the individual subject's measurement at each time point. Black line is the averaged value at each timepoint and its change over each follow up appointment.

Graph 2. IOPI Tongue Protrusion Measurement – App Group



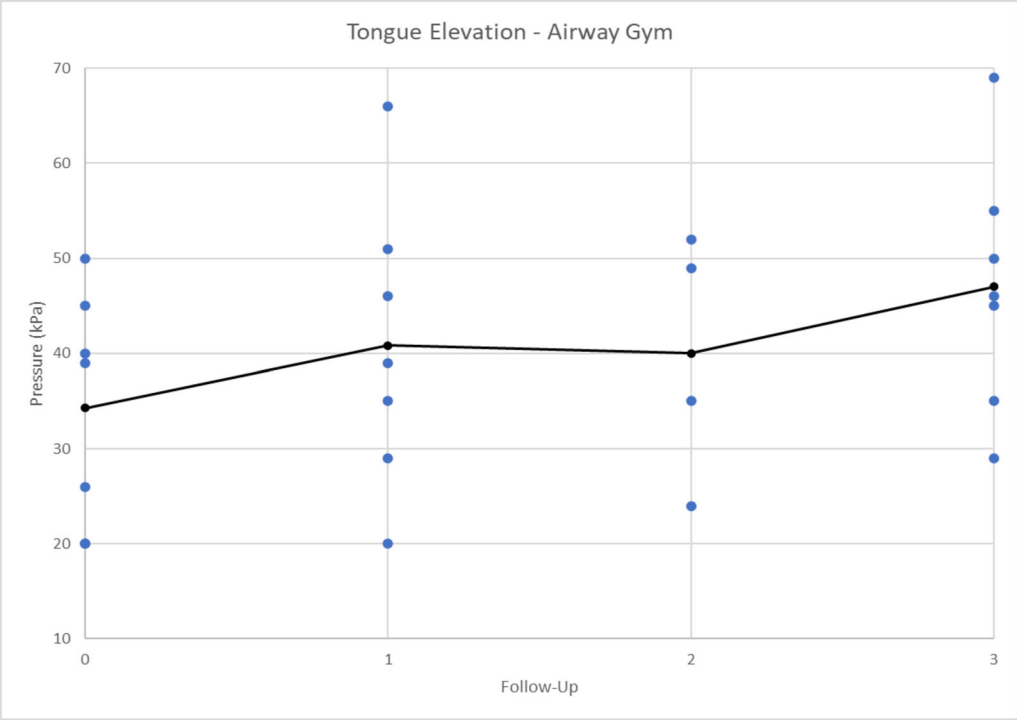
a. Blue dots plot the individual subject's measurement at each time point. Black line is the averaged value at each timepoint and its change over each follow up appointment.

Graph 3. IOPI Post. Tongue Elevation Measurement – Analog Group



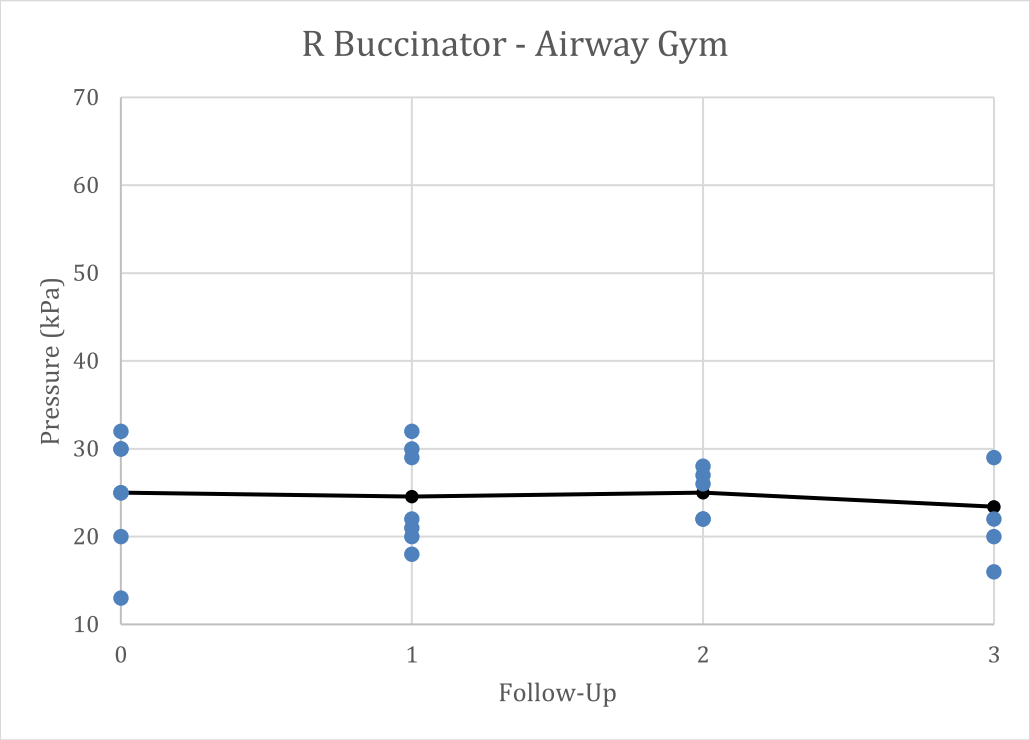
a. Blue dots plot the individual subject's measurement at each time point. Black line is the averaged value at each timepoint and its change over each follow up appointment.

