

# Nasopharyngoscopic evaluation of oral appliance therapy for obstructive sleep apnoea

A.S.L. Chan\*,\*\*,\*, R.W.W. Lee\*,\*\*,\*, V.K. Srinivasan\*, M.A. Darendeliler\*, R.R. Grunstein\* and P.A. Cistulli\*,\*\*,\*

ABSTRACT: This study aimed to explore the effect of mandibular advancement splints (MAS) on upper airway anatomy during wakefulness in obstructive sleep apnoea (OSA).

Patients commencing treatment for OSA with MAS were recruited. Response to treatment was defined by a  $\geqslant 50\%$  reduction in the apnoea/hypopnoea index. Nasopharyngoscopy was performed in the supine position.

Nasopharyngoscopy was performed in 18 responders and 17 nonresponders. Mandibular advancement caused an increase in the calibre of the velopharynx (mean $\pm$ sem +40 $\pm$ 10%), with relatively minor changes occurring in the oropharynx and hypopharynx. An increase in cross-sectional area of the velopharynx with mandibular advancement occurred to a greater extent in responders than nonresponders ( $\pm$ 56 $\pm$ 16% versus  $\pm$ 22 $\pm$ 13%; p<0.05). Upper airway collapse during the Müller manoeuvre, relative to the baseline cross-sectional area, was greater in nonresponders than responders in the velopharynx ( $\pm$ 94 $\pm$ 4% versus  $\pm$ 99%; p<0.01) and oropharynx ( $\pm$ 37 $\pm$ 6% versus  $\pm$ 16 $\pm$ 3%; p<0.01). When the Müller manoeuvre was performed with mandibular advancement, airway collapse was greater in nonresponders than responders in the velopharynx ( $\pm$ 80 $\pm$ 11% versus  $\pm$ 9 $\pm$ 37%; p<0.001), oropharynx ( $\pm$ 36 $\pm$ 6% versus  $\pm$ 20 $\pm$ 5%; p<0.05) and hypopharynx ( $\pm$ 64 $\pm$ 6% versus -42 $\pm$ 6%; p<0.05).

These results indicate that velopharyngeal calibre is modified by MAS treatment and this may be useful for predicting treatment response.

KEYWORDS: Mandibular advancement splints, nasopharyngoscopy, obstructive sleep apnoea

andibular advancement splints (MAS) are an alternative to continuous positive airway pressure (CPAP) for the treatment of obstructive sleep apnoea (OSA) [1]. Although CPAP is the treatment of choice for OSA, its obtrusive nature limits its clinical effectiveness. MAS are an efficacious treatment for OSA in 60–70% of patients [2]. They are a simpler form of treatment and are often considered by patients to be more acceptable compared to CPAP [3].

The clinical practice parameters of the American Academy of Sleep Medicine recommend the use of MAS for the treatment of mild-to-moderate OSA; or for patients with severe OSA who are unable to tolerate or refuse treatment with CPAP [4]. Treatment of OSA with MAS has been shown to have a beneficial impact on a number of important clinical end-points, including the polysomnographic indices of OSA [5, 6], subjective and objective measures of sleepiness [5–7], blood

pressure [8–11], aspects of neuropsychological functioning [8, 12] and quality of life [8].

MAS mechanically protrude the mandible with the aim of preventing collapse of the upper airway during sleep [1]. However, the mechanisms by which MAS improve OSA are not well understood and little is known about the effect of mandibular advancement on the anatomy of the upper airway. Nasopharyngoscopic assessment during wakefulness has been shown to be a useful approach to assessing the upper airway and may be able to predict the presence of OSA [13, 14] and response to other treatments, such as uvulopalatopharyngoplasty [15]. The primary aim of the present study was to evaluate the mechanism of action of MAS by assessing their effect on upper airway anatomy using nasopharyngoscopy performed during wakefulness in patients with OSA. As a secondary aim, the potential of this approach for identifying responders and nonresponders was also evaluated.

### ΔΕΕΙΙ ΙΔΤΙΩΝΙS

\*Centre for Sleep Health and Research, Dept of Respiratory Medicine, Royal North Shore Hospital, St Leonards, #Woolcock Institute of Medical Research, University of Sydney, \*Dept of Orthodontics, Faculty of Dentistry, Sydney Dental Hospital, University of Sydney, and \*Dept of Respiratory and Sleep Medicine, St George Hospital, University of New South Wales, Sydney, NSW, Australia.

