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Long-term exposure to wind turbine noise and redemption of antihypertensive medication: A nationwide cohort study

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ABSTRACT

Noise from wind turbines (WTs) has been reported more annoying than traffic noise at similar levels, and concerns have been raised about whether WT noise (WTN) can increase risk for cardiovascular disease. We aimed to investigate if long-term exposure to WTN increases risk for hypertension, estimated as redemption of prescriptions for antihypertensive drugs. We identified all Danish dwellings within a radius of 20 WT heights from a WT and 25% randomly selected dwellings within 20–40 WT heights radius. Using data on WT type and hourly wind conditions at each WT, we estimated hourly outdoor (10–10,000 Hz) and low frequency (LF: 10–160 Hz) indoor WTN for all dwellings, and aggregated it as long-term nighttime running means. From nationwide registries, we identified 535,675 persons age 25–85 years living in these dwellings for > 1 year from 1996 to 2013, of whom 83,729 fulfilled our case definition of redeeming ≥ 2 prescriptions and ≥ 180 defined daily doses of antihypertensive drugs within a year. Data were analyzed using Poisson regression according to categories of WTN exposure and adjustment for individual and area-level covariates. We found no associations between 5-year mean exposure to WTN during night and redemption of antihypertensives, with hazard ratios (HR) of 0.91 (95% confidence intervals (CI): 0.78–1.06) for outdoor WTN ≥ 42 dB(A) and of 1.06 (CI: 0.83–1.35) for indoor LF WTN ≥ 15 dB(A) when compared to the reference WTN levels (< 24 dB(A) and < 5 dB(A), respectively). The lack of association was consistent across sub-populations of people living on farms, far from major roads and with high validity of the noise estimate. For people younger than 65 years we found HRs of 0.81 (95% CI: 0.67–0.98) and 0.94 (95% CI: 0.68–1.30) for outdoor WTN ≥ 42 dB(A) and indoor WTN ≥ 15 dB(A), respectively, whereas for people above 65 years the corresponding HRs were 1.17 (95% CI: 0.90–1.52) and 1.28 (95% CI: 0.87–1.88). In conclusion, the present study does not support an association between WTN and redemption of antihypertensive medication.

1. Introduction

Global interest in renewable energy has resulted in advancements in wind energy technologies and installation of more and larger wind turbines (WTs). However, neighbors to WTs have reported exposure to WT noise (WTN) to be annoying (Janssen et al., 2011; Michaud et al., 2016b; Schmidt and Klokke, 2014; Van Kamp and Van den Berg, 2018). Also, some studies found WTN to disturb nighttime sleep (Schmidt and Klokke, 2014), although more recent studies have suggested no direct associations between WTN and sleep (Jalali et al., 2016; Michaud et al., 2016c; Van Kamp and Van den Berg, 2018).

Furthermore, concern of whether WTN can increase risk of cardiovascular disease has been raised, as exposure to traffic noise has consistently been linked with hypertension, myocardial infarction and stroke (Dimakopoulou et al., 2017; Eriksson et al., 2010; Fuks et al., 2017; Heritier et al., 2017; Sørensen et al., 2011; van Kempen and Babisch, 2012; Vienneau et al., 2015). The believed pathophysiologic pathways behind are activation of a general stress response and disturbance of sleep, leading to a rise in cardiovascular risk factors, such as endothelial dysfunction, atherosclerosis, oxidative stress, high blood pressure and a weakened immune system (Kalsch et al., 2014; Munzel et al., 2017; Schmidt et al., 2015; Schmidt et al., 2013; van Kempen and

Abbreviations: AHT, antihypertensives; CI, confidence intervals; HR, hazard ratios; LF, low frequency; WT, wind turbines; WTN, wind turbine noise

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Babisch, 2012).

Results on traffic noise and cardiovascular disease are not readily applicable to WTN. Levels of WTN are lower than traffic noise in urban settings. In Denmark, 30% of all dwellings are exposed to road traffic noise levels exceeding 58 dB(A), whereas Danish legislation does generally not allow WTN to exceed 44 dB(A) (at 8 m/s) at dwellings. However, at comparable noise levels, studies have found WTN to be associated with a higher proportion of annoyed residents than traffic noise (Janssen et al., 2011), potentially because WTN, which depends on wind speed and direction, is less predictable for those exposed than road traffic noise. Also, amplitude modulation gives WTN a rhythmic quality different from traffic noise. 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, as typically used in studies of traffic noise (Jeffery et al., 2014). Lastly, WTs are mainly located in rural areas, where the auditory impact of WTs may be more noticeable than in urbanized areas.

Only few studies, all of cross-sectional design, have investigated associations between WTN and cardiovascular disease. A study combining a Dutch and two Swedish study population(s), with a total of 1755 participants, found no associations between outdoor A-weighted WTN or WTN annoyance and self-reported high blood pressure or cardiovascular disease (Pedersen, 2011). Furthermore, a study of 1238 Canadians found no associations between estimated A-weighted residential WTN and self-reported prevalent high blood pressure, use of antihypertensive drugs or heart disease (Michaud et al., 2016b). Also, as part of the Canadian study, hair cortisol was measured in 675 participants, and resting systolic and diastolic blood pressure and heart rate were measured in 1077 participants according to standardized procedures (Michaud et al., 2016a). However, no associations were found between 1-year mean residential outdoor WTN (estimated) and any of these measures of stress or cardiovascular disease (Michaud et al., 2016a).

In the present study, we aim to investigate associations between long-term residential exposure to WTN and redemption of prescriptions for antihypertensives (AHT) as a proxy for hypertension, in a nationwide register-based study, combining data on WTN, residential addresses, prescriptions and socioeconomic indicators over the period from 1996 to 2013.