Graph 4. IOPI Post. Tongue Elevation Measurement – App Group



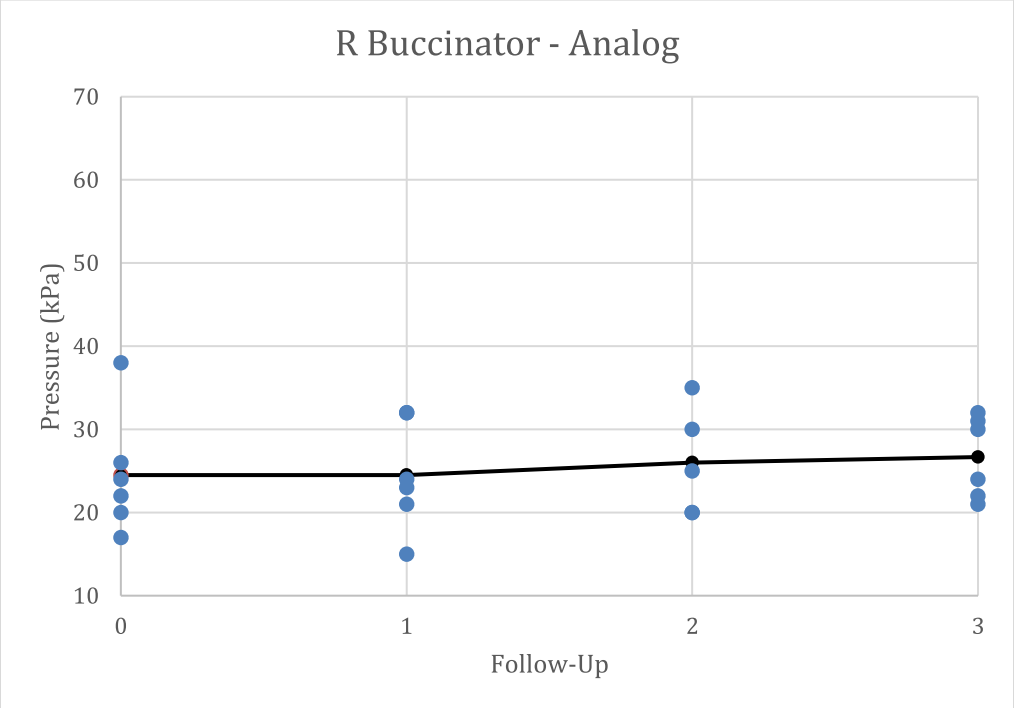
a. Blue dots plot the individual subject's measurement at each time point. Black line is the averaged value at each timepoint and its change over each follow up appointment.

Graph 5. IOPI Right Buccinator Measurement – Airway Gym



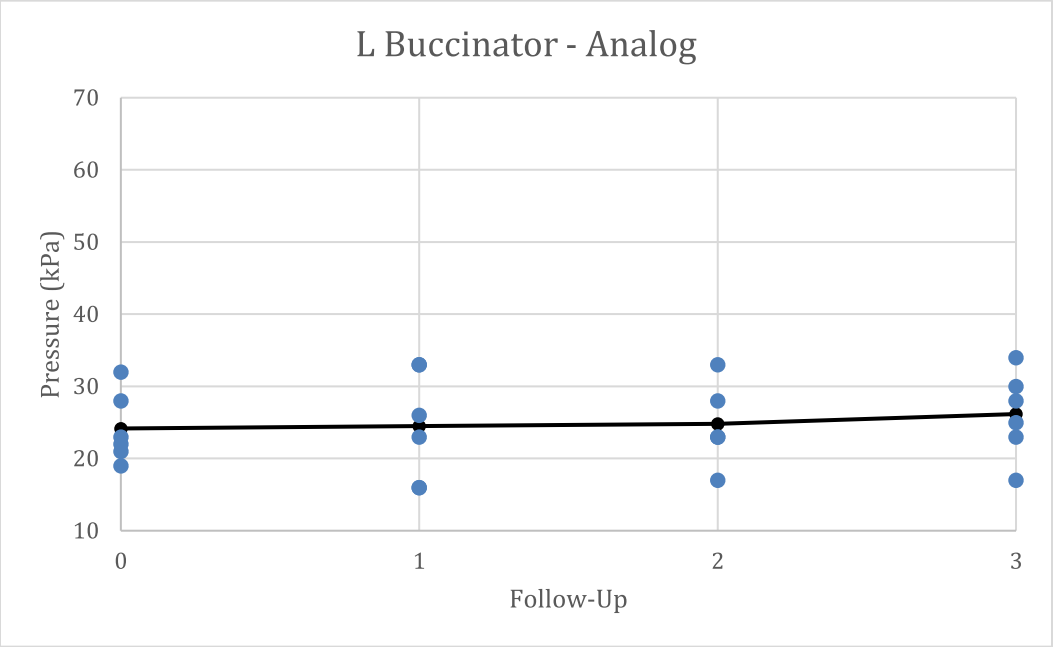
a. Blue dots plot the individual subject's measurement at each time point. Black line is the averaged value at each timepoint and its change over each follow up appointment.

