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Self-reported short and long sleep duration, sleep debt and insomnia are associated with several types of infections: Results from the Norwegian practice-based research network in general practice – PraksisNett

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ABSTRACT

Objective: The objective was to assess the association between self-reported infections and sleep duration, sleep debt, chronic insomnia, and insomnia severity.
Methods: In total, 1023 participants were recruited from the Norwegian practice-based research network in general practice to a cross-sectional online survey with validated questions about sleep habits and insomnia symptoms (Bergen Insomnia Scale (BIS) and Insomnia Severity Index (ISI)), and whether they had experienced various infections during the last three months. Data were analyzed with chi-square tests and logistic regressions with adjustment for relevant confounders.
Results: Self-reported short sleep duration (<6 h) was significantly associated with increased odds of throat infection (OR = 1.60), ear infection (OR = 2.92), influenzalike illness (OR = 1.81) and gastrointestinal infection (OR = 1.91) whereas long sleep duration (>9 h) was associated with increased odds of throat (OR = 3.33) and ear infections (OR = 5.82), compared to sleep duration of 6–9 h, respectively. Sleep debt of >2 h was associated with increased odds of the common cold (OR = 1.67), throat infection (OR = 2.58), ear infection (OR = 2.84), sinusitis (OR = 2.15), pneumonia/bronchitis (OR = 3.97), influenzalike illness (OR = 2.66), skin infection (OR = 2.15), and gastrointestinal infection (OR = 2.80), compared to no sleep debt. Insomnia (based on BIS and ISI) was associated with throat infection (OR = 2.06, 2.55), ear infection (OR = 2.43, 2.45), sinusitis (OR = 1.82, 1.80), pneumonia/bronchitis (OR = 2.23, 3.59), influenzalike illness (OR = 1.77, 1.90), skin infection (OR = 1.64, 2.06), gastrointestinal infection (OR = 1.94, 3.23), and eye infection (OR = 1.99, 2.95).
Conclusions: These novel findings support the notion that people who have insufficient sleep or sleep problems are at increased risk of infections.

1. Introduction

The association between sleep and infectious diseases is understudied. An extensive review on the sleep-immune crosstalk, which focused on how sleep and the immune system interact, suggested more studies [1]. It is assumed that sleep of adequate duration and quality may reduce the risk of infections, improve infection outcomes and enhance vaccination responses [1–4]. This notion is supported with data from two large population cohorts, where an insomnia diagnosis causally predisposed for influenza, upper respiratory infections and severe COVID-19 [5]. A study on influenza vaccination compared habitual sleep with restricted sleep (time in bed was restricted to 4 h per night for 4 days before and 2 days after the vaccination), and found that influenza-virus-specific antibody titers after vaccination were doubled in participants with

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habitual sleep compared to restricted sleep [6]. Furthermore, research shows that a single night without sleep following vaccination against hepatitis A, hepatitis B, H1N1 (swine flu) reduced the antigen-specific antibody response [1]. These latter two studies suggest that severe sleep restriction impacts the immune system. How more modest sleep deprivation affects the risk of infections is uncertain and warrants further studies.

A recent cross-sectional study among patients visiting their general practitioner (GP) showed that both chronic insomnia and short and long sleep duration were associated with increased risk of self-reported infections within the last three months. Furthermore, short sleep duration and chronic insomnia were also associated with increased risk of antibiotic use [7]. The reason why the patients visited their GP was not registered in that study, and this may represent a bias as having an acute illness may influence sleep. In addition, this previous study did not assess the role of sleep need. Habitual sleep duration and sleep need vary considerably between individuals [8], and some people may feel rested after relatively few hours. Thus, to compare individuals who fulfil their sleep need with people who do not, may enhance our understanding of the association between sleep and infections. Sleep debt can be calculated as the difference between self-reported sleep need and sleep duration, and increasing levels of sleep debt are assumed to be associated with poorer health outcomes [9,10].

Based on this backdrop, the aims of the present study were to examine associations between self-reported sleep duration, sleep debt, chronic insomnia, and different levels of insomnia severity, and a wide variety of infections. We hypothesized that short and long sleep duration (<6 h and >9 h), increasing sleep debt, chronic insomnia, and increasing insomnia severity would be positively associated with infections.

2. Materials and methods

2.1. Study design and participants

Norway has a well-functioning primary care system, and all citizens are entitled to enlist with a GP. Most GPs work in small collaborations with less than 10 colleagues and support staff.

GPs from different parts of Norway participate in the Norwegian practice-based research network in General Practice – PraksisNett (www.praksisnett.no). The network facilitates recruitment of primary care patients to research. The GPs surgeries are connected to the network through an advanced IT infrastructure named Snow. In the Snow system, no central database is required, and all patient data are stored within the IT infrastructure in each GP surgery ensuring the anonymity of patient information [11]. This Snow infrastructure enables identification of potential study participants based on e.g., diagnoses.

Table 1
Characteristics of total study sample of participants invited by the General Practitioner.

