The clinical impact of customised positive airway pressure (PAP) therapy interfaces (3DPiPPIn): a single site randomised controlled trial

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Abstract

Introduction: Positive Airway Pressure (PAP) therapy is the recognised treatment for sleep disordered breathing (SDB), delivered via a tight-fitting face mask (interface). Conventional interfaces do not consider facial geometries, often resulting in poor fit and ineffective therapy. Three-dimensional printing of customised interfaces may improve comfort and outcomes.

Objectives: To evaluate the clinical impact of customised versus conventional oronasal interfaces in adults with OSA. The primary outcome was residual Apnoea Hypopnea Index(AHI) at six months; secondary outcomes included interface leak, therapy concordance, and patient-reported symptoms.

Methods: A Randomised Controlled Trial (RCT) with 160 adults naïve to PAP therapy and diagnosed with SDB (AHI ≥15 events/hr). Randomisation was minimised by age and ethnicity. Structured light facial scans (POP2, Revopoint, China) were used to produce 3D-printed moulds (Fuse 30+, Formlabs, USA) for silicone-injected oronasal customised interface cushions.

AHI was compared using quantile regression to account for the skewed distribution of the AHI data. Secondary outcomes were compared using logistic, quantile and linear regressions.

Results: 160 participants were recruited (Intervention: 82, Control: 78). Customised interfaces were associated with a 1.5 (events/hr) increase in AHI (p=0.059), higher interface leak (difference in medians 30.0L/min, 95% CI 7.36 to 40.14, p <0.0001) and lower compliance (difference in compliance = 0.78, 95% CI 0.05 to 1.54, p =0.04) at six months.

Conclusions: This trial did not demonstrate customised oronasal interfaces were superior to conventional interfaces. Further refinement in design and production is needed to realise their potential benefits.

Trial registration: ISRCTN: 74082423

What is already known on this topic – Prior studies investigating 3D printed customised interface for PAP therapy users have been limited to either mannequin models, healthy volunteers, or were of very short durations (≤14 days). Our trial

provides clinically relevant, real-world data on a novel technological application designed to address a key limitation in current PAP therapy: the mismatch between commercial interfaces and individual facial morphology.

What this study adds - Although we did not find a statistically significant difference in AHI at six months (primary endpoint), there was an unexpected trend toward reduced therapy concordance and increased interface leak in the customised group.

How this study might affect research, practice or policy - these findings suggest that the clinical use of 3D-printed interfaces is feasible, although further refinement in manufacturing is required to optimise fit and performance.

Introduction

Obstructive sleep apnoea (OSA) is a common condition that affects an estimated 1.6 million people in the UK, relating to 14% of the population [1 2]. Positive Airway Pressure (PAP) provides positive pressure throughout the respiratory cycle, splinting the upper airway, thus relieving OSA. PAP is delivered via a tight-fitting interface attached to the patient's face. PAP improves morbidity, mortality and quality of life (QoL)[3]. The effectiveness of PAP is dependent upon interface fit. Patients often find the interface uncomfortable, limiting treatment adherence [4]. Furthermore, interface leaks have been found to cause high residual Apnoea Hypopnea Index (AHI) [5], persistent nocturnal desaturations [6] and ultimately failure of PAP therapy [7]. Pressure ulcers related to the interface are a documented side effect of PAP therapy, which limits a patient's ability to concord with treatment [8 9]. Similarly, patients are known to develop skin reactions and have reported side effects of oronasal dryness, nasal congestion, sinus or ear pain, gastric bloating and eye irritation associated with both PAP therapy itself and the interface [4 10 11]. Interfaces are currently limited to conventional interfaces supplied by PAP device manufacturers, which come in limited sizes and do not consider different facial geometries. Ineffective therapy due to a high interface leak is commonly observed which might affect morbidity and mortality and escalating healthcare utilisation, particularly in respiratory failure groups. There is a need to develop new solutions to the clinical problems of interfaces faced by clinicians, patients and their carers.

Several authors [12-24] have developed manufacturing pipelines for both nasal and oronasal customised PAP therapy interfaces. Furthermore, our multidisciplinary team developed and tested the feasibility of a customised PAP therapy device and have previously described the manufacturing process in detail [25]. Figure 1 displays an example of the customised oronasal interface for readers' convenience. Although nasal interfaces have been demonstrated to increase concordance, minimise AHI and minimise leak, oronasal interfaces can be used successfully [26]. We developed a customised oronasal interface as clinical experience informed us that patients experience more issues with interface fit with this type of interface. Furthermore, most studies to date have investigated customised nasal interfaces meaning there is a literature gap regarding oronasal interfaces. This was supported by patient and public involvement and engagement groups. A RCT was necessary to determine the clinical

effectiveness of the new customised oronasal interface. This RCT aimed to evaluate the clinical impact of customised oronasal PAP interfaces in adults with OSA. The primary outcome was AHI at six months, with secondary outcomes including mask leak, therapy concordance, and patient reported symptoms.