Graph 6. IOPI Right Buccinator Measurement – Analog



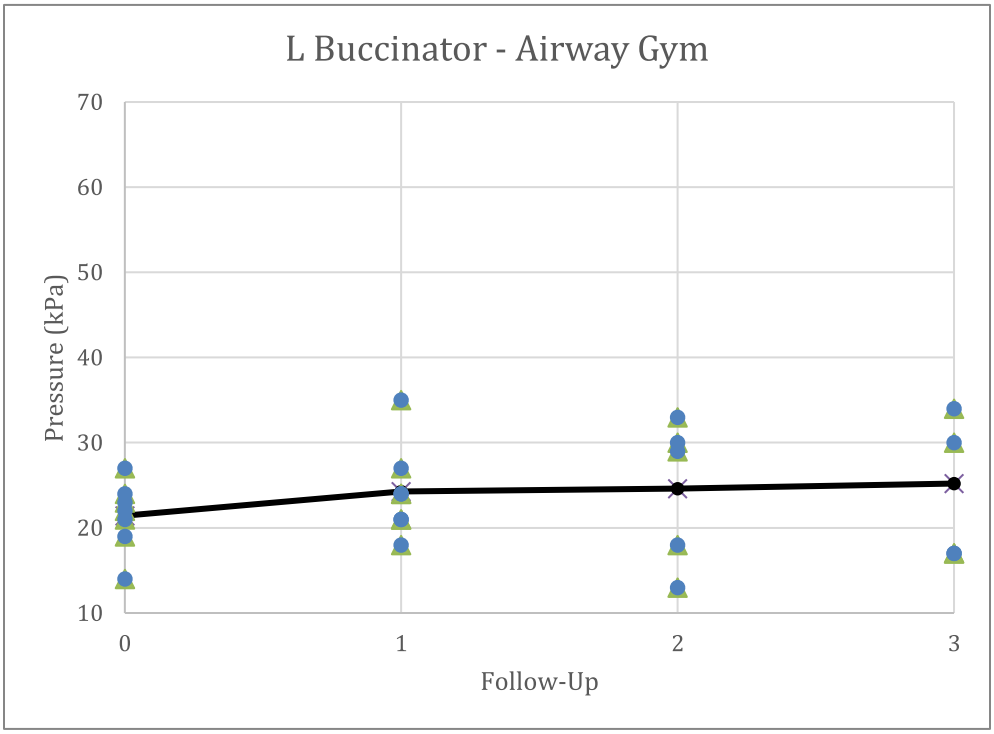
a. Blue dots plot the individual subject's measurement at each time point. Black line is the averaged value at each timepoint and its change over each follow up appointment.

Graph 7. IOPI Left Buccinator Measurement – Analog Group



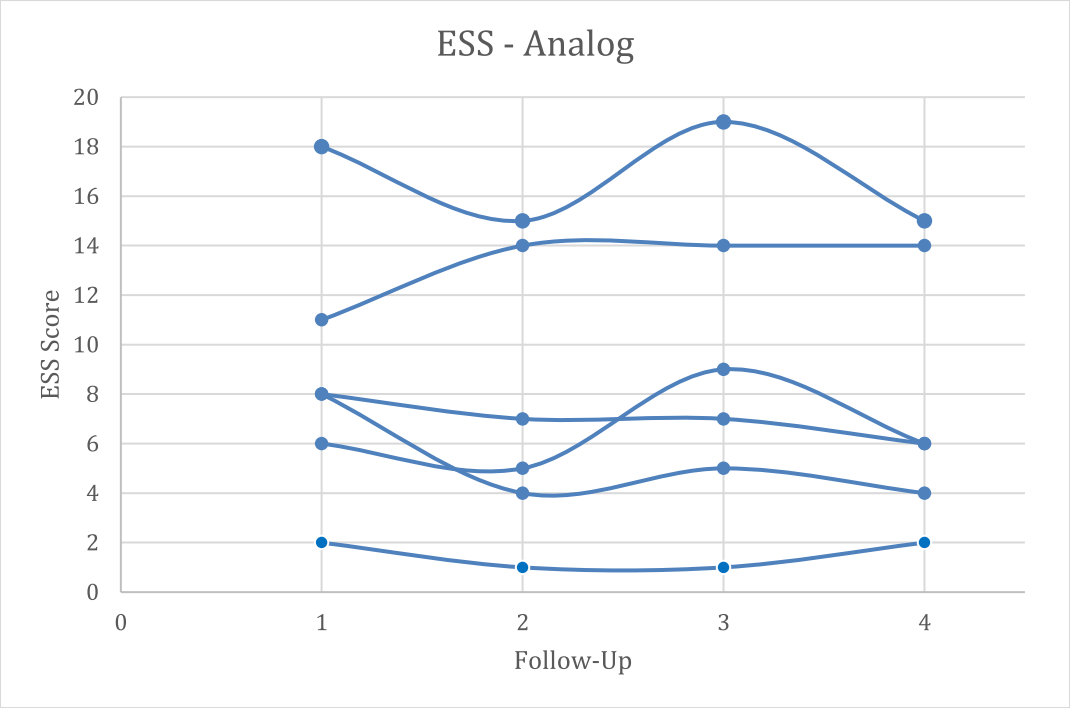
a. Blue dots plot the individual subject's measurement at each time point. Black line is the averaged value at each timepoint and its change over each follow up appointment.

