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Original Article

Obstructive sleep apnea and road traffic accidents: a Danish nationwide cohort study

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ABSTRACT

Study objectives: In this nationwide study, we investigate the risk and severity of all road traffic accidents in patients with obstructive sleep apnea (OSA).
Methods: We used the unique Danish registries to identify all Danish citizens receiving a diagnosis of OSA between 1995 and 2015. As a reference cohort, we randomly selected 10 sex- and age-matched citizens for each patient. We used Poisson regression to calculate the incidens rate ratio (IRR) for all road traffic accidents (motor vehicle, bicycle, and pedestrian) in both groups, and Cox proportional regression analysis to compare risk of first motor vehicle accident. Lastly, we used Fischers' Exact test to compare severity of motor vehicle accident between the two groups-
Results: We identified 48,168 patients with OSA, covering up to 24 years of follow-up. Patients with OSA had an increased risk of road traffic accidents when compared with the reference cohort (hazard ratio, 1.15; 95% CI, 1.10–1.20; IRR: 1.19; 95% CI, 1.14–1.29), especially motor vehicle accidents (hazard ratio, 1.29; 95% CI, 1.18–1.39; IRR 1.30; 95% CI, 1.20–1.42). The risk of accidents as pedestrian or bicyclist were not increased. Further, patients with OSA had a tendency to be involved in more severe motor vehicle accidents.
Conclusions: This is the first nationwide study to estimate the risk of all road traffic accidents in patients with OSA. Our estimates show that patients with OSA have an increased risk of motor vehicle accidents, and greater severity of accidents, when compared with a large reference cohort.

1. Introduction

Obstructive sleep apnea (OSA) is a common chronic disease, affecting approximately 25% of adults in the US, with similar incidences in other western countries [1–3]. The disease is characterized by recurrent partial or complete upper airway obstruction during sleep. This reduce or abolish airflow, leading to hypoxemia, sleep fragmentation, excessive daytime sleepiness, slow cognitive processing, and impaired reaction time [4–6]. The reported delays in both cognitive processing and reaction time have been linked to motor vehicle accidents [7,8].

Patients with OSA are often reported as having an increased risk of motor vehicle accidents and near-misses events in a motor vehicle, with most studies reporting data on professional drivers [9–16]. Indeed, a recent cohort study by Pocobelli et al. reported a moderate increased risk of motor vehicle accidents of 17 percent in patients with OSA from the north-western United States, whereas a study from 2009 by Tregear et al. found a relative risk of 2.4 when comparing patients with OSA with drivers without OSA [12,17]. In a timespan of two years, patients with a high risk of OSA had an prevalence of falling asleep while driving of 37 percent with 10 percent resulting in motor vehicle accident [18]. In contrast, these numbers were 17 percent and 7 percent in the general population. The correlation between OSA and motor vehicle accidents is believed to be multifactorial, as excessive daytime sleepiness, inattention, diminished alertness, and patients with OSA falling asleep while driving have been described [18–21].

There remains little doubt in the literature, that patients with OSA have an increased risk of motor vehicle accident. Nonetheless, the level of the actual true increased risk is still debatable, as novel

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studies reports a lower risk compared to studies from previous decades. No nationwide studies have ever estimated the risk and incidence rate of motor vehicle accident in patients with OSA, or compared the risk to a large reference cohort. Additionally, few good-quality epidemiological studies exist, and the incidence of other road traffic accidents remains largely unknown [16].

In this study, we used the unique Danish registers to estimate the risk of all road traffic accidents (including motor vehicle accident, bicycle, pedestrian), and examine the severity of accidents in a nationwide cohort of patients with OSA compared to a large reference cohort covering up to 24 years of follow-up.

2. Materials and methods

This study was approved by The Central Denmark Region Research Committee (1-16- 02- 558- 20). The requirement for informed consent was waived given the nature of the study.