2. Methods

2.1. Study base and estimation of noise

2.1.1. Identification and classification of Danish WTs

In Denmark, it is mandatory for all WT owners to report geographical coordinates and cadastral codes of their WT(s) to the Master Data Register of Wind Turbines, established and maintained by the Danish Energy Agency. The register also contains WT coordinates from the Danish Geodata Agency for WTs in operation (at the time of data extraction). Using this register, we identified 7860 WTs in operation any time between 1980 and 2013. We excluded all offshore WTs ($n = 517$). In case of disagreement between the geographical locations recorded in the register, the WT location was validated against historical topographic maps and aerial photographs. We found 314 WTs that were wrongly recorded in the Master Data Register, and these were assigned new coordinates. Also, 87 WTs were excluded as no credible location could be established. For the resulting 7256 WTs, we gathered information on height, model, type and operational settings (where relevant), and each WT was classified into one of 99 noise spectra classes, with detailed information on the noise spectrum from 10 to 10,000 Hz in thirds of octaves for wind speeds from 4 to 25 m/s. These noise classes were made from existing measurements of noise spectra for Danish WTs (Backalarz et al., 2016; Sondergaard and Backalarz, 2015).

2.1.2. Simulation of wind conditions and metrological parameters at all WTs

For each WT location, we estimated the hourly wind speed and direction at hub height for the period 1982–2013, using mesoscale model simulations performed with the Weather Research and Forecasting model (Hahmann et al., 2015; Peña and Hahmann, 2017). These simulations also provided data on temperature and relative humidity at 2 m height as well as the atmospheric stability at each WT location.

2.1.3. Modelling of WTN

The modelling of WTN has been described in details in (Backalarz et al., 2016). In summary, we initially identified the buildings eligible for detailed noise modelling, defined as all Danish dwellings that could experience at least 24 dB(A) outdoor noise or 5 dB(A) indoor LF noise (10–160 Hz) under the unrealistically extreme scenario that all WTs ever in operation in Denmark were simultaneously operating at a wind speed of 8 m/s with downwind sound propagation in all directions. Subsequently, we modelled WTN exposure in detail for the 553,066 eligible buildings, calculating noise levels in 1/3 octave bands from 10 to 10,000 Hz with the Nord2000 noise propagation model (Kragh et al., 2001), using the simulated time-varying weather conditions as input variables. The Nord2000 model has been successfully validated for WTs (Sondergaard et al., 2009). For each dwelling, we calculated the hourly noise contribution from all WTs within a 6 km radius. These hourly modelled values were then aggregated as means for the nighttime period (10 PM to 7 AM), which we considered the most relevant time-window as people are most likely at home and sleep during these hours. We calculated outdoor A-weighted sound pressure level (10–10,000 Hz) – a metric commonly used in health studies (Michaud et al., 2016a; Pedersen, 2011), and A-weighted indoor LF (10–160 Hz) sound pressure level, as 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).

For each dwelling, for each night, we determined validity scores for the indoor and the outdoor noise estimates. The scores summed up information for all contributing WTs on the number and quality of the data used to determine the WTN spectra classes, and how closely the simulated meteorological conditions of each hour resembled the conditions under which the relevant WTN spectra were measured.

To enable calculation of indoor LF noise, we obtained information on noise attenuation for each dwelling. We classified all dwellings into one of six sound insulation classes based on building characteristics in the Building and Housing register (Christensen, 2011): “1½-story houses” (residents assumed to sleep on the second floor), “light façade” (e.g. wood), “aerated concrete” (and similar materials including timber framing), “farm houses” (remaining buildings in the registry classified as farms), “brick buildings” and “unknown” (assigned the mean attenuation value of the five previous classes). The frequency-specific attenuation values for these six insulation classes are shown in (Backalarz et al., 2016).

2.2. Study population

The study was based on the Danish population and the study population defined as follows: We found all 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 between 20 and 40 WT heights from a WT. Thereby, we included all persons living close to WTs, as well as a large population living in the same areas, but with little or no exposure. We excluded hospitals, residential institutions and dwellings situated within 100 m of areas classified as “town center”, because type of dwellings, traffic conditions and lifestyle in town centers may differ substantially from the main study population. Subsequently, all persons aged 25–85 years living at least one year in these “inclusion dwellings”

from five years before WT erection until 2013 were identified using the Danish Civil Registration System (Schmidt et al., 2014). We applied this extended timeframe to ensure inclusion of persons living in exactly the same dwellings before erection (or after decommissioning) of a WT. People entered the study population after living one year in the dwelling. For this population, we established complete address histories from five years before study entry until five years after moving from the inclusion dwelling. Persons without complete address history five years preceding entry were excluded. Furthermore, we censored at date of missing an address after start of follow-up. Finally, combining the information on address histories with the WTN exposure information for all dwellings provided information on daily WTN levels for each study participant for the entire follow-up period.

The study was approved by the Danish Data Protection Agency (J.nr: 2014-41-2671). By Danish Law, ethical approval and informed consent are not required for entirely register-based studies.

2.3. Covariates

Selection of potential confounders was done *a priori*. From the registries of Statistics Denmark, we obtained information on age, sex and areal level (10,000 m²) mean household income (in 2008) together with socioeconomic variables collected for each year in the follow-up period and entered as time-dependent in the statistical models: highest attained educational level, personal income, marital status and work market affiliation. Information on type of dwelling was obtained from the building and housing register (Christensen, 2011). As proxies for local road traffic noise and air pollution, we identified the distance from each dwelling to the nearest road with an average daily traffic count of ≥ 5000 vehicles (in 2005) as well as a variable summarizing the total amount of kilometers driven by vehicles within 500 m of the residence each day as the product of street length and traffic density added up for all street lines within a 500-m circle around the address.

