# The Evaluation the Toffee Full Face Mask for the Treatment of Obstructive Sleep Apnea

**NCT04615832**

**DATE:** 25th of June 2021

Fisher & Paykel HEALTHCARE

Fisher & Paykel
HEALTHCARE

# Clinical Investigation Plan
# 25th June 2021

[redacted]

Revision A: 25 June 2021

This page is left intentionally blank.

[redacted]

## Review and Approval

[redacted]

# Contents

# 1. Revision History

| Rev | Date | Author | Description of Changes |
|---|---|---|---|
| A | 25 June 2021 | [redacted] | [redacted] |

## 1.1. List of Abbreviations

[redacted]

# 2. Document Information

## 2.1. Purpose and Scope

The purpose of this document is to outline the clinical trial protocol for:

[redacted]

The purpose of the Clinical Investigation Plan (CIP) is to provide research personnel at the investigation sites in New Zealand with sufficient information about the scope of the clinical trial, and the activities associated with completing procedures to an acceptable standard, as per what is stipulated by the sponsor company, Fisher & Paykel Healthcare. Ltd. (FPH), in New Zealand (NZ). The CIP will be updated if there is significant change to the protocol being applied. The Principal Investigator (PI) will acknowledge the receipt of this CIP, as well as subsequent amendments.

[redacted]

## 2.2. Confidentiality Statement

This CIP contains commercially sensitive and confidential information belonging to FPH and is provided for the sole purpose of enabling an evaluation of a possible collaboration between FPH and the investigation sites to undertake the proposed clinical trial. As such, this CIP must remain confidential at all times, and any disclosure, distribution, or reproduction of this CIP beyond its intended purpose is strictly prohibited.

## 2.3. Persons Authorized to Amend the Clinical Investigation Protocol

[redacted]

## 2.4. Literature Review

[redacted]

[redacted]

## 2.5. Study justification

[redacted] The aim of this clinical trial is to evaluate the performance, comfort, usability, and reliability of the Toffee Full Face mask in a home environment, with regards to participant views on overall experience, satisfaction, and acceptance.

[redacted]

## 2.6. Study synopsis

This will be a prospective, multi-arm, randomized, and non-blinded clinical trial, designed to evaluate the performance, comfort, and usability of the FPH Toffee Full Face mask amongst participants who have been prescribed PAP therapy by a physician. [redacted]

[redacted]

### 2.7. Study Site

[redacted]

### 2.8. Clinical trial guidelines

This clinical trial will be conducted in accordance with ICH and GCP guidelines. No deviation from the protocol will be implemented without prior review and approval from the sponsor, except where it may be necessary to eliminate an immediate hazard to a participant. In such case, the deviation will be reported to the sponsor as soon as possible. Although the sponsor and the investigator are the same company, the sponsor will not be the investigator. To ensure roles are clearly defined and kept independent, there is a DOA, located within tab 3.1 of CIA-284, to clearly delineate tasks to be carried out by each of the clinical research personnel.

## 3. Investigator Information

### 3.1. Principal Investigator

| | |
|---|---|
| Name: | Bhavi Ogra |
| Address: | 15 Maurice Paykel Place, East Tamaki, 2013, Auckland, NZ |
| Email: | bhavi.ogra@fphcare.co.nz |
| Phone: | +64 09 574 0123 Ext 7882 |
| Mobile: | +64 210488581 |
| Professional Position: | Clinical Research Manager |
| Country of Residence: | NZ |

### 3.2. Institutions

| | |
|---|---|
| Name: | Hawke's Bay Memorial Hospital (HBDHB) |
| Name of Contact: | Colleen Lockwood |
| Address: | 398 Omahu Road, Camberley, Hastings 4120, NZ |
| Email: | colleen.lockwood@hbdhb.govt.nz |
| Phone: | +64 6 878 8109 Ext. 6604 |
| Professional Position: | Sleep Scientist – Recruitment Coordinator |
| Country of residence: | NZ |

| | |
|---|---|
| Name: | WellSleep, Bowen Hospital |
| Name of Contact: | Angela Campbell |
| Address: | 98 Churchill Drive, Crofton Downs, Wellington, 6035, NZ |
| Email: | angela.campbell@otago.ac.nz |