CORRESPONDENCE
P.A. Cistulli
Centre for Sleep Health and Research
Dept of Respiratory Medicine
Royal North Shore Hospital
St Leonards
NSW 2065
Australia

E-mail: cistullip@med.usyd.edu.au

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European Respiratory Journal Print ISSN 0903-1936 Online ISSN 1399-3003 Preliminary results of this study have been previously reported in the form of abstracts [16–18].

# **METHODS**

# **Subjects**

Patients commencing treatment of OSA with a custom-made MAS were recruited from sleep disorders clinics at two university teaching hospitals: Royal North Shore Hospital (St Leonards, New South Wales, Australia) and St George Hospital (Kogarah, New South Wales). Recruitment aimed to include patients with a broad range of severity of OSA, representative of patients in sleep disorders clinics, so as to allow the comparison of nasopharyngoscopic findings in responders and nonresponders. The specific inclusion criteria were the presence of at least two symptoms of OSA (snoring, witnessed apnoeas, fragmented sleep or daytime sleepiness) and evidence of OSA on polysomnography (apnoea/ hypopnoea index (AHI)  $\geq 10$  events·h<sup>-1</sup>). Patients were excluded if they had periodontal disease, insufficient number of teeth or an exaggerated gag reflex. The study was approved by the institutional ethics committees of the Northern Sydney Central Coast Area Health Service (New South Wales), the Sydney South West Area Health Service (New South Wales), the University of Sydney (New South Wales), the South Eastern Sydney Illawarra Area Health Service (New South Wales), and the University of New South Wales (New South Wales). Written informed consent was obtained from all patients.

# MAS

A custom-made two-piece MAS was used (SomnoDent MAS; SomnoMed Ltd, Crows Nest, New South Wales, Australia), the design features and efficacy of which have previously been published [5, 6, 9, 19–21]. Acclimatisation occurred over a period of ~6–8 weeks. During this time, the appliance was incrementally titrated until the maximum comfortable limit of mandibular advancement was achieved.

# Polysomnography

Polysomnography, as previously described [6], was performed to confirm the diagnosis of OSA and to determine treatment outcome, and was scored according to standard criteria [22, 23]. Apnoeas were defined by a cessation of airflow for  $\geqslant 10$  s in association with oxygen desaturation of  $\geqslant 3\%$  or an arousal. Hypopnoeas were defined by a reduction in the amplitude of airflow, as measured using nasal pressure or thoraco-abdominal wall movement, by >50% of the baseline measurement for  $\geqslant 10$  s, in association with oxygen desaturation of  $\geqslant 3\%$  or an arousal.

# Treatment outcome

The definition of treatment outcome was based on the results of polysomnography, as previously described [5, 6, 21]. "Responders" were defined as patients with a reduction in AHI of  $\geqslant$ 50%; "nonresponders" were defined as patients with a reduction in AHI of <50%. This somewhat liberal definition reflects clinical practice, with patients often obtaining clinical benefit despite incomplete resolution of OSA.

# Nasopharyngoscopy

A video-endoscopy system (Olympus Medical Systems Corp., Tokyo, Japan) was used for nasopharyngoscopy. Nasopharyngoscopy was performed by a single operator after the completion of acclimatisation to treatment with MAS and the maximum comfortable limit of mandibular advancement was achieved. It was performed with patients in the supine position and the Frankfort plane perpendicular to horizontal. Prior to the procedure, patients were given instructions for the Müller manoeuvre and given time to practise the manoeuvre until they were comfortable performing it. For the Müller manoeuvre, patients were asked to perform a maximal inspiration against a closed airway. Following the administration of topical anaesthetic nasal spray (4% lignocaine), the nasopharyngoscope was inserted into the nose and pharynx. Digital images of the velopharynx, oropharynx and hypopharynx were obtained. For each of these segments, images were taken during tidal breathing and the Müller manoeuvre, both with and without mandibular advancement. In order to ensure consistent magnification, the position of the scope, marked at the nares, was maintained when obtaining images for a given airway segment. Visual monitoring during the procedure ensured that an orthogonal view was maintained and captured for subsequent analysis. Mandibular advancement was provided using the patients' custom-made MAS.