	Number	Percentage (%)
Gender		
Male	397	40.2
Female	590	59.7
Do not want to say/other	1	0.1
Age (years)		
25-40	269	27.3
41-55	402	40.8
56-70	315	31.9
Marital status		
Single	163	16.5
Married/cohabiting	735	74.5
Divorced/separated	76	7.7
Widow/widower	12	1.2
Country of birth		
Norway	890	90.3
Other European country	73	7.4
Asia	11	1.1
Africa	3	0.3
America	8	0.8
Oceania	1	0.1
Children living at home		
No	584	59.1
Yes	404	40.9
Educational level		
Primary school	51	5.2
Secondary school	261	26.6
College/university	669	68.2
Sleep duration		
<6 h	230	23.9
6–9 h	716	74.5
>9 h	15	1.6
Sleep need		
<6 h	26	2.7
6–9 h	896	93.3
>9 h	38	4.0
Sleep debt		
No	252	26.3
15 min-2 hours	566	59.0
>2 h	142	14.8
Bergen Insomnia Scale		
No insomnia	426	47.3
Chronic insomnia	475	52.7
Insomnia Severity Index		
No insomnia	388	41.6
Subthreshold insomnia	333	35.7
Insomnia	211	22.6

Table 2
Self-reported infections during the last three months in the total sample of participants invited by the general practitioner.

	Number	Percentage (%)
Common cold		
No	439	49.1
Yes	456	50.9
Throat infection		
No	780	87.2
Yes	114	12.8
Ear infection		
No	856	95.7
Yes	38	4.3
Sinusitis		
No	800	89.5
Yes	94	10.5
Pneumonia/bronchitis		
No	858	96.0
Yes	36	4.0
COVID-19		
No	733	82.1
Yes	160	17.9
Influenzalike illness		
No	613	68.5
Yes	282	31.5
Skin infection		
No	698	78.0
Yes	197	22.0
Gastrointestinal infection		
No	717	80.1
Yes	178	19.9
Urinary infection		
No	846	94.5
Yes	49	5.5
Venereal disease		
No	877	98.1
Yes	17	1.9
Eye infection		
No	821	91.8
Yes	73	8.2

In the present study, PraksisNett was used to identify potential participants aged 25–70 years to a study focusing on sleep and infections. Lists of their own eligible patients were made electronically available for GPs within the network, and 29 GPs sent out invitations to patients for participation in the study. Only the GP knew the identity of the identified patients, and the GP sent an electronic invitation through the National online health services (www.helsenorge.no) in Norway (including a link to the online survey) to the patients. The GPs decided which patients to invite from the lists, and they were instructed to exclude patients who they considered not eligible for participation (e.g., due to terminal disease, acute life crisis etc.). The GPs were instructed to invite about 20 patients from a list of patients who had been diagnosed with a sleep problem during the last year (P06 in the International Classification of Primary Care, 2nd edition – ICPC-2) and about 40 patients from a list of patients without a diagnosed sleep problem during the last year. The reason for this procedure was to ensure enough patients with a sleep problem. To increase the number of participants, 12 of the GPs invited patients on two separate occasions. The goal was to include about 900 patients as power analysis suggested that this number would be appropriate. Based on an estimation of about 30% response rate, we therefore aimed at inviting a total of 3000 patients. The invitations were sent out between March 2022 and January 2023. Patients responded to the invitation by clicking on the link and thereby entering the online survey (provided by Surveyxact by Ramboll; www.surveyxact.no) in which they were presented with information about the study. Only patients who consented to participate received the survey questions.

2.2. Survey items analyzed in the present study

Patients were asked about the following socio-demographic variables: gender (male; female; do not want to say/other), age (25–70 years), marital status (single; married/cohabiting; divorced/separated; widow/widower), country of birth (Norway; other European country; Asia; Africa; America; Oceania), children living at home (no; yes), educational level (primary school; secondary school; college/university).

Habitual daily sleep duration was self-reported from a drop-down menu with 15 min intervals ("0 min" up until "more than 12 h") and categorized into <6 h, 6–9 h, and >9 h. Sleep need (how many hours of sleep per day do you need to feel rested?) was also indicated from a similar drop-down menu. Sleep debt was calculated as the difference between sleep need and sleep duration and split into three categories (no sleep debt; 15 minutes-2 hours; >2 h).

Insomnia symptoms were measured with two validated questionnaires, Bergen Insomnia Scale and Insomnia Severity Index. Bergen Insomnia Scale (BIS) [12] consists of six items, and was in the present study used as a proxy for chronic insomnia as indicated by the diagnostic criteria in the Diagnostic and Statistical Manual for Mental Disorders version 5 (DSM-5) and International Classification of Sleep Disorders-3 (ICSD-3) [13,14]. The BIS items are scored along an eight-point scale indicating the number of days per week during the last three months for which a specific insomnia symptom is experienced (0–7 days). The items refer to sleep onset (sleep latency exceeding 30 min), wake after sleep onset (more than 30 min), early

Table 3
Association between sleep duration and different types of infection.