[redacted]

Phone: +64 4 920 8819
Professional Position: Manager
Country of residence: NZ

Name: Fisher & Paykel Healthcare
Name of Contact: Rebecca Thomson
Address: 15 Maurice Paykel Place, East Tamaki, 2013, Auckland, NZ
Email: rebecca.thomson@fphcare.co.nz
Phone: +64 09 574 0123 Ext 7675
Professional Position: Senior Clinical Research Scientist
Country of residence: NZ

# 4. Sponsor Information

## 4.1. Primary Sponsor

Name: Fisher & Paykel Healthcare Ltd.
Name of Contact: Chris Nightingale
Address: 15 Maurice Paykel Place, East Tamaki, 2013, Auckland, NZ
Phone: +64 9 5740123 | Extension: 7879
Email: chris.nightingale@fphcare.co.nz
Position: General Manager - OSA
Residence: NZ

## 4.2. Clinical Researchers

[redacted]

[redacted]

[redacted]

# 5. Clinical trial objectives

## 5.1. Hypothesis

[redacted]

## 5.2. Objectives

Primary objectives:

- To evaluate the Toffee Full Face mask for comfort, sealing performance, aesthetics, and usability in a home environment when used for the delivery of PAP therapy

[redacted]

## 5.3. Population

A sample of 45 participants, who currently use a full-face mask, will be recruited for the clinical trial by the investigation site. [redacted]

## 5.4. Enrolment eligibility

Inclusion criteria:

- Persons who are ≥22 years of age
- Persons who weigh ≥66 lbs (30 kgs)
- Persons who have been prescribed PAP (APAP, BPAP or CPAP) therapy by a physician
- Persons who are compliant with PAP therapy for ≥4 hours per night for 70% of nights for at least two weeks prior to enrolment in the trial
- Persons who are currently using a full face mask
- Persons who have an IPAP pressure of < 30 $cmH_2O$
- Persons who currently use a PAP therapy device with data recording capabilities
- Persons who are fluent in spoken and written English
- Persons who possess the capacity to provide informed consent

Exclusion criteria:

- Persons who are intolerant to PAP therapy
- Persons who are required to use PAP therapy for more than 12 hours per day or for extensive periods other than sleep or naps
- Persons using nasal or nasal pillows masks
- Persons who possess, or suffer from, anatomical or physiological conditions which make PAP therapy inappropriate
- Persons who are pregnant or think they may be pregnant
- Persons who use a PAP therapy machine for the delivery of medicines, except supplemental $O_2$
- Persons who currently have cold or flu like symptoms at the time of recruitment
- Persons who have tested positive for COVID-19 within the previous 28 days prior to enrolment

Participants can be current users of any full-face mask.

[redacted]

[redacted]

### 5.5. Informed consent

Participants will be pre-screened for eligibility according to the inclusion and exclusion criteria and recruited by the three investigation sites from their database of patients by email or phone (using the RS, Appendix 15.1). If a patient is willing to participate in the clinical trial, informed consent will be obtained, individually or in groups, at the investigation site during Visit 1. A CI or the PI identified in the Delegation of Authority (DOA) will be present to witness the informed consent taking place and to answer any questions potential participants have relating to the clinical trial. Participants will be given the opportunity to read over the Informed Consent Form (ICF; Appendix 17.2), before being given an overview of clinical trial procedures and risks associated with partaking, by the CI or PI. All participants will be provided with a photocopy of the signed ICF before clinical trial procedures commence. No further physical or electronic copies of ICFs will be created. Each enrolled participant will be allocated a unique and random pre-generated 4-digit Subject Identification Number (SIN), which will be recorded in the Subject Identification Log (SIL). The SIL and all ICFs will be stored separate to all other clinical trial documentation at the investigation site to maintain anonymity of the feedback obtained from participants during the clinical trial. Details of the informed consent, such as the date and time it was obtained from participants, as well as the activities that were consented to, will also be recorded in the Case Report Form (CRF).

