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Original Article

The relationship between nightmares, depression and suicide

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ABSTRACT

Objective: Previous studies investigating the association between nightmares and suicide have yielded different results. We aimed to investigate whether nightmares, directly or indirectly, influence the incidence of suicide.

Methods: We used a prospective cohort study, based on 40,902 participants with a mean follow-up duration of 19.0 years. Cox proportional hazards models with attained age as time-scale were fitted to estimate hazard ratios (HR) of suicide with 95% confidence intervals (CI) as a function of the presence or absence of depression and nightmares. Mediation analysis was used to asses to what extent the relationship between nightmares and the incidence rate of suicide could be mediated by depression.

Results: No association was observed between nightmares and the incidence of suicide among participants without depression. Compared with non-depressed participants without nightmares, the incidence of suicide among participants with a diagnosis of depression was similar among those with and without nightmares (HR 12.3, 95% CI 5.55–27.2 versus HR 13.2, 95% CI 7.25–24.1). The mediation analysis revealed no significant effects of nightmares on suicide incidence. However, the incidence of depression during follow-up was higher among those who suffered from nightmares than among those who did not ($p < 0.001$).

Conclusions: Our findings indicate that nightmares have no influence on the incidence rate of suicide, but may reflect pre-existing depression. This is supported by a recent discovery of a strong genetic correlation of nightmares with depressive disorders, with no evidence that nightmares would predispose to psychiatric illness or psychological problems. Interventions targeting both depression and nightmares, when these conditions co-occur, may provide additional therapeutic benefit.

1. Introduction

Suicide is a major public health concern with heterogeneous etiology. On an individual level, the interplay between predisposing, mediating, and precipitating factors contribute to the risk of developing suicidal behavior [1]. Improved recognition and understanding of individual factors influencing suicidal behavior may facilitate the detection of high-risk individuals.

Nightmares are terrifying or disturbing dreams, usually involving threats to survival, safety or physical integrity, able to awaken the sleeper [2]. Nightmares can be posttraumatic as part of a posttraumatic stress reaction, idiopathic or drug induced [3]. Frequent nightmares have been related to both general psychopathology [4] and psychiatric disorders, in particular post-traumatic stress disorder [3–5], major depressive disorder [6], schizophrenia [6], and borderline personality disorder [7]. Evidence suggests that nightmares may persist over long periods of time

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[8–10]. As with other sleep disorders, nightmares have been associated with increased risk of suicidal ideation, suicide attempts and death by suicide [11–20].

The association between depression and suicidal behavior is well-documented, and most studies investigating the influence of nightmares on suicidal behavior have reported that the prevalence of nightmares increases with depressive symptoms [11–20]. Depressive symptoms may thus act as a confounder of the relationship between suicidal behavior and nightmares. However, while some studies have reported that nightmares might significantly increase suicidal behavior after controlling for depression [14–16], other studies indicate that depressive symptoms could be aggravated by low sleep quality and mediate the association between nightmares and suicide risk [19,20]. It is thus unclear whether nightmares represent an independent risk factor for suicidal behavior or whether the association between nightmares and suicide risk is mediated by psychiatric conditions.

Most previous studies investigating the influence of nightmares on suicidal behavior have used clinical samples that may not reflect the general population. Using a large Swedish cohort with a mean follow-up time of 19.0 years, we aimed to study the relationship between nightmares, depression and the incidence of suicide, and investigate whether nightmares, directly or indirectly, influence the incidence rate of suicide.

2. Methods

In September 1997, the Swedish National March Cohort [21] was established during a four-day nationwide fundraising event organized by the Swedish Cancer Society. Participants were invited to fill out a 36-page questionnaire regarding demographic, lifestyle, and medical information. All participants received written information regarding the purpose of the study and provided written informed consent to participate. They also provided their national registration number, a unique identifier assigned to all Swedish residents, which enabled us to follow the cohort by linkage to multiple nation-wide, continuously updated and essentially complete databases. The study was approved by the Regional Ethics Committee in Stockholm.

