



Original Article

The epidemiology of sleep disorders in Israel: results from a population-wide study



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ABSTRACT

Background: Studies on the prevalence of sleep disorders have found great variability due to different data collection methods and case definitions. We aimed at assessing the prevalence of sleep disorders in a large, unselected population using validated clinical patient records.

To the best of our knowledge, this is the first large clinically based study on sleep disorders.

Methods: This retrospective study used the computerized data of 2.3 million members of Maccabi Healthcare Services (MHS) public mandated health provider. Among enrolled MHS members alive in June 2018, electronic medical records were searched from January 2010 for sleep disorders using diagnosis codes, sleep medications, and recorded sleep studies.

Results: A total of 195,201 patients (9% of the total MHS population) were identified. Patients were 48.3% men and the average age at diagnosis was 50.4 years (SD = 20.9). Prevalence increased with age; 3.2% in children under 10 years, 5.2% in young adults, and 22.3% among seniors aged 75 or older.

The two most prevalent disorders were insomnia (7.4%), and sleep-related breathing disorders (2%). Less prevalent disorders included central disorders of hypersomnolence (100 per 100,000), circadian rhythm sleep–wake disorders (49 per 100,000), parasomnias (140 per 100,000), and sleep-related movement disorders (20 per 100,000).

Conclusions: The overall prevalence of sleep disorders including insomnia and sleep related breathing disorders in Israel were similar to other western countries despite stressful life events of ongoing war and terrorism. The large sample size allowed us to calculate the prevalence of more rare sleep disorders, which have been generally less known.

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1. Introduction

Sleep disorders are a category of medical conditions that affect the ability to sleep well on a regular basis. Diagnostic classification of sleep disorders according to standardized definitions is important because it improves awareness of the conditions, promotes a broad differential diagnosis, and facilitates a systematic diagnostic

approach. The International Classification of Sleep Disorders (ICSD) is the most widely used classification system for sleep disorders. The third edition of the ICSD (ICSD-3) includes the following seven major categories of sleep disorders: (1) insomnia (defined as difficulty falling asleep or maintaining sleep, early-morning awakening or non-restorative sleep with associated daytime consequences); (2) sleep-related breathing disorders (sleep apnea, characterized by abnormal respiration during sleep); (3) central disorders of hypersomnolence (daytime sleepiness that is not due to another sleep disorder); (4) circadian rhythm sleep–wake disorders (characterized by a chronic or recurrent sleep disturbance due to alteration of the circadian system or misalignment between the environment and an individual's sleep–wake cycle); (5) parasomnias (undesirable physical events or experiences that occur before, during or

Abbreviations: MHS, Maccabi healthcare services; ICSD, international classification of sleep disorders; AHI, the Apnea–hypopnea index; MSLT, multiple sleep latency test; CPAP, continuous positive airway pressure; SES, socio-economic status.

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after sleep); (6) sleep-related movement disorders (characterized by simple, stereotypic movements that disturb sleep); and (7) other sleep disorders that cannot be appropriately classified [1–3].

Lack of proper sleep can have a negative impact on daily functions such as mood, attention and concentration abilities, and overall health [4]. For example, insomnia has been linked to major depressive illness [5]. Additionally, the long-term effects of sleep apnea include the development of hypertension, myocardial hypertrophy, atherosclerosis, and coronary artery disease; contributing to the progression of heart failure and increased mortality rates [4].

Age and gender are the most clearly identified demographic risk factors; for insomnia, with an increased prevalence in women and older adults [6]. In women, insomnia and sleep apnea are more prevalent with the onset of menopause [7].

Insomnia and sleep apnea are the most common sleep disorders [8]. However, these estimates are based on studies using various definitions and methods of measurement. A review article on epidemiological sleep disorder studies found that insomnia was self-reported by nearly one third of the responders, but a clinically valid diagnosis was available for only 6–15% [9]. Sleep apnea research studies on adults have also yielded great variability, prevalence estimates range from 9% to 38%, while only 2% of women and 4% of men are likely to meet diagnostic criteria including one symptom of disturbed sleep [9,10].