2.4. Identification of outcome

We collected information on redeemed prescriptions for AHT from the Danish National Prescription Registry, containing data on all prescription drugs sold in Denmark since 1995 (Kildemoes et al., 2011). The register includes information on the name and type of drug according to the Anatomic Therapeutic Chemical (ATC) system (2012), date of dispensing and number of defined daily doses dispensed (DDD: assumed average maintenance dose per day for a drug used for its main indication in adults (2012)). The indication for prescribing and prescribed daily dose is not available. We used these data to identify people who redeemed prescriptions for orally administered AHT (ATC: C02, C03, C07–C09). To increase specificity towards hypertensive indications, we only counted people as cases once they within a year had redeemed 2 or more prescriptions and > 180 DDDs. In a sensitivity analysis, we attempted to further increase specificity towards hypertension by applying the same criteria but excluding diuretics (ATC: C03) from the list of ATC codes included, as they have a range of non-hypertensive indications.

As cases redeeming AHT upon start of the register could include prevalent cases from before start of the register, thus we excluded all persons with a redeemed prescription for AHT before 1996. Also, we excluded people with diabetes or admitted to a hospital with a cardiovascular diagnosis (ICD8: 390–458; ICD10: I00–I99) before study entry using national health registers (Carstensen et al., 2011; Lynge et al., 2011).

2.5. Statistical methods

Log-linear Poisson regression analysis was used to calculate hazard ratios (HRs) for redemption of AHT according to outdoor WTN (< 24 , $24 - < 30$, $30 - < 36$, $36 - < 42$, and ≥ 42 dB(A)) or indoor LF WTN

(< 5 , $5 - < 10$, $10 - < 15$, and ≥ 15 dB(A)) exposure, calculated as running means over the previous 1- and 5-years. At present, the level below which WTN has no biological impact is unknown and we chose the exposure groups *a priori*. For dwellings located so far from WTs as to never have WTN above 24 dB(A) outdoor and 5 dB(A) indoor, or when WTs were not operating due to wind conditions, we applied a value of -20 dB(A) when calculating running means. Follow-up started after living one year in the recruitment dwelling, turning 25 years or 1 January 1996, whichever came last, and ended at 31 December 2013, death, age 85 years, five years after moving from inclusion dwelling, having no recorded address in Denmark for 8 or more days, disappearance, diagnosis of cardiovascular disease or diabetes 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 years, in five-year categories). Furthermore, we adjusted for highest attained education (updated annually: basic or high school, vocational, higher and unknown;), personal income (updated annually: 20 equal sized annual categories and unknown), marital status (married/registered partnership and other), work-market affiliation (updated annually: employed, retired and other), area level average disposable income (updated when moving: 20 equal sized categories and unknown), type of dwelling (updated when moving: farm, single-family detached house and other), distance to road with ≥ 5000 vehicles per day (updated when moving: < 500 m, $500 - < 1000$ m, $1000 - < 2000$ m and ≥ 2000 m), and traffic load within 500 m radius of dwelling (updated when moving and annually: 1st and 2nd quartile and above median). Subjects were allowed to change between categories of covariates and exposure variables over time.

We used Poisson models including an interaction term and stratified analyses, to investigate sex and age (above and below 65 years) as potential effect-modifiers. Furthermore, we investigated associations between 5-year mean exposures and redemption of AHT in sub-populations for whom we hypothesized that a potential association between exposure and risk could be more conspicuous: living in dwelling classified as a farm (a large proportion of the highly exposed lives on farms, and we hypothesize that there is less variation in lifestyle and other exposures among this sub-population compared to the whole population, potentially reducing susceptibility to residual confounding in this group); nearest WT with a total height of > 35 m; high validity of noise estimate; dwelling far from major road (> 2 km to nearest road with > 5000 vehicles/day); and low tree coverage ($< 5\%$ of the area within 500 m of dwelling covered by forest, thicket, groves, single trees and hedgerows; we applied a 500 m buffer as we assumed that vegetation further apart would be near indiscernible from background noise). Data were analyzed using SAS 9.3 (SAS Institute Inc. Cary, NC, USA).

3. Results

We identified 744,438 adults (age 25–84 years) living more than one year in one of the ‘inclusion dwellings’ (i.e. within 40 heights of a WT). We excluded persons who emigrated ($n = 44,106$) or disappeared ($n = 1573$) prior to entry, who had an unknown address for eight or more consecutive days in the five years prior to entry ($n = 59,313$), or who lived in hospitals or institution at study start of follow-up ($n = 1586$). Also, we excluded 70,779 persons redeeming AHT before start of follow-up, and 31,406 persons admitted to hospital with a cardiovascular disease or diabetes before start of follow-up. The final study population included 535,675 persons of whom 83,729 redeemed AHT corresponding to our main case definition during 4,213,896 person-years.

People exposed to high levels of outdoor WTN (≥ 42 dB(A); 1-year mean) at start of follow-up were more likely to be men, younger, enter the study population before 2005, married, working, live in areas with higher household incomes, live at farms, live far from a major road, and

Table 1

Characteristics of the study population at start of follow-up according to residential A-weighted exposure to outdoor wind turbine noise calculated as mean exposure during the preceding year.