Graph 8. IOPI Left Buccinator Measurement – App Group



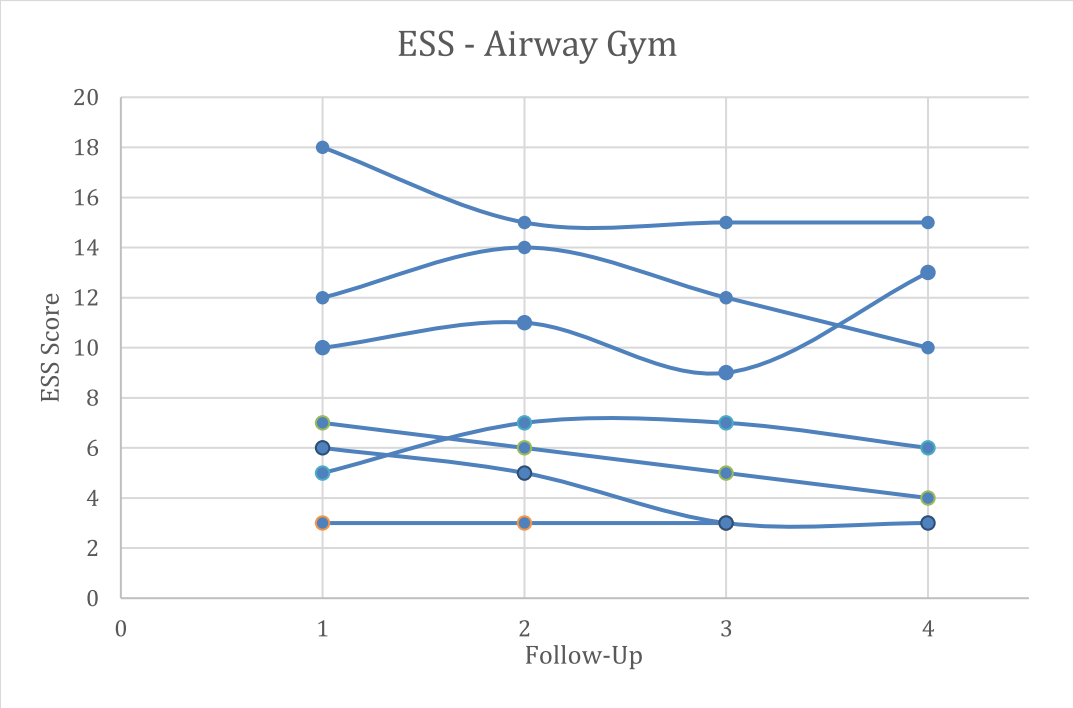
a. Blue dots plot the individual subject's measurement at each time point. Black line is the averaged value at each timepoint and its change over each follow up appointment.

Graph 9. Epworth Sleepiness Scale Responses – Analog Group



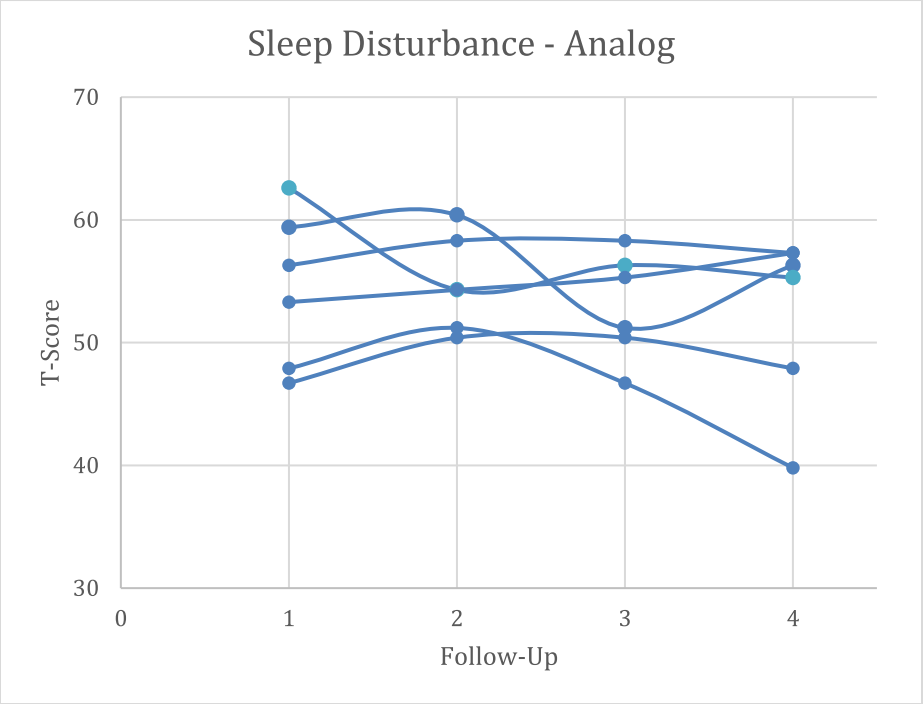
a. Each line demarcates an individual's response at each point between baseline and final visit and its change through time