Patient and public involvement and engagement

A patient advisory group was established. Patients with experience of PAP therapy were involved in all stages of the research cycle.

Methods

The protocol has been previously described[27] but is described briefly here for the benefit of the reader.

Study design

The study design was a randomised controlled trial (RCT), via block randomisation by computerised random number generator (Sealedenvelope.com). Minimisation was by age (<65, ≥65) and ethnicity (Asian, Black and Caucasian). Ethnicity and age are the biggest factors affecting facial geometry[28 29] and thus were included in the minimisation. The primary outcome was residual AHI at the primary end point of six months. Residual AHI was chosen as the primary outcome measure since it is known that where interface fit is poor, residual AHI has been shown to be high[5 30]. The RCT was designed as a pragmatic trial and was embedded into existing clinical pathways.

Study participants

Inclusion criteria

- Diagnosis of sleep-disordered breathing (SDB): AHI ≥15 events/hour
- Patients naive to domiciliary PAP therapy
- Age ≥18years

Exclusion criteria

- AHI <15
- Excessive facial hair, which patient was unwilling to shave
- Age <18years
- Existing facial pressure ulcers
- Unable to provide informed consent

- Known allergy to silicone
- Keloid scarring
- Previous domiciliary PAP therapy

A sample size of 160, with 80 per group, was required for a power of 80%, with a significance of 5%, assuming an effect size of 0.50 and allowing for a 20% dropout rate.

Devices

The device was a 3D printed customised oronasal mask designed to be used with PAP therapy. The manufacturing process has been described extensively elsewhere[25]; in brief, structured light facial scans (POP2, Revopoint, China) were captured for each patients and the 3D surface images processed to produce moulds for 3D printing (Fuse 30+, Formlabs, USA). Silicone was injected in the 3D printed patient specific moulds to produce *c*ustomised oronasal interface cushions. The comparator was an off the shelf oronasal interface. The PAP therapy devices used were Prisma Smart and Prisma 25S (Lowenstein. Germany). Auto CPAP (Prisma Smart) and Auto S mode (Prisma 25S) were used in all patients, with minimum pressure 4cmH_2O and maximum pressure of 20cmH_2O and 25cmH_2O respectively. This protocol was reviewed and granted a favourable opinion by the Hampshire B Research Ethics Committee (REC reference: 22/SC/0405).

Analysis

Patient characteristics were reported with descriptive statistics using frequencies, median (IQR) and mean (SD) when appropriate, according to data type and distribution. The hypothesis was tested by comparing the difference between the groups in residual AHI (the primary outcome) at the primary endpoint (six months) using quantile regression, adjusting for score at baseline and stratification variables (age as a binary variable and ethnicity). Quantile regression was used to account for the skewed distribution of the AHI data, providing a more robust analysis than mean-based methods[31]. It estimates the effects of covariates at different points of the outcome distribution, without assuming normality. A quantile regression was chosen over a linear regression as the data were skewed and could not be transformed to normality. The 50th centile was chosen as there was no clinical threshold or guideline

that suggested an alternative centile was appropriate. Analysis was conducted on an intention-to-treat basis.

For secondary outcome measures, differences between groups were compared using appropriate regression adjusting for respective scores at baseline and stratification variables. Logistic regression was used for binary data, linear regression for normally distributed data, and quantile regression for skewed data. Throughout, Caucasian ethnicity and age <65 years were the reference group, as this was the largest group.

Study data were collected and managed using REDCap (Research Electronic Data Capture) electronic data capture tools hosted at University College London[32 33]. Data were analysed using Excel and R in R studio.

Results

685 patients were screened between January 2023 and May 2024, with the target of 160 participants recruited (Fig 2). 72%(n=56) of the control group completed the trial versus 51%(n=42) in the intervention group (p=0.007). There were no demographic factors or baseline disease characteristics associated with the higher dropout rate in the intervention group (descriptive comparisons only; see Online supplement 1.). A complete case analysis is reported throughout the remainder of these results.

