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Hypoxic burden captures sleep apnoea-specific nocturnal hypoxaemia

Ali Azarbarzin *, Scott A. Sands, Luigi Taranto-Montemurro, Susan Redline, and Andrew Wellman

Division of Sleep and Circadian Disorders, Brigham and Women's Hospital and Harvard Medical School, 221 Longwood Avenue, Boston, MA 02115, USA

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This commentary refers to 'How to assess nocturnal hypoxaemic burden in Cardiology?', by D. Linz and M. Baumert, on page 2988.

We thank Drs Linz and Baumert[1] for their comments on the importance of our study[2] and for emphasizing the need for using better metrics than the apnoea–hypopnoea index to capture the cardiovascular risks of obstructive sleep apnoea (OSA). The main objective of our article[2] was to develop an 'OSA-specific' metric that can be easily quantified in clinical settings and cross-validated in independent cohorts. Our study applied rigorous statistical models to examine the ability of the OSA-specific hypoxic burden to predict mortality beyond conventional polysomnography parameters.

There are a growing list of candidate metrics to predict OSA outcomes, including the recent paper by Baumert *et al.*[3] The hypoxic burden, presented in our article,[2] was designed to capture the OSA-specific nocturnal burden, whereas T90-related metrics, including the hypoxaemic burden developed by Baumert *et al.*,[3] are not OSA-specific but will vary in response to varied exposures (such as from chronic obstructive pulmonary disease or obesity hypoventilation) that may be unrelated to upper airway obstruction and OSA.

Indeed, if the goal was only to predict cardiovascular outcomes, metrics such as circulatory time could potentially be stronger candidates.[4] However, these metrics, including those related to T90, do not provide direct information on the targets for OSA treatment (e.g. continuous positive airway pressure), which mostly address episodic airway obstruction. Additionally, T90-related measures depend on somewhat arbitrary absolute thresholds (e.g. 90%), which may not apply across populations. Indeed, we found that SpO_2 values $\leq$90% are rare in women and T93, not T90, predicted mortality in women.[5]

In addition, in contrast to Baumert *et al.*[3] findings, we were unable to find a significant association between T90 and CV mortality in the MrOS study[2] [possibly due to different cardiovascular mortality event data used; our analysis relied on a sample with larger number of adjudicated CV events (440 vs. 185)] which led us to consider that the OSA-specific hypoxic burden was more informative than the T90 in this respect. We also disagree with the notion that to quantify the hypoxic burden, comprehensive sleep studies are required. Indeed, in our current algorithm, only the airflow and SpO_2 signals are required, and these signals are available in the home sleep apnoea testing devices and sleep laboratories, underscoring the clinical relevance of our work.

Conflict of interest: A.A. receives grants from American Heart Association, American Academy of Sleep Medicine, and Somnifix and serves as consultant for Somnifix and Apnimed outside this study. S.A.S. receives personal fees as a consultant for Cambridge Sound Management, Nox Medical and Merck outside the submitted work. L.T.-M. reports personal fees from Novion Pharmaceuticals, personal fees from Cambridge Sound Management, outside the submitted work; reports personal fees from Cambridge Sound Management, personal fees from Apnimed, outside this work. He has also a financial interest in Apnimed, Inc., a company developing pharmacologic therapies for sleep apnoea. S.R. reports grants from NIH, during the conduct of the study; grants from Jazz Pharma, grants from Beckman Coulter, outside the submitted work. A.W. works as a consultant for Somnifix, Cambridge Sound Management, Nox, Bayer, Philips, Apnimed, Inspire, and Galvani, and has received grants from Somnifix and Sanofi. He also has a financial interest in Apnimed Corp., a company developing pharmacologic therapies for sleep apnoea. A.W.'s and L.T.-M.'s interests were reviewed and are managed by Brigham and Women's Hospital and Partners HealthCare in accordance with their conflict of interest policies.

* Corresponding author. Tel: +16177325619, Email: aazarbarzin@bwh.harvard.edu

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