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Original Article

Ten-year trend in sleeping pills use in Switzerland: the CoLaus study

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ABSTRACT

Objective: The aim of this study was to assess the trends and determinants of sleeping pill consumption in the general population.
Methods: This was a prospective study that included 4329 participants (2379 women, 51.9 ± 10.4 years) living in the city of Lausanne, Switzerland, followed up for an average of 10.9 years. Benzodiazepines and benzodiazepine receptor agonists were considered as sleeping pills.
Results: The prevalence (95% confidence interval [CI]) of sleeping pills use was 8.0% (7.2–8.9) at baseline and 8.4 (7.6–9.3) after 10.9 years. Overall, sleeping pills use was higher among women, elderly individuals, and individuals reporting a history of anxiety and depression. During the 10.9-year follow-up, 85.8% of participants never used sleeping pills, 2.7% used the sleeping pills at all assessments, and 11.5% shifted from using to quitting (and vice versa). On multivariate analysis, the factors associated with "always" sleeping pills use were as follows: female gender (relative risk ratio and [95% CI] = 1.80 [1.14–2.85]); older age (7.05 [3.56–14.0] for 65 + vs < 45 years); lower educational level (2.06 [1.06–3.99] for mandatory vs university); anxiety (5.61 [3.61–8.71] for yes/no); and depression (3.75 [2.47–5.69] for yes/no). The same factors were also associated with occasional sleeping pills use (ie, shifters): relative risk ratios and 95% CI = 1.56 (1.26–1.94), 2.37 (1.72–3.26), 1.35 (0.98–1.87), 3.40 (2.59–4.45), and 2.50 (1.99–3.15) for female gender, older age, lower educational level, and anxiety and depression, respectively.
Conclusion: During a 10.9-year follow-up, one out of seven participants (14.2%) used sleeping pills at least once during the study period. Sleeping pills use is more frequent among individuals with anxiety or depression, elderly individuals, and women.

1. Introduction

Sleep disorders are commonly experienced across adulthood [1]. Approximately one-third of adults complain of insomnia symptoms [2], with prevalence estimates ranging from 19% [3] to 44% [4] due to different diagnostic criteria. The increasing prevalence of sleep disorders [5,6] has been paralleled by an increase in the prescription of sleep medications (ie, sleeping pills) [7].

However, sleeping pills have long been controversial due to side effects and health outcomes [8]. Benzodiazepines, used for decades as effective agents for the short-term control of insomnia, have been widely reported to cause harm (eg, higher risk of falls and fractures [9–12] and cognitive disturbances, particularly among older people) [13]. Newer, nonbenzodiazepine agents (so-called "Z-drugs" such as zolpidem and zopiclone) are supposed to have a lower potential for abuse and dependence [14], although this statement has been challenged [14]. Z-drugs can also cause adverse effects because of their effects on human performance and driving [15,16]. Since the 1980s [17], recommendations regarding the prescription of sleeping pills have been issued [18–20]. According to these recommendations, psychological and behavioral interventions (in particular, cognitive-behavioral therapy) are the treatment of choice for chronic insomnia. Although chronic hypnotic medication may be indicated for individuals with severe or refractory insomnia or chronic comorbid illness [21], sleeping pills should ideally be prescribed for short periods not exceeding three weeks [18,19], to limit adverse events and the potential risk for

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developing tolerance and dependency, in particular with benzodiazepines. Still, it is estimated that 0.7–3.0% of the adult general population takes sleeping pills [8,22–24], and that more than one-third of these individuals do so on a long-term basis [23]. Sleeping pills use is more prevalent among elderly individuals [25–27], and is frequently associated with depression [23,28,29] or comorbidity [27].

Despite the importance of understanding the profile of sleeping pills (benzodiazepines and Z-drugs) users and the pattern of change in their use, these issues have not been extensively studied in longitudinal studies. Thus, this study aimed (1) to assess the prevalence and the pattern of change of sleeping pill use, and (2) to examine factors associated with, and determinants of, change in the use of sleeping pills.

2. Methods

2.1. Study population and design

The CoLaus study is an ongoing prospective survey investigating the biological and genetic determinants of cardiovascular risk factors (CVRF) and cardiovascular disease (CVD) in the population of Lausanne, Switzerland. The study was approved by the Institutional Ethics Committee of the University of Lausanne (decision reference 33/09). Detailed descriptions of the study design have been reported elsewhere [30]. A simple, nonstratified random sample of the Lausanne population between 35 and 75 years of age was drawn. Inclusion criteria were written informed consent and willingness to take part in the examination and to provide blood samples. Recruitment began in June 2003, ended in May 2006, and included 6733 participants, with a participation rate of 41%. The baseline evaluation included an interview, a physical examination, a blood sampling, and a set of self-completed questionnaires.