Those enrolled in the trial had similar demographics in terms of age, ethnicity, and sex compared to those who declined to participate (Table 1). Anthropometric and physiological measures were similar at baseline and prevalence of comorbidities and medications were comparable between the control and intervention groups (Table 1). All patients were initially started on CPAP; two required transition to bi-level PAP therapy due to high remnant AHI on treatment.

At the primary endpoint of six months the median (IQR) AHI in the control group was 1.3 [0.6 to 2.6], compared to 3.3 [1.4 to 8.3] in the intervention group. At six months, median AHI was not different between the customised and conventional interface groups(Q50 1.5, 95% CI 0.7 to 3.1, p=0.059).

Table 2 presents the descriptive results for the secondary outcome measures at six months. The three-month outcome data is available in online supplement 2. Secondary outcomes are not adequately powered and are thus exploratory in nature.

The intervention was associated with higher interface leak (Difference in medians 30.0, 95% CI 7.36 to 40.14, p <0.0001) and lower compliance (hh:mm) at six months (difference in compliance = 0.78, 95% CI 0.05 to 1.54, p =0.04). At six months, there was no difference in odds of being compliant between the control and intervention group (Odds Ratio (OR) = 0.53, 95% CI: 0.22 to 1.24, p =0.150). At six months, there was no difference in the risk of developing a pressure ulcer between the intervention and control groups (OR 1.87, 95% CI: 0.39 to 10.1, p =0.434). There was no difference in excessive daytime sleepiness (EDS) symptoms between the control and intervention groups at six months (difference between control and intervention = 0.36, 95% CI -1.61 to 2.33, p =0.72). There was a significantly lower SWIFT score in the intervention groups at six months (difference between control and intervention = -0.27, 95% CI -2.97 to 2.42, p =0.051). There was no difference in S^3-NIV score between the intervention groups at six months (difference between control and intervention = 0.13, 95% CI -0.65 to 0.91, p =0.74). Online supplement 3 shows the results of the interface questionnaire at six months. At six months, there were no differences between the groups in any of the questions posed.

Discussion

This study is the first RCT in adult patients assessing customised oronasal PAP therapy interfaces over a medium-term duration. To date, other authors have conducted studies on healthy individuals or have only reviewed short-term outcomes (max 14 days)[12-18 20-22 34 35].

This negative trial demonstrated no statistically significant or clinically meaningful difference in AHI between off-the-shelf and customised oronasal PAP therapy interfaces. Previous authors have suggested a minimally clinically important difference (MCID) in AHI of 5 events/hr[3], which would mean the 95% confidence interval (3.12) is below the MCID, further indicating no clinically meaningful difference. The results of this study do not indicate superiority of customised oronasal PAP therapy interfaces with the current design and technologies. With further product refinement and development of 3D printing technologies, there is potential for customised interfaces to be a solution in the future. Clinicians and patients will undoubtedly be disappointed to hear that current technologies are not yet adequate to enable customised PAP therapy interfaces to be routine.

Cheng et al.[23] report on an RCT comparing conventional nasal cushions with customised nasal cushions. Their customised cushion was created using computer numerical control (CNC) rather than 3D printing. They report a significant difference between the two groups in residual AHI ($p<0.001$); however, the report lacks other statistical information (differences between groups and confidence intervals), and the customised cushion was nasal rather than oronasal interface, meaning results are not comparable to this study. Furthermore, the duration of 14 days might not be long enough to gain adequate control of OSA.

There are conflicting results between existing literature and this study regarding the impact of customised interfaces on unintentional leak, with some authors reporting no difference[15 16], others in favour of the customised design[12 13] and others favouring off the shelf interfaces[35]. The conflicting results could be due to different interface styles used. Other factors that are known to impact interface leak, include: nasal obstruction, BMI, fat distribution, age and sex[36]. These patient factors have not been considered in previous study designs, nor fully in this study design. Furthermore, Lowenstein do not publish a threshold on the acceptable leak as a set figure; therefore, it is not possible to report if the leak was within acceptable limits. The higher interface leak observed in the customised group could be due to a number of factors. Facial scans were acquired in the supine position and thus the customisation process does not take into account possible face deformation when lying and different sleeping positions during the night. Furthermore, the customised interfaces were heavier than the conventional interfaces to avoid damage during manufacturing. It was outside of the scope of this study to compare the material properties of the silicone used between customised and conventional interfaces, but this may further explain the differences observed in interface leak. Refinement of the customised interfaces production processes could include possible face deformation when lying and exploring different materials like more compliant silicone and considering alternative manufacturing approaches which reduce the weight of the customised interface.