Given the fundraising nature and nearly 3600 Swedish cities and villages participating in the event, the number of individuals offered a questionnaire could not be assessed. In total, 43,863 participants completed the questionnaire. Those with incorrect national registration number were excluded (n = 11) as were those who were younger than 18 years (n = 1732) or had emigrated or died (n = 55) before the start of follow-up. In the present study, we also excluded participants with missing values on self-reported depressive symptoms (n = 721) or nightmares (n = 442). After applying the exclusion criteria, our final study population included 40,902 participants (64% women and 36% men) followed prospectively for death by suicide until the end of April, 2018. Mean age was 51.2 years (SD 16.0) with an age range between 18 and 94 years.

2.1. Exposure assessment

Information regarding diagnoses of psychiatric disorders was obtained from the Swedish Patient Register. A diagnosis of depression was defined as having received ICD-8 codes 296.0–296.3, 296.8–296.9, 298.0 or 300.4 or ICD-9 codes 296B-E, 298A or 300E before baseline or ICD-10 codes F31–F33 during follow-up. Depressive symptoms were assessed by asking the participants to estimate how often they felt sad, low-spirited or depressed. The response alternatives were never/seldom, sometimes, often or always/almost always. The reference group was represented by those who never or seldom experienced depressive symptoms. The Karolinska Sleep Questionnaire [22] was used to assess the prevalence and frequency of nightmares. Answer alternatives were never, seldom, sometimes, mostly or always. The reference group was represented by those who never or seldom experienced nightmares. In some of the analyses, we also dichotomized nightmares into yes (sometimes, mostly, or always experiencing nightmares) or no (never or seldom experiencing nightmares). Since few participants reported often or always having nightmares, they were merged with those who sometimes reported nightmares into the exposed group. In order to elucidate the relationship between measures of depression, nightmares and death by suicide, the participants were further categorized based on both a diagnosis of depression, self-reported depressive symptoms and frequency of nightmares.

2.2. Follow-up and outcome

The cohort was followed from baseline on October 1, 1997. Follow-up ended at the time of death, emigration or April 30, 2018, whichever occurred first. Using the individually unique Swedish national registration numbers, mortality data was obtained by linkage to the Swedish Cause of Death Register held by the National Board for Health and Welfare. A total of 8640 deaths occurred during the follow-up period. Of these, 69 were suicides (ICD-10 codes X60-X84 and Y10–Y34).

2.3. Statistical analysis

Differences in baseline variables across categories of nightmare frequency were assessed using one-way analysis of variance (ANOVA) for continuous variables and the Kruskal–Wallis test for categorical variables. Cox proportional hazards models with attained age as time-scale were used to estimate hazard ratios of suicide (HRs) with 95% confidence intervals (CI) for participants categorized by depressive symptoms and nightmares. A trend test for a dose response relationship regarding the frequency of nightmares and suicide incidence rate was performed by using a categorical variable for nightmare frequency (never/seldom, sometimes, often, or always) in a Cox proportional hazards model. Residual analyses were conducted to study the proportionality hazard assumption, based on the Schoenfeld residual plots and statistical tests.

Among participants without a diagnosis of depression at baseline, we used a logistic regression model to assess the risk of receiving a diagnosis of depression during follow-up among those who suffered from nightmares at baseline, compared to those who never or seldom had nightmares. Mediation analysis using Cox models under the rare outcome assumption was carried out to asses to what extent the relationship between nightmares and the incidence of suicide was mediated by depression [23,24]. The effects were estimated on the HR scale and the CI's were calculated using the delta method. Participants with a diagnosis of depression at baseline were excluded in the mediation analyses.