The follow-up visits were similar to the baseline evaluation. The first follow-up visit took place between April 2009 and September 2012, on average 5.6 years after the baseline (median 5.4 years, range 4.5–8.8 years). The second follow-up visit was conducted between May 2014 and April 2017, on average 10.9 years after the baseline data (median 10.7 years, range 8.8–13.6 years).

2.2. Definitions of the use of sleeping pills and categories of use

At each visit, participants indicated which medicines, either prescribed or obtained over-the-counter, they were currently taking. Medicines were coded according to the Anatomical Therapeutics Chemical (ATC) Classification System of the World Health Organization. For this study, only benzodiazepines (ATC code starting with N03AE, N05BA, and N05BC) and benzodiazepine receptor agonists (BzRAs) or Z-drugs (ATC code starting with N05CF) were considered. Although other medications are commonly used off label for the treatment of insomnia, such as sedating antidepressants, antihistamines, analgesics, or antipsychotics, we did not consider these treatments for this analysis because these treatments could have been prescribed for other reasons (ie, for the treatment of depression, for allergies, or for pain control) and not as sleeping pills. For each survey (baseline and follow-ups), sleeping pill intake was categorized as yes/no based on the presence/absence of at least one medicine related to benzodiazepines or Z-drugs.

Trends in sleeping pills intake were defined as never (no sleeping pills at baseline and both follow-ups); always (sleeping pills at baseline and at both follow-ups); and shifters (sleeping pills in one or two assessments but not at all three time points).

2.3. Covariates

Sociodemographic and lifestyle factors were assessed by self-completed questionnaires. Age was categorized into 10-year age groups (ie, 35–44 years, 45–54 years, etc). Marital status was defined as living alone (ie, single, divorced or widowed) or living in couple (ie, married or cohabiting). Smoking status was categorized into never, former, and current as reported. Educational level was classified into university education, high school, apprenticeship, and mandatory education. Alcohol consumption was evaluated by the number of alcoholic beverage units (ie, one glass of wine, one can or glass of beer, one shot of spirits) consumed per week, and subjects were categorized as drinkers or nondrinkers. Country of birth was categorized into Switzerland and other.

Body weight and height were measured with participants barefoot and in light indoor clothes. Body weight was measured in kilograms to the nearest 100 g using a Seca (Hamburg, Germany) scale. Height was measured to the nearest 5 mm using a Seca (Hamburg, Germany) height gauge. Body mass index (BMI) was categorized as normal ($18.5 < \text{BMI} < 25$ kg/m^2), overweight ($25 \leq \text{BMI} < 30$ kg/m^2), and obese (≥ 30 kg/m^2). As the number of underweight ($\text{BMI} \leq 18.5$ kg/m^2) participants was small, they were included in the normal-weight group.

Depression and anxiety were assessed by questionnaire interview. Depression or anxiety was considered as present if the participant answered positively to the questions “Have you ever been told that you have/had depression that needed treatment?” and “Have you ever been told that you have/had anxiety or panic attacks?” respectively. A sensitivity analysis was performed using data from the PsyCoLaus study, which assessed psychiatric disorders in a subsample of the CoLaus study [31].

2.4. Exclusion criteria

We excluded participants who did not complete both follow-up visits and participants with had missing baseline (2003–2006) data for any of the covariates. For the sensitivity analysis, participants who did not attend the PsyCoLaus study were excluded.

2.5. Statistical analysis

Statistical analysis was performed using Stata software version 15.1 (Stata Corp, College Station, TX, USA). Descriptive results were expressed as number and percentage of participants for categorical variables or as mean ± standard deviation (SD) for continuous variables. Bivariate analysis was performed using a χ^2 test for categorical variables and Student t test for continuous variables. Multivariable analysis was performed using multinomial (polytomous) logistic regression using never users as reference, and results were expressed as multivariable-adjusted relative risk ratios (RRR) and 95% confidence intervals (CI). Statistical significance was considered for a two-tailed test with $p < 0.05$.