2.1. Study population

We used several medical registries in this nationwide descriptive cohort study. Registration and collection of data from all hospitals and outpatient clinics in Denmark is mandatory, with linkage of different registers made possible by the use of the unique personal identification number, the civil registration number, assigned to all Danish individuals at birth or immigration [22]. The Danish healthcare system is publicly financed, with equal accessibility for all registered Danish residents. We used the Danish National Patient Registry (DNPR) to identify all Danish citizens older than 15 year of age receiving a diagnosis of OSA between 1995 and 2005 [23]. The DNPR contains information on all hospital admissions in Denmark, dates of admission and discharge, surgical procedures, and discharge diagnoses coded according to the International Classification of Diseases, 10th Revision (ICD-10). To identify patients with OSA, we used the ICD-10 codes DG473 and DG4732. To identify patients with OSA treated with continuous positive airway pressure (CPAP) we used the code ZZ3915. As adjusting covariates, we used Denmarks Statistics to get information on Socio-Economic Classification from The Employment Classification Module for both patients with OSA and the comparison cohort based on information on the main source of income and employment for each individual.

A random reference sample matched by sex and birth year with the included patients with OSA was drawn using the Danish Civil Registration System, ensuring a ratio of 10 citizens per patient. To eliminate the risk of immortal time bias, date of diagnosis was used as the date of matching between patients with sleep apnea and their references.

2.2. Assessment of road traffic accidents

We linked the study population with the Danish Road Traffic Accidents Register using the civil registration number. The data source is police reports on traffic accidents resulting in personal injuries. This register contains information on road traffic accidents in Denmark from 1993 through 2019. The register includes all traffic accidents resulting in personal injuries that come to the attention of the police, including minor injuries, serious injuries, and fatal accidents. It contains information on several aspects of the road traffic accidents, eq. type of traffic accident (motor vehicle, bicycle or pedestrian) and severity of accident. We only included motor vehicle accidents where the subject was the actual driver.

2.3. Statistical analysis

Continuous variables were reported as mean and SD. Comparisons of means were performed by unpaired t test. Categorical variables were summarized by percentages or frequencies. Comparisons of categorical baseline characteristics between patients and the reference cohort were performed by Fisher's exact test. We followed patients with OSA from their first hospital contact, inpatient or outpatient, until death or December 31, 2020 (whichever came first). Comparisons of incidences of first episode of road traffic accident between patients with OSA and their matched references were performed by Cox regression with age as time scale. In each matching cluster, individuals entered the risk set at the age of diagnosis of the patient with OSA. SEs were calculated taking matching clusters into account. Through the matching and choice of time scale, the analyses are adjusted for sex, attained age, and birth year. Furthermore, we adjusted for socioeconomic status. We used Poisson regression to calculate the incidence rate ratio for all road traffic accidents (as one person can commit multiple events) in patients with OSA and the reference cohort with same adjustments as Cox regression. To evaluate the influence of comorbidities on our estimates, we conducted a sensitivity analysis adjusting for diabetes mellitus, hypertension, and cerebrovascular events. In sub-analyses, we compared patients with OSA treated with CPAP with their matched references. Comparison between patients with OSA treated with and without CPAP were additionally adjusted for age at diagnosis, calendar time (in order to accommodate for any differences in usage of CPAP over time), and sex. Finally, we made a sub-analysis investigating severity of motor vehicle accidents regardless of time of diagnosis. All analyses were performed using Stata 16 (StataCorp LP, TX).

3. Results

We identified 48,168 patients with OSA (mean age, 64 years; 78% male) diagnosed between 1995 and 2015 in Denmark. Baseline characteristics are presented in Table 1.

A total of 7.009 patients had died, with a median age of death of 69 years. Mean follow-up was 12.5 years, with a maximum follow-up of 24 years. The reference cohort was composed of 481,680 individuals from the general population (mean age, 64 years; 78% male).

3.1. Risk of road traffic accidents

We found 841 events of road traffic accidents among patients with OSA, and 6413 events in the reference group between 1995 and 2015 in Denmark, see Table 2.

The majority of events were motor vehicle accidents, followed by bicycle accidents and pedestrians. Motor vehicle accidents were more frequently occurring among patients, whereas more references were involved in accidents as a pedestrian. For patients with OSA, the overall risk of road traffic accidents was increased when compared with the reference group (hazard ratio, 1.15; 95% CI, 1.10–1.20 and IRR: 1.19; 95% CI, 1.14–1.29) (Table 3).

The risk was higher when only investigating motor vehicle accidents (hazard ratio, 1.29; 95% CI, 1.18–1.39 and IRR 1.30; 95% CI, 1.20–1.42), whereas the risk of bicycle accidents was lower in patients with OSA. The risk of accidents as pedestrians did not significantly differ between patients with OSA and the reference cohort. When adjusting for diabetes mellitus, hypertension, and cerebrovascular events in our model, a decrease in our estimates were observed compared to our primary analysis.