All analyses were adjusted for a number of potential confounding variables. In presence of confounding, the adjusted estimates of the beta's coefficient will change compared to the crude estimate. The final analyses were adjusted for sex, educational level, occupation, smoking, sleep duration, hypnotic use, and presence of cardiovascular disease at baseline When appropriate, adjustments were also made for depressive disorders, anxiety disorders, and psychotic disorders, or self-reported depressive symptoms and self-reported anxiety symptoms.

Educational level was summarized into a binary variable, based on having reached a university degree. Occupation was categorized

into working, retired, student, unemployed, long-term sick-leave or other. Smoking was categorized into never, past or current smokers. Habitual sleep duration was represented by a continuous variable for sleep duration (number or hours per weekday night). Hypnotic use was dichotomized into yes or no. Information regarding diagnoses of cardiovascular disease (ICD-10 codes I00–I99), anxiety disorders (F40–F48), and psychotic disorders (F20–F29) at baseline was obtained from the Swedish Patient Register and the variables were dichotomized into those who had a diagnosis and those who had not. Anxiety symptoms were assessed by asking the participants to estimate how often they felt worried, tensed or anxious. The response alternatives were never/seldom, sometimes, often or always/almost always. The reference group was represented by those who never or seldom experienced anxiety symptoms.

Adjustments were also made for the following potential confounding variables; body mass index (BMI), physical activity, alcohol consumption, coffee consumption, insomnia, and cancer. However, these factors only had minor influence on the results and were therefore not kept in the final analyses. BMI was calculated by dividing weight in kilograms by height in meters squared, and categorized into underweight (<18.5 kg/m^2), normal weight (18.5–24.99 kg/m^2), overweight (25–30 kg/m^2) or obese (>30 kg/m^2). Physical activity was based on reported responses on weekly exercise levels ranging from none or easy physical activity to hard physical activity and dichotomized into those active (more than 120 min) or inactive (120 min or less). Alcohol consumption was categorized into drinkers, non-drinkers or unknown. We further adjusted for alcohol as a continuous variable (gram per months). Coffee consumption was categorized into 0, 1–4, 5–7 or >7 cups of coffee per day. Insomnia symptoms were assessed by asking participants to estimate how often they experienced difficulties initiating sleep, difficulties maintaining sleep, early-morning awakenings, not rested at awakening and daytime sleepiness. The response alternatives were never, seldom, sometimes, mostly or always. Insomnia was defined as mostly or always experiencing any of the nocturnal insomnia symptoms (difficulties initiating sleep, difficulties maintaining sleep and early-morning awakenings), as well as mostly or always experiencing symptoms of non-restorative sleep (not rested at awakening and daytime sleepiness). Information regarding diagnoses of cancer (ICD-10 codes C00–C97) was obtained from the Cancer Register and was dichotomized into those who had a diagnosis and those who had not.

The proportion of missing data in the potential confounding variables was 6.7% for smoking habits, 4.6% for sleep duration, 4.3% for BMI, 1.7% for coffee consumption, 1.2% for insomnia status, and less than 1% for occupational level, educational level, physical activity, and alcohol consumption. We therefore conducted supplementary analyses after imputing missing data using the multiple imputation chained equation procedure.

Since low incidence rate affects statistical power, we performed a power analysis, described in detail in Supplementary Table 1. All analyses were performed using Statistical Analysis System 9.4. All statistical tests were two-sided, and p values less than 0.05 were considered statistically significant.

3. Results

Characteristics of participants at baseline, overall and by category of nightmare frequency, are presented in Table 1. The occurrence of nightmares was highly correlated to other sleep-related difficulties and measures of depression. A larger proportion of women reported having nightmares. Generally, nightmare sufferers had a lower educational level than those who reported never or seldom having nightmares. They reported lower physical activity, higher BMI, and were more often smokers. They were more likely to have a diagnosis of cardiovascular disease or cancer, compared to those who reported never or seldom having nightmares.