2.6. Ethics statement

The institutional Ethics Committee of the University of Lausanne, which afterwards became the Ethics Commission of Canton Vaud (www.cer-vd.ch), approved the baseline CoLaus study (reference 16/03, decisions of 13 January and 10 February 2003); the approval was renewed for the first (reference 33/09, decision of 23 February 2009) and the second (reference 26/14, decision of 11 March 2014) follow-ups. (The full decisions of the CER-VD can be obtained from the authors upon request.) The study was performed in agreement with the Declaration of Helsinki and its former amendments, and in accordance with the applicable Swiss

Table 1
Prevalence of sleeping pill use at the different evaluations of the CoLaus study, Lausanne, Switzerland.

	2003–2006	2009–2012	2014–2017
Overall	8.0 (7.2–8.9)	7.3 (6.5–8.1)	8.4 (7.6–9.3)
Gender			
Female	10.5 (9.3–11.8)	9.8 (8.6–11.0)	10.6 (9.3–11.9)
Male	5.0 (4.1–6.0)	4.3 (3.4–5.2)	5.8 (4.8–6.9)
Age group, y			
35–44	4.3 (3.3–5.6)	3.5 (2.6–4.6)	5.0 (3.9–6.3)
45–54	7.4 (6.0–9.0)	7.0 (5.7–8.5)	8.4 (6.9–10.0)
55–64	10.3 (8.6–12.2)	9.3 (7.7–11.2)	10.0 (8.3–11.8)
65+	13.8 (11.0–17.1)	12.9 (10.2–16.0)	13.6 (10.9–16.8)
Body mass index			
Normal	7.4 (6.3–8.5)	7.0 (5.9–8.1)	7.6 (6.5–8.8)
Overweight	9.0 (7.6–10.5)	7.5 (6.3–8.9)	9.3 (7.9–10.8)
Obese	7.8 (5.8–10.3)	7.8 (5.8–10.3)	9.2 (7.0–11.9)
Anxiety			
No	5.8 (5.1–6.6)	5.8 (5.1–6.6)	6.7 (5.9–7.5)
Yes	31.5 (26.8–36.5)	23.2 (19.0–27.8)	27.0 (22.5–31.8)
Depression			
No	5.3 (4.6–6.1)	4.9 (4.2–5.7)	6.6 (5.8–7.4)
Yes	22.0 (19.0–25.3)	19.4 (16.5–22.5)	17.8 (15–20.8)

Results are expressed as percentage and (95% confidence interval).

legislation. All participants gave their signed informed consent before entering the study.

3. Results

3.1. Selection and characteristics of participants

Of the initial 6733 participants, 4239 (64.3%, mean age 51.9 ± 10.4 years, 55% women and 45% men) were retained for the analysis. The exclusion criteria are indicated in Supplemental Fig. 1. Sociodemographic, lifestyle, and psychometric characteristics of the participants who were included or excluded are summarized in Supplemental Table 1. Excluded participants were more frequently men, living alone, not born in Switzerland, obese, current smokers, and those with lower education levels as well as higher anxiety and depression symptoms.

3.2. Prevalence of sleeping pills use

Prevalence rates of the use of sleeping pills at baseline and both follow-ups are summarized in Table 1. Overall, sleeping pills use slightly increased from 8.0% at baseline to 8.4% at second follow-up. At all three time points, the use of sleeping pills was higher among women, older individuals, and those reporting a history of anxiety or depression.

At baseline, 4.8% of participants reported using benzodiazepines alone, 2.7% reported using Z-drugs alone, and 0.5% reported using both benzodiazepines and Z-drugs. The corresponding percentages at the first follow-up were 4.1%, 2.5% and 0.7%, and 4.7%, 3.0% and 0.7% at the second follow-up. Benzodiazepines represented 62.4% of sleeping pills at baseline, the corresponding values being 60.5% and 59.6% for the first and the second follow-ups.

3.3. Pattern of change of sleeping pills use and its determinants

The pattern of change of sleeping pills use is presented in Fig. 1. Although the majority of participants (85.8%) reported never using sleeping pills during the 10.9-year follow-up, 2.7% used the sleeping pills at all assessments. Meanwhile, more than one-tenth of the participants shifted from using to quitting (and vice versa) among the three assessments over the 10.9-year study period.

