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SLEEP DURATION AND MULTIMORBIDITY IN LUXEMBOURG. RESULTS FROM THE EUROPEAN HEALTH EXAMINATION SURVEY, 2013-2015

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Contributorship statement

MRC and SS conceptualized and designed the study. MRC and VB performed the statistical analysis. MRC, SS and T.T.M interpreted the data. MRC drafted the article. SS supervised the study. All authors participated in the revision of the article. All authors contributed to and have approved the final manuscript.

Abstract

Objectives: We estimated the prevalence of short sleep duration and multimorbidity in Luxembourg, and assessed whether sleep duration was associated with multimorbidity after adjusting for socio-demographic and behavioral characteristics.

Design: Cross-sectional study.

Participants: Data from 1508 Luxembourg residents (48% men and 52% women) aged 25 to 64 years came from the European Health Examination Survey 2013-2015.

Outcome measures: Short sleep duration and multimorbidity.

Results: Participants reported sleeping 7.86hrs/night when not having to work the next day, nearly 1hr more than during work days. Nearly half of participants reported having been diagnosed with ≥2 chronic conditions/diseases. Short sleep duration was linearly associated with the number of chronic conditions when participants did not have work the next day (OR: 2.52, 95% CI: 1.44, 4.41 and OR: 2.78, 95% CI: 1.65, 4.68 for 2, and ≥3 chronic conditions/diseases, respectively), independently of socioeconomic and behavioral characteristics. The effect was stronger when participants had to work the next day (OR: 3.03, 95% CI: 1.34, 6.84, and OR: 3.46, 95% CI: 1.56, 7.66, for 2 and ≥3 chronic conditions/diseases, respectively).

Conclusions: Health promotion programs should aim at improving and promoting healthy sleeping and its possible benefits on chronic disease outcomes, which in turn can help reducing the risk of multimorbidity in middle-aged adults.

Keywords: Sleep duration; multimorbidity; chronic diseases; Luxembourg; European Health Examination Survey

Strengths and limitations of this study

- This is the first study in Luxembourg on the prevalence of sleep patterns, with a focus on short and long sleep duration, and their relationship with multimorbidity.

- Short sleep duration, difficulties in sleeping through the night, sleep disorders and sleeping medication, all are a public health challenges in Luxembourg.

- In the present study, short sleep duration was linearly associated with the number of chronic conditions

- As both sleep problems and multimorbidity are highly prevalent in Luxembourg, health promotion programs should be addressed to improve and promote healthy sleeping habits among the general population, which in turn may help reducing the risk of multimorbidity

- Limitations of the present study include the subjective measure of sleep duration, the cross-sectional design of the study (not allow to establish a causal link) and the low participation rate.

Data sharing statement: Extra data can be accessed by emailing Dr Laetitia Huiart, Head of the Population Health Department, LIH (laetitia.huiart@lih.lu) and the Principal Investigator of EHES-LUX2013-2015, Dr Maria Ruiz-Castell (maria.ruiz@lih.lu) and fill out a request form.

Introduction

A healthy lifestyle includes healthy sleep habits. Sleep patterns influence several physiological and psychological processes such as inflammation, cognitive function, glucose regulation and energy balance (1-3). Short sleep duration, poor sleep quality, and sleep-related disorders can result in sleep deficiency and impact on individual health (4). According to the Centers for Disease Control and Prevention (CDC), insufficient sleep is associated with health problems such as chronic diseases, poor quality of life, mental health, risk of accidents, and lower productivity at work (5). Adequate sleep duration is one of the dimensions needed for a good sleep health (6). The American Academy of Sleep Medicine and Sleep Research Society considers that for an adult it is recommended at least 7 hours of sleep per night (4). However, a high percentage of the population sleeps less than the recommended 7 hours (7).

Several factors may affect sleep such as physical activity or eating behaviors, but also socioeconomic factors including job status, marital status and ethnicity (8, 9). Studies have observed an association between lower education, unemployment and both short and long sleep duration (10, 11), while factors such as physical activity and healthy diet seem to improve sleep quality (12, 13). Moreover, diet intake (energy and total fat intake) and nutrients seem to be associated with both short and long sleep duration through multifactorial factors including behaviors (e.g., time and hours of intake) and variations in hormones related to appetite, such as leptin (14).

Epidemiologic data suggest an association between sleep duration and poor sleep quality with cardiometabolic health (e.g. hypertension, diabetes, obesity, cardiovascular diseases), mental problems (e.g. depression), and mortality (15-18). The observed relationship between short sleep duration and mortality would be especially critical in adults under 65 years of age (18). Few studies so far have focused on possible relationships between sleep patterns and multimorbidity (19, 20). Multimorbidity is defined as the presence of two or more chronic diseases in the same individual (21), and is associated with disability, functional decline, frailty, poor quality of life and mortality (22). In the context of ageing societies, multimorbidity is an increasing global phenomenon (23); although its occurrence usually increases with age, a large proportion of individuals younger than 65 are also affected (24). Definitions of multimorbidity vary, however, and the prevalence differs based on changing definitions, which in turn present significant challenges when attempting to compare results between populations and studies (22).

The aim of the present study was to estimate the prevalence of short sleep duration and multimorbidity in Luxembourg, as well as to assess whether sleep duration was associated with multimorbidity after adjusting for socio-demographic and behavioral characteristics.

Methods

Study population and recruitment

Data was drawn from the European Health Examination Survey in Luxembourg (EHES-LUX). EHES-LUX is a representative cross-sectional population-based survey carried out by the Luxembourg Institute of Health with the objectives of assessing the health status of the population of the Grand-Duchy of Luxembourg, develop national and European health indicators, identify the needs of the population, and evaluate health behaviors. EHES-LUX was conducted between February 2013 and January 2015. Individuals were randomly selected in a one-stage sampling procedure from the national health insurance registry (95% social coverage). Institutionalized individuals (e.g. hospitals, elderly homes) were not included. A total of 1508 residents (excluding 21 pregnant women) of Luxembourg aged 25 to 64 participated in the survey (participation rate of 24.1%) (25). Of them, 7 participants did not reported their sleep habits. A total of 1501 participants had information on multimorbidity and sleep habitsParticipants signed an informed consent and were interviewed by trained nurses who also conducted medical examinations. Questionnaires included several health modules (e.g. sleep habits, nutritional habits, health care, working and living conditions) as well as demographic and socioeconomic characteristics. Medical examinations included measurements such as blood pressure and anthropometry. Sampling weights were calculated to be generalized to the population of Luxembourg in terms of age, sex and district of residence. The study national research ethics committee (Comité national d'éthique de Recherche-CNER) approved the study and it was notified to the Luxemburgish National Commission for Data Protection.

Patient involvement

Participants were not involved in the development of the research question, study design, recruitment or the conduction of the study. Upon request, results from the medical examination were forwarded to the study participants and their medical doctors. General results were presented to the general public in national health activities

Sleep

Sleep duration was assessed using two questions: 1) "How many hours do you normally sleep at night when you have to work the next day?", and 2) "How many hours do you normally sleep at

night when you don't have to work the next day?". Responses to the first question were categorized in short sleep duration (<6hrs/night), medium sleep duration (6-7hrs/night), and long sleep duration (>7hrs/night), in line with most of previously published studies. Responses to the second question were categorized in short sleep duration (<7hrs/night), medium sleep duration (7-8hrs/night), and long sleep duration (>8hrs/night) .

Difficulty in sleeping the night was assessed based on the question "Do you have difficulties in sleeping through the night?". Diagnosis of sleep disorders was assessed using the question "Have you ever been told by a doctor or another health professional that you have a sleep disorder?". Sleep medication was assessed using the question "In the past 2 weeks, have you used other types of medicines that were prescribed to you, such as sleeping tablets?". Sleepiness was defined as a score of ≥11 on the Epworth Sleepiness Scale (26).

Multimorbidity

Participants were asked if they ever had a chronic disease or condition diagnosed by a medical doctor (e.g., hypertension, high cholesterol, diabetes, coronary heart disease or angina pectoris, heart attack or its chronic consequences, stroke or its chronic consequences, stomach or duodenal ulcer, cirrhosis or other liver disease, urinary incontinence, kidney problems, chronic back or neck disorder, rheumatoid arthritis, arthrosis, osteoporosis, cancer, severe headache as migraine or chronic anxiety). Based on this information, the variable "ever being diagnosed with a chronic disease or condition" was generated with four categories: 0, 1, 2 and ≥3 chronic disease or condition. Multimorbidity was defined as having two or more chronic diseases or conditions diagnosed by a medical doctor.

Explanatory variables

Sociodemographic characteristics included age, sex and immigration status. As Portuguese are the largest immigrant community in Luxembourg, immigration status was categorized in non-immigrant, immigrant born in Portugal and immigrant born in other countries. Socioeconomic status included education (primary, secondary and tertiary education completed) and job status (unemployed; managers/professionals; technical/clerical/service occupation; skilled/unskilled workers).

Lifestyles included smoking (never; current; ex-smokers), alcohol consumption (never; ex-drinkers; drinkers), physical activity (never; ≤ 3hrs/week of sports, fitness, and/or recreational activities which lasted at least 10 consecutive minutes; >3hrs/week of sports, fitness, and/or recreational activities which lasted at least 10 consecutive minutes), and vegetable and fruit consumption (< 1 portion/ day, 1–4 portions/day, ≥ 5 portions/day). Weight and height were measured by trained

nurses and used to calculate body mass index (BMI; kg/m^2). BMI was categorized as normal body weight (<25 kg/m^2), overweight (25-29.99 kg/m^2) and obesity (≥30kg/m^2).

Statistical data analysis

Means and frequencies were used for descriptive purposes. We calculated the prevalence of sleep disorders, short and long sleep duration, chronic conditions/diseases and multimorbidity. Percentages did not include missing values. A chi-square test (χ2) or Student t-test were used to analyze associations between the prevalence of sleep duration and covariates and the prevalence of multimorbidy and covariates. The association between sleep duration and chronic conditions/diseases was assessed using multinomial logistic regression models (reference for sleep duration when having to work the next day was 6-7h per night and reference for sleep duration when not having to work the next day was 7-8h) adjusted for sociodemographic characteristics, socieconomic status and physical activity. We considered a P<0.05 statistically significant. To be representative of the population and avoid biased estimates, the observations were weighted. Participants with missing values on sleep habits and or murltimorbidity were not included in the present analysis. Analyses were performed using STATA 14.0 and and SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Table 1 shows the prevalence of chronic conditions/diseases, multimorbidity, sleep duration and sleep disorders. Nearly half of participants reported being diagnosed with two or more chronic conditions/ diseases, and nearly a third of participants reported being diagnosed with three or more chronic conditions/diseases. More than 8% of participants were diagnosed with a sleep disorder and a third reported having difficulties in sleeping through the night. Participants reported sleeping 7.86hrs/night when they did not have to work the next day, nearly one hour more than when they had to work the next day (6.95hrs/night).

Participant characteristics by chronic conditions/diseases are shown in **Table 2**. More men than women presented three or more chronic diseases. Higher number of chronic diseases/conditions increased with age: those aged 55 to 64 presented more chronic conditions compared to those aged 25-34. Immigrants born in Portugal presented more chronic conditions than non-immigrants and other immigrants. Participants being less educated and unemployed presented more chronic conditions compared to those employed and highly educated. Participants being less physically active and with obesity presented more chronic conditions/diseases than those being more physically active and with a lower BMI.

Participant characteristics by sleep duration are shown in **Table 3**. When participants had to work the following day, more men than women reported a medium sleep duration. Short sleep duration was more likely among immigrants born in Portugal, participants with lower education and skilled/unskilled workers. Short sleep duration was less common among those being physically active and with a BMI less than 25 Kg/m^2. When participants did not have to work the next day, short sleep duration was more common among older individuals, immigrants born in Portugal, unemployed people, and those being less physically active. Long sleep duration was observed among participants with lower education. No differences in sleep duration were observed between men and women.

Table 4 shows results from multinomial logistic regression analyses examining the association between sleep duration and chronic conditions/diseases, and adjusted by sociodemographic characteristics, socioeconomic position and physical activity. Among participants who reported sleep hours when they did not have to work the next day, those sleeping less hours (<7h) were 2.35 and 2.85 times as likely to report having 2 and 3 or more chronic conditions after adjusting for covariates. In models adjusted for different indicators of socioeconomic status, sociodemographic and physical activity, the strength of associations between sleep duration and multimorbidity remained statistically significant. The same association (although more accentuated) was observed in those participant with a job at the moment of the survey who reported the number of sleep hours when they had to work the next day: those sleeping less hours (<6h) were 3.07 and 3.70 times as likely to report having 2 and 3 or more chronic conditions after adjusting for covariates.

Estimates of sleep problems and chronic conditions are presented in **Table S1**. The prevalence of sleep problems was high, with 1 out 3 participants having difficulties in sleeping the night through, nearly 8% of participants diagnosed with a sleep disorder and 4.26% taking sleeping medication. In all cases, the percentage of participants with sleep problems increased with the number of chronic diseases.

Discussion

Sleep problems are highly prevalent in Luxembourg, where nearly 34% of the resident population aged 25-64 reported having difficulties sleeping through the night, 8.21% having been diagnosed a sleep disorder, and 4.26% taking sleep medication. Moreover, 6.08% and 28.82% of the Luxembourg population reported sleeping respectively less than 6 hours and less than 7 hours per night during working days. The latter decreased to 13.52% when participants did not have to work on the following day. Luxembourg residents sleep on average 6.95hrs/night when they have to work the following day, nearly one hour less than when they do not have to work the next day. Results

are similar to those observed in other countries (27, 28), although in countries such as Brazil the prevalence of short sleep duration was of nearly 22% (29), and in the United States values reached up to 34.8% in 2014 (30). However, in the present study the age range from 25 to 64 years must be taken into account since it does not include adults over 65 years old who usually sleep less hours. This means that the prevalence of the Luxembourg population sleeping less than the recommended hours is likely to be higher.