3.2. Severity of motor vehicle accidents

There were no significant differences in fatal motor vehicle accidents when comparing patients with OSA with the reference cohort, see Table 4.

Table 1
Characteristics of patients with OSA and matched references.

Variable	Cases n = 48,168	References n = 481,680	p-value
Age, year, mean (SD)	64.2 (13)	64.2 (13)	0.9681
Sex, male (%)	77.7	77.7	–
Age at diagnosis, years, mean (SD)	53,5 (12.9)	–	–
Follow-up, y (min–max)	12.5 (4–24)	–	–
CPAP, n (%)	12,875 (26.7)	–	–
Dead, n (%)	7009 (14.6)	64,515 (13.4)	
Age at death, years, mean (SD)	69.4(11.3)	70 (10.7)	
Socioeconomic status			
Owner of business or employee with high income, n (%)	4870 (10.1)	64,654 (13.4)	<0.0001
Employee with middle or low income, n (%)	12,901 (26.8)	129,499 (26.9)	0.635
Unemployed, social benefits, students or pensioners, n (%)	28,887 (60.0)	255,164 (53.0)	<0.0001
Other, n (%)	1326 (2,8)	30,077 (6.2)	<0.0001
Missing, n (%)	184 (0.4)	2286 (0.5)	0.004
Comorbidity			
Diabetes Mellitus, n (%)	5748 (11.9)	22,172 (4.6)	<0.0001
Hypertension, n (%)	5913 (12.3)	26, 284 (5.5)	<0.0001
Cerebrovascular events, n (%)	3736 (7.8)	26,165 (5.4)	<0.0001

CPAP = Continuous Positive Airway Pressure.

Table 2
Overview of road traffic accidents and characteristics of motor vehicle accidents.

Variable	Cases n = 48,168	References n = 481,680	p-value
Road traffic accident, n (%)	841 (1.73)	6413 (1.32)	<0.0001
Motor Vehicle, n (%)	673 (1.4)	4737 (0.98)	<0.0001
Bicycle, n (%)	116 (0.24)	1278 (0.26)	0.328
Pedestrian, n (%)	48 (0.1)	345 (0.07)	0.035
Motor Vehicle Accidents	**Cases n=673**	**References n=4737**	**p-value**
Age, mean (SD)	63.4 (13.2)	63.5 (12.4)	0.717
Age at diagnosis, years, mean (SD)	49,1 (12.8)	–	–
Sex, male (%)	91.5	90.0	0.214
Alcohol intoxicated, n (%)[a]	38 (5.7)	302 (6.4)	0.498
No seatbelt or helmet, n (%)	42 (6.2)	253 (5.3)	0.319

[a] Above 0.049% blood alcohol concentration.

Table 3
Risk of road traffic accidents in patients with OSA compared with matched references.

Variable	No. Of cases	IRR	HR	Sensitivity analysis: IRR[a]	Sensitivity analysis: HR[a]
Road traffic accident	841	1.19 (1.14–1.29)	1.15 (1.10–1.20)	1.16 (1.07–1.24)	1.08 (1.01–1.17)
Motor Vehicle	673	1.30 (1.20–1.42)	1.29 (1.18–1.39)	1.26 (1.16–1.37)	1.20 (1.10–1.30)
Bicycle	116	0.81 (0.67–0.98)	0.85 (0.77–0.95)	0.81 (0.66–0.98)	0.73 (0.59–0.91)
Pedestrian	48	1.21 (0.89–1.65)	1.14 (0.83–1.55)	1.14 (0.84–1.55)	0.97 (0.67–1.36)

HR = Hazard ratio. IRR = Incidence rate ratio.
[a] Adjusted for covariates from the primary analysis and three additional covariates: diabetes mellitus, hypertension, and cerebrovascular events.

The occurrence of severe motor vehicle accidents was higher among patients with OSA compared with the reference cohort, however, the difference was not significant. Correspondently, significantly more references were left unharmed following their accident. When including events prior to the OSA diagnosis, patients with OSA would have a significantly higher occurrence of both mild and severe accidents.

Table 4
Accident severity of motor vehicle accidents.