The segments of the upper airway were defined by anatomical landmarks. The velopharynx was defined by the level of the uvula, the oropharynx was defined by the base of the tongue and the hypopharynx was defined by the tip of the epiglottis. Video-editing software was used to capture frames from the digital video recording of the nasopharyngoscopy. Image analysis software (ImageJ; National Institutes of Health, Bethesda, MD, USA) was used to determine cross-sectional areas of the upper airway lumen. Airway measurements were made using nasopharyngoscopic images captured during quiet tidal breathing and during a maximal Müller manoeuvre, both with and without mandibular advancement. The cross-section of the airway was defined by a manual segmentation process to identify the edge of the airway lumen at specific anatomical landmarks. The quantitative analysis of nasopharyngoscopic images has previously been shown to be a useful approach in the evaluation of the upper airway [14], and we have previously shown (unpublished data) good intra-observer reproducibility using this technique (mean ± SD coefficient of variation  $3.6 \pm 1.3\%$ ) when making repeated measurements on the same nasopharyngoscopic images. Image analysis was performed without knowledge of the treatment outcome on polysomnography. For the purposes of assessing the association between nasopharyngoscopic findings and the treatment response on polysomnography, an increase in the crosssectional area of the lumen of the upper airway was based on any increase in the quantitative assessment of the crosssectional area on the nasopharyngoscopic images.

# Statistical analysis

Statistical analyses were performed using a statistical software package (SPSS 13.0 for Windows; SPSS, Inc., Chicago, IL, USA). Descriptive statistics for clinical characteristics of patients and cross-sectional areas of the upper airway lumen are presented as mean ±SD and mean ±SEM, respectively. Continuous variables were compared using an unpaired t-test or Mann–Whitney Utest, as appropriate. Categorical variables were compared using the Chi-squared test or the Fisher's exact test. Logistical regression analysis was performed using a forward step-wise procedure. Statistical significance was accepted if p<0.05.



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# **RESULTS**

# Clinical characteristics of patients

35 patients were recruited for this study. Of these patients, 18 were responders and 17 were nonresponders. There was no significant difference between responders and nonresponders in the degree of mandibular advancement (mean  $\pm$  SD  $5.8\pm2.2$  mm, representing 75% of maximum mandibular protrusion). In responders, treatment with MAS resulted in a reduction of AHI to  $6.8\pm7.9$  events  $\cdot h^{-1}$ , with 66.7% of patients achieving a complete response (reduction of AHI to <5 events  $\cdot h^{-1}$ ) and 33.3% achieving a partial response ( $\geqslant50\%$  reduction in AHI, but with residual AHI of  $\geqslant5$  events  $\cdot h^{-1}$ ). There were no significant differences between responders and nonresponders with respect to age, sex, body mass index or baseline AHI. The clinical characteristics of patients are shown in table 1.

# Nasopharyngoscopy

Nasopharyngoscopy was performed in all patients. The procedure was generally well tolerated, with no major complications. Imaging of the oropharynx and hypopharynx was not able to be completed in two patients due to exaggerated gag reflexes. A further patient did not have imaging of the oropharynx.

# **Changes in cross-sectional areas of upper airway lumen** *Mandibular advancement*

Mandibular advancement increased the velopharyngeal cross-sectional area in both responders and nonresponders (mean  $\pm$  sem  $\pm$  10%), with an increase in the lateral dimension of the velopharynx by  $\pm$  25  $\pm$  3% and an increase in the anteroposterior dimension of the velopharynx by  $\pm$  17  $\pm$  6%. However, the extent of the increase in the velopharyngeal cross-sectional area, relative to the baseline cross-sectional area, was significantly greater in responders than nonresponders. Relatively smaller increases in cross-sectional area were produced by mandibular advancement in the oropharynx ( $\pm$ 1.8  $\pm$ 3.1%) and hypopharynx ( $\pm$ 8.9  $\pm$ 7.1%), and there were no significant differences in the change in cross-sectional area with mandibular advancement between responders and nonresponders in these segments.