Substantial uncertainty was found in studies assessing the prevalence of other sleep disorders because of scarce clinically-based data [9].

Insomnia is often a consequence of stress and anxiety [11]. The Israeli population is characterized by its relatively frequent exposure to war and terrorism, immigration society, and Holocaust legacy [12].

Currently, there is limited research on sleep disorders in Israel, only scarce data from selected populations are available [13,14], and neither study was based on large clinically valid data. Thus, the objectives of this real-world clinical-based study were to better understand the scope and prevalence of sleep disorders in Israel

using doctor recorded patient information including diagnosis, medication, and sleep studies from a large population.

2. Methods

2.1. Setting

Data were extracted from the computerized database of Maccabi Healthcare Services (MHS), the second largest health care provider in Israel with over two million members, representing 25% of the population [15]. Data were automatically collected and included information regarding all diagnoses, comorbidities, hospitalizations, emergency department visits, physician visits, outpatient specialist visits, medication purchases, laboratory test results, and imaging. Each individual participant had a unique identification code in the system valid for all encounters.

Socio-economic status (SES) was categorized from 1 to 10 based on the poverty index of the member's enumeration area, as defined by Israel's 2008 national census. The poverty index was based on household income, educational level, crowding, physical conditions, and car ownership [16].

The study was approved by the MHS Ethics Board.

2.2. Sleep disorders assessments and definitions

Eligible patients for the study included all MHS members from January 1st 2010 to June 30th 2018 who belong to at least one of the following sleep disorder categories according their definitions. Patients were required to be alive and enrolled in MHS during June 2018.

The prevalence rates for each disorder were calculated. The conditions investigated and inclusion requirements are provided in Table 1. The study entry date was defined as the earliest date of dispensed medication or diagnosis.

Two types of sleep studies were performed to establish the diagnosis patients. The apnea–hypopnea index (AHI) is used for

Table 1
Sleep disorders definitions.

Sleep disorder	Study inclusion requirement
Insomnia	<ul style="list-style-type: none"> Any medication indicated for insomnia in Israel dispensed for at least six months during one year (see list of medications in Appendix I) or A physician diagnosis of insomnia (according to the International Classification of Diseases version 9 with clinical modifications (ICD-9-CM) codes (see all diagnosis codes in Appendix II)). <p>A more specific definition included only long-term use of a relevant sleep medication with or without a validating diagnosis.</p>
Sleep-related breathing disorders	<ul style="list-style-type: none"> Positive Apnea–Hypopnea Index (AHI) (AHI > 5/h) or A physician diagnosis of sleep apnea following a sleep study (without a documented AHI result) or Continuous positive airway pressure (CPAP) use.
Central disorders of hypersomnolence	<ul style="list-style-type: none"> Multiple sleep latency test (MSLT) or A physician diagnosis of central disorders of hypersomnolence.
Circadian rhythm sleep–wake disorders	<ul style="list-style-type: none"> A relevant physician diagnosis.
Parasomnias	<ul style="list-style-type: none"> A relevant physician diagnosis.
Sleep-related movement disorders	<ul style="list-style-type: none"> A relevant physician diagnosis of periodic limb movement^a.

^a In order to keep the sensitivity of the sleep-related movement disorder we have decided not to include the restless legs syndrome (RLS), which could occur not at sleep.

Table 2
Demographic data for patients with sleep disorders.