Multimorbidity was also highly prevalent in Luxembourg, especially when taking into account the fact that the study population was up to 65 years, which represents a relatively young population since multimorbidity prevalence naturally increases with age (22). Nearly half of participants had two or more chronic diseases and 31% had three or more chronic diseases/conditions. The most prevalent diseases were chronic low back disorder or other chronic back defect followed by hypercholesterolemia, arthrosis and hypertension.

Short sleep duration was also more common among immigrants. The relationship between immigration status and sleep patterns remains unclear, with some studies showing a protective effect and others observing an opposite effect, possibly related to the stress linked to the migratory processes, cultural adaptation, or working conditions in the host country (31, 32). In our study, Portuguese immigrants were more likely to sleep less than 6h per night during work days. Portuguese are the most important immigrant community in Luxembourg, accounting for 16% of the 46% immigrant population living in Luxembourg. Compared to Luxembourgish natives, Portuguese immigrants have a lower socioeconomic status (33) (including income, education and employment) which could partly explain why the Portuguese have a greater likelihood of being short sleepers. Job status seems to play an important role, since the effect is not significant when compared to short sleep duration when not having to work the next day.

In our study, long sleep duration was more common in women. This was in line with other studies which showed that men usually sleep less hours, though women reported having more sleep problems (34). However, this relationship is complex and could depend on family composition (e.g. single parents have shorter sleep duration, particularly women) (35).

Physical activity was associated with sleep duration but only during days when not having to work the next day. Physical activity would reduce the likelihood of short and/or long sleep duration and maintain an optimal duration. Studies have observed an association between physical activity and sleep, improving quality of sleep, sleep efficiency, and total sleep time (12, 36).

In our study we observed that short sleep duration was significantly linearly associated with the number of chronic conditions independently of socioeconomic and behavioral characteristics, an

effect accentuated during working days, when sleep hours are reduced. Our results are in line with those from other studies that have observed an association between sleep and number of chronic diseases, although previous studies have been usually performed in populations of older adults (e.g. over 50 years old) (19, 37). As observed by Koyanagi et al., sleep problems increase with the number of diseases in both low and high income countries independent of their economic development (19). These associations could explain the observed relationship of sleep duration (below the recommended 7 hours) and poor sleep quality with mortality, even among adults younger than 65 years old (18). It is not clear if sleep problems are a consequence of chronic diseases (e.g. pathologies themselves affect sleep) or part of the cause (sleep predispose the individual to more diseases or exacerbates the symptoms), although it is plausible that sleep problems and chronic diseases are linked by a bidirectional association (38).

Although both sleep problems and the number of chronic diseases increase with age, and are more prevalent in older adults, our study shows that the prevalence is also high in adults under 65 and the association begins much earlier. It is therefore necessary to detect these problems earlier in order to improve individual health and general wellbeing and reduce mortality, particularly in the context of ageing populations burdened by the accumulation of multiple chronic conditions over time.

In terms of potential mechanisms to corroborate the biological plausibility of the link between sleep problems and multimorbidity, sleep deprivation has been associated with a number of chronic conditions, including cardio-metabolic and neurodegenerative disease, cancer, musculoskeletal disorders, and mental problems (15, 16). In addition, sleep problems often cluster with major behavioral risk factors such as cigarette smoking, heavy drinking, and physical inactivity, which may in turn increase the risk of chronic disease. Furthermore, there is experimental evidence corroborating the plausibility of deleterious effects of lack of sleep on endocrine, immune, neurovegetative and inflammatory pathways (1-3).

Limitations of the present study include the subjective measure of sleep duration (self-reported number of hours of sleep) instead of an objective measure (e.g. actigraphy, polysomnography). However, in the absence of an objective measure, there is a moderate correlation between both objective and subjective measurements, a correlation that is high during weekdays possibly due to routines (39), but may be attenuate based on certain individual characteristics (e.g. presence of pathologies such as depression, sociodemographic characteristics) (40). Other limitations include the fact that we did not include other sleep problems such as insomnia or sleep apnea nor environmental factors such as noise, traffic or commuting, all of which could affect sleep duration. In addition, multimorbidity was also self-reported and due to a limited predetermined list of

diseases in the questionnaire, participants may have not reported some conditions they may have had and underestimate the prevalence of multimorbidity. Information on non- responders was not available and despite being a representative sample of the Luxembourg population (in terms of age, sex and district) we could not determine the possibility of a non-response bias. Finally, it should be noted that the design of the study (cross-sectional) does not allow to ascertain a causal link between sleep and multimorbidity; in addition, the low participation rate may affect the generalizability of our results.

This is the first study in Luxembourg on the prevalence of sleep patterns, with a focus on short and long sleep duration, and their relationship with multimorbidity. Short sleep duration, having difficulties in sleeping the night through, sleep disorders and sleeping medication are a public health problem, especially when associated with a number of chronic conditions and diseases, thus producing a negative impact on the wellbeing and general health status of the population. As both sleep problems and multimorbidity are highly prevalent in Luxembourg, health promotion programs should be addressed to improve and promote healthy sleeping habits among the general population, which in turn may be beneficial on a number of chronic disease outcomes.

Acknowledgements

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Table 1. Chronic diseases/conditions, multimorbidity and sleep: European Health Examination Survey in Luxembourg (N =1508).

	N (%) / Mean ± SD
Hypertension	250 (16.59)
High cholesterol	458 (30.39)
Diabetes	69 (4.58)
Coronary heart disease or angina pectoris	26 (1.73)
Myocardial infarction or chronic consequences of myocardial infarction	14 (0.93)
Stroke or chronic consequences of stroke	11 (0.73)
Stomach or duodenal ulcer	81 (5.37)
Cirrhosis of the liver or other liver disease	46 (3.05)
Urinary incontinence, problems in controlling the bladder	74 (4.91)
Kidney problems	108 (7.17)
Chronic low back disorder or other chronic back defect	489 (32.47)
Chronic neck disorder or other chronic neck defect	246 (16.32)
Rheumatoid arthritis	88 (5.85)
Arthrosis	292 (19.38)
Osteoporosis	44 (2.92)
Cancer	54 (3.59)
Severe headache such as migraine	271 (17.98)
Chronic anxiety	98 (6.50)
Depression	204 (13.54)
Number of chronic diseases	
0	405 (27.00)
1	362 (24.13)
≥2 (multimorbidity)	733 (49.00)
≥3	465 (31.00)
Sleep	
Diagnosis of sleep disorder	122 (8.21)
Sleepiness [a]	118 (7.89)
Have difficulties in sleeping the night through	510 (33.89)
Sleeping medication	64 (4.26)
Sleep duration	

Hours when you have to work the next day (N=1,152-working)	6.95±0.97
<6hrs/night	70 (6.08)
6-7hrs/night	761 (66.06)
>7hrs/night	321 (27.86)
Hours when you don't work the next day (N=1,501)	7.86±1.30
<7hrs/night	203 (13.52)
7-8hrs/night	878 (58.49)
>8hrs/night	420 (27.98)

N=number, SD=standard deviation

[a] Measured with Epworth Sleepiness Scale

Table 2. Participant characteristics by chronic conditions/diseases: European Health Examination Survey in Luxembourg (N =1508).

	Chronic conditions/diseases				
	0	1	2	≥3	P[a]
Sex					
Men	199 (27.72)	199 (27.72)	143 (19.92)	177 (24.65)	<0.001
Women	206 (26.34)	163 (20.84)	125 (15.98)	288 (36.83)	
Age					
25-34	130 (43.62)	86 (28.86)	48 (16.11)	34 (11.41)	<0.001
35-44	156 (34.29)	119 (26.15)	69 (15.16)	111 (24.40)	
45-54	83 (18.16)	111 (24.29)	98 (21.44)	165 (36.11)	
55-64	36 (12.41)	46 (15.86)	53 (18.28)	155 (53.45)	
Immigration					
Luxembourg	184 (23.44)	197 (25.10)	144 (18.34)	260 (33.12)	<0.001
Portugal	52 (23.85)	42 (19.27)	45 (20.64)	79 (36.24)	
Other	169 (34.00)	123 (24.75)	79 (15.90)	126 (25.35)	
Education					
Primary	68 (18.38)	75 (20.27)	64 (17.30)	163 (44.05)	<0.001
Secondary	133 (23.05)	142 (24.61)	106 (18.37)	196 (33.97)	
Tertiary	203 (37.04)	145 (26.46)	97 (17.70)	103 (18.80)	
Job					
Not working	58 (16.67)	56 (16.09)	58 (16.67)	176 (50.57)	<0.001
managers/professionals	168 (35.59)	138 (29.24)	73 (15.47)	93 (19.70)	
technicians/clerical/service occupation	119 (29.38)	89 (21.98)	76 (18.77)	121 (29.88)	

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skilled/unskilled workers	60 (21.90)	79 (28.83)	61 (22.26)	74 (27.01)	
Smoking					
Never	239 (29.25)	209 (25.58)	145 (17.75)	224 (27.42)	0.026
Current	90 (26.01)	75 (21.68)	63 (18.21)	118 (34.10)	
Ex-smoker	74 (22.09)	78 (23.28)	60 (17.91)	123 (36.72)	
Alcohol					
Never	30 (27.78)	21 (19.44)	20 (18.52)	37 (34.26)	0.055
Drinkers	365 (27.53)	328 (24.74)	234 (17.65)	399 (30.09)	
Ex-drinkers	8 (12.50)	13 (20.31)	14 (21.88)	29 (45.31)	
Fruits and vegetables consumption					
<1 portion/day	126 (27.39)	112 (24.35)	87 (18.91)	135 (29.35)	0.597
1-4 portions/day	223 (27.81)	183 (22.82)	142 (17.71)	254 (31.67)	
≥5 portions/day	55 (23.31)	66 (27.97)	39 (16.53)	76 (32.20)	
Physical Activity					
Never	130 (21.35)	133 (21.84)	125 (20.53)	221 (36.29)	<0.001
<=3h/week	151 (29.84)	130 (25.69)	77 (15.22)	148 (29.25)	
>3h/week	121 (31.84)	98 (25.79)	65 (17.11)	96 (25.26)	
BMI	25.27 ± 4.06	26.04 ± 4.89	26.66 ± 4.96	28.07 ± 5.56	<0.001
<25	212 (33.02)	169 (26.32)	112 (17.45)	149 (23.21)	<0.001
25-30	152 (27.39)	131 (23.60)	100 (18.02)	172 (30.99)	
>=30	41 (13.62)	61 (20.27)	55 (18.27)	144 (47.84)	

Values are: numbers (%) for categorical variables and means±standard deviation for continuous variables. BMI: Body Mass Index.[a] χ2 test for categorical variables, t-test for continuous variables.

Table 3. Participant's characteristics by Sleep duration: European Health Examination Survey in Luxembourg (N =1508).

	Sleep hours when you have to work the next day (N=1,152-working)				Sleep hours when you do NOT work the next day (N=1,501)			
	6-7hrs/night	<6hrs/night	>7hrs/night	P [a]	7-8hrs/night	<7hrs/night	>8hrs/night	P [a]
Sex								
Men	419 (70.78)	41 (6.93)	132 (22.30)	<0.001	442 (56.52)	106 (13.55)	234 (29.92)	0.193
Women	342 (61.07)	29 (5.18)	189 (33.75)		436 (60.64)	97 (13.49)	186 (25.87)	
Age	43.08 ± 9.04	45.18 ± 8.90	42.66 ± 9.01	0.107	45.47 ± 10.01	48.44 ± 9.62	42.38 ± 9.74	<0.001
25-34	168 (64.62)	10 (3.85)	82 (31.54)	0.452	157 (52.86)	22 (7.41)	118 (39.73)	<0.001
35-44	264 (67.52)	23 (5.88)	104 (26.60)		272 (59.78)	51 (11.21)	132 (29.01)	
45-54	252 (65.80)	27 (7.05)	104 (27.15)		270 (58.82)	70 (15.25)	119 (25.93)	
55-64	77 (65.25)	10 (8.47)	31 (26.27)		179 (61.72)	60 (20.69)	51 (17.59)	
Immigration								
Luxembourg	406 (66.56)	28 (4.59)	176 (28.85)	0.011	500 (63.61)	77 (9.80)	209 (26.59)	<0.001
Portugal	104 (62.65)	20 (12.05)	42 (25.30)		105 (48.17)	48 (22.02)	65 (29.82)	
Other	251 (66.76)	22 (5.85)	103 (27.39)		273 (54.93)	78 (15.69)	146 (29.38)	
Education								
Primary	147 (63.36)	25 (10.78)	60 (25.86)	0.004	186 (50.27)	89 (24.05)	346 (62.91)	<0.001
Secondary	278 (65.11)	28 (6.56)	121 (28.34)		343 (59.55)	76 (13.19)	37 (6.73)	
Tertiary	335 (68.37)	17 (3.47)	128 (28.16)		346 (62.91)	157 (27.26)	167 (30.36)	
Job								
Not working	NA	NA	NA		204 (58.62)	92 (26.44)	52 (14.94)	<0.001

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managers/professionals	319 (67.58)	16 (3.39)	137 (29.03)	0.023	292 (61.73)	31 (6.55)	150 (31.71)	
technicians/clerical/service occupation	267 (65.60)	29 (7.13)	111 (27.27)		239 (58.44)	43 (10.51)	127 (31.05)	
skilled/unskilled workers	175 (64.10)	25 (9.16)	73 (26.74)		143 (52.77)	37 (13.65)	91 (33.58)	
Smoking								
Never	431 (65.11)	38 (5.74)	193 (29.15)	0.736	477 (58.46)	92 (11.27)	247 (30.27)	0.013
Current	179 (68.32)	18 (6.87)	65 (24.81)		193 (55.46)	59 (16.95)	96 (27.59)	
Ex-smoker	151 (66.52)	14 (6.17)	62 (27.31)		207 (61.61)	52 (15.48)	77 (22.92)	
Alcohol								
Never	41 (60.29)	4 (5.88)	23 (33.82)	0.037	59 (54.13)	17 (15.60)	33 (30.28)	0.005
Drinkers	702 (66.79)	60 (5.71)	289 (27.50)		790 (59.44)	168 (12.64)	371 (27.92)	
Ex-drinkers	18 (54.55)	6 (18.18)	9 (27.27)		29 (46.77)	18 (29.03)	15 (24.19)	
Fruits and vegetables consumption								
<1 portion/day	246 (66.13)	23 (6.18)	103 (27.69)	0.903	257 (55.75)	66 (14.32)	138 (29.93)	0.438
1-4 portions/day	403 (65.53)	40 (6.50)	172 (27.97)		485 (60.40)	108 (13.45)	210 (26.15)	
≥5 portions/day	111 (67.68)	7 (4.27)	46 (28.05)		135 (57.20)	29 (12.29)	72 (30.51)	
Physical Activity								
Never	288 (63.86)	40 (8.87)	123 (27.27)	0.016	319 (52.21)	119 (19.48)	173 (28.31)	<0.001
<=3h/week	272 (65.70)	17 (4.11)	125 (30.19)		302 (59.80)	46 (9.11)	157 (31.09)	
>3h/week	200 (70.42)	12 (4.23)	72 (25.35)		254 (66.67)	38 (9.97)	89 (23.36)	
BMI	26.50 ± 5.00	27.64 ± 4.61	25.82 ± 4.62	0.0097	26.57 ± 5.06	27.56 ± 5.38	26.13 ± 4.78	0.004
<25	329 (65.93)	18 (3.61)	152 (30.46)	0.008	382 (59.50)	72 (11.21)	188 (29.28)	0.183

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25-30	280 (64.22)	35 (8.03)	121 (27.75)	316 (57.14)	81 (14.65)	156 (28.21)
>=30	151 (69.91)	17 (7.87)	48 (22.22)	179 (58.88)	49 (16.12)	76 (25.00)

Values are: numbers (%) for categorical variables and means±standard deviation for continuous variables. BMI: Body Mass Index. NA: not available.

