Research

Long-Term Exposure to Wind Turbine Noise and Risk for Myocardial Infarction and Stroke: A Nationwide Cohort Study

Aslak Harbo Poulsen,[1] Ole Raaschou-Nielsen,[1,3] Alfredo Peña,[2] Andrea N. Hahmann,[2] Rikke Baastrup Nordsborg,[1] Matthias Ketzel,[3,5] Jørgen Brandt,[3] and Mette Sørensen[1,4]

[1]Diet, Genes and Environment, Danish Cancer Society Research Center, Copenhagen, Denmark
[2]DTU Wind Energy, Technical University of Denmark, Roskilde, Denmark
[3]Department of Environmental Science, Aarhus University, Roskilde, Denmark
[4]Department of Natural Science and Environment, Roskilde University, Roskilde, Denmark
[5]Global Center for Clean Air Research (GCARE), University of Surrey, United Kingdom

BACKGROUND: Noise from wind turbines (WTs) is reported as more annoying than traffic noise at similar levels, raising concerns as to whether WT noise (WTN) increases risk for cardiovascular disease, as observed for traffic noise.

OBJECTIVES: We aimed to investigate whether long-term exposure to WTN increases risk of myocardial infarction (MI) and stroke.

METHODS: We identified all Danish dwellings within a radius 20 times the height of the closest WT and 25% of the dwellings within 20–40 times the height of the closest WT. Using data on WT type and simulated hourly wind at each WT, we estimated hourly outdoor and low frequency (LF) indoor WTN for each dwelling and derived 1-y and 5-y running nighttime averages. We used hospital and mortality registries to identify all incident cases of MI ($n = 19,145$) and stroke ($n = 18,064$) among all adults age 25–85 y ($n = 717,453$), who lived in one of these dwellings for $\geq$one year over the period 1982–2013. We used Poisson regression to estimate incidence rate ratios (IRRs) adjusted for individual- and area-level covariates.

RESULTS: IRRs for MI in association with 5-y nighttime outdoor WTN >42 (vs. <24) dB(A) and indoor LF WTN >15 (vs. <5) dB(A) were 1.21 [95% confidence interval (CI): 0.91, 1.62; 47 exposed cases] and 1.29 (95% CI: 0.73, 2.28; 12 exposed cases), respectively. IRRs for intermediate categories of outdoor WTN [24–30, 30–36, and 36–42 dB(A) vs. <24 dB(A)] were slightly above the null and of similar size: 1.08 (95% CI: 1.04, 1.12), 1.07 (95% CI: 1.00, 1.12), and 1.06 (95% CI: 0.93, 1.22), respectively. For stroke, IRRs for the second and third outdoor exposure groups were similar to those for MI, but near or below the null for higher exposures.

CONCLUSIONS: We did not find convincing evidence of associations between WTN and MI or stroke. https://doi.org/10.1289/EHP3340

Introduction

During recent decades, focus on renewable energy has increased globally, and advancements in wind energy technologies have resulted in an increased number of wind turbines (WTs). WT noise (WTN) has consistently been associated with annoyance among people living near WTs (Janssen et al. 2011; Michaud et al. 2016a; Schmidt and Klokker 2014), and some studies have indicated that WTN may also disturb sleep (Schmidt and Klokker 2014), although results are inconsistent (Jalali et al. 2016; Michaud et al. 2016b).

Long-term exposure to transportation noise has been associated with higher risk for myocardial infarction (MI) and stroke (Hansell et al. 2013; Héritier et al. 2017; Sørensen et al. 2011; Vienneau et al. 2015). The pathophysiologic pathways are believed to involve activation of a general stress response and disturbance of sleep, in turn leading to increases in cardiovascular risk factors, including blood pressure, endothelial dysfunction, and oxidative stress, as well as a weakened immune system (Münzel et al. 2017a; Schmidt et al. 2013, 2015; van Kempen and Babisch 2012). This assocation has raised concerns about whether WTN may increase risk for cardiovascular disease.

The findings on traffic noise and health are not readily applicable to WTN. Generally, levels of WTN are considerably lower than levels of traffic noise found in urban settings; e.g., in Denmark app. 30% of all dwellings are exposed to levels of road traffic noise that exceed 58 dB(A), whereas Danish legislation does not allow WTN to exceed 44 dB(A) (at 8 m/s) at dwellings (except WT owners erecting WTs on their private property) (Miljø- og Fødevareministeriet 2011; Miljøministeriet 2007). However, at comparable noise levels, WTN has been associated with a higher proportion of annoyed residents than traffic noise (Janssen et al. 2011). A potential explanation for this increased annoyance is that WTN depends on wind speed and direction, making it less predictable for the exposed population than road traffic noise, which often follows a distinct pattern with high levels during rush hours and lower levels during the night. Also, amplitude modulation gives WTN a rhythmic quality that is different from that of road traffic noise. It has therefore 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 (Waye et al. 2003), rather than the full spectrum A-weighted noise, as typically used in studies of traffic noise (Jeffery et al. 2014). Last, WTs are mainly located in rural areas, where the auditory impact of WTs may be more pronounced due to lower levels of background noise in general, together with an expectation of a quieter environment among rural residents in comparison with expectations of people living in more densely populated areas.

Only a few studies have investigated whether residential outdoor WTN is associated with cardiovascular risk factors or diseases. The studies were all of cross-sectional design. A study based on two Swedish study populations and one Dutch study population, with a total of 1,755 participants, found no associations between WTN and self-reported high blood pressure or cardiovascular disease, for neither A-weighted WTN nor indoor or outdoor WT annoyance (Pedersen 2011). Similarly, a Canadian study of 1,238 participants living within 12 km of a WT found no associations between estimated A-weighted residential WTN and self-reported prevalent high blood pressure, medication for high blood pressure, or heart disease (Michaud et al. 2016a). Furthermore, the Canadian

study found no associations between 1-y mean residential outdoor WTN (modeled) and measurements of blood pressure, heart rate, or hair cortisol (Michaud et al. 2016c).

We aimed to prospectively investigate whether long-term residential exposure to WTN is associated with risk for MI and stroke in a nationwide register-based study. We combined data on WT position and type, simulated meteorological conditions and WTN, residential addresses, socioeconomic indicators, and development of disease over the period 1982–2013.