	Insomnia, N = 160,222	Sleep-related breathing disorders, N = 43,115	Central disorders of hypersomnolence, N = 2189	Circadian rhythm sleep–wake disorders, N = 1069	Parasomnias, N = 2998	Sleep-related movement disorders, N = 440	Any sleep disorder, N = 195,201
Sex, males, n (%)	68,910 (43.0%)	30,914 (71.7%)	1075 (49.1%)	610 (57.1%)	1764 (58.8%)	279 (63.4%)	94,186 (48.3%)
Age at diagnosis, mean (SD)	51.2 (21.2)	51.0 (17.0)	40.2 (19.5)	31.8 (17.3)	28.2 (28.0)	55.8 (18.4)	50.4 (20.9)
Low SES (1–4), n (%)	25,975 (16.2%)	6452 (15%)	303 (13.8%)	109 (10.2%)	424 (14.1%)	51 (11.6%)	31,300 (16%)

Table 3
Prevalence by sleep disorder.

	Insomnia, N = 160,222	Sleep-related breathing disorders, N = 43,115	Central disorders of hypersomnolence, N = 2189	Circadian rhythm sleep-wake disorders, N = 1069	Parasomnias, N = 2998	Sleep-related movement disorders, N = 440	Any sleep disorder, N = 195,201
Crude prevalence, % (95% CI)	7.4% (7.36–7.43)	2% (1.97–2.01)	1 per 1000 (1–1.1 per 1000)	0.49 per 1000 (0.46–0.52 per 1000)	1.4 per 1000 (1.34–1.43 per 1000)	0.2 per 1000 (0.19–0.22 per 1000)	9% (8.97–9.05)
Adjusted prevalence, ^a % (95% CI)	6.7% (6.67–6.77)	1.8% (1.78–1.83)	1.1 per 1000 (0.98–1.11 per 1000)	0.53 per 1000 (0.49–0.58 per 1000)	1.4 per 1000 (1.31–1.46 per 1000)	0.18 per 1000 (0.16–0.21 per 1000)	8.2% (8.17–8.28)
Crude prevalence in adults, % (95% CI)	9.7% (9.62–9.72)	2.7% (2.69–2.74)	1.3 per 1000 (1.2–1.4 per 1000)	0.52 per 1000 (0.49–0.56 per 1000)	0.9 per 1000 (0.83–0.93 per 1000)	0.28 per 1000 (0.25–0.31 per 1000)	11.7% (11.70–11.81)

^a Age standardized according WHO.

sleep-related breathing disorders and the multiple sleep latency test (MSLT) for central disorders of hypersomnolence.

- (1) AHI is defined as the number of apneic or hypopneic episodes per hours of sleep. Patients were stratified into those without sleep apnea (AHI < 5/h), those with mild sleep apnea (AHI ≥ 5 to <15/h), moderate sleep apnea (AHI ≥ 15 to <30/h), and severe sleep apnea (AHI ≥ 30/h) [17].
- (2) MSLT is a widely used and standardized method for quantifying the degree of daytime sleepiness [18]. These medical tests are performed at the Assuta institute of sleep medicine. Patients complaining of relevant sleep symptoms were referred to the tests by their primary care physicians.

2.3. Statistical methods

Descriptive statistics of patient data were performed and expressed as means and standard deviations (SD) for continuous variables and as number and percentage for dichotomous variables.

Age and sex specific prevalence rates were calculated for MHS population in 2018.

The 95% Confidence Interval (CI) was provided for the prevalence rates.

For comparing the prevalence of sleep apnea, data from the 2005–2006 National Health and Nutrition Examination Surveys (NHANES) [19] was used. It provided self-reported clinically diagnosed sleep apnea data representative of the non-institutionalized civilian population of the United States.

All analyses were conducted using standard statistical software (IBM-SPSS version 24, Inc.).

3. Results

A total of 195,201 patients met the sleep disorder inclusion criteria (accounting for 9% of the total MHS population and 8.2% after world health organization (WHO) – age standardizations, 11.7% of MHS adults), with approximately 20,000 incident cases per year. Patients were 48.3% men and age at diagnosis was 50.4 years (SD = 20.9) (Table 2). More than one sleep disorder was recorded (primarily insomnia sleep apnea) in 7.3% of patients.

