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Published in:
Environmental Health Perspectives

DOI:
10.1289/EHP9146

Publication date:
2021

Document Version
Publisher's PDF, also known as Version of record

Citation for published version (APA):
Thacher, J. D., Poulsen, A. H., Hvidtfeldt, U. A., Raaschou-Nielsen, O., Brandt, J., Geels, C., Khan, J., Münzel, T., & Sørensen, M. (2021). Long-term exposure to transportation noise and risk for type 2 diabetes in a nationwide cohort study from denmark. *Environmental Health Perspectives*, *129*(12), Article 127003. https://doi.org/10.1289/EHP9146

A Section 508–conformant HTML version of this article is available at https://doi.org/10.1289/EHP9146.

Long-Term Exposure to Transportation Noise and Risk for Type 2 Diabetes in a Nationwide Cohort Study from Denmark

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Background: Epidemiologic studies have linked transportation noise to increased morbidity and mortality, particularly for cardiovascular outcomes. However, studies investigating metabolic outcomes such as diabetes are limited and have focused only on noise exposures estimated for the loudest residential façade.

Objectives: We aimed to examine the influence of long-term residential exposure to transportation noise at the loudest and quietest residential façades and the risk for type 2 diabetes.

Methods: Road traffic and railway noise exposures (Lden) at the most and least exposed façades were estimated for all dwellings in Denmark during 1990–2017. Aircraft noise was estimated in 5-dB categories. Ten-year time-weighted mean noise exposures were estimated for 3.56 million individuals ≥35 years of age. From 2000 to 2017, 233,912 incident cases of type 2 diabetes were identified using hospital and prescription registries, with a mean follow-up of 12.9 y. We used Cox proportional hazards models adjusting for individual- and area-level covariates and long-term residential air pollution. The population-attributable fraction (PAF) was also computed.

Results: Hazard ratios (HRs) and 95% confidence intervals (CIs) for type 2 diabetes in association with 10-dB increases in 10-y mean road traffic noise at the most and least exposed façades, respectively, were 1.05 (95% CI: 1.04, 1.05) and 1.09 (95% CI: 1.08, 1.10). Following subsequent adjustment for fine particulate matter [particulate matter ≤2.5 μm in aerodynamic diameter] (10-y mean), the HRs (CIs) were 1.03 (95% CI: 1.03, 1.04) and 1.08 (95% CI: 1.07, 1.09), respectively. For railway noise, the HRs per 10-dB increase in 10-y mean exposure were 1.03 (95% CI: 1.02, 1.04) and 1.02 (95% CI: 1.01, 1.04) for the most and least exposed façades, respectively. Categorical models supported a linear exposure–outcome relationship for road traffic noise and, to a lesser extent, for railway noise. Aircraft noise >45 dB was associated with a 1–4% higher likelihood of type 2 diabetes compared with those who were unexposed. We found road traffic and railway noise associated with a PAF of 8.5% and 1.4%, respectively, of the diabetes cases.

Discussion: Long-term exposure to road, railway, and possibly aircraft traffic noise was associated with an increased risk of type 2 diabetes in a nationwide cohort of Danish adults. Our findings suggest that diabetes should be included when estimating the burden of disease due to transportation noise. https://doi.org/10.1289/EHP9146

Introduction

Over the past decade, a growing number of studies have linked exposure to transportation noise with increased morbidity and mortality, particularly cardiovascular health effects (Kempen et al. 2018; Münzel et al. 2020; Thacher et al. 2020a). In the European Union around a quarter of the population is exposed to noise levels exceeding the guideline value of 55 dB (WHO 2018). Transportation noise is considered to be a detrimental environmental exposure (Hänninen et al. 2014), and, according to the World Health Organization (WHO), 1–1.6 million healthy life-years are lost annually from traffic-related noise in Europe (WHO 2011).

Noise is believed to act through an indirect pathway, with cognitive perception of noise followed by arousal of the autonomic nervous system, which, via the hypothalamus–pituitary–adrenal and sympathetic–adrenal–medulla axes, stimulates the release of stress hormones (e.g., cortisol) (Babisch 2002; Münzel et al. 2018). In addition, nighttime noise exposure can affect sleep quality and duration (Basner and McGuire 2018). This, in turn, may lead to low-grade inflammation, reduce insulin sensitivity, and impair glucose regulation and lead to the dysregulation of appetite-regulating hormones, all of which are involved in the etiology of type 2 diabetes (Münzel et al. 2017). Furthermore, transportation noise has been linked with important risk factors for diabetes, such as obesity (Pyko et al. 2017) and physical inactivity (Roswall et al. 2017).

In the most recent WHO environmental noise guidelines, the WHO concluded that depending on the noise source, the evidence linking transportation noise with diabetes was of very low to moderate quality and that better quality evidence and refined exposure–outcome relationships were needed (Kempen et al. 2018). Several prospective studies of road traffic noise and diabetes were conducted after this review, including four that reported positive associations that persisted after adjustment for air pollution (Clark et al. 2017; Eze et al. 2017; Ohlwein et al. 2019; Shin et al. 2020) and one that found no association after adjustment for fine particulate matter [PM ≤2.5 μm in aerodynamic diameter ($PM_{2.5}$)] or NO_2 (Jørgensen et al. 2019). In addition, a recent meta-analysis of five studies reported a pooled relative risk (RR) of 1.11 [95% confidence interval (CI): 1.08, 1.15] for type 2 diabetes with a 10-dB increase in the estimated A-weighted sound pressure level due to road traffic noise during the day, evening, and night (L_{den}) (Vienneau et al. 2019a). Railway and aircraft noise have received less attention, but three studies of railway noise and diabetes reported no associations (Eze et al. 2017; Roswall et al. 2018; Sørensen et al. 2013). Of three studies on aircraft noise, one suggested a positive association (Eze et al. 2017), one found an association only among women (Eriksson et al. 2014), and the third was a small study that found no clear

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Supplemental Material is available online (https://doi.org/10.1289/EHP9146).

The authors declare they have no actual or potential competing financial interests.

Received 15 February 2021; Revised 1 November 2021; Accepted 4 November 2021; Published 2 December 2021.

evidence of an association (Dimakopoulou et al. 2017). Overall, the evidence linking noise and diabetes is still lacking, especially with regard to railway and aircraft noise.

Earlier studies have focused on noise exposure at the most exposed façade of individual residences, and, to date, no study has reported on the association between type 2 diabetes and transportation noise at the least exposed façade. Many dwellings have a quieter side, which is likely where bedrooms would be placed, and, given that the effects of transportation noise are believed to be partially mediated through sleep disturbance, noise during sleep may be more consequential than exposure during the day (Héritier et al. 2018; Münzel et al. 2017). Therefore, the investigation of transportation noise exposure at multiple façades in relation to type 2 diabetes is warranted.

We aimed to examine the association between long-term residential exposure to road traffic and railway noise at the most and least exposed façades and the risk for type 2 diabetes using a nationwide cohort from Denmark, with register-based information on address history, incident diabetes, and individual- and area-level socioeconomic confounders. We also aimed to estimate the number of type 2 diabetes cases attributable to road traffic and railway noise in Denmark.

Methods

Study Population

The present study was based on the total Danish population, which was identified and followed across health and administrative registers using personal identification numbers. All Danish residential addresses were identified using the Danish Building and Housing Register (Christensen 2011) and subsequently linked to the Danish Civil Registration System, which contains information on address history for all individuals residing in Denmark (Schmidt et al. 2014).

All persons residing in Denmark from 1 January 2000 until 31 December 2017 were identified. Individuals were enrolled into this study base on 1 January 2000 or at 35 years of age, whichever came last. Address history from the 10 y prior to enrollment until censoring was ascertained for all participants. We excluded any persons with an incomplete address history during the 10-y period prior to enrollment. This study was approved by local ethical committees, and the study was conducted according to the Helsinki Declaration.