The determinants of the pattern of use of sleeping pills at baseline and follow-ups are summarized in Table 2 (bivariate analysis) and Table 3 (multivariable analysis). On bivariate analysis, gender, age group, education level, living alone, alcohol

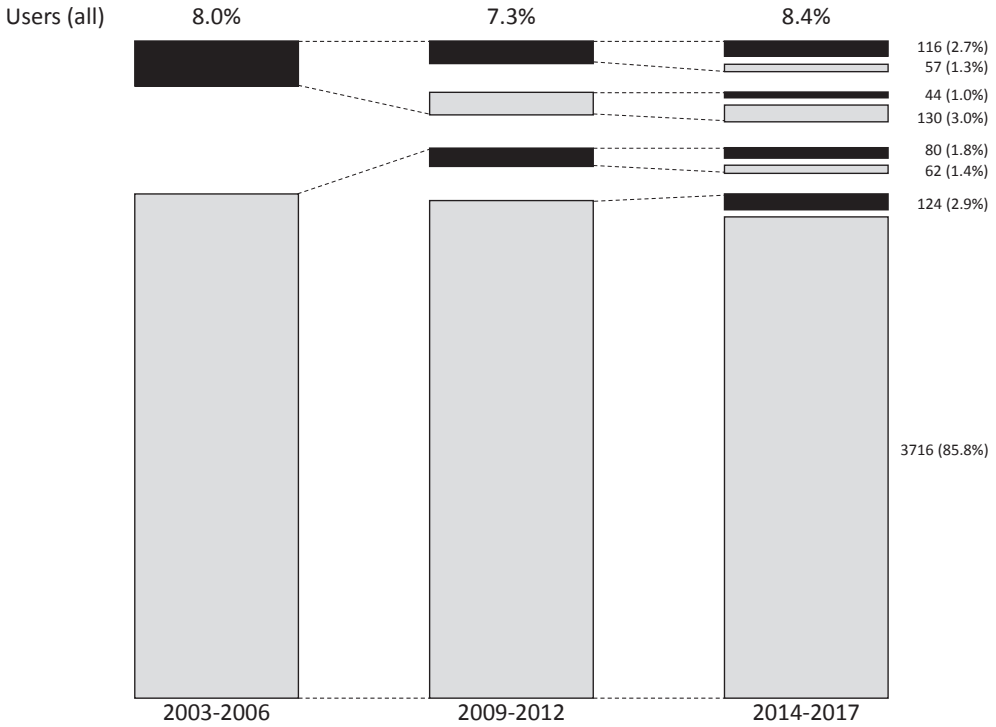

Fig. 1. Trends in sleeping pills use. Black rectangles indicate users; the height of the rectangles is proportional to the prevalence rates. Figures on the right-hand side indicate number of participants and (prevalence rate) according to their trajectories. Never users represent 85.8% of the sample; always users represent 2.7%; the other categories (shifters) represent 11.5% of the sample.

Table 2
Bivariate analysis of the factors associated with sleeping pill use, CoLaus study, Lausanne, Switzerland.

	Never	Always	Shifters	p
Overall	3716 (85.8)	116 (2.7)	497 (11.5)	
Gender				<0.001
Female	1950 (52.5)	87 (75.0)	342 (68.8)	
Male	1766 (47.5)	29 (25.0)	155 (31.2)	
Age group, y				<0.001
35–44	1220 (32.8)	13 (11.2)	105 (21.1)	
45–54	1130 (30.4)	27 (23.3)	154 (31.0)	
55–64	949 (25.5)	45 (38.8)	151 (30.4)	
65+	417 (11.2)	31 (26.7)	87 (17.5)	
Educational level				<0.001
University education	851 (22.9)	14 (12.1)	84 (16.9)	
High school	997 (26.8)	31 (26.7)	119 (23.9)	
Apprenticeship	1310 (35.3)	36 (31.0)	190 (38.2)	
Mandatory education	558 (15.0)	35 (30.2)	104 (20.9)	
Smoking status				0.208
Never	1550 (41.7)	41 (35.3)	201 (40.4)	
Former	1277 (34.4)	40 (34.5)	159 (32.0)	
Current	889 (23.9)	35 (30.2)	137 (27.6)	
Body mass index category				0.452
Normal	1905 (51.3)	50 (43.1)	245 (49.3)	
Overweight	1320 (35.5)	49 (42.2)	186 (37.4)	
Obese	491 (13.2)	17 (14.7)	66 (13.3)	
Marital status				<0.001
Alone	1133 (30.5)	51 (44.0)	192 (38.6)	
In couple	2583 (69.5)	65 (56.0)	305 (61.4)	
Born in Switzerland				0.447
No	1359 (36.6)	36 (31.0)	177 (35.6)	
Yes	2357 (63.4)	80 (69.0)	320 (64.4)	
Alcohol drinker				<0.001
No	911 (24.5)	38 (32.8)	159 (32.0)	
Yes	2805 (75.5)	78 (67.2)	338 (68.0)	
Anxiety				<0.001
No	3505 (94.3)	73 (62.9)	380 (76.5)	
Yes	211 (5.7)	43 (37.1)	117 (23.5)	
Depression				<0.001
No	3238 (87.1)	60 (51.7)	323 (65)	
Yes	478 (12.9)	56 (48.3)	174 (35)	