The crude prevalence rate of insomnia in the general population of MHS was 7.4% ($n = 160,222$): 35% of them used chronic insomnia medications (Table 3). When limiting the insomnia definition to patients with dispensed sleep medications, patients with sleep disorders declined to 101,953 patients (4.7% and 6.5% of the total and adult MHS population, respectively) (Appendix III). The prevalence of insomnia increased with age. Insomnia was more prevalent in males until age 34, over age 45 the prevalence rates in females were much higher than in males (Fig. 1, Fig. 2a).

The prevalence of sleep-related breathing disorder was 2% ($n = 43,115$), with major difference between males (2.9%) vs. females (1.1%), particularly among adults (4.1% vs. 1.4%, respectively). Overall, sleep related breathing disorders increased until age 55–64 and decreased thereafter, similar to the prevalence of patients with more than one sleep disorder (Fig. 1). The adjusted prevalence of sleep-related breathing disorders in males was higher in all age groups than among females, but the ratio between male to female decreased from 5:1 in young adults to 2:1 after menopause age (Fig. 2b).

The prevalence of parasomnias in MHS population was 140 per 100,000 ($n = 2998$) and 90 per 100,000 for adult, followed by hypersomnolence with 100 per 100,000 ($n = 2189$) and 130 per 100,000 for adults (when narcolepsy was investigated on its own the prevalence was 27 per 100,000), circadian rhythm sleep-wake disorder with 49 per 100,000 ($n = 1069$) and 52 per 100,000 for

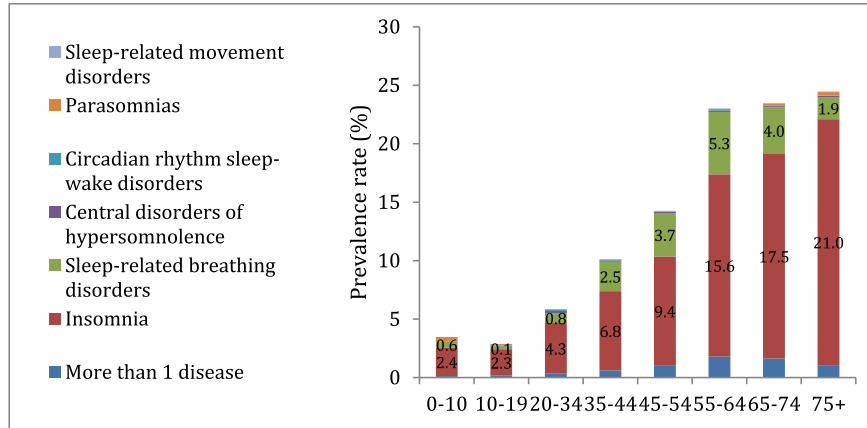


Fig. 1. Age-specific prevalence (%) of sleep disorders, Maccabi Healthcare Services 2010–2018.