[a] $\chi2$ test for categorical variables, t-test for continuous variables.

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Table 4. Results of multinomial logistic regression measuring the association between sleep duration and chronic conditions in models adjusted for participants socieconomic characteristics and physical activity: European Health Examination Survey in Luxembourg (N =1508).

| | Sleep duration work the next day (N=1,152-working) | | | | Sleep duration do NOT work the next day (N=1,501) | | | |
| | Short (<6hrs/night) | | Long (>7hrs/night) | | Short (<7hrs/night) | | Long (>8 hrs/night) | |
	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)
Chronic conditions/diseases								
0	1	1	1	1	1	1	1	1
1	1.51 (0.66, 3.46)	1.50 (0.65, 3.50)	0.90 (0.64, 1.26)	0.91 (0.64, 1.28)	1.53 (0.88-2.63)	1.48 (0.84-2.59)	0.79 (0.58, 1.08)	0.84 (0.61, 1.16)
2	3.34 (1.52, 7.33)	3.07 (1.36, 6.92)	0.95 (0.65, 1.40)	0.94 (0.63, 1.40)	2.63 (1.54, 4.50)	2.35 (1.34, 4.12)	0.88 (0.62, 1.24)	1.01 (0.70, 1.44)
≥3	3.68 (1.75, 7.69)	3.70 (1.66, 8.22)	0.89 (0.62, 1.27)	0.82 (0.56, 1.21)	3.84 (2.39, 6.15)	2.85 (1.69, 4.81)	0.74 (0.54, 1.01)	0.98 (0.70, 1.38)
Immigration								
Luxembourg		1		1		1		1
Portugal		2.13 (1.01-4.48)		0.85 (0.53-1.37)		1.77 (1.07-2.93)		1.15 (0.76-1.73)
Other		1.72 (0.93-3.20)		0.92 (0.68-1.25)		2.47 (1.68-3.64)		1.28 (0.97-1.69)
Sex								
Men		1		1		1		1
Women		0.63 (0.36-1.09)		1.79 (1.36-2.36)		0.79 (0.56-1.12)		1.28 (1.00-1.64)
Age		1.00 (0.97-1.03)		1.00 (0.98-1.01)		1.00 (0.98-1.02)		0.97 (0.96-0.99)
Education								
Primary		1		1		1		1
Secondary		0.80 (0.40-1.59)		0.96 (0.62-1.50)		0.58 (0.38-0.88)		0.85 (0.59-1.23)
Tertiary		0.45 (0.17-1.18)		0.94 (0.55-1.60)		0.31 (0.17-0.56)		0.76 (0.48-1.19)
Job status								
Unemployed						1		1
managers/professionals		1		1		0.59 (0.33-1.04)		1.92 (1.24-2.96)
technicians/clerical/service occupation		1.46 (0.68-3.11)		0.88 (0.62-1.26)		0.59 (0.37-0.94)		1.83 (1.23-2.73)
skilled/unskilled workers		0.97 (0.39-2.42)		1.07 (0.66-1.75)		0.44 (0.26-0.74)		2.10 (1.34-3.30)
Physical Activity								

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Never	1	1	1	1
≤3h/week	0.61 (0.33-1.14)	1.09 (0.79-1.50)	0.60 (0.40-0.91)	0.96 (0.72-1.28)
>3h/week	0.59 (0.29-1.19)	0.93 (0.65-1.33)	0.54 (0.34-0.83)	0.70 (0.51-0.97)

Note. OR: Odds ratio; AOR: Ajusted Odds ratio; 95% CI: 95% confidence interval.

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SupplementaryTable S1. Sleep problems and duration by chronic conditions/diseases: European Health Examination Survey in Luxembourg.

Variables	Total	Chronic diseases /conditions				P
		0	1	2	≥3	
Diagnosis of sleep disorder (N=1486)	122 (8.21)	11 (9.02)	13 (10.66)	22 (18.03)	76 (62.30)	<0.001
Sleepiness	118 (7.89)	25 (21.19)	26 (22.03)	18 (15.25)	49 (41.53)	0.071
Have difficulties in sleeping the night through (N=1505)	510 (33.89)	84 (16.63)	79 (15.64)	93 (18.42)	249 (49.31)	
Sleep duration						
Num sleep hours when you have to work the next day (N=1,152-working)						
<6h	70 (6.08)	10 (14.29)	13 (18.57)	19 (27.14)	28 (40.00)	0.006
6-7h	761 (66.06)	232 (30.73)	206 (27.28)	133 (17.62)	184 (24.37)	
≥8h	321 (27.86)	103 (32.09)	87 (27.10)	56 (17.45)	75 (23.36)	
Num sleep hours when you do NOT work the next day (N=1,501)						
≤6h	203 (13.52)	25 (12.38)	34 (16.83)	43 (21.29)	100 (49.50)	<0.001
7-8h	878 (58.49)	245 (28.00)	227 (25.94)	150 (17.14)	253 (28.91)	
>8h	420 (27.98)	133 (31.89)	100 (23.98)	75 817.99)	109 (26.14)	

Values are: numbers (%) [a] $\chi 2$ test for categorical variable

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STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	8, 12
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 2 and 3
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 4

		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	6

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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SLEEP DURATION AND MULTIMORBIDITY IN LUXEMBOURG. RESULTS FROM THE EUROPEAN HEALTH EXAMINATION SURVEY IN LUXEMBOURG, 2013-2015

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SLEEP DURATION AND MULTIMORBIDITY IN LUXEMBOURG. RESULTS FROM THE EUROPEAN HEALTH EXAMINATION SURVEY IN LUXEMBOURG, 2013-2015

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Word count: 3401; **Abstract:** 202; **Tables:** 4; **References:** 43

Conflict of interest: The authors declare that they have no conflict of interest.

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Contributorship statement

MRC and SS conceptualized and designed the study. MRC and VB performed the statistical analysis. MRC, SS and T.T.M interpreted the data. MRC drafted the article. SS supervised the study. All authors participated in the revision of the article. All authors contributed to and have approved the final manuscript.

Abstract

Objectives: We estimated the prevalence of short sleep duration and multimorbidity in Luxembourg, and assessed whether sleep duration was associated with multimorbidity after adjusting for socio-demographic and behavioral characteristics.

Design: Cross-sectional study.

Participants: Data from 1508 Luxembourg residents (48% men and 52% women) aged 25 to 64 years came from the European Health Examination Survey 2013-2015.

Outcome measures: Short sleep duration and multimorbidity.

Results: Participants reported sleeping 6.95hrs/night during work days, nearly 1hr less than during non-work days (7.86hrs/night). Nearly half of participants reported having been diagnosed with ≥2 chronic conditions/diseases. Short sleep duration was linearly associated with the number of chronic conditions when participants did not have to work the next day (OR: 1.93, 95% CI: 1.09, 3.40 and OR: 1.77, 95% CI: 1.02, 3.07 for 2, and ≥3 chronic conditions/diseases, respectively), independently of socioeconomic and behavioral characteristics. The effect was stronger when participants had to work the next day (OR: 2.89, 95% CI: 1.27, 6.56, and OR: 2.98, 95% CI: 1.30, 6.87, for 2 and ≥3 chronic conditions/diseases, respectively).

Conclusions: Health promotion programs should aim at improving and promoting healthy sleeping and its possible benefits on chronic disease outcomes, which in turn can help reducing the risk of multimorbidity in middle-aged adults.

Keywords: Sleep duration; multimorbidity; chronic diseases; Luxembourg; European Health Examination Survey

Strengths and limitations of this study

- This is the first study in Luxembourg on the prevalence of sleep patterns, with a focus on short and long sleep duration, and their relationship with multimorbidity.
- The present study was drawn from the European Health Examination Survey in Luxembourg (EHES-LUX), a representative cross-sectional population-based survey.
- Limitations of the present study include the subjective self-reported measure of sleep duration, the cross-sectional design of the study (not allowing to establish a causal link), and the low participation rate.

Data sharing statement: Extra data can be accessed by emailing Dr Laetitia Huiart, Head of the Population Health Department, LIH (laetitia.huiart@lih.lu) and the Principal Investigator of EHES-LUX2013-2015, Dr Maria Ruiz-Castell (maria.ruiz@lih.lu) and fill out a request form.

Introduction

A healthy lifestyle includes healthy sleep habits. Sleep patterns influence several physiological and psychological processes such as inflammation, immune responses, mental and cognitive function, glucose regulation and energy balance (1-3). Short sleep duration, poor sleep quality, and sleep-related disorders can result in sleep deficiency and impact on individual health (4). According to the Centers for Disease Control and Prevention (CDC), insufficient sleep is associated with health problems such as chronic diseases, poor quality of life, mental health, risk of accidents, and lower productivity at work (5). Adequate sleep duration is one of the dimensions needed for good sleep health (6). The American Academy of Sleep Medicine and Sleep Research Society considers that for an adult an average sleep duration of at least 7 hours per night should be recommended (4). However, a high percentage of the population sleeps less than the recommended 7 hours (7). Several factors may affect sleep such as physical activity patterns or eating behaviors, but also socioeconomic factors including job status, marital status and ethnicity (8, 9). Studies have observed an association of lower education and unemployment with both short and long sleep duration (10, 11), while factors such as physical activity and healthy diet seem to improve sleep quality (12, 13). Moreover, diet intake (energy and total fat intake) and nutrients seem to be associated with both short and long sleep duration through multifactorial factors including eating patterns (e.g., time and hours of intake) and variations in hormones related to appetite, such as leptin (14).

Epidemiologic data suggest an association of abnormal sleep duration and poor sleep quality with cardiometabolic problems (e.g. hypertension, diabetes, obesity, cardiovascular diseases), mental disorders (e.g. depression), and mortality (15-18). The observed relationship between short sleep duration and mortality would be especially critical in adults under 65 years of age (18). Few studies so far have focused on possible relationships between sleep patterns and multimorbidity (19, 20). Multimorbidity is defined as the presence of two or more chronic diseases in the same individual (21), and is associated with disability, functional decline, frailty, poor quality of life and mortality (22). In the context of ageing societies, multimorbidity is an increasing global phenomenon (23); its occurrence usually increases with age, though a large proportion of individuals younger than 65 are also affected (24). Definitions of multimorbidity vary, however, and the prevalence differs based on changing definitions, which in turn present significant challenges when attempting to compare results between populations and studies (22).

The aim of the present study was to estimate the prevalence of short sleep duration and multimorbidity in Luxembourg, as well as to assess whether sleep duration was associated with multimorbidity after adjusting for socio-demographic and behavioral characteristics.

Methods

Study population and recruitment

Data were drawn from the European Health Examination Survey in Luxembourg (EHES-LUX). EHES-LUX is a representative cross-sectional population-based survey carried out by the Luxembourg Institute of Health with the objectives of assessing the health status of the population of the Grand-Duchy of Luxembourg, develop national and European health indicators, identify the needs of the population, and evaluate health behaviors. EHES-LUX was conducted between February 2013 and January 2015. Individuals were randomly selected in a one-stage sampling procedure from the national health insurance registry (95% social coverage). Institutionalized individuals (e.g. hospitals, elderly homes) were not included. A total of 1508 residents (excluding 21 pregnant women) of Luxembourg aged 25 to 64 participated in the survey (participation rate of 24.1%) (25). Of them, 7 participants did not reported their sleep habits. A total of 1501 participants had information on multimorbidity and sleep habits. Participants signed an informed consent and were interviewed by trained nurses who also conducted medical examinations. Questionnaires included several health modules (e.g. sleep and nutritional habits, health care, working and living conditions) as well as demographic and socioeconomic characteristics. Medical examinations included measurements such as blood pressure and anthropometry. Sampling weights were calculated to be generalized to the population of Luxembourg in terms of age, sex and district of residence. The study national research ethics committee (Comité national d'éthique de Recherche-CNER) approved the study and it was notified to the Luxemburgish National Commission for Data Protection.

Patient involvement

Participants were not involved in the development of the research question, study design, recruitment or the conduction of the study. Upon request, results from the medical examination were forwarded to the study participants and their medical doctors. General results were presented to the general public in a range of dissemination activities.