There was a significant correlation between a diagnosis of depression and self-reported depressive symptoms (correlation coefficient = 0.38, $p < 0.001$). Baseline characteristics among participants with different frequencies of depressive symptoms are presented in Table 2. Participants who reported depressive symptoms had longer sleep duration on average, compared to those who never or seldom experienced depressive symptoms, and they considerably more often suffered from insomnia symptoms. They were more often smokers and reported a lower level of physical activity. Women were overrepresented among those with self-reported depressive symptoms.

During a mean follow-up time of 19.0 years (SD 4.0), 69 deaths by suicide occurred (64% men and 36% women). The mean time from baseline to suicide was 9.0 years (SD 5.0). Often or always having nightmares was associated with a significantly increased incidence of suicide. However, after adjustment, statistical significance was lost (Table 3).

When participants were categorized based on a diagnosis of depression and nightmares, no association was observed between nightmares and death by suicide among those without a diagnosis of depression (HR 1.00, 95% CI 0.44–2.28) (Table 4). Compared with participants without a diagnosis of depression or nightmares, there was a more than 12-fold increased incidence of suicide among depressed participants, whereas nightmares did not further increase the risk. There were no significant gender differences (Table 4). Similar results were obtained when participants instead were categorized based on subjective depressive and anxiety symptoms without considering psychiatric diagnoses (Table 5).

3.1. Incidence of depression by nightmare frequency

Among participants without a diagnosis of depression at baseline, the odds of depression during follow-up was higher among those who suffered from nightmares than among those who did not (OR 1.35, 95% CI 1.19–1.53). When the analysis was stratified by gender, similar results were obtained for women (OR 1.37, 95% CI 1.19–1.57) and men (OR 1.30, 95% CI 1.02–1.66). There was also a trend showing increasing incidence of receiving a diagnosis of depression during follow-up with increasing frequency of nightmares at baseline (p value for trend <0.001).

3.2. Mediation analysis

The total effect of nightmares on the incidence of suicide, estimated on the HR scale, was 1.07 (95% CI 0.49–2.37). The direct effect was 1.02 (95% CI 0.57–1.83) and the indirect effect, mediated by depression, was 1.05 (95% CI 0.62–1.80). Estimates were similar when women and men were analyzed separately. There was no interaction between a diagnosis of depression and nightmares with regard to suicide risk.

Our results remained almost identical after carrying out the analyses on the multiple imputed data (data not shown).

4. Discussion

In the present cohort, comprising 40,902 participants with a mean follow-up of 19.0 years, we found no evidence suggesting that nightmares influence the incidence of suicide.

Nightmare frequency was highly correlated with self-reported depressive and anxiety symptoms, sleep duration, and insomnia. These results are in accordance with previous research showing an

Table 1
Baseline characteristics, overall and by frequency of nightmares.

