risk relative to mPAP probably varies across different patient subgroups or by individual. We acknowledge that true threshold effects are uncommon in human disease and that future studies might further widen the mPAP continuum corresponding to clinical risk to even lower levels. Nonetheless, an important opportunity exists now to view pulmonary hypertension in clinically relevant terms.

In conclusion, the current standard for defining pulmonary hypertension excludes a sizeable population of at-risk patients who would be captured by adjusting the mPAP level defining pulmonary hypertension to 19 mm Hg or higher. In changing this definition, we would acknowledge the pathological implications of an mPAP of 19–24 mm Hg and appropriately increase awareness, clinical monitoring, and efforts to modify risk factors for these previously undiagnosed patients. We do not advocate for pulmonary vasodilator therapy in this population, because many of these patients might have pulmonary hypertension due to left heart disease or parenchymal lung disease. Rather, future clinical trials including this patient group are needed to clarify the true framework for specific treatment eligibility. Overall, updating the clinical definition of pulmonary hypertension to an mPAP of 19 mm Hg or higher is a fundamental and important step towards potentially reducing morbidity associated with this disease.

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Challenges in obstructive sleep apnoea

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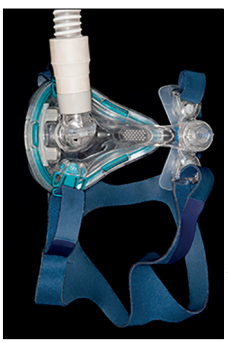
Obstructive sleep apnoea (OSA) is very common with a growing prevalence over the past two decades that at least partly reflects the rising prevalence of obesity.[1] OSA is traditionally diagnosed on the basis of frequency of sleep-disordered breathing events measured during overnight polysomnography, but this approach is poorly suited to the clinical evaluation of large at-risk populations. In addition, a large prospective randomised trial[2] cast doubt on previous evidence supporting beneficial effects of continuous positive airway pressure (CPAP) on cardiovascular outcomes. Considering these challenges, a conference was held in October 2016 in Baveno, Italy, where 19 European experts in OSA, selected from the Sleep-Disordered Breathing Group of the European Respiratory Society and from the European Sleep Research Society discussed current issues regarding the diagnosis and management of OSA, and identified future research priorities and potential new practices.

Four key questions were addressed. First, what constitutes clinically significant OSA syndrome? The widely accepted definition of OSA based on an apnoea-hypopnoea frequency (using the apnoea-hypopnopea index [AHI]) of greater than 5 during sleep associated with daytime symptoms such as excessive daytime sleepiness (EDS), should be reevaluated for several reasons. First, recent general population studies in Switzerland[3] and Iceland[4] indicate a prevalence of AHI greater than 15 in up to 50% of the adult male population. Second, EDS correlates poorly with AHI from sleep studies, undermining the clinical reliability of syndrome definition and severity grading based on these variables. Therefore, new approaches are required for the assessment of clinical significance, particularly due to increasing recognition of different clinical[5] and pathophysiological[6] OSA phenotypes. Furthermore, current OSA severity grading is based on polysomnography and is less reliable in ambulatory sleep studies that do not include sleep staging.[7]

Second, what is the best way to diagnose a clinically significant OSA syndrome? The gold standard for diagnosis by overnight polysomnography in a sleep laboratory is impractical for the routine investigation of OSA. New technologies with novel signal recordings such as peripheral arterial tonometry and non-contact sensor technology, in addition to novel evaluation of existing variables such as oximetry, capnometry, electrocardiography, and pulse-wave analysis, might provide alternative approaches for the ambulatory assessment of suspected OSA. Variables separate from sleep studies, such as biomarkers and a non-dipping nocturnal blood pressure pattern, could also provide information on clinical significance. However, many of these diagnostic approaches still require full evaluation.

Third, what role does OSA play in the development of comorbidities? OSA is associated with multiple comorbidities, especially cardiovascular and metabolic,[8] but the role of OSA as an independent risk factor is less clear. Although multiple basic mechanisms relating to OSA have been identified that might contribute to comorbidity, including sympathetic excitation, inflammation, and oxidative stress, in addition to metabolic and endothelial dysfunction,[9] the causal association of OSA in clinical comorbidity is not yet fully established. The evidence is strongest for some cardiovascular comorbidities such as hypertension and atrial fibrillation, but relatively weak for others such as cancer. Furthermore, recent negative studies regarding cardiovascular outcomes of CPAP therapy question the importance of OSA in the development of comorbidities.