Methods

The study was based on the Danish population, where all citizens since 1968 can be tracked in and across all Danish health and administrative registers by means of a personal identification number that is maintained by the Central Population Register (Schmidt et al. 2014).

Locating and Classifying WTs

We identified all WTs (7,860) in operation in Denmark at any time between 1980 and 2013 using the administrative Master Data Register of Wind Turbines, a registry maintained by the Danish Energy Agency (Energistyrelsen 2014). In Denmark, it is mandatory for all WT owners to report geographical coordinates and cadastral codes of their WT(s) to the registry. Furthermore, for WTs in operation at the time of data extraction (May 2014), the register also contained coordinates from the Danish Geodata Agency. In case of disagreement between these coordinates and geographical locations reported by WT owners, the WT location was validated against aerial photographs and historical topographic maps. We excluded 517 offshore WTs and 87 WTs for which no credible location was found. Moreover, 314 WTs wrongly recorded in the Master Data Register were assigned new coordinates based on maps and aerial photographs. Information on height, model, type, and operational settings was collected through the Master Data Register of Wind Turbines, and each WT was classified into one of 99 noise spectra classes, with detailed noise spectrum information 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 sound power for Danish WTs (Backalarz et al. 2016; Sondergaard and Backalarz 2015).

Wind Conditions

For each WT location, we estimated the wind speed and direction at hub height for each hour over the period 1982–2013, using mesoscale model simulations performed with the Weather Research and Forecasting model (Hahmann et al. 2015; Peña and Hahmann 2017).

Noise Modeling

The WTN exposure modeling has been described in detail elsewhere (Backalarz et al. 2016). In summary, we first identified buildings that might have WTN discernable above background noise, which we defined as having $\geq 24\,\mathrm{dB(A)}$ outdoor WTN or $\geq 5\,\mathrm{dB(A)}$ indoor LF WTN (10–160 Hz) under the unrealistically extreme scenario that all WTs ever operational in Denmark were simultaneously operating at a wind speed of 8 m/s with downwind sound propagation in all directions (to ensure that no eligible buildings were excluded). Second, 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 to 10,000 Hz, using the Nord2000 noise propagation model (Kragh et al. 2001), and taking into account the hourly estimates of wind speed and direction at hub height during the period

1982–2013. The Nord2000 model has been successfully validated for WTs (Søndergaard et al. 2009). For each dwelling, we calculated the noise contribution from all WTs within a 6-km radius hour by hour. Noise contributions from WTs beyond 6 km were not evaluated because they could not appreciably affect the noise estimate. These modeled values were then aggregated over the nighttime period [2200 to 0700 hours (10 P.M. to 7 A.M.)], which we considered the most relevant time window as people are most likely at home and asleep during these hours. We calculated outdoor A-weighted sound pressure level, which is the metric most commonly used in noise and health studies (Michaud et al. 2016c; Pedersen 2011), as well as A-weighted indoor LF (10–160 Hz) sound pressure level. LF noise penetrates buildings well and has been suggested as an important component of WTN in relation to health (Jeffery et al. 2014).

We determined a validity score for the indoor and the outdoor noise estimates as follows: For estimation of WTN, WTs were grouped into 99 noise spectra classes with similar noise profiles. The noise spectra for each class was determined from existing noise data describing the noise spectra of all WT-models within each class, typically for 8 m/s wind speed and since 2006 also for 6 m/s wind speed. For some WTs, data were available for other wind speeds. In WT classes with many WT models, more data were available than in classes with few WTs. In general, fewer data were available for old or rare WT types. For each dwelling time point (hour by hour), the validity score reflects information for all contributing WTs on *a*) the number and quality of measurement data used to determine the WTN spectra classes, and *b*) how closely the simulated meteorological conditions for that hour resembled the conditions under which the relevant WTN spectra were measured. These validity data were then combined for all WTs contributing noise to a given dwelling on a given night and subsequently aggregated over the past 1 and 5 y following the running exposure periods for each participant. The higher the number of this score, the more reliable the noise estimate was assumed to be. Finally, we dichotomized validity by the median among those dwellings exposed to outdoor WTN >30 or indoor LF WTN $>10\,\mathrm{dB(A)}$. This method was used because WTN and the likelihood of a high validity score is by definition correlated, and we wanted to focus on highly exposed subjects with comparatively high validity for that noise level.

For the calculation of indoor LF noise, all dwellings were classified into one of six sound insulation classes, based on building attributes in the Building and Housing register (Christensen 2011): "1½-story houses" (residents assumed to sleep on the second floor with most sound transmitted through the roof), "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 each of the six classes are shown in Backalarz et al. 2016.

Study Population and Exposure Assignment

To define the study population, we first identified a set of "inclusion dwellings," which were all Danish dwellings located within a radius of 20 times the height of a neighboring WT at any time during the years 1982–2013, plus a random selection of 25% of all dwellings within a radius of 20–40 WT heights from at least one WT during the same period. These criteria were selected to ensure that the study population would include all people living within a radius of 20 times the height of one or more WTs, plus people living in the same areas, but with little or no WTN exposure. We excluded all hospitals and residential institutions and all dwellings situated within 100 m of areas classified as a "town

center" (i.e., the central part of larger towns, characterized by multistory adjoined buildings) in GIS data from the Danish Geodata Agency (dataset: KORT10, precision ± 1 m, data from 2013), as traffic conditions and lifestyle in town centers may differ substantially from the main study population.

We subsequently used the Danish Civil Registration System (Schmidt et al. 2014) to identify the study cohort, defined as all adults (age 25–84 y) who lived in one of these inclusion dwellings any time between five years before the erection of the first neighboring WT and the end of 2013. Including people before and after a WT was operational ensured inclusion of subjects living in exactly the same dwellings but with no exposure. For this population, we then established complete migration histories (including also town centers and other addresses not counted as inclusion dwellings) from five years before start of follow-up until five years after moving from the inclusion dwelling. This method allowed us to assign daily residential WTN exposure to each member of the cohort based on all dwellings they had lived in during that period. Subjects without complete geocodable address history for the period five years before start of follow-up were excluded (later holes in address history resulted in censoring).

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 entirely register-based studies.