Variable	Total	Nightmares			P-value for difference between groups
		Often, always	Sometimes	Never, seldom	
N	40,902	407	7496	32,999	
Mean age (SD)	51.2 (16.0)	50.0 (19.1)	50.5 (16.7)	51.4 (15.7)	0.003
Women, n (%)	26,301 (64)	291 (72)	5489 (73)	20,521 (62)	<0.001
University degree, n (%)	11,534 (28)	88 (22)	1815 (24)	9631 (29)	<0.001
Working, n (%)	20,274 (50)	138 (34)	3388 (45)	16,748 (51)	<0.001
Retired, n (%)	10,603 (26)	128 (31)	1928 (26)	8547 (26)	0.036
Student, n (%)	1604 (3.9)	37 (9.1)	415 (5.5)	1152 (3.5)	<0.001
Unemployed, n (%)	821 (2.0)	15 (3.7)	184 (2.5)	622 (1.9)	<0.001
Long-term sick-leave, n (%)	670 (1.6)	21 (5.2)	197 (2.6)	452 (1.4)	<0.001
Other, n (%)	1850 (4.5)	30 (7.4)	359 (4.8)	1461 (4.4)	0.038
Difficulty falling asleep, n (%)	2243 (5.5)	131 (32)	701 (9.4)	1411 (4.3)	<0.001
Difficulty maintaining sleep, n (%)	2922 (7.1)	136 (33)	897 (12)	1889 (5.7)	<0.001
Early morning awakening, n (%)	3550 (8.7)	117 (29)	950 (13)	2483 (7.5)	<0.001
Tired at awakening, n (%)	5934 (15)	142 (35)	1526 (20)	4266 (13)	<0.001
Daytime sleepiness, n (%)	2955 (7.2)	129 (32)	884 (12)	1942 (5.9)	<0.001
Insomnia, n (%)	2350 (5.8)	127 (31)	748 (10)	1475 (4.5)	<0.001
Mean sleep duration, hours/night (SD)	6.8 (1.0)	6.4 (1.4)	6.8 (1.1)	6.9 (1.0)	<0.001
Often/always depressive symptoms, n (%)	2565 (6.3)	142 (35)	942 (13)	1481 (4.5)	<0.001
Often/always anxiety symptoms, n (%)	3785 (9.4)	156 (39)	1367 (19)	2262 (7.0)	<0.001
Current smokers, n (%)	2957 (7.2)	50 (12)	742 (9.9)	2165 (6.6)	<0.001
Past smokers, n (%)	10,506 (26)	92 (23)	1917 (26)	8497 (26)	0.340
BMI, kg/m^2 (SD)	24.6 (3.5)	25.1 (4.1)	24.7 (3.8)	24.6 (3.5)	0.025
Low physical activity, n (%)	6492 (16)	101 (25)	1227 (16)	5164 (16)	<0.001
Coffee, no of cups/daily (SD)	2.9 (1.8)	2.6 (1.9)	2.8 (1.8)	2.9 (1.8)	<0.001
Alcohol drinkers, n (%)	36,011 (88)	351 (86)	6595 (88)	29,065 (88)	0.516
Standard glasses of alcohol per week (SD)	6.3 (4.3)	6.0 (4.5)	6.1 (4.3)	6.3 (4.3)	<0.001
Cancer, n (%)	2558 (6.3)	35 (8.6)	538 (7.2)	1985 (6.0)	<0.001
Cardiovascular disease, n (%)	4458 (11)	81 (20)	939 (13)	3438 (11)	<0.001

Differences in baseline variables across categories of nightmare frequency were assessed using one-way analysis of variance (ANOVA) for continuous variables and the Kruskal–Wallis test for categorical variables.

Table 2
Baseline characteristics among subjects with different frequencies of self-reported depressive symptoms.

