Why Do We Need Combination Therapy?
CPAP adherence is poor

- Adherence is poor
  - 50-60% abandon CPAP within first 12 months¹,²
  - Adherence (hours of use) rates range from 30-60%³

- Non adherent users
  - Start skipping nights during week one of treatment
  - Remain non adherent⁴

- 16 years after this pattern of poor adherence was first described in the literature it remains largely unchanged⁴

¹Propescu et al 2001; ²Galetke et al 2011; ³Weaver and Sawyer 2010; ⁴Weaver & Sawyer 2009
Trending Away From FFM

**FFM – Now Reconsidered**

- FFM masks require higher pressure than nasal masks to maintain patency. *Valentin A et al. Sleep J 2011*

- Pressure in FFM causes more upper airway obstruction than a nasal mask by either displacing the mandible posteriorly or increasing upper airway collapsibility by virtue of mouth-opening. *Tero, Sleep J 2011*

**Why Prescribed?**

- First choice for Mouth breathers

- Increased Reimbursement ($20-40) DME

- Proactively Rx @ VA due to long wait times for PAP intervention (bad press)
Results of Poor Mask Fit

50% of patients quit CPAP therapy within the first year

- Poor mask fit leads patients, on average, to try 3–5 generic masks in the first month.

- Patients who switched their mask are at a seven-fold higher risk for abandoning therapy after switch than those who did not.

- Mask acceptance is correlated with fewer mask leaks (p=0.002) and higher pressure therapy (p=0.042)

O₂ Vent Airway™

3. Valentin A et al. Sleep J 2011
4. Tero, Sleep J 2011
Oral Appliances Not Efficacious For All Patients

• Mandibular advancement splints (MAS) are not as efficacious as continuous positive airway pressure (CPAP)

• Effectiveness of both treatments on general health outcomes, cognitive function, and quality of life appears to be equivalent

• The main barrier for the implementation of MAS treatment in clinical practice is the interindividual variability in response to MAS treatment.

• Several prediction tools have been proposed to enhance patient selection for MAS treatment

• Phenotyping obstructive sleep apnea patients may reveal patient characteristics that enable the prediction of response to MAS treatment

Our Sleep Treatment Platform is personalising sleep medicine

More patients achieving success* with minimal intervention

<table>
<thead>
<tr>
<th>Traditional lower jaw advancement (competitor products)</th>
<th>Oventus O₂Vent™</th>
<th>Oventus O₂Vent™ + EPAP</th>
<th>Oventus O₂Vent™ + Connect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mandibular advancement splints</td>
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- **41%** of patients treated successfully
- **54%** of patients treated successfully
- **78%** of patients treated successfully
- **100%** of patients treated successfully

Cumulative Treatment Success Using Oventus Treatment Platform

2. Victor Lai, Benjamin Tong, Carolin Tran, Andrea Ricciardello, Michele Donegan, Nicholas Murray, Jayne Carberry and Danny Eckert Combination therapy with mandibular advancement and expiratory positive airway pressure valves reduces OSA severity. Abstract Submitted Sleep DownUnder Brisbane 2018

* AHI < 10 and 50% reduction

* Traditional Jaw Advancement mouth guard
What Is Oventus Airway Technology Doing and How Can Clinicians Use it?

A Personalised Approach to Medicine

- Ability to treat nasal obstruc ters as well as non-nasal obstruc ters
  - Benjamin Tong, Jason Amatoury, Jayne Carberry and Danny Eckert. The effects of posture and mandibular advancement on nasal resistance and obstructive sleep apnea treatment outcome with a novel oral appliance therapy device. Neuroscience Research Australia (NeuRA) and the University of New South Wales, Sydney, Australia. Poster and Abstract World Sleep Prague 2017.

- Where Mandibular advancement alone may not be able to
  - Ng AT1, Qian J, Cistulli PA. Oropharyngeal collapse predicts treatment response with oral appliance therapy in obstructive sleep apnea. Sleep 2006 May;29(5):666-7
What Is Oventus Airway Technology Doing and How Can Clinicians Use it?

A Personalised Approach to Medicine

• Reduces pharyngeal pressure swings (collapsibility) and reduces residual events compared to MAS alone
  
  
  – Amatoury J, Tong B, Nguyen C, Szollosi I, Eckert DJ THE ROLE OF A NOVEL ORAL APPLIANCE THERAPY DEVICE ON PHARYNGEAL PRESSURE SWINGS AND CPAP REQUIREMENTS DURING SLEEP IN OBSTRUCTIVE SLEEP APNEA: A PILOT STUDY. Abstract Supplement AADSM Boston 2017
What Is Oventus Airway Technology Doing and How Can Clinicians Use it?