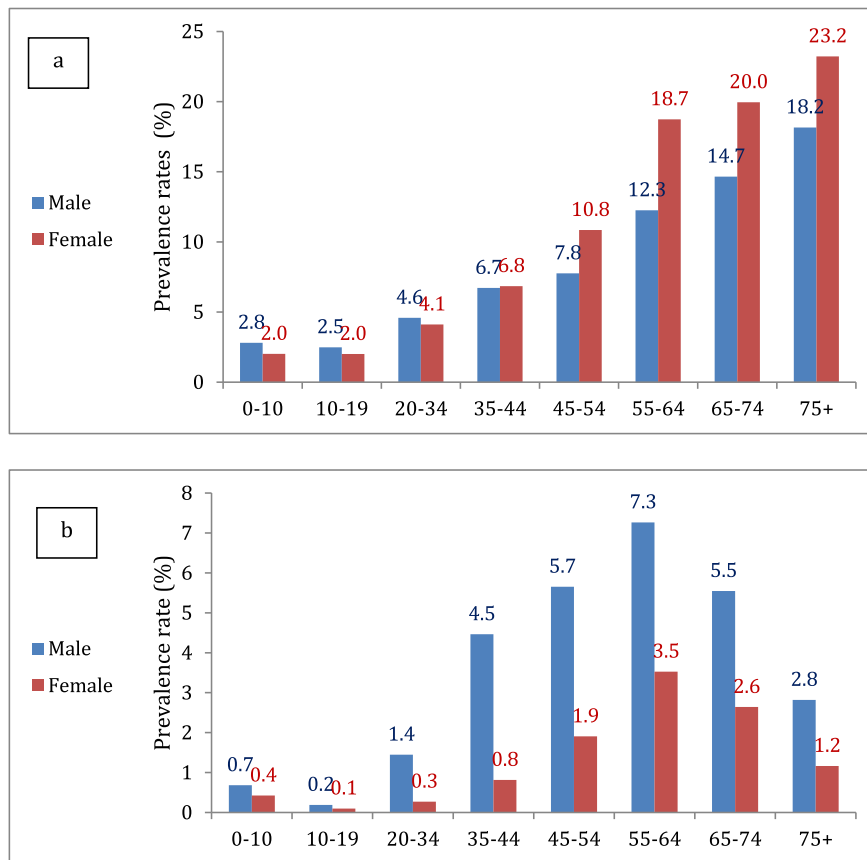


Fig. 2. Age- and sex-specific prevalence (%) of (a) insomnia (b) sleep-related breathing disorders.

adults, and sleep-related movement disorder 20 per 100,000 ($n = 440$). No relevant cases were found belong to other sleep disorders (Table 3).

4. Discussion

To the best of our knowledge, this is the first large clinically-based study to present findings of sleep disorders from a national health care provider database. The data are based on physician diagnoses, relevant drug use and sleep tests unlike some studies

that have used patient self-reporting, questionnaires, and survey information without physician involvement.

The overall age-standardized prevalence of sleep disorders was 8.2% in our analysis and was consistent with the overall prevalence of clinically validated sleep disorders in the USA (10%) [8].

The results of this population-based study indicate that despite stressful life circumstances, the prevalence of insomnia, the major sleep disorder in Israel, was comparable with other western countries, falling within the range shown in international studies (6–15%) [9]. Research studies on the prevalence of mood and anxiety disorders in Israel also reached similar conclusions [12].

Our broad definition for insomnia included chronic sleep medication use and physician diagnosis without differentiation between transient and chronic insomnia. Meanwhile, other previous studies have shown that insomnia was mostly chronic and lasted at least one year in 85% of cases [9].

The prevalence of sleep-related breathing disorders found in the study (4.1% in male and 1.4% in females) is comparable with previous international reports [9,10,20,21], but lower than the NHANES 2005–2006 study [19] (5.3% in males and 2.7% in females, respectively). The ratio between men and women of 2.9 in our study was also similar to the ratio of 3.3 in American studies [20,21]. In addition, decreased disorder was also seen in post-menopausal women.

Comparing the results of less common sleep disorders to other studies is difficult because of scarce clinically-based data in the literature. The study findings indicated a much lower prevalence compared to previous international studies using self-reported outcomes without physician assessment. The calculated prevalence of hypersomnolence (including hypersomnia, narcolepsy) in self-reporting studies (3.9–16%) [9] is far greater than 0.13% found in the study results. The prevalence of narcolepsy diagnosis by MSLT was 0.027%, comparable to 0.02–0.067% in Europe and North

America and 0.04% in Saudi Arabia [9]. Differences in assessment methods may also explain the significant differences found for parasomnias (1.9–3.2% in the adult population [22] compared 0.09% in our study), and for circadian rhythm sleep disorders (1.3–1.7 per 1000 in adult population [23] vs. 0.52 per 1000 in our study).