	Sleep duration			χ2 (df)	p-value[1]
	<6 h	6–9 h	>9 h		
Common cold				2.7 (2)	0.263
No	97 (44.3%)	334 (50.5%)	8 (53.3%)		
Yes	122 (55.7%)	327 (49.5%)	7 (46.7%)		
Throat infection				**9.2 (2)**	**0.010**
No	184 (84.0%)	586 (88.8%)	10 (66.7%)		
Yes	35 (16.0%)	74 (11.2%)	5 (33.3%)		
Ear infection				**12.7 (2)**	**0.002**
No	202 (92.2%)	641 (97.1%)	13 (86.7%)		
Yes	17 (7.8%)	19 (2.9%)	2 (13.3%)		
Sinusitis				2.5 (2)	0.284
No	190 (86.8%)	597 (90.5%)	13 (86.7%)		
Yes	29 (13.2%)	63 (9.5%)	2 (13.3%)		
Pneumonia/bronchitis				3.2 (2)	0.202
No	206 (94.1%)	637 (96.5%)	15 (100.0%)		
Yes	13 (5.9%)	23 (3.5%)	0 (0.0%)		
COVID-19				1.4 (2)	0.490
No	184 (84.0%)	538 (81.6%)	11 (73.3%)		
Yes	35 (16.0%)	121 (18.4%)	4 (26.7%)		
Influenzalike illness				**15.0 (2)**	**<0.001**
No	127 (58.0%)	476 (72.0%)	10 (66.7%)		
Yes	92 (42.0%)	185 (28.0%)	5 (33.3%)		
Skin infection				2.7 (2)	0.256
No	162 (74.0%)	524 (79.3%)	12 (80.0%)		
Yes	57 (26.0%)	137 (20.7%)	3 (20.0%)		
Gastrointestinal infection				**16.9 (2)**	**<0.001**
No	156 (71.2%)	551 (83.4%)	10 (66.7%)		
Yes	63 (28.8%)	110 (16.6%)	5 (33.3%)		
Urinary infection				2.4 (2)	0.295
No	205 (93.6%)	628 (95.0%)	13 (86.7%)		
Yes	14 (6.4%)	33 (5.0%)	2 (13.3%)		
Venereal disease				2.2 (2)	0.334
No	214 (97.7%)	649 (98.3%)	14 (93.3%)		
Yes	5 (2.3%)	11 (1.7%)	1 (6.7%)		
Eye infection				3.0 (2)	0.220
No	195 (89.0%)	612 (92.7%)	14 (93.3%)		
Yes	24 (11.0%)	48 (7.3%)	1 (6.7%)		

χ2, Pearson chi-square. df, degrees of freedom. Significant results are indicated in bold.

morning awakening (more than 30 min), non-restorative sleep, daytime impairment, and dissatisfaction with sleep. Chronic insomnia was defined as scoring 3 days per week or more on at least one of the first three items, as well as 3 days per week or more on at least one of the latter two items. Cronbach's alpha for the BIS was 0.86 in the present sample. Insomnia Severity Index (ISI) is a seven-item instrument which assesses perceived severity of nocturnal and daytime symptoms of insomnia during the last two weeks [15]. Each item is rated on a scale of 0–4 for a total score ranging from 0 to 28. A score of 0–7 indicates no insomnia, 8–14 subthreshold insomnia, and 15–28 indicates moderate to severe insomnia. Cronbach's alpha for the ISI was 0.91 in the present sample.

The participants reported whether they had experienced the following infections during the last three months (no/yes): common cold, throat infection, ear infection, sinusitis, pneumonia/bronchitis, COVID-19, influenzalike illness, skin infection (erysipelas, herpes labialis, etc.), gastrointestinal infection with vomit and/or diarrhea, urinary infection (cystitis, pyelonephritis), venereal disease (chlamydia, genital herpes), and eye infection.

2.3. Ethics

The study was approved by the Regional Committee for Medical and Health Related Research Ethics (REK sør-øst, application number 268606). Only participants who consented to participate received the survey questions.

2.4. Statistics

Data analyses were conducted with SPSS, version 28 (IBM SPSS Statistics). The associations between sleep duration (<6 h vs. 6–9 h vs. >9 h) and different types of infections were explored using Pearson chi-square statistics. Similarly, the associations between sleep debt (no sleep debt vs. 15 min-2 hours vs. >2 h), chronic insomnia (BIS: no vs. yes), and insomnia severity (ISI: no vs. subthreshold vs. insomnia) and different types of infections were explored with Pearson chi-square statistics. Furthermore, both crude and adjusted (for gender, age, marital status, country of birth, children living at home, and educational level) logistic regression analyses were conducted with the different infections as dependent variables (no = 0; yes = 1) and sleep duration, sleep debt, chronic insomnia, and insomnia severity as independent variables. The adjusting variables were chosen since they are known to potentially influence sleep [16]. Significance level was set to .05.

3. Results

The GPs sent out a total of 2492 invitations to potential participants. In all, 1023 consented to participate, 72 declined, and the rest did not respond to the invitation. Response rate was 41.1% (1023/2492).

Table 1 presents the characteristics of the study sample. About 60% of the participants were female, and mean age was 48.7

Table 4
Association between sleep debt and different types of infection.