Transportation Noise Assessment

We gathered information on all residential addresses in Denmark (address and geocode) from the Building and Housing Registry and then estimated transportation noise at the most and least exposed façades for each dwelling. Traffic noise levels at the most and least exposed façades were calculated as the equivalent continuous A–weighted sound pressure level (L_{Aeq}) at each address for the day (L_d; 0700–1900 hours), evening (L_e; 1900–2200 hours), and night (L_n; 2200–0700 hours) and was expressed as L_{den} (where den = day, evening, night).

Road traffic noise exposure at the most ($L_{den}max$) and least ($L_{den}min$) exposed façades were estimated for all residential addresses in Denmark for the years 1995, 2000, 2005, 2010, and 2015 and has been described in detail previously (Thacher et al. 2020b). Noise calculations were performed according to the Nordic prediction method for road traffic noise using SoundPLAN (version 8.0; SoundPLAN Nord ApS). Input variables for the noise model comprised three-dimensional building polygons (linked with the address and exact floor of each residence), road attributes—comprising annual mean daily traffic, traffic composition and speed, road type (motorways, rural highways, roads wider than 6 m, roads 3- to 6-m wide, and other roads), noise barriers, embankments, and terrain. Traffic information was collected from a national database (Jensen and Hillig 2019). Urban areas, roads, and bodies of water were assumed to be reflecting surfaces, and all other topography was assumed to be absorbent.

In 1997 and 2021, railway noise exposure at the most ($L_{den}max$) and least ($L_{den}min$) exposed façades was estimated using Nord2000 (Kragh 2001). Railway noise was estimated for all dwellings situated within 1,000 m of any Danish rail line, yielding railway noise estimates for around 710,000 addresses. Dwellings >1,000 m from a rail line were classified as having no railway noise exposure. Model input variables comprised yearly average daily train type, lengths, and speed gathered by the Danish railway traffic administration. Data on terrain was gathered from Geodanmark (2012) for 2012, and a digitalized ground model was produced and included in the model to account for the attenuation and impedance effects of terrain, berms, noise barriers, and buildings (Thacher et al. 2020b) Reflection loss for buildings was set to 1 dB, and the model accounted for up to two façade reflections.

Based on the five annual estimates for road and the two annual estimates for rail, we used linear interpolation to estimate noise at all Danish dwellings during each year from 1995 to 2017. Subsequently, we linked these estimates to person-specific address histories to calculate time-weighted 5- and 10-y running means for $L_{den}max$ and $L_{den}min$, accounting for exposure at all addresses during the study period (based on the exact date of each change in residential address). The time-weighted averages were calculated as arithmetic averages on the sound pressure scale followed by logarithmic transformation to the decibel scale. All values <35 dB were considered as a lower limit of ambient noise and were assigned the value of 35 dB. We did not evaluate L_n as a separate exposure because L_n levels at the most and least exposed façades were significantly correlated with the corresponding maximum and minimum exposure estimates based on L_{den} ($R_S = 0.99$ and 0.97, respectively).

Aircraft noise was calculated in 5-dB categories from noise maps generated by local authorities using the Danish Airport Noise Simulation Model and the Integrated Noise Model (Liasjø and Granøien 1993), and, for the Copenhagen airport, aircraft noise contour modeling following the European Civil Aviation Conference guidelines was used (European Civil Aviation Conference 1997). Aircraft noise was assessed for each airfield separately for various years and frequencies. For airfields with multiple yearly estimates, noise levels were extrapolated to the closest year, whereas for airfields with single estimates, noise levels were assigned throughout the follow-up period. For aircraft noise, all values <45 dB were set to 45 dB, given that the noise maps did not permit a lower cutoff. Those with aircraft noise levels ≤45 dB were assigned to the reference group. Aircraft noise was not modeled as a time-weighted average; therefore, exposure corresponded to the yearly exposure at the address at time of diagnosis.

Identification of Cases

Incident diabetes cases were identified by linking personal identification numbers to the National Patient Register, started in 1978 (Lynge et al. 2011), and the National Prescription Register, started in 1995 and which compiles data on all dispensed drugs in Denmark, classifying them according to the Anatomical Therapeutic Chemical classification system (ATC), as well as collecting data on date and number of defined daily doses (Kildemoes et al. 2011). Type 2 diabetes cases were defined as two interactions with the hospital or pharmacy relating to type 2 diabetes with *a*) an *International Classification of Disease, Eighth Revision* (ICD 8; WHO 1966) or an *International*

Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10; WHO 2016) type 2 diabetes diagnosis (ICD-8, code 250; ICD-10 code E11) and *b*) at least one dispensed prescription for low blood glucose-exclusive insulin or insulin analogs [ATC codes A10B (excluding saxenda—A10BJ02) or a combination of lixisenatide and insulin glargine, as well as liraglutide and insulin degludec (A10AE54 and A10AE56)]. Participants were classified as incident cases on the date of the second contact, thus providing higher sensitivity. Participants with type 1 diabetes [ICD-8 code 249 or ICD-10 code E10 or at least one dispensed prescription with insulin or insulin analogs (ATC codes A10A, excluding A10AE54 and A10AE56)] or type 2 diabetes before baseline were excluded. Participants classified as having incident type 1 diabetes after baseline were censored ($n = 10{,}524$).

Covariates

Covariates were selected *a priori* based on current literature (indicating an association with both exposure and outcome) and availability. From registries at Statistics Denmark, we gathered time-varying (yearly) individual-level information on the highest achieved education (mandatory, secondary or vocational, medium or long education), marital status (married/cohabitating, single), occupational status (unemployed, blue collar, low-level white collar, high-level white collar, and retired), disposable income (in quintiles), and country of origin [Danish and non-Danish (immigrant—western/nonwestern origin; descendant—western/nonwestern origin)]. In addition, we gathered data on four time-varying neighborhood-level (parish) sociodemographic characteristics comprising the proportion of inhabitants in each parish with: low income (lowest quartile of household disposable income), unemployment, manual labor, and only basic education (primary and lower secondary education). In 2017, Denmark had 2,160 parishes with a median number of 1,032 inhabitants and an average area of 16.2 km^2. Information on residence type (single family, semidetached, and multistory buildings) for each address was extracted from the Building and Housing Register and evaluated as an effect modifier.

Annual mean $PM_{2.5}$ and NO_2 concentrations were calculated for the years 2000, 2010, and 2015 using the Danish multiscale dispersion modeling system—the Danish Eulerian Hemispheric Model (DEHM)/Urban Background Model (UBM)/AirGIS modeling system—for all Danish addresses. Next, annual averages from yearly changes in urban background levels using DEHM/UBM were estimated for each person's residence/s for the years 1990–2017. Details of the DEHM/UBM/AirGIS modeling system have been described previously (Khan et al. 2019). Briefly, it is a high-resolution dispersion modeling system that integrates contributions from local, urban, and regional sources of $PM_{2.5}$ and NO_2 that are estimated using three models operating at different scales; the DEHM, the UBM, and the Operational Street Pollution Model (Ketzel et al. 2013). The DEHM/UBM/AirGIS modeling system has been validated and used in multiple studies [e.g., Ketzel et al. (2013) and Khan et al. (2019)].

Using Basemap02 (Aarhus University), we estimated the green space as area percentages of 36 land-use classes within 150- and 1,000-m radius buffers around all the included addresses (Levin et al. 2017). We assigned land with recreational areas, forest, and wet or dry open nature land as high-quality green space, and modeled the total percentage of high-quality green space in each buffer.