Our results are probably more representative of clinical practice than the shorter duration trials, given PAP therapy is a long rather than short-term treatment. Our data suggest that manufacturing an oronasal mask with an acceptable leak is more challenging than manufacturing a nasal or nasal pillow interface with an acceptable interface leak.

The average concordance with PAP therapy within this research trial was low, with only 44% of the control and 25% of the intervention group being considered concordant with treatment at six months. Although >4hrs/night of PAP therapy use is internationally recognised as adequate for symptom relief[37], a recent review[38] has suggested that for AHI to be controlled PAP therapy use needs to be >6hrs/night. Therefore, the inadequate use of PAP therapy might not facilitate full control of AHI. There is a complex relationship between AHI, interface leak, symptoms, side effects and concordance, with all these variables impacting each other. Concordance was not the primary outcome but is an important factor to consider given the relationship between concordance and symptoms, as well as the potential impact on cardiovascular risk for some phenotypes. Although there is no MCID for PAP therapy concordance, both the linear regression (compliance measured as hours) and logistic regression (compliance as a binary measure) demonstrated clinically important reduced concordance in the intervention group. The impact of customised PAP therapy interfaces on concordance over six months appears to be a novel finding of this research. Tong et al.[39] undertook a cohort study of existing poorly concordant CPAP users, issued them with customised nasal pillow interfaces and reviewed them after one month. They reported a statistically significant (p=0.016) increase in CPAP usage, although even with the customised interface, the median nightly use was only 3.8 hours. This suggests factors other than the CPAP interface were involved in the low concordance in this group.

Given the paucity of reporting of medical device-related pressure ulcers in home PAP therapy, it is difficult to know if the prevalence reported here is above or below what would be expected. The data from this study seems to be in keeping with the limited data published by other authors[13 20 25]. Previous data suggest that, even in healthy subjects and short-term use, at least blanchable erythema occurs with both off-the-shelf and customised PAP therapy interfaces. Patients with SDB OSA will have other difficult-to-mitigate risk factors increasing the prevalence of pressure ulcers and skin damage, for example, obesity and diabetes.

Within this clinical trial symptoms associated with OSA were measured using ESS and SWIFT. Improvement in EDS is a key goal of PAP therapy treatment[3]. Interestingly, other authors have not considered the impact on EDS with customised interfaces, this

is perhaps because most studies to date have been in healthy subjects who would not be suffering from EDS, or the studies were of short duration.

Our results showed no difference in comfort at six months between the control and intervention groups. Comfort has been a focus of other authors investigating customised interfaces. There were conflicting results for comfort, including both no difference between customised and conventional interfaces[15 35] and in favour of customised interfaces[16 20 21 23 24 39 40]. It is difficult to compare the results of these studies with our study due to the different mask styles used, follow-up periods and study designs. All authors to date, including our study, have self-developed questionnaires. This means the psychometric properties of these questionnaires are not known, and results should be interpreted with caution.

Limitations

There were several limitations to this trial. It was only feasible to assess medium-term (six-month) outcomes within the scope of the funding. Off-the-shelf interfaces are marketed as lasting approximately a year, and so the durability of the customised interfaces beyond six months has not been tested. Furthermore, due to funding, it was not possible to blind assessors, leading to potential reporting bias. However, (unpublished) intra-rater and inter-rater reliability analysis of AHI suggested this was minimal. The interventional nature of the trial means it was not possible to blind participants, which could lead to reporting bias. This was a single-site study and may not be representative of other healthcare settings, regions, or patient populations, potentially reducing generalisability. It was not possible to include a health economics assessment due to funding constraints.

The dropout rate was higher than anticipated overall, and was higher in the intervention group. This may reflect the challenges of acclimatising to a novel device or the additional burden associated with trialling a non-standard interface. While our study was not designed to explore reasons for attrition, these findings highlight the importance of incorporating strategies to support concordance and acceptability in future trials of PAP therapy-based interventions. They also underline the need to anticipate higher dropout rates in power calculations when designing studies of novel PAP interfaces. . The therapeutic pressure was not collected, which could be a potential confounding factor. Additionally, the population were overall poorly

concordant with PAP therapy, which introduces variability and confounding factors that might not be fully accounted for. We did not measure other factors known to impact concordance, such as behavioural and psychological components, and so could not account for them. Were a trial design to include concordance as a primary outcome, it would be important to include these aspects in the trial design. The 3DPiPPIn Patient and Public Involvement group have expressed frustration at the limitation of providing customised masks within a clinical trial, and that, due to regulations, the customised masks cannot be utilised outside of the clinical trial.