	Sleep debt			χ2 (df)	p-value[1]
	No	15 min-2 hours	>2 h		
Common cold				**10.5 (2)**	**0.005**
No	136 (56.9%)	250 (47.7%)	53 (40.2%)		
Yes	103 (43.1%)	274 (52.3%)	79 (59.8%)		
Throat infection				**13.0 (2)**	**0.001**
No	217 (90.8%)	460 (88.0%)	103 (78.0%)		
Yes	22 (9.2%)	63 (12.0%)	29 (22.0%)		
Ear infection				**8.9 (2)**	**0.012**
No	231 (96.7%)	505 (96.6%)	120 (90.9%)		
Yes	8 (3.3%)	18 (3.4%)	12 (9.1%)		
Sinusitis				**8.8 (2)**	**0.012**
No	224 (93.7%)	465 (88.9%)	111 (84.1%)		
Yes	15 (6.3%)	58 (11.1%)	21 (15.9%)		
Pneumonia/bronchitis				**10.6 (2)**	**0.005**
No	233 (97.5%)	505 (96.6%)	120 (90.9%)		
Yes	6 (2.5%)	18 (3.4%)	12 (9.1%)		
COVID-19				0.2 (2)	0.920
No	195 (81.9%)	428 (81.8%)	110 (83.3%)		
Yes	43 (18.1%)	95 (18.2%)	22 (16.7%)		
Influenzalike illness				**22.3 (2)**	**<0.001**
No	186 (77.5%)	356 (68.1%)	71 (53.8%)		
Yes	54 (22.5%)	167 (31.9%)	61 (46.2%)		
Skin infection				**14.3 (2)**	**<0.001**
No	207 (86.6%)	394 (75.2%)	97 (73.5%)		
Yes	32 (13.4%)	130 (24.8%)	35 (26.5%)		
Gastrointestinal infection				**27.7 (2)**	**<0.001**
No	205 (85.4%)	428 (81.8%)	84 (63.6%)		
Yes	35 (14.6%)	95 (18.2%)	48 (36.4%)		
Urinary infection				2.2 (2)	0.333
No	225 (93.8%)	499 (95.4%)	122 (92.4%)		
Yes	15 (6.3%)	24 (4.6%)	10 (7.6%)		
Venereal disease				1.0 (2)	0.619
No	233 (97.5%)	515 (98.5%)	129 (97.7%)		
Yes	6 (2.5%)	8 (1.5%)	3 (2.3%)		
Eye infection				2.4 (2)	0.299
No	225 (94.1%)	475 (90.8%)	121 (91.7%)		
Yes	14 (5.9%)	48 (9.2%)	11 (8.3%)		

χ2, Pearson chi-square. df, degrees of freedom. Significant results are indicated in bold.

Table 5
Association between chronic insomnia (Bergen Insomnia Scale) and different types of infection.

	Chronic insomnia		χ2 (df)	p-value[1]
	No	Yes		
Common cold			3.3 (1)	0.07
No	221 (52.4%)	218 (46.1%)		
Yes	201 (47.6%)	255 (53.9%)		
Throat infection			**11.9 (1)**	**<0.001**
No	385 (91.4%)	395 (83.5%)		
Yes	36 (8.6%)	78 (16.5%)		
Ear infection			**4.5 (1)**	**0.034**
No	410 (97.4%)	446 (94.3%)		
Yes	11 (2.6%)	27 (5.7%)		
Sinusitis			**7.8 (1)**	**0.005**
No	390 (92.6%)	410 (86.7%)		
Yes	31 (7.4%)	63 (13.3%)		
Pneumonia/bronchitis			**4.8 (1)**	**0.028**
No	411 (97.6%)	447 (94.5%)		
Yes	10 (2.4%)	26 (5.5%)		
COVID-19			1.6 (1)	0.205
No	337 (80.2%)	396 (83.7%)		
Yes	83 (19.8%)	77 (16.3%)		
Influenzalike illness			**18.0 (1)**	**<0.001**
No	319 (75.6%)	294 (62.2%)		
Yes	103 (24.4%)	179 (37.8%)		
Skin infection			**9.8 (1)**	**0.002**
No	349 (82.7%)	349 (73.8%)		
Yes	73 (17.3%)	124 (26.2%)		
Gastrointestinal infection			**18.2 (1)**	**<0.001**
No	364 (86.3%)	353 (74.6%)		
Yes	58 (13.7%)	120 (25.4%)		
Urinary infection			0.2 (1)	0.681
No	397 (94.1%)	449 (94.9%)		
Yes	25 (5.9%)	24 (5.1%)		
Venereal disease			0.0 (1)	1.000
No	413 (98.1%)	464 (98.1%)		
Yes	8 (1.9%)	9 (1.9%)		
Eye infection			**5.8 (1)**	**0.016**
No	397 (94.3%)	424 (89.6%)		
Yes	24 (5.7%)	49 (10.4%)		

χ2, Pearson chi-square with continuity correction. df, degrees of freedom. Significant results are indicated in bold.

(SD = 12.0) years. More than 90% reported being born in Norway, and most participants reported college or university education. Short sleep duration (<6 h) was reported by 23.9% and long sleep duration (>9 h) by 1.6%. Only 2.7% reported a sleep need of <6 h and 4.0% a sleep need of >9 h (Table 1). Based on sleep duration and sleep need, sleep debts of 15 min-2 hours and >2 h were calculated to be 59.0% and 14.8%, respectively. Based on BIS, chronic insomnia was present in 52.7%, whereas ISI showed subthreshold insomnia and insomnia in 35.7% and 22.6%, respectively (Table 1).

Table 2 presents the percentage of self-reported infections experienced during the last three months. The percentage of infections ranged from 50.9% (common cold) to 1.9% (venereal disease).

Table 3 presents the associations between sleep duration and different types of infections. In general, participants with a sleep duration between 6 and 9 h reported fewer infections than short (<6 h) and long (>9 h) sleepers. In chi-square tests, the difference in relation to these three sleep duration categories was significant for throat infection, ear infection, influenzalike illness, and gastrointestinal infection.