Sleep

Sleep duration was assessed using two questions: 1) "How many hours do you normally sleep at night when you have to work the next day?", and 2) "How many hours do you normally sleep at

night when you don't have to work the next day?". Responses to the first question were categorized as short sleep duration (<6hrs/night), medium sleep duration (6-8hrs/night), and long sleep duration (>8hrs/night), in line with previously published studies (8, 26, 27). Responses to the second question were categorized in short sleep duration (≤6hrs/night), medium sleep duration (7-8hrs/night), and long sleep duration (>8hrs/night) . The main reason why we used two different cutoffs was due to the marked difference observed between sleep hours during workdays and non-work days (approximately one-hour difference). Therefore, the number of participants who were at the extremes (e.g. < 6 hours and >8hours during the days when not having to work the next day) had very small sample size.

Sleep disorders and sleep quality were assessed with the following variables: difficulty in sleeping the night, diagnosis of sleep disorders, sleep medication and sleepiness. Difficulty in sleeping the night was assessed based on the question "Do you have difficulties in sleeping through the night?". Diagnosis of sleep disorders was assessed using the question "Have you ever been told by a doctor or another health professional that you have a sleep disorder?". Sleep medications were assessed using the question "In the past 2 weeks, have you used other types of medicines that were prescribed to you ?". The question was aimed at answering about several medications including sleep tablets. Sleepiness was defined as a score of ≥11 on the Epworth Sleepiness Scale (28).

Multimorbidity

Participants were asked if they ever had a chronic disease or condition diagnosed by a medical doctor (e.g., hypertension, high cholesterol, diabetes, cardiovascular diseases, stomach or duodenal ulcer, cirrhosis or other liver disease, urinary incontinence, kidney problems, chronic back or neck disorder, rheumatoid arthritis, arthrosis, osteoporosis, cancer, severe headache as migraine or chronic anxiety). Cardiovascular diseases included coronary heart disease or angina pectoris, heart attack or its chronic consequences, stroke or its chronic consequences. Based on this information, the variable "ever being diagnosed with a chronic disease or condition" was generated with four categories: 0, 1, 2 and ≥3 chronic disease or condition. Multimorbidity was defined as having two or more chronic diseases or conditions diagnosed by a medical doctor.

Explanatory variables

Sociodemographic characteristics included age, sex and immigration status. As Portuguese are the largest immigrant community in Luxembourg, immigration status was categorized in non-immigrant, immigrant born in Portugal, and immigrant born in other countries. Socioeconomic status included education (primary, secondary and tertiary education completed) and job status

(unemployed; managers/professionals; technical/clerical/service occupation; skilled/unskilled workers).

Lifestyles included smoking (never; current; ex-smokers), alcohol consumption (never; ex-drinkers; drinkers), physical activity (never; ≤ 3hrs/week of sports, fitness, and/or recreational activities which lasted at least 10 consecutive minutes; >3hrs/week of sports, fitness, and/or recreational activities which lasted at least 10 consecutive minutes), and vegetable and fruit consumption (< 1 portion/ day, 1–4 portions/day, ≥ 5 portions/day). Weight and height were measured by trained nurses and used to calculate body mass index (BMI; kg/m^2). BMI was categorized as normal body weight (<25 kg/m^2), overweight (25-29.99 kg/m^2) and obesity (≥30kg/m^2).

Statistical data analysis

Means and frequencies were used for descriptive purposes. We calculated the prevalence of sleep disorders, short and long sleep duration, chronic conditions/diseases and multimorbidity. Percentages did not include missing values. A chi-square test (χ2) or Student t-test were used to analyze associations between the prevalence of sleep duration and covariates and the prevalence of multimorbidy and covariates. The association between sleep duration and chronic conditions/diseases was assessed using multinomial logistic regression models (reference for sleep duration when having to work the next day was 6-8hrs per night and reference for sleep duration when not having to work the next day was 7-8hrs) adjusted for sociodemographic characteristics, behavioural risk factors (e.g. BMI, smoking, alcohol consumption and physical activity), as well as for measures of sleep disorders and sleep quality. We did sensitivity analysis using the same categories for sleep duration for working days and days when not having to work the following day (<6hrs/night; 6-8hrs/night; >8hrs/night). We considered a P<0.05 statistically significant. To be representative of the population and avoid biased estimates, the observations were weighted. Participants with missing values on sleep habits and or murltimorbidity were not included in the present analysis. Analyses were performed using STATA 14.0 and and SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Table 1 shows the prevalence of chronic conditions/diseases, multimorbidity, sleep duration and sleep disorders. Nearly half of participants reported being diagnosed with two or more chronic conditions/ diseases, and nearly a third of participants reported being diagnosed with three or more chronic conditions/diseases. The most prevalent diseases were chronic low back disorder or other chronic back defect followed by hypercholesterolemia, arthrosis and hypertension. More than 8% of participants were diagnosed with a sleep disorder, a third reported having difficulties in sleeping

through the night and 4.3% reported taking sleep medication. Participants reported sleeping 7.86hrs/night when they did not have to work the next day, nearly one hour more than when they had to work the next day (6.95hrs/night). Moreover, 6.08% of the Luxembourg population reported sleeping less than 6 hours during working days, a percentage that was reduced to almost half (3.93%) when participants did not have to work the next day.

Participant characteristics by chronic conditions/diseases are shown in **Table 2**. More men than women presented three or more chronic diseases. Higher number of chronic diseases/conditions increased with age: those aged 55 to 64 presented more chronic conditions compared to those aged 25-34. Immigrants born in Portugal presented more chronic conditions than non-immigrants and other immigrants. Participants being less educated and unemployed presented more chronic conditions compared to those employed and highly educated. Participants being less physically active and with obesity presented more chronic conditions/diseases than those being more physically active and with a lower BMI.

Participant characteristics by sleep duration are shown in **Table 3**. When participants had to work the following day, more men than women reported a medium sleep duration. Short sleep duration was more likely among immigrants born in Portugal, participants with lower education and skilled/unskilled workers. Short sleep duration was less common among those being physically active and with a BMI less than 25 Kg/m². When participants did not have to work the next day, short sleep duration was more common among older individuals, immigrants born in Portugal, unemployed people, and those being less physically active. Long sleep duration was observed among participants with lower education. No differences in sleep duration were observed between men and women.

Table 4 shows results from multinomial logistic regression analyses examining the association between sleep duration and chronic conditions/diseases, and adjusted by sociodemographic characteristics, behavioural risk factors, socioeconomic position, as well as for measures of sleep disorders and sleep quality. Among participants who reported sleep hours when they did not have to work the next day, those sleeping less hours (≤6h) were 1.93 and 1.77 times as likely to report having 2 and 3 or more chronic conditions after adjusting for covariates. In fully adjusted models, the strength of associations between sleep duration and multimorbidity remained statistically significant. The same association (although more accentuated) was observed in those participant with a job at the moment of the survey who reported the number of sleep hours when they had to work the next day: those sleeping less hours (<6h) were 2.89 and 2.98 times as likely to report having 2 and 3 or more chronic conditions after adjusting for covariates.

Estimates of sleep problems and chronic conditions are presented in **Table S1**. The prevalence of sleep problems was high, with one out of three participants having difficulties in sleeping the night through and nearly 8% of participants diagnosed with a sleep disorder. In all cases, the percentage of participants with sleep problems increased with the number of chronic diseases. Sensitivity analysis examining the association between sleep duration and chronic conditions/diseases are presented in **Table S2**, using the same cut points for sleep duration categories for both workdays and non-work days. We observed the same trend as in Table 4 with consistent associations of short sleep duration with the number of chronic conditions.

Discussion

Results from the present nationwide population-based study show for the first time in Luxembourg the prevalence of sleep patterns, with a focus on short and long sleep duration, as well as their association with multimorbidity. The prevalence of short sleep duration in Luxembourg is 6.08% when having to work the following day, and 3.93% when not having to work the following day. Results are similar to those observed internationally (27, 29), although in countries such as Brazil the prevalence of short sleep duration was nearly 22% (30), and in Portugal and the United States values reached up to 20% in 2015-2016 and 11.8% in 2014, respectively (31, 32). However, in the present study the age range from 25 to 64 years must be considered since it does not include adults over 65 years old who generally sleep less hours. This means that the overall prevalence of the Luxembourg population sleeping less than the recommended hours is likely to be higher, when including older adults as well.

Multimorbidity is highly prevalent in Luxembourg, especially when taking into account the fact that the study population was up to 65 years, which represents a relatively young population, as multimorbidity prevalence naturally increases with age (22). Nearly half of participants had two or more chronic diseases and 31% had three or more chronic diseases/conditions.

In our study, we observed that short sleep duration was significantly associated with the number of chronic conditions independently of socioeconomic, behavioral characteristics and sleep disorders, an effect accentuated during working days, when sleep hours are reduced. Our results are in line with those from other studies that observed an association between sleep and number of chronic diseases, although previous studies have been usually performed in populations of older adults (e.g. over 50 years old) (19, 33). As observed by Koyanagi et al., sleep problems increase with the number of diseases in both low and high income countries independent of their economic development (19). These associations could explain the observed relationship between sleep duration (under the recommended 7 hours) and poor sleep quality with mortality, even among

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adults younger than 65 years old (18). It is not clear if sleep problems are a consequence of chronic diseases (e.g. conditions affecting sleep) or part of the cause (sleep predispose the individual to more diseases or exacerbates the symptoms), although it is plausible that both sleep problems and chronic diseases are linked by a bidirectional association (34). Although both sleep deprivation and the number of chronic diseases increase with age, and are more prevalent in older adults, our study shows that the prevalence is also high in adults under 65 and the association begins much earlier. It is therefore necessary to detect these problems earlier in order to improve individual health and general wellbeing and reduce mortality, particularly in the context of ageing populations burdened by the accumulation of multiple chronic conditions over time. In our study, we also observed that short sleep duration was associated with immigration status, at least for the sleep categories during non-working days. The relationship between immigration status and sleep patterns remains unclear, possibly related to stress linked to the migratory process, cultural adaptation, or working conditions in the host country (35, 36). In our study, Portuguese immigrants were more likely to sleep less than 6h per night during workdays and less than 7h during non-working days. Portuguese are the largest immigrant community in Luxembourg, accounting for 16% of the 46% immigrant population living in Luxembourg. Compared to Luxembourgish natives, Portuguese immigrants have a lower socioeconomic status (37) (including income, education and employment) which could partly explain why they have a greater likelihood of being short sleepers. However, after adjusting for sleep disorders the association with short sleep duration was only maintained for non-work-days.

In our study, long sleep duration was more common in women. This was in line with other studies showing that men usually sleep less hours, although women reported having more sleep problems (38). However, this relationship is complex and could depend on family composition (e.g. single parents have shorter sleep duration, particularly women) (39).

In terms of potential mechanisms to corroborate the biological plausibility of the link between short sleep duration and multimorbidity, sleep deprivation has been associated with a number of chronic conditions, including cardio-metabolic and neurodegenerative disease, cancer, musculoskeletal disorders, and mental problems (15, 16). Experimental evidence corrobores the plausibility of deleterious effects of lack of sleep on endocrine, immune, neurovegetative and inflammatory pathways (1-3). Sustained sleep deprivation could be related to chronic conditions through its impact on the ciercadian rhythm and its association with hormonal (e.g. insulin resistance and decrease leptin) and autonomic nervous system changes (increase the activity of the sympathetic nervous system) (40).

In addition, sleep deprivation often cluster with other behavioral risk factors such as cigarette smoking, heavy drinking, and physical inactivity, which may in turn increase the risk of chronic disease. However, in our study, we only observed an association between physical activity and short sleep duration during days when not having to work the following day, with no association observed between short sleep duration and smoking or alcohol consumption. Regular physical activity would reduce the likelihood of short and/or long sleep duration and maintain an optimal duration. Studies have observed an association between physical activity and sleep, improving quality of sleep, sleep efficiency, and total sleep time (12, 41).

Limitations of the present study include the subjective measure of sleep duration (self-reported number of hours of sleep) instead of an objective measure (e.g. actigraphy, polysomnography). However, in the absence of an objective measure, there is a moderate correlation between objective and subjective measurements, a correlation that is high during weekdays possibly due to routines (42), but may be attenuated based on certain individual characteristics (e.g. presence of conditions such as depression, sociodemographic characteristics) (43). Other limitations include the fact that we did not include other sleep problems such as insomnia or sleep apnea nor environmental factors such as noise, traffic or commuting, all of which could affect sleep duration. In addition, multimorbidity was also self-reported based on a restricted list of diseases in the questionnaire, therefore participants may have not reported additional conditions, which may produce a possible underestimation of multimorbidity prevalence. Information on non-responders was not available, and despite being a representative sample of the Luxembourg population (in terms of age, sex and district), we could not determine the possibility of a non-response bias. In our study, we only included the number of sleep hours during the night, without including nap times. For this reason, the categories used here are slightly different from the recommendations of daily sleep hours. Finally, it should be noted that the study design (cross-sectional) does not allow to ascertain a causal link between sleep and multimorbidity; in addition, the low participation rate may affect the generalizability of our results.

This is the first study in Luxembourg on the prevalence of sleep patterns, with a focus on short and long sleep duration, and their relationship with multimorbidity. Sleep deprivation, having difficulties in sleeping the night through, sleep disorders and sleeping medication represent a neglected public health problem, especially when associated with a number of chronic conditions and diseases, thus producing a negative impact on the wellbeing and general health status of the population. Sleep hygiene should be considered as an additional important health behavior along with diet, smoking and physical activity, both in clinical and public health practice. As both sleep

problems and multimorbidity are highly prevalent in Luxembourg, health promotion programs should be developed to improve and promote healthy sleeping habits among the general population, which in turn may be beneficial in the prevention and management of a number of chronic disease outcomes, including the occurrence of multimorbidity.

Acknowledgements

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Table 1. Chronic diseases/conditions, multimorbidity and sleep: European Health Examination Survey in Luxembourg (N =1508).

