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Impact of Long-Term Exposure to Wind Turbine Noise on Redemption of Sleep Medication and Antidepressants: A Nationwide Cohort Study

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Background: Noise from wind turbines (WTs) is associated with annoyance and, potentially, sleep disturbances.

Objectives: Our objective was to investigate whether long-term WT noise (WTN) exposure is associated with the redemption of prescriptions for sleep medication and antidepressants.

Methods: For all Danish dwellings within a radius of 20-WT heights and for 25% of randomly selected dwellings within a radius of 20-to 40-WT heights, we estimated nighttime outdoor and low-frequency (LF) indoor WTN, using information on WT type and simulated hourly wind. During follow-up from 1996 to 2013, 68,696 adults redeemed sleep medication and 82,373 redeemed antidepressants, from eligible populations of 583,968 and 584,891, respectively. We used Poisson regression with adjustment for individual and area-level covariates.

Results: Five-year mean outdoor nighttime WTN of ≥42 dB was associated with a hazard ratio (HR) = 1.14 [95% confidence interval (CI): 0.98, 1.33) for sleep medication and HR = 1.17 (95% CI: 1.01, 1.35) for antidepressants (compared with exposure to WTN of <24 dB). We found no overall association with indoor nighttime LF WTN. In age-stratified analyses, the association with outdoor nighttime WTN was strongest among persons ≥65 y of age, with HRs (95% CIs) for the highest exposure group (≥42 dB) of 1.68 (1.27, 2.21) for sleep medication and 1.23 (0.90, 1.69) for antidepressants. For indoor nighttime LF WTN, the HRs (95% CIs) among persons ≥65 y of age exposed to ≥15 dB were 1.37 (0.81, 2.31) for sleep medication and 1.34 (0.80, 2.22) for antidepressants.

Conclusions: We observed high levels of outdoor WTN to be associated with redemption of sleep medication and antidepressants among the elderly, suggesting that WTN may potentially be associated with sleep and mental health. https://doi.org/10.1289/EHP3909

Introduction

Over the last several decades, wind power deployment has increased markedly worldwide, with a rise in the global cumulative wind capacity from 23 GW in 2001 to 487 GW in 2016 (GWEC 2017). In Denmark, wind power provides more than 40% of the national electricity consumption, which is the highest proportion worldwide. This has led to a growing number of persons being exposed to noise from wind turbines (WTs), followed by a rise in the number of persons complaining that WT noise (WTN) impacts their lives negatively through noise annoyance, disturbance of sleep, and other adverse health effects (Schmidt and Klokker 2014).

Epidemiological studies have consistently found that emission of noise from WTs is associated with annoyance (Guski et al. 2017; Hongisto et al. 2017; Michaud et al. 2016d). Exposure–response curves show that WTN is associated with a higher proportion of highly annoyed persons than traffic noise at comparable levels (Janssen et al. 2011; Michaud et al. 2016d). Potential explanations include that WTN, which depends on wind speed and direction, is less predictable for those exposed than other noise sources such as road traffic noise. In addition, onshore WTs are typically erected in rural areas, where people often expect silent surroundings and where the sound from WTs may be more noticeable than in urbanized areas. Furthermore, amplitude modulation gives WTN a rhythmic quality different from traffic noise, and it has been suggested that the characteristics of WTN relevant for annoyance may be better captured by metrics focusing on amplitude modulation or low-frequency (LF) noise, rather than the full spectrum A-weighted noise (Jeffery et al. 2014; Schäffer et al. 2016).

Studies have indicated that exposure to WTN is associated with the disturbance of sleep, and the potential mechanisms include a direct association with nighttime noise, disturbance of sleep through annoyance, or a combination of the two (Bakker et al. 2012). A meta-analysis from 2015 based on 1,039 persons from six cross-sectional studies using questionnaires to assess information on sleep disturbance, found that exposure to WTN increased the odds for self-reported sleeping problems (Onakpoya et al. 2015). The investigators, however, wrote that the results should be interpreted with caution due to large variations in the estimations of noise and self-reported sleep disturbance across the included studies. Since the meta-analysis in 2015, a Japanese study of 1,079 persons found that outdoor WTN levels >40 dB were associated with self-reported insomnia (Kageyama et al. 2016). Interestingly, a cross-sectional Canadian study of 1,238 persons found no associations between 1-y mean outdoor WTN and various measures of sleep, including both subjective self-reported information of sleep quality and use of sleep medication as well as objective measures of sleep (Michaud et al. 2016a, 2016b). Thus, it remains uncertain from which exposure levels and to what extent WTN disturbs sleep.

A few studies have investigated whether WTN is associated with mental health, which was mainly assessed as self-reported quality of life (Feder et al. 2015; Jalali et al. 2016; Onakpoya et al. 2015). While a systematic review from 2015 based on four cross-sectional studies concluded that living in areas with WTs might be associated with decreased quality of life (Onakpoya et al. 2015), a recent large Canadian study found no association (Feder

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et al. 2015). In addition, a study based on 31 participants with self-reported information on quality of life before and after installation of WTs, found a worsening in different components of quality of life such as the mental component score (Jalali et al. 2016). Last, the large Canadian study also investigated whether outdoor 1-y WTN noise was associated with self-reported anxiety or depression medication but found no association (Michaud et al. 2016b).

The existing studies on WTN and sleep and mental health are generally of cross-sectional design and rely on active participation and self-reported data. We aimed to investigate whether long-term residential exposure to WTN was associated with the redemption of prescriptions for sleep medication and antidepressants in a prospective, nationwide register-based cohort.