Table 4 presents the associations between sleep debt and different types of infections. Increasing sleep debt dose-dependently increased the risk of reporting to have experienced common cold, throat infection, ear infection, sinusitis, pneumonia/bronchitis, influenzalike illness, skin infection, and gastrointestinal infection.

Table 5 presents the associations between chronic insomnia and different types of infections. Chronic insomnia increased the risk of reporting to have experienced throat infection, ear infection, sinusitis, pneumonia/bronchitis, influenzalike illness, skin infection, gastrointestinal infection, and eye infection.

Table 6 presents the associations between insomnia severity and different types of infections. Increasing insomnia severity dose-dependently increased the risk of reporting to have experienced throat infection, ear infection, pneumonia/bronchitis, influenzalike illness, skin infection, gastrointestinal infection, and eye infection.

Table 7 shows logistic regression analyses with the different types of infection as the dependent variable. In line with the results from the chi-square tests, adjusted analyses showed that both short and long sleep duration predicted increased odds of throat infection and ear infection, and short sleep duration predicted increased odds of influenzalike illness and gastrointestinal infection. Odds ratio (OR) ranged from 1.60 to 5.82. For sleep debt, the adjusted logistic regression analyses indicated a dose-dependent association, with a sleep debt of >2 h predicting increased odds of common cold (OR = 1.67), throat infection (OR = 2.58), ear infection (OR = 2.84), sinusitis (OR = 2.15), pneumonia/bronchitis (OR = 3.97), influenzalike illness (OR = 2.66), skin infection (OR = 2.15), and gastrointestinal infection (OR = 2.80). For chronic insomnia and insomnia severity, the adjusted logistic regression analyses showed similar findings in which there were increased odds of throat infection, ear infection, sinusitis, pneumonia/bronchitis, influenzalike illness, skin infection, gastrointestinal infection, and eye infection (Table 7). COVID-19, urinary infection, and venereal disease did not show any association with sleep duration, sleep debt, chronic insomnia, and insomnia severity.

4. Discussion

Short and long sleep duration, sleep debt, and insomnia were all associated with higher odds of experiencing infections. For sleep debt and insomnia severity, the associations were clearly dose-dependent. These significant associations were evident for several types of infections, such as throat infection, ear infection, sinusitis, pneumonia/bronchitis, influenzalike illness, skin infection, and gastrointestinal infection. However, no associations were present between the sleep variables (sleep duration, sleep debt, and insomnia) and COVID-19, urinary infection, and venereal disease.

Sufficient sleep of good quality is assumed to reduce the risk of infections [1,3,4], but studies are few. In a recent study with patients visiting their GP, we found associations between insomnia, short and long sleep duration and risk of infection and antibiotic use [7] in line with the present findings. However, that study did not report any associations specifically for respiratory infections, in contrast to the present findings. Most other studies on the association between sleep and infections have investigated respiratory infections, and the general findings are that short sleep duration and sleep problems do infer an increased risk [17–19]. Furthermore, an experimental study showed that the susceptibility for rhinovirus infection (the common cold) is increased in people sleeping less than 6 h [20]. In the present study we found an association between short sleep duration (<6 h) and several respiratory infections but not the common cold. However, when looking at sleep debt, we found that >2 h difference between sleep need and sleep duration significantly increased the odds also for the common cold. We do believe that investigating sleep debt may enhance our understanding of the association between sleep and infections, because some people may have short sleep duration and still feel rested [8]. It is likely that sleep is associated with risk of infections especially among those individuals who do not fulfil their sleep need. The present findings underscore this, where the associations between sleep debt and odds of infection

Table 6
Association between insomnia (Insomnia Severity Index) and different types of infection.

	Insomnia Severity Index			χ2 (df)	p-value[1]
	No insomnia	Subthreshold	Insomnia		
Common cold				1.5 (2)	0.476
No	187 (50.3%)	161 (50.0%)	91 (45.3%)		
Yes	185 (49.7%)	161 (50.0%)	110 (54.7%)		
Throat infection				**14.8 (2)**	**<0.001**
No	343 (92.2%)	272 (84.7%)	165 (82.1%)		
Yes	29 (7.8%)	49 (15.3%)	36 (17.9%)		
Ear infection				**6.6 (2)**	**0.037**
No	360 (96.8%)	310 (96.6%)	186 (92.5%)		
Yes	12 (3.2%)	11 (3.4%)	15 (7.5%)		
Sinusitis				**7.2 (2)**	**0.027**
No	345 (92.7%)	279 (86.9%)	176 (87.6%)		
Yes	27 (7.3%)	42 (13.1%)	25 (12.4%)		
Pneumonia/bronchitis				**9.5 (2)**	**0.009**
No	364 (97.8%)	308 (96.0%)	186 (92.5%)		
Yes	8 (2.2%)	13 (4.0%)	15 (7.5%)		
COVID-19				1.7 (2)	0.432
No	298 (80.3%)	265 (82.6%)	170 (84.6%)		
Yes	73 (19.7%)	56 (17.4%)	31 (15.4%)		
Influenzalike illness				**16.8 (2)**	**<0.001**
No	283 (75.9%)	207 (64.5%)	123 (61.2%)		
Yes	90 (24.1%)	114 (35.5%)	78 (38.8%)		
Skin infection				**14.4 (2)**	**<0.001**
No	313 (84.1%)	240 (74.5%)	145 (72.1%)		
Yes	59 (15.9%)	82 (25.5%)	56 (27.9%)		
Gastrointestinal infection				**36.1 (2)**	**<0.001**
No	325 (87.1%)	259 (80.7%)	133 (66.2%)		
Yes	48 (12.9%)	62 (19.3%)	68 (33.8%)		
Urinary infection				0.1 (2)	0.940
No	353 (94.6%)	304 (94.7%)	189 (94.0%)		
Yes	20 (5.4%)	17 (5.3%)	12 (6.0%)		
Venereal disease				1.1 (2)	0.570
No	367 (98.7%)	314 (97.8%)	196 (97.5%)		
Yes	5 (1.3%)	7 (2.2%)	5 (2.5%)		
Eye infection				**10.9 (2)**	**0.004**
No	353 (94.9%)	293 (91.3%)	175 (87.1%)		
Yes	19 (5.1%)	28 (8.7%)	26 (12.9%)		