Statistical Methods

Cox proportional hazards models, with age as the underlying time scale, were used to estimate hazard ratios (HRs) per 10-dB increase in road traffic and railway noise at the most ($L_{den}max$) and least ($L_{den}min$) exposed façades, and HRs for aircraft noise exposures of 45–49, 50–54, 55–59, and ≥60 dB compared with ≤45-dB exposure. Aircraft noise was included as a categorical variable because this exposure was quantified only in 5-dB buffers. Follow-up began on the 1 January 2000 or at 35 years of age, whichever came last, and participants were censored on the date of type 1 or type 2 diabetes classification, death, emigration, missing address, or end of follow-up (31 December 2017), whichever came first. Exposures to road and railway noise and traffic-related air pollution were modeled as 5- and 10-y time-weighted means, taking into account all current and historical addresses in the respective periods.

The proportional hazards assumption was assessed on the basis of the correlation between the scaled Schoenfeld residuals and the rank order of event time. Deviation from the assumption ($p < 0.01$; Table S1) was identified for calendar-year, sex, civil status, income, and occupational status; therefore, all analyses were performed with these variables as strata.

HRs for the association between transportation noise and type 2 diabetes were calculated with increasing adjustment, beginning with adjustment for age, sex, and calendar-year (2-y categories) only (Model 1). Our primary model (Model 2) was mutually adjusted for all three transportation-related noise sources and was additionally adjusted for individual-level civil status, income, country of origin, occupational status (unemployed, blue collar, low-level white collar, high-level white collar, and retired), and green space (both 150- and 1,000-m buffers); and parish-level percentages (continuous) of residents with low income, only basic education, who were unemployed, and who performed manual labor. Models of railway noise as a continuous variable also included a time-varying indicator term for any exposure (vs. none) to account for participants who did not live within 1,000 m of a rail line (during each corresponding time window). Models 1 and 2 were conducted as complete case analyses with the same population number in all analyses.

We also modeled 10-y mean $L_{den}max$ and $L_{den}min$ exposures as categorical variables, with adjustment for Model 2 covariates. For road traffic noise, we estimated HRs for categorical exposures representing 3-dB exposure increments (corresponding to a doubling of acoustical energy) relative to reference categories of 35–<45 dB for road $L_{den}max$ and 35–<40 dB for road $L_{den}min$, consistent with previous studies (Sørensen et al. 2021b; Thacher et al. 2021). For railway noise, we estimated HRs for 3-dB exposure categories (ranging from 35–<38 to ≥70 dB for rail $L_{den}max$, and 35–<38 to ≥65 dB for rail $L_{den}min$) relative to no exposure (i.e., using participants who had no railway noise exposure during the 10-y period as the reference group). In addition, we calculated HRs according to exposure to none (reference), one, two, or three transportation noise sources (road, railway, and aircraft) ≥45, ≥50, and ≥55 dB $L_{den}max$ (three separate analyses).

In sensitivity analyses, we further adjusted Model 2 for time-dependent $PM_{2.5}$, using 5- or 10-y means, as for the primary noise variable (Model 3). In addition, we repeated Model 2 with mutual adjustment for $L_{den}min$ and $L_{den}max$, and additional adjustment for NO_2 (time-dependent, 10-y mean), NO_2 and $PM_{2.5}$, and highest attained education, respectively. All models were performed as complete case analyses. With the exception of models adjusted for highest attained education, which was not available for most people born before 1921 (7% missing), all analyses were based on the same study population.

Potential effect modification by sex, population density, highway noise as primary road traffic noise source (yes/no), building type (at time of diabetes classification), green space, individual

income, and $PM_{2.5}$ (above/below median over entire follow-up period) were assessed by introducing an interaction term into the model (Model 2, 10-y means) and tested by Wald's test to calculate a global *p*-value (across all strata). Addresses in close proximity to highways and corresponding road traffic noise levels ($L_{den}max$) from highway noise were identified by the Danish Road Directory (Danish Road Directory 2016). Persons were considered to have highway noise as their primary source of road traffic noise if the difference between our estimated 1-y mean road $L_{den}max$ was <5 dB higher than the Road Directory's estimated level. Thus, indicating that their primary road traffic noise exposure came from highways. Effect modification by building type and population density were investigated because we aimed to assess whether the potential masking of the association between transportation noise and diabetes by competing noise sources, such as noise from neighbors, restaurants, or bars, was higher among those living in multistory buildings and/or in high population density areas. Furthermore, noise exposures may be estimated with greater error for residents of multistory buildings and areas with high population density given that high buildings and narrow streets may increase the number of reflective surfaces (Thacher et al. 2020b) and our model only includes first and second order reflections. A $p_{interaction}$ of <0.05 was considered statistically significant.

To facilitate the interpretation of our findings, we estimated the population-attributable fraction (PAF) and population-attributable risk (PAR) using the noise exposure distributions and estimated Model 2 HRs for 10-y mean road traffic and railway $L_{den}max$ (for comparability with previous studies). Specifically, we estimated $PAF = [\Sigma(Pi \times RRi) - 1\}/\Sigma(Pi \times RRi)]$ where Pi = proportion of the population in exposure category i (using categories representing 3-dB increases in exposure), and RRi = HR for exposure category i compared with reference level (35–< 45 dB for road noise and those without exposure to railway noise, respectively). We estimated $PAR = PAR\%/100 \times Nd$, where $PAR\% = Pe/100 \times (RR - 1)/(Pe/100 \times (RR - 1) + 1) \times 100[\%]$, Pe = percentage of the population exposed (in the aforementioned $L_{den}max$ categories representing 3-dB increases in exposure) and Nd = the number of people diagnosed with type 2 diabetes in Denmark during 2017, among those ≥35 years of age ($n = 14{,}325$, from the National Board of Health) (WHO 2011). We used the statistical software R (version 4.0.4#; R Development Core Team) to evaluate proportional hazards, and SAS (version 9.4; SAS Institute Inc.) was used for all remaining statistical analyses.

Results

Of the study base comprising 4,033,990 persons ≥35 years of age, we excluded 103,206 with type 1 ($n = 17{,}663$) or type 2 (85,543) diabetes before baseline, 366,467 (9%) with incomplete address histories during the 10 y prior to baseline, and 326 individuals with missing covariate information, yielding a study population of 3,563,991 individuals with a mean follow-up of 12.9 y. In total, 233,912 incident cases of type 2 diabetes were identified. On average we identified 13,759 cases of type 2 diabetes per year (Figure S1).

Compared with participants exposed to a 10-y mean road $L_{den}max \leq 55$ dB at baseline, those with exposures >55 dB were slightly more likely to be male, be younger, live alone, have medium or high education, work in white collar occupations, have a lower proportion of high-quality green space close to home, live in multistory buildings, live in higher population densities, and be exposed to higher levels of NO_2 (Table 1). In general, road traffic and railway (>35 dB) $L_{den}max$ distributions were normally distributed, whereas $L_{den}min$ distributions were skewed to the right (Figure S2). Median noise levels (25th and 75th percentiles) at baseline were 56.9 (50.9 and 61.9) and 44.9 dB (40.9 and 49.3) for road traffic $L_{den}max$ and $L_{den}min$, respectively (Table S2). Corresponding median noise level estimates for railway noise (among the 33.6% of participants with any exposure) were 53.0 (46.9 and 57.9) and 45.8 dB (40.8 and 50.4) for $L_{den}max$ and $L_{den}min$, respectively. Median 10-y mean $PM_{2.5}$ and NO_2 levels at baseline were 15.1 and 16.7 $\mu g/m^3$, respectively. Road traffic noise and air pollution exposures were low to moderately correlated ($R_S = 0.12$ and 0.40 for $L_{den}max$ with $PM_{2.5}$ and NO_2,

Table 1. Baseline sociodemographic characteristics of the study population (Denmark 2000–2017, $N = 3{,}563{,}991$).