Methods

Study Base and Modeling of Noise

In Denmark, all WT owners are required to report the cadastral code and geographical coordinate of their WT(s) to the national Master Data Register of Wind Turbines. For WTs in operation at the time of data extraction, this register also included WT coordinates from the Danish Geodata Agency. In this register, we identified 7,860 WTs in operation at any time during the period 1980–2013. We then excluded 517 offshore WTs. In case of disagreement between the geographical information recorded in the register, the WT location was validated against historical topographic maps and aerial photographs. New coordinates were assigned to the 314 WTs that were incorrectly recorded in the register, and 87 WTs were excluded because no credible location could be established, leaving 7,256 WTs for noise modeling. For these WTs, we collected information on model, type, height, and operational settings (where relevant). Subsequently, each WT was classified into one of 99 noise spectra classes, with detailed information on the noise spectrum from 10–10,000 Hz in thirds of octaves for wind speeds from 4–25 m/s. The noise classes were determined from existing measurements of noise spectra for Danish WTs (Backalarz et al. 2016; Sondergaard and Backalarz 2015).

We estimated the hourly wind speed and direction at hub height for each WT location for the period 1982–2013. This was done using mesoscale model simulations performed with the Weather Research and Forecasting model (Hahmann et al. 2015; Peña and Hahmann 2017). For each WT location, the simulations also provided data on relative humidity and temperature at a height of 2 m and data on atmospheric stability, which were all used for noise modeling.

The modeling of WTN has been described in detail elsewhere (Backalarz et al. 2016). Briefly, we initially identified buildings eligible for detailed noise modeling, defined as all dwellings that could experience at least 24 dB outdoor noise or 5 dB indoor LF noise (10–160 Hz) under the (unrealistic) scenario that all WTs ever operational in Denmark were operating at the same time at 8 m/s wind speed, with downwind sound propagation in all directions. Subsequently, we performed a detailed modeling of noise exposure for the 553,066 buildings identified as eligible in the first step, calculating noise levels in one-third octave bands from 10–10,000 Hz with the Nord2000 noise propagation model (Kragh et al. 2001) and using the simulated hourly weather conditions as input variables. The Nord2000 model has been successfully validated for WTs (Sondergaard et al. 2009). For each dwelling, we modeled hourly noise contributions from all WTs within a 6-km radius. These modeled values were averaged over the nighttime period (2200–0700 hours), which we considered the most relevant time window because people are likely to be in their homes and asleep at that time. We calculated outdoor A-weighted sound pressure level (10–10,000 Hz)—a metric commonly used in health studies (Michaud et al. 2016c; Pedersen 2011)—and A-weighted indoor LF (10–160 Hz) sound pressure level because LF noise is less attenuated by distance and passage through typical building materials and has been proposed to be an important component of WTN in relation to health (Jeffery et al. 2014). We did not model WTN in detail for situations where the 24-dB outdoor noise and 5-dB indoor LF noise limit would not be exceeded even under the unrealistic scenario that all WTs ever operational in Denmark were operating at the same time at 8 m/s wind speed, with downwind sound propagation in all directions given that people living in these buildings would, regardless of exposure level, be categorized in the reference category.

The quality of the noise spectra available for different WT models differed, and these spectra were typically only described at certain wind speeds. We therefore determined a validity score that for each night and dwelling summed up information for all contributing WTs on the number of measurements used to determine the WTN spectra class and how closely the simulated meteorological conditions of each night resembled the conditions under which the relevant WTN spectra were measured.

In the calculation of indoor LF noise, we classified all dwellings into one of six sound insulation classes based on building characteristics listed in the Building and Housing register (Christensen 2011): "1½-story houses" (inhabitants presumed to sleep on second floor), "light façade" (e.g., wood), "aerated concrete" (as well as similar materials such as timber framing), "farm houses" (remaining buildings classified as farms in the registry), "brick buildings," and "unknown" (which were assigned the mean attenuation value of the five other classes). The frequency-specific attenuation values for these insulation classes have been presented previously by Backalarz et al. (2016).

Study Population

We found all Danish dwellings ever situated within a radius of 20-WT heights of a WT as well as a random selection of 25% of all dwellings situated 20-to 40-WT heights away. We excluded residential institutions, hospitals, and dwellings situated within 100 m of areas classified as a "town center" because the type of dwellings, traffic, and lifestyle in town centers may differ substantially from town center–type areas of the main study population. All inhabitants between 25 and 85 y of age and living at least 1 y in one of these dwellings determining eligibility for the study ("eligibility dwellings"), from 5 y before WT erection (from start of follow-up in 1996) until 2013, were subsequently found in the Danish Civil Registration System (Schmidt et al. 2014). This extended time frame ensured the inclusion of people living in exactly the same dwellings before erection (or after decommissioning) of a WT. Persons were included in the study population after living 1 y in an eligibility dwelling. Afterward, we obtained complete address histories from 5 y before study entry until 5 y after moving from the eligibility dwelling for all persons living at least 1 y in an eligibility dwelling. Persons with an incomplete address history for the 5 y preceding entry were excluded.

The study was approved by the Danish Data Protection Agency (J.nr: 2014-41-2,671). By Danish Law, ethical approval and informed consent are not required for studies based entirely on registries.