	treatment outcome		
	Responders#	Nonresponders <sup>¶</sup>	
Patients n	18	17	
Male %	77.8	82.4	
Age yrs	$53.7 \pm 11.9$	55.8 ± 10.1	
BMI kg·m <sup>-2</sup>	$29.3 \pm 4.7$	$31.0 \pm 4.6$	
Baseline AHI events h	-1 29.3 + 15.7	24.1 + 11.2	

TABLE 1 Clinical characteristics of nationts according to

Data are presented as mean $\pm$  sp, unless otherwise stated. BMI: body mass index; AHI: apnoea/hypopnoea index; MAS: mandibular advancement splints. "Responders" were defined as patients with a  $\geqslant$ 50% reduction in AHI; "Nonresponders" were defined as patients with a <50% reduction in AHI;

 $6.8 \pm 7.9$ 

66.7

# Müller manoeuvre

The Müller manoeuvre resulted in collapse of the velopharynx, oropharynx and hypopharynx in both responders and nonresponders. However, the extent of collapse, relative to the baseline cross-sectional area, was significantly greater in nonresponders than responders in the velopharynx and oropharynx. In the hypopharynx, there was no significant difference in the extent of collapse between responders and nonresponders.

# Müller manoeuvre with mandibular advancement

When the Müller manoeuvre was performed with mandibular advancement, the extent of collapse, relative to the baseline cross-sectional area, was significantly greater in nonresponders than responders in the velopharynx, oropharynx and hypopharynx.

The changes in the cross-sectional areas of the velopharynx, oropharynx and hypopharynx with the Müller manoeuvre and mandibular advancement are shown in figures 1, 2 and 3. Representative nasopharyngoscopic images of the velopharynx from a responder and nonresponder are shown in figures 4 and 5.

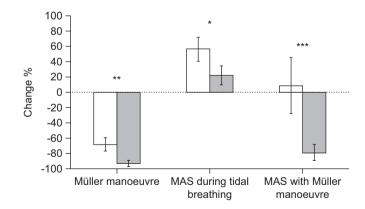
# Nasopharyngoscopic findings and treatment outcome

Increase in cross-sectional area of airway lumen with mandibular advancement

An increase in the velopharyngeal cross-sectional area with mandibular advancement was significantly associated with a treatment response on polysomnography (sensitivity 88.9%, specificity 47.1%, positive predictive value 64.0%, negative predictive value 80.0%; p<0.05). An increase in the cross-sectional area of the oropharynx or hypopharynx was not significantly associated with treatment outcome.

Increase in cross-sectional area of airway lumen during Müller manoeuvre with mandibular advancement

An increase in the cross-sectional area of the airway lumen when the Müller manoeuvre was performed with mandibular advancement (relative to when the Müller manoeuvre was performed without mandibular advancement) was associated with a treatment response on polysomnography for the velopharyngeal



**FIGURE 1.** The changes in cross-sectional area of the velopharynx with the Müller manoeuvre and mandibular advancement, relative to the baseline cross-sectional area. The bars and whiskers represent mean  $\pm$  sem, respectively. Responders ( $\square$ ): n=18; nonresponders ( $\square$ ): n=17. MAS: mandibular advancement splints. \*: p<0.05; \*\*: p<0.01; \*\*\*: p<0.001.

AHI with MAS events · h-1

Complete responders %+

 $26.8 \pm 23.9$ 

<sup>†: &</sup>quot;Complete responders" were defined as patients with a post-treatment AHI of <5 events·h<sup>-1</sup>.

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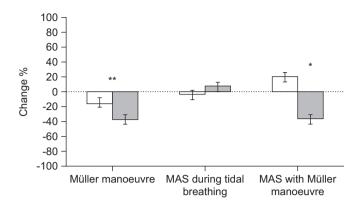


FIGURE 2. The changes in cross-sectional area of the oropharynx with the Müller manoeuvre and mandibular advancement, relative to the baseline cross-sectional area. The bars and whiskers represent mean±sem, respectively. Responders (□): n=15; nonresponders (□): n=17. MAS: mandibular advancement splints. \*: p<0.05; \*\*: p<0.01.