Characteristics at entry	Outdoor wind turbine noise				
	< 24 dB(A) (N = 413,372)	24–30 dB(A) (N = 84,639)	30–36 dB(A) (N = 30,014)	36–42 dB(A) (N = 6343)	≥ 42 dB(A) (N = 1307)
Men	51%	51%	52%	53%	53%
Age					
< 40 years	47%	57%	58%	54%	47%
40–50 years	21%	19%	19%	21%	24%
50–60 years	15%	13%	13%	14%	17%
≥ 60 years	17%	12%	11%	11%	12%
Year of entry					
1996–2000	57%	42%	44%	53%	72%
2001–2005	13%	21%	21%	21%	17%
2006–2010	20%	22%	21%	17%	8%
2011–2013	10%	15%	14%	9%	3%
Personal income					
Quartile 1 (low)	17%	19%	18%	20%	19%
Quartile 2	23%	26%	26%	25%	23%
Quartile 3	27%	28%	28%	26%	24%
Quartile 4 (high)	26%	22%	23%	22%	28%
Unknown	7%	4%	5%	6%	6%
Highest attained education					
Basic or high school	33%	34%	34%	35%	37%
Vocational	43%	47%	47%	47%	40%
High	17%	17%	16%	16%	21%
Unknown	6%	3%	2%	3%	3%
Marital status					
Married	55%	48%	48%	50%	61%
Divorced/widow(er)	13%	13%	12%	11%	11%
Never married	32%	39%	40%	39%	28%
Affiliation to work market					
Working	72%	75%	77%	77%	81%
Retired	14%	12%	10%	10%	8%
Other	14%	13%	13%	13%	11%
Area-level income ^a					
Quartile 1 (low)	23%	19%	13%	11%	14%
Quartile 2	27%	31%	30%	28%	21%
Quartile 3	28%	30%	33%	34%	36%
Quartile 4 (high)	20%	17%	19%	20%	23%
Unknown	2%	3%	5%	7%	6%
Type of dwelling					
Farm	12%	17%	27%	40%	41%
Single-family detached house	63%	63%	61%	51%	50%
Others	25%	20%	12%	9%	9%
Distance to major road ^b					
< 500 m	39%	25%	18%	16%	17%
500–2000 m	27%	28%	27%	26%	25%
≥ 2000 m	34%	47%	55%	58%	57%
Traffic load within 500 m (10 ³ vehicle km/day) ^c					
< 2.5	31%	42%	57%	69%	66%
2.5–5.3	24%	26%	24%	13%	16%
5.3–9.7	19%	20%	14%	12%	9%
> 9.7	26%	12%	6%	6%	8%
Tree coverage within 500 m ^c					
< 5%	12%	18%	23%	30%	29%
5–20%	61%	68%	67%	63%	62%
> 20%	27%	14%	10%	7%	9%

^a Average disposable household income among all households in a 100 * 100 m grid cell.

^b Major road defined as ≥ 5000 vehicles per day.

^c In a 500 m radius around the dwelling.

have low traffic load and little tree coverage near their dwelling compared to people exposed to < 24 dB(A) (Table 1). Personal income and education did not show marked differences according to exposure level. Similar tendencies were seen when comparing people exposed to high and low levels of indoor LF WTN, except that people exposed to ≥ 5 dB(A) entered the study later than people exposed to < 5 dB(A) (Supplement Table 1). We found high correlations between the WTN exposures averaged over 1- and 5-years, whereas the correlation between indoor and outdoor WTN was lower (Supplement Table 2).

At start of follow-up, 78% of the study population lived in dwellings

exposed to < 24 dB(A) outdoor WTN and 97% lived in dwellings exposed to < 5 dB(A) indoor LF WTN (1-year mean, Table 2). Within each of the exposure categories above the reference (≥ 24 dB(A) for outdoor and ≥ 5 dB(A) for indoor LF WTN), the median exposure was close to the lower cut-point of the category (Table 2). The majority of the people living in dwellings with a 1-year mean exposure of ≥ 36 dB(A) outdoor WTN lived < 500 m from a WT at start of follow-up. Only small differences in height of the nearest WT were seen when comparing people exposed to < 36 dB(A) and 36–42 dB(A), whereas for the highest exposure group (≥ 42 dB(A)), there was a much higher proportion of

Table 2

Characteristics of wind turbines at the dwellings of the study participants at start of follow-up, according to residential exposure to outdoor and indoor low frequency (LF) wind turbine noise calculated as mean exposure during the preceding year.

Wind turbine characteristics at study dwellings at entry	Outdoor wind turbine noise					Indoor LF wind turbine noise			
	< 24 dB(A) (N = 413,372)	24–30 dB(A) (N = 84,639)	30–36 dB(A) (N = 30,014)	36–42 dB(A) (N = 6343)	≥ 42 dB(A) (N = 1307)	< 5 dB(A) (N = 513,645)	5–10 dB(A) (N = 17,949)	10–15 dB(A) (N = 3787)	≥ 15 dB(A) (N = 294)
Wind turbine noise levels									
Median	– ^a	26 dB(A)	32 dB(A)	37 dB(A)	45 dB(A)	– ^a	6 dB(A)	11 dB(A)	16 dB(A)
10% percentile	– ^a	24 dB(A)	30 dB(A)	36 dB(A)	42 dB(A)	– ^a	5 dB(A)	10 dB(A)	15 dB(A)
90% percentile	– ^a	29 dB(A)	34 dB(A)	40 dB(A)	50 dB(A)	– ^a	9 dB(A)	13 dB(A)	18 dB(A)
Outdoor wind turbine noise (1-year mean)									
< 24 dB(A)	100%	–	–	–	–	80%	0%	–	–
24–30 dB(A)	–	100%	–	–	–	15%	33%	0%	–
30–36 dB(A)	–	–	100%	–	–	4%	47%	46%	2%
36–42 dB(A)	–	–	–	100%	–	0%	17%	38%	48%
≥ 42 dB(A)	–	–	–	–	100%	0%	3%	15%	50%
Indoor LF wind turbine noise (1-year mean)									
< 5 dB(A)	100%	93%	66%	26%	7%	100%	–	–	–
5–10 dB(A)	0%	7%	28%	48%	37%	–	100%	–	–
10–15 dB(A)	–	0%	6%	23%	45%	–	–	100%	–
≥ 15 dB(A)	–	–	0%	2%	11%	–	–	–	100%
Distance to nearest wind turbine									
< 500 m	1%	17%	58%	94%	97%	7%	36%	67%	93%
500–2000 m	53%	82%	41%	5%	1%	56%	63%	33%	6%
≥ 2000 m	46%	1%	1%	1%	1%	37%	1%	1%	1%
Total height, nearest wind turbine									
< 35 m	34%	18%	22%	31%	65%	32%	11%	12%	19%
35–70 m	54%	63%	63%	58%	33%	56%	62%	57%	62%
70–100 m	10%	17%	14%	9%	1%	11%	23%	28%	17%
≥ 100 m	2%	2%	1%	1%	0%	1%	3%	3%	2%