	N (%) / Mean ± SD
Hypertension	250 (16.59)
High cholesterol	458 (30.39)
Diabetes	69 (4.58)
Coronary heart disease or angina pectoris	26 (1.73)
Myocardial infarction or chronic consequences of myocardial infarction	14 (0.93)
Stroke or chronic consequences of stroke	11 (0.73)
Stomach or duodenal ulcer	81 (5.37)
Cirrhosis of the liver or other liver disease	46 (3.05)
Urinary incontinence, problems in controlling the bladder	74 (4.91)
Kidney problems	108 (7.17)
Chronic low back disorder or other chronic back defect	489 (32.47)
Chronic neck disorder or other chronic neck defect	246 (16.32)
Rheumatoid arthritis	88 (5.85)
Arthrosis	292 (19.38)
Osteoporosis	44 (2.92)
Cancer	54 (3.59)
Severe headache such as migraine	271 (17.98)
Chronic anxiety	98 (6.50)
Depression	204 (13.54)
Number of chronic diseases	
0	405 (27.00)
1	362 (24.13)

≥2 (multimorbidity)	733 (49.00)
≥3	465 (31.00)
Sleep	
Diagnosis of sleep disorder	122 (8.21)
Sleepiness [a]	118 (7.89)
Have difficulties in sleeping the night through	510 (33.89)
Sleeping medication	64 (4.26)
Sleep duration	
Hours when you have to work the next day (N=1,152-working)	6.95±0.97
<6hrs/night	70 (6.08)
6-8hrs/night	1,040 (90.28)
>8hrs/night	42 (3.65)
Hours when you don't work the next day (N=1,501)	7.86±1.30
≤6hrs/night	203 (13.52)
7-8hrs/night	878 (58.49)
>8hrs/night	420 (27.98)

N=number, SD=standard deviation

[a] Measured with Epworth Sleepiness Scale

Table 2. Participant characteristics by chronic conditions/diseases: European Health Examination Survey in Luxembourg (N =1508).

	Chronic conditions/diseases				
	0	1	2	≥3	P[a]
Sex					
Men	199 (27.72)	199 (27.72)	143 (19.92)	177 (24.65)	<0.001
Women	206 (26.34)	163 (20.84)	125 (15.98)	288 (36.83)	
Age					
25-34	130 (43.62)	86 (28.86)	48 (16.11)	34 (11.41)	<0.001
35-44	156 (34.29)	119 (26.15)	69 (15.16)	111 (24.40)	
45-54	83 (18.16)	111 (24.29)	98 (21.44)	165 (36.11)	
55-64	36 (12.41)	46 (15.86)	53 (18.28)	155 (53.45)	
Immigration					
Luxembourg	184 (23.44)	197 (25.10)	144 (18.34)	260 (33.12)	<0.001
Portugal	52 (23.85)	42 (19.27)	45 (20.64)	79 (36.24)	
Other	169 (34.00)	123 (24.75)	79 (15.90)	126 (25.35)	
Education					
Primary	68 (18.38)	75 (20.27)	64 (17.30)	163 (44.05)	<0.001
Secondary	133 (23.05)	142 (24.61)	106 (18.37)	196 (33.97)	
Tertiary	203 (37.04)	145 (26.46)	97 (17.70)	103 (18.80)	
Job					
Not working	58 (16.67)	56 (16.09)	58 (16.67)	176 (50.57)	<0.001
managers/professionals	168 (35.59)	138 (29.24)	73 (15.47)	93 (19.70)	
technicians/clerical/service occupation	119 (29.38)	89 (21.98)	76 (18.77)	121 (29.88)	

skilled/unskilled workers	60 (21.90)	79 (28.83)	61 (22.26)	74 (27.01)	
Smoking					
Never	239 (29.25)	209 (25.58)	145 (17.75)	224 (27.42)	0.026
Current	90 (26.01)	75 (21.68)	63 (18.21)	118 (34.10)	
Ex-smoker	74 (22.09)	78 (23.28)	60 (17.91)	123 (36.72)	
Alcohol					
Never	30 (27.78)	21 (19.44)	20 (18.52)	37 (34.26)	0.055
Drinkers	365 (27.53)	328 (24.74)	234 (17.65)	399 (30.09)	
Ex-drinkers	8 (12.50)	13 (20.31)	14 (21.88)	29 (45.31)	
Fruits and vegetables consumption					
<1 portion/day	126 (27.39)	112 (24.35)	87 (18.91)	135 (29.35)	0.597
1-4 portions/day	223 (27.81)	183 (22.82)	142 (17.71)	254 (31.67)	
≥5 portions/day	55 (23.31)	66 (27.97)	39 (16.53)	76 (32.20)	
Physical Activity					
Never	130 (21.35)	133 (21.84)	125 (20.53)	221 (36.29)	<0.001
<=3h/week	151 (29.84)	130 (25.69)	77 (15.22)	148 (29.25)	
>3h/week	121 (31.84)	98 (25.79)	65 (17.11)	96 (25.26)	
BMI	25.27 ± 4.06	26.04 ± 4.89	26.66 ± 4.96	28.07 ± 5.56	<0.001
<25	212 (33.02)	169 (26.32)	112 (17.45)	149 (23.21)	<0.001
25-30	152 (27.39)	131 (23.60)	100 (18.02)	172 (30.99)	
>=30	41 (13.62)	61 (20.27)	55 (18.27)	144 (47.84)	

Values are: numbers (%) for categorical variables and means±standard deviation for continuous variables. BMI: Body Mass Index.[a] χ2 test for categorical variables, t-test for continuous variables.

Table 3. Participant's characteristics by Sleep duration: European Health Examination Survey in Luxembourg (N =1508).

	Sleep hours when you have to work the next day (N=1,152-working)				Sleep hours when you do NOT work the next day (N=1,501)			
	<6hrs/night	6-8hrs/night	>8hrs/night	P [a]	≤6hrs/night	7-8hrs/night	>8hrs/night	P [a]
Sex								
Men	41 (6.93)	537 (90.71)	14 (2.36)	0.031	97 (13.49)	436 (60.64)	186 (25.87)	0.193
Women	29 (5.18)	503 (89.82)	28 (5.00)		106 (13.55)	442 (56.52)	234 (29.92)	
Age	45.18 ± 8.90	43.02 ± 9.02	41.40 ± 9.40	0.072	48.44 ± 9.62	45.47 ± 10.01	42.38 ± 9.74	<0.001
25-34	10 (3.85)	237 (91.15)	13 (5.00)	0.264	22 (7.41)	157 (52.86)	118 (39.73)	<0.001
35-44	23 (5.88)	352 (90.03)	16 (4.09)		51 (11.21)	272 (59.78)	132 (29.01)	
45-54	27 (7.05)	347 (90.60)	9 (2.35)		70 (15.25)	270 (58.82)	119 (25.93)	
55-64	10 (8.47)	104 (88.14)	4 (3.39)		60 (20.69)	179 (61.72)	51 (17.59)	
Immigration								
Luxembourg	28 (4.59)	558 (91.48)	24 (3.93)	0.015	77 (9.80)	500 (63.61)	209 (26.59)	<0.001
Portugal	20 (12.05)	139 (83.73)	7 (4.22)		48 (22.02)	105 (48.17)	65 (29.82)	
Other	22 (5.85)	343 (91.22)	11 (2.93)		78 (15.69)	273 (54.93)	146 (29.38)	
Education								
Primary	25 (10.78)	198 (85.34)	9 (3.88)	0.002	89 (24.05)	186 (50.27)	346 (62.91)	<0.001
Secondary	28 (6.56)	380 (88.99)	19 (4.45)		76 (13.19)	343 (59.55)	37 (6.73)	
Tertiary	17 (3.47)	459 (93.67)	14 (2.86)		157 (27.26)	346 (62.91)	167 (30.36)	
Job								
Not working	NA	NA	NA	0.004	92 (26.44)	204 (58.62)	52 (14.94)	<0.001
managers/professionals	16 (3.39)	440 (93.22)	16 (3.39)		31 (6.55)	292 (61.73)	150 (31.71)	
technicians/clerical/service occupation	29 (7.13)	367 (90.17)	11 (2.70)		43 (10.51)	239 (58.44)	127 (31.05)	
skilled/unskilled workers	25 (9.16)	233 (85.35)	15 (5.49)		37 (13.65)	143 (52.77)	91 (33.58)	
Smoking								

Never	38 (5.74)	597 (90.18)	27 (4.08)	0.850	92 (11.27)	477 (58.46)	247 (30.27)	0.013
Current	18 (6.87)	237 (90.46)	7 (2.67)		59 (16.95)	193 (55.46)	96 (27.59)	
Ex-smoker	14 (6.17)	205 (90.31)	8 (3.52)		52 (15.48)	207 (61.61)	77 (22.92)	
Alcohol								
Never	4 (5.88)	58 (85.29)	6 (8.82)	0.006	17 (15.60)	59 (54.13)	33 (30.28)	0.005
Drinkers	60 (5.71)	957 (91.06)	34 83.24)		168 (12.64)	790 (59.44)	371 (27.92)	
Ex-drinkers	6 (18.18)	25 (75.76)	2 (6.06)		18 (29.03)	29 (46.77)	15 (24.19)	
Fruits and vegetables consumption								
<1 portion/day	23 (6.18)	337 (90.59)	12 (3.23)	0.858	66 (14.32)	257 (55.75)	138 (29.93)	0.438
1-4 portions/day	40 (6.50)	551 (89.59)	24 (3.90)		108 (13.45)	485 (60.40)	210 (26.15)	
≥5 portions/day	7 (4.27)	151 (92.07)	6 (3.66)		29 (12.29)	135 (57.20)	72 (30.51)	
Physical Activity								
Never	40 (8.87)	387 (85.81)	24 (5.32)	0.002	119 (19.48)	319 (52.21)	173 (28.31)	<0.001
<=3h/week	17 (4.11)	385 (93.00)	12 (2.90)		46 (9.11)	302 (59.80)	157 (31.09)	
>3h/week	12 (4.23)	266 (93.66)	6 (2.11)		38 (9.97)	254 (66.67)	89 (23.36)	
BMI	27.64 ± 4.61	26.33 ± 4.89	25.52 ± 5.01	0.049	27.56 ± 5.38	26.57 ± 5.06	26.13 ± 4.78	0.004
<25	18 (3.61)	457 (91.58)	24 (4.81)	0.011	72 (11.21)	382 (59.50)	188 (29.28)	0.183
25-30	35 (8.03)	390 (89.45)	11 (2.52)		81 (14.65)	316 (57.14)	156 (28.21)	
>=30	17 (7.87)	192 (88.89)	7 (3.24)		49 (16.12)	179 (58.88)	76 (25.00)	

Values are: numbers (%) for categorical variables and means±standard deviation for continuous variables. BMI: Body Mass Index. NA: not available.

[a] $\chi 2$ test or Fisher's exact test for categorical variables, t-test for continuous variables.

Table 4. Results of multinomial logistic regression measuring the association between sleep duration and chronic conditions in models adjusted for participants socieconomic characteristics and physical activity: European Health Examination Survey in Luxembourg (N =1508).

	Sleep duration work the next day (N=1,146-working)				Sleep duration do NOT work the next day (N=1,501)			
	Short (<6h)		Long (>8h)		Short (≤6h)		Long (>8h)	
	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)
Chronic conditions/diseases								
0	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1	1.72 (0.76, 3.87)	**1.68 (0.72, 3.88)**	1.88 (0.84, 4.21)	1.84 (0.79, 4.26)	1.53 (0.88, 2.63)	1.27 (0.72, 2.23)	0.79 (0.58, 1.08)	0.84 (0.61, 1.16)
2	3.22 (1.47, 7.05)	**2.89 (1.27, 6.56)**	1.99 (0.83, 4.76)	1.87 (0.75, 4.65)	2.63 (1.54, 4.50)	**1.93 (1.09, 3.40)**	0.88 (0.62, 1.24)	1.11 (0.77, 1.59)
≥3	4.06 (1.95, 8.43)	**2.98 (1.30, 6.87)**	0.86 (0.31, 2.43)	0.94 (0.31, 2.89)	3.84 (2.39, 6.15)	**1.77 (1.02, 3.07)**	0.74 (0.54, 1.01)	1.10 (0.76, 1.60)
Immigration								
Luxembourg		1.00		1.00		1.00		1.00
Portugal		1.64 (0.88, 3.06)		0.70 (0.25, 1.94)		**1.89 (1.09, 3.27)**		1.24 (0.81, 1.89)
Other		1.90 (0.87, 4.16)		0.68 (0.31, 1.50)		**2.50 (1.66, 3.76)**		1.27 (0.95, 1.68)
Sex								
Men		1.00		1.00		1.00		1.00
Women		**0.48 (0.26, 0.87)**		**2.32 (1.12, 4.80)**		**0.67 (0.45, 0.99)**		**1.33 (1.02, 1.73)**
Age		0.99 (0.96, 1.02)		0.98 (0.95,1.02)		1.00 (0.98, 1.02)		**0.97 (0.96, 0.99)**
Education								
Primary		1.00		1.00		1.00		1.00
Secondary		0.85 (0.41, 1.78)		1.43 (0.53, 3.88)		**0.66 (0.41, 1.04)**		0.90 (0.61, 1.31)
Tertiary		0.50 (0.18, 1.37)		0.97 (0.26, 3.65)		**0.35 (0.18, 0.66)**		0.75 (0.47, 1.20)
Job status								
Unemployed						1.00		1.00
managers/professionals		1.00		1.00		0.56 (0.31, 1.02)		**2.08 (1.33, 3.25)**
technicians/clerical/service occupation		1.51 (0.70, 3.27)		0.63 (0.24, 1.64)		**0.61 (0.37, 0.95)**		**1.99 (1.32, 3.01)**

skilled/unskilled workers	1.14 (0.45, 2.90)	1.96 (0.64, 5.99)	**0.49 (0.28, 0.86)**	**2.17 (1.36, 3.47)**
Physical Activity				
Never	1.00	1.00	1.00	1.00
≤3h/week	0.60 (0.32, 1.15)	0.47 (0.22, 1.00)	**0.64 (0.41, 0.99)**	0.91 (0.67, 1.22)
>3h/week	0.64 (0.31, 1.34)	0.40 (0.16, 1.04)	**0.60 (0.37, 0.95)**	**0.69 (0.50, 0.97)**
BMI				
Normal	1.00	1.00	1.00	1.00
Overweight	1.55 (0.82, 2.93)	0.61 (0.28, 1.32)	1.00 (0.66, 1.52)	1.06 (0.80, 1.40)
Obese	1.12 (0.52, 2.41)	0.64 (0.25, 1.66)	0.76 (0.46, 1.23)	0.84 (0.59, 1.20)
Smoking				
Never	1.00	1.00	1.00	1.00
Current	0.94 (0.51, 1.76)	0.63 (0.26, 1.57)	1.12 (0.73, 1.71)	0.89 (0.65, 1.22)
Ex-smokers	0.81 (0.40, 1.63)	1.14 (0.49, 2.66)	0.97 (0.63, 1.50)	0.85 (0.61, 1.18)
Alcohol				
Never	1.00	1.00	1.00	1.00
Drink	3.82 (0.78, 18.70)	1.13 (0.19, 6.70)	2.29 (0.89, 5.90)	1.21 (0.53, 2.77)
Ex-drinker	1.29 (0.37, 4.56)	0.45 (0.16, 1.24)	1.29 (0.64, 2.61)	1.10 (0.67, 1.80)
Sleeping medication	2.61 (0.87, 7.87)	0.00 (0.00, >999.99)	1.61 (0.78, 3.32)	1.58 (0.75, 3.32)
Sleep disorder diagnosis	0.99 (0.40, 2.51)	0.83 (0.14, 4.74)	1.32 (0.76, 2.30)	1.04 (0.61, 1.78)
Difficulties in sleeping the night	1.72 (0.97, 3.04)	0.90 (0.42, 1.93)	**2.35 (1.62, 3.42)**	**0.62 (0.46, 0.83)**
Sleepiness	**2.83 (1.39, 5.78)**	0.86 (0.23, 3.20)	**2.45 (1.42, 4.25)**	0.71 (0.42, 1.19)

Note. OR: Odds ratio; AOR: Ajusted Odds ratio; 95% CI: 95% confidence interval.