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- **MAS + Airway** Increases response rate in MAS non-responders.

- **MAS + Airway + EPAP** Increases response rate in MAS + Airway non-responders
  - Victor Lai, Benjamin Tong, Carolin Tran, Andrea Ricciardiello, Michelle Donegan, Nicholas Murray, Jayne Carberry and Danny Eckert Combination therapy with mandibular advancement and expiratory positive airway pressure valves reduces OSA severity. Abstract Submitted Sleep DownUnder Brisbane 2018
What Is Oventus Airway Technology Doing and How Can Clinicians Use it?

A Personalised Approach to Medicine

- Reduces CPAP pressure requirements, eliminates the need for a full face mask and allows mouth breathing while delivering nCPAP
  - Benjamin Tong, Carolin Tran, Andrea Ricciardiello, Michelle Donegan, Nicholas Murray, Alan Chiang, Irene Szollosi, Jason Amatoury and Danny Eckert. Combination therapy with CPAP plus MAS reduces CPAP therapeutic requirements in incomplete MAS responders. Abstract Submitted Sleep DownUnder Brisbane 2018

- Treating nasal obstruction patients where traditional CPAP may not be able to
How Oventus Airway Technology is truly differentiated
Delivers consistent airflow. Addresses common sites of obstruction.

- Oventus Airway Technology addresses multiple levels of obstruction.
- Mandibular positioning primarily manages tongue based obstruction, i.e. 20% of primary obstructions
- Allowing airflow through Oventus ‘Airway Technology has a similar effect to pumping via CPAP
- Oventus improves efficacy of oral appliance therapy by 30-50%

Combining mandibular advancement with its proprietary oral airway, Oventus Airway Technology uniquely addresses both sites of primary upper airway blockage and secondary airway collapse.

What is nasal EPAP?

- Mechanical one-way valve (Provent™) applied over each nostril
  - Provides high resistance to expiration -> high airway pressures during expiration -> reduces upper airway collapsibility
  - Hyperinflation of lungs -> increased ‘tracheal traction’ -> reduces upper airway collapsibility

Friedman, M., et al. (2016).

Functional Residual Capacity

Upper Airway Area

Could Nasal EPAP Complement MAS?

1. Nasal EPAP therapy reduces AHI, ODI, arousals per hour and daytime sleepiness
2. MAS primarily widens retro-palatal region and nasal EPAP may widen the hypo-pharyngeal region
3. ~50% of patients on MAS therapy have incompletely resolved OSA

Could combination therapy of MAS with nasal and oral EPAP reduce OSA severity in these patients?

AHI with nasal EPAP

Oxygen Desaturation Index (ODI): number of >3% oxygen desaturations/hour of sleep

Apnoea-hypopnoea index (AHI): number of apnoic (≥90% airflow cessation) or hypopnoeic (>30% airflow cessation with arousal/≥3% oxygen desaturation) events/hour of sleep

Care of Prof Danny Eckert NeuRA
ORAL ePAP “Oventus ExVent™”

Controlling Mouth Breathing
IMPROVING UPPER AIRWAY PHYSIOLOGY

• Mouth breathing results from increased resistance in the nose and/or soft palate collapse
• Increased resistance leads to negative pressure swings that cause arousals and a switch to mouth breathing
• Mouth breathing leads to a highly unstable airway
• Oventus Airway Technology + controlled exhalation reduces negative pressure swings and AHI while simultaneously increasing internal pressure in the airway and/or maintaining stability during exhalation with or without nCPAP
• The valve at the front of the airway or “ExVent™” achieves this
Oventus Airway Technology + PEEP delivering low resistance inhalation and controlled exhalation

Soft Palate Collapses and a switch to device breathing occurs

Neg pressure swings reduced due to air being delivered through device airway and oropharyngeal airway, supported by PEEP

Increased nasal resistance

Low resistance inhalation and PEEP targeted to the oropharynx via $O_2$ ExVent and Oventus Airway
1. Nasal EPAP therapy reduces AHI, ODI, arousals per hour and daytime sleepiness
2. MAS primarily widens retro-palatal region and nasal EPAP may widen the hypo-pharyngeal region
3. ~50% of patients on MAS therapy have incompletely resolved OSA

Could combination therapy of MAS with nasal and oral EPAP reduce OSA severity in these patients?