Baseline characteristics	Road traffic noise at most exposed façade[a] ≤55 dB ($n = 1{,}474{,}613$)	Road traffic noise at the most exposed façade[a] >55 dB ($n = 2{,}089{,}378$)
Individual level		
Men (%)	47.1	48.3
Age [y (mean ± SD)]	52.7 ± 14.8	48.8 ± 15.6
Civil status (%)		
Married or cohabiting	77.8	70.7
Widow(er) or divorced	13.6	14.5
Single	8.6	14.8
Individual income (%)		
Low (Q 1)	19.8	20.2
Medium (Q 2–4)	59.0	60.5
High (Q 5)	21.2	19.3
Country of origin (%)		
Danish	99.0	98.5
Non-Danish[b]	1.0	1.5
Occupational status (%)		
Unemployed	4.4	6.0
Blue collar	36.0	35.3
White collar	28.0	31.8
Retired	31.6	26.9
Highest attained education (%)		
Mandatory education	32.0	28.8
Secondary or vocational education	43.7	42.5
Medium or long education	17.1	21.7
Unknown	7.2	7.0
Building type (%)		
Single-family house	69.9	54.4
Semidetached house	14.6	11.7
Multistory building	15.3	33.6
Other	0.2	0.32
Population density [persons/km^2 (%)]		
≤100	27.5	25.2
101–2,000	59.7	47.5
2,001–5,000	10.2	15.2
≥5,000	2.6	12.1
Address level		
High-quality green space [radius (m) (mean ± SD)]		
150	8.3 ± 11.6	7.6 ± 11.3
1,000	15.8 ± 10.5	14.8 ± 10.2
Air pollution [$\mu g/m^3$ (10-y mean ± standard deviation)]		
$PM_{2.5}$	17.6 ± 1.8	17.8 ± 2.4
NO_2	18.5 ± 5.6	23.7 ± 9.1
Area level		
Area-level SES [% (mean ± SD)]		
Low income	4.2 ± 1.9	4.9 ± 2.4
Only basic education	12.7 ± 3.6	11.5 ± 3.9
Unemployed	1.5 ± 0.6	1.6 ± 0.6
Manual labor	15.7 ± 3.5	13.9 ± 4.0

Note: Data were complete for all variables except highest attained education due to exclusion of observations with incomplete data for other covariates (7% missing). NO_2, nitrogen dioxide; $PM_{2.5}$, fine particulate matter (PM ≤2.5 μm in aerodynamic diameter); Q, quintile; SD, standard deviation; SES, socioeconomic status.
[a]Based on 10-y mean exposure.
[b]Non-Danish consists of immigrants of western/non-western origin as well as descendants who were of western/non-western origin.

Table 2. Associations between residential exposure to road traffic, railway, and aircraft noise and risk for type 2 diabetes ($N = 3{,}563{,}991$).

		Type 2 diabetes		
Noise exposure	Cases (n)	Model 1[a] HR (95% CI)	Model 2[b] HR (95% CI)	Model 3[c] HR (95% CI)
Road traffic per 10 dB [years mean exposure ($L_{den}max$)]				
5	233,912	1.06 (1.06, 1.07)	1.04 (1.03, 1.04)	1.03 (1.02, 1.03)
10	233,912	1.07 (1.07, 1.08)	1.05 (1.04, 1.05)	1.03 (1.03, 1.04)
Road traffic per 10 dB [years mean exposure ($L_{den}min$)]				
5	233,912	1.08 (1.07, 1.08)	1.09 (1.08, 1.09)	1.07 (1.07, 1.08)
10	233,912	1.08 (1.08, 1.09)	1.09 (1.08, 1.10)	1.08 (1.07, 1.09)
Railway per 10 dB [years mean exposure ($L_{den}max$)]				
5	233,912	1.06 (1.05, 1.07)	1.03 (1.02, 1.04)	1.02 (1.01, 1.03)
10	233,912	1.06 (1.05, 1.07)	1.03 (1.02, 1.04)	1.02 (1.01, 1.03)
Railway per 10 dB [years mean exposure ($L_{den}min$)]				
5	233,912	1.09 (1.07, 1.11)	1.02 (1.00, 1.03)	1.01 (1.00, 1.03)
10	233,912	1.09 (1.07, 1.10)	1.02 (1.01, 1.04)	1.01 (1.00, 1.03)
Aircraft, categorical (dB)				
<45	223,539	Reference	Reference	Reference
45–49	4,948	1.01 (0.98, 1.03)	1.02 (1.00, 1.05)	1.03 (1.00, 1.06)
50–54	4,007	1.02 (0.99, 1.05)	1.04 (1.02, 1.07)	1.04 (1.01, 1.07)
55–59	1,113	1.01 (0.96, 1.08)	1.03 (0.97, 1.09)	1.03 (0.97, 1.10)
≥60	305	1.02 (0.91, 1.14)	1.03 (0.92, 1.15)	1.03 (0.92, 1.15)

Note: Covariate data were complete for all three of the models. CI, confidence interval; HR, hazard ratio; $L_{den}max$, noise at the most exposed façade; $L_{den}min$, noise at the least exposed façade; $PM_{2.5}$, fine particulate matter (PM ≤2.5 μm in aerodynamic diameter).
[a]Adjusted for age (by design), sex (male/female), and calendar-year (2-y periods).
[b]Model 1 plus adjustment for civil status [married/cohabitating, widow(er)/divorced, single], income (in quintiles), country of origin (Danish, non-Danish), occupational status (unemployed, blue collar, low-level white collar, high-level white collar, retired), green space (150- and 1,000-m buffers), area-level percentage (continuous) of population with low income, with only basic education, who are unemployed, and who performed manual labor, as well as mutual road traffic, railway, and aircraft noise adjustment (road and rail (continuous), indicator term for any railway noise exposure (yes/no), aircraft noise (<45, 45–49, 50–54, 55–59, and ≥60 dB).
[c]Model 2 plus adjustment for $PM_{2.5}$, 5- and 10-y means respectively.

respectively), and the correlation between $L_{den}max$ and $L_{den}min$ was $R_S = 0.45$ for road traffic noise and 0.90 for railway noise (Table S3). Correlations between high-quality green space and road traffic noise or railway noise were low ($R_S = -0.05$ to 0.08) (Table S4). For road and railway noise, correlations between 5- and 10-y mean exposure for $L_{den}max$, as well as for $L_{den}min$, were high ($R_S \geq 0.83$) (Table S4).

Road traffic $L_{den}max$ and $L_{den}min$ were associated with type 2 diabetes for both time windows of exposure (Table 2). Associations with a 10-dB increase in road traffic $L_{den}min$ tended to be stronger than corresponding associations with road traffic $L_{den}max$ [HR = 1.09 (95% CI: 1.08, 1.10) vs. 1.05 (95% CI: 1.04, 1.05), 10-y exposure] (Model 2). Associations were weaker after additional adjustment for $PM_{2.5}$ (Model 3) for both $L_{den}max$ [HR = 1.03 (95% CI: 1.03, 1.04), 10-y exposure] and $L_{den}min$ [HR = 1.08 (95% CI: 1.07, 1.09), 10-y exposure] (Table 2). The association between road traffic noise $L_{den}max$ and $L_{den}min$ with type 2 diabetes was generally consistent with a linear exposure–outcome relationship (Figure 1; Table S5).