## 6. Investigational Product

### 6.1. Identification of the Medical Device

[redacted]

### 6.2. Pre-Clinical Testing

[redacted]

### 6.3. Device Risk Analysis and Management

[redacted]

## 6.4. Additional Precautions

[redacted]

## 6.5. Previous Clinical Experience

[redacted]

## 6.6. Essential Requirements of the Relevant Directive

Essential requirements are not applicable as this clinical trial is being conducted in New Zealand.

[redacted]

# 7. Clinical Investigation Design

## 7.1. Type of Investigation

This will be a multi-arm, randomized, crossover and non-blinded clinical trial.

## 7.2. Controls and Bias

No control group will be used in this clinical trial as it is designed to test Toffee Full Face mask for the for comfort, sealing performance, aesthetics, and usability in a home environment.

## 7.3. Equipment

## 7.4. Endpoints

Primary endpoint:

1. The Toffee Full Face mask facilitates the continued delivery of PAP therapy when used in the home

Secondary endpoints:

2. The Toffee Full Face mask, including the cushion and headgear, is comfortable when used for the delivery of PAP therapy in the home
3. The Toffee Full Face mask performs (e.g. minimal leak) adequately when used for the delivery of PAP therapy in the home
4. The Toffee Full Face mask is easy to disassemble/re-assemble when required for cleaning
5. The Toffee Full Face mask sizing guide is accurate in predicting the correct size for the participants

## 7.5. Event timeline

[redacted]

## 7.6. Participant Compensation

## 7.7. Variables

## 7.8. Measurements

[redacted]

[redacted]

## 7.10. Participant Procedure

[redacted]

[redacted]

[redacted]

[redacted]

Additionally, the PI may withdraw a participant at any time for the following reasons:

- Protocol violation
- Safety concerns
- Serious illness
- AE/SAE

The reason for participant discontinuation in the clinical trial is to be recorded in the CRF.

### 7.12. Follow-Up Plan

Participants will receive standard care from their healthcare provider throughout and after the completion of the clinical trial.

### 7.13. Foreseeable Complications

From the Manufacturer and User Facility Device Experience database, the common reported injuries from PAP therapy and associated interface use are pressure sores, leading to cuts, rashes, and skin abrasions and breakdown. Allergic reaction to materials in the interface can occur. Common complaints are discomfort and soreness on the areas of contact with the interface. Participants on the clinical trial are informed that they can switch back to their usual mask if required. In instances of malfunction or damage, the investigational product and its components may be replaced, as recorded in the CRF.

## 8. Clinical Trial Documentation

### 8.1. Consent and Recruitment

[redacted]

### 8.2. Case Report Form

[redacted]

### 8.4. Insurance Statement

[redacted]

### 8.5. Record of Deviations

[redacted]

## 9. Statistical Analysis

### 9.1. Statistical Design

[redacted]

Next, the following data analysis strategy will be employed.

1. For each participant and requirement, it will be determined if the requirement is met by the participants' response(s) to associated questions.
2. Minitab will be used to perform a one-sided one-proportion test on each requirement using the confidence limit to confirm that the acceptance criteria has been met:

   $H_0$: proportion = Reliability Limit
   $H_1$: proportion > Reliability Limit
   Acceptance criteria:
   $P \leq 0.05$ to reject $H_0$

FPH as the sponsor may consult an external statistician to assist with or review the analysis of the data.