Graph 10. Epworth Sleepiness Scale Responses – Analog Group



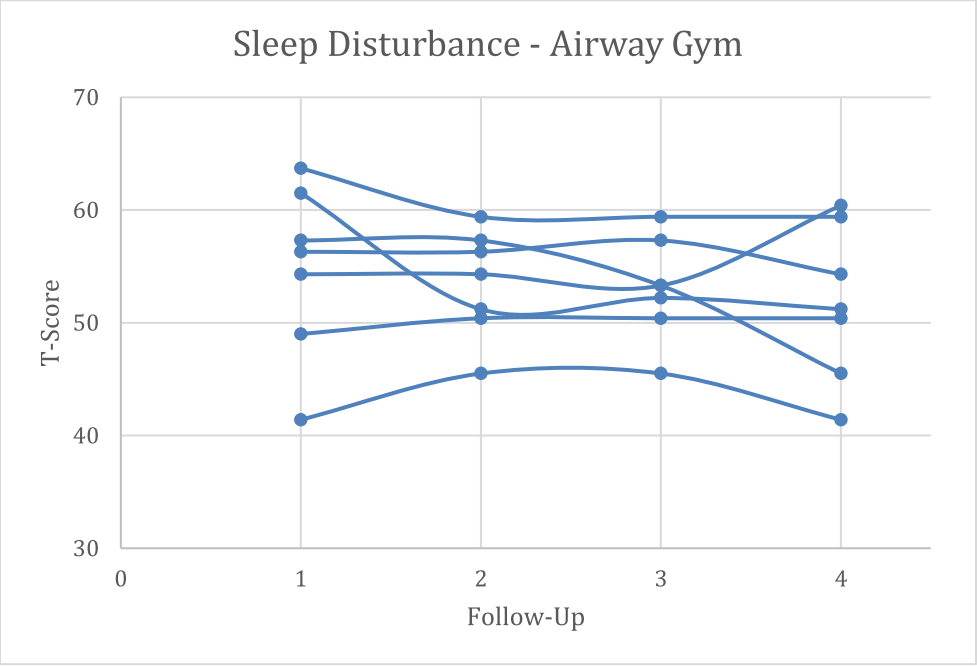
a. Each line demarcates an individual's response at each point between baseline and final visit and its change through time

Graph 11. Sleep Disturbance Short Form 8b Responses – Analog Group



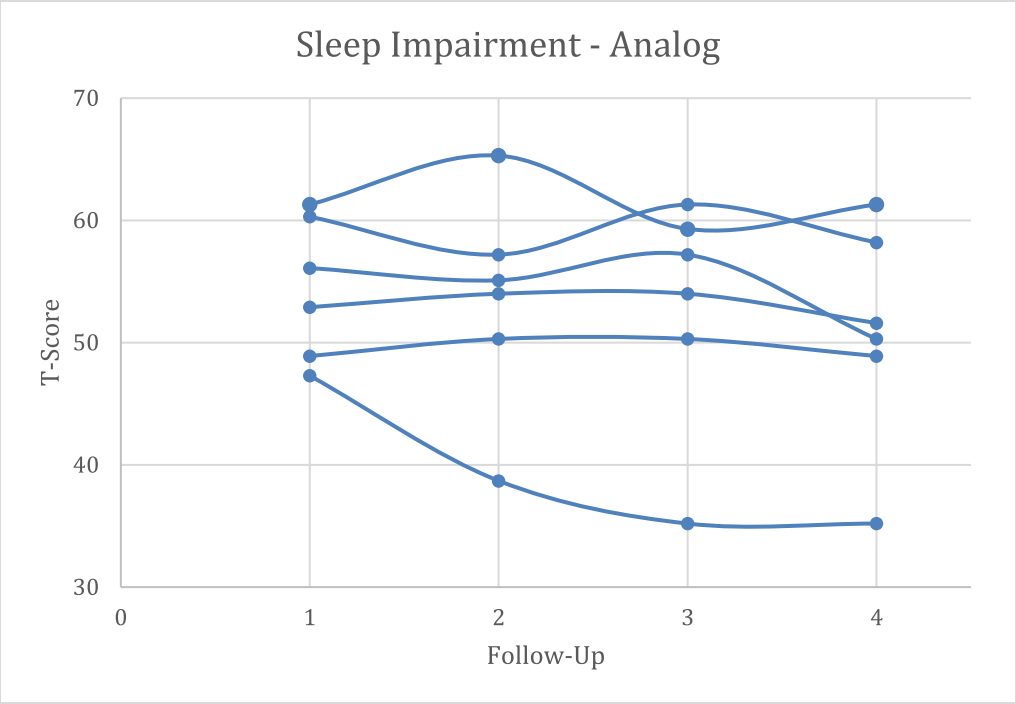
a. Each line demarcates an individual's response at each point between baseline and final visit and its change through time

