Positive airway pressure therapy and all-cause and cardiovascular mortality in people with obstructive sleep apnoea

G Audley, MB ChB, Dip HIV Man (SA), FCP (SA), MMed

Pulmonology Fellow, Stellenbosch University and Tygerberg Academic Hospital.
ggaudley@gmail.com

Obstructive sleep apnea (OSA) is a highly prevalent condition worldwide and a major contributor to neurocognitive and cardiovascular disease.[1] It is well established that the mainstay of OSA treatment is positive airway pressure therapy (PAP), however, there has been a lack of robust data to conclusively establish its role in reducing mortality and morbidity.

A recent systematic review and metanalysis by Zhang and colleagues[2] which combined existing randomised controlled trials (RCTs), and confounder-adjusted non-randomised controlled trials (NRCTs), clearly showed the the benefits of PAP in reducing all-cause and cardiovascular mortality in OSA patients. The risk of all-cause mortality (HR 0·63, 95% CI 0·56–0·72; p<0·0001) and cardiovascular mortality (0·45, CI 0·29–0·72; p<0·0001) was significantly lower in the PAP group than in the no-PAP group. Furthermore, this clinical benefit increased with longer durations of PAP use.

Interestingly, this study demonstrates PAP's efficacy where previous research have largely failed to show a statistically significant benefit. When dissecting this study's findings, it becomes clear that to date there is a paucity of large RCTs that are adequately powered to demonstrate a statistically significant reduction in mortality metrics. Although the RCT arm of the study's metanalysis trended towards mortality benefit, it is only when the markedly larger NRCT arm is incorporated that the statistical benefit becomes clear. The use of confounder adjusted NRCTs (through propensity score matching a regression analysis) in this metanalysis by Zhang and colleagues is important for several reasons. Firstly, RCTs typically have smaller sample sizes and shorter follow-up durations compared with NRCTs, making them more likely to be underpowered for detecting mortality outcomes.This was clearly shown in the above-mentioned study where the metanalysis of RCTs only contributed 5-thousand patients while the NRCTs contributed over 1-million patients to the the all-cause mortality analysis. Secondly, the strict inclusion criteria in RCTs often exclude patients with complex comorbidities or severe OSA (largely due to ethical concerns of allocating a patient with severe disease to a placebo arm). NRCTs, however, would generally include a wider spectrum of OSA patients and thus provide a better 'real-world' perspective on the effects of PAP on OSA. Lastly, investigating the effects of PAP therapy is inherently challenging. Standardising adherence to PAP in a research setting is fraught with challenges which typically limit sample sizes in more rigorous RCTs. The markedly larger sample sizes of NRCTs likely diminishes the impact of this variability in adherence and allows for a more generalisable assessment.

This study convincingly demonstrates the benefit of PAPs in reducing all-cause and cardiovascular mortality in OSA. Whether these findings are generalisable to the South African context remains open for further research.

1. Benjafield A V, Ayas NT, Eastwood PR, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med 2019;7(8):687-698. https://doi.org/10.1016/s2213-2600(19)30198-5
2. Benjafield AV, Pepin JL, Cistulli PA, et al. Positive airway pressure therapy and all-cause and cardiovascular mortality in people with obstructive sleep apnoea: a systematic review and meta-analysis of randomised controlled trials and confounder-adjusted, non-randomised controlled studies. Lancet Respir Med 2025;13(5):403-413. https://doi.org/10.1016/s2213-2600(25)00002-5