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# Sleep apnea in the general population

Phenotype, risk factors, burden  
of disease and sex-differences

Fré Bauters

Thesis submitted to fulfill the requirements for the degree of  
Doctor in Medical Sciences

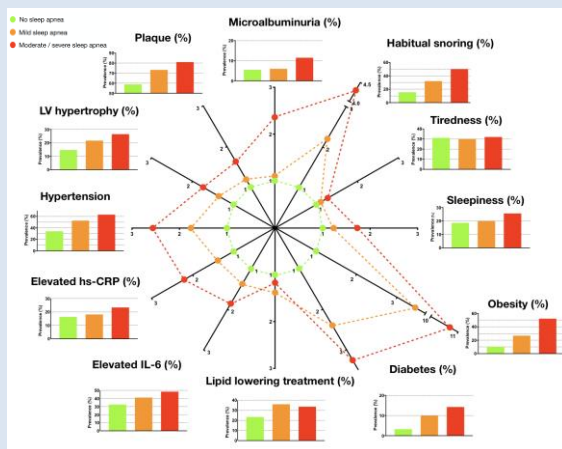
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## Introduction

Sleep apnea is a sleep-related breathing disorder with a high occurrence in the general population. The apnea/hypopnea-index (AHI) is the conventional measure for sleep apnea diagnosis and severity classification. The most important risk factors are obesity, increasing age and male sex. There is a strong, independent relationship of moderate to severe sleep apnea with hypertension and other cardiovascular diseases. However, the clinical presentation and cardiovascular risk are highly variable amongst sleep apnea patients. Susceptibility is not just explained by the AHI, and it remains unclear which subtypes are more susceptible for worse outcome. Particularly the group with mild sleep apnea may have important public health implications, because of the large size of the group and the opportunity for early interventions.

## Phenotype and risk factor burden

In the Asklepios study, a community-based Belgian cohort study including more than 2000 participants, we examined the prevalence and the phenotype of sleep apnea, as well as its cardiovascular risk correlates, through extensive clinical and cardiovascular assessment combined with home sleep recordings. We showed that mild sleep apnea is a distinct phenotype in the general population, demonstrating a higher cardiovascular, inflammatory and metabolic risk profile compared to those without sleep apnea. Adjustment for obesity resulted in a marked, but partial attenuation of the observed effects of sleep apnea on markers of cardiovascular damage/risk.



## Screening questionnaires

We demonstrated that the diagnostic performance of two well-known screening tests, NoSAS and the STOP-Bang, have an acceptable sensitivity in men, however, in women the low sensitivities make them not useful for screening. The potential of these screening tests can be optimized using sex-specific cut-offs resulting in an important increase of the sensitivity in women. The diagnostic performance indices of sleep questionnaires should be evaluated and reported in a sex-stratified fashion, as results from mixed-sex populations can overestimate test performance in each sex. These findings are novel, clinically relevant and should impact clinical practice and our understanding about the best application of the screening questionnaires, especially in women.

## Sex-differences in susceptibility for hypertension

We examined the sex-related differences in the relationship between hypertension, blood pressure and sleep apnea. We demonstrated an age-adjusted graded association of higher blood pressure and hypertension rate with increasing AHI in both sexes, even within the normal range of AHI. These associations were present at a distinctly lower AHI in women compared to men. Additional adjusting for obesity attenuated the associations, especially in men. The graded associations were dissimilar between men and women, suggesting different susceptibility.

## Future perspectives

Upcoming research should be performed in a sex-stratified manner. Addressing this research gap and achieving a better understanding of sex differences could allow to move towards a more precise and personalized management of women and men with sleep apnea, and could improve decision-making from a public health perspective.



## Curriculum vitae

Fré Bauters obtained her Master degree in Medicine at Ghent University (summa cum laude) in 2001. Subsequently, she had her training in Internal Medicine and in Respiratory Medicine. Since 2008, she works as a Pulmonologist and staff member at Ghent University Hospital, Belgium, with a focus on sleep-related breathing disorders. Since 2011, she works as a co-investigator at the Asklepios project.



## Main publications

Sex differences in the association between arterial hypertension, blood pressure and sleep apnea in the general population. [Bauters FA](#), Hertegonne KB, Pevernagie D, De Buyzere M, Chirinos JA, Rietzschel ER  
*Journal of Clinical Sleep Medicine*. 2021;17:1057-1066

Sex-specific sleep apnea screening questionnaires: closing the performance gap in women. [Bauters FA](#), Loof S, Hertegonne KB, Chirinos JA, De Buyzere ML, Rietzschel ER  
*Sleep Medicine*.2020;67:91-98

Phenotype and risk burden of sleep apnea: a population-based cohort study. [Bauters FA](#), Hertegonne KB, De Buyzere ML, Joos GF, Chirinos JA, Rietzschel ER  
*Hypertension*. 2019; 74(4):1052-1062

The Link Between Obstructive Sleep Apnea and Cardiovascular Disease. [Bauters F](#), Rietzschel ER, Hertegonne KB, Chirinos JA  
*Current Atherosclerosis Reports*.2016;18(1):1