Covariates

We selected potential confounders *a priori*. From Statistics Denmark, we obtained data on age and sex, personal income

(time-dependent), highest attained educational level (time-dependent), work-market affiliation (time-dependent), marital status (time-dependent), and areal-level (10,000 m^2) mean household income. The type of dwelling was extracted from the Building and Housing Register (Christensen 2011). As proxies for local road traffic noise and air pollution, we identified for each dwelling the total daily distance driven by vehicles within a 500-m radius as well as the distance to the nearest road with an average daily traffic count of ≥5,000 vehicles (in 2005).

Redemption of Sleep Medication and Antidepressants

We collected information on redeemed prescriptions for sleep medication and antidepressants from the Danish National Prescription Registry, which contains data on all prescription drugs sold in Denmark since 1995 (Kildemoes et al. 2011). The register includes the date of dispensing as well as information on the name and type of drug prescribed according to the Anatomic Therapeutic Chemical (ATC) system (WHO Collaborating Centre for Drug Statistics Methodology 2012). The indication for prescribing was not available. We used these data to identify persons who redeemed prescriptions for orally administered sleep medication (ATC: N05CC-CF, N05CH except N05CD08or antidepressants [ATC: N06AA, AB, AF, AG, AX except N06AX12 and Yntreve® (from ATC group N06AX21)].

Because cases redeeming prescriptions upon start of the register in 1995 could have included prevalent cases from before the start of the register, we excluded all persons with a redeemed relevant prescription before 1996 or the start of the follow-up period.

Statistical Analyses

Log-linear Poisson regression analysis was used to calculate hazard ratios (HRs) for redemption of sleep medication or depression (as two separate outcomes) according to outdoor nighttime WTN (<24, 24 to <30, 30 to <36, 36 to <42, and ≥42 dB) or indoor nighttime LF WTN (<5, 5 to <10, 10 to <15, and ≥15 dB) exposure, calculated as running means over the preceding 1 and 5 y. The categorizations were determined *a priori*. At present, there are no standards regarding categorizations of WTN. After consulting acoustical experts we chose <24 dB outdoor and <5 dB indoor LF WTN as references because the acousticians evaluated that WTN in all likelihood would be inaudible below these levels. For outdoor WTN, the upper limit of 42 dB was chosen because this is the regulatory WTN limit in Denmark (at a wind speed of 6 m/s) and, therefore, of interest from an administrative point of view, and the intermediate cut points chosen were 30 and 36 dB, which separated categories by 6 dB.

When calculating running means, we applied a value of −20 dB for situations in which noise had not been estimated (when wind conditions or the distance to WTs made WTN above 24 dB outdoor or 5 dB indoor impossible). We started follow-up after participants had been living 1 y in the recruitment dwelling, turned 25 y of age or 1 January 1996, whichever came last, and stopped at 31 December 2013, 85 y of age, disappearance, death, 5 y after moving from the eligibility dwelling, having no recorded address in Denmark for ≥8 d, or at date of fulfilling our case criteria, whichever came first.

We adjusted all analyses for sex, calendar year (1996–1999, 2000–2004, 2005–2009, and 2010–2013) and age (25–85 y of age, in 5-y categories). Furthermore, we adjusted for education (basic or high school, vocational, higher, and unknown), personal income (20 annual categories of equal size and unknown), marital status (married or registered partnership and other), work-market affiliation (employed, retired, and other), area-level average disposable income (20 categories of equal size and unknown), type of dwelling (farm, single-family detached house, and other), traffic load within a 500-m radius of the dwelling (first and second quartile and above median) and distance to the nearest road with >5,000 vehicles per day (<500 m, 500 to <1,000 m, 1,000 to <2,000 m and ≥2,000 m). Subjects were allowed to change between categories of covariates and exposure variables over time.

We investigated sex and age (above and below 65 y of age) as potential effect modifiers in the Poisson model by stratified analysis and by including an interaction term. Furthermore, we investigated associations between 5-y mean exposures and redemption of sleep medication and antidepressants in subpopulations for whom we hypothesized that a potential association between exposure and risk could be more conspicuous: living on a farm (potentially less variation in lifestyle and other exposures in this subpopulation, which may reduce the potential for residual confounding in this group, although it is important to note that this subpopulation may differ substantially from the study population); nearest WT with a total height of >35 m; high validity of noise estimate; dwelling far from major road (>2 km to the nearest road with >5,000 vehicles per day); and low tree coverage defined as less than 5% covered by forest, thicket, groves, single trees, or hedgerows within 500 m of the dwelling (because we assumed that vegetation beyond this distance would be nearly indiscernible from background noise). Data were analyzed using SAS (version 9.3; SAS Institute Inc.).

Results

We identified 758,736 adults (25–84 y of age) living ≥1 y in one of the dwellings determining eligibility. We excluded persons who had emigrated ($n = 43{,}794$) or did not have a registered address in the address registry ($n = 1{,}573$) prior to entry, who had an unknown address for ≥8 consecutive days in the 5 y prior to entry ($n = 59{,}318$), or who lived in hospitals or institutions at study start of follow-up ($n = 1{,}586$). In addition, we excluded 26,700 persons who, before the start of the follow-up period, had redeemed both sleep medication and antidepressants. After exclusion of 41,797 people redeeming sleep medication before the start of follow-up, the final study population for the sleep medication analyses was 583,968 people of whom 68,696 had redeemed sleep medication during 4,974,043 person-years. The final study population for antidepressants analyses was 584,891 people (after exclusion of 40,874 people who had redeemed antidepressants before the start of follow-up) of whom 82,373 redeemed antidepressants during 4,986,327 person-years. The median age at first redemption was 56.9 y (5th–95th percentiles: 31.8–80.3) for sleep medication and 54.2 y (5th–95th percentiles: 29.9–81.3) for antidepressants.