A 10-dB increase in railway $L_{den}max$ and $L_{den}min$ was associated with type 2 diabetes, with Model 2 HRs of 1.03 (95% CI: 1.02, 1.04) and 1.02 (95% CI: 1.01, 1.04), respectively (Table 2). Attenuation in effect estimates for railway $L_{den}max$ [HR = 1.02 (95% CI: 1.01, 1.03)] and $L_{den}min$ [HR = 1.01 (95% CI: 1.00, 1.03)] were observed following adjustment for $PM_{2.5}$ (Model 3). Exposure–outcome curves for railway $L_{den}max$ and $L_{den}min$ (relative to no railway noise exposure as the reference category) both suggested nonlinear associations, with weaker associations for the highest exposure categories (although estimates are very imprecise) and a flat slope in the middle of each distribution (Figure 1; Table S6).

For aircraft noise, those exposed to ≥60 dB had an HR = 1.03 (95% CI: 0.92, 1.15) (Model 2) compared with those with no aircraft noise exposure, and similar HRs were observed for the other exposure categories (Table 2). Model 2 HRs were slightly stronger than Model 1 estimates, but further adjustment for $PM_{2.5}$ (Model 3) did not influence associations.

HRs increased in magnitude as the number of transportation noise sources with $L_{den}max \geq 50$ and 55 dB increased (Figure 2; Table S7). For example, compared with those without any noise sources with $L_{den}max \geq 50$ dB, HRs for exposures to one, two, and three noise sources ≥50 dB were 1.07 (95% CI: 1.06, 1.08), 1.13 (95% CI: 1.12, 1.15), and 1.20 (95% CI: 1.10, 1.30), respectively. The pattern was similar for $L_{den}max \geq 45$ dB, although the association was strongest for two noise sources above the threshold.

In the sensitivity analyses of association with road traffic noise (based on 10-y mean exposure) when we included $L_{den}max$ and $L_{den}min$ simultaneously in the model, the association with road traffic $L_{den}min$ was similar to the primary model, whereas estimates for $L_{den}max$ remained positive but closer to the null (Table S8). For road traffic noise, associations weakened after additional adjustment for NO_2 alone, and for NO_2 and $PM_{2.5}$ (e.g., for road $L_{den}max$, HRs went from 1.05 to 1.02). In contrast with findings for road traffic noise, mutual adjustment for railway $L_{den}max$ and $L_{den}min$ had no impact on the association with $L_{den}max$, whereas the association with $L_{den}min$ became null [HR = 1.00 (95% CI: 0.99, 1.02)]. Compared with our primary model, estimated associations with railway and aircraft noise were essentially unchanged after adjustment for NO_2 only and NO_2 plus $PM_{2.5}$. Relative to Model 2 estimates, HRs declined only slightly for road $L_{den}max$ and the two highest exposure

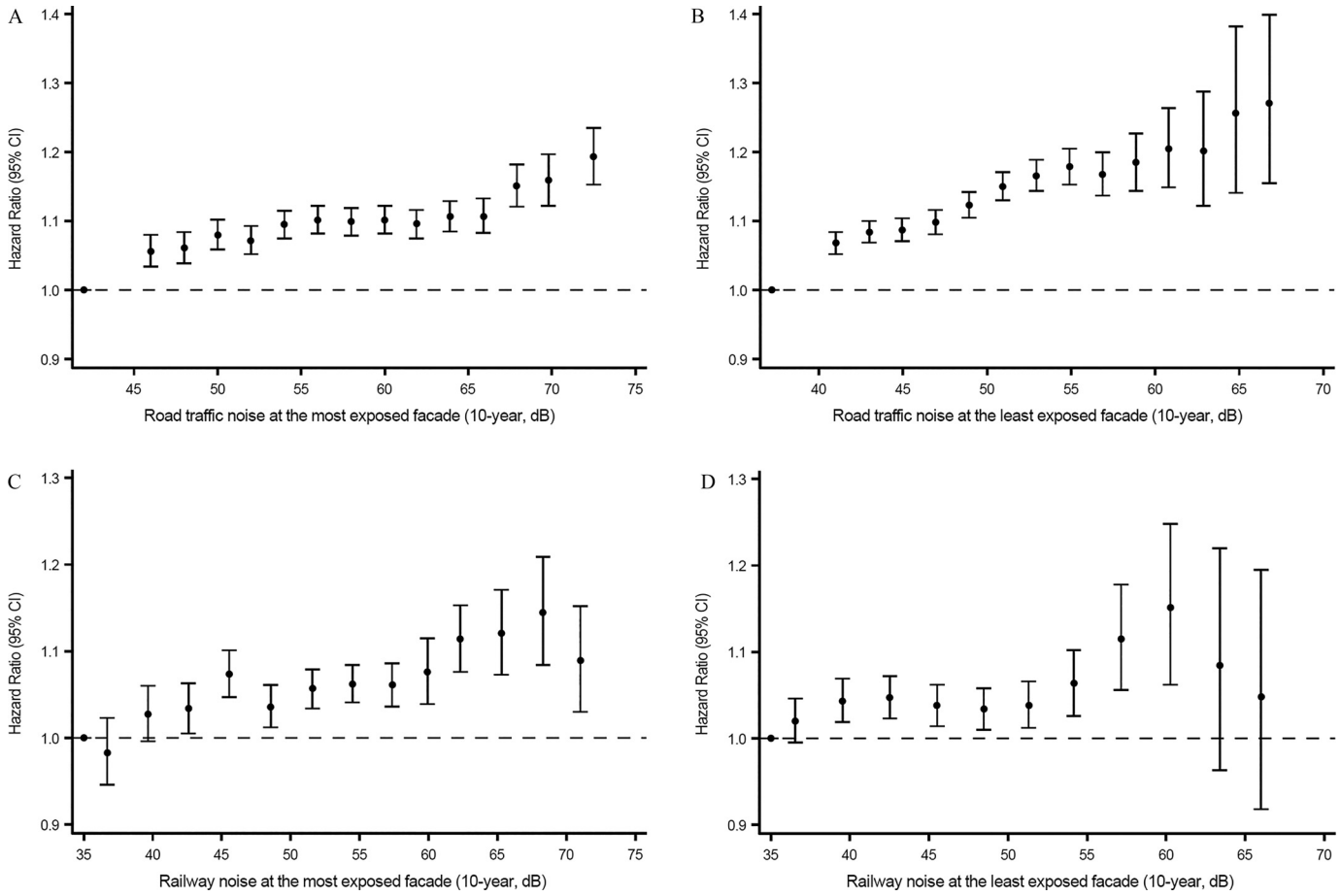

Figure 1. Hazard ratios (95% confidence intervals) for incident type 2 diabetes in association with 10-y mean residential exposures to (A) road traffic noise at the most exposed façade, (B) road traffic at the least exposed façade, (C) railway noise at the most exposed façade, and (D) railway noise at the least exposed façade relative to the reference category for each exposure ($N = 3{,}563{,}991$). All models were adjusted for individual-level age, sex, calendar-year (2-y periods), civil status [married/cohabitating, widow(er)/divorced, single], income (quintiles), country of origin (Danish, non-Danish), occupational group (unemployed, blue collar, low-level white collar, high-level white collar, retired), green space (in 150- and 1,000-m buffers), and aircraft noise (<45, 45–49, 50–54, 55–59, and ≥60 dB), and area-level percentage of population with low income, with only basic education, who are unemployed, and who performed manual labor. Models of road traffic noise were also adjusted for 10-y mean railway noise (continuous) and an indicator term for any railway noise (yes/no); models of railway noise were also adjusted for 10-y mean road traffic noise (continuous) and an indicator term for any railway noise (yes/no). See Tables S5 and S6 for corresponding numeric data and numbers of cases in each exposure category. Note: CI, confidence interval.

categories for aircraft noise after further adjustment for highest attained education, whereas associations with road $L_{den}min$, railway noise, and lower levels of aircraft noise exposure were unchanged (Table S8).