^a Exposure distribution below reference level not presented as exact estimation was not undertaken for most situations.

dwellings located near low WTs (< 35 m). For indoor LF WTN, a larger proportion of those exposed to ≥ 10 dB(A) lived > 500 m from a WT at entry (especially in the 10–15 dB(A) group) and a much lower proportion lived near a WT < 35 m as compared with outdoor exposure ≥ 36 dB(A) (Table 2).

We found no overall associations between long-term exposure to outdoor WTN or indoor LF WTN and redemption of AHT neither for the main case definition nor for a case definition with higher specificity towards hypertensive indications (disregarding prescriptions for diuretics; Table 3). Generally, adjustment for potential confounders resulted in estimates closer to unity. For outdoor WTN, the point estimates for AHT above 42 dB(A) tended to remain below one (e.g. for 5-year exposure in relation to the main case definition HR: 0.91 and 95% CI: 0.78–1.06). Although we observed that some estimates were significantly above (e.g. 5-year outdoor WTN of 24–30 dB(A) for the main case definition; HR: 1.03 and 95% 1.01–1.05) and below unity (e.g. 1-year outdoor WTN ≥ 42 dB(A) for the strict case definition; HR: 0.78 and 95% CI: 0.61–0.98) no indications of dose-response relationships were observed.

We found indications of effect-modification by age, as for people above 65 years of age when redeeming AHT, HRs seemed to increase at high exposures to outdoor WTN as well as at high exposures to indoor LF WTN, whereas for people below 65 years no or even a decreased HR was observed in the highest exposure groups (Table 4). This interaction was borderline statistically significant for outdoor WTN. We found no indication of sex as a significant modifier of the relationship between WTN and redemption of AHT, although among women the HR was 1.27 (95% CI: 0.91–1.76) in the ≥ 15 dB(A) indoor LF WTN exposure group. The number of cases was low in this exposure group and similar tendencies were not observed for high exposure to outdoor WTN.

When investigating the association between exposure to outdoor and indoor LF WTN and risk for redeeming AHT in different sub-populations, we generally observed similar estimates across sub-populations as for the whole population, with no overall association between

WTN and redemption of AHT (Table 5). However, when confining the study population to people with high validity of the noise estimate, we observed a HR of 1.25 for people exposed to ≥ 15 dB(A) indoor LF WTN. The confidence intervals were, however, large and spanned unity (0.88–1.77) and the same tendency was not observed for outdoor WTN.

4. Discussion

We did not find long-term nighttime exposure to outdoor or indoor LF WTN to be associated with redemption of AHT in a large prospective study. The lack of association between WTN and redemption of AHT was consistent across two case definitions with increasing specificity as well as across various strata, including distance to a major road, validity of the noise estimate and total height of the nearest WT. There were some indications of an interaction with age.

A major strength of the present study is the prospective nationwide design with information on potential individual socioeconomic, area-level socioeconomic and environmental confounders, the large number of cases identified through a nationwide register (Kildemoes et al., 2011) with high validity (Rasmussen et al., 2016), and access to complete residential moving history for the study period. We modelled exposure to WTN using input data of high quality (hourly wind speed and direction at all WTs and detailed WTN spectra for all types of WTs) and state-of-the art exposure models, allowing us to model noise during night, where most people are at home sleeping. Also, we modelled the potentially more biologically relevant indoor LF WTN, where we took sound insulation characteristics of type of dwelling into account, although we were only able to differentiate into few insulation categories, based on relatively crude information. Further strengths were modelling of WTN for all dwellings in Denmark that might experience WTN, and inclusion of subjects from the same areas but with little or no exposure.

A major weakness of our study is that we use redemption of prescriptions for drugs with the indication of hypertension as a proxy for

Table 3

Associations between mean 1- and 5-year exposure to outdoor and indoor low frequency wind turbine noise and redemption of prescriptions for antihypertensives.