Variable	Total	Self-reported depressive symptoms			P-value for difference between groups
		Often or always	Sometimes	Never or seldom	
N	40,902	2565	20,792	17,545	
Mean age (SD)	51.2 (16.0)	52.6 (15.6)	50.6 (16.1)	46.1 (16.0)	<0.001
Women, n (%)	26,301 (64)	1988 (78)	14,573 (70)	9740 (56)	<0.001
University degree, n (%)	11,534 (28)	755 (29)	5765 (28)	5014 (29)	0.065
Working, n (%)	20,274 (50)	1220 (48)	10,073 (48)	8981 (51)	<0.001
Retired, n (%)	10,603 (26)	395 (15)	5179 (25)	5029 (29)	<0.001
Student, n (%)	1604 (3.9)	191 (7.5)	943 (4.5)	470 (2.7)	<0.001
Unemployed, n (%)	821 (2.0)	87 (3.4)	464 (2.2)	270 (1.5)	<0.001
Long-term sick-leave, n (%)	670 (1.6)	104 (4.1)	382 (1.8)	184 (1.1)	<0.001
Other, n (%)	1850 (4.5)	113 (4.4)	726 (3.5)	597 (3.4)	0.035
Difficulty falling asleep, n (%)	2243 (5.5)	511 (20)	1295 (6.2)	437 (2.5)	<0.001
Difficulty maintaining sleep, n (%)	2922 (7.1)	533 (21)	1759 (8.5)	630 (3.6)	<0.001
Early morning awakening, n (%)	3550 (8.7)	542 (21)	2039 (10)	969 (5.5)	<0.001
Tired at awakening, n (%)	5934 (15)	985 (38)	3365 (16)	1584 (9.0)	<0.001
Daytime sleepiness, n (%)	2955 (7.2)	719 (28)	1685 (8.1)	551 (3.1)	<0.001
Insomnia, n (%)	2350 (5.8)	591 (23)	1353 (6.5)	406 (2.3)	<0.001
Mean sleep duration, hours/night (SD)	6.8 (1.0)	6.9 (0.8)	6.8 (1.0)	6.6 (1.2)	<0.001
Often/always nightmares, n (%)	407 (1.0)	142 (5.5)	206 (1.0)	59 (0.3)	<0.001
Sometimes nightmares, n (%)	7496 (18)	942 (37)	4784 (23)	1770 (10)	<0.001
Current smokers, n (%)	2957 (7.2)	317 (12)	1594 (7.7)	1046 (6.0)	<0.001
Past smokers, n (%)	10,506 (26)	640 (25)	5319 (26)	4547 (26)	0.514
BMI, kg/m^2 (SD)	24.6 (3.5)	24.6 (3.3)	24.6 (3.6)	24.7 (4.1)	0.462
Low physical activity, n (%)	6492 (16)	568 (22)	3326 (16)	2598 (15)	<0.001
Coffee, no of cups/daily (SD)	2.9 (1.8)	2.9 (1.8)	2.8 (1.8)	2.8 (2.0)	<0.001
Alcohol drinkers, n (%)	36,011 (88)	2254 (88)	18,360 (88)	15,397 (88)	0.251
Standard glasses of alcohol per week (SD)	6.3 (4.3)	6.5 (4.4)	6.2 (4.2)	5.9 (4.2)	<0.001
Cancer, n (%)	2558 (6.3)	164 (6.4)	1355 (6.5)	1039 (5.9)	0.054
Cardiovascular disease, n (%)	4458 (11)	274 (11)	2307 (11)	1877 (11)	0.432

Differences in baseline variables across categories of nightmare frequency were assessed using one-way analysis of variance (ANOVA) for continuous variables and the Kruskal–Wallis test for categorical variables.

Table 3
HR with 95% CI of death by suicide among subjects who suffer from nightmares, compared to those who never or seldom have nightmares.

Nightmares	N	Person years	Deaths (%)	HR (95% CI)[a]	HR (95% CI)[b]	HR (95% CI)[c]	HR (95% CI)[d]
Never/seldom	32,999	628,389	52 (0.16)	1.0 (reference)	1.0 (reference)	1.0 (reference)	1.0 (reference)
Sometimes	7496	141,425	14 (0.19)	1.41 (0.78–2.56)	1.10 (0.60–2.01)	1.03 (0.56–1.90)	1.04 (0.56–1.92)
Often/always	407	7342	3 (0.74)	**5.78 (1.80–18.6)**	2.90 (0.86–9.75)	2.45 (0.70–8.53)	2.27 (0.65–7.89)
P value for trend				**0.04**	0.36	0.53	0.55

[a] Adjusted for gender.
[b] Adjusted for gender, occupational status, educational status, smoking, sleep duration, hypnotic use, and cardiovascular disease.
[c] Adjusted for gender, occupational status, educational status, smoking, sleep duration, hypnotic use, cardiovascular disease, depressive disorders, anxiety disorders, and psychotic disorders.
[d] Adjusted for gender, occupational status, educational status, smoking, sleep duration, hypnotic use, cardiovascular disease, self-reported depressive symptoms, and self-reported anxiety symptoms. Significant HRs are in bold.