SupplementaryTable S1. Sleep problems and duration by chronic conditions/diseases: European Health Examination Survey in Luxembourg.

Variables	Total	Chronic diseases /conditions				P
		0	1	2	≥3	
Diagnosis of sleep disorder (N=1486)	122 (8.21)	11 (9.02)	13 (10.66)	22 (18.03)	76 (62.30)	<0.001
Sleepiness	118 (7.89)	25 (21.19)	26 (22.03)	18 (15.25)	49 (41.53)	0.071
Have difficulties in sleeping the night through (N=1505)	510 (33.89)	84 (16.63)	79 (15.64)	93 (18.42)	249 (49.31)	
Sleep duration						
Num sleep hours when you have to work the next day (N=1,152-working)						
<6h	70 (6.08)	10 (14.29)	13 (18.57)	19 (27.14)	28 (40.00)	0.006
6-7h	761 (66.06)	232 (30.73)	206 (27.28)	133 (17.62)	184 (24.37)	
≥8h	321 (27.86)	103 (32.09)	87 (27.10)	56 (17.45)	75 (23.36)	
Num sleep hours when you do NOT work the next day (N=1,501)						
≤6h	203 (13.52)	25 (12.38)	34 (16.83)	43 (21.29)	100 (49.50)	<0.001
7-8h	878 (58.49)	245 (28.00)	227 (25.94)	150 (17.14)	253 (28.91)	
>8h	420 (27.98)	133 (31.89)	100 (23.98)	75 817.99)	109 (26.14)	

Values are: numbers (%) [a] χ2 test for categorical variable

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SupplementaryTable S2. Results of multinomial logistic regression measuring the association between sleep duration (Short (<6hrs/night); long (>8hrs/night) and chronic conditions in models adjusted for participants sociodemographic characteristics, behavioural risk factors and measures of sleep disorders and sleep quality: European Health Examination Survey in Luxembourg (N =1508). Sensitivity analysis.

| | Sleep duration work the next day (N=1,146-working) | | | | Sleep duration do NOT work the next day (N=1,501) | | | |
| | Short (<6h) | | Long (>8h) | | Short (<6h) | | Long (>8h) | |
	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)
Chronic conditions/diseases								
0	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
1	1.72 (0.76, 3.87)	1.68 (0.72, 3.88)	1.88 (0.84, 4.21)	1.84 (0.79, 4.26)	3.08 (0.65, 14.62)	2.61 (0.53, 12.95)	0.77 (0.57, 1.05)	0.83 (0.60, 1.14)
2	3.22 (1.47, 7.05)	2.89 (1.27, 6.56)	1.99 (0.83, 4.76)	1.87 (0.75, 4.65)	6.03 (1.35, 26.97)	3.59 (0.75, 17.23)	0.83 (0.59, 1.15)	1.04 (0.73, 1.49)
≥3	4.06 (1.95, 8.43)	2.98 (1.30, 6.87)	0.86 (0.31, 2.43)	0.94 (0.31, 2.89)	17.27 (4.36, 68.47)	5.38 (1.20, 24.13)	0.65 (0.48, 0.88)	1.06 (0.74, 1.53)
Immigration								
Luxembourg		1.00		1.00		1.00		1.00
Portugal		1.64 (0.88, 3.06)		0.70 (0.25, 1.94)		2.74 (1.02, 7.37)		1.16 (0.77, 1.74)
Other		1.90 (0.87, 4.16)		0.68 (0.31, 1.50)		2.90 (1.37, 6.15)		1.16 (0.88, 1.53)
Sex								
Men		1.00		1.00		1.00		1.00
Women		0.48 (0.26, 0.87)		2.32 (1.12, 4.80)		0.44 (0.21, 0.90)		1.38 (1.06, 1.78)
Age		0.99 (0.96, 1.02)		0.98 (0.95,1.02)		1.01 (0.97, 1.05)		0.98 (0.96, 0.99)
Education								
Primary		1.00		1.00		1.00		1.00
Secondary		0.85 (0.41, 1.78)		1.43 (0.53, 3.88)		1.00 (0.45, 2.24)		0.98 (0.68, 1.41)
Tertiary		0.50 (0.18, 1.37)		0.97 (0.26, 3.65)		0.52 (0.16, 1.66)		0.87 (0.55, 1.37)
Job status								
Unemployed						1.00		1.00
managers/professionals		1.00		1.00		0.42 (0.13, 1.35)		2.21 (1.42, 3.44)
technicians/clerical/service occupation		1.51 (0.70, 3.27)		0.63 (0.24, 1.64)		0.84 (0.37, 1.88)		2.16 (1.44,3.24)
skilled/unskilled workers		1.14 (0.45, 2.90)		1.96 (0.64, 5.99)		0.17 (0.05, 0.62)		2.35 (1.49, 3.70)

Physical Activity				
Never	1.00	1.00	1.00	1.00
≤3h/week	0.60 (0.32, 1.15)	0.47 (0.22, 1.00)	0.58 (0.25, 1.33)	0.96 (0.72, 1.28)
>3h/week	0.64 (0.31, 1.34)	0.40 (0.16, 1.04)	0.79 (0.34, 1.82)	0.74 (0.54, 1.03)
BMI				
Normal	1.00	1.00	1.00	1.00
Overweight	1.55 (0.82, 2.93)	0.61 (0.28, 1.32)	0.95 (0.44, 2.04)	1.06 (0.80, 1.39)
Obese	1.12 (0.52, 2.41)	0.64 (0.25, 1.66)	0.66 (0.27, 1.59)	0.87 (0.61, 1.23)
Smoking				
Never	1.00	1.00	1.00	1.00
Current	0.94 (0.51, 1.76)	0.63 (0.26, 1.57)	1.06 (0.49, 2.30)	0.89 (0.66, 1.20)
Ex-smokers	0.81 (0.40, 1.63)	1.14 (0.49, 2.66)	0.70 (80.31, 1.61)	0.85 (0.62, 1.17)
Alcohol				
Never	1.00	1.00	1.00	1.00
Drink	3.82 (0.78, 18.70)	1.13 (0.19, 6.70)	1.39 (0.32, 6.08)	1.02 (0.46, 2.27)
Ex-drinker	1.29 (0.37, 4.56)	0.45 (0.16, 1.24)	0.68 (0.22, 2.09)	1.04 (0.65, 1.69)
Sleeping medication	2.61 (0.87, 7.87)	0.00 (0.00, >999.99)	1.72 (0.64, 4.65)	1.46 (0.72, 2.99)
Sleep disorder diagnosis	0.99 (0.40, 2.51)	0.83 (0.14, 4.74)	1.69 (0.76, 3.78)	0.99 (0.60, 1.67)
Difficulties in sleeping the night	1.72 (0.97, 3.04)	0.90 (0.42, 1.93)	6.47 (2.83, 14.80)	0.57 (0.43, 0.77)
Sleepiness	2.83 (1.39, 5.78)	0.86 (0.23, 3.20)	1.32 (0.49, 3.57)	0.62 (0.37, 1.01)

Note. OR: Odds ratio; AOR: Ajusted Odds ratio; 95% CI: 95% confidence interval.

STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	8, 12
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 2 and 3
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 4

		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	6

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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SLEEP DURATION AND MULTIMORBIDITY IN LUXEMBOURG. RESULTS FROM THE EUROPEAN HEALTH EXAMINATION SURVEY IN LUXEMBOURG, 2013-2015

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SLEEP DURATION AND MULTIMORBIDITY IN LUXEMBOURG. RESULTS FROM THE EUROPEAN HEALTH EXAMINATION SURVEY IN LUXEMBOURG, 2013-2015

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Contributorship statement

MRC and SS conceptualized and designed the study. MRC and VB performed the statistical analysis. MRC, SS and T.T.M interpreted the data. MRC drafted the article. SS supervised the study. All authors participated in the revision of the article. All authors contributed to and have approved the final manuscript.

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Abstract

Objectives: We estimated the prevalence of short sleep duration and multimorbidity in Luxembourg, and assessed whether sleep duration was associated with multimorbidity after adjusting for socio-demographic and behavioral characteristics.

Design: Cross-sectional study.

Participants: Data from 1508 Luxembourg residents (48% men and 52% women) aged 25 to 64 years came from the European Health Examination Survey 2013-2015.

Outcome measures: Short sleep duration and multimorbidity.

Results: Participants reported sleeping 6.95hrs/night during work days, nearly 1hr less than during non-work days (7.86hrs/night). Nearly half of participants reported having been diagnosed with ≥2 chronic conditions/diseases. Short sleep duration was associated with the number of chronic conditions (OR: 4.65, 95% CI: 1.48, 14.51, OR: 7.30, 95% CI: 2.35, 22.58, OR: 6.79, 95% CI: 2.15, 21.41 for 1, 2, and ≥3 chronic conditions/diseases, respectively), independently of socioeconomic and behavioral characteristics.

Conclusions: Health promotion programs should aim at improving and promoting healthy lifestyles among the general population to improve sleep habits as well as decrease multimorbidity in middle-aged adults.

Keywords: Sleep duration; multimorbidity; chronic diseases; Luxembourg; European Health Examination Survey

Strengths and limitations of this study

- This is the first study in Luxembourg on the prevalence of sleep patterns, with a focus on short and long sleep duration, and their relationship with multimorbidity.
- The present study was drawn from the European Health Examination Survey in Luxembourg (EHES-LUX), a representative cross-sectional population-based survey.
- Limitations of the present study include the subjective self-reported measure of sleep duration, the cross-sectional design of the study (not allowing to establish a causal link), and the low participation rate.

Data sharing statement: Extra data can be accessed by emailing Dr Laetitia Huiart, Head of the Population Health Department, LIH (laetitia.huiart@lih.lu) and the Principal Investigator of EHES-LUX2013-2015, Dr Maria Ruiz-Castell (maria.ruiz@lih.lu) and fill out a request form.

Introduction

A healthy lifestyle includes healthy sleep habits. Sleep patterns influence several physiological and psychological processes such as inflammation, immune responses, mental and cognitive function, glucose regulation and energy balance (1-3). Short sleep duration, poor sleep quality, and sleep-related disorders can result in sleep deficiency and impact on individual health (4). According to the Centers for Disease Control and Prevention (CDC), insufficient sleep is associated with health problems such as chronic diseases, poor quality of life, mental health, risk of accidents, and lower productivity at work(5)[5] (5). Adequate sleep duration is one of the dimensions needed for good sleep health (6). The American Academy of Sleep Medicine and Sleep Research Society considers that for an adult an average sleep duration of at least 7 hours per night should be recommended (4). However, a high percentage of the population sleeps less than the recommended 7 hours (7). Several factors may affect sleep such as physical activity patterns or eating behaviors, but also socioeconomic factors including job status, marital status and ethnicity (8, 9). Studies have observed an association of lower education and unemployment with both short and long sleep duration (10, 11), while factors such as physical activity and healthy diet seem to improve sleep quality (12, 13). Moreover, diet intake (energy and total fat intake) and nutrients seem to be associated with both short and long sleep duration through multifactorial factors including eating patterns (e.g., time and hours of intake) and variations in hormones related to appetite, such as leptin (14).

Epidemiologic data suggest an association of abnormal sleep duration and poor sleep quality with cardiometabolic problems (e.g. hypertension, diabetes, obesity, cardiovascular diseases), mental disorders (e.g. depression), and mortality (15-18). The observed relationship between short sleep duration and mortality would be especially critical in adults under 65 years of age (18). Few studies so far have focused on possible relationships between sleep patterns and multimorbidity (19, 20). Multimorbidity is defined as the presence of two or more chronic diseases in the same individual (21), and is associated with disability, functional decline, frailty, poor quality of life and mortality (22). In the context of ageing societies, multimorbidity is an increasing global phenomenon (23); its occurrence usually increases with age, though a large proportion of individuals younger than 65 are also affected (24). Definitions of multimorbidity vary, however, and the prevalence differs based on changing definitions, which in turn present significant challenges when attempting to compare results between populations and studies (22).

