Positive airway pressure in obesity hypoventilation syndrome: is it worth it?

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Over the past decade, increasing attention has been paid to the evaluation and management of obesity hypoventilation syndrome (OHS).[1] This disorder is characterised by daytime hypercapnia and three main phenotypes of sleep disordered breathing, including severe obstructive sleep apnoea (OSA), combined OSA and OHS and isolated OHS.[2] Rising rates of global obesity along with a greater awareness of the significant health and social costs of this disorder have been driving factors fuelling interest in how best to manage those with OHS. Although the cornerstone of treatment has been to address sleep breathing abnormalities using positive airway pressure (PAP) therapy, the mode of therapy which optimises outcomes in the most cost-effective manner has been less clear.[3–6]

In many centres, OHS has become a major indication for home ventilation, with most individuals prescribed bilevel therapy.[7] However, OHS can present as chronic respiratory failure as a consequence of OSA, OSA and OHS or lone OHS, with the OSA and OSA-OHS phenotypes accounting for more than 90% of individuals diagnosed with OHS, 70% of whom will have apnoea-hypopnea indices>30 events/hour.[4] Although continuous single level PAP therapy (CPAP) does not directly provide inspiratory assistance to increase tidal volumes, correction of upper airway obstruction in conjunction with increased resting lung volumes, resetting of the respiratory centres, reduced WOB and prevention of expiratory flow limitation[8] can improve gas exchange, alleviate symptoms and improve quality of life. Several medium-term randomised studies[3 5 6] and one long term randomised trial[9] comparing CPAP to bilevel therapy have failed to find significant differences between these therapies in terms of resolving waking chronic respiratory failure, improving quality of life, therapy adherence, incidence of new cardiovascular events or mortality in those individuals with OHS and coexistent OSA.[10] Evidence is limited, but a proportion of stable OHS patients treated initially with bilevel therapy can be stepped down to CPAP therapy, at least in the medium term, without compromising awake blood gases, quality of life or sleep quality,[11] although a number of patients will experience treatment failure following step-down from NIV and therefore require careful monitoring.[12]

With all of these data, a robust economic analysis evaluating the longer-term cost effectiveness of CPAP compared with bilevel therapy has been lacking. In this issue of Thorax, Masa and colleagues[13] provide a post hoc analysis of data obtained from the second stage of the Pickwick Project,[9] comparing the cost and cost effectiveness of bilevel therapy (spontaneous-timed mode with volume targeted pressure support) and CPAP over the longer term in the management of OHS with the specific phenotype of severe concomitant OSA. Two hundred and fifteen patients were enrolled initially in this trial, with data from 204 patients available for the cost effectiveness analysis. Using hospitalisation days/year as the primary outcome, the effectiveness of therapy slightly favoured bilevel therapy although this was then more than offset by the higher costs of bilevel devices compared with CPAP. As a consequence, the overall cost-effectiveness relationship favoured CPAP. Furthermore, this cost effectiveness relationship, whether expressed in hospitalisation days or in monetary terms, also favoured CPAP in both high and low adherence subgroups. Based on this and previous data showing bilevel therapy and CPAP provide similar outcomes in terms of clinical improvements as well as hospital resource utilisation,[9] and as CPAP is also more cost effective, CPAP should be considered first line treatment for stable ambulant OHS patients with severe OSA.