Outcome	Cases n = 673	References n = 4737	p-value
Dead, n (%)	21 (3.12)	148 (3.12)	0.989
Severe, n (%)	126 (18.72)	791 (16.7)	0.188
Minor, n (%)	117 (17.38)	711 (15.1)	0.109
Unharmed, n (%)	409 (60.8)	3087 (65.17)	0.028

3.3. Risk of motor vehicle accidents in patients treated with CPAP

The baseline characteristics of patients with OSA treated with CPAP and their matched references did not differ, see Table 5.

We found a total of 113 events among patients treated with CPAP and 819 events in the reference cohort. The risk of motor vehicle accidents was significantly higher in patients when compared to the references (hazard ratio, 1.35; 95% CI, 1.10–1.66 and IRR 1.29; 95% CI, 1.06–1.58). Baseline characteristics and comparison between patients with OSA treated with CPAP and patients with OSA treated without CPAP is shown in Table 6.

The prevalence of motor vehicle accidents was substantially lower in patient treated with CPAP, and the incidence rate ratios were significantly decreased. The hazard ratio of motor vehicle accident was comparable between the two groups.

Table 5
Characteristics of patients with OSA treated with CPAP and the risk of motor vehicle accidents in patients with OSA treated with CPAP compared with matched references.

Variable	CPAP n = 12,875	References n = 128,750	P-value
Sex, male (%)	78.3	78.3	–
Age, year, mean (SD)	62.7 (12.7)	62.7 (12.7)	0.890
Age at diagnosis, year, mean (SD)	55.4 (12.5)	–	–
Motor vehicle accidents, n (%)	113 (0.88)	819 (0.64)	0.002
Age at accident, year, mean (SD)	54.7 (11.3)	55.2 (12.3)	0.470
Variable	No. of cases	IRR	HR
Motor Vehicle Accidents	113	1.29 (1.06–1.58)	1.35 (1.10–1.66)

CPAP = Continuous Positive Airway Pressure. HR = Hazard ratio. IRR = Incidence rate ratio.

Table 6
Characteristics of patients with OSA treated with or without CPAP and the risk of motor vehicle accidents compared between the two groups.

Variable	CPAP n = 12,875	No CPAP n = 35,293	P-value
Sex, male (%)	78.3	77.7	0.174
Age, year, mean (SD)	62.7 (12.7)	64.7 (13.4)	<0.0001
Age at diagnosis, year, mean (SD)	55.4 (12.5)	52.7 (12.9)	<0.0001
Motor vehicle accidents, n (%)	113 (0.88)	560 (1.57)	<0.0001
Age at accident, year, mean (SD)	54.7 (11.3)	54.4 (13.3)	0.941
Age at diagnosis for patients involved in accident, year, mean (SD)	52.1 (11.5)	48.5 (13.0)	0.007
Variable	No. of cases	IRR	HR
Motor Vehicle Accidents	113	0.75 (0.60–0.91)	0.82 (0.67–1.02)

CPAP = Continuous Positive Airway Pressure. HR = Hazard ratio. IRR = Incidence rate ratio.

4. Discussion

We present the first nationwide study to estimate the risk of all road traffic accidents in patients with OSA compared to a large reference cohort covering a long-term follow-up of up to 24 years. We have demonstrated that the risk of motor vehicle accidents is increased in patients with OSA, whereas the risk of bicycle accidents and as pedestrians is not increased. Patients with OSA had a tendency to be involved in more severe accidents.

Our results are supportive of the existing literature, and, thereby, the presumed link between OSA and an increased occurrence of motor vehicle accidents. Our sensitivity analysis showed that diabetes mellitus, hypertension, and cerebrovascular events could explain some of the observed association, however, a moderate increased risk persisted. The increased risk of motor vehicle accidents found in our study is comparable with the risk described in previous studies, albeit in the lower end of the scale [11–13,17,21]. As mentioned, a meta-analysis from Tregear et al., in 2009 demonstrated a relative risk of 2.4, considerably higher than our estimate. A potential explanation might be, as the authors mention, that the majority of studies included was of low quality due to lack of adjustments and self-reported data acquisition. Interestingly, our estimates were quite similar to the findings in a novel US cohort study, reporting a 17 percent increased risk of first motor vehicle accidents. Despite similarities in study design, the study by Pocobelli et al. does not address risk of recurrent events and only have a follow-up time of 2.2 years. Still, these data might be taken as support for the notion, that the actual true increased risk of motor vehicle accidents for patients with OSA is to be found in this range.