Graph 12. Sleep Disturbance Short Form 8b Responses – App Group



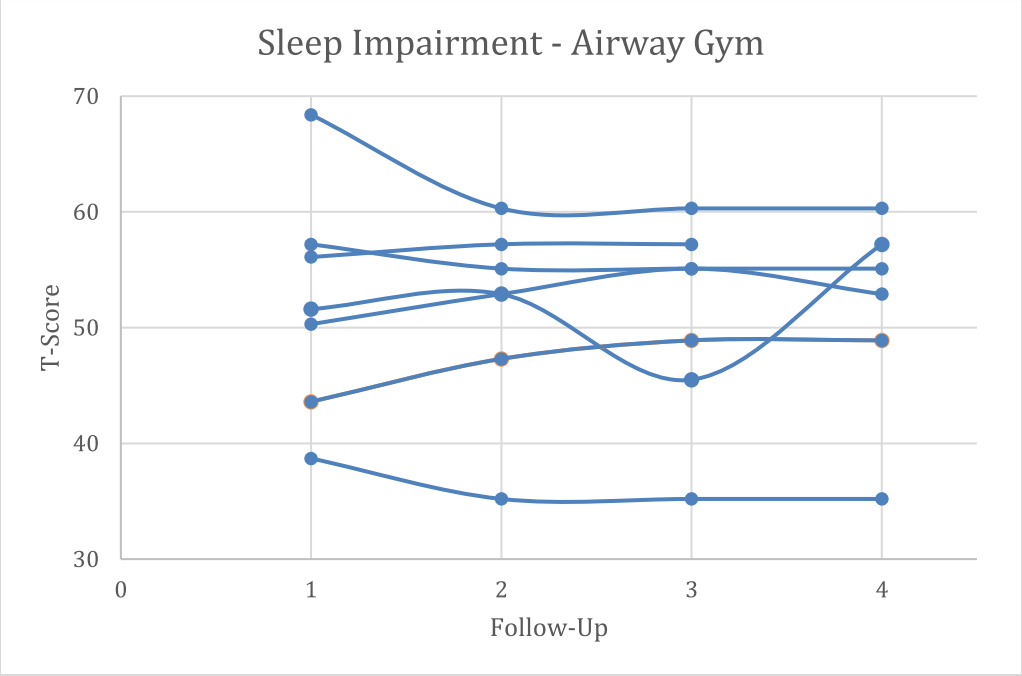
a. Each line demarcates an individual's response at each point between baseline and final visit and its change through time

Graph 13. Sleep Impairment Short Form 8a Responses – Analog Group



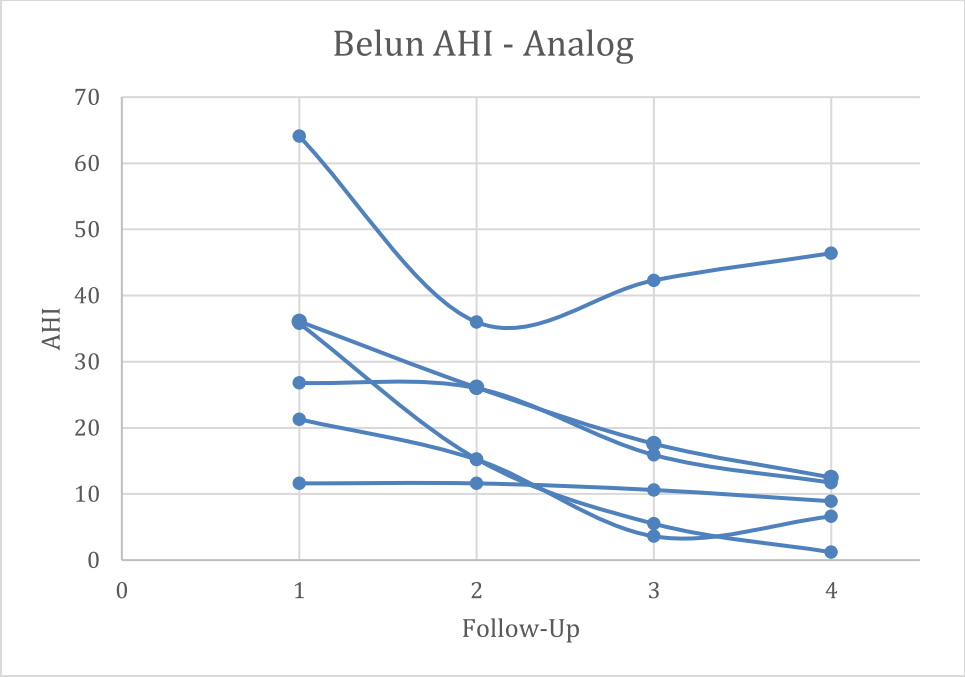
a. Each line demarcates an individual's response at each point between baseline and final visit and its change through time