Exposure	Antihypertensive medication, all			Antihypertensive medication, excl. diuretics ^a		
	N cases	Crude ^b HR (95% CI)	Adjusted ^c HR (95% CI)	N cases	Crude ^b HR (95% CI)	Adjusted ^c HR (95% CI)
Outdoor 1-year mean WTN						
< 24 dB(A)	60,378	1 (ref)	1 (ref)	33,669	1 (ref)	1 (ref)
24–30 dB(A)	16,703	1.03 (1.01–1.05)	1.02 (1.00–1.04)	9272	1.01 (0.99–1.03)	1.00 (0.98–1.02)
30–36 dB(A)	5501	0.99 (0.96–1.01)	1.00 (0.97–1.03)	3095	0.97 (0.93–1.01)	0.98 (0.95–1.02)
36–42 dB(A)	998	0.95 (0.89–1.01)	0.99 (0.93–1.06)	562	0.95 (0.87–1.03)	0.99 (0.91–1.08)
≥ 42 dB(A)	149	0.85 (0.72–0.99)	0.92 (0.78–1.08)	70	0.73 (0.58–0.92)	0.78 (0.61–0.98)
Outdoor 5-year mean WTN						
< 24 dB(A)	60,348	1 (ref)	1 (ref)	33,562	1 (ref)	1 (ref)
24–30 dB(A)	16,791	1.04 (1.03–1.06)	1.03 (1.01–1.05)	9415	1.02 (1.00–1.05)	1.02 (0.99–1.04)
30–36 dB(A)	5429	1.01 (0.99–1.04)	1.03 (1.00–1.06)	3072	0.99 (0.95–1.03)	1.01 (0.97–1.04)
36–42 dB(A)	997	0.98 (0.92–1.04)	1.03 (0.97–1.10)	535	0.93 (0.85–1.01)	0.97 (0.89–1.06)
≥ 42 dB(A)	164	0.85 (0.73–0.99)	0.91 (0.78–1.06)	84	0.79 (0.64–0.98)	0.84 (0.68–1.04)
Indoor LF 1-year mean WTN						
< 5 dB(A)	78,461	1 (ref)	1 (ref)	43,561	1 (ref)	1 (ref)
5–10 dB(A)	4291	0.96 (0.93–0.99)	0.99 (0.96–1.02)	2523	0.95 (0.92–0.99)	0.98 (0.94–1.02)
10–15 dB(A)	908	0.91 (0.86–0.98)	0.97 (0.91–1.04)	542	0.91 (0.83–0.99)	0.96 (0.88–1.05)
≥ 15 dB(A)	69	0.85 (0.67–1.07)	0.93 (0.74–1.18)	42	0.86 (0.63–1.16)	0.93 (0.69–1.26)
Indoor LF 5-year mean WTN						
< 5 dB(A)	79,039	1 (ref)	1 (ref)	43,870	1 (ref)	1 (ref)
5–10 dB(A)	3870	0.96 (0.93–0.99)	0.99 (0.96–1.03)	2300	0.95 (0.91–0.99)	0.98 (0.93–1.02)
10–15 dB(A)	757	0.93 (0.87–1.00)	0.99 (0.93–1.07)	459	0.91 (0.83–1.00)	0.97 (0.88–1.06)
≥ 15 dB(A)	63	0.96 (0.75–1.23)	1.06 (0.83–1.35)	39	0.97 (0.71–1.33)	1.05 (0.77–1.44)

HR: hazard ratio; CI: confidence interval; WTN: wind turbine noise; LF: low frequency.

^a Redemption of prescriptions for antihypertensive excluding diuretics.^b Adjusted for age, sex and calendar year.^c Adjusted for age, sex, calendar year, personal income, education, marital status, work-marked affiliation, area-level socioeconomic status, type of dwelling, traffic load in 500 m radius and distance to major road.

hypertension. This results in a reduction in outcome sensitivity, as we lack information on people with undiagnosed hypertension and people who do not redeem prescriptions. However, as hypertension is a major risk factor for cardiovascular disease, diagnosing this condition ranks high at the general practitioners. Redemption of AHT is most likely a

result of repeated blood pressure measurements and clinical examination in accordance with clinical guidelines, and thus, the specificity is expected to be higher than a measurement at one point in time (which is often used in cross-sectional studies). The few previous studies that investigated associations between WTN and hypertension, defined

Table 4

Associations between 5-year exposure to wind turbine noise and redemption of antihypertensives according to sex and age.

Sub-populations	Outdoor wind turbine noise			p ^b	Indoor low frequency wind turbine noise			p ^b
	Exposure categories	N cases	Adjusted HR (95% CI) ^a		Exposure categories	N cases	Adjusted HR (95% CI) ^a	
Sex				0.24				0.29
Men	< 24 dB(A)	27,825			< 5 dB(A)	36,877	1 (ref)	
	24–30 dB(A)	8147	1.05 (1.02–1.07)		5–10 dB(A)	1957	1.00 (0.95–1.04)	
	30–36 dB(A)	2702	1.02 (0.98–1.06)		10–15 dB(A)	375	0.95 (0.86–1.05)	
	36–42 dB(A)	483	0.99 (0.90–1.08)		≥ 15 dB(A)	28	0.88 (0.60–1.27)	
	≥ 42 dB(A)	80	0.86 (0.69–1.07)					
Women	< 24 dB(A)	32,523	1 (ref)		< 5 dB(A)	42,162	1 (ref)	
	24–30 dB(A)	8644	1.02 (1.00–1.04)		5–10 dB(A)	1913	0.99 (0.95–1.04)	
	30–36 dB(A)	2727	1.04 (1.00–1.08)		10–15 dB(A)	382	1.04 (0.94–1.15)	
	36–42 dB(A)	514	1.07 (0.98–1.17)		≥ 15 dB(A)	35	1.27 (0.91–1.76)	
	≥ 42 dB(A)	84	0.96 (0.78–1.19)					
Age				0.06				0.33
< 65 years	< 24 dB(A)	37,310	1 (ref)		< 5 dB(A)	48,887	1 (ref)	
	24–30 dB(A)	10,468	1.03 (1.01–1.06)		5–10 dB(A)	2555	0.98 (0.94–1.02)	
	30–36 dB(A)	3487	1.02 (0.98–1.05)		10–15 dB(A)	524	1.00 (0.92–1.09)	
	36–42 dB(A)	630	0.99 (0.91–1.07)		≥ 15 dB(A)	37	0.94 (0.68–1.30)	
	≥ 42 dB(A)	108	0.81 (0.67–0.98)					
≥ 65 years	< 24 dB(A)	23,038	1 (ref)		< 5 dB(A)	30,152	1 (ref)	
	24–30 dB(A)	6323	1.03 (1.00–1.06)		5–10 dB(A)	1315	1.03 (0.97–1.09)	
	30–36 dB(A)	1942	1.06 (1.01–1.11)		10–15 dB(A)	233	0.98 (0.86–1.11)	
	36–42 dB(A)	367	1.11 (1.00–1.23)		≥ 15 dB(A)	26	1.28 (0.87–1.88)	
	≥ 42 dB(A)	56	1.17 (0.90–1.52)					

HR: hazard ratio; CI: confidence interval.