Whereas the risk of motor vehicle accidents is well-described in patients with OSA, the risk of traffic accidents as a pedestrian or bicyclist is not. To our knowledge, we are the first to describe the risk of these accidents isolated in patients with OSA, as other studies have included them as part of motor vehicle accidents. Previous studies have, however, suggested that sleep deprivation among Korean adolescents was associated with bicycle accidents, and children with OSA had an increased risk of pedestrian injury [24,25]. Our results are interesting, as patients with OSA demonstrated a lower risk of bicycle accidents. The most logical and probable explanation is that patients with OSA are less active and less likely to ride a bicycle, and that the risk factors associated with OSA (excessive daytime sleepiness, inattention, reduced alertness and falling asleep) is diminished when physically active. The later might also explain why patients with OSA had a similar risk of accidents as pedestrians compared with the reference cohort.

Patients with OSA had a tendency to be involved in more severe motor vehicle accidents, however, the difference were only significant for unharmfull events. The tendency of patients with OSA being involved in more severe accidents were more evident in the study from Mulgraw et al. who described a threefold increase in the odds of accidents with personal injury among patients with OSA [11]. Given that we only choose to include events after time of diagnosis and the authors of this single centre study choose to include crashes occurring 3 years prior to polysomnography, some differences between our results were to be expect. Our sub-analysis of all motor vehicle accidents regardless of time of diagnosis did indeed show a significant difference in the occurrence of severe and mild accidents. The occurrence of fatal accidents were, however, identical between patients and references. This finding might be a result of immontal bias, as there will undoubly be some fatal accidents among undiagnosed patients with OSA occurring in the reference group. It should be noted that, given the nature of the registers, we only included accidents that were reported to the police. This could potentially introduce bias, as drivers with OSA may underreport accidents for fear of having their licence suspended. While speculative, we belive the tendency we describe to be reflective of the actual truth.

The effects of CPAP treatment were ambiguous in the present study, as the occurrence of motor vehicle accidents were noticeable lower in patients treated with CPAP compared to patients treated without CPAP, however, the risk of motor vehicle accidents was

significantly higher in patients treated with CPAP when compared with matched references. Although it have been suggested that driving simulator performance remains impaired in patients with severe OSA after CPAP treatment, our findings are perhaps somewhat surprising, given that the majority of previous studies investigating the effects of CPAP treatment have reported a beneficial effect on the risk of motor vehicle accidents [14,17–26]. Indeed, the review by Tregear et al. reports that after just 2–7 days of treatment with CPAP, patients with OSA have a reduced risk of accidents with rates of motor vehicle crashes similar to that of individuals without OSA [12]. Similar findings were reported by Karimi et al. who found a 70% reduction in motor vehicle accidents if patients with OSA complied to at least 4 h of CPAP therapy per night [21]. These differences might be due to the different study designs, as we included the entire Danish cohort of OSA patients with a matched reference cohort covering up to 24 years of follow-up. In contrast, Karimi et al. estimated the rate of motor vehicle accidents in a smaller control population. We cannot, however, exclude that these discrepancies in relation to our study is caused by issues with compliance, as Karimi et al. used a non-naturalistic design by providing regular follow-up and monitoring, which might improve the compliance to treatment among their patients. Low compliance to CPAP treatment is well-documented among patients with OSA and might, consequently, influence this sub-analysis negatively [27]. The present study is unable to control for therapy adherence, as both patients returning their CPAP and patients with low compliance are categorised as receiving CPAP treatment. Consequently, this sub-analysis should be interpreted with caution.

4.1. Limitations

The present study has a number of strengths compared with previous studies in the area of OSA and motor vehicle accidents, and adds to the field in several aspects. Our study is the first nationwide study with a mean long-term follow up of more than 12 years. Using the unique Danish registries to gain information on OSA diagnosis and road traffic accident, the risk of selection- and recall-bias should be eliminated.