### 9.2. Sample Size

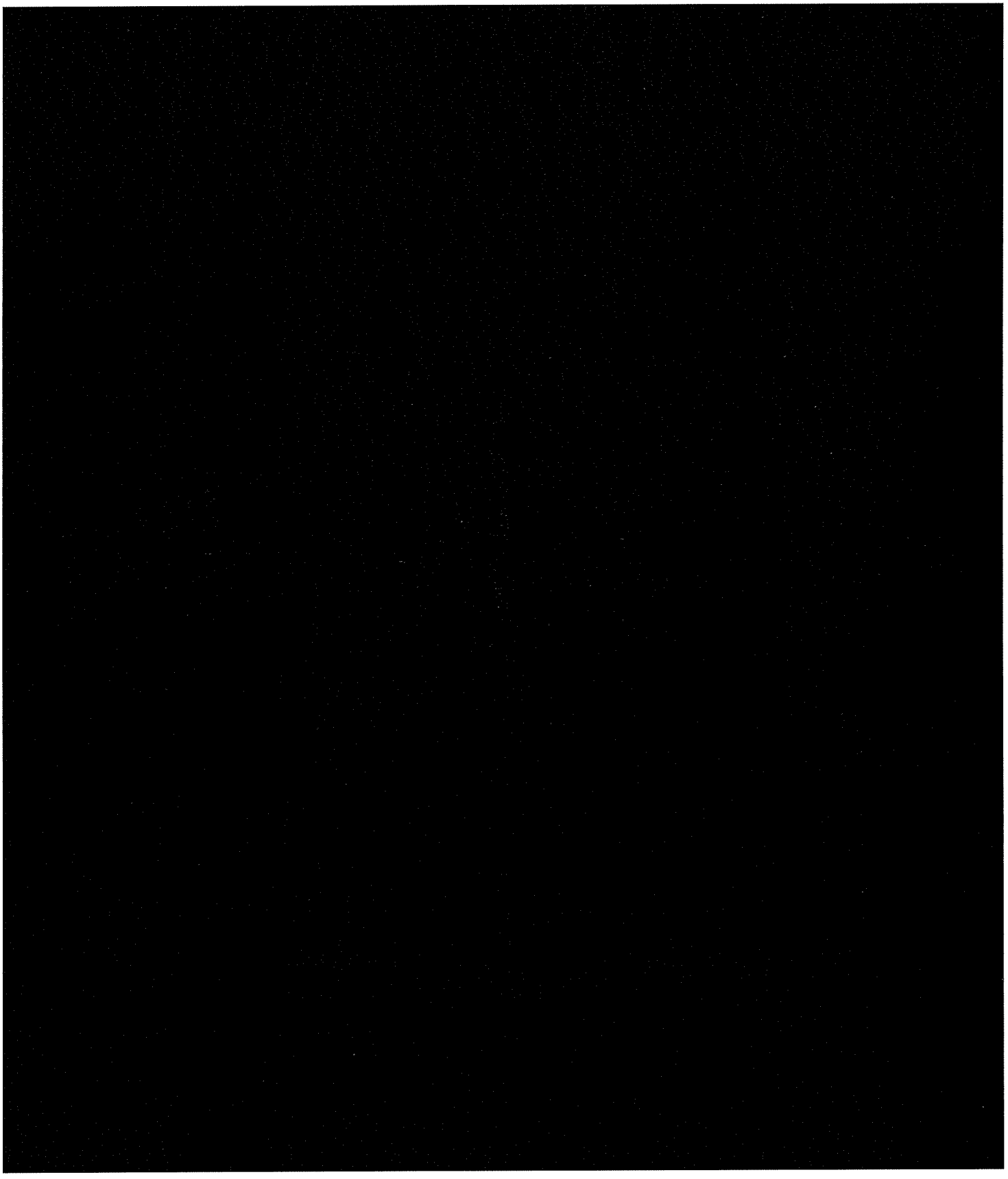
The recruitment goal for the Toffee Full Face product validation will be 45 participants.

For each requirement challenged by the product validation, the outcome for each participant will be recorded as a pass or fail. Therefore, in order to evaluate the validation criteria, the analysis will be performed using a 95% confidence interval for the proportion of successes, where the lower confidence limit must be greater than the proportion pre-defined for each validation requirement.