The aim of the present study was to estimate the prevalence of short sleep duration and multimorbidity in Luxembourg, as well as to assess whether sleep duration was associated with multimorbidity after adjusting for socio-demographic and behavioral characteristics.

Methods

Study population and recruitment

Data were drawn from the European Health Examination Survey in Luxembourg (EHES-LUX). EHES-LUX is a representative cross-sectional population-based survey carried out by the Luxembourg Institute of Health with the objectives of assessing the health status of the population of the Grand-Duchy of Luxembourg, develop national and European health indicators, identify the needs of the population, and evaluate health behaviors. EHES-LUX was conducted between February 2013 and January 2015. Individuals were randomly selected in a one-stage sampling procedure from the national health insurance registry (95% social coverage). Institutionalized individuals (e.g. hospitals, elderly homes) were not included. A total of 1508 residents (excluding 21 pregnant women) of Luxembourg aged 25 to 64 participated in the survey (participation rate of 24.1%) (25). Of them, 7 participants did not reported their sleep habits. A total of 1501 participants had information on multimorbidity and sleep habits. Participants signed an informed consent and were interviewed by trained nurses who also conducted medical examinations. Questionnaires included several health modules (e.g. sleep and nutritional habits, health care, working and living conditions) as well as demographic and socioeconomic characteristics. Medical examinations included measurements such as blood pressure and anthropometry. Sampling weights were calculated to be generalized to the population of Luxembourg in terms of age, sex and district of residence. The study national research ethics committee (Comité national d'éthique de Recherche-CNER) approved the study and it was notified to the Luxemburgish National Commission for Data Protection.

Patient involvement

Participants were not involved in the development of the research question, study design, recruitment or the conduction of the study. Upon request, results from the medical examination were forwarded to the study participants and their medical doctors. General results were presented to the general public in a range of dissemination activities.

Sleep

Sleep duration was assessed using two questions: 1) "How many hours do you normally sleep at night when you have to work the next day?", and 2) "How many hours do you normally sleep at

night when you don't have to work the next day?". We calculated a weighted average of sleep duration for each participant by assigning weights of 5/7 to working days and 2/7 to non-working days (26, 27). Responses were categorized as short sleep duration (<6hrs/night), medium sleep duration (6-9hrs/night), and long sleep duration (>9hrs/night), in line with previously published studies and sleep time duration recommendations (4, 8, 28).

Sleep disorders and sleep quality were assessed with the following variables: difficulty in sleeping the night, diagnosis of sleep disorders, sleep medication and sleepiness. Difficulty in sleeping the night was assessed based on the question "Do you have difficulties in sleeping through the night?". Diagnosis of sleep disorders was assessed using the question "Have you ever been told by a doctor or another health professional that you have a sleep disorder?". Sleep medications were assessed using the question "In the past 2 weeks, have you used other types of medicines that were prescribed to you ?". The question was aimed at answering about several medications including sleep tablets. Sleepiness was defined as a score of ≥11 on the Epworth Sleepiness Scale (29).

Multimorbidity

Participants were asked if they ever had a chronic disease or condition diagnosed by a medical doctor (e.g., hypertension, high cholesterol, diabetes, cardiovascular diseases, stomach or duodenal ulcer, cirrhosis or other liver disease, urinary incontinence, kidney problems, chronic back or neck disorder, rheumatoid arthritis, arthrosis, osteoporosis, cancer, severe headache as migraine or chronic anxiety). Cardiovascular diseases included coronary heart disease or angina pectoris, heart attack or its chronic consequences, stroke or its chronic consequences. Based on this information, the variable "ever being diagnosed with a chronic disease or condition" was generated with four categories: 0, 1, 2 and ≥3 chronic disease or condition. Multimorbidity was defined as having two or more chronic diseases or conditions diagnosed by a medical doctor.

Explanatory variables

Sociodemographic characteristics included age, sex and immigration status. As Portuguese are the largest immigrant community in Luxembourg, immigration status was categorized in non-immigrant, immigrant born in Portugal, and immigrant born in other countries. Socioeconomic status included education (primary, secondary and tertiary education completed) and job status (unemployed; managers/professionals; technical/clerical/service occupation; skilled/unskilled workers).

Lifestyles included smoking (never; current; ex-smokers), alcohol consumption (never; ex-drinkers; drinkers), physical activity (never; ≤ 3hrs/week of sports, fitness, and/or recreational activities which lasted at least 10 consecutive minutes; >3hrs/week of sports, fitness, and/or recreational

activities which lasted at least 10 consecutive minutes), and vegetable and fruit consumption (< 1 portion/ day, 1–4 portions/day, ≥ 5 portions/day). Weight and height were measured by trained nurses and used to calculate body mass index (BMI; kg/m^2). BMI was categorized as normal body weight (<25 kg/m^2), overweight (25-29.99 kg/m^2) and obesity (≥30kg/m^2).

Statistical data analysis

Means and frequencies were used for descriptive purposes. We calculated the prevalence of sleep disorders, short and long sleep duration, chronic conditions/diseases and multimorbidity. Percentages did not include missing values. A chi-square test (χ2) or a two-way analysis of variance (ANOVA) were used to analyze associations between the prevalence of sleep duration and covariates and the prevalence of multimorbidity and covariates. The association between sleep duration and chronic conditions/diseases was assessed using multinomial logistic regression models (reference for sleep duration was 6-9hrs per night) adjusted for sociodemographic characteristics, behavioural risk factors (e.g. BMI, smoking, alcohol consumption and physical activity), as well as for measures of sleep disorders and sleep quality We considered a $P<0.05$ statistically significant. To be representative of the population and avoid biased estimates, the observations were weighted. Participants with missing values on sleep habits and or murltimorbidity were not included in the present analysis. Analyses were performed using STATA 14.0 and and SAS version 9.4 (SAS Institute Inc., Cary, NC, USA).

Results

Table 1 shows the prevalence of chronic conditions/diseases, multimorbidity, sleep duration and sleep disorders. Nearly half of participants reported being diagnosed with two or more chronic conditions/ diseases, and nearly a third of participants reported being diagnosed with three or more chronic conditions/diseases. The most prevalent diseases were chronic low back disorder or other chronic back defect followed by hypercholesterolemia, arthrosis and hypertension. More than 8% of participants were diagnosed with a sleep disorder, a third reported having difficulties in sleeping through the night and 4.3% reported taking sleep medication. Participants reported sleeping 7.86hrs/night when they did not have to work the next day, nearly one hour more than when they had to work the next day (6.95hrs/night). Moreover, 5.13% of the Luxembourg population reported sleeping less than 6 hours/night and 1.79% reported sleeping more than 9hours/night. . Participant characteristics by chronic conditions/diseases are shown in **Table 2**. More men than women presented three or more chronic diseases. Higher number of chronic diseases/conditions increased with age: those aged 55 to 64 presented more chronic conditions compared to those aged 25-34. Immigrants born in Portugal presented more chronic conditions than non-immigrants and

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other immigrants. Participants being less educated and unemployed presented more chronic conditions compared to those employed and highly educated. Participants being less physically active and with obesity presented more chronic conditions/diseases than those being more physically active and with a lower BMI.

Participant characteristics by sleep duration are shown in **Table 3**. More men than women reported a medium sleep duration. Short sleep duration was more likely among immigrants born in Portugal, participants with lower education and skilled/unskilled workers. Short sleep duration was less common among those being physically active and with a BMI less than 25 Kg/m^2.

Table 4 shows results from multinomial logistic regression analyses examining the association between sleep duration and chronic conditions/diseases, and adjusted by sociodemographic characteristics, behavioural risk factors, socioeconomic position, as well as for measures of sleep disorders and sleep quality. Participants sleeping less hours (<6h) were 7.30and 6.79 times as likely to report having 2 and 3 or more chronic conditions after adjusting for covariates. In fully adjusted models, the strength of associations between sleep duration and multimorbidity remained statistically significant.

Estimates of sleep problems and chronic conditions are presented in **Table S1**. The prevalence of sleep problems was high, with one out of three participants having difficulties in sleeping the night through and nearly 8% of participants diagnosed with a sleep disorder. In all cases, the percentage of participants with sleep problems increased with the number of chronic diseases.

Discussion

Results from the present nationwide population-based study show for the first time in Luxembourg the prevalence of sleep patterns, with a focus on short and long sleep duration, as well as their association with multimorbidity. The prevalence of short sleep duration in Luxembourg is 5.13% .Results are similar to those observed internationally (28, 30), although in countries such as Brazil the prevalence of short sleep duration was nearly 22% (31), and in Portugal values of short sleep duration defined as ≤5hrs reached up to 20% in 2015-2016 (32). However, in the present study the age range from 25 to 64 years must be considered since it does not include adults over 65 years old who generally sleep less hours. This means that the overall prevalence of the Luxembourg population sleeping less than the recommended hours is likely to be higher, when including older adults as well.

Multimorbidity is highly prevalent in Luxembourg, especially when taking into account the fact that the study population was up to 65 years, which represents a relatively young population, as

multimorbidity prevalence naturally increases with age (22). Nearly half of participants had two or more chronic diseases and 31% had three or more chronic diseases/conditions.

In our study, we observed that short sleep duration was significantly associated with the number of chronic conditions independently of socioeconomic, behavioral characteristics and sleep disorders. Our results are in line with those from other studies that observed an association between sleep and number of chronic diseases, although previous studies have been usually performed in populations of older adults (e.g. over 50 years old) (19, 33). As observed by Koyanagi et al., sleep problems increase with the number of diseases in both low and high income countries independent of their economic development (19). These associations could explain the observed relationship between sleep duration (under the recommended 7 hours) and poor sleep quality with mortality, even among adults younger than 65 years old (18). It is not clear if sleep problems are a consequence of chronic diseases (e.g. conditions affecting sleep) or part of the cause (sleep predispose the individual to more diseases or exacerbates the symptoms), although it is plausible that both sleep problems and chronic diseases are linked by a bidirectional association (34). In terms of potential mechanisms to corroborate the biological plausibility of the link between short sleep duration and multimorbidity, reduced sleep duration has been associated with a number of chronic conditions, including cardio-metabolic and neurodegenerative disease, cancer, musculoskeletal disorders, and mental problems (15, 16). Pain caused by certain chronic diseases, as well as the medications/treatments used and mood disorders (e.g. anxiety, depression) could have an impact on sleep (35). In turn, sleep disturbances could worsen the health status. Experimental evidence corrobores the plausibility of deleterious effects of lack of sleep on endocrine, immune, neurovegetative and inflammatory pathways (1-3). Sustained short sleep duration could be related to chronic conditions through its impact on the circadian rhythm and its association with hormonal (e.g. insulin resistance and decrease leptin) and autonomic nervous system changes (increase the activity of the sympathetic nervous system) (36). Although both reduced sleep duration and the number of chronic diseases increase with age, and are more prevalent in older adults, our study shows that the prevalence is also high in adults under 65 and the association begins much earlier. It is therefore necessary to detect these problems earlier in order to improve individual health and general wellbeing and reduce mortality, particularly in the context of ageing populations burdened by the accumulation of multiple chronic conditions over time. In our study, we also observed that short sleep duration was associated with immigration status. The relationship between immigration status and sleep patterns remains unclear, possibly related to stress linked to the migratory process, cultural adaptation, or working conditions in the host country (37, 38). In our study, Portuguese immigrants were more

likely to sleep less than 6h per night during workdays and less than 7h during non-working days. Portuguese are the largest immigrant community in Luxembourg, accounting for 16% of the 46% immigrant population living in Luxembourg. Compared to Luxembourgish natives, Portuguese immigrants have a lower socioeconomic status (39) (including income, education and employment) which could partly explain why they have a greater likelihood of being short sleepers. However, after calculating the weight average for sleep hours and adjusting for sleep disorders, the association with short sleep duration disappeared.

In our study, long sleep duration was more common in women. This was in line with other studies showing that men usually sleep less hours, although women reported having more sleep problems (40). However, this relationship is complex and could depend on family composition (e.g. single parents have shorter sleep duration, particularly women) (41).

In addition, short sleep suration often cluster with other behavioral risk factors such as cigarette smoking, heavy drinking, and physical inactivity, which may in turn increase the risk of chronic disease. However, in our study, we only observed an association between physical activity and short sleep duration, with no association observed between short sleep duration and smoking or alcohol consumption. Regular physical activity would reduce the likelihood of short and/or long sleep duration and maintain an optimal duration. Studies have observed an association between physical activity and sleep, improving quality of sleep, sleep efficiency, and total sleep time (12, 42).

Limitations of the present study include the subjective measure of sleep duration (self-reported number of hours of sleep) instead of an objective measure (e.g. actigraphy, polysomnography). However, in the absence of an objective measure, there is a moderate correlation between objective and subjective measurements, a correlation that is high during weekdays possibly due to routines (43), but may be attenuated based on certain individual characteristics (e.g. presence of conditions such as depression, sociodemographic characteristics) (44). Other limitations include the fact that we did not include other sleep problems such as insomnia or sleep apnea nor environmental factors such as noise, traffic or commuting, all of which could affect sleep duration. In addition, multimorbidity was also self-reported based on a restricted list of diseases in the questionnaire, therefore participants may have not reported additional conditions, which may produce a possible underestimation of multimorbidity prevalence. Information on non-responders was not available, and despite being a representative sample of the Luxembourg population (in terms of age, sex and district), we could not determine the possibility of a non-response bias. In our study, we only included the number of sleep hours during the night, without including nap times. Moreover, we did not have information on the number of days that participants were working and assumed that most

were working 5 days per week. Finally, it should be noted that the study design (cross-sectional) does not allow to ascertain a causal link between sleep and multimorbidity; in addition, the low participation rate may affect the generalizability of our results.

This is the first study in Luxembourg on the prevalence of sleep patterns, with a focus on short and long sleep duration, and their relationship with multimorbidity. Short sleep duration, having difficulties in sleeping the night through, sleep disorders and sleeping medication represent a neglected public health problem, especially when associated with a number of chronic conditions and diseases, thus producing a negative impact on the wellbeing and general health status of the population. Sleep hygiene should be considered as an additional important health behavior along with diet, smoking and physical activity, both in clinical and public health practice. As both sleep problems and multimorbidity are highly prevalent in Luxembourg, health promotion programs should be developed to improve and promote healthy lifestyles among the general population to improve sleep habits as well as decrease multimorbidity.