Graph 14. Sleep Impairment Short Form 8a Responses – App Group



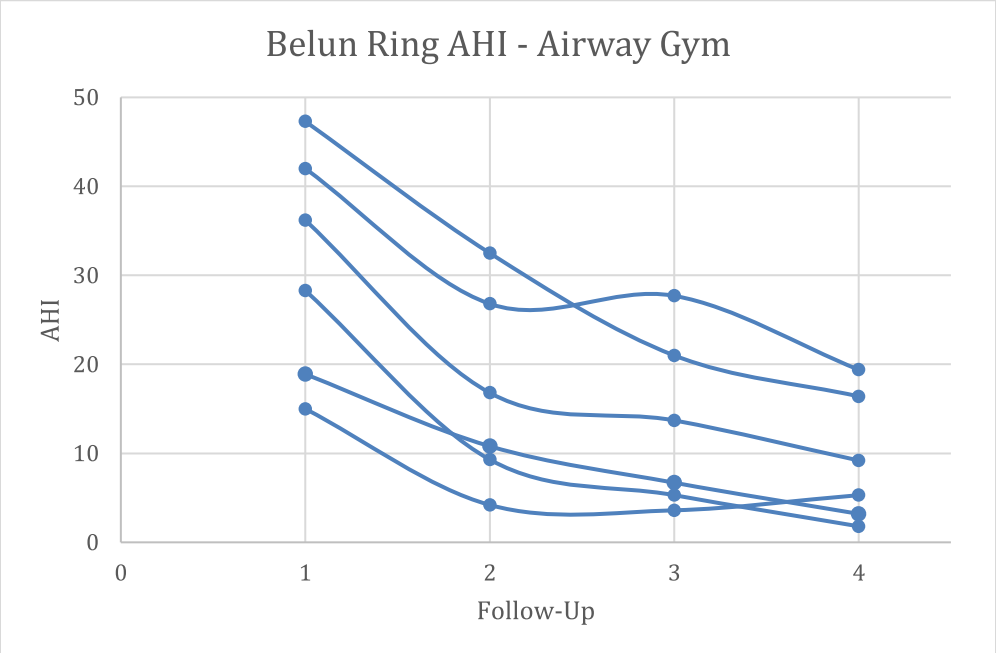
a. Each line demarcates an individual's response at each point between baseline and final visit and its change through time

Graph 15. AHI Readings by Belun Ring Technology – Analog Group



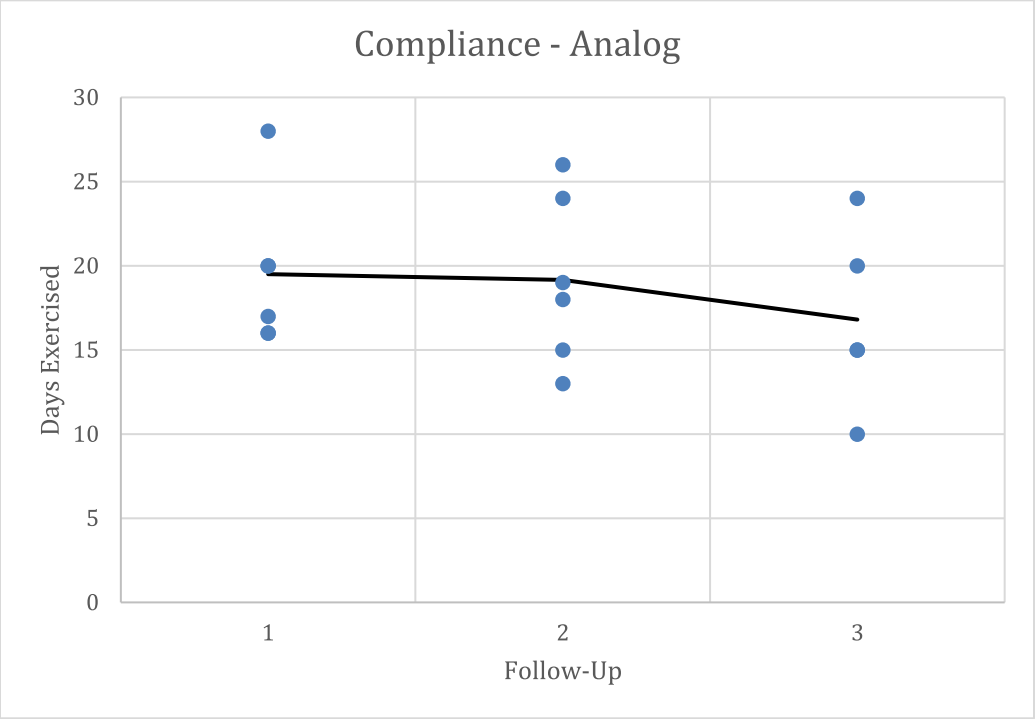
a. Each line demarcates an individual's AHI reading by Belun Ring and its change through time. Baseline AHI reading was obtained through the subject's most recent Polysomnography