The need for research focusing on developing patient-specific interfaces for PAP therapy that are acceptable to patients and avoid side effects such as leaks, pressure ulcers, and ineffective PAP therapy is a priority[41]. The outcomes from this trial could inform the design and manufacturing processes of future customised PAP therapy interfaces and support future trial conduct. For example, the pragmatic trial design proved beneficial in a recruiting a representative population. Future research should focus on product development and bench studies, there would need to be significant improvements in manufacturing processes before further clinical trials would be appropriate. There is no standardised questionnaire for interface comfort or specifically side effects associated with CPAP and future research could develop one. Further research into responders and non-responders is warranted; this would ensure trials investigate the populations most likely to benefit from customised interfaces. It might be more appropriate to consider a trial design for those already established on PAP therapy, rather than those naive to therapy, thus navigating the issues of non-concordance. Future research should include a health economics assessment.

Conclusion

This particular customised oronasal interface did not confer benefit over a conventional interface. Future refinement of design and production may yield different results. Further product development is required before future clinical trials should be considered.

Author contributions

Conceptualization: SKM Methodology: SKM, SM, CK, EM, SS, EM, SH, Resources: SKM, FG Data Curation: SKM, FG Writing - Original Draft: SKM, Writing - Review and

Editing: All authors Supervision: SM, EM, SS, CK, SH Project administration: FG, SKM Funding acquisition: All authors Guarantor: Silvia Schievano

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Data availability statement

Data supporting this study cannot be made available due to ethical, legal and commercial reasons.

Summary competing interest statements: SKM: Educational grants from Dolby Vivisol. FG: Nil to declare. DR: Nil to declare. CK: Nil to declare. OO: Nil to declare. SM: consultancy for Philips Respironics and Fisher and Paykel, educational and small research grants from Dolby Vivisol. SH: Nil to declare. EM: Nil to declare. SS: Nil to declare.

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Tables

Table 1 Demographics of those screened and enrolled into the trial

	Screened n=525	**Control n=78**	**Intervention n=82**
Age (years)	53.8(13.6)	54.21 (13.26)	54.37 (11.70)

Sex n (%)			
Male	365(69)	58(74)	66(80)
Female	160(31)	20(26)	16(20)
Ethnicity n (%)			
Asian	74 (14)	15(19)	15(18)
Black	38(7)	9(12)	11(14)
Caucasian	231(44)	54(69)	56(68)
Other	182(35)	-	-
Respiratory rate (bpm)	-	14(6)	14(3)
SpO_2	-	96 (6)	96(1)
Waterlow score	-	4 (2)	4 (2)
BMI Kg/m^2	-	34.94 (6.72)	35.16 (7.02)
Rockwood Frailty Score n(%)			
Very fit	-	-	-
Well	-	38(49)	42(51)
Managing well	-	37(47)	3745)
Vulnerable	-	1(1)	2(2)
Mildly frail	-	-	-
Moderately frail	-	2(2)	1(1)
Severely frail	-	-	-
Very severely frail	-	-	-
Terminally ill	-	-	-
Smoking Status n (%)			
Current smoker	-	8(10)	6(7)
Ex-smoker	-	33(42)	36(44)
Never smoker	-	37(47)	40(49)

Alcohol consumption (units/week)		6.1(12.6)	5.0(7.4)
Past medical history n(%)			
Alzheimer's disease	-	0	0
Current steroid use	-	12(15)	9(11)
Oxygen therapy prescription	-	0	0
Cardiovascular disease	-	37(47)	37(47)
Diabetes mellitus	-	14(18)	16(20)
COPD	-	0	0
Hip fractures	-	2(3)	0
Heart failure	-	2(3)	3(4)
Limb paralysis	-	0	1(1)
Lower limb oedema	-	4(5)	5(6)
Malignancy	-	8(10)	3(4)
Parkinson's disease	-	0	0
Rheumatoid arthritis	-	0	2(2)
Urinary tract infection	-	17(22)	17(21)
Medications n(%)			
Anticoagulants	-	15(12)	16(13)
Cardiovascular disease	-	41(32)	38(31)
Diabetes	-	13(10)	15(12)
Diuretics	-	5(4)	10(8)
Steroids	-	1(1)	0(0)
Baseline sleep study Mean(SD)			
AHI (events/hr)	-	38.1(17.0)	39.5(20.1)
ODI (events/hr)	-	31.3(19.8)	29.5(18.7)
Mean SpO_2	-	91.8(2.4)	91.5(2.7)