Covariates

Selection of potential confounders was done *a priori*. From the registries of Statistic Denmark, we obtained information on age and sex, highest attained educational level (time-dependent, updated yearly), personal income (time-dependent, updated yearly), marital status (time-dependent, updated yearly), work-market affiliation (time-dependent, updated yearly), and areal level ($10,000 \, m^2$) mean household income (year 2010) (Baadsgaard and Quitzau 2011; Jensen and Rasmussen 2011; Petersson et al. 2011). 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 ≥5,000 vehicles (in 2005) as well as total distance driven by vehicles within 500 m of the residence each day as the product of street length and traffic density.

Identification of Outcome

Cases with MI and stroke were identified by linking the personal identification number of each member of the study population to the nationwide Danish National Patient Register, which started in 1977 (Lynge et al. 2011), and the Danish Register of Causes of Death from 1970 (Helweg-Larsen 2011). We defined stroke cases using the International Classification of Diseases (ICD) 8 codes 431–434 and 436 or ICD10 codes I61, I63, and I64, and cases of MI as ICD8 code 410 or ICD10 code I21. The subgroup of ischemic strokes was defined as ICD8 432–434 or ICD10 I63. We considered only incident events (from either register) and excluded all persons with events prior to start of follow-up.

Statistical Methods

Log-linear Poisson regression analysis was used to calculate incidence rate ratios (IRRs) for MI and stroke according to outdoor [<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 y and 5 y. We performed categorical analyses to avoid concealment

of potential effects at high exposures due to forced linearity dictated by the vast majority of our population exposed to less than the (as-yet-unknown) levels potentially associated with the health outcomes. The categorizations were determined *a priori*. At present, there are no standards regarding categorizations of WTN. After consulting acousticians, we chose <24 dB(A) outdoor and <5 dB(A) indoor LF WTN as the references, as the acousticians evaluated that WTN in all likelihood will be inaudible below these levels. For outdoor WTN, the upper limit of 42 dB(A) was chosen as this is the regulatory WTN limit in Denmark (at wind speed 6 m/s) and therefore of interest from an administrative point of view, and the intermediate cut points chosen were 30 dB(A) and 36 dB(A), which separated categories by 6 dB(A). For indoor LF WTN, the Danish regulatory limit was 20 dB(A), and we chose intermediate cut points of 10 dB(A) and 15 dB(A). However, there were very few cases exposed to levels >20 dB(A), and we therefore chose >15 dB(A) as the highest exposure category.

For dwellings located so far from WTs as to never have WTN above 24 dB(A) outdoors and 5 dB(A) indoors, or when WTs were not operating due to wind conditions, a value of −20 dB(A) was used to represent close to no noise in calculating the average. Follow-up was started after residents had lived one year in the recruitment dwelling, turning 25 y or 1 January 1982, whichever came last, and follow-up ended at time of MI (in analyses of MI) or stroke (in analyses of stroke), death, age 85 y, disappearance, or having no recorded address geocodes for more than seven consecutive days, 31 December 2013, or five years after moving from the inclusion dwelling, whichever came first. In addition, we estimated IRRs for the subgroup of strokes diagnosed as ischemic and censured all other types of stroke at time of diagnosis.

All analyses were adjusted for sex, calendar year (1982–1984, 1985–1989, 1990–1994, 1995–1999, 2000–2004, 2005–2009, and 2010–2013) and age (25–84 y, in five-year categories). Additionally, we adjusted for marital status [currently married/registered partnership and other (never or formerly married)], education (basic or high school, vocational, higher, and unknown), work-market affiliation [employed, retired, and other (e.g., under education or unemployed)], personal income (20 equal-sized annual categories, and an unknown income category), area-level average mean household income (20 equal-sized categories, and an unknown income category; data from 2010), dwelling classification (farm, single-family detached house, and other (e.g., apartments and terraced housing), distance to road with ≥5,000 vehicles per day (<500 m, 500 − < 1,000 m, 1,000 − < 2,000 m and ≥2,000 m), and traffic load within 500 m radius of dwelling (first, and second quartile, and above median; quartiles calculated in larger sample of Danish addresses). Subjects were allowed to change between categories of covariates (yearly and/or at change of address) and exposure variables over time.

We used Poisson models, including an interaction term, to investigate sex and age (above and below 65 y) as potential (multiplicative) effect modifiers. Also, we conducted a number of sensitivity analyses in subpopulations for whom we hypothesized that a potential association between modeled exposure and risk could be more pronounced. First, we investigated association among cases with a diagnosis of MI or stroke after year 2000 (persons diagnosed with MI or stroke before year 2000 were censored at diagnosis and not counted as cases), reflecting improved diagnostic practices and more comprehensive data on more modern WTs. Second, we looked only at people while they were living in dwellings classified as farms (a large proportion of the highly exposed people live on farms, and we hypothesize that there is less variation in lifestyle and other exposures among this subpopulation in comparison with the whole population, potentially reducing susceptibility to residual confounding in

Table 1. Characteristics of the populations for study of MI and stroke, 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.