Table 4
HR with 95% CI of death by suicide among subjects with different combinations of depression and nightmares, compared to subjects without a diagnosis of depression who never or seldom experience nightmares, overall and stratified by gender.

Depression diagnosis	Nightmares	N	Person years	Deaths (%)	P value for mortality rate difference	HR (95% CI)[a]	HR (95% CI)[b]
No	Never/seldom	31,643	603,205	32 (0.1)	0.94	1.0 (reference)	1.0 (reference)
No	Sometimes/often/always	7243	136,370	7 (0.1)		1.16 (0.51–2.64)	1.00 (0.44–2.28)
Yes	Never/seldom	1356	25,184	20 (1.5)	0.97	**16.5 (9.39–28.9)**	**12.3 (5.55–27.2)**
Yes	Sometimes/often/always	660	12,398	10 (1.5)		**20.2 (9.83–41.3)**	**13.2 (7.25–24.1)**
Women							
No	Never/seldom	19,585	381,273	9 (0.05)	0.78	1.0 (reference)	1.0 (reference)
No	Sometimes/often/always	5263	102,010	3 (0.06)		1.27 (0.34–4.70)	1.08 (0.29–4.04)
Yes	Never/seldom	936	17,819	8 (0.85)	0.94	**19.1 (7.36–49.7)**	**15.2 (5.67–40.5)**
Yes	Sometimes/often/always	517	9910	5 (0.97)		**22.0 (7.35–66.1)**	**13.3 (4.05–43.5)**
Men							
No	Never/seldom	12,058	221,932	23 (0.19)	0.85	1.0 (reference)	1.0 (reference)
No	Sometimes/often/always	1980	34,360	4 (0.20)		1.11 (0.38–3.20)	0.96 (0.33–2.79)
Yes	Never/seldom	420	7365	12 (2.8)	0.73	**15.3 (7.58–30.7)**	**12.6 (6.08–26.0)**
Yes	Sometimes/often/always	143	2488	5 (3.5)		**19.4 (7.35–51.0)**	**12.6 (4.45–35.9)**

We used the test-based method to calculate p values.
[a] Adjusted for gender when appropriate.
[b] Adjusted for gender when appropriate, occupational status, educational status, smoking, sleep duration, hypnotic use, cardiovascular disease, anxiety disorders, and psychotic disorders. Significant HRs are in bold.

Table 5
HR with 95% CI of death by suicide among subjects with different combinations of self-reported depressive symptoms and nightmares, compared to those who never or seldom experience depressive symptoms or nightmares.

Depressive symptoms	Nightmares	N	Person years	Deaths (%)	P value for mortality rate difference	HR (95% CI)[a]	HR (95% CI)[b]
Never, seldom	Never/seldom	15,716	298,394	10 (0.06)	0.91	1.0 (reference)	1.0 (reference)
Never, seldom	Sometimes/often/always	1829	33,663	1 (0.05)		0.98 (0.12–7.48)	0.94 (0.11–6.69)
Sometimes	Never/seldom	15,802	301,377	36 (0.23)	0.95	**4.47 (2.21–9.04)**	**3.90 (1.92–7.92)**
Sometimes	Sometimes/often/always	4990	94,167	11 (0.22)		**4.95 (2.09–11.7)**	**3.61 (1.49–8.71)**
Often, always	Never/seldom	1481	28,617	6 (0.41)	0.83	**9.23 (3.32–25.6)**	**6.01 (2.13–17.4)**
Often, always	Sometimes/often/always	1084	20,937	5 (0.46)		**12.4 (4.16–36.8)**	**5.66 (1.78–18.0)**

We used the test-based method to calculate p values.
[a] Adjusted for gender.
[b] Adjusted for gender, occupational status, educational status, smoking, sleep duration, hypnotic use, cardiovascular disease, and self-reported anxiety symptoms. Significant HRs are in bold.

association between nightmare frequency and the general level of psychopathology, mood and anxiety disorders, and other sleep disorders [3–7].