In subgroup analyses, the association between a 10-dB increase in 10-y road traffic $L_{den}max$ and type 2 diabetes was stronger among people living in areas with lower vs. higher population density [e.g., HR = 1.05 (95% CI: 1.04, 1.06) and 1.02 (95% CI: 1.00, 1.05) for ≤100 and ≥5,000 persons/km^2, respectively, $p_{interaction} = 0.06$], and among those with highways as their primary source of road traffic noise exposure [HR = 1.10 (95% CI: 1.07, 1.13) vs. 1.04 (95% CI: 1.04, 1.05), $p_{interaction} < 0.01$], for those living in single-family homes compared with semidetached homes and multistory buildings [HR = 1.05 (95% CI: 1.05, 1.06) vs. 1.01 (95% CI: 0.99, 1.02) and 0.99 (95% CI: 0.98, 1.00), respectively, $p_{interaction} < 0.01$], and those exposed to higher levels of $PM_{2.5}$ [HR = 1.05 (95% CI: 1.04, 1.06) and 1.03 (95% CI: 1.02, 1.04) for 10-y mean $PM_{2.5}$ ≥15.1 vs. <15.1 μg/m^3, respectively, $p_{interaction} < 0.01$] (Figure 3; Table S9). For road traffic $L_{den}min$, similar tendencies were observed for population density, house type, and $PM_{2.5}$. Associations with road $L_{den}max$ and $L_{den}min$ differed by sex, but in opposite directions, with stronger associations among females for $L_{den}max$ [HR = 1.06 (95% CI: 1.05, 1.06) vs. 1.04 (95% CI: 1.03, 1.04), $p_{interaction} < 0.01$], and stronger associations among males for $L_{den}min$ [HR = 1.10 (95% CI: 1.09, 1.11) vs. 1.08 (95% CI: 1.07, 1.09), $p_{interaction} = 0.01$] (Table S9). For both $L_{den}min$ and $L_{den}min$, no clear associations were observed for income or green space.

For railway $L_{den}max$ and $L_{den}min$, associations were stronger among those with higher income quintiles compared with the lowest income quintile, particularly for railway $L_{den}min$ [HR = 1.10 (95% CI: 1.05, 1.15) vs. 0.99 (95% CI: 0.96, 1.01), $p_{interaction} < 0.01$] (Table S10). Sex, population density, building type, and greenspace did not interact with railway $L_{den}max$ or $L_{den}min$ ($p_{interaction} > 0.05$).

Assuming that our estimates of exposure and Model 2 associations with 10-y mean road $L_{den}max$ were accurate and unbiased, we estimated that 8.5% of type 2 diabetes cases were attributable to road traffic noise and 1.4% were attributable to railway noise. Thus resulting in 1,211 and 207 incident cases of type 2 diabetes, respectively, in Denmark in 2017.

Discussion

This nationwide cohort study adds to the growing body of literature linking transportation noise and type 2 diabetes and suggests

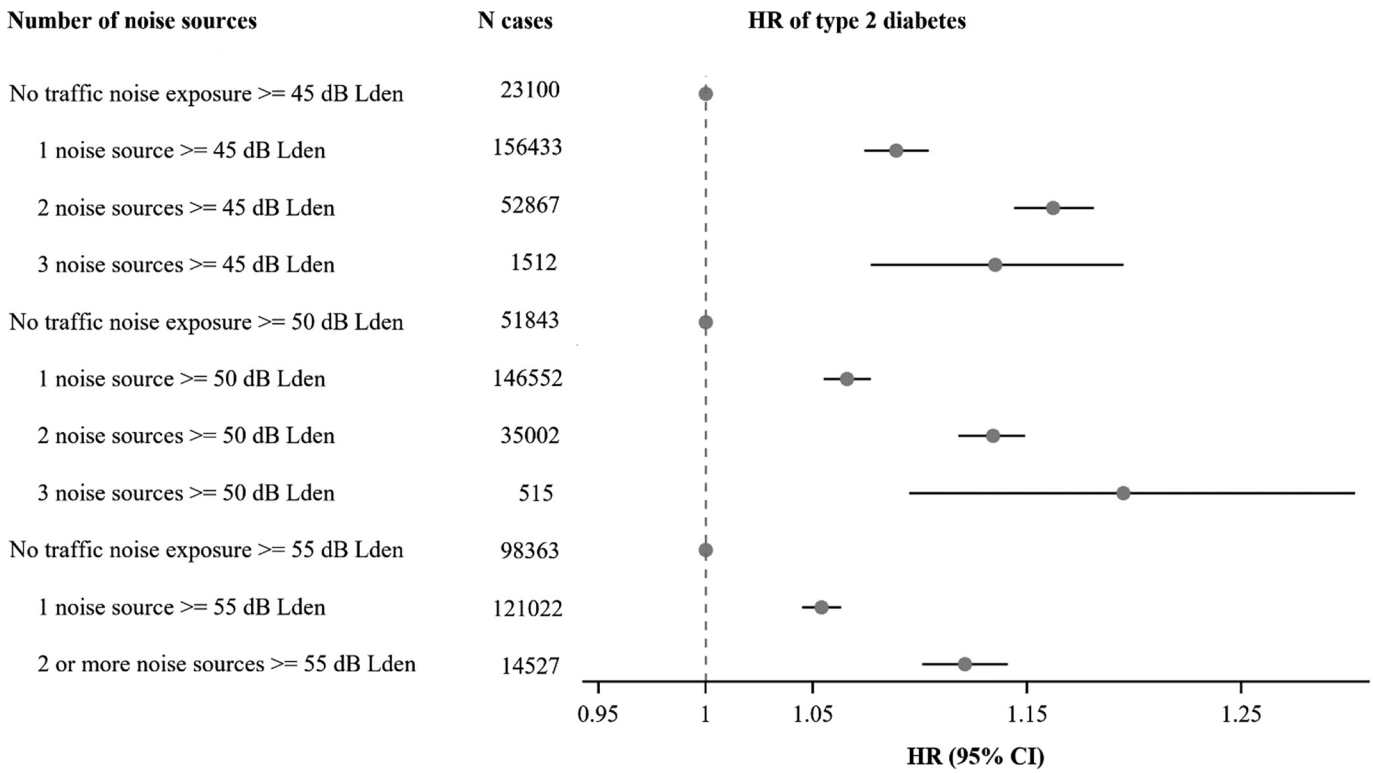

Figure 2. Hazard ratios (95% confidence intervals) for incident type 2 diabetes in association with the number of transportation noise sources with 10-y mean $L_{den}max \geq 45$, 50, or 55 dB, respectively, relative to the risk among participants with no individual source of transportation noise at or above the threshold ($N = 3{,}563{,}991$). All models were adjusted for individual-level age, sex, calendar-year (2-y periods), civil status [married/cohabitating, widow(er)/divorced, single], income (quintiles), country of origin (Danish, non-Danish), occupational group (unemployed, blue collar, low-level white collar, high-level white collar, retired), and green space (in 150- and 1,000-m buffers), and area-level percentage of population with low income, with only basic education, who are unemployed, and who performed manual labor. See Table S7 for corresponding numeric data and numbers of cases in each exposure category. Note: CI, confidence interval; HR, hazard ratio; L_{den}, noise levels during day, evening, and night; $L_{den}max$, noise at the most exposed façade.

that combined exposure from multiple noise sources may be particularly harmful. Road traffic and railway noise exposures (10-y mean) were associated with an increased risk of type 2 diabetes, with evidence of stronger associations as exposures increased, particularly for road traffic noise. Associations also remained positive after additional adjustment for $PM_{2.5}$ and NO_2 exposure, although, with the exception of associations with road traffic $L_{den}min$, HRs were closer to the null. Our results for aircraft noise suggest an association with type 2 diabetes among those exposed to aircraft noise >45 dB. Road traffic $L_{den}min$ was more strongly associated with type 2 diabetes than $L_{den}max$. Associations between road traffic noise and type 2 diabetes tended to be stronger among individuals living in areas with lower population densities, those living in single-family homes, and those with higher exposure to $PM_{2.5}$.