The prevalence of insomnia increased by age and the ratio between the genders switched once women reached menopause, as found by previous reports [5]. The age-adjusted prevalence of insomnia was similar to the results from the Leger (France) [24] and Ohayon (Spain) [25] studies (shown in Fig. 3). The prevalence was similar up to age 64, but in Israel the prevalence was significantly higher among seniors 65 or older (Fig. 3).

Unlike other countries, a large portion of the older Israeli population included immigrants, which may influence the insomnia prevalence, as was found in previous study with 61% reported insomnia complaint among older Russian immigrants [26].

The adjusted prevalence of sleep-related breathing disorders in males increased until age 65, similar to studies from the USA [20,21] (Fig. 4), and to NHANES 2005–2006 data [19]. For females, the prevalence in our study was lower for all age groups than the NHANES (Fig. 2b and Appendix IV). While our definition for sleep-related breathing disorders was according to an AHI > 5

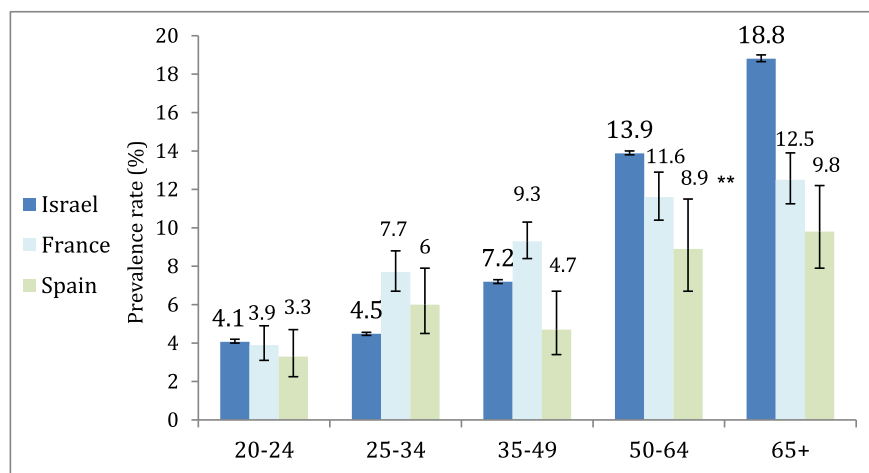


Fig. 3. Insomnia prevalence (%) and 95% confidence intervals by age in current study and previous reports from France [24] and Spain [25].

*Age group in France study was 18–24, and in the Spain study was 15–24. **In the Spain study, the prevalence was 6.6 for 45–54 years, and 8.9% for 55–64 years.

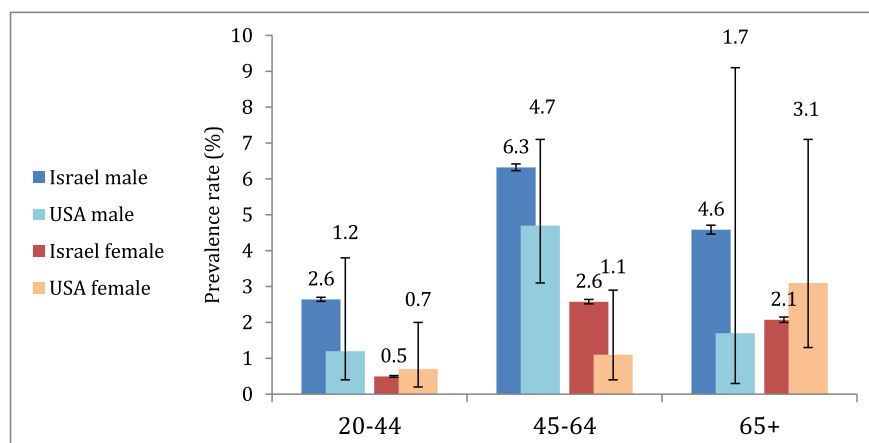


Fig. 4. Age- and sex-specific prevalence (%) and 95% confidence intervals of sleep-related breathing disorders in current study and previous reports from USA [20,21].

test result and physician diagnosis, NHANES data were ascertained by participants' self-report who were told by doctor to have sleep apnea.