χ2, Pearson chi-square. df, degrees of freedom. Significant results are indicated in bold.

were more pronounced than the associations between short sleep duration and infection. These findings are novel, as no previous study has investigated the association between sleep debt and risk of infections.

The associations between sleep duration, sleep debt, insomnia and infections were strong, and stronger the more sleep was insufficient or disturbed. For instance, there was a dose-dependent association with influenzalike illness where 22.5% among those with no sleep debt, 31.9% among those with a sleep debt of 15 minutes-2 hours, and 46.2% among those with a sleep debt of >2 h reported to have experienced such illness during the last three months. For gastrointestinal infection, these numbers were 14.6%, 18.2%, and 36.4%, again clearly showing the dose-dependent association with increasing sleep debt. Sleep disturbances are common in patients with gastrointestinal disease [21], but few studies have investigated whether insufficient or poor sleep may increase the risk of gastrointestinal infection. Our data are cross-sectional; hence, we cannot infer cause-and-effect. Thus, our data cannot tell whether insufficient and poor sleep are causing these infections or whether the infections are causing insufficient and poor sleep.

Experimental research on humans has shown that sleep deprivation and/or sleep problems are associated with increased levels of inflammatory blood markers and decreased vaccine responses [1,6,20,22]. In a Norwegian study among nurses, short sleep duration (<6 h) was associated with lower levels of interleukin-1beta and higher levels of tumor necrosis factor-alpha [23]. Furthermore, cohort studies show that insomnia causally predisposes for influenza, upper respiratory infections and severe COVID-19 [5]. These data suggest that it is more likely that insufficient sleep and insomnia are causing increased risk of infections than vice versa. However, more longitudinal studies are needed to entangle these associations.

Long sleep duration (>9 h) was associated with increased odds of throat and ear infections, but not the other infections. Long sleep duration is more common among patients with cardiovascular disease, diabetes and obesity [24], and has also been linked to depression, low educational level, low physical activity level, and high drinking and smoking rates [25]. Thus, the association between long sleep duration and infection may be related to these comorbidities. Since very few individuals (only 15) reported >9 h sleep duration, these data need to be interpreted with caution.

We did not find any associations between the sleep variables and COVID-19, urinary infection, or venereal disease. For COVID-19 this was a bit surprising, but one possible explanation may be that the SARS-CoV-2 virus is so contagious that people get infected when exposed, even if there is no sleep debt or sleep problem. In line with this, a recent study showed that shift/night work was not associated with increased risk of COVID-19. However, when infected, the shift/night workers suffered from more severe illness [26]. Whether this was the case in the present study is unknown. In the previous study with patients visiting their GP, we found that chronic insomnia was associated with increased risk of urinary infection [7], in contrast to the present findings. Sleep duration was, however, not significantly associated with urinary infection in the

Table 7
Logistic regression analyses with type of infection (no = 0; yes = 1) as the dependent variable and sleep duration, sleep debt, chronic insomnia, and insomnia severity as predictors.

	Common cold (n = 895) OR (95% CI)		Throat infection (n = 894) OR (95% CI)		Ear infection (n = 894) OR (95% CI)	
	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
Sleep duration						
6–9 h	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
<6 h	1.29 (0.95–1.75)	1.36 (0.99–1.89)	1.51 (0.98–2.23)	**1.60 (1.02–2.50)**	**2.84 (1.45–5.57)**	**2.92 (1.45–5.85)**
>9 h	0.89 (0.32–2.49)	0.74 (0.26–2.13)	**3.96 (1.32–11.90)**	**3.33 (1.06–10.48)**	**5.19 (1.09–24.63)**	**5.82 (1.12–30.09)**
Sleep debt						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
15 min-2 hours	**1.45 (1.06–1.97)**	1.20 (0.87–1.66)	1.35 (0.81–2.25)	1.22 (0.72–2.06)	1.03 (0.44–2.40)	1.10 (0.46–2.64)
>2 h	**1.97 (1.28–3.03)**	**1.67 (1.05–2.64)**	**2.78 (1.52–5.07)**	**2.58 (1.37–4.87)**	**2.89 (1.15–7.26)**	**2.84 (1.06–7.63)**
Chronic insomnia						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	1.29 (0.99–1.67)	1.27 (0.96–1.69)	**2.11 (1.39–3.21)**	**2.06 (1.34–3.19)**	**2.26 (1.11–4.61)**	**2.43 (1.15–5.10)**
Insomnia severity						
No insomnia	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Subthreshold	1.01 (0.75–1.36)	0.96 (0.70–1.31)	**2.13 (1.31–3.46)**	**2.05 (1.25–3.37)**	1.07 (0.46–2.45)	1.06 (0.45–2.48)
Insomnia	1.22 (0.87–1.72)	1.27 (0.88–1.84)	**2.58 (1.53–4.35)**	**2.55 (1.48–4.39)**	**2.42 (1.11–5.28)**	**2.45 (1.08–5.52)**