Characteristics at start of follow-up	Outdoor wind turbine noise				
	<24 dB(A) MI/stroke ($N = 587,866/589,098$)	24–30 dB(A) MI/stroke ($N = 86,280/86,194$)	30–36 dB(A) MI/stroke ($N = 29,869/29,888$)	36–42 dB(A) MI/stroke ($N = 6,063/6,050$)	≥42 dB(A) MI/stroke ($N = 1,171/1,171$)
Men	50/50%	51/51%	52/52%	53/53%	54/54%
Age					
<40 years	43/42%	60/60%	63/63%	65/65%	68/68%
40–50 years	19/19%	16/16%	16/16%	17/17%	17/17%
50–60 years	15/15%	11/11%	10/10%	10/10%	8/8%
≥60 years	23/23%	14/14%	10/10%	8/7%	6/6%
Year of start of follow-up					
1982–1990	23/23%	6/6%	6/6%	9/9%	16/16%
1990–2000	39/39%	27/27%	28/28%	35/35%	49/49%
2000–2010	29/29%	50/50%	39/39%	44/44%	31/31%
2010–2013	8/8%	18/18%	16/16%	12/12%	4/4%
Personal income					
Quartile 1 (low)	19/19%	19/19%	18/18%	18/18%	16/16%
Quartile 2	23/23%	28/28%	28/28%	27/27%	25/25%
Quartile 3	24/24%	28/28%	28/28%	28/28%	27/27%
Quartile 4 (high)	23/23%	21/21%	21/21%	21/21%	26/26%
Unknown	12/12%	4/4%	5/5%	6/6%	5/5%
Highest attained education					
Basic or high school	35/35%	33/33%	32/32%	31/31%	33/33%
Vocational	37/37%	46/46%	48/48%	49/49%	46/46%
High	15/15%	18/18%	18/18%	18/18%	19/19%
Unknown	13/13%	3/3%	2/2%	2/2%	2/2%
Marital status					
Married	57/57%	41/41%	40/40%	39/39%	45/45%
Divorced/widow(er)	15/15%	16/16%	15/15%	14/14%	13/13%
Never married	28/28%	43/43%	45/45%	47/47%	42/42%
Affiliation to work market					
Working	65/65%	70/70%	73/74%	75/76%	77/77%
Retired	19/19%	16/16%	12/12%	10/9%	7/8%
Other[a]	16/16%	14/14%	14/14%	15/15%	16/16%
Area-level income[b]					
Quartile 1 (low)	24/23%	22/22%	15/15%	12/12%	15/15%
Quartile 2	28/28%	29/29%	29/29%	27/27%	21/21%
Quartile 3	27/27%	29/29%	32/32%	33/33%	33/33%
Quartile 4 (high)	19/19%	17/17%	19/19%	21/22%	25/25%
Unknown	3/3%	3/3%	5/5%	7/7%	6/6%
Type of dwelling					
Farm	13/13%	14/14%	23/23%	34/34%	34/34%
Single-family detached house	62/62%	60/60%	61/61%	52/52%	54/54%
Others[c]	25/25%	25/26%	17/17%	14/13%	12/12%
Distance to major road[d]					
<500 m	36/36%	25/25%	19/19%	18/18%	20/20%
500–2,000 m	27/27%	30/30%	28/28%	27/27%	27/27%
≥2,000 m	37/37%	45/45%	53/53%	55/55%	53/53%
Traffic load[e]					
<2.5 million vehicles	33/33%	40/40%	54/54%	67/67%	63/63%
2.5-5.3 million vehicles	25/25%	27/27%	25/25%	13/13%	16/16%
5.3-9.7 million vehicles	19/19%	21/21%	15/15%	13/13%	12/12%
>9.7 million vehicles	23/23%	12/12%	6/6%	7/7%	9/9%
Tree coverage[e]					
<5%	13/13%	17/17%	21/21%	28/28%	28/28%
5–20%	63/63%	68/68%	68/68%	63/64%	63/63%
>20%	24/24%	15/15%	11/11%	8/8%	9/9%

[a]Include under education and unemployed among others.
[b]Average mean household income among all households in a 100×100 m grid cell.
[c]Include apartments and terraced housing among others.
[d]Major road defined as ≥5,000 vehicles per day.
[e]In a 500 meters radius around the dwelling.

this group). Third, we investigated people while their nearest WT had a total height of >35 m (the WTN may qualitatively differ, for example, in terms of frequency composition by WT size, and there is less likelihood that the WT is owned by those exposed). Fourth,

we addressed exposure misclassification by looking at people with validity of the cumulated noise estimate better than the median. As exposure misclassification among individuals with very low exposure was unlikely to be sufficient to alter exposure categorization,

Table 2. Characteristics of wind turbines at the dwellings of the study participants at start of follow-up, according to residential exposure to outdoor wind turbine noise calculated as mean exposure during the preceding year.

Wind turbine characteristics at of the study population dwellings at start of follow-up	Outdoor wind turbine noise				
	<24 dB(A) MI/stroke (N = 587,866/589,098)	24–30 dB(A) MI/stroke (N = 86,280/86,194)	30–36 dB(A) MI/stroke (N = 29,869/29,888)	36–42 dB(A) MI/stroke (N = 6,063/6,050)	≥42 dB(A) MI/stroke (N = 1,171/1,171)
Indoor LF wind turbine noise (1-year mean)					
<5 dB(A)	100%	93/92%	64/64%	27/27%	7/7%
5–10 dB(A)	0%	7/7%	30/30%	45/45%	38/38%
10–15 dB(A)	0%	0/0%	6/6%	26/26%	43/43%
≥15 dB(A)	0%	0/0%	0/0%	3/3%	12/12%
Distance to nearest wind turbine					
<500 m	1/1%	17/17%	52/52%	91/91%	95/95%
500–2,000 m	37/37%	79/79%	45/45%	7/7%	2/2%
≥2,000 m	61/61%	4/4%	3/3%	2/2%	3/3%
Total height, nearest wind turbine					
<35 m	41/41%	19/19%	23/23%	35/35%	71/71%
35–70 m	41/41%	59/59%	60/60%	52/52%	27/27%
70–100 m	9/9%	20/20%	16/16%	12/12%	1/1%
≥100 m	1/1%	2/2%	2/2%	1/1%	0/0%

Note: LF, low frequency.

the median was calculated only among those individuals with exposures ≥10 dB(A) LF or 30 dB(A) in indoor and outdoor analyses, respectively. Fifth, we investigated effects in people living in dwellings located far from a major road (>2,000 m to nearest road with >5,000 vehicles/day, as exposure to traffic noise may mask WTN). Last, we investigated associations among people in dwellings with low tree coverage [<5% of the area within 500 m of dwelling covered by forest, thicket, groves, single trees, and hedgerows, according to GIS data (dataset KORT10, precision ± 1 m) from the Danish Geodata Agency, as vegetation noise may mask WTN]. Data were analyzed using SAS (version 9.3; SAS Institute Inc.).

Results

We identified 844,228 adults (25–84 y) living ≥one year in the inclusion dwellings between 1982–2013. We excluded persons who had emigrated (n = 44,049) or disappeared (n = 1,570) prior to start of follow-up, who had unknown address for eight or more consecutive days in the five years prior to start of follow-up (n = 78,830; 98% had address holes of more than 30 d and 64% of more than a year), and who lived in hospitals or institution at study start of follow-up (n = 2,004). Also, we excluded all persons diagnosed with MI (n = 6,526 only relevant for the MI study population) or stroke (n = 5,374, only relevant for the stroke

study population) before start of follow-up. The final study population was 711,249 persons for the MI analyses, of whom 19,145 (2.7%) developed MI during 7,440,090 person-years, and 712,401 persons for the stroke analyses, of whom 18,064 (2.5%) developed stroke during 7,466,239 person-years.