The two populations for the study of redemption of sleep medication and antidepressants, respectively, were very similar with regard to characteristics at entry (Table 1). For both of these study populations, persons exposed to ≥36-dB outdoor nighttime WTN were at entry younger, more often working, more often living on farms and in areas with higher income, more often living far from a major road and with low traffic density, and more often living in a dwelling with low tree coverage as compared with persons exposed to <36 dB (Table 1). Furthermore, persons exposed to ≥42-dB outdoor nighttime WTN entered the study earlier, had slightly higher education levels, had higher personal incomes, and were more often married as compared with persons exposed to <42 dB. We found similar tendencies for indoor nighttime LF WTN as for outdoor nighttime WTN, although for this exposure, participants in both of the two high-exposure categories (10–15 and ≥15 dB) had higher educations and more often were never married (see Table S1). Furthermore, both of the two high-

Table 1. Characteristics of the populations for study of redemption of sleep medication and antidepressants, respectively, at start of follow-up according to residential A-weighted exposure to outdoor wind turbine noise calculated as mean exposure during the preceding year.

	Outdoor wind turbine noise		
Characteristics at entry	<36 dB Sleep/antidepressants (n = 575,899/576,857) (%)	36–42 dB Sleep/antidepressants (n = 6,704/6,637) (%)	≥42 dB Sleep/antidepressants (n = 1,365/1,397) (%)
Men	52/52	54/54	53/54
Age (y)			
<40	45/43	51/50	46/44
40–50	19/19	20/20	23/22
50–60	16/16	15/15	18/18
≥60	21/22	15/15	13/15
Year of entry			
1996–2000	55/57	56/57	73/74
2001–2005	14/14	19/20	17/17
2006–2010	20/20	16/15	7/7
2011–2013	10/9	9/8	3/3
Personal income			
Quartile 1 (low)	20/20	21/21	20/21
Quartile 2	24/23	25/24	22/22
Quartile 3	26/26	26/25	24/23
Quartile 4 (high)	25/25	22/23	28/28
Unknown	6/6	6/6	7/6
Highest attained education			
Basic or high school	35/35	36/36	37/37
Vocational	43/42	45/45	39/38
High	16/16	15/15	21/21
Unknown	6/7	4/4	3/4
Marital status			
Married	55/56	52/53	62/63
Divorced/widow(er)	14/14	12/12	11/11
Never married	31/30	36/36	27/26
Attachment to labor market			
Working	69/69	75/75	80/78
Retired	18/19	13/13	9/11
Other	13/13	12/12	11/11
Area-level income[a]			
Quartile 1 (low)	23/23	11/11	14/14
Quartile 2	28/28	28/28	21/21
Quartile 3	28/28	34/34	35/36
Quartile 4 (high)	19/19	20/20	24/23
Unknown	2/2	7/7	6/6
Type of dwelling			
Farm	13/13	40/40	40/41
Single-family detached house	62/62	51/51	51/50
Others	24/24	9/9	9/9
Distance to major road (m)[b]			
<500	35/35	17/17	18/18
500–2,000	27/27	26/26	25/25
≥2,000	37/37	57/57	58/57
Traffic load within 500 m (10^3 vehicles km/d)[c]			
<2.5	34/34	69/69	66/67
2.5–5.3	25/25	13/13	16/15
5.3–9.7	19/19	12/13	9/10
>9.7	22/23	6/6	8/8
Tree coverage (%)[c]			
<5	13/13	30/29	29/28
5–20	63/63	63/63	62/63
>20	24/24	7/7	9/9

[a]Average disposable household income among all households in a 100 × 100 m grid cell.
[b]Major road defined as ≥5,000 vehicles per day.
[c]In a 500-m radius around the dwelling.

exposure categories (10–15 and ≥15 dB) entered the study later than persons exposed to <10 dB.

We found that 78% of the sleep medication–study population and 79% of the antidepressant-study population at entry lived in dwellings with <24-dB outdoor nighttime WTN and that, for both study populations, 97% lived in dwellings with indoor nighttime LF WTN <5 dB (see Table S2). Of those exposed to WTN above 42 dB or 15 dB LF, the majority lived within 500 m of a WT, whereas in the reference population less than 10% lived <500 m from a WT. In addition, we found that people with outdoor nighttime WTN exposure of ≥42 dB more often had a shorter WT (<35 m) as the nearest WT, whereas people with indoor nighttime LF WTN of ≥10 dB more often had a higher WT (>70 m) as their nearest WT (see Table S2). We found high correlations for both outdoor and indoor WTN between 1- and 5-y mean exposures, whereas the correlations between indoor and outdoor WTN were lower (see Table S3).

In adjusted analyses, we found that persons exposed to 5-y mean outdoor nighttime WTN levels >42 dB had a 14% higher risk of redeeming sleep medication [HR = 1.14 (95% CI: 0.98,

Table 2. Associations between mean 1- and 5-y exposure to residential A-weighted outdoor wind turbine noise and redemption of prescriptions for sleep medication and antidepressants.

