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Occupational noise exposure and risk of incident stroke: a pooled study of five Scandinavian cohorts

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ABSTRACT

Objectives To investigate the association between occupational noise exposure and stroke incidence in a pooled study of five Scandinavian cohorts (NordSOUND).

Methods We pooled and harmonised data from five Scandinavian cohorts resulting in 78 389 participants. We obtained job data from national registries or questionnaires and recoded these to match a job-exposure matrix developed in Sweden, which specified the annual average daily noise exposure in five exposure classes (L_{Aeq8h}): <70, 70–74, 75–79, 80–84, ≥85 dB(A). We identified residential address history and estimated 1-year average road traffic noise at baseline. Using national patient and mortality registers, we identified 7777 stroke cases with a median follow-up of 20.2 years. Analyses were conducted using Cox proportional hazards models adjusting for individual and area-level potential confounders.

Results Exposure to occupational noise at baseline was not associated with overall stroke in the fully adjusted models. For ischaemic stroke, occupational noise was associated with HRs (95% CI) of 1.08 (0.98 to 1.20), 1.09 (0.97 to 1.24) and 1.06 (0.92 to 1.21) in the 75–79, 80–84 and ≥85 dB(A) exposure groups, compared with <70 dB(A), respectively. In subanalyses using time-varying occupational noise exposure, we observed an indication of higher stroke risk among the most exposed (≥85 dB(A)), particularly when restricting analyses to people exposed to occupational noise within the last year (HR: 1.27; 95% CI: 0.99 to 1.63).

Conclusions We found no association between occupational noise and risk of overall stroke after adjustment for confounders. However, the non-significantly increased risk of ischaemic stroke warrants further investigation.

Key messages

What is already known about this subject?
- Health impacts of environmental noise are a growing concern, and there is limited evidence available on occupational noise and risk for stroke.

What are the new findings?
- We found no association between occupational noise and overall stroke.
- However, a non-significant increased risk of ischaemic stroke warrants further investigation.
- In time-varying occupational noise exposure analyses, we observed tendencies for recent occupational exposures to be associated with higher risk of stroke compared with exposures further back in time.

How might this impact on policy or clinical practice in the foreseeable future?
- The findings contribute to better knowledge of the health effects of occupational noise and stroke.
- Efforts to protect workers from occupational noise should continue to minimise the potential health risks among workers.

INTRODUCTION

Stroke is a leading cause of morbidity and mortality, and until effective stroke prevention strategies are widely implemented, the disease burden is expected to increase.[1] The identification of modifiable risk factors is a crucial step in prevention, and research has increasingly focused on the role of the working environment in stroke aetiology.[2]

Noise is a frequent occupational exposure that may increase risk for stroke through a stress response induced by acute high noise exposure which activates the pituitary-adrenal-cortical and sympathetic-adrenal medullary axes, thereby triggering the release of stress hormones,[3] and increases in heart rate, blood pressure and vasoconstriction.[4 5] In support, a systematic review found occupational noise associated with a higher risk of hypertension and cardiovascular disease.[6] Also, a small experimental trial in 48 participants found that daytime

occupational noise affected night-time sleep quality, which is a risk factor for stroke.[7] Finally, both stress and sleep disturbance are known to promote an unhealthy lifestyle,[8 9] which may also increase the risk of stroke.[2]

WHO and the International Labour Organization (ILO) recently conducted a systematic review of studies investigating the risk of stroke in workers exposed to noise ≥85 dB(A).[10] The authors found an indication for a higher risk for incident stroke with a pooled relative risk of 1.11 (95% CI 0.88 to 1.39)[10] based on a Danish cohort study of 164 247 workers and a Swedish cohort of 5753 males.[11 12] Additionally, after pooling three studies from Sweden (n=194 501),[13] Australia (n=2796)[14] and Canada (n=27 499),[15] the systematic review reported a RR of 1.02 (95% CI 0.93 to 1.12) for stroke mortality.[10] Other studies on occupational noise and stroke, not included in the WHO/ILO review, included two studies relying on self-reported exposure and outcome, which found no or small positive associations between occupational noise and stroke morbidity.[16 17] Additionally, a Japanese study (n=14 568) found an association between self-reported occupational noise exposure and intracerebral haemorrhage, but not with cerebral infarction or subarachnoid haemorrhage.[18] Overall, studies investigating occupational noise and stroke are heterogeneous in design, assessment of occupational noise and definition of stroke, which hampers synthesising findings and WHO/ILO review highlights the need for more high-quality longitudinal studies.

Road traffic noise has been associated with stroke.[19–22] More than 20% of the European Union population lives in areas where traffic noise levels are considered harmful to health.[23] Additionally, according to the sixth European Working Conditions Survey, 28% of workers in 2015 were exposed to excessive noise for at least a quarter of their time at work.[24] Therefore, many people will be exposed to high levels of noise at both work and at home, with poor access to a restorative, silent environment. Despite this, few studies have investigated the joint effect. A Swedish study investigating associations between road traffic noise, occupational noise and myocardial infarction, found that exposure to multiple noise sources increased the risk of myocardial infarction with each additional exposure.[25]

We aimed to test the hypothesis that occupational noise exposure is associated with a higher risk of stroke in a pooled study of five Scandinavian cohorts, containing incident stroke data from national registries, harmonised variables on potential socioeconomic and lifestyle confounders and job data merged to the same Job Exposure Matrix (JEM). Also, we aimed to investigate interactions between exposure to occupational and road traffic noise in relation to the risk of stroke.

METHODS

Study population

This study is based on five Scandinavian cohorts participating in the '*Nordic studies on occupational and traffic noise in relation to disease*' (NordSOUND) project (www.nordsound.dk): The Swedish National Study of Aging and Care in Kungsholmen,[26] the Stockholm part of the Screening Across the Lifespan Twin Study,[27] both based in Stockholm County, and using the same methodology for environmental exposure assessment within the CEANS project (Cardiovascular Effects of Air pollution and Noise in Stockholm)[19]; from Gothenburg, the Primary Prevention Study (PPS)[28]; from Malmö, the Malmö Diet and Cancer Study (MDC)[29]; and from Copenhagen/Aarhus, Denmark, the Diet, Cancer and Health cohort (DCH).[30] Cohort details are shown in online supplemental table 1. Data were pooled after variables were recoded according to a common codebook.

Exposure assessment

Occupational noise exposure was estimated through a JEM developed in Sweden.[31] The JEM is based on occupational measurements and specifies the annual average of the daily 8-hour equivalent A-weighted sound pressure level in five exposure classes: <70, 70–74, 75–79, 80–84, ≥85 dB(A) (L_{Aeq8h}). It is based on an earlier validated JEM with three exposure classes,[31] updated recently to use new measurement reports. The noise exposure information used for the JEM was derived from measurement reports collected from occupational medicine clinics, occupation health services and companies across Sweden.[31] The JEM contains 321 job families and was developed using the Nordic Occupational Classification (NYK)-83 coding system, which covers the period 1970–2004 in 5-year time bands. In NordSOUND, individual information on occupations was retrieved from national registers or through questionnaires filled in at baseline (participant recruitment date, online supplemental table 1). The occupation was then coded in different occupational coding systems in accordance with the system used in each country. To match the JEM with cohort data, the JEM was manually recoded by an occupational hygienist into two additional occupational code systems used in the NordSOUND cohorts. In total, three versions of the