Total Sleep Time SpO_2 <90% (%)	-	18.4(18.3)	20.5(19.4)
Epworth Sleepiness Score		8.5 [5.3 to 13.0]	9.0 [5.0 to 14.0]
Sleepiness-Wakefulness Inability and Fatigue		10.0[5.0 to 16.0]	9.0 [3.0 to 16.0]

Mean ±SD are presented with Median [IQR] in square brackets. n (%) are denoted in the demographic column where applicable. AHI: Apnoea Hypopnea Index, BMI: Body Mass Index, bpm: breaths per minute, COPD: Chronic Obstrucitve Pulmonary Disease, ODI: Overnight Desaturation Index,

Table 2: Descriptive summary between control and intervention group for the secondary outcome measures at 6 months

	Control	**Intervention**
Interface leak(L/min) at 6 months	2.5 [0.0 to 13.1]	32.5 [12.5 to 45.0]
Incidence of pressure ulcers at 6 months n (%)	3(4.8)	4(9.5)
Location of pressure ulcer		
Bridge of nose	3(100)	4(100)
Grade of pressure ulcer		
Early warning sign	1(33.3)	
Grade 1	1(33.3)	3(75)
Grade 2	1(33.3)	1(25)
Grade 3		
Grade 4		
Compliance with PAP therapy (hh:mm) at 6 months	05:47(01:47)	04:58(01:56)
Compliance with PAP therapy (%) at 6 months	66.5 [32.2 to 97.0]	57.0 [17.0 to 79.2]
Compliant with PAP therapy (≥4hrs/night on average on ≥70% of nights) at 6 months n(%)	25(44.6)	13(31)
Epworth Sleepiness Score at 6 months	6.0 [3.0 to 8.25]	5.0 [3.0 to 9.0]

Sleepiness-Wakefulness and Fatigue at 6 months	Inability	6.5 [2.3 to 9.0]	4.5 [1.0 to 9.5]
S^3-NIV at 6months		6.7 [5.5 to 7.5]	7.0 [6.1 to 8.0]

Mean ±SD are presented with Median [IQR] in square brackets. n (%) are denoted in the demographic column where applicable. PAP: Positive Airway Pressure,

References

1. Lyons MM, Bhatt NY, Pack AI, et al. Global burden of sleep-disordered breathing and its implications. *Respirology* 2020;25(7):690-702. doi: 10.1111/resp.13838
2. British Lung Foundation. Obstructive Sleep Apnoea (OSA) Toolkit for commissioning and planning local NHS services in the UK. London: British Lung Foundation, 2015.
3. National Institute for Clinical Excellence. Obstructive sleep apnoea/hypopnoea syndrome and obesity hypoventilation syndrome in over 16s. NICE guideline [NG202]. https://www.nice.org.uk/guidance/ng202: NICE, 2021.
4. Bachour A, Vitikainen P, Virkkula P, et al. CPAP interface: satisfaction and side effects. *Sleep and Breathing* 2013;17(2):667-72. doi: 10.1007/s11325-012-0740-0
5. Schellhas V, Glatz C, Beecken I, et al. Upper airway obstruction induced by non-invasive ventilation using an oronasal interface. *Sleep and Breathing* 2018;22(3):781-88. doi: 10.1007/s11325-018-1640-8
6. Gonzalez-Bermejo J, Morelot-Panzini C, Arnol N, et al. Prognostic value of efficiently correcting nocturnal desaturations after one month of non-invasive ventilation in amyotrophic lateral sclerosis: a retrospective monocentre observational cohort study. *Amyotrophic lateral sclerosis & frontotemporal degeneration* 2013;14(5-6):373-9. doi: 10.3109/21678421.2013.776086 [published Online First: 2013/03/27]
7. Hess DR. The evidence for noninvasive positive-pressure ventilation in the care of patients in acute respiratory failure: a systematic review of the literature. *Respiratory care* 2004;49(7):810-29. doi: 10.4187/respcare.04490730
8. Kakkar RK, Berry RB. Positive Airway Pressure Treatment for Obstructive Sleep Apnea. *CHEST* 2007;132(3):1057-72. doi: 10.1378/chest.06-2432
9. Pepin JL, Leger P, Veale D, et al. Side effects of nasal continuous positive airway pressure in sleep apnea syndrome. Study of 193 patients in two French sleep centers. *Chest* 1995;107(2):375-81. doi: 10.1378/chest.107.2.375 [published Online First: 1995/02/01]
10. Mehta S, Hill NS. Noninvasive Ventilation. *American journal of respiratory and critical care medicine* 2001;163(2):540-77. doi: 10.1164/ajrccm.163.2.9906116