Results are expressed as number of participants and (percentage). Between-group analysis was performed using the χ^2 test.

Table 3
Multivariable analysis of the factors associated with sleeping pill use, CoLaus study, Lausanne, Switzerland.

	Always	p	Shifters	p
Gender				
Male	1 (ref)		1 (ref)	
Female	1.80 (1.14–2.85)	0.012	1.56 (1.26–1.94)	<0.001
Age group				
35–44	1 (ref)		1 (ref)	
45–54	2.14 (1.09–4.23)	0.028	1.53 (1.17–2.01)	0.002
55–64	4.14 (2.18–7.86)	<0.001	1.73 (1.32–2.28)	<0.001
65+	7.05 (3.56–14.0)	<0.001	2.37 (1.72–3.26)	<0.001
Educational level				
University education	1 (ref)		1 (ref)	
High school	1.31 (0.68–2.54)	0.420	1.02 (0.75–1.38)	0.903
Apprenticeship	1.03 (0.54–1.97)	0.925	1.17 (0.88–1.55)	0.286
Mandatory education	2.06 (1.06–3.99)	0.033	1.35 (0.98–1.87)	0.070
Marital status				
Alone	1 (ref)		1 (ref)	
In couple	0.89 (0.60–1.33)	0.577	0.95 (0.77–1.17)	0.643
Alcohol drinker				
No	1 (ref)		1 (ref)	
Yes	0.94 (0.61–1.44)	0.776	0.86 (0.69–1.07)	0.176
Anxiety				
No	1 (ref)		1 (ref)	
Yes	5.61 (3.61–8.71)	<0.001	3.40 (2.59–4.45)	<0.001
Depression				
No	1 (ref)		1 (ref)	
Yes	3.75 (2.47–5.69)	<0.001	2.50 (1.99–3.15)	<0.001

Results are expressed as relative risk ratio and (95% confidence interval). Statistical analysis using multinomial logistic regression, using never users as reference group.

consumption, and reporting anxiety or depression symptoms were associated with the pattern of sleeping pills change (Table 2). Multivariable analysis adjusting for all covariates indicated that, relative to never users, gender, age group and reporting anxiety or depression symptoms were significantly and independently associated both with sleeping pills use (always users and occasional users, ie, shifters) (Table 3).

Sensitivity analysis restricted to the participants assessed by the PsyCoLaus study ($n = 2808$) led to similar findings (Supplemental Table 2). Exceptions were that, despite RRRs >1 as in the original analysis, female gender was no longer associated with always use, and mandatory education was no longer associated with occasional use. Finally, living in couple was negatively associated with always use of sleeping pills (Supplemental Table 2).

4. Discussion

Few studies have assessed the long-term use of sleeping pills in the general population. Our results show that, during a 10.9 year study period, one out of seven participants took sleeping pills, and that a significant percentage of the population appears to use sleeping pills in an almost continuous manner.

4.1. Prevalence of sleeping pills use

Prevalence of sleeping pills use varied between 7.3% and 8.4%, a value higher than reported in the United States (3.0%) [8], in several European countries (4.3–6.8%) [23], and in a previous study conducted in Switzerland (2.8%) [22]. Conversely, the prevalence rates observed in our study were in agreement with those in recent studies conducted in Brazil (7.6%) [32] and in British Columbia (8.4%) [33]. The reasons for the higher prevalence of sleeping pills use in our study are not straightforward, and can only be speculated; possible explanations include an older age of our sample or the fact that the study was conducted in the French-speaking part of Switzerland, where prescription rates tend to be higher than in the German-speaking part [34]. Still, it would be of interest for our study to be replicated in other parts of Switzerland to confirm or disconfirm our findings.