	Sinusitis (n = 894) OR (95% CI)		Pneumonia/bronchitis (n = 894) OR (95% CI)		COVID-19 (n = 893) OR (95% CI)	
	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
Sleep duration						
6–9 h	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
<6 h	1.45 (0.91–2.31)	1.44 (0.88–2.34)	1.75 (0.87–3.51)	1.64 (0.81–3.36)	0.85 (0.56–1.28)	0.91 (0.60–1.39)
>9 h	1.46 (0.32–6.61)	1.16 (0.25–5.47)	NA	NA	1.62 (0.51–5.16)	1.72 (0.53–5.66)
Sleep debt						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
15 min-2 hours	**1.86 (1.03–3.36)**	1.56 (0.85–2.86)	1.38 (0.54–3.53)	1.39 (0.53–3.65)	1.01 (0.68–1.50)	0.99 (0.66–1.50)
>2 h	**2.83 (1.40–5.69)**	**2.15 (1.04–4.46)**	**3.88 (1.42–10.60)**	**3.97 (1.37–11.52)**	0.91 (0.52–1.60)	0.95 (0.53–1.72)
Chronic insomnia						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	**1.93 (1.23–3.04)**	**1.82 (1.13–2.92)**	**2.39 (1.14–5.02)**	**2.23 (1.04–4.78)**	0.79 (0.56–1.11)	0.82 (0.58–1.17)
Insomnia severity						
No insomnia	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Subthreshold	**1.92 (1.16–3.20)**	**1.83 (1.08–3.08)**	1.92 (0.79–4.69)	1.80 (0.73–4.45)	0.86 (0.59–1.27)	0.88 (0.59–1.30)
Insomnia	**1.82 (1.02–3.22)**	1.80 (0.98–3.30)	**3.67 (1.53–8.81)**	**3.59 (1.46–8.87)**	0.74 (0.47–1.18)	0.80 (0.49–1.28)

	Influenzalike illness (n = 895) OR (95% CI)		Skin infection (n = 895) OR (95% CI)		Gastrointestinal infection (n = 895) OR (95% CI)	
	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
Sleep duration						
6–9 h	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
<6 h	**1.86 (1.36–2.56)**	**1.81 (1.30–2.52)**	1.35 (0.94–1.92)	1.28 (0.89–1.84)	**2.02 (1.42–2.89)**	**1.91 (1.32–2.76)**
>9 h	1.29 (0.43–3.81)	0.99 (0.33–3.03)	0.96 (0.27–3.44)	0.79 (0.22–2.90)	2.51 (0.84–7.47)	1.89 (0.61–5.81)
Sleep debt						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
15 min-2 hours	**1.62 (1.13–2.30)**	**1.53 (1.06–2.21)**	**2.13 (1.40–3.25)**	**2.07 (1.35–3.19)**	1.30 (0.85–1.98)	1.24 (0.81–1.92)
>2 h	**2.96 (1.87–4.67)**	**2.66 (1.65–4.31)**	**2.33 (1.36–3.99)**	**2.15 (1.23–3.76)**	**3.35 (2.02–5.54)**	**2.80 (1.65–4.75)**
Chronic insomnia						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	**1.89 (1.41–2.52)**	**1.77 (1.31–2.40)**	**1.70 (1.23–2.35)**	**1.64 (1.17–2.30)**	**2.13 (1.51–3.02)**	**1.94 (1.36–2.79)**
Insomnia severity						
No insomnia	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Subthreshold	**1.73 (1.25–2.41)**	**1.62 (1.15–2.26)**	**1.81 (1.25–2.64)**	**1.75 (1.20–2.57)**	**1.62 (1.08–2.44)**	1.52 (1.00–2.30)
Insomnia	**1.99 (1.38–2.89)**	**1.90 (1.29–2.80)**	**2.05 (1.35–3.10)**	**2.06 (1.34–3.18)**	**3.46 (2.27–5.27)**	**3.23 (2.08–5.02)**