Acknowledgements

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Table 1. Chronic diseases/conditions, multimorbidity and sleep: European Health Examination Survey in Luxembourg (N =1508).

	N (%) / Mean ± SD
Hypertension	250 (16.59)
High cholesterol	458 (30.39)
Diabetes	69 (4.58)
Coronary heart disease or angina pectoris	26 (1.73)
Myocardial infarction or chronic consequences of myocardial infarction	14 (0.93)
Stroke or chronic consequences of stroke	11 (0.73)
Stomach or duodenal ulcer	81 (5.37)
Cirrhosis of the liver or other liver disease	46 (3.05)
Urinary incontinence, problems in controlling the bladder	74 (4.91)
Kidney problems	108 (7.17)
Chronic low back disorder or other chronic back defect	489 (32.47)
Chronic neck disorder or other chronic neck defect	246 (16.32)
Rheumatoid arthritis	88 (5.85)
Arthrosis	292 (19.38)
Osteoporosis	44 (2.92)
Cancer	54 (3.59)
Severe headache such as migraine	271 (17.98)
Chronic anxiety	98 (6.50)
Depression	204 (13.54)
Number of chronic diseases	
0	405 (27.00)
1	362 (24.13)

≥2 (multimorbidity)	733 (49.00)
≥3	465 (31.00)
Sleep	
Diagnosis of sleep disorder	122 (8.21)
Sleepiness [a]	118 (7.89)
Have difficulties in sleeping the night through	510 (33.89)
Sleeping medication	64 (4.26)
Sleep duration	
Total sleep duration (N=1,170)	
<6hrs/night	60 (5.13%)
6h-9hrs/night	1089 (93.08%)
>9hrs/night	21 (1.79%)
Hours when you have to work the next day (N=1,152-working)	6.95±0.97
Hours when you don't work the next day (N=1,501)	7.86±1.30

N=number, SD=standard deviation

[a] Measured with Epworth Sleepiness Scale

Missing values ranged from 2 to 13 observations

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Table 2. Participant characteristics by chronic conditions/diseases: European Health Examination Survey in Luxembourg (N =1508).

	Chronic conditions/diseases				
	0	1	2	≥3	P^a
Sex					
Men	199 (27.72)	199 (27.72)	143 (19.92)	177 (24.65)	<0.001
Women	206 (26.34)	163 (20.84)	125 (15.98)	288 (36.83)	
Age					
25-34	130 (43.62)	86 (28.86)	48 (16.11)	34 (11.41)	<0.001
35-44	156 (34.29)	119 (26.15)	69 (15.16)	111 (24.40)	
45-54	83 (18.16)	111 (24.29)	98 (21.44)	165 (36.11)	
55-64	36 (12.41)	46 (15.86)	53 (18.28)	155 (53.45)	
Immigration					
Luxembourg	184 (23.44)	197 (25.10)	144 (18.34)	260 (33.12)	<0.001
Portugal	52 (23.85)	42 (19.27)	45 (20.64)	79 (36.24)	
Other	169 (34.00)	123 (24.75)	79 (15.90)	126 (25.35)	
Education					
Primary	68 (18.38)	75 (20.27)	64 (17.30)	163 (44.05)	<0.001
Secondary	133 (23.05)	142 (24.61)	106 (18.37)	196 (33.97)	
Tertiary	203 (37.04)	145 (26.46)	97 (17.70)	103 (18.80)	
Job					
Not working	58 (16.67)	56 (16.09)	58 (16.67)	176 (50.57)	<0.001
managers/professionals	168 (35.59)	138 (29.24)	73 (15.47)	93 (19.70)	

technicians/clerical/service occupation	119 (29.38)	89 (21.98)	76 (18.77)	121 (29.88)	
skilled/unskilled workers	60 (21.90)	79 (28.83)	61 (22.26)	74 (27.01)	
Smoking					
Never	239 (29.25)	209 (25.58)	145 (17.75)	224 (27.42)	0.026
Current	90 (26.01)	75 (21.68)	63 (18.21)	118 (34.10)	
Ex-smoker	74 (22.09)	78 (23.28)	60 (17.91)	123 (36.72)	
Alcohol					
Never	30 (27.78)	21 (19.44)	20 (18.52)	37 (34.26)	0.055
Drinkers	365 (27.53)	328 (24.74)	234 (17.65)	399 (30.09)	
Ex-drinkers	8 (12.50)	13 (20.31)	14 (21.88)	29 (45.31)	
Fruits and vegetables consumption					
<1 portion/day	126 (27.39)	112 (24.35)	87 (18.91)	135 (29.35)	0.597
1-4 portions/day	223 (27.81)	183 (22.82)	142 (17.71)	254 (31.67)	
≥5 portions/day	55 (23.31)	66 (27.97)	39 (16.53)	76 (32.20)	
Physical Activity					
Never	130 (21.35)	133 (21.84)	125 (20.53)	221 (36.29)	<0.001
<=3h/week	151 (29.84)	130 (25.69)	77 (15.22)	148 (29.25)	
>3h/week	121 (31.84)	98 (25.79)	65 (17.11)	96 (25.26)	
BMI	25.27 ± 4.06	26.04 ± 4.89	26.66 ± 4.96	28.07 ± 5.56	<0.001
<25	212 (33.02)	169 (26.32)	112 (17.45)	149 (23.21)	<0.001
25-30	152 (27.39)	131 (23.60)	100 (18.02)	172 (30.99)	
>=30	41 (13.62)	61 (20.27)	55 (18.27)	144 (47.84)	

Values are: numbers (%) for categorical variables and means±standard deviation for continuous variables. BMI: Body Mass Index. [a] $\chi 2$ test for categorical variables, t-test for continuous variables.

Missing values ranged from 8 to 13 observations.

Table 3. Participant's characteristics by Sleep duration: European Health Examination Survey in Luxembourg.

	Sleep duration (N=1,170)			
	<6hrs/night	6-9hrs/night	>9hrs/night	P[a]
Sex				
Men	35 (5.85)	559 (93.48)	4 (0.67)	0.007
Women	25 (4.37)	530 (92.66)	17 (2.97)	
Age	44.88 ± 8.53	43.00 ± 9.04	42.11 ± 10.43	0.26
25-34	8 (3.03)	251 (95.08)	5 (1.89)	0.50
35-44	22 (5.53)	367 (92.21)	9 (2.26)	
45-54	22 (5.70)	360 (93.26)	4 (1.04)	
55-64	8 (6.56)	111 (90.98)	3 (2.46)	
Immigration				
Luxembourg	23 (3.75)	581 (94.78)	9 (1.47)	0.02
Portugal	17 (10.00)	151 (88.82)	2 (1.18)	
Other	20 (5.17)	357 (92.25)	10 (2.58)	
Education				
Primary	21 (8.90)	212 (89.83)	3 (1.27)	0.007
Secondary	25 (5.81)	395 (91.86)	10 (2.33)	
Tertiary	14 (2.80)	478 (95.60)	8 (1.60)	
Job				
Not working	0 (0.00)	19 (95.00)	1 (5.00)	0.05
managers/professionals	15 (3.18)	450 (95.34)	7 (1.48)	
technicians/clerical/service occupation	23 (5.64)	376 (92.16)	9 (2.21)	
skilled/unskilled workers	22 (8.15)	244 (90.37)	4 (1.48)	
Smoking				
Never	32 (4.79)	625 (93.56)	11 (1.65)	0.84
Current	15 (5.60)	249 (92.91)	4 (1.49)	
Ex-smoker	13 (5.58)	214 (91.85)	6 (2.58)	
Alcohol				
Never	4 (5.63)	63 (88.73)	4 (5.63)	0.03
Drinkers	52 (4.89)	996 (93.61)	16 (1.50)	
Ex-drinkers	4 (11.43)	30 (85.71)	1 (2.86)	
Fruits and vegetables consumption				
<1 portion/day	19 (5.04)	351 (93.10)	7 (1.86)	0.72
1-4 portions/day	36 (5.76)	578 (92.48)	11 (1.76)	
≥5 portions/day	5 (2.99)	159 (95.21)	3 (1.80)	
Physical Activity				
Never	36 (7.81)	413 (89.59)	12 (2.60)	0.003
<=3h/week	12 (2.86)	401 (95.48)	7 (1.67)	

>3h/week	12 (4.15)	275 (95.16)	2 (0.69)	
BMI	27.57 ± 4.80	26.36 ± 4.87	25.27 ± 6.53	0.10
<25	16 (3.16)	477 (94.27)	13 (2.57)	0.003
25-30	30 (6.80)	409 (92.74)	2 (0.45)	
>=30	14 (6.31)	202 (90.99)	6 (2.70)	

Values are: numbers (%) for categorical variables and means±standard deviation for continuous variables. BMI: Body Mass Index. NA: not available.

[a] χ2 test or Fisher's exact test for categorical variables, ANOVA for continuous variables.

Table 4. Results of multinomial logistic regression measuring the association between sleep duration and chronic conditions in models adjusted for participants sociodemographic characteristics, behavioural risk factors and measures of sleep disorders and sleep quality: European Health Examination Survey in Luxembourg (N=1,170).

	Sleep duration			
	Short (<6h)		Long (>9h)	
	OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)
Chronic conditions/diseases				
0	1.00	1.00	1.00	1.00
1	**4.55 (1.49-13.88)**	**4.65 (1.48-14.51)**	2.94 (0.93-9.19)	2.66 (0.80-8.85)
2	**7.65 (2.55-22.91)**	**7.30 (2.35-22.58)**	0.86 (0.16-4.54)	0.82 (0.14-4.67)
≥3	**9.45 (3.25-27.41)**	**6.79 (2.15-21.41)**	1.27 (0.31-5.24)	0.73 (0.13-3.88)
Immigration				
Luxembourg		1.00		1.00
Portugal		1.66 (0.71-3.89)		0.86 (0.14-5.08)
Other		**1.96 (1.00-3.82)**		1.80 (0.61-5.31)
Sex				
Men		1.00		1.00
Women		**0.48 (0.24-0.93)**		**4.57 (1.22-17.09)**
Age		0.99 (0.95-1.02)		0.98 (0.93-1.04)
Education				
Primary		1.00		1.00
Secondary		0.77 (0.35-1.71)		1.79 (0.36-8.85)
Tertiary		0.36 (0.12-1.11)		1.07 (0.14-7.85)
Job status				
Unemployed				
managers/professionals		1.00		1.00
technicians/clerical/service occupation		1.17 (0.50-2.68)		1.47 (0.40-5.39)

skilled/unskilled workers	0.96 (0.36-2.55)	2.00 (0.33-11.91)
Physical Activity		
Never	1.00	1.00
≤3h/week	**0.47 (0.22-0.98)**	0.33 (0.10-1.09)
>3h/week	0.73 (0.34-1.56)	0.23 (0.04-1.08)
BMI		
Normal	1.00	1.00
Overweight	1.49 (0.74-2.98)	0.29 (0.06-1.39)
Obese	0.94 (0.40-2.16)	1.25 (0.35-4.40)
Smoking		
Never	1.00	1.00
Current	0.92 (0.46-1.84)	1.13 (0.30-4.15)
Ex-smokers	0.88 (0.42-1.86)	3.30 (0.98-11.00)
Alcohol consumption		
Never	1.00	1.00
Drink	2.21 (0.39-12.48)	0.60 (0.05-7.13)
Ex-drinker	1.14 (0.31-4.10)	0.32 (0.07-1.44)
Sleeping medication	1.89 (0.56-6.35)	NA
Sleep disorder diagnosis	1.39 (0.55-3.49)	NA
Difficulties in sleeping the night	**2.12 (1.14-3.92)**	1.34 (0.45-3.90)
Sleepiness	**3.37 (1.57-7.21)**	1.09 (0.20-5.77)

Note. OR: Odds ratio; AOR: Ajusted Odds ratio; 95% CI: 95% confidence interval.

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SupplementaryTable S1. Sleep problems and duration by chronic conditions/diseases: European Health Examination Survey in Luxembourg.

Variables	Total	Chronic diseases /conditions				P
		0	1	2	≥3	
Diagnosis of sleep disorder (N=1486)	122 (8.21)	11 (9.02)	13 (10.66)	22 (18.03)	76 (62.30)	<0.001
Sleepiness	118 (7.89)	25 (21.19)	26 (22.03)	18 (15.25)	49 (41.53)	0.071
Have difficulties in sleeping the night through (N=1505)	510 (33.89)	84 (16.63)	79 (15.64)	93 (18.42)	249 (49.31)	
Sleep duration						
Num sleep hours when you have to work the next day (N=1,152-working)						
<6h	70 (6.08)	10 (14.29)	13 (18.57)	19 (27.14)	28 (40.00)	0.006
6-7h	761 (66.06)	232 (30.73)	206 (27.28)	133 (17.62)	184 (24.37)	
≥8h	321 (27.86)	103 (32.09)	87 (27.10)	56 (17.45)	75 (23.36)	
Num sleep hours when you do NOT work the next day (N=1,501)						
≤6h	203 (13.52)	25 (12.38)	34 (16.83)	43 (21.29)	100 (49.50)	<0.001
7-8h	878 (58.49)	245 (28.00)	227 (25.94)	150 (17.14)	253 (28.91)	
>8h	420 (27.98)	133 (31.89)	100 (23.98)	75 817.99)	109 (26.14)	

Values are: numbers (%) [a] χ2 test for categorical variable

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STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	6
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	8, 12
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8
		(*b*) Describe any methods used to examine subgroups and interactions	
		(*c*) Explain how missing data were addressed	8
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 2 and 3
		(b) Indicate number of participants with missing data for each variable of interest	
Outcome data	15*	Report numbers of outcome events or summary measures	8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 4

		(*b*) Report category boundaries when continuous variables were categorized	7-8
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	6

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.