The notable strengths of this study include the large numbers of patients followed up over a significantly long period of time to capture a range of healthcare use. Additionally, there was no cross over of participants, and the therapies used are in line with accepted management of this patient group. Analysis of the data was also performed using different models including those related to therapy adherence and health-related quality of life, with all providing findings consistent with those produced by the primary cost effectiveness analysis. However, it is also important to note the limitations of the study, fully acknowledged by the authors. The study was powered for superiority of bilevel therapy above CPAP based on a mean hospital admission rate of 2.5 days per patient-year. The power calculation was based on a 20% treatment difference with a reduction of 0.5 hospitalisation days per patient year in the bilevel group. The observed overall mean hospitalisation days per patient-year was 1.5 days (1·4 days bilevel and 1·6 days CPAP). Clinical superiority would have been difficult to achieve as the event rate was lower than expected, with the change in the mean difference for the primary outcome falling within the 95% confidence intervals. The risk is of a sample size underpowered to fully address the question. Further, this was a post hoc analysis of data, which may have introduced some biases which were not accounted for. Since cost-effectiveness depends on the costs of both the equipment and those related to utilisation of healthcare services, this ratio may vary from one country to another, although it would still appear to favour CPAP. In addition, the cost effectiveness analysis was based on hospital resource use and there were limited data on outpatient and primary care resource utilisation with the economic consequence of work absence being disregarded.

There are considerable economic and practical consequences of these findings. Bilevel therapy is often commenced as long term therapy after a single night overnight PAP titration study showing 'failure' of CPAP to fully correct nocturnal gas exchange. A lack of data around the effectiveness of CPAP longer term no doubt has been a deterrent to the wider spread use of this less complex therapy in OHS with OSA. However, data provided by the Pickwick project now provides this evidence, demonstrating longer term outcomes are similar whether CPAP or bilevel therapy are used,[9] although with

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some improvements evolving a little more slowly in those managed with bilevel therapy over the first one or 2 months of treatment.[3 14] Since CPAP devices are considerably less expensive than those providing bilevel therapy, as well as being less complex to set up and titrate, access to treatment by OHS patients may be fast-tracked or enhanced by commencing with CPAP as initial therapy. Nevertheless, given there is individual variability in the response to PAP, it remains critical patients are monitored closely to ensure an appropriate response to therapy is achieved.[1]

Finally, more work is needed to identify specific characteristics of OHS patients with concurrent OSA who are most likely to fail CPAP in order to reduce healthcare costs and provide more focused therapy options. Indeed, comparison of data from Spanish trials with the data from the trials from the United Kingdom[5] and Australia[3 6] show a 10 $kg.m^{-2}$ difference in BMI in the enrolled patients, raising the question as to the difference in clinical effectiveness between CPAP and bilevel therapy in the obese and superobese cohorts. Perhaps a future target would be weight reduction[15] but until we have further trials we will need to address some of these questions with well-designed individual participant meta-analyses merging available randomised controlled trials.

Contributors All authors were involved in the writing, editing and reviewing the submitted work.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests AJP reports personal fees from ResMed, Philips and Sanofi Genzyme for lecturing; clinical advisory board membership for Philips on the management of COPD. JLP reports grants and personal fees from ResMed, Philips, Agiradom, Astra Zeneca, SEFAM; research support from Mutualia and Air Liquide Foundation; grants from Fisher and Paykel and Vitalaire; he has also received personal fees from JAZZ pharmaceuticals and ITAMAR. NH reports personal fees for lecturing from Philips, Resmed, Fisher-Paykel held by Guy's and St Thomas' Charity; unrestricted grants from Philips, Resmed and Fisher Paykel, with the funds held and managed by Guy's and St Thomas' NHS Foundation Trust; financial support from Philips for development of the MYOTRACE technology that has patent filed in Europe (US patent pending); membership of the Pulmonary Research Advisory Board for Philips with the funds for this role held by Guy's and St Thomas' NHS Foundation Trust; and is Joint Editor-in-Chief for Thorax.

Patient consent for publication Not required.

Provenance and peer review Commissioned; externally peer reviewed.

To cite Piper A, Pépin JL, Hart N. *Thorax* 2020;**75**:439–440.

Accepted 19 February 2020
Published Online First 26 March 2020

Linked

► http://dx.doi.org/10.1136/thoraxjnl-2019-213622

Thorax 2020;**75**:439–440.
doi:10.1136/thoraxjnl-2019-214403

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