Benzodiazepines were more often prescribed than Z-drugs, although a small decrease was found during the 10.9-year follow-up period. This finding is in agreement with an older European study [23] and with a recent Israeli study [35] but not with a US study [8]. The reasons for the higher prescription rates of benzodiazepines could be their lower price, their variety, and their anxiolytic properties [20].

A small percentage of participants (0.5%) reported simultaneously taking benzodiazepines and Z-drugs. A likely explanation is that benzodiazepines were prescribed as anxiolytics and not as sleeping pills. Still, a study conducted in Norway reported that 27.9% of the long-term recurrent users of Z-drugs also used benzodiazepines, and 33.9% used opioids [36]. Hence, the combination Z-drugs and benzodiazepines might indicate the presence of psychological or psychiatric issues.

4.2. Pattern of change of sleeping pills use and its determinants

Always users represented 2.7% of the sample, a value in agreement with one study (3.0%) [33] but higher than reported in a UK (0.69%) [37] and a US (0.3%) [8] study. A possible explanation is that we based our definition of always users on the presence of sleeping pills use at all assessments, whereas no information was available regarding sleeping pills use between assessments. Hence, it is

possible that our prevalence rates of always users could be overestimated. Indeed, a recent review showed that the prevalence of long-term users varies from 6% to 76% among sleeping pills users in the general population, depending on the definition used [38]. Nevertheless, it would be important to replicate this study using pharmacy records or health care claims to identify always users.

Women and older participants had a higher likelihood of being sleeping pills users, a finding in agreement with the literature [8,22,25–27,32]. The higher prevalence rates among elderly subjects are likely related to increases in sleep disorders with age and in women, increased number of medications [39], higher rates of insomnia and presence of several comorbidities [40]. The higher prevalence rates among women could be related to a higher prevalence of anxiety [41] and depression in women [42], even if gender remained significantly associated with sleeping pills use after adjustment for those diseases. Hence, other factors than anxiety and depression must mediate the association between female gender and sleeping pills use.

Participants reporting anxiety or depression had a higher likelihood of being sleeping pills users. The association between sleeping pills use and depression had also been reported in Brazil [28,32], in Canada [26] and in several European countries [23,29]. The association of always sleeping pills use and anxiety has also been reported in several studies [29,38]. Whether sleeping pills are used to treat the disease (anxiety or depression) or the comorbid sleep disorder related to them (insomnia) remains to be assessed, as it has been suggested that practitioners tend to prescribe more anxiolytics than antidepressants for subjects with depression [23].

4.3. Study strengths and limitations

The major strength of this study is that it is one of the few longitudinal studies assessing determinants in pattern of change in sleeping pills use in a population-based sample.

This study has also some limitations. First, a significant number of participants had to be excluded, and excluded participants had a higher frequency of lower education and of anxiety and depression symptoms. Therefore, the prevalence of sleeping pills use might have been underestimated, as several factors associated with exclusion were also associated with a higher frequency of sleeping pills use. Still, as it was not ethically possible to retain the participants in the cohort; this is the best estimation available regarding trends in sleeping pills use. Future studies should rely on pharmacy records or on health care claims [43] to minimize losses to follow-up. Second, our study relied on self-reported medication use, and some participants might have omitted reporting that they took sleeping pills. This would have decreased the prevalence of sleeping pill use, but would not change the determinants of sleeping pill use and change. Furthermore, it has been reported that self-reported medication use adequately agrees with pharmacy records [44,45]; hence, the likelihood of a reporting bias is low. Finally, it was not possible to know whether benzodiazepines were prescribed as anxiolytics or as sleeping pills (or both); thus, the prevalence of sleeping pills users might be overestimated. Conversely, as we did not consider other types of medications that aid sleep such as antidepressants, antihistamines, or melatonin, so the overestimation rate might be modified.

5. Conclusion

In a population-based prospective study, during a 10.9-year follow-up, approximately one out of seven participants used sleeping pills. Sleeping pills use is more frequent among women, elderly individuals, and individuals with anxiety or depression.

Author contributions

N.A. made part of the statistical analyses and wrote most of the article; P.M.V. collected data, made part of the statistical analysis and wrote part of the article; P.V., J.H.-R., and R.H. revised the article for important intellectual content. P.M.V. had full access to the data and is the guarantor of the study.

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Conflict of interest

The authors report no conflict of interest.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2018.06.022.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2018.06.022.

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