The prevalence of sleep disorders was investigated using information including clinical diagnoses and medical tests from a large database as opposed to patient self-reports. Less frequent sleep disorders rarely researched by other studies were also explored.

One limitation to physician diagnoses from electronic medical records is the variability in diagnostic definitions used by physicians, especially for the rare categories, coupled with physicians' less experience in sleep disorders. For sleep apnea and central disorders of hypersomnolence which were diagnosed by specific tests, some selection bias may exist in patients who were sent but did not do the sleep test.

In summary, the overall prevalence of sleep disorders in Israel, including insomnia and sleep related breathing disorders individually, were similar to other western countries. Contrary to expectations stemming from Israel's stressful life circumstances, no

indication of increased prevalence of insomnia or other sleep disorders were found.

Acknowledgments

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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.2019.10.010>.

Appendix I. Medication list for insomnia

Medication name	Generic	Code ATC	Group
BONDORMIN TAB 0.25 MG(20)	BROTIZOLAM	N05CD09	Benzodiazepines
BONDORMIN 0.25 MG 10TAB	BROTIZOLAM	N05CD09	Benzodiazepines
BROTIZOLAM-TEVA 0.25 MG 10TAB	BROTIZOLAM	N05CD09	Benzodiazepines
ROHYPNOL	FLUNITRAZEPAM	N05CD03	Benzodiazepines
HYPNODORM	FLUNITRAZEPAM	N05CD03	Benzodiazepines
HYPNODORM 2 MG 10TAB	FLUNITRAZEPAM	N05CD03	Benzodiazepines
ROHIPNOL 1 MG 20TAB	FLUNITRAZEPAM	N05CD03	Benzodiazepines
NUMBON 5 MG 20TAB	NITRAZEPAM	N05CD02	Benzodiazepines
NITRAZEPAM TAB 5M	NITRAZEPAM	N05CD02	Benzodiazepines
AMBIEN CR 12.5 MG 28TAB	ZOLPIDEM	N05CF02	Z-drugs
AMBIEN CR 6.25 MG 28TAB	ZOLPIDEM	N05CF02	Z-drugs
STILNOX 10 MG 20TAB	ZOLPIDEM	N05CF02	Z-drugs
STILNOX 10 MG 20TAB	ZOLPIDEM	N05CF02	Z-drugs
ZODORM 10 MG 20 TAB	ZOLPIDEM	N05CF02	Z-drugs
IMOVANE 7.5 MG 20TAB	ZOPICLONE	N05CF01	Z-drugs
NOCTURNO LS 20TAB	ZOPICLONE	N05CF01	Z-drugs
NOCTURNO 7.5 MG 20TAB	ZOPICLONE	N05CF01	Z-drugs
ZOPICLONE 7.5 MG 20 TAB	ZOPICLONE	N05CF01	Z-drugs
DORMINOL NIGHT	HOP CONES DRY EXTR, VALERIAN ROOT DRY EXT	N05CM09	OTC
SONGHA NIGHT 30	VALERIAN, MELISSA	N05CM09	OTC
SLEEP AID 16 TAB	DOXYLAMINE SUCCINATE	R06AA09	OTC
SLEEP AID 25 MG 16TAB	DOXYLAMINE SUCCINATE	R06AA09	OTC
TONIGHT TABS 25 MG X10	DOXYLAMINE SUCCINATE	R06AA09	OTC
UNISOM	DOXYLAMINE SUCCINATE	R06AA09	OTC
UNISOM 25 MG 8TAB	DOXYLAMINE SUCCINATE	R06AA09	OTC
CIRCADIN 2 MG 30TAB	MELATONIN	N05CH01	MELATONIN
CIRCADIN 2 MG 21TAB	MELATONIN	N05CH01	MELATONIN