	Sleep medication			Antidepressants		
Outdoor wind turbine noise	Cases (*n*)	Crude HR (95% CI)[a]	Adjusted HR (95% CI)[b]	Cases (*n*)	Crude HR (95% CI)[a]	Adjusted HR (95% CI)[b]
1-y mean exposure (dB)						
<24	50,262	1 (Ref)	1 (Ref)	60,205	1 (Ref)	1 (Ref)
24–30	13,032	0.98 (0.96, 0.99)	1.01 (0.99, 1.03)	15,782	0.98 (0.96, 1.00)	1.00 (0.98, 1.02)
30–36	4,415	0.96 (0.93, 0.99)	1.04 (1.00, 1.07)	5,295	0.95 (0.93, 0.98)	1.01 (0.99, 1.04)
36–42	842	0.95 (0.89, 1.02)	1.05 (0.98, 1.13)	930	0.89 (0.84, 0.95)	0.99 (0.93, 1.05)
≥42	145	0.99 (0.84, 1.17)	1.08 (0.92, 1.28)	161	0.99 (0.85, 1.15)	1.12 (0.96, 1.31)
5-y mean exposure (dB)						
<24	50,559	1 (Ref)	1 (Ref)	60,315	1 (Ref)	1 (Ref)
24–30	13,021	1.00 (0.98, 1.02)	1.03 (1.01, 1.05)	15,958	1.01 (0.99, 1.02)	1.02 (1.00, 1.04)
30–36	4,133	0.97 (0.93, 1.00)	1.03 (1.00, 1.06)	5,016	0.96 (0.94, 0.99)	1.02 (0.99, 1.05)
36–42	814	0.98 (0.92, 1.05)	1.08 (1.00, 1.15)	899	0.92 (0.86, 0.98)	1.01 (0.95, 1.08)
≥42	169	1.06 (0.91, 1.23)	1.14 (0.98, 1.33)	185	1.05 (0.90, 1.21)	1.17 (1.01, 1.35)

Note: CI, confidence interval; HR, hazard ratio; Ref, reference.
[a]Adjusted for age, sex, and calendar-year.
[b]Adjusted for age, sex, calendar-year, personal income, education, marital status, work-market affiliation, area-level socioeconomic status, type of dwelling, traffic load in a 500-m radius, and distance to nearest major road.

1.33)] and a 17% higher risk of redeeming antidepressants [HR = 1.17 (95% CI: 1.01, 1.35)] when compared to persons exposed to <24 dB (Table 2). For antidepressants, similar, although weaker, tendencies were seen for 1-y mean exposures to outdoor nighttime WTN, with HRs for the ≥42-dB exposure group of 1.12 (0.96, 1.31). For sleep medication, risk estimates remained close to the null even at high exposure. In general, the unadjusted risk estimates were lower than the adjusted risk estimates, with no clear suggestions of increased risk. The most influential confounder was dwelling type. For indoor nighttime LF WTN, we found no association between 1- or 5-y exposure and risk of redeeming sleep medication or antidepressants (Table 3).

In analyses stratified by age, we found that outdoor nighttime WTN exposure among persons >65 y of age was associated with a higher risk of redeeming sleep medication, whereas for persons <65 y of age there was no association (Table 4). Furthermore, among persons >65 y of age, the association with outdoor nighttime WTN seemed to follow an exposure–response relationship, with HR = 1.22 (95% CI: 1.08, 1.38) in the 36–42 dB exposure group and HR = 1.68 (95% CI: 1.27, 2.21) in the ≥42 dB exposure group. Similar tendencies were seen for people redeeming antidepressants, with HR = 1.27 (95% CI: 1.13, 1.43) in the 36–42 dB exposure group and HR = 1.23 (95% CI: 1.09, 1.69) in the ≥42 dB exposure group among persons >65 y of age. There were also indications of a higher risk of redeeming antidepressants among persons <65 y of age in the highest outdoor WTN exposure group. When stratifying the indoor nighttime LF WTN analyses by age, we found similar tendencies as for outdoor nighttime WTN for both outcomes, with HRs among persons >65 y of age of 1.13 (95% CI: 0.97, 1.32) for 10–15 dB and 1.37 (95% CI: 0.81, 2.31) for ≥15 dB for redemption of sleep medication and of 1.09 (95% CI: 0.94, 1.26) for 10–15 dB and 1.34 (95% CI: 0.80, 2.22) for ≥15 dB for redemption of antidepressants (Table 5). We found no associations between indoor nighttime LF WTN and any of the two outcomes among persons <65 y of age.

In outdoor nighttime WTN analyses stratified by sex, we found for sleep medication that although the *p*-value for interaction was below 0.05, the HRs in the two highest exposure categories were almost identical, whereas for antidepressants, the association seemed to be confined to men (Table 4). For indoor nighttime LF WTN, we found no marked differences in risks between men and women for redeeming either sleep medication or antidepressants (Table 5). However, for indoor exposure, the number of cases exposed to ≥15 dB was small.

When investigating effects of outdoor nighttime WTN in different subpopulations, we found that among people living on farms or with low tree coverage, the increase in risk in the highest exposure group disappeared for both sleep medication and antidepressants (see Table S4). For the other subpopulations investigated, we found no consistent patterns when comparing results for sleep medication and antidepressants. For example, for highly exposed people living far from major roads, the HR for antidepressants = 1.25 (95% CI: 1.00, 1.55), whereas for sleep

Table 3. Associations between mean 1- and 5-y exposure to residential indoor low-frequency wind turbine noise and redemption of prescriptions for sleep medication and antidepressants.