(sensitivity 83.3%, specificity 76.5%, positive predictive value 78.9%, negative predictive value 81.3%; p<0.001) and hypopharyngeal segments (sensitivity 58.8%, specificity 87.5%, positive predictive value 83.3%, negative predictive value 66.7%; p<0.01). An increase in the cross-sectional area of the oropharynx when the Müller manoeuvre was performed with mandibular advancement (relative to when the Müller manoeuvre was performed without mandibular advancement) was not significantly associated with treatment outcome.

The association between an increase in the cross-sectional area of the velopharynx when the Müller manoeuvre was performed with mandibular advancement (relative to when the Müller manoeuvre was performed without mandibular advancement) and the treatment response on polysomnography is shown in table 2. In responders, the mean increase in the velopharyngeal cross-sectional area, in absolute terms, when the Müller manoeuvre was performed with mandibular advancement (relative to when the Müller manoeuvre was performed without mandibular advancement) was mean ± SEM +77.8 ± 32.3%, compared to  $\pm 14.2 \pm 9.0\%$  in nonresponders (p<0.05). As shown in table 2, a relative increase of  $\geq 5\%$  in the velopharyngeal crosssectional area during the Müller manoeuvre with mandibular advancement (relative to when the Müller manoeuvre was performed without mandibular advancement) was observed in 83.3% of responders, compared to 23.5% of nonresponders.

# Logistic regression analysis

These nasopharyngoscopic findings were considered in a logistic regression analysis. This identified an increase in the cross-sectional area of the velopharynx when the Müller manoeuvre was performed with mandibular advancement (relative to when the Müller manoeuvre was performed without mandibular advancement) as a predictor of a treatment response on polysomnography (p<0.01). The inclusion of other nasopharyngoscopic findings did not significantly improve the prediction model.

Intra-observer reproducibility of nasopharyngoscopic findings As the velopharynx was shown to be of importance in the mechanism of action of mandibular advancement and as a

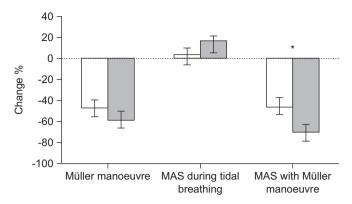
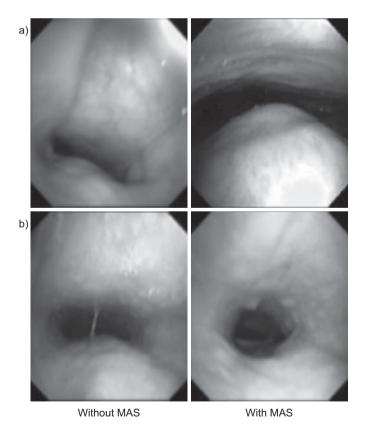


FIGURE 3. The changes in cross-sectional area of the hypopharynx with the Müller manoeuvre and mandibular advancement, relative to the baseline cross-sectional area. The bars and whiskers represent mean±sem, respectively. Responders (□): n=16; nonresponders (□): n=17. MAS: mandibular advancement splints. \*: p<0.05.

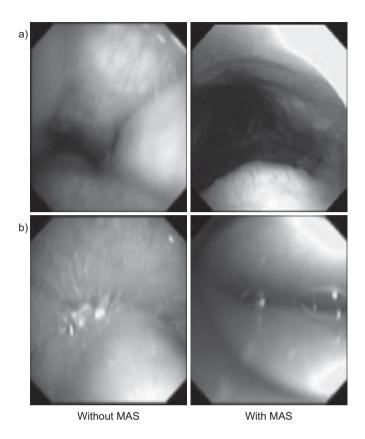
potential predictor of treatment outcome, the reproducibility of the nasopharyngoscopic evaluation of cross-sectional area of the velopharynx, during tidal breathing and the Müller manoeuvre, was assessed in a random subset of patients in this study (n=5) by assessing the variation of these measurements when repeated by the same operator. The reproducibility was very



**FIGURE 4.** Representative nasopharyngoscopic images of the velopharynx from a) a responder and b) a nonresponder during tidal breathing. In the responder, mandibular advancement can be seen to increase the calibre of the velopharynx. This effect does not occur in the nonresponder. MAS: mandibular advancement splints.