Care of Prof Danny Eckert NeuRA
Sydney NeuRA Study – Effect of Oral EPAP on MAD + Oventus Airway Technology Treatment Failures (n=13)

- 69% of previous O₂Vent™ treatment failures improved their treatment outcome
- 44% of O₂Vent™ treatment failures achieved >50% AHI RDN
- 33% of previous O₂Vent™ treatment failures achieved AHI ≤ 10
- Appears to work well in patients with increased nasal resistance
- The increased nasal resistance may be working as a natural PEEP valve
Sydney NeuRA Study – Effect of Oro-nasal EPAP on MAD + Oventus Airway Technology Treatment Failures (n=13)

- Oro-nasal EPAP “ONEPAP”
- Titratable true PEEP valve delivering constant pressure on exhalation
- 54% of previous O₂Vent™ treatment failures achieve AHI ≤ 10 & >50% RDN
- 31% of previous treatment failures AHI ≤ 5
A True Titratable PEEP Valve vs “Flapper”

• “Flapper” has a linear flow-pressure curve
• The harder the patient exhales the higher the pressure ramps to
• This can cause discomfort and/or feelings of claustrophobia
• A true PEEP valve the maximum pressure can be set by adjusting the titration mechanism
• The curve flattens out at a certain pressure level even as flow increases.
Positional obstructive sleep apnoea (POSA), commonly defined as supine to non-supine apnoea/hypopnea index (AHI) ratio of ≥ 2).

Twenty patients with sdOSA

Sleep positional trainer (SPT) reduced the time spent in supine sleeping position compared to baseline and MAD therapy.

Both MAD and SPT were individually effective in reducing the overall apnea/hypopnea index (AHI) significantly when compared to baseline from 20.8 (15.1; 33.6)/h at baseline to 11.0 (6.7; 13.8)/h and to 11.1 (3.5; 17.7)/h with MAD or SPT, respectively.

The combination of SPT + MAD further reduced the overall AHI to 5.7 (3.6; 7.4), which was significantly lower than with MAD alone (p < 0.001) and SPT alone (p < 0.008), respectively.

NeuRA Nasal Resistance Study (n=7)

• **Results:** Awake nasal resistance tended to increase from seated, to supine, to lateral body positions (2.5±0.7, 3.6±1.2, 4.3±1.6 cmH₂O/ml/s, respectively).

• Mandibular advancement did not systematically alter nasal resistance in either the seated (3.1±0.9 cmH₂O/ml/s) or supine positions (4.7±2.1 cmH₂O/ml/s).

• Oral appliance therapy reduced the median supine non-REM AHI from 34.4 [5.1, 55.0] to 7.0 [3.1, 22.7] events/h sleep, p=0.03).
• CPAP pressure required to eliminate all obstructive events on the combination therapy was reduced from 9.4 ± 2.3 to 7.3 ± 1.4 cm H₂O (p = 0.001)

• The residual apnea hypopnea index on the MAD decreased from 11.2 ± 3.9 to 3.4 ± 1.5 on the combination therapy (p < 0.001).

• The number of oxygen desaturations was also less with the combination therapy than with MAD (p < 0.001)

• Both the MAD and the combination therapy were effective in reducing daytime sleepiness from 12.7 ± 2.1 at baseline to 9.7 ± 3.1 (p = 0.04) and 7.5 ± 4.1 (p = 0.007), respectively.

14 male patients were included.

The residual AHI and ODI on combination therapy (CT) was lower than that on MAD or PAP.

The residual % TST-SpO2<90% was lower than that on MAD and similar to that on PAP.

The therapeutic pressure on CT was on average 9.2 cm H2O lower than that on PAP 19cm H2O.

For the 11 patients who completed CT, only CT reduced ESS compared to pretreatment value.

No treatment had significant impact on % slow wave sleep or overnight change of blood pressure.

For patients who completed CT, the average usage was 5.9±1.7 hr/night at 12th week and 6.4±1.5 hr/night at a median follow-up of 36.5-months.