The statistical power of this one-proportion test, i.e. the probability of not making a type II error, is determined by the sample size. To estimate an adequate sample size to achieve 80% power, the Minitab power and sample size tool was used. Data from the most recent clinical trial (TR-32203) was used as an estimate for the population proportion, this was recalculated at the test report stage with the actual proportion found, in order to confirm its validity. Where there was no comparable data from the past clinical trial, data from previous validation trials of recent products was leveraged. Formal calculation by validation requirement are present in TP-2163 but are not required to present individually here in this CIP. From the calculations, a sample size of 40 has been determined as the minimum sample size for 95% confidence across all requirements. Therefore, the recruitment goal for the Toffee Full face product

validation will be 45 participants to ensure that at least 40 participants complete the clinical investigation accounting for potential dropouts.

### 9.3. Pass and Fail Criteria



[redacted]

### 9.4. Statistical Termination

No interim analysis will be conducted as statistical outcomes will not change the conduct of the clinical trial.

### 9.5. Statistical Procedure Deviations

Statistical procedure deviations will be reported to the PI and the sponsor. Deviations from the original statistical plan will be explained in the final investigation report.

### 9.6. Selection Criteria

All participants who consent and whom are fitted with the Toffee Full Face mask and use in home, will be included in the analysis unless clear reason for exclusion are present such as definitive proof of wearing a different mask during the intervention period. Any data points that are excluded will be documented clearly with the reason for their exclusion.

## 10. Data Management

### 10.1. Data Management

[redacted]

### 10.2. Monitoring Arrangements

[redacted]

### 10.3. Data Management

[redacted]

[redacted]

# 11. Adverse Events and Termination

An AE is any adverse change from the participant's baseline condition, and is considered as any unfavorable and unintended sign or symptom or disease that occurs over the course of the clinical trial, whether related or unrelated to PAP therapy. All clinically significant AEs occurring during the clinical trial that were not present prior to the commencement of PAP therapy, will be recorded in the CRF, source document, and Adverse Event Log, and followed up by the PI until resolution or stabilization occurs in accordance with GCP. The collection of AE data will commence once the participant is consented into the trial and up to 24 hours after the Toffee Full face mask is returned following and the participant has completed the study. After this 24-hour period, AE information will no longer be collected.

Serious adverse events (SAE) are considered those which result in any of the following outcomes, regardless of their relationship to PAP therapy:

- Death
- Life-threatening AE
- Unplanned in-patient hospitalization or prolongation of existing hospitalization
- Persistent or significant disability or incapacity
- Congenital abnormality or birth defect

All SAEs will be recorded on a Serious Adverse Event Form, and any additional material or medical records will be de-identified by the PI or CI before it is affixed to the document.

Due to the nature of the delivery of PAP therapy, there are a number of expected side effects that may occur when using the Toffee full-face mask. These are disclosed in the PIS/ICF and will be documented in the CRF but not as adverse events. These are also documented below in Section 11.2.

## 11.1. Emergency Contact Details

| | |
|---|---|
| Name: | Bhavi Ogra |
| Address: | 15 Maurice Paykel Place, East Tamaki, Auckland 2013 |
| Phone: | +64 09 574 0123 Ext 7882 |
| Email: | bhavi.ogra@fphcare.co.nz |
| Professional Position: | Clinical Research Manager |

| | |
|---|---|
| Name: | Rebecca Thomson |
| Address: | 15 Maurice Paykel Place, East Tamaki, Auckland 2013 |
| Phone: | +64 09 574 0123 Ext 7675 |
| Email: | rebecca.thomson@fphcare.co.nz |
| Professional Position: | Senior Clinical Research Scientist |

## 11.2. Foreseeable Adverse Events

[redacted]

[redacted]

### 11.3. Reporting Adverse Events

Any SAEs, due to any cause, that occur during the clinical trial period, must be reported immediately, or within the next business day, by telephone to the sponsor. In addition to the initial telephone report, a SAEF must be completed and sent via email to the sponsor. All SAEs must also be recorded on the AE log. Additionally, all SAE's must be reported to HDEC as per HDECs reporting requirements.