Despite the clear strengths of the present study, we need to address some of the inherent limitations of register-based studies. Firstly, the validity of our estimates always depends on the accuracy of the OSA diagnosis generated by the physicians. The validity of the diagnosis in the DNPR is generally considered moderate to high. In an attempt to improve the completeness of our data, we decided only to include patients diagnosed after 1994, thereby also including all patients diagnosed in an outpatient clinic. Regarding external validity of our findings, we cannot extrapolate our findings to the large group of undiagnosed patients with OSA in the general population. Additionally, our cases are likely to still suffer from clinical referral bias, given that many patients with OSA have other clinical conditions potentially associated with increased risk of road traffic accidents. Despite our sensitivity analysis, this may consequently account for some of the significance of the association demonstrated in the present study.

Finally, given the nature of the Danish registries, we do not have detailed clinical information (e.g., apnea-hypopnea index or therapy adherence) or information on other factors that can contribute to the occurrence of motor traffic accidents, e.g., the number of miles driven (degree of exposure), time of accidents, legal drug consumption, driver experience, degree of sleepiness, sleep duration, and circadian factors. Although socioeconomic status is correlated to some of these variables it can only be considered a crude surrogate [28,29].

5. Conclusion

With this nationwide study, we are the first to have estimated the risk of all road traffic accidents in an entire population of patients with OSA. Our results clearly validate the presumed link between OSA and occurrence of motor vehicle accidents, as we demonstrate a moderate but significant increased risk of motor vehicle accidents in patients with OSA when compared to a large reference cohort. Our data suggests that not only is the risk of motor vehicle accidents increased, but also that the severity of accidents is higher among patients with OSA. In contrast, patients with OSA did not have an increased risk of being involved in accidents while biking or as a pedestrian.

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Credit author statement

NU, SU and JB designed the study. NU and SU made the analysis. SLC assisted all the data analysis. NU and CR took the lead in writing the manuscript. All authors aided in interpreting the results and worked on the manuscript. All authors discussed the results and commented on the manuscript.

Conflict of interest

None.

The ICMJE Uniform Disclosffigure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2022.04.003.

References

[1] Gottlieb DJ, Punjabi NM. Diagnosis and management of obstructive sleep apnea: a review. JAMA 2020;323(14):1389–400. https://doi.org/10.1001/jama.2020.3514.
[2] Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 2002;165(9):1217–39. https://doi.org/10.1164/rccm.2109080.
[3] Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc 2008;5(2):136–43. https://doi.org/10.1513/pats.200709-155MG.
[4] Dempsey JA, Veasey SC, Morgan BJOC. Pathophysiology of sleep apnea. Physiol Rev 2010 Jan;90(1):47–112. https://doi.org/10.1152/physrev.00043.2008.
[5] George CFP. Sleep apnea, alertness, and motor vehicle crashes. Am J Respir Crit Care Med 2007;176(10):954–6. https://doi.org/10.1164/rccm.200605-629PP.
[6] Young T, Palta M, Dempsey J, et al. Burden of sleep apnea: rationale, design, and major findings of the Wisconsin sleep cohort study. Wis Med J 2009;108(5):246–9.
[7] Gottlieb DJ, Ellenbogen JM, Bianchi MT, et al. Sleep deficiency and motor vehicle crash risk in the general population: a prospective cohort study. BMC Med 2018;16(1):1–10. https://doi.org/10.1186/s12916-018-1025-7.
[8] Hiestand D, Phillips B. Obstructive sleep apnea syndrome: assessing and managing risk in the motor vehicle operator. Curr Opin Pulm Med 2011;17(6):412–8. https://doi.org/10.1097/MCP.0b013e32834b96a4.
[9] Ward KL, Hillman DR, James A, et al. Excessive daytime sleepiness increases the risk of motor vehicle crash in obstructive sleep apnea. J Clin Sleep Med 2013 Oct 15;9(10):1013–21. https://doi.org/10.5664/jcsm.3072.
[10] Basoglu OK, Tasbakan MS. Elevated risk of sleepiness-related motor vehicle accidents in patients with obstructive sleep apnea syndrome: a case-control study. Traffic Inj Prev 2014;15(5):470–6. https://doi.org/10.1080/15389588.2013.830213.
[11] Mulgrew AT, Nasvadi G, Butt A, et al. Risk and severity of motor vehicle crashes in patients with obstructive sleep apnoea/hypopnoea. Thorax 2008;63(6):536–41. https://doi.org/10.1136/thx.2007.085464.
[12] Tregear S, Reston J, Schoelles K, et al. Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. J Clin sleep Med JCSM Off Publ Am Acad Sleep Med 2009;5(6):573–81.
[13] Ellen RLB, Marshall SC, Palayew M, et al. Systematic review of motor vehicle crash risk in persons with sleep apnea. J Clin sleep Med JCSM Off Publ Am Acad Sleep Med 2006;2(2):193–200.
[14] Terán-Santos J, Jiménez-Gómez A, Cordero-Guevara J. The association