	Sleep medication			Antidepressants		
Indoor low-frequency wind turbine noise	Cases (*n*)	Crude HR (95% CI)[a]	Adjusted HR (95% CI)[b]	Cases (*n*)	Crude HR (95% CI)[a]	Adjusted HR (95% CI)[b]
1-year mean exposure (dB)						
<5	64,617	1 (Ref)	1 (Ref)	77,360	1 (Ref)	1 (Ref)
5–10	3,299	0.94 (0.91, 0.98)	1.03 (0.99, 1.06)	4,073	0.93 (0.91, 0.96)	1.01 (0.98, 1.04)
10–15	726	0.96 (0.89, 1.03)	1.08 (1.00, 1.16)	882	0.92 (0.86, 0.98)	1.03 (0.97, 1.10)
≥15	54	0.93 (0.71, 1.22)	1.05 (0.81, 1.38)	58	0.82 (0.63, 1.06)	0.96 (0.74, 1.24)
5-y mean exposure (dB)						
<5	65,202	1 (Ref)	1 (Ref)	77,995	1 (Ref)	1 (Ref)
5–10	2,911	0.97 (0.93, 1.01)	1.05 (1.01, 1.09)	3,663	0.96 (0.93, 1.00)	1.04 (1.00, 1.07)
10–15	542	0.93 (0.86, 1.02)	1.04 (0.96, 1.14)	672	0.90 (0.84, 0.97)	1.01 (0.94, 1.10)
≥15	41	0.92 (0.68, 1.25)	1.03 (0.76, 1.40)	43	0.80 (0.59, 1.07)	0.94 (0.70, 1.27)

Note: CI, confidence interval; HR, hazard ratio; Ref, reference.
[a]Adjusted for age, sex, and calendar-year.
[b]Adjusted for age, sex, calendar-year, personal income, education, marital status, work-market affiliation, area-level socioeconomic status, type of dwelling, traffic load in a 500-m radius, and distance to nearest major road.

Table 4. Associations between 5-y exposure to outdoor wind turbine noise and redemption of sleep medication and antidepressants according to age and sex.

Subpopulations	Exposure categories (dB)	Sleep medication			Antidepressants		
		Cases (n)	Adjusted HR (95% CI)[a]	p-Value[b]	Cases (n)	Adjusted HR (95% CI)[a]	p-Value[b]
Age (y)				0.003			0.0001
<65	<24	33,895	1 (Ref)		41,630	1 (Ref)	
	24–30	8,691	1.03 (1.01, 1.05)		10,979	1.02 (1.00, 1.04)	
	30–36	2,833	1.02 (0.98, 1.06)		3,532	1.00 (0.96, 1.03)	
	36–42	550	1.02 (0.94, 1.11)		610	0.92 (0.85, 1.00)	
	≥42	118	1.00 (0.84, 1.20)		146	1.15 (0.98, 1.36)	
≥65	<24	16,664	1 (Ref)		18,685	1 (Ref)	
	24–30	4,330	1.03 (0.99, 1.06)		4,979	1.02 (0.98, 1.05)	
	30–36	1,300	1.06 (1.00, 1.12)		1,484	1.07 (1.01, 1.13)	
	36–42	264	1.22 (1.08, 1.38)		289	1.27 (1.13, 1.43)	
	≥42	51	1.68 (1.27, 2.21)		39	1.23 (0.90, 1.69)	
Sex				0.03			0.08
Men	<24	22,204	1 (Ref)		25,379	1 (Ref)	
	24–30	6,067	1.06 (1.03, 1.10)		7,047	1.04 (1.01, 1.06)	
	30–36	1,950	1.05 (1.00, 1.10)		2,274	1.03 (0.99, 1.08)	
	36–42	381	1.08 (0.97, 1.19)		423	1.06 (0.96, 1.16)	
	≥42	79	1.15 (0.92, 1.44)		97	1.39 (1.14, 1.69)	
Women	<24	28,355	1 (Ref)		34,936	1 (Ref)	
	24–30	6,954	1.00 (0.97, 1.03)		8,911	1.01 (0.98, 1.03)	
	30–36	2,183	1.01 (0.97, 1.06)		2,742	1.01 (0.97, 1.05)	
	36–42	433	1.08 (0.98, 1.19)		476	0.98 (0.89, 1.07)	
	≥42	90	1.14 (0.92, 1.40)		88	1.00 (0.81, 1.23)	

Note: CI, confidence interval; HR, hazard ratio; Ref, reference.
[a]Adjusted for age, sex, calendar-year, personal income, education, marital status, work-market affiliation, area-level socioeconomic status, type of dwelling, traffic load in a 500-m radius and distance to nearest major road.
[b]p for interaction.

medication, it remained unchanged. Among persons with high validity of the outdoor noise estimate, we found that the risk for redeeming antidepressants was slightly higher than in the overall analysis [HR = 1.25 (95% CI: 0.89, 1.74)], and for sleep medication, the risk estimate among persons exposed to 36–42 dB increased, whereas the risk in the highest exposure group disappeared [HR = 0.81 (95% CI: 0.52, 1.27); 19 cases; see Table S4]. With regard to indoor LF WTN in the same subpopulations, we found the lack of association for both outcomes to be consistent among people living on farms, whose nearest WT was ≥35 m, living far from a major road and with low tree coverage, whereas among people redeeming sleep medication/antidepressants after 2005, the estimate in the highest exposure group (≥15 dB) was increased [HR = 1.12 (95% CI: 0.79, 1.57); see Table S5]. There was a tendency toward a slight increase in risk for redeeming sleep medication in the highest exposure group among people with a high validity of the noise estimate [HR = 1.20 (95% CI: 0.75, 1.90)], whereas for redeeming antidepressants, the lack of an association remained [HR = 0.92 (95% CI: 0.57, 1.49)].

Discussion

We found that high levels of long-term nighttime exposure to outdoor WTN seemed associated with redemption of sleep medication and antidepressants in a large prospective study, whereas

Table 5. Associations between 5-y exposure to indoor low-frequency wind turbine noise and redemption of sleep medication and antidepressants according to age and sex.