11. Mandal S, Ramsay M, Suh E-S, et al. External Heated Humidification During Non-Invasive Ventilation Set Up: Results from a pilot cross-over clinical trial. *European Respiratory Journal* 2020:1901126. doi: 10.1183/13993003.01126-2019

12. Borras-Novell C, Causapie MG, Murcia M, et al. Development of a 3D Individualized Mask for Neonatal Non-Invasive Ventilation. *Int J Bioprint* 2022;8(2):516. doi: 10.18063/ijb.v8i2.516 [published Online First: 20220224]

13. Willox M, Metherall P, McCarthy AD, et al. Custom-made 3D printed masks for children using non-invasive ventilation: a comparison of 3D scanning technologies and specifications for future clinical service use, guided by patient and professional experience. *J Med Eng Technol* 2021;45(6):457-72. doi: 10.1080/03091902.2021.1921869 [published Online First: 2021/05/22]

14. Bockstedte M, Xepapadeas AB, Spintzyk S, et al. Development of Personalized Non-Invasive Ventilation Interfaces for Neonatal and Pediatric Application Using Additive Manufacturing. *J Pers Med* 2022;12(4) doi: 10.3390/jpm12040604 [published Online First: 20220408]

15. Martelly E, Rana S, Shimada K. Design and Fabrication of Custom-Fit BiPAP and CPAP Masks Using Three-Dimensional Imaging and Three-Dimensional Printing Techniques. *Journal of Medical Devices* 2021;15(2) doi: 10.1115/1.4049981

16. Duong K, Glover J, Perry AC, et al. Feasibility of three-dimensional facial imaging and printing for producing customised nasal masks for continuous positive airway pressure. *ERJ Open Research* 2021;7(1) doi: 10.1183/23120541.00632-2020

17. Simpson R, Pascoe J, Letcher J, et al. Customized, 3D-Printed Nasal Masks for the Delivery of Noninvasive Positive Airway Pressure in Patients with Obstructive Sleep Apnea, Preliminary Findings. *A69 SRN: CLINICAL AND PHYSIOLOGICAL INSIGHTS INTO THE MANAGEMENT OF SDB* 2020:A2433-A33. doi: 10.1164/ajrccm-conference.2020.201.1_MeetingAbstracts.A2433

18. Personalized 3D-printed CPAP masks improve CPAP effectiveness in children with OSA and craniofacial anomalies. Combined Otolaryngology Spring Meetings April; 2015.

19. Rouchié B, Mattana G, Piro B, et al. Development of a test bench for ventilation masks through 2D and 3D printing processes. *Sensors and Actuators A: Physical* 2024;367 doi: 10.1016/j.sna.2023.115001

20. Shikama M, Nakagami G, Noguchi H, et al. Development of personalized fitting device with 3-dimensional solution for prevention of niv oronasal mask-related pressure ulcers. *Respiratory care* 2018;63(8):1024-32. doi: 10.4187/respcare.05691

21. Wu YY, Acharya D, Xu C, et al. Custom-Fit Three-Dimensional-Printed BiPAP Mask to Improve Compliance in Patients Requiring Long-Term Noninvasive Ventilatory Support. *Journal of Medical Devices* 2018;12(3):031003-03-8. doi: 10.1115/1.4040187

22. Martin-Gonzalez A, Morras de la Torre B, Bergon-Sendin E, et al. Feasibility of three-dimensional nasal imaging and printing in producing customized nasal masks for non-invasive ventilation in extremely low birth weight infant: A pilot study. *Int J Bioprint* 2023;9(1):627. doi: 10.18063/ijb.v9i1.627 [published Online First: 20221028]

23. Cheng YL, Hsu DY, Lee HC, et al. Clinical verification of patients with obstructive sleep apnea provided with a customized cushion for continuous positive airway pressure. *The Journal of prosthetic dentistry* 2015;113(1):29-34.e1. doi: 10.1016/j.prosdent.2014.01.030 [published Online First: 2014/10/05]

24. Hsu D-Y, Cheng Y-L, Bien M-Y, et al. Development of a method for manufacturing customized nasal mask cushion for CPAP therapy. *Australasian physical & engineering sciences in medicine* 2015;38(4):657-64. doi: 10.1007/s13246-015-0383-0