between sleep apnea and the risk of traffic accidents. Cooperative Group Burgos-Santander. N Engl J Med 1999;340(11):847–51. https://doi.org/10.1056/NEJM199903183401104.
[15] Lloberes P, Levy G, Descals C, et al. Self-reported sleepiness while driving as a risk factor for traffic accidents in patients with obstructive sleep apnoea syndrome and in non-apnoeic snorers. Respir Med 2000;94(10):971–6. https://doi.org/10.1053/rmed.2000.0869.
[16] Bonsignore MR, Randerath W, Schiza S, et al. European Respiratory Society statement on sleep apnoea, sleepiness and driving risk. Eur Respir J 2021;57(2). https://doi.org/10.1183/13993003.01272-2020.
[17] Pocobelli G, Akosile MA, Hansen RN, et al. Obstructive sleep apnea and risk of motor vehicle accident. Sleep Med 2021;85:196–203. https://doi.org/10.1016/j.sleep.2021.07.019.
[18] Gonçalves M, Amici R, Lucas R, et al. Sleepiness at the wheel across Europe: a survey of 19 countries. J Sleep Res 2015;24(3):242–53. https://doi.org/10.1111/jsr.12267.
[19] Bonsignore MR, Marrone O, Fanfulla F. Sleep apnea, sleepiness, and driving risk. Sleep Med Clin 2019;14(4):431–9. https://doi.org/10.1016/j.jsmc.2019.08.001.
[20] Howard ME, Desai AV, Grunstein RR, et al. Sleepiness, sleep-disordered breathing, and accident risk factors in commercial vehicle drivers. Am J Respir Crit Care Med 2004;170(9):1014–21. https://doi.org/10.1164/rccm.200312-1782OC.
[21] Karimi M, Hedner J, Häbel H, et al. Sleep apnea related risk of motor vehicle accidents is reduced by continuous positive airway pressure: Swedish traffic accident registry data. Sleep 2015;38(3):341–9. https://doi.org/10.5665/sleep.4486.
[22] Schmidt M, Pedersen L, Sørensen HT. The Danish civil registration system as a tool in epidemiology. Eur J Epidemiol 2014;29(8):541–9. https://doi.org/10.1007/s10654-014-9930-3.
[23] Lynge E, Sandegaard JL, Rebolj M. The Danish national patient register. Scand J Publ Health 2011. https://doi.org/10.1177/1403494811401482.
[24] Avis Kristin T, Karen L, Gamble DCS. Obstructive sleep apnea syndrome (OSAS) increases pedestrian injury risk in children. J Pediatr 2015;January;166(1):109–14. https://doi.org/10.1016/j.jpeds.2014.09.032 [Obstructive].
[25] Kim SY, Sim S, Kim SGCH. Sleep deprivation is associated with bicycle accidents and slip and fall injuries in Korean adolescents. PLoS One 2015 Aug 17;10(8):e0135753. https://doi.org/10.1371/journal.pone.0135753.
[26] Findley LJ, Smith C, Hooper J, et al. Treatment with nasal CPAP decreases automobile accidents in patients with sleep apnea. Am J Respir Crit Care Med 2000;161(3 I):857–9. https://doi.org/10.1164/ajrccm.161.3.9812154.
[27] Yetkin O, Kunter EGH. CPAP compliance in patients with obstructive sleep apnea syndrome. Sleep Breath 2008 Nov;12(4):365–7.
[28] Whitlock G, Norton R, Clark T, et al. Motor vehicle driver injury and marital status: a cohort study with prospective and retrospective driver injuries. Inj Prev 2004;10(1):33–6. https://doi.org/10.1136/ip.2003.003020.
[29] Patel Sanjay R, Malhotra Atul, Gottlieb Daniel J, White DP, Hu Frank B. Correlates of long sleep duration. Sleep 2006 July;29(7):881–9.