### 11.4. Early Termination

The clinical trial may be discontinued at any time on the advice of the responsible investigator or on the basis of new information regarding safety or efficacy arising. Additionally, the clinical trial may be terminated if progress is unsatisfactory. The following documentation is required if the appropriate party terminates a clinical trial.

- PI: If the PI terminates or suspends a clinical trial without prior agreement of the sponsor, the PI should inform the institution, where required by the applicable regulatory requirements and the PI/institution should promptly inform the sponsor and HDEC, and should provide the sponsor and HDEC a detailed written explanation of the termination or suspension.

- Sponsor: If the sponsor terminates or suspends a clinical trial, the PI should promptly inform the institution, when and where required by the applicable regulatory requirements, and the PI/institution should promptly inform HDEC and provide a detailed written explanation of the termination or suspension.

- HDEC: If HDEC terminates or suspends its approval/favorable opinion of a clinical trial, the PI should inform the institution, when and where required by the applicable regulatory requirements. The PI/institution should promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.

## 12. Publication Policy

[redacted]

# 13. Approval

[redacted]

# 14. References


1. Senaratna, C. V. *et al.* Prevalence of obstructive sleep apnea in the general population: A systematic review. *Sleep Medicine Reviews* (2017).doi:10.1016/j.smrv.2016.07.002

2. Balachandran, J. S., Masa, J. F. & Mokhlesi, B. Obesity hypoventilation syndrome: Epidemiology and diagnosis. *Sleep Medicine Clinics* (2014). doi:10.1016/j.jsmc.2014.05.007

3. Aurora, R. N. *et al.* Practice parameters for the surgical modifications of the upper airway for obstructive sleep apnea in adults. *Sleep* (2010). doi:10.1093/sleep/33.10.1408

4. Sullivan, C. E., Berthon-Jones, M., Issa, F. G. & Eves, L. Reversal of Obstructive Sleep Apnoea by Continuous Positive Airway Pressure applied through the nares. *Lancet* (1981). doi:10.1016/S0140-6736(81)92140-1

5. Kryger, M., Roth, T. & Dement, W. *Principles and Practice of Sleep Medicine*. (Elsevier, 2016).

6. Ramar, K. *et al.* Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: An update for 2015. *J. Clin. Sleep Med.* (2015). doi:10.5664/jcsm.4858

7. Silva, R. S. *et al.* An orientation session improves objective sleep quality and mask acceptance during positive airway pressure titration. *Sleep Breath.* (2008). doi:10.1007/s11325-007-0138-6