	Urinary infection (n = 895) OR (95% CI)		Venereal disease (n = 894) OR (95% CI)		Eye infection (n = 894) OR (95% CI)	
	Crude	Adjusted	Crude	Adjusted	Crude	Adjusted
Sleep duration						
6–9 h	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
<6 h	1.30 (0.68–2.48)	1.01 (0.51–1.97)	1.38 (0.47–4.01)	1.24 (0.39–3.95)	1.57 (0.94–2.63)	1.50 (0.88–2.56)
>9 h	2.93 (0.63–13.51)	1.86 (0.37–9.45)	4.21 (0.51–34.92)	2.33 (0.25–21.87)	0.91 (0.12–7.07)	1.02 (0.13–8.17)
Sleep debt						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
15 min-2 hours	0.72 (0.37–1.40)	0.68 (0.34–1.38)	0.60 (0.21–1.76)	0.47 (0.16–1.45)	1.62 (0.88–3.00)	1.63 (0.87–3.07)
>2 h	1.23 (0.54–2.82)	0.91 (0.37–2.21)	0.90 (0.22–3.67)	0.45 (0.10–2.07)	1.46 (0.64–3.32)	1.33 (0.55–3.20)
Chronic insomnia						
No	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Yes	0.85 (0.48–1.51)	0.62 (0.33–1.16)	1.00 (0.38–2.62)	0.72 (0.25–2.06)	**1.91 (1.15–3.17)**	**1.99 (1.17–3.36)**
Insomnia severity						
No insomnia	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Subthreshold	0.99 (0.51–1.92)	0.80 (0.40–1.59)	1.64 (0.51–5.21)	1.29 (0.39–4.24)	1.78 (0.97–3.24)	1.84 (1.00–3.39)
Insomnia	1.12 (0.54–2.34)	0.86 (0.39–1.93)	1.87 (0.54–6.55)	1.21 (0.31–4.75)	**2.76 (1.49–5.12)**	**2.95 (1.54–5.63)**

CI, confidence interval. NA, not applicable. The logistic regression analyses were adjusted for gender, age, marital status, country of birth, children living at home, and educational level. Significant results are indicated in bold.

previous or the present study. Very few participants reported venereal disease, making the statistical analyses on possible associations with sleep variables uncertain. More studies on different types of infections are warranted to enhance our understanding of the potential underlying mechanisms behind the association with insufficient sleep and insomnia.

In the present study we used two different validated insomnia instruments. Bergen Insomnia Scale was used to categorize participants into chronic insomnia or not, based on DSM-5 and ICSD-3 criteria [13,14]. Thus, time frame for BIS was symptoms during the last three months. Insomnia Severity Index asks about symptoms during the last two weeks, and we used this scale for categorizing insomnia into no insomnia, subthreshold insomnia, and insomnia. The scales also differ regarding how the questions are phrased. BIS focuses on how many days per week an individual uses more than 30 min for sleep onset, wake after sleep onset, or early morning awakening, whereas ISI focuses on whether sleep onset, wake after sleep onset, or early morning awakening are experienced as problematic (no, mild, moderate, severe, very severe). Similar associations between these two scales and infections support the notion that insomnia symptoms are indeed associated with increased infection risk. Furthermore, the use of ISI enabled us to investigate whether insomnia was dose-dependently associated with infections, and this was confirmed for several types of infections.

Several strengths and limitations are worth considering. One strength was that we assessed insomnia with two validated instruments [12,15] as stated above. However, we need to acknowledge that these insomnia instruments may not accurately differentiate between insomnia and other sleep disorders. For instance, high scores on both scales may also be seen in participants with obstructive sleep apnea or circadian rhythm sleep-wake disorders [27]. The response rate was acceptable for this type of study [28], and higher than expected. We anticipated a response rate of about 30% but reached the goal of 900 participants with fewer invitations sent by the GPs. We believe that the present procedure in which the GPs were provided with lists of eligible patients, and the patients received invitations to participate from their personal GP with an electronically provided link to the survey, ensured a higher response rate. We also like to note that the reported response rate was based on how many consented to participate among the ones who were invited. However, we do not know if all invitations sent by the GPs were read. Only 72 out of 1095 participants who entered the website declined to participate. Thus, we believe that the results are likely generalizable to the general adult population. All data were based on self-report, which represents an important limitation. Thus, neither sleep duration nor infections were objectively assessed. Other limitations include recall bias [29], social desirability bias [30], and the common method bias [31]. Furthermore, due to the cross-sectional design, no causal inferences can be made in terms of the relationship between the study variables.

To conclude, both short and long sleep duration, increasing sleep debt, chronic insomnia, and increasing insomnia severity were associated with higher odds of infections. The clear dose-dependent association with sleep debt and insomnia severity are novel findings. Our study supports the notion that people who have insufficient sleep or sleep problems more often experience infections. Future studies are needed to explore whether sleep interventions can be potential targets for reducing this risk of infections.

CRediT authorship contribution statement

Bjørn Bjorvatn: Conceptualization, Methodology, Formal analysis, Investigation, Resources, Writing – original draft, Project administration, Funding acquisition. **Guri Rørtveit:** Conceptualization, Methodology, Investigation, Resources, Writing – review & editing, Project administration, Funding acquisition. **Ingrid Rebnord:** Conceptualization, Methodology, Writing – review & editing. **Siri Waage:** Conceptualization, Methodology, Writing – review & editing. **Knut Erik Emberland:** Conceptualization, Methodology, Writing – review & editing. **Ingeborg Forthun:** Conceptualization, Methodology, Investigation, Resources, Writing – review & editing, Project administration, Funding acquisition.

Declaration of competing interest

BB reports to have served as consultant for F. Hoffmann-La Roche Ltd, and received honoraria for lectures from AGB-Pharma AB. The other authors do not report any conflict of interest.

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