Graph 16. AHI Readings by Belun Ring Technology – App Group



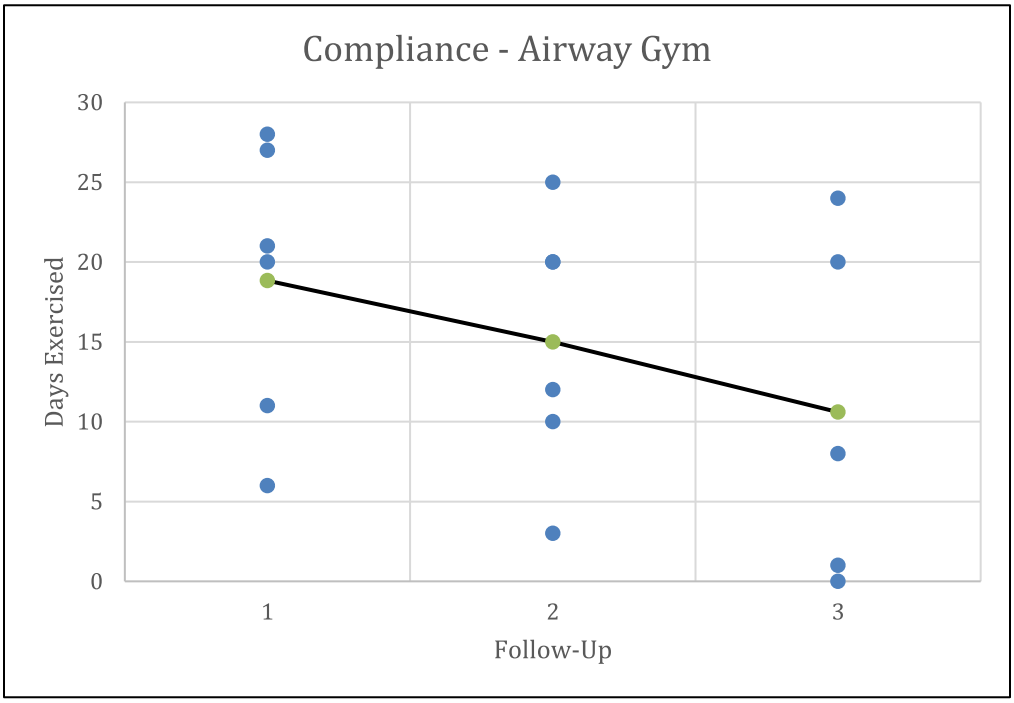
a. Each line demarcates an individual's AHI reading by Belun Ring and its change through time. Baseline AHI reading was obtained through the subject's most recent Polysomnography

Graph 17. Compliance By Days Exercised Out of a Month – Analog Group



a. Blue dot indicates an individual's compliance at each follow-up appointment. Black line is the averaged compliance at each timepoint and its change through time.

Graph 18. Compliance By Days Exercised Out of a Month – Analog Group



a. Blue dot indicates an individual's compliance at each follow-up appointment. Black line is the averaged compliance at each timepoint and its change through time.

IRB Administration Offices
UH IRB Phone: 216.844.1529
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INITIAL APPROVAL

Principal Investigator:	Juan Palomo
Title:	The impact of technology in the myofunctional therapy treatment of Obstructive Sleep Apnea Syndrome
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IRB Office:	CWRU IRB
Approval Date:	5/10/2024
Effective Date:	5/10/2024
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Type of Submission:	Initial Study
Type of Review:	Expedited
Documents Reviewed:	• CWRU Biomedical irb-consent - 7.1.24.pdf, Category: Consent Form; • Airway Gym App Screenshots.pdf, Category: Other; • Study Advertisement.pdf, Category: Other; • Study Advertisement - 5.16.24.pdf, Category: Recruitment Materials; • PSQI Questionnaire, Category: Other; • Myofunctional Exercise Routine.pdf, Category: Other; • StopBang Questionnaire, Category: Other; • IOPI Description.pdf, Category: Other; • Belun_ Ring - Belun Technology.pdf, Category: Other; • AAO Demographic Questionnaire.pdf, Category: Other; • Thesis Protocol - 6.29.24.pdf, Category: IRB Protocol; • sample-written-recruitment-script.pdf, Category: Recruitment Materials; • IOPI Diagram.pdf, Category: Other; • Myofunctional Therapeutic Exercises Compliance Form.pdf, Category: Other;

The IRB has reviewed this submission.

- Per Federal regulation, changes MAY NOT be made to any element of the current research without prior IRB approval, except to eliminate an immediate and apparent hazard to subjects enrolled in the study.

The UH IRB operates under HHS Federalwide Assurance (FWA) number 00003937 and IRB registration numbers 00000684, 00001691 and 00008600. The CWRU IRB operates under DHHS FWA00004428 and IRB registration number 00000683.