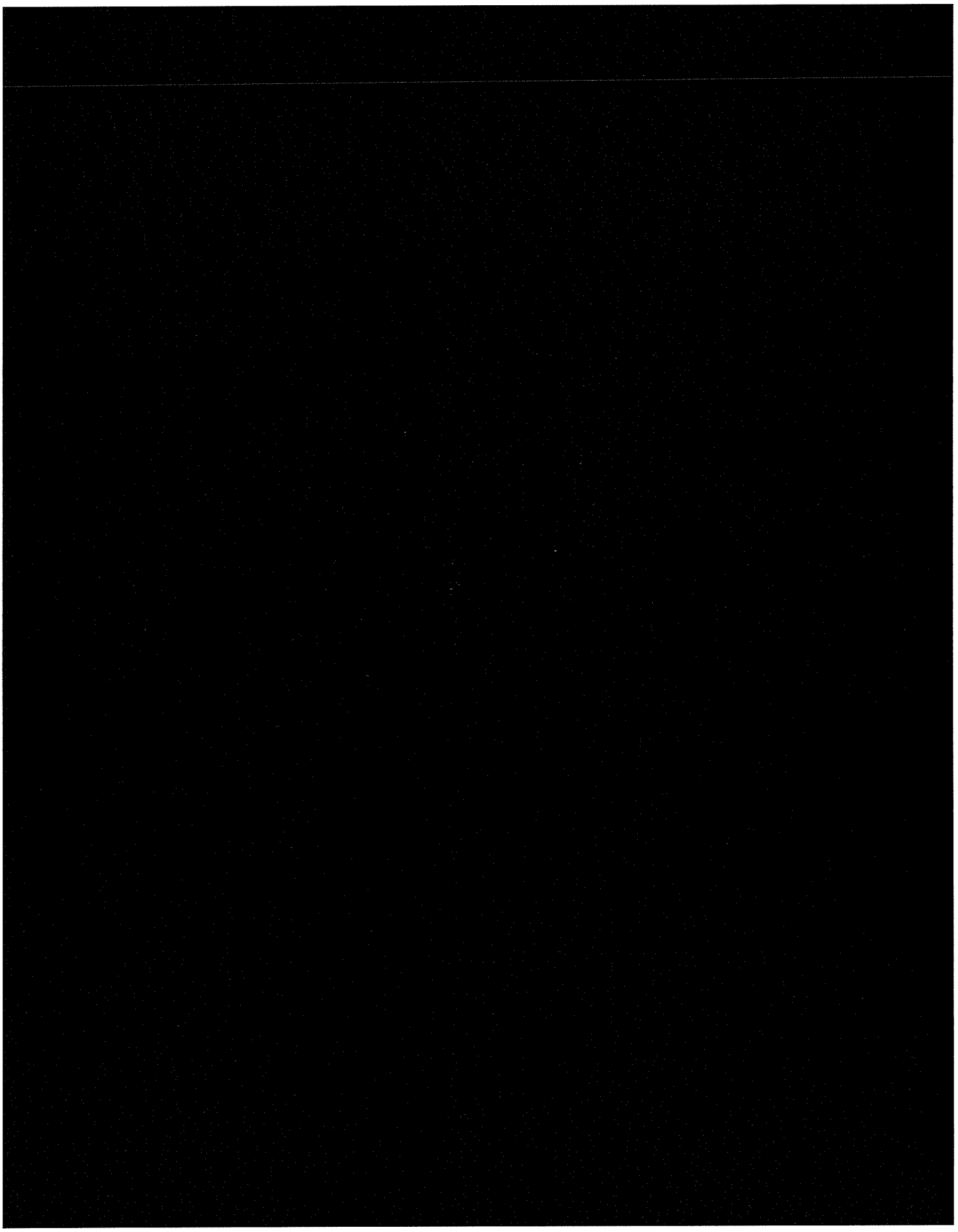
8. 2018 Census place summaries | Stats NZ. *Stats.govt.nz* (2020). at <https://www.stats.govt.nz/tools/2018-census-place-summaries/new-zealand#ethnicity-culture-and-identity>

9. Schwab RJ, Badr SM, Epstein LJ, Gay PC, Gozal D, Kohler M, Lévy P, Malhotra A, Phillips BA, Rosen IM, Strohl KP. An official American Thoracic Society statement: continuous positive airway pressure adherence tracking systems. The optimal monitoring strategies and outcome measures in adults. American journal of respiratory and critical care medicine. 2013 Sep 1;188(5):613-20. (16)

10. Baltzan MA, Dabrusin R, Garcia-Asensi A, Sully JL, Parenteau M, Tansimat G, Kassissia I, Wolkove N. Leak profile inspection during nasal continuous positive airway pressure. Respiratory care. 2011 May 1;56(5):591-5. (17)

11. Teschler H, Stampa J, Ragette R, Konietzko N, Berthon-Jones M. Effect of mouth leak on effectiveness of nasal bilevel ventilatory assistance and sleep architecture. European Respiratory Journal. 1999 Dec 1;14(6):1251-7. (18)

# 15. Appendix



[redacted]

[redacted]

[redacted]

[redacted]

[redacted]