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**FIGURE 5.** Representative nasopharyngoscopic images of the velopharynx from a) a responder and b) a nonresponder during the Müller manoeuvre. In the responder, mandibular advancement improves the patency of the velopharynx during the Müller manoeuvre. In the nonresponder, there is persistent velopharyngeal collapse despite mandibular advancement. MAS: mandibular advancement splints.

good, with mean  $\pm$  SD coefficients of variation of  $7.6\pm2.1\%$  and  $5.3\pm5.8\%$  for measurements made during tidal breathing and the Müller manoeuvre, respectively.

# **DISCUSSION**

There has been increasing evidence to support the use of MAS for the treatment of OSA in clinical practice. Overall,  $\sim\!60\text{--}70\%$  of patients achieve a reduction of  $\geqslant\!50\%$  in AHI, with a reduction of AHI to  $<\!5$  events·h<sup>-1</sup> occurring in 35–40% of patients [5, 6]. Although less efficacious than CPAP for improving AHI, MAS are a simpler form of treatment and are often considered by patients to be a more acceptable treatment modality [24]. However, the mechanisms by which MAS improve OSA are not well understood and little is known about the actual effect of mandibular advancement on the anatomy of the upper airway.

The key findings of this study are that mandibular advancement causes an increase in the calibre of the velopharynx, with relatively minor changes occurring in the oropharynx and hypopharynx, and that nasopharyngoscopy performed during wakefulness is able to discern anatomical differences in the upper airway between those who respond to treatment with MAS and those who do not. The extent of collapse of the velopharynx and oropharynx during the Müller manoeuvre

TABLE 2

The association between an increase in the cross-sectional area of the velopharynx when the Müller manoeuvre was performed with mandibular advancement (relative to when the Müller manoeuvre was performed without mandibular advancement) and the treatment response on polysomnography

	Patients n	Increase#	No increase
Responders	18	15	3
Nonresponders	17	4	13

#: of ≥5% in relative terms.

was greater in nonresponders than responders. Mandibular advancement produced a greater degree of increase of the velopharyngeal calibre in responders than nonresponders. When the Müller manoeuvre was performed with mandibular advancement, the extent of collapse of the velopharynx, oropharynx and hypopharynx was greater in nonresponders than responders. The study cohort was typical of a population of OSA patients seen in a sleep disorders clinic, with a broad range of anthropomorphic characteristics and OSA severity, and thus, the results of this study are likely to have good generalisability.

The results of this study suggest that the velopharynx is an important site in the mechanism of action of MAS treatment, consistent with the findings of previous studies [25-27]. These studies, performed in both anaesthetised patients [27] and awake patients with OSA [25, 26], found that advancement of the mandible improved the patency of the velopharynx. The effect of mandibular advancement on the velopharyngeal closing pressure has also been shown to be important in achieving control of sleep-disordered breathing [28], and there have been studies indicating that the velopharyngeal segment may be relevant for the prediction of treatment outcome [26, 29]. All of this challenges the traditional notion that the mechanism of action of MAS is to mechanically advance the mandible and produce an increase in oropharyngeal dimensions. The precise reason for this effect on the velopharynx is unclear, but soft tissue structures within the palatoglossal and palatopharyngeal arches connect the mandible, tongue, lateral pharyngeal walls and soft palate. It has been proposed that such soft tissue connections may be stretched by mandibular advancement [30]. These structural changes are associated with a reduction in the collapsibility of the upper airway during sleep [31]. The importance of upper airway neuromuscular reflexes in the mechanism of action of MAS remains uncertain.

Given the anatomical basis of OSA [32], and the differences between responders and nonresponders observed in this study, upper airway imaging has the potential to be useful for predicting treatment outcome. Magnetic resonance imaging (MRI) of the upper airway has previously been used to show that the effect of mandibular advancement on the calibre of the upper airway differs between responders and nonresponders [26]. During the Müller manoeuvre, an improvement in upper airway patency on MRI with mandibular advancement was found to be associated with a successful treatment outcome,

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whereas persistence of upper airway collapse with mandibular advancement was associated with treatment failure [33]. Druginduced "sleep" nasopharyngoscopy has also been used to select patients whose airway patency improves with mandibular advancement for treatment with MAS [34]. The awake nasopharyngoscopic approach used in this study has more direct application to the clinical practice setting.