^a Adjusted for age, sex, calendar-year, personal income, education, marital status, work-marked affiliation, area-level socioeconomic status, type of dwelling, traffic load in 500 m radius and distance to major road.^b P for interaction.

Table 5
Associations between 5-year exposure to wind turbine noise and redemption of antihypertensives in different sub-populations.

Sub-populations	Outdoor wind turbine noise			Indoor low frequency wind turbine noise		
	Exposure categories	N cases	Adjusted HR (95% CI) ^a	Exposure categories	N cases	Adjusted HR (95% CI) ^a
All ^b	< 24 dB(A)	60,348	1 (ref)	< 5 dB(A)	79,039	1 (ref)
	24–30 dB(A)	16,791	1.03 (1.01–1.05)	5–10 dB(A)	3870	0.99 (0.96–1.03)
	30–36 dB(A)	5429	1.03 (1.00–1.06)	10–15 dB(A)	757	0.99 (0.93–1.07)
	36–42 dB(A)	997	1.03 (0.97–1.10)	≥ 15 dB(A)	63	1.06 (0.83–1.35)
	≥ 42 dB(A)	164	0.91 (0.78–1.06)			
Living on a farm	< 24 dB(A)	6234	1 (ref)	< 5 dB(A)	9491	1 (ref)
	24–30 dB(A)	2926	1.00 (0.96–1.05)	5–10 dB(A)	1335	0.98 (0.93–1.04)
	30–36 dB(A)	1545	1.00 (0.94–1.05)	10–15 dB(A)	374	1.02 (0.92–1.13)
	36–42 dB(A)	463	1.07 (0.98–1.18)	≥ 15 dB(A)	34	1.08 (0.77–1.52)
	≥ 42 dB(A)	66	0.89 (0.70–1.13)			
Total height of nearest wind turbine ≥ 35 m	< 24 dB(A)	47,032	1 (ref)	< 5 dB(A)	62,917	1 (ref)
	24–30 dB(A)	14,688	1.03 (1.01–1.05)	5–10 dB(A)	3626	1.00 (0.97–1.04)
	30–36 dB(A)	4701	1.04 (1.01–1.07)	10–15 dB(A)	712	1.01 (0.93–1.08)
	36–42 dB(A)	799	1.06 (0.98–1.13)	≥ 15 dB(A)	56	1.04 (0.80–1.35)
	≥ 42 dB(A)	91	1.12 (0.91–1.37)			
High validity score of noise estimate ^c	< 24 dB(A)	45,258	1 (ref)	< 5 dB(A)	42,295	1 (ref)
	24–30 dB(A)	11,051	1.04 (1.01–1.06)	5–10 dB(A)	1729	1.02 (0.97–1.07)
	30–36 dB(A)	3579	1.04 (1.01–1.08)	10–15 dB(A)	383	1.08 (0.98–1.19)
	36–42 dB(A)	531	1.06 (0.97–1.15)	≥ 15 dB(A)	32	1.25 (0.88–1.77)
	≥ 42 dB(A)	29	0.95 (0.66–1.37)			
Dwelling ≥ 2000 m from major road ^d	< 24 dB(A)	20,016	1 (ref)	< 5 dB(A)	29,066	1 (ref)
	24–30 dB(A)	8117	1.04 (1.01–1.07)	5–10 dB(A)	2199	1.00 (0.95–1.04)
	30–36 dB(A)	2966	1.00 (0.96–1.09)	10–15 dB(A)	479	0.99 (0.90–1.08)
	36–42 dB(A)	585	1.01 (0.93–1.09)	≥ 15 dB(A)	46	1.08 (0.81–1.44)
	≥ 42 dB(A)	106	0.98 (0.81–1.18)			
< 5% tree coverage ^e	< 24 dB(A)	6393	1 (ref)	< 5 dB(A)	9683	1 (ref)
	24–30 dB(A)	2842	1.01 (0.96–1.05)	5–10 dB(A)	922	1.00 (0.94–1.07)
	30–36 dB(A)	1316	1.07 (1.01–1.14)	10–15 dB(A)	257	1.05 (0.93–1.19)
	36–42 dB(A)	287	0.98 (0.87–1.11)	≥ 15 dB(A)	23	0.88 (0.58–1.32)
	≥ 42 dB(A)	47	0.89 (0.67–1.18)			

HR: hazard ratio; CI: confidence interval.

^a Adjusted for age, sex, calendar-year, personal income, education, marital status, work-marked affiliation, area-level socioeconomic status, type of dwelling, traffic load in 500 m radius and distance to major road.

^b Corresponding to HRs and CIs in Tables 3 and 4.

^c Includes only study participants with validity score better than the median among those with exposures ≥ 36 dB(A) for outdoor and ≥ 10 dB(A) for indoor WTN. The validity score reflects the estimated uncertainty associated with all aspects of noise estimation at a specific address and day.