In comparison with people exposed to 1-y mean outdoor WTN <24 dB(A), the likelihood of being male, <40 years of age, living on a farm, living in areas with high area-level income and low tree coverage increased with increasing levels of outdoor WTN, whereas the likelihood of having high levels of traffic, major roads nearby, or being retired decreased (Table 1). People exposed ≥24 dB(A) were likely to have higher levels of education than those exposed to <24 dB, and exposure to ≥42 dB(A) WTN was associated with higher income. In general, similar tendencies as those for outdoor WTN were seen when looking at indoor LF WTN levels, except that no differences in gender distribution were found, and the likelihood of high personal income decreased with increased WTN levels (Table S1). Also, when comparing people with outdoor or indoor WTN above the respective reference levels, the latter tended to enter the study later, live further from major roads, have lower tree coverage, and more likely have vocational training as highest attained education level.

People exposed to outdoor WTN above 30 dB(A) were more frequently exposed to levels of indoor LF WTN above the

Table 3. Characteristics of wind turbines at the dwellings of the study participants at start of follow-up, according to residential exposure to indoor low frequency wind turbine noise calculated as mean exposure during the preceding year.

Wind turbine characteristics at of the study population dwellings at start of follow-up	Indoor LF wind turbine noise			
	<5 dB(A) MI/stroke (N = 688,489/689,608)	5–10 dB(A) MI/stroke (N = 18,465/18,497)	10–15 dB(A) MI/stroke (N = 3,996/3,997)	≥15 dB(A) MI/stroke (N = 299/299)
Outdoor wind turbine noise (1-year mean)				
<24 dB(A)	85/85%	0/0%	0/0%	0/0%
24–30 dB(A)	12/12%	35/35%	1/1%	0/0%
30–36 dB(A)	3/3%	48/48%	48/48%	2/2%
36–42 dB(A)	0/0%	15/15%	39/39%	53/53%
≥42 dB(A)	0/0%	2/2%	13/13%	45/45%
Distance to nearest wind turbine				
<500 m	5/5%	30/30%	63/63%	91/91%
500–2,000 m	42/42%	68/68%	35/35%	7/7%
≥2,000 m	54/54%	2/2%	2/2%	2/2%
Total height, nearest wind turbine				
<35 m	38/38%	11/11%	11/11%	24/25%
35–70 m	44/44%	59/59%	54/54%	56/56%
70–100 m	10/10%	26/26%	31/31%	18/17%
≥100 m	1/1%	4/4%	4/4%	2/2%

Note: LF, low frequency.

Table 4. Associations between mean 1- and 5-year exposure to residential A-weighted outdoor wind turbine noise and risk of myocardial infarction and stroke.

Outdoor wind turbine noise	Myocardial infarction				Stroke			
	Person-years	N cases	Crude IRR (95% CI)[a]	Adjusted IRR (95% CI)[b]	Person-years	N cases	Crude IRR (95% CI)[a]	Adjusted IRR (95% CI)[b]
1-year mean exposure								
<24 dB(A)	5,543,711	13,916	1 (ref)	1 (ref)	5,562,511	13,136	1 (ref)	1 (ref)
24–30 dB(A)	1,313,384	3,756	1.10 (1.06-1.14)	1.09 (1.05-1.13)	1,318,515	3,596	1.06 (1.02-1.10)	1.08 (1.04-1.12)
30–36 dB(A)	467,029	1,200	1.05 (0.99-1.11)	1.08 (1.02-1.15)	468,658	1,136	1.03 (0.97-1.10)	1.10 (1.03-1.17)
36–42 dB(A)	96,282	228	0.99 (0.87-1.13)	1.07 (0.94-1.22)	96,736	175	0.84 (0.72-0.97)	0.92 (0.80-1.07)
≥42 dB(A)	19,685	45	1.09 (0.81-1.46)	1.21 (0.90-1.63)	19,819	21	0.62 (0.41-0.95)	0.71 (0.46-1.08)
5-year mean exposure								
<24 dB(A)	5,644,428	14,151	1 (ref)	1 (ref)	5,664,088	13,205	1 (ref)	1 (ref)
24–30 dB(A)	1,265,628	3,616	1.09 (1.05-1.13)	1.08 (1.04-1.12)	1,270,239	3,566	1.07 (1.03-1.11)	1.09 (1.05-1.13)
30–36 dB(A)	425,855	1,119	1.04 (0.97-1.10)	1.07 (1.00-1.12)	427,200	1,095	1.04 (0.98-1.11)	1.10 (1.03-1.17)
36–42 dB(A)	85,193	212	0.99 (0.87-1.14)	1.06 (0.93-1.22)	85,595	175	0.87 (0.75-1.01)	0.95 (0.82-1.11)
≥42 dB(A)	18,986	47	1.10 (0.82-1.46)	1.21 (0.91-1.62)	19,117	23	0.62 (0.41-0.94)	0.69 (0.46-1.05)

Note: CI, confidence interval; IRR, incidence rate ratio.
[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 500-m radius, and distance to major road.

reference level than were people exposed to lower levels of outdoor WTN, and a similar pattern was observed for indoor LF WTN (Tables 2 and 3). Among dwellings exposed to ≥36 dB(A) outdoor WTN or ≥10 dB(A) indoor LF WTN, the vast majority were located <500 m from a WT. With regard to height of the nearest WT, 71% of the dwellings with ≥42 dB(A) were located near low WTs (35 m) in comparison with percentages between 19 and 41 for the lower exposure groups, whereas for indoor LF WTN, height of nearest WT distributed more evenly across the exposure groups.