Subpopulations	Exposure categories (dB)	Sleep medication			Antidepressants		
		Cases (n)	Adjusted HR (95% CI)[a]	p-Value[b]	Cases (n)	Adjusted HR (95% CI)[a]	p-Value[b]
Age (y)				0.40			0.06
<65	<5	43,617	1 (Ref)		53,739	1 (Ref)	
	5–10	2,062	1.05 (1.00, 1.09)		2,640	1.02 (0.98, 1.06)	
	10–15	381	1.01 (0.91, 1.12)		490	0.99 (0.90, 1.08)	
	≥15	27	0.91 (0.63, 1.33)		28	0.81 (0.56, 1.17)	
≥65	<5	21,585	1 (Ref)		24,256	1 (Ref)	
	5–10	849	1.06 (0.99, 1.13)		1,023	1.10 (1.03, 1.17)	
	10–15	161	1.13 (0.97, 1.32)		182	1.09 (0.94, 1.26)	
	≥15	14	1.37 (0.81, 2.31)		15	1.34 (0.80, 2.22)	
Sex				0.18			0.70
Men	<5	29,017	1 (Ref)		33,206	1 (Ref)	
	5–10	1,393	1.08 (1.02, 1.14)		1,687	1.06 (1.01, 1.11)	
	10–15	248	1.00 (0.88, 1.13)		306	1.00 (0.89, 1.12)	
	≥15	23	1.27 (0.84, 1.91)		21	1.04 (0.68, 1.60)	
Women	<5	36,185	1 (Ref)		44,789	1 (Ref)	
	5–10	1,518	1.02 (0.97, 1.08)		1,976	1.02 (0.98, 1.07)	
	10–15	294	1.09 (0.97, 1.22)		366	1.03 (0.93, 1.14)	
	≥15	18	0.83 (0.52, 1.32)		22	0.86 (0.57, 1.30)	

Note: CI, confidence interval; HR, hazard ratio; Ref, reference.
[a]Adjusted for age, sex, calendar-year, personal income, education, marital status, work-market affiliation, area-level socioeconomic status, type of dwelling, traffic load in a 500-m radius, and distance to nearest major road.
[b]p for interaction.

for long-term indoor nighttime LF WTN, no associations were found. We found the strongest associations between outdoor nighttime WTN and redemption of sleep medication and antidepressants among persons >65 y of age compared with those <65 y of age. In addition, for persons >65 y of age, high levels of indoor nighttime LF WTN seemed to be associated with redemption of sleep medication.

Our finding of an association between high exposure to outdoor nighttime WTN and redemption of sleep medication is in accordance with most (Kageyama et al. 2016; Onakpoya et al. 2015) but not all (Michaud et al. 2016a) studies on WTN and sleep problems (high exposure was generally defined as >40–41 dB in these studies). In support of our results on high outdoor nighttime WTN and depression, most (Jalali et al. 2016; Onakpoya et al. 2015) but not all (Feder et al. 2015) of the few studies investigating WTN and self-reported mental health indicated that living in areas with WTs could decrease the quality of life. Overall, this suggests that high levels of outdoor nighttime WTN is associated with sleep disturbance and depression, although it is important to note that most previous studies were cross-sectional (which hampers conclusions on causality), relied on active participation and self-reported data, and were based on much smaller study populations than the current study. That we see similar associations for both sleep and antidepressant medication for outdoor WTN strengthens the plausibility of both because it is well established that disturbed sleep and mental health problems, including depression, interact through a complex bidirectional relationship (Anderson and Bradley 2013; Lopresti et al. 2013). It is, however, noteworthy that we found no association between indoor nighttime LF WTN and redemption of sleep medication or antidepressants even though this exposure estimate likely better reflects exposure during sleep. In a recent study based on the current study population, we found indications that high levels of indoor LF WTN during the night may trigger cardiovascular events, whereas for outdoor nighttime WTN we found no association (Poulsen et al. 2018). A potential explanation is that outdoor WTN may be associated with a higher overall annoyance than indoor LF WTN given that people are disturbed during their outdoor activities during the day. However, further research is needed to elucidate this possibility, particularly because studies on both traffic and WT noise have indicated that the effect of annoyance on the association between noise exposure, sleep disturbance, and mental health is complex and as yet not fully understood (Bakker et al. 2012; Frei et al. 2014; Fyhri and Aasvang 2010; Héritier et al. 2014; WHO 2009).

We found stronger associations with WTN among the elderly, especially with regard to sleep medication, where the association seemed confined to persons >65 y of age, with a positive exposure–response relationship starting at relatively low WTN levels. Furthermore, for this age group, high levels of indoor nighttime LF WTN also seemed to be associated with the redemption of sleep medication. A potential explanation is that the elderly may be particularly susceptible to health effects from WTN given that a number of changes in sleep structure occur with age (Cooke and Ancoli-Israel 2011; Wolkove et al. 2007). Older people generally spend more time in the lighter stages of sleep (stage 1 and 2) and less time in deep sleep and REM sleep, which could lead to higher risk for awakenings due to nighttime WTN. Furthermore, the nocturnal sleep time of elderly is reduced and more fragmented, with an increased number of arousals and awakenings, and thus they are potentially more easily disturbed by noise, worry, and annoyance. In addition, one might speculate that persons >65 y of age are more likely to be retired from work and therefore at home during the daytime, which could potentially increase annoyance due to WTN and help explain the increased HRs observed for outdoor exposure.

