

## RESEARCH LETTER

## Cardiovascular event rates in the MOSAIC trial: 2-year follow-up data

**Abstract** The Multicentre Obstructive Sleep Apnoea Intervention Cardiovascular (MOSAIC) trial investigated the effect of continuous positive airway pressure (CPAP) on both sleepiness and predicted cardiovascular risk over 6 months in minimally symptomatic patients with obstructive sleep apnoea. Although there was clear benefit in terms of Epworth Sleepiness Score, there was no improvement in blood pressure and predicted vascular risk score. In order to calculate the required size of future trials, with real vascular events as the endpoint, the rate of such events in this population is needed. 188 patients from the original trial were followed for 2 years. The overall number of new vascular events over the 2 years was 25, and all-cause mortality was 4. There was a weak statistically significant reduction in vascular events in the CPAP group ( $p=0.049$ ). Large-scale randomised trials are needed to determine if CPAP causes a real reduction in vascular events in minimally symptomatic patients. Based on our figures, future trials of CPAP versus no treatment would need to randomise approximately 2540 patients to not miss a real reduction in vascular events and over 6000 for mortality.

### INTRODUCTION

In a non-randomised trial, patients treated with continuous positive airway pressure (CPAP) for severe obstructive sleep apnoea (OSA) had fewer cardiovascular events than untreated severe OSA patients.<sup>1</sup> However, the MOSAIC randomised study of minimally symptomatic patients did not show a reduction in blood pressure or predicted 5-year cardiovascular risk score with CPAP<sup>2</sup>; although, in a subset, CPAP improved endothelial function.<sup>3</sup> In the full cohort of patients at 6 months, vascular event rates were lower than anticipated in both the CPAP and standard treatment arms. This may be in part due to increasing use of vascular risk reduction therapies. There is a need to establish the true vascular event rate in such patients, and thus the required size of future trials if they are not to miss a clinically relevant reduction in cardiovascular events.

### METHODS

The MOSAIC trial was a multicentre, randomised controlled parallel, hospital trial in patients with confirmed OSA (oxygen desaturation index  $>7.5$  h) but insufficient symptoms to warrant CPAP therapy. Patients were randomised to 6 months of auto-adjusting CPAP therapy or standard care. Patients from the Oxford cohort of the MOSAIC trial ( $n=188$ ) were subsequently followed over 2 years for new vascular events. Vascular events included a wide range of diagnoses (table 1) and the researcher (CT) verifying these events was blind to the treatment allocation. CPAP versus control comparison was based on intention to treat.

### RESULTS

Overall, there were 25 cardiovascular events over the 2 years of follow-up in the 188 patients. There was a weak statistically significant reduction in the rate of new vascular events in the CPAP group (8/94) compared with best medical care (17/94),  $p=0.049$ . There was no significant difference in any one single type of vascular event (table 1).

### DISCUSSION

Vascular events are a common cause of morbidity and mortality in all patients with OSA.<sup>4</sup> It is not known if CPAP reduces real vascular risk in minimally symptomatic patients. Our research has shown a weak statistically significant reduction in cardiovascular events, a tertiary outcome in the MOSAIC trial and

thus not definitive. Further research is needed to see if there is a benefit in terms of real cardiovascular risk for this group of patients. In terms of the size of a future study, to ensure not missing a relative risk reduction of 30% (absolute risk reduction of 4%) in vascular events, with a power of 90%, one would need to randomise 2540 patients to CPAP versus no therapy, over 2 years follow-up. This bodes well for large-scale trials currently being conducted, such as the SAVE study in patients with OSA and an already high vascular risk.<sup>5</sup> However, over 6000 would need randomising if mortality was the endpoint.

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**Table 1** Vascular events by type

	No CPAP	CPAP	Total
Cardiovascular death	2	1	3
Angina	1	1	2
Hypertension	1	2	3
Myocardial infarction	0	2	2
Diabetes mellitus	4	1	5
Peripheral vascular disease	0	0	0
Atrial fibrillation	2	0	2
Transient ischaemic attack	1	0	1
Stroke	1	0	1
Coronary angioplasty	1	0	1
Coronary stent	2	1	3
Coronary artery bypass graft	1	0	1
Endarterectomy	1	0	1
Total	17	8	25
All-cause mortality	3	1	4

Standard care compared with CPAP.  
CPAP, continuous positive airway pressure.

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