Previous studies investigating transportation noise and diabetes have concentrated on noise at the most exposed façade ($L_{den}max$). Our findings for road $L_{den}max$ are generally in agreement with these studies, most of which have also reported positive associations with diabetes (Clark et al. 2017; Dimakopoulou et al. 2017; Eze et al. 2017; Ohlwein et al. 2019; Roswall et al. 2018; Shin et al. 2020). However, a recent meta-analysis reported a pooled RR estimate of 1.11 (95% CI: 1.08, 1.15) per 10-dB increase in road traffic L_{den} at the most exposed façade (Vienneau et al. 2019a), which is stronger than our estimated HR of 1.05 (95% CI: 1.04, 1.05) for a 10-dB increase in 10-y mean road $L_{den}max$ (Model 2). Stronger estimates of association in previous studies may reflect selection bias in cohort studies based on active participation (Eze et al. 2017; Ohlwein et al. 2019; Roswall et al. 2018) or inadequate adjustment strategies in registry-based studies (Clark et al. 2017; Shin et al. 2020). All these studies were adjusted for air pollution, either for $PM_{2.5}$ (Clark et al. 2017; Ohlwein et al. 2019), NO_2 (Clark et al. 2017; Eze et al. 2017; Ohlwein et al. 2019; Shin et al. 2020), or nitrogen oxides (Roswall et al. 2018), and for all but one (Jørgensen et al. 2019) the effect estimates remained elevated after adjustment, strongly suggesting that transportation noise is a risk factor for type 2 diabetes, independent from air pollution. Our estimates were slightly attenuated after adjustment for $PM_{2.5}$ but remained positive. In addition, stratified analyses suggested that associations with road traffic noise were stronger among those with $PM_{2.5}$ exposures $\geq 15.1\ \mu g/m^3$.

Our study is novel in regard to assessing noise exposure at the least exposed façade, which we hypothesize to be a relevant exposure in relation to diabetes risk. Because people often choose to have their bedroom in the quietest room possible, presumably away from a noisy road, noise at this side may better describe exposure during sleep. Disturbance of sleep is a risk factor for diabetes through effects on glucose metabolism, insulin resistance, and appetite regulation (Basner and McGuire 2018). In agreement with this hypothesis, the association with type 2 diabetes was stronger for road traffic noise exposure at the quite side ($L_{den}min$). This suggests that $L_{den}min$ may provide a better measure of etiologically relevant exposure to noise at night than $L_{den}max$. If confirmed in future studies, this has public health implications because future preventive actions toward road traffic noise should focus on reducing noise in the bedroom.

Associations between type 2 diabetes and noise sources that are not strongly correlated with road traffic noise or air pollution would support noise as an important metabolic risk factor. We

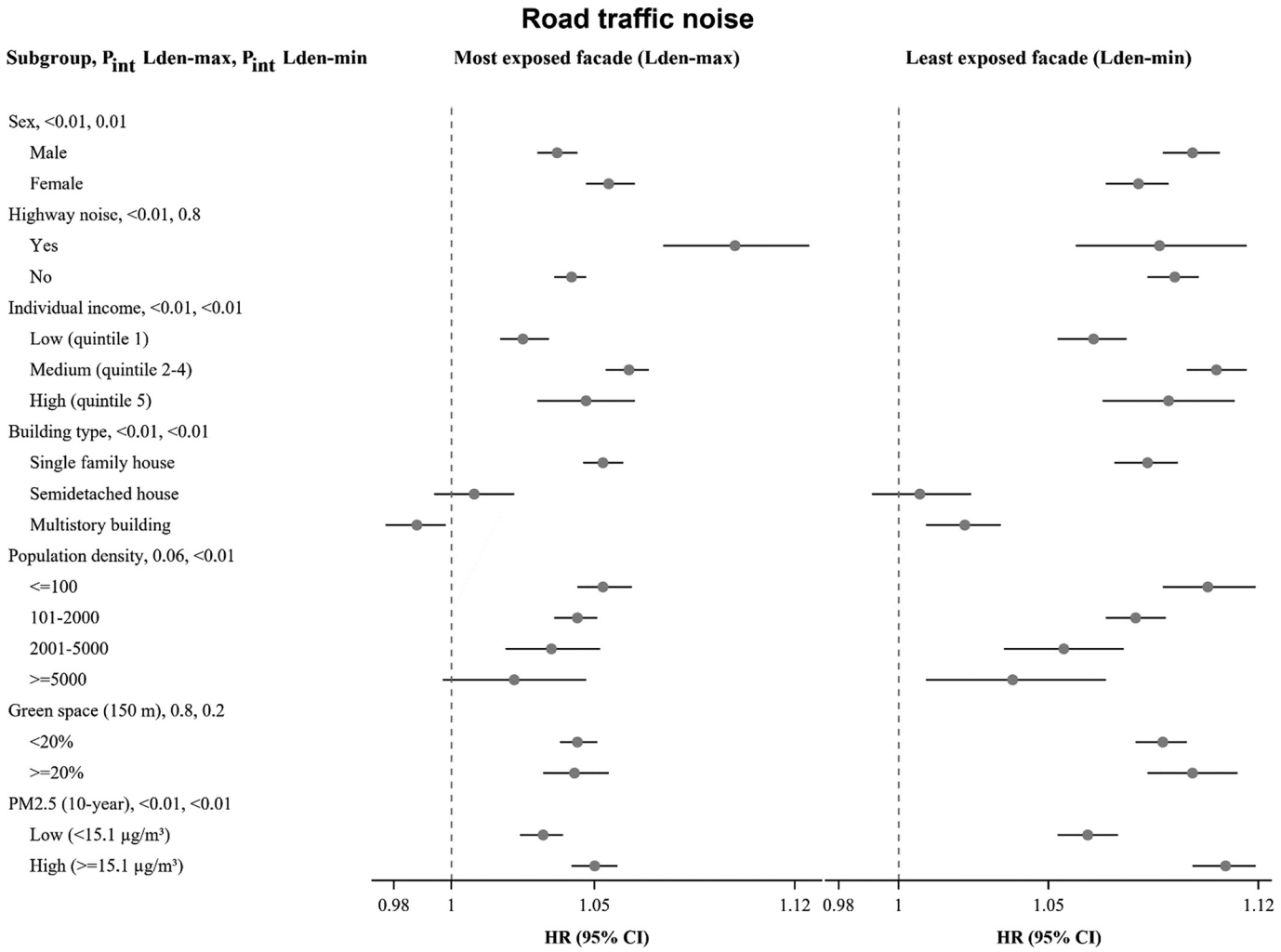

Figure 3. Hazard ratios (95% confidence intervals) for incident type 2 diabetes in association with 10-y mean road traffic noise (linear, per 10 dB) at the most and least exposed façades according to potential effect modifiers ($N = 3{,}563{,}991$). Highway noise was classified as "yes" if highways were the primary source of road traffic noise during the 10-y period. $PM_{2.5}$ exposures were categorized based on 10-y mean values. Values next to each modifier name are *p*-values for $L_{den}max$ and $L_{den}min$, respectively, based on Wald's tests for models with interaction terms. Excluding modifiers, as appropriate, all models were adjusted for individual-level age, sex, calendar-year (2-y periods), civil status [married/cohabitating, widow(er)/divorced, single], income (quintiles), country of origin (Danish, non-Danish), occupational group (unemployed, blue collar, low-level white collar, high-level white collar, retired), green space (in 150- and 1,000-m buffers), aircraft noise (<45, 45–49, 50–54, 55–59, and ≥60 dB), and area-level percentage of population with low income, with only basic education, who are unemployed, and who performed manual labor. Models of road traffic noise were also adjusted for 10-y mean railway noise (continuous) and an indicator term for any railway noise (yes/no). See Table S9 for corresponding numeric data and numbers of cases in each modifier subgroup. Note: CI, confidence interval; HR, hazard ratio; $L_{den}max$, noise at the most exposed façade; $L_{den}min$, noise at the least exposed façade; $PM_{2.5}$, fine particulate matter (PM ≤2.5 µm in aerodynamic diameter).