Exposure to 1- or 5-y mean outdoor WTN above the reference level (<24 dB(A)) was positively associated with point estimates for MI in all exposure groups in the adjusted analyses; however, IRRs did not increase monotonically with increasing exposures (Table 4). Associations were significant for the 24–30 dB(A) and 30–36 dB(A) exposure groups (e.g., for 5-y exposure with IRRs of 1.08; 95% CI: 1.04, 1.12; 3,616 MI events and 1.07; 95% CI: 1.00, 1.12; 1,119 MI events, respectively) and similar but not significant for the 36–42 dB(A) group (IRR = 1.06; 95% CI: 0.93, 1.22; 212 MI events), whereas the IRR for the highest exposure group (≥42 dB(A)) was 1.21 (95% CI: 0.91, 1.62) based on 47 MI events.

For indoor LF WTN, we found no associations between 1-y mean exposure and risk of MI. For the 5-y exposure time window, we observed IRRs of 1.02 (95% CI: 0.95, 1.11), 1.08 (95% CI: 0.91, 1.28) and 1.29 (95% CI: 0.73, 2.28) for people exposed

to 5–10 dB(A), 10–15 and ≥15 dB(A), respectively in comparison with exposure levels <5 dB(A) (Table 5). Only 12 persons with MI were exposed ≥15 dB(A). In all analyses, IRRs increased with adjustment for potential confounders (i.e., closer to or past the null for crude IRRs <1.0, further from the null for crude IRRs >1.0).

IRRs for stroke did not show consistent patterns of associations with 1- and 5-y outdoor WTN or indoor LF WTN (Tables 4 and 5). IRRs for 5-y outdoor WTN relative to the <24 dB(A) reference group were 1.09 (95% CI: 1.05, 1.13; 3,566 stroke events), 1.10 (95% CI: 1.03, 1.17; 1,095 stroke events), 0.95 (95% CI: 0.82, 1.11; 175 stroke events), and 0.69 (95% CI: 0.46, 1.05; 23 stroke events) for the 24–30, >30 − 36, >36 − 42, and ≥42 dB(A) exposure groups, respectively (Table 4). For indoor LF WTN, all IRRs were null or inverse and nonsignificant (Table 5). As for MI analyses, adjustment for potential confounders resulted in slightly higher IRRs. IRRs for ischemic stroke were similar, with adjusted IRRs of 0.78 (95% CI: 0.42, 1.45; 10 stroke events) for ≥42 vs. <24 dB(A) 5-y outdoor WTN, and 0.94 (95% CI: 0.35, 2.52; 4 stroke events) for ≥15 vs. <5 dB(A) indoor 5-y LF WTN (Table S2).

In general, patterns of associations between 5-y exposures and MI were similar to estimates from the main models when restricted to population or outcome subgroups, albeit often based on reduced populations of small size (Table 6 and 7). For situations with high validity of the noise estimate, the IRR for MI

Table 5. Associations between mean 1- and 5-year exposure to residential A-weighted indoor low frequency wind turbine noise and risk of myocardial infarction and stroke.

Indoor low frequency wind turbine noise	Myocardial infarction				Stroke			
	Person-years	N cases	Crude IRR (95% CI)[a]	Adjusted IRR (95% CI)[b]	Person-years	N cases	Crude IRR (95% CI)[a]	Adjusted IRR (95% CI)[b]
1-year mean exposure								
<5 dB(A)	7,031,863	18,189	1 (ref)	1 (ref)	7,056,494	17,157	1 (ref)	1 (ref)
5–10 dB(A)	329,970	780	0.97 (0.91-1.05)	1.04 (0.96-1.12)	331,166	749	0.94 (0.87-1.01)	1.02 (0.95-1.10)
10–15 dB(A)]	72,551	165	0.97 (0.83-1.13)	1.09 (0.93-1.27)	72,847	148	0.88 (0.75-1.04)	1.00 (0.85-1.18)
≥15 dB(A)	5,706	11	0.80 (0.44-1.44)	0.92 (0.51-1.67)	5,732	10	0.76 (0.41-1.40)	0.89 (0.48-1.65)
5-year mean exposure								
<5 dB(A)	7,097,455	18,319	1 (ref)	1 (ref)	7,122,406	17,288	1 (ref)	1 (ref)
5–10 dB(A)	283,001	681	0.96 (0.89-1.04)	1.02 (0.95-1.11)	283,933	656	0.92 (0.85-1.00)	0.99 (0.92-1.07)
10–15 dB(A)]	55,408	133	0.97 (0.82-1.15)	1.08 (0.91-1.28)	55,660	111	0.81 (0.67-0.97)	0.91 (0.75-1.10)
≥15 dB(A)	4,226	12	1.11 (0.63-1.96)	1.29 (0.73-2.28)	4,239	9	0.87 (0.45-1.67)	1.02 (0.53-1.96)

Note: CI, confidence interval; IRR, incidence rate ratio.
[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 500-m radius and distance to major road.

Table 6. Associations between 5-year exposure to outdoor wind turbine noise and risk of myocardial infarction in different subpopulations.