MAD + PAP

• 92 OSA patients aged 25 to 85 years (mean 55 years)
• Mean polysomnogram-determined diagnostic AHI value was 37.6 (standard deviation (sd): 25.9)
• Half (n=46) met the diagnostic threshold for severe OSA (AHI ≥30), a quarter (n=23) had moderate OSA (AHI 15–29.9), and the remainder (n=23) had mild OSA (AHI 5–14.9)
• 65 patients (70.7%) tolerated PAP/MAS therapy, having used it for 14.0 months on average (sd: 11.1)
• Tolerance was higher in patients with severe OSA (76.1%) than mild OSA (69.8%), this difference was not statistically significant (P = 0.421)
• Patients with severe OSA were more likely to have had the follow-up polysomnogram than those with mild OSA (P = 0.023)
• In these patients, AHI values decreased from an untreated mean of 48.0 (sd: 28.3) events/hour to a treated mean of 3.1 events/hour (sd: 3.8) (P < 0.001), indicating that, on average, PAP/MAS eliminated OSA.

http://www.sleepreviewmag.com/2015/03/dental-clinicians-observations-combination-therapy-pap-intolerant-patients/
Pilot Study $O_2$Vent™ T +/- PAP Connection

$O_2$Vent™ W AND OPTIMA™ + EXVENT™ +/- Nasal epap or cpap

- Reduced pressure requirements by 66%
- Simultaneous nCPAP delivery and physiologic mouth breathing
- Mask and strap free ultra low pressure PAP delivery

In Development - Launch 2019

Amatoury J, Tong B, Nguyen C, Szollosi I, Eckert DJ THE ROLE OF A NOVEL ORAL APPLIANCE THERAPY DEVICE ON PHARYNGEAL PRESSURE SWINGS AND CPAP REQUIREMENTS DURING SLEEP IN OBSTRUCTIVE SLEEP APNEA: A PILOT STUDY. Abstract Supplement AADSM Boston 2017
Oventus Airway Technology – Coming Soon….

O₂Vent™ Connect PAP Connection

- Nasal PAP delivers pressure and flow
- Controlled exhalation with easy inhalation allows mouth breathing while putting a floor under pharyngeal pressure
All of These Results Can Be Achieved From September

$O_2$ VENT™ W AND OPTIMA™ + EXVENT™ +/- NASAL EPAP OR CPAP
How Can we use the Oventus Treatment Platform to Enhance Patient Outcomes?

A Personalised Approach to Medicine

The Oventus Treatment Platform Cumulative Success*

- MAS 41% Treatment success\(^1\)
- Oventus O\(_2\)Vent\(^{TM}\) 54% Treatment success\(^1\)
- Oventus O\(_2\)Vent\(^{TM}\) + EPAP 78% Treatment Success\(^2\)
- Oventus O\(_2\)Vent\(^{TM}\) + Connect 100% Treatment Success\(^3\)


2. Victor Lai, Benjamin Tong, Carolin Tran, Andrea Ricciardiello, Michelle Donegan, Nicholas Murray, Jayne Carberry and Danny Eckert Combination therapy with mandibular advancement and expiratory positive airway pressure valves reduces OSA severity. Abstract Submitted Sleep DownUnder Brisbane 2018


*\(\text{AHI} \leq 10\) and >50% reduction
WHERE TO NEXT?
Fig. 2 Individual effects on tailored therapy on the severity of sleep-disordered breathing. Individual data comparing apnea-hypopnea index (AHI) and Epworth sleepiness scale (ESS) at baseline and post-tailored therapy. Changes following treatment with trazodone and acetazolamide are represented as solid line, those following treatment with acetazolamide, compression stockings, and hypocaloric diet are represented as dashed lines, and those following treatment with trazodone are represented with point dashed lines. Note as AHI was reduced in all but one subject. Means and standard deviations are represented by a white circle and vertical bars, respectively.
100% anatomical compromise (but of variable magnitude)

37% low arousal threshold

36% poor muscle responsiveness

36% unstable respiratory control (high loop gain)

MAD + Pharma

Combination therapy: Supplemental O$_2$ and a hypnotic (eszopiclone) reduces OSA Severity

Edwards et al, Sleep (2016)
Oventus Optima™
ExVent™ and ONEPAP™
Comprehensive Dental Sleep Treatment Platform

Designed specifically for Sleep Groups

- The Dental Sleep Program is comprehensive and will assist Sleep Groups to maximise patient outcomes by providing the systems, support, training and resources required to run a professional Dental Sleep Medicine clinic utilising Oventus’ proprietary airway technology and digital workflow
QUESTIONS?
THANK YOU