estimated a 2–3% increase in type 2 diabetes likelihood per 10-dB increase in railway noise, which was only weakly correlated with road traffic noise ($R_S = 0.17$ and 0.25 for 10-y road and rail $L_{den}max$ and $L_{den}min$, respectively). To our knowledge, only three studies have investigated the association between railway noise and diabetes, all reporting no association (Eze et al. 2017; Roswall et al. 2018; Sørensen et al. 2013). If railway noise has a weak effect on type 2 diabetes, it might be difficult to detect in smaller studies. Railway noise also may be perceived as less annoying compared with road traffic noise (Murphy and King 2014). In addition, in Denmark most trains are passenger trains and do not operate throughout the night. This could partly explain why we did not see major differences between railway $L_{den}max$ and $L_{den}min$ in relation to type 2 diabetes, in contrast with road traffic noise in the present study. In addition, we saw a positive association with aircraft noise, further supporting the association between noise and type 2 diabetes. To date, only three studies have reported on the association between aircraft noise and diabetes, with two suggesting positive associations (Eriksson et al. 2014; Eze et al. 2017) and the third reporting no association (Dimakopoulou et al. 2017).

In general, as the number of transportation noise sources with $L_{den}max$ above a given threshold increased, a stronger association with type 2 diabetes was also observed. This is in agreement with earlier studies of sleep effects and annoyance in association with concomitant exposure to various noise sources (Griefahn et al. 2006; Miedema 2004). Furthermore, our results are in line with the multiple environmental stressors theory, which states that multiple stressors potentially augment the effect of one another (Stansfeld and Matheson 2003). These results could suggest that exposure to more noise and/or an increasing number of noise sources may be particularly harmful.

Interestingly, we found weaker associations between road traffic noise and type 2 diabetes among individuals residing in multistory or semidetached buildings, as well as living in areas with high population densities. A potential explanation is that we

anticipated the highest degree of exposure misclassification among those living in multistory buildings and/or in areas with high population density because inner-city areas with smaller streets and high-rise structures may have higher estimation error due to multiple reflections, and our model only includes first and second order reflections (Thacher et al. 2020b). However, a Swiss study assessed the influence of misclassifying floor of a residence in relation to myocardial infarction mortality and concluded that no substantial difference was observed (Vienneau et al. 2019a). Similar to our findings, Vienneau et al. (2019b) also reported stronger associations between noise and myocardial infarction mortality among people living in areas with more single-family homes, which they suggested could be related to more accurate classification of noise in less urban areas. Furthermore, noise from competing noise sources, such as noise from restaurants, bars, or neighbors may result in a masking of the potential effect of road traffic noise on diabetes. Last, this leveling-off may be due to that residents who are more sensitive to noise may have moved away from highly exposed areas. We also found a stronger association between road $L_{den}max$ and type 2 diabetes among persons whose primary noise exposure came from highways, but not for $L_{den}min$. In a Danish report, highway noise was found to be two to three times more annoying compared with road traffic noise from other streets at similar noise levels (Danish Road Directory 2016). This suggests that for road $L_{den}max$, perceived noise annoyance may be on the pathway from noise exposure to outcome (Babisch et al. 2013).

The present study has several key strengths. We used the entire Danish population (≥35 years of age), which largely reduced the risk of selection bias and yielded a higher generalizability of our findings. The substantial sample size, coupled with lengthy follow-up time, provided high statistical power. Furthermore, the ability to identify historical addresses and exact floor of each residence allowed for the calculation of 10-y average noise exposure, as well as the use of complete residential historical data to estimate time-varying exposure that accounted for residential mobility, is a strength. The use of the high-quality national hospital and prescription registries (Pottegård et al. 2017; Schmidt et al. 2015) to identify incident type 2 diabetes cases is a strength, resulting in less outcome misclassification than studies using a single administrative registry to define diabetes (Clark et al. 2017; Shin et al. 2020). In addition, previous studies on transportation noise and diabetes have not differentiated between type 1 and type 2 diabetes, whereas in the present study we selected only type 2 diabetes cases. The validated and state-of-the-art modeling of transportation noise and air pollution at the exact individual address level (Khan et al. 2019; Ström 1997) are also important strengths, reducing the risk for exposure misclassification, compared with, for example, studies using postal codes as a proxy for individual address (Clark et al. 2017; Shin et al. 2020), which has been suggested to attenuate the magnitude of association (Vienneau et al. 2019b). Last, the inclusion of noise at the least exposed façade is a major strength.

Covariate data in the present study were based on administrative registries, and the lack of data on personal lifestyle factors—for example, body mass index (BMI), diet, physical activity, smoking, and alcohol use—is a limitation and could result in an overestimation. However, a recent study from Denmark showed that further adjustment for lifestyle factors had a very limited effect on risk estimates for air pollution and cardiometabolic disease that were already adjusted for various area- and individual-level covariates (Sørensen et al. 2021a). We did have information on individual- and area-level sociodemographic confounders, which could capture some aspects of lifestyle and behavioral habits; nevertheless, we cannot rule out residual confounding. However, given the consistent findings of transportation noise as a risk factor for overweight, adjusting for BMI could result in overadjustment (Eriksson et al. 2014; Foraster et al. 2018; Pyko et al. 2017). We could not focus on nighttime noise (L_n) specifically because road traffic $L_{den}max$ and $L_{den}min$ are correlated with L_n ($R_S = 0.99$ and 0.97, respectively). For all noise exposures, we did not account for personal noise abatement initiatives, time spent at home, or window-opening habits, which potentially influence precise exposure. Last, we excluded those with incomplete address history at baseline, which may have led to some selection bias.

In conclusion, long-term exposure to road traffic noise, especially at the least exposed façade, was associated with type 2 diabetes in a nationwide cohort of Danish residents ≥35 years of age, with evidence of a linear exposure–outcome relationship. In addition, associations with road traffic noise persisted after adjustment for long-term exposure to ambient air pollution. Significant positive associations were also estimated for railway noise, and nonsignificant positive associations were estimated for aircraft noise above the reference level. These findings provide further support for transportation noise as an important metabolic risk factor and indicate that diabetes should be considered in future assessments of the burden of disease due to transportation noise.

Acknowledgments

M.S. conceived the study and was in charge of overall direction and planning. M.S. and O.R.N. secured funding. J.D.T. conducted the analyses and took the lead in writing the manuscript and was the guarantor. J.B., C.G., and J.K. conducted modeling of air pollution. T.M. is primary investigator of the German Center for Cardiovascular Research, Partner Site Rhine-Main, Mainz, Germany. All authors contributed to the interpretation of the results and provided critical feedback to the manuscript.

This project was funded by the Independent Research Fund Denmark (grant 7016-00036B) and the Health Effects Institute (HEI) (Assistance Award R-82811201).

Research described in this article was conducted under contract to the HEI, an organization jointly funded by the U.S. Environmental Protection Agency (EPA; Assistance Award R-82811201), and certain motor vehicle and engine manufacturers. The contents of this article do not necessarily reflect the views of the HEI, or its sponsors, nor do they necessarily reflect the views and policies of the U.S. EPA or motor vehicle and engine manufacturers.

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