The standard clinical pathway for commencing treatment with MAS involves an initial medical assessment (including objective confirmation of OSA and its severity), followed by a dental assessment [1]. As not all patients achieve a successful outcome when treated with MAS, the development of a simple and clinically useful tool to predict which patients will respond would aid the appropriate selection of patients. Although there are a number of anthropomorphical, physiological, cephalometrical and polysomnographical parameters that have been associated with a better treatment outcome [6, 19, 21, 29, 35-38], there have been no prospective studies demonstrating the ability to predict the outcome of treatment using these parameters, either singly or in combination. A recent development has been the use of single-night titration of mandibular advancement during sleep to determine the polysomnographic response and the amount of mandibular advancement required to achieve a response [39, 40], but further studies are needed to assess its utility in clinical practice. Nasopharyngoscopy is widely available and easily performed, and could therefore be a useful prediction tool.

In order to have clinical utility, the nasopharyngoscopic findings needed to predict the outcome of treatment with MAS would have to be easily recognisable. In this study, an increase in the velopharyngeal calibre with mandibular advancement, and an increase in the velopharyngeal and hypopharyngeal calibre when the Müller manoeuvre was performed with mandibular advancement (relative to when the Müller manoeuvre was performed without mandibular advancement) were significantly associated with a treatment response on polysomnography. Although a segmentation process with quantification of cross-sectional areas was used to determine the changes in the airway lumen in this study, it is possible that these nasopharyngoscopic findings could be observed in clinical practice by qualitative assessment of crosssectional areas because of the magnitude of the changes. An increase in the velopharyngeal calibre when the Müller manoeuvre was performed with mandibular advancement appeared to have the best performance characteristics, with a positive predictive value of 78.9% and negative predictive value of 81.3%. This nasopharyngoscopic finding was identified as a predictor of a treatment response in the logistic regression analysis and the inclusion of other nasopharyngoscopic findings did not improve the prediction model. The intra-observer reproducibility of the nasopharyngoscopic assessment of velopharyngeal calibre, during tidal breathing and the Müller manoeuvre, was good.

There are a number of important limitations of this study. There was the potential for selection bias as patients commencing treatment of OSA with a custom-made MAS were recruited, rather than *de novo* patients with OSA. The higher proportion (48.6%) of nonresponders in this study proved useful for examining differences in nasopharyngoscopic findings. The

definition of treatment outcome, with response to MAS defined by a reduction in AHI of  $\geq 50\%$ , could be criticised for including those who only obtained a partial response. However, we intentionally used this definition because it reflects clinical practice, with patients often obtaining clinical benefit despite incomplete resolution of OSA. The custom-made MAS used in this study was of a single device design, which may limit the extent to which the results can be generalised to other devices. With regard to the nasopharyngoscopy, it is possible that the effect of the Müller manoeuvre could have varied as a result of differences in intraluminal pressure generated by patients. However, the complexity of measuring intraluminal pressure would be a barrier to the use of such a method in clinical practice, so we chose to evaluate a clinically useful method and were able to demonstrate good intra-observer reproducibility. The study was also performed during wakefulness and thus the effects of mandibular advancement observed in this study may not be identical to the changes that occur during sleep. Finally, before such a method can be translated to clinical practice, it needs to be validated in a prospective cohort. This is important as, in this study, mandibular advancement was provided using the custommade MAS. In a prospective study, nasopharyngoscopic prediction would need to be made prior to construction of the MAS. Furthermore, a prediction model would generally be expected to have less predictive value in a validation cohort compared to the original derivation cohort. It would also be important to clarify the effects of inter-observer variability, as a prediction tool that can only be performed by a single operator would not have clinical utility, and assess whether the predictive utility of nasopharyngoscopy can be improved by combining it with other methods, such as flow/volume curves [21].

In conclusion, this study indicates that velopharyngeal calibre is modified by MAS treatment, and that nasopharyngoscopy performed during wakefulness is able to identify anatomical differences in the upper airway between those who respond to treatment with MAS and those who do not. Such a method may have clinical utility in predicting the outcome of treatment of OSA with MAS, and improve the selection of patients for this treatment modality.

# **SUPPORT STATEMENT**

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# STATEMENT OF INTEREST

Statements of interest for M.A. Darendeliler, R.R. Grunstein and P.A. Cistulli, and for the study itself can be found at www.erj.ersjournals.com/misc/statements.dtl

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