^d Major road defined as ≥ 5000 vehicles per day.

^e In a 500 m radius around the dwelling.

hypertension as self-reported high blood pressure, self-reported intake of AHT or measured systolic and diastolic blood pressure (Michaud et al., 2016a; Michaud et al., 2016b; Pedersen, 2011). Similar to the present study, these studies did not find any associations between residential WTN exposure and hypertension, suggesting that WTN is not associated with hypertension. However, these studies were all cross-sectional, they were based on much smaller study populations than the present study and hypertension or use of AHT was self-reported, and more studies are needed before a final conclusion can be made.

Although hypertension is the primary indication for most drugs defined as AHT, some of these drugs are also used for treatment of other conditions, including heart disease and diabetes. To reduce misclassification of the outcome, we therefore censored persons when diagnosed with cardiovascular disease or diabetes. In a sensitivity analysis, we increased specificity even further by excluding diuretics entirely from our case identification algorithm (although thereby decreasing sensitivity), as these drugs have a range of entirely different indications e.g. oedema. We found similar results for the more restrictive case definition as for the main case definition, indicating that low specificity does not explain the lack of association between WTN and redemption of AHT observed in the present study.

A main problem when investigating hypertension is that many people have hypertension without being diagnosed, resulting in a substantial underreporting in both studies using self-reported data and registry studies such as the present. In Denmark, it has been estimated

that 30% of people with hypertension are not aware of this; a number that decreases with increasing age, probably due to a more frequent contact with the health care system (Kronborg et al., 2009). We cannot completely rule out surveillance bias, as one might speculate that people living near WTs may contact the health care system more frequently than people living far from a WT due to concern regarding WTN. Also, we did see some indications of effect-modification by age, as for people above 65 years we observed that high levels of outdoor or indoor LF WTN seemed associated with higher HRs, and for outdoor WTN there was a borderline statistically significant interaction together with some suggestion of a dose-response relationship. Elevated risk estimates among people above 65 years could suggest that they constitute a more susceptible population with regard to exposure to WTN, but also that in this age group there is less underreporting of hypertension, due to more frequent contact with the health care system, thus including a more “true” distribution of cases and non-cases. Also, one might speculate that people above 65 are more likely to be at home during daytime, which could potentially explain the increased HRs for outdoor exposure. On the other hand, we found marginal but borderline significant risk increase even at the lowest exposure levels, indicating that non-causal factors may have influenced the results. Furthermore, although the HRs for ≥ 42 dB(A) outdoor and ≥ 15 dB(A) indoor LF WTN were somewhat elevated in the older age group, the CIs spanned unity and there were relatively few cases with high exposure to WTN, and chance remains a likely explanation for these observations. In addition,

the finding of a borderline statistically significant effect modification by age for outdoor exposure was partly driven by a statistically significant reduction in risk among the highly exposed younger than 65 years. We do not have any plausible biological explanation as to how high levels of outdoor WTN could protect this age group from redeeming AHT, and with increased risk in the 24–30 dB(A) exposure group, there were no indications of a dose-response relationship, suggesting a chance finding. The indications of an association among people over 65 years, however, call for further investigations of older persons in designs with a more complete registration of hypertension than in the present.

Due to the register-based nature of the study, we did not have access to potential lifestyle confounders, such as dietary habits, tobacco smoking and physical activity, which is a weakness. However, we found that adjustment for individual and area-level socioeconomic variables generally brought the estimates closer to unity. For outdoor WTN, the HRs were marginally but borderline significantly elevated, except in the highest exposure category where they remain slightly decreased, which all together suggests some minor residual confounding. Also, confining the dataset to people living on farms – a sub-population where lifestyle patterns are expected to be more similar than for the whole study population – yielded HRs that were similar to the HRs obtained for the whole population, which again indicates that residual confounding is not prominent in the present study. Lastly, studies have indicated that noise from traffic may be associated with lifestyle, such as higher waist circumference and low physical activity (Christensen et al., 2015; Eriksson et al., 2014; Foraster et al., 2016; Roswall et al., 2017), suggesting that these are intermediates and not only potential confounders on the pathway between noise and disease.

Other limitations include the rather crude adjustment for local road traffic noise, using traffic load and distance to major road. However, residual confounding by traffic noise is unlikely to be a large problem in our study, as we obtained similar estimates among people living far from major roads as compared to the whole study population. Also, although the Nord2000 has been successfully validated for WTs (Søndergaard et al., 2009), there is inevitable uncertainty in the modelled noise exposure. We did not perform validation by measurements in the present study, as this is generally not recommendable, because it is very difficult to produce measurements that are not polluted by other noise sources, such as traffic noise and leaf rustle. Any uncertainty on the noise estimate is likely to be non-differential, influencing the estimates towards unity. To investigate this further, we used a validity score for the noise estimate of each person. Although this validity score does not cover all features of uncertainty of the noise modelling, our finding of similar estimates for outdoor WTN among people with a high validity score compared to the whole population suggests that exposure misclassification is not a major issue for outdoor WTN. For indoor LF WTN, we observed that the HR in the highest exposure group increased among people with a high validity score indicating that exposure misclassification may have affected the results. However, there were relatively few cases ($n = 37$) in this exposure group and the CIs spanned unity, and thus the observed increase in the HR may be due to chance.

In conclusion, we found no overall association between long-term nighttime exposure to outdoor or indoor LF WTN and redemption of AHT, which is in accordance with the sparse literature within the area. The lack of association was consistent across a number of sub-populations. We did however find weak indications of an association between both WTN exposure types and redeeming AHT among people over 65 years, which calls for more studies.

Competing financial interests declaration

All authors declare no competing financial interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.envint.2018.08.054>.

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