Sub-populations	Exposure categories	Outdoor wind turbine noise		
		Person-years	N cases	Adjusted IRR (95% CI)[a]
All[b]				
	<24 dB(A)	5,644,428	14,151	1 (ref)
	24–30 dB(A)	1,265,628	3,616	1.08 (1.04-1.12)
	30–36 dB(A)	425,855	1,119	1.07 (1.00-1.12)
	36–42 dB(A)	85,193	212	1.06 (0.93-1.22)
	≥42 dB(A)	18,986	47	1.21 (0.91-1.62)
Diagnosis of MI after 2000				
	<24 dB(A)	3,288,875	8,590	1 (ref)
	24–30 dB(A)	948,866	2,643	1.04 (0.99-1.08)
	30–36 dB(A)	312,238	814	1.04 (0.97-1.12)
	36–42 dB(A)	55,170	131	1.00 (0.84-1.19)
	≥42 dB(A)	9,074	27	1.36 (0.93-1.98)
Living on a farm				
	<24 dB(A)	726,414	1,408	1 (ref)
	24–30 dB(A)	250,387	504	0.98 (0.88-1.08)
	30–36 dB(A)	129,503	277	1.04 (0.91-1.18)
	36–42 dB(A)	37,124	80	1.07 (0.86-1.35)
	≥42 dB(A)	7,345	15	1.13 (0.68-1.87)
Total height of nearest wind turbine ≥35 m				
	<24 dB(A)	3,922,187	10,116	1 (ref)
	24–30 dB(A)	1,042,138	2,999	1.08 (1.03-1.12)
	30–36 dB(A)	339,990	893	1.07 (1.00-1.15)
	36–42 dB(A)	58,893	147	1.06 (0.90-1.25)
	≥42 dB(A)	7,175	26	1.54 (1.04-2.26)
High validity score of noise estimate[c]				
	<24 dB(A)	4,349,483	10,161	1 (ref)
	24–30 dB(A)	780,854	2,220	1.16 (1.11-1.22)
	30–36 dB(A)	256,089	654	1.11 (1.03-1.21)
	36–42 dB(A)	39,720	102	1.19 (0.98-1.45)
	≥42 dB(A)	3,164	9	1.43 (0.74-2.75)
Dwelling ≥2,000 m from major road[d]				
	<24 dB(A)	1,977,176	5,128	1 (ref)
	24–30 dB(A)	609,642	1,825	1.12 (1.06-1.18)
	30–36 dB(A)	235,000	629	1.07 (0.98-1.16)
	36–42 dB(A)	48,496	115	1.01 (0.84-1.22)
	≥42 dB(A)	10,943	30	1.28 (0.89-1.84)
Less than 5 % tree coverage[e]				
	<24 dB(A)	670,421	1,571	1 (ref)
	24–30 dB(A)	222,014	613	1.12 (1.02-1.22)
	30–36 dB(A)	98,341	254	1.12 (0.98-1.27)
	36–42 dB(A)	24,062	64	1.25 (0.98-1.61)
	≥42 dB(A)	5,202	9	0.92 (0.48-1.78)

Note: CI, confidence interval; IRR, incidence rate ratio.
[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 500-m radius and distance to major road.
[b]Corresponding to IRRs and CIs in Table 4.
[c]Includes only study participants with validity score better than the median among those with exposures ≥30 dB(A) outdoor wind turbine noise. 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 ≥5,000 vehicles per day.
[e]In a 500-m radius around the dwelling.

among people with outdoor WTN ≥42 dB(A) was 1.43 (95% CI: 0.74, 2.75; 9 MI events) and for indoor LF WTN ≥15 dB(A) the corresponding IRR was 1.55 (95% CI: 0.64, 3.72; 5 MI events). When restricted to subjects living in inclusion dwellings where the height of the closest WT was ≥35 m, the IRR for outdoor WTN ≥42 dB(A) was increased relative to the main model (IRR = 1.54; 95% CI: 1.04, 2.26; 26 MI events), whereas the IRR for indoor LF WTN ≥15 dB(A) was similar to the main model (IRR = 1.36; 95% CI: 0.75, 2.45; 11 MI events). Conversely, when we restricted to people living in dwellings with less than 5% tree coverage within a 500-m radius of their dwelling, indoor LF WTN ≥15 dB(A) was associated with an IRR for MI of 2.43 (95% CI: 1.26, 4.67; 9 MI events), whereas the corresponding IRR for outdoor WTN ≥42 dB(A) was 0.92 (95% CI: 0.48, 1.78; 9 MI events).

For stroke, we observed patterns of associations between 5-y exposures of outdoor or indoor LF WTN and risk for stroke to be similar in comparison with estimates from the main models when restricted to population or outcome subgroups (Tables S3 and S4). In analyses restricted to people with high validity score of the exposure estimate, IRRs could not be shown for the highest exposure group for both exposures as the categories contained three stroke events or less, which cannot be presented due to Danish anonymity legislation.

We found no significant effect modification by sex (all $p > 0.07$) or age (all $p > 0.22$) for neither indoor nor outdoor noise in relation to MI or stroke (Tables S4 and S5).

Discussion

For both long-term nighttime outdoor WTN above 42 dB(A) and indoor LF WTN above 15 dB(A), we found slightly elevated relative risk estimates for MI in comparison with exposures below 24 dB(A) and 5 dB(A), respectively, but the number of cases

Table 7. Associations between 5-year exposure to indoor low frequency wind turbine noise and risk of myocardial infarction in different subpopulations.

Subpopulations	Exposure categories	Person-years	N cases	Adjusted IRR (95% CI)[a]
		Indoor low frequency wind turbine noise		
All[b]				
	<5 dB(A)	7,097,455	18,319	1 (ref)
	5–10 dB(A)	283,001	681	1.02 (0.95-1.11)
	10–15 dB(A)	55,408	133	1.08 (0.91-1.28)
	≥15 dB(A)	4,226	12	1.29 (0.73-2.28)
Diagnosis of MI after 2000				
	<5 dB(A)	4,312,355	11,496	1 (ref)
	5–10 dB(A)	249,411	584	1.00 (0.92-1.08)
	10–15 dB(A)	49,101	115	1.06 (0.88-1.27)
	≥15 dB(A)	3,358	10	1.33 (0.71-2.47)
Living on a farm				
	<5 dB(A)	1,017,885	2,025	1 (ref)
	5–10 dB(A)	103,730	205	0.97 (0.84-1.13)
	10–15 dB(A)	26,980	47	0.90 (0.68-1.21)
	≥15 dB(A)	2,177	7	1.62 (0.77-3.40)
Total height of nearest wind turbine ≥35 m				
	<5 dB(A)	5,063,410	13,427	1 (ref)
	5–10 dB(A)	254,128	624	1.04 (0.95-1.12)
	10–15 dB(A)	49,379	119	1.07 (0.89-1.28)
	≥15 dB(A)	3,465	11	1.36 (0.75-2.45)
High validity score of noise estimate[c]				
	<5 dB(A)	4,122,053	9,636	1 (ref)
	5–10 dB(A)	124,062	305	1.16 (1.04-1.31)
	10–15 dB(A)	25,344	59	1.12 (0.86-1.44)
	≥15 dB(A)	1,547	5	1.55 (0.64-3.72)
Dwelling ≥2,000 m from major road[d]				
	<5 dB(A)	2,684,822	7,269	1 (ref)
	5–10 dB(A)	158,807	364	0.97 (0.88-1.08)
	10–15 dB(A)	34,642	85	1.11 (0.89-1.37)
	≥15 dB(A)	2,985	9	1.33 (0.69-2.56)
Less than 5 % tree coverage[e]				
	<5 dB(A)	933,801	2,304	1 (ref)
	5–10 dB(A)	67,112	159	1.08 (0.92-1.27)
	10–15 dB(A)	17,311	39	1.05 (0.76-1.44)
	≥15 dB(A)	1,816	9	2.43 (1.26-4.67)