For redemption of antidepressants, we observed similar trends as for sleep medication: The association with outdoor WTN during the night was stronger and started at lower levels among elderly compared with their younger counterparts, and there was a suggestion of an association with high levels of indoor nighttime LF WTN. As described above, there is a strong association between sleep and depression (Anderson and Bradley 2013; Lopresti et al. 2013), and the observed association between WTN and depression mainly among the elderly could be explained by a WTN-induced disturbance of sleep as well as a higher WTN-annoyance due to spending more time at home. In addition, depression in late life may present differently from depression in younger adults, with higher prevalence of, for example, sleep disturbance, loss of interest, and fatigue (Christensen et al. 1999; Fiske et al. 2009), and the incidence of diagnosed depression in later life is generally found to be lower than at younger ages (Büchtemann et al. 2012; Fiske et al. 2009).

Strengths of our study include the prospective nationwide design with access to residential moving history for the study period and the identification of a large number of cases through high-quality nationwide registers with high coverage and data quality (Kildemoes et al. 2011; Pottegård et al. 2017; Schmidt et al. 2014). We also had access to information on individual and area-level confounders though national registries with high coverage and validity (Baadsgaard and Quitzau 2011; Jensen and Rasmussen 2011; Petersson et al. 2011) as well as information on environmental confounders. Furthermore, we applied state-of-the art exposure models to estimate exposures to WTN using input data of high quality on hourly wind speed and direction at all WTs and detailed WTN spectra for all types of WTs, which allowed us to model noise during nighttime, which we found to be the most relevant time period. First, during the daytime, many people will be away from home, whereas during the nighttime, we expect the majority of the population to be at home, and second, for the sleeping medication outcome, this is the relevant time window, but for depression, nighttime exposure is also very relevant because we expect disturbance of sleep to be on the mechanistic pathway. In addition, by taking sound insulation characteristics of the types of dwelling into account, we estimated the potentially more biologically relevant indoor LF WTN, although we were only able to differentiate this into a few insulation categories. Other strengths include the modeling of WTN for all Danish dwellings potentially exposed to WTN and the inclusion of persons from the same geographical areas but with little or no WTN exposure.

The drugs used to define the outcomes in the current study are only available by prescription in Denmark and the redemption of these prescriptions is registered in an almost complete national register (Kildemoes et al. 2011). Furthermore, all Danes have access to free universal healthcare and subsidized drug costs. We therefore had an excellent sensitivity and specificity toward redemption of sleep and antidepressant medication. There are, however, some challenges associated with interpreting them as proxies for sleep or depressive disorders. A 2013 survey of 160,000 randomly selected Danes found the prevalence of sleep problems and "feeling depressed/unhappy" to be 41% and 29%, respectively. In the current study, 12% of the study population redeemed sleep medication and 14% redeemed antidepressants. This reflects that only people with more severe problems are likely to both contact a physician and to qualify for these drugs. Although we expect the lack of information on people with undiagnosed sleep problems and depression to be nondifferential with regard to exposure, it impairs sensitivity towards sleep

disturbances or depressive conditions in general and our results, therefore, pertain most directly to more severe sleep or depressive conditions. Furthermore, our reliance on prescription data reduced specificity towards sleep and depressive conditions because some of the included drugs, particularly the antidepressants, also have other indications, primarily for anxiety-related conditions. Any bias resulting from this will depend on both the prevalence of these conditions among our cases and their association with WTN.

Due to the register-based nature of the study, we did not have access to potential lifestyle confounders, such as physical activity and alcohol consumption, and other factors that might affect the studied associations, such as orientation of the bedroom and hearing loss. This is a weakness of our study. We found that adjustment for individual and area-level socioeconomic variables generally tended to increase estimates in the highest exposure group. It is conspicuous that we found no association for either outcome when restricting analyses to people living on farms given that lifestyle and other exposures are expected to be more similar within this subpopulation as compared with the whole population. However, attitudes towards WTN and health behavior may also differ, which might contribute to the lack of association in this group. Another potential explanation is a healthy-worker bias, and in exploratory analyses restricted to farm dwellers >65 y of age, we found that exposure to ≥42 dB was associated with an increased risk for the use of sleep medication, whereas no association was observed for antidepressants.

Other limitations include the rather crude adjustment for local road traffic noise, using traffic load and distance to the nearest major road. However, residual confounding by traffic noise is unlikely to be a major problem in the current study because we obtained similar estimates among people living far from major roads as compared with the whole study population. In addition, there is inevitable uncertainty in the modeled noise exposure, particularly in indoor LF, where we had to rely on relatively crude data on building sound insulation. This uncertainty is likely to be nondifferential, influencing the estimates towards unity. To investigate this further, we used a validity score, which captured some of the features of uncertainty of the noise modeling. For outdoor WTN, we observed that for situations with high validity WTN, the risk estimates for antidepressants were largely unaffected, whereas for sleep medication, the estimate for 36–42 dB was elevated and for ≥42 dB, decreased. However, for sleeping medication, only 19 of the 169 cases exposed to ≥42 dB had a high validity score, resulting in high uncertainty for this subanalysis.

Conclusions

In conclusion, in a large nationwide population, we found suggestions of an association between exposure to high levels of outdoor nighttime WTN and increased risk of first-time redemption of sleep medication and antidepressants. This association was strongest among the elderly. We found no consistent associations for indoor nighttime LF WTN. Given that this was the first prospective study on this topic and that we had only a few cases for many of the groups, independent replication is desirable.

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