25. Mansell SK, Olsen O, Gowing F, et al. 3DPiPPIN: 3D printing of positive airway pressure (PAP) therapy interfaces: a single site feasibility study. *Journal of Medical Engineering & Technology* 2025:1-11. doi: 10.1080/03091902.2025.2532648

26. Mansell SK, Devani N, Shah A, et al. Current treatment strategies in managing side effects associated with domiciliary positive airway pressure (PAP) therapy for patients with sleep disordered breathing: A systematic review and meta-analysis. *Sleep Medicine Reviews* 2023:101850. doi: 10.1016/j.smrv.2023.101850

27. Mansell SK, Mandal S, Ridout D, et al. Clinical impact of customised positive airway pressure (PAP) therapy interfaces versus usual care in the treatment of patients with sleep-disordered breathing (3DPiPPIn): a randomised controlled trial protocol. *BMJ Open* 2024;14(11):e087234. doi: 10.1136/bmjopen-2024-087234

28. Farkas LG, Katic MJ, Forrest CR, et al. International anthropometric study of facial morphology in various ethnic groups/races. *J Craniofac Surg* 2005;16(4):615-46. doi: 10.1097/01.scs.0000171847.58031.9e

29. Farkas LG, Eiben OG, Sivkov S, et al. Anthropometric measurements of the facial framework in adulthood: age-related changes in eight age categories in 600 healthy white North Americans of European ancestry from 16 to 90 years of age. *J Craniofac Surg* 2004;15(2):288-98. doi: 10.1097/00001665-200403000-00027

30. Genta PR, Kaminska M, Edwards BA, et al. The Importance of Mask Selection on Continuous Positive Airway Pressure Outcomes for Obstructive Sleep Apnea. An Official American Thoracic Society Workshop Report. *Annals of the American Thoracic Society* 2020;17(10):1177-85. doi: 10.1513/AnnalsATS.202007-864ST

31. Koenker R, Bassett G. Regression Quantiles. *Econometrica* 1978;46(1):33-50. doi: 10.2307/1913643

32. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *Journal of biomedical informatics* 2009;42(2):377-81. doi: 10.1016/j.jbi.2008.08.010

33. Harris PA, Taylor R, Minor BL, et al. The REDCap consortium: building an international community of software platform partners. *Journal of biomedical informatics* 2019;95:103208. doi: 10.1016/j.jbi.2019.103208

34. Mansell S, Oliver O, Smith L, et al. 3D Printing Positive Pressure Interfaces (3dpippin): Results From a Two-Phase Feasibility Trial. *American journal of respiratory and critical care medicine* 2025;211(Abstracts):A6945-A45. doi: 10.1164/ajrccm.2025.211.Abstracts.A6945

35. Nam J-G, Kim DH, Lee T-H. Application and limitations of facial computed tomography and three-dimensional scanner images for patient-specific three-dimensional printing of a nose mask. *Journal of Cosmetic Medicine* 2022;6(1):27-33. doi: 10.25056/JCM.2022.6.1.27

36. Lebret M, Arnol N, Martinot JB, et al. Determinants of Unintentional Leaks During CPAP Treatment in OSA. *Chest* 2018;153(4):834-42. doi: 10.1016/j.chest.2017.08.017 [published Online First: 2017/08/30]

37. Weaver TE, Maislin G, Dinges DF, et al. Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep* 2007;30(6):711. doi: 10.1093/sleep/30.6.711

38. Chaplin H, Ward K. How many hours per night is enough? A systematic integrative review to identify optimal hours of CPAP therapy use for sleep apnoea. *Health Sciences Review* 2022;5 doi: 10.1016/j.hsr.2022.100061

39. Tong BK, Cistulli PA, Ledger S, et al. A novel three-dimensional-printed customized nasal mask for improving CPAP adherence and satisfaction for the treatment of obstructive sleep apnea. *Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine* 2025;21(1):9-16. doi: 10.5664/jcsm.11340

40. Tanoto N, Friedland Y, Collier RC, et al. THREE-DIMENSIONAL printed continuous positive airway pressure masks in children with maxillofacial deformities with obstructive sleep apnea. *Otolaryngology Case Reports* 2024;31:100602. doi: 10.1016/j.xocr.2024.100602

41. Argent AC. Noninvasive Ventilatory Support: The Detail Lies in the Interface. *Respiratory care* 2015;60(11):1708-10. doi: 10.4187/respcare.04492 [published Online First: 2015/10/24]

Figure legends

Figure 1 Example customised oronasal PAP therapy interface

Figure 2 Consort diagram