Nightmares were not associated with an increased incidence of suicide among non-depressed participants, and did not further increase the incidence of suicide associated with depression. Mediation analysis showed no evidence suggesting that nightmares directly influence suicide risk. However, among participants without a diagnosis of depression at baseline, nightmare sufferers had an increased probability of receiving a diagnosis of depression during follow-up. Our findings indicate that nightmares may reflect pre-existing depression.

In accordance with previous studies suggesting a gender difference in nightmare frequency [25], women tended to report nightmares more often than men. We also observed a gender difference in the prevalence of self-reported depressive symptoms and depressive disorders, which has also previously been well-documented [26]. Our study was also in line with the consistent finding that men have higher suicide mortality rates than women [27]. Although there are gender differences in nightmare frequency, in the prevalence of depressive symptoms and depressive disorders, as well as in suicide mortality rates, our finding that nightmares have no direct influence on suicide incidence applied to both women and men.

Nightmare distress, the extent to which nightmares compromise daytime functioning and well-being, has been associated with mental complaints such as anxiety and depression rather than with nightmare frequency [28,29]. Since nightmares are potentially modifiable, and the clinical efficacy of psychological treatments is well-documented [2], interventions in order to reduce clinically significant nightmare symptoms are important, particularly in the context of psychiatric comorbidity.

There are substantial genetic effects on the disposition to nightmares [8]. A recent genome-wide association study,

examining the genetics of nightmares, indicate that shared genetics may account for the observed association between nightmares and depression, and thus contribute to the comorbidity of these conditions [30]. Furthermore, analysis of directionality showed that psychiatric traits were predictors for nightmares, whereas no evidence was observed suggesting that nightmares would predispose to psychiatric illness or psychological problems [30]. More research in this area is warranted since knowledge of the role of genetics in nightmares and depression might be applied in developing preventative strategies in the future.

The strengths of this prospective cohort study are the large sample size, the long follow-up duration, and the almost complete follow-up ascertained by linking baseline information with nationwide, continuously updated registers. The study provides detailed information of high quality regarding exposure information [21].

Weaknesses are that all self-reported information was only measured at baseline. Potential changes in the occurrence of nightmares during the follow-up period would go undetected. However, evidence suggests that nightmares may persist over long periods of time [8–10]. Another limitation is that the participants were not provided with a definition of nightmares and we were unable to differentiate between nightmares with intense emotional impact that awakens the sleeper and bad dreams with no temporal relationship between the content of the dream and waking up. However, the gender difference in nightmare frequency is not affected by nightmare definition [25], indicating that there is a continuum from bad dreams to nightmares with comparable etiological factors. When the participants were categorized by measures of depression and nightmares, relatively few deaths by suicide occurred in each category, and our results should therefore be interpreted with caution. Furthermore, apart from self-reported use of hypnotics, we did not have the opportunity to adjust the analyses for medications that have been associated with the occurrence of nightmares, such as selective serotonin reuptake inhibitors [31].

Since subjects were recruited during a fund-raising event in order to support cancer research, the cohort may be prone to a potential healthy volunteer bias. However, while poor response rates and incomplete follow-up is a problem in many population-based studies, the shortcomings of a non-representative sample must be weighed against the fact that choosing a restricted sample can increase the feasibility of the study, the prevalence of the exposure and completeness of the follow-up. These factors all increase the validity and precision of the study. For example, the level of missing data was very low in our study.

In conclusion, our findings indicate that nightmares have no influence on the incidence rate of suicide, but may reflect pre-existing depression. This is supported by a recent discovery of a strong genetic correlation of nightmares with depressive disorders, with no evidence that nightmares would predispose to psychiatric illness or psychological problems. Interventions targeting both depression and nightmares, when these conditions co-occur, may provide additional therapeutic benefit.

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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.2020.11.018.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2020.11.018.

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