Appendix II. Diagnosis list for sleep disorders

Sleep disorder category	ICD-9 codes	
Insomnia	327	
	327.0	
	327.00	
	327.01	
	327.02	
	327.09	
	780.52	
	307.41	
	307.42	
	307.43	
	307.44	
	307.48	
	307.49	
	780.50	
	Sleep-related breathing disorders	327.2
		327.20
		327.21
327.22		
327.23		
327.24		
327.25		
327.26		
327.27		
327.29		
780.57		
780.51		
780.53		
Central disorders of hypersomnolence	347	
	347.0	
	347.00	
	347.01	
	347.1	
	347.9	
	347.10	
	347.11	
	327.10	
	327.11	
	327.12	
	327.13	
	327.14	
	327.15	
327.19		
780.54		

(continued)

Sleep disorder category	ICD-9 codes
Circadian rhythm sleep–wake disorders	327.3
	327.30
	327.31
	327.32
	327.33
	327.34
	327.35
	327.36
	327.37
	327.39
Parasomnias	780.55
	780.56
	307.45
	327.4
	327.40
	327.41
	327.42
	327.43
	327.44
	327.49
Sleep-related movement disorders	307.46
	307.47
	327.5
	327.51
	327.52
	327.53
	327.59
	780.58
	307.4
	327.8
Other sleep disorders	780.59

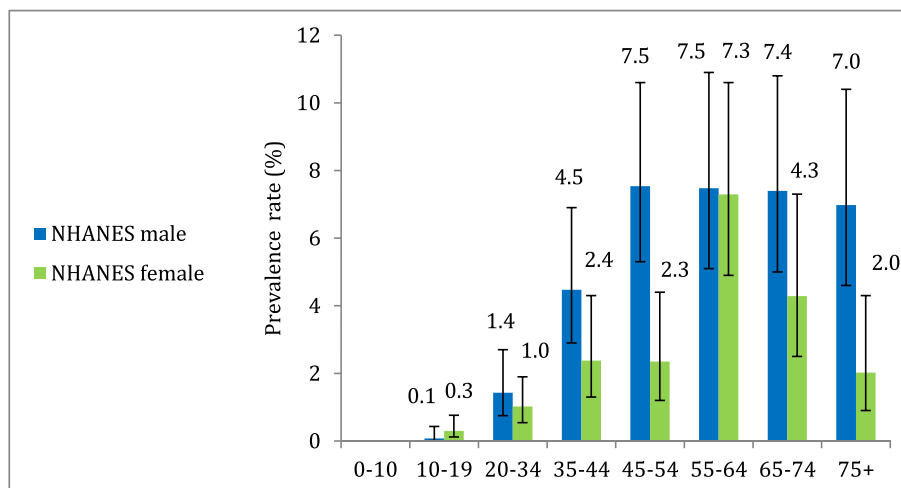
Appendix III. Insomnia specific definition^a

	Any sleep disorder: specific definition, <i>n</i> = 101,953
Sex, males, <i>n</i> (%)	53,266 (52.2%)
Age at diagnosis, mean (SD)	56.4 (18.3)
Low SES (1–4), <i>n</i> (%)	15,820 (15.5%)
Crude prevalence, % (95% CI)	4.7% (4.68–4.73)
Adjusted prevalence, ^b % (95% CI)	4.1% (4.06–4.13)
Crude prevalence in adults, % (95% CI)	6.5% (6.45–6.53)

^aThe specific definition of sleep disorders based only on chronic sleep medications users for insomnia. There were 56,987 patients with chronic medications for insomnia.

^bAge standardized according to WHO.

Appendix IV. Age- and sex-specific prevalence (%) and 95% confidence intervals of sleep-related breathing disorders from NHANES 2005–2006 data [19].



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