Note: CI, confidence interval; IRR, incidence rate ratio.
[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 500-m radius, and distance to major road.
[b]Corresponding to IRRs and CIs in Table 5.
[c]Includes only study participants with validity score better than the median among those with exposures ≥10 dB(A) LF indoor wind turbine noise. 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 ≥5,000 vehicles per day.
[e]In a 500-m radius around the dwelling.

were low in the highest exposure groups, and the associations were not statistically significant. There was no monotonic exposure–response relationship between WTN and MI, especially for outdoor WTN, where we found slightly increased relative risks of similar size in the three intermediate exposure groups. The IRRs for MI in the highest exposure group for both indoor LF and outdoor WTN were unchanged or slightly higher across different subpopulations in comparison with the IRRs in the main analysis. For stroke, all levels of indoor LF WTN were associated with IRRs close to unity, whereas for outdoor WTN, we observed IRRs above unity in the intermediate exposure groups and below unity in the highest exposure groups.

A major strength of this study is the prospective nationwide design with information on potential socioeconomic and environmental confounders, the large number of incident cases identified through a high-quality nationwide register (Helweg-Larsen 2011; Lynge et al. 2011), and access to complete residential address history for the entire exposure and follow-up period. Also, we estimated long-term exposure to WTN using a state-of-the-art exposure model that used detailed WTN spectra for all WT types and allowed for time varying wind direction, wind speed, and climatic conditions. The later information was modeled hour by hour for each WT position, which allowed us to estimate noise levels specifically for nighttime, when people are most likely to be at home sleeping. Additionally, we estimated exposure to the potentially more biologically relevant indoor noise, accounting for different housing sound insulation properties, although we could only differentiate into few insulation categories, based on relatively crude information. Further strengths were estimation of WTN for all dwellings in Denmark that might experience WTN, the access to a number of individual and area-level socioeconomic variables, and that we accounted for living on a farm, which is conceivably associated with many differences in lifestyle and environment.

Due to the register-based nature of the study, we did not have access to detailed potential lifestyle confounders, such as dietary habits, obesity, and physical activity, which is a study weakness. It is, however, important to note that adjusting for lifestyle in studies of noise is not straightforward, as studies have indicated that traffic noise may be associated with factors such as obesity, physical activity, and smoking habits (Christensen et al. 2015; Eriksson et al. 2014; Foraster et al. 2016; Pyko et al. 2015; Roswall et al. 2017; Roswall et al. 2018), suggesting that these are intermediaries and not confounders on the pathway between noise and disease. Another limitation is the rather crude adjustment for local road traffic noise, using traffic load and distance to major road. However, residual confounding by traffic noise is

probably not a major issue in the present study, as adjusting for the traffic-related proxies resulted in only minor changes on the second decimal in estimates (data not shown), and we obtained similar estimates among people living far from major roads in comparison with the whole study population. Another limitation is potential bias from missing data.

The Nord2000 has been successfully validated for WTs (Sondergaard et al. 2009). Even so, there is inevitable exposure misclassification in the modeled noise-exposure metrics. This circumstance is unlikely to depend on the case status and will in most cases influence the estimates towards the null. Although not covering all aspects of uncertainty pertaining to the noise estimates, our validity score allowed us to look further into this uncertainty. Although based on small numbers, our finding of a higher IRR for MI for both outdoor and indoor LF WTN among people with a high validity score indicates that exposure misclassification may have affected the results. For stroke, the number of highly exposed cases was too small (<4), precluding meaningful interpretation. It was also a limitation that we could not model exposure from WTs before 1982. However, only 103 cohort members were recruited due to living within a 1000 m of one of the relatively small WT operating before 1982. Lastly, statistical power was impaired for the highest exposure groups by the small number of cases with high exposure to WTN.

The few previous studies that investigated associations between WTN and cardiovascular disease found no indications of an association (Michaud et al. 2016a; Michaud et al. 2016c; Pedersen 2011). However, these studies were all cross-sectional, they were based on much smaller study populations than the present study, they had more crude exposure models, and the diagnosis of cardiovascular disease was self-reported, which makes direct comparison with the present study difficult.

We found that long-term high exposure to WTN was associated with slightly elevated point estimates for MI, both for exposure to outdoor WTN and for exposure to the potentially more biologically relevant indoor WTN noise. This pattern persisted across a range of subpopulations, for whom we hypothesized that a potential association between exposure and outcome could be more pronounced, such as high validity of the noise estimate and living far from major roads. However, the numbers of MI cases in the highest exposure groups were small, and the CIs were wide. Furthermore, we did not observe any monotonic exposure–response trends. This observation was most evident for outdoor WTN, where small and almost identical increases in risk were found for the three intermediate exposure groups. Also, because the biological mechanisms behind an effect of noise on disease are believed similar for MI and stroke (Münzel et al. 2017b) and because traffic noise has been associated with both diseases (Hansell et al. 2013; Héritier et al. 2017; Sørensen et al. 2011; Vienneau et al. 2015), we expected similar results for MI and stroke in the present study. However, for outdoor WTN above 42 dB(A), the IRR was below unity for stroke. We are not aware of plausible biological mechanisms to explain a protective effect of WTN. Also, numbers of highly exposed stroke cases were small, the CI was wide, and the IRR was noninsignificant; furthermore, high exposure to the potentially more biologically relevant indoor WTN noise was not associated with a decreased risk for stroke. The discrepant results for MI and stroke among the highly exposed in the present study further underscores that the observed IRRs for MI and stroke should be interpreted with caution.

In conclusion, although we found the highest levels of WTN to be associated with the highest relative risk for incident MI, numbers of highly exposed cases were small, and the associations were nonsignificant. Inverse or null associations between high

exposures and stroke were also based on a small number of cases. Therefore, it is not possible to draw firm conclusions from our finding. Future studies should, if possible, include larger numbers of highly exposed individuals.

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