Fourth, what are the changing indications for CPAP therapy? CPAP remains the most effective therapy for OSA but there are uncertainties regarding its use in selected patient populations, such as those with highly symptomatic mild OSA, and the possible benefits of CPAP to comorbidities. Initially, prospective observational studies demonstrated reduced cardiovascular morbidity and mortality with long-term CPAP therapy,[10] however, recent long-term randomised prospective studies have failed to confirm these findings. In particular, the recent SAVE trial[2] showed no benefit of CPAP in the secondary prevention of cardiovascular disease in non-sleepy patients with AHI greater than 15, although the findings were limited by poor CPAP compliance. Furthermore, benefits to glycaemic control in patients with OSA and comorbid diabetes mellitus following CPAP therapy remain uncertain.[11] Thus, while symptomatic benefits of CPAP in OSA are well established, further research is required to clarify benefits, if any, of CPAP in ameliorating comorbidity.



Dr P. Marazzi/SPL

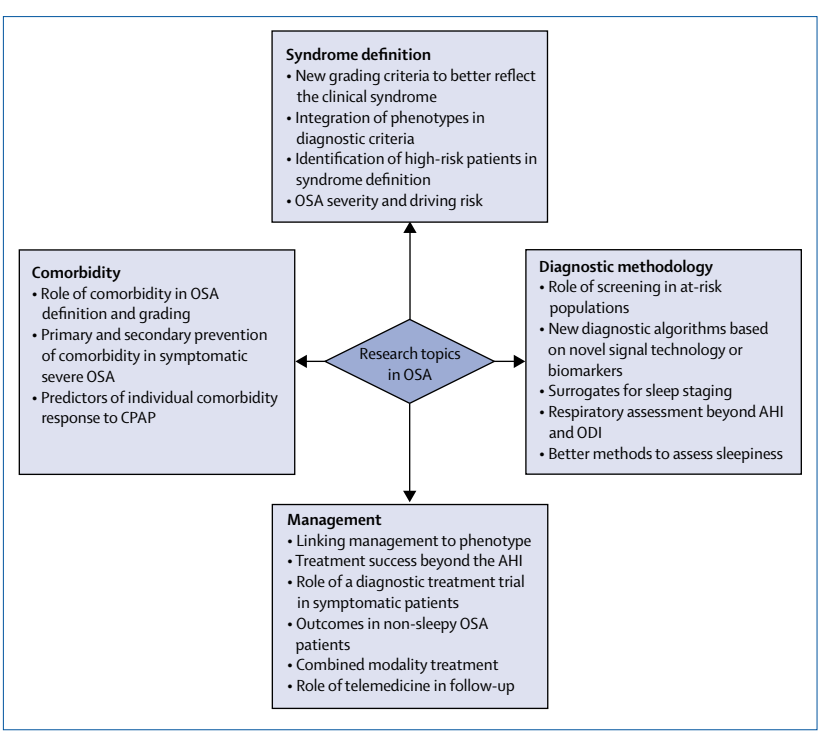


Figure: **Proposed topics for future research in obstructive sleep apnoea (OSA)**
AHI=apnoea-hypopnoea index. ODI=oxygen desaturation index. CPAP=continuous positive airway pressure.

These considerations indicate that major questions regarding OSA diagnosis and management remain unanswered (figure). New approaches to syndrome definition are required that consider different clinical phenotypes and the high general prevalence of sleep-disordered breathing. Certain comorbidities strongly associated with OSA could also be included in severity grading. New diagnostic approaches are required that incorporate novel technologies providing surrogates for sleep staging, respiratory evaluation other than AHI, and the role of biomarkers in disease classification.

Personalised patient management could be facilitated by linking treatment selection with clinical and pathophysiological phenotype, and by evaluation of treatment success beyond AHI, but these aspects require further validation. Finally, research is urgently required to evaluate possible benefits to cardiovascular outcomes in patients with severe symptomatic OSA compliant with CPAP, to address the limitations of the SAVE trial.[2]

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See appendix for full list of members

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Members of the Baveno Working Group are listed in the appendix.

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COPD exacerbations: transforming outcomes through research

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"Would you tell me, please, which way I ought to go from here?"

"That depends a good deal on where you want to get to."

L Carroll—Alice in Wonderland

The time has come for a revolution in the prevention and mitigation of COPD exacerbations. In the UK, national audit data demand urgent attention; admissions to hospital for COPD exacerbations rose by 13% between 2008 and 2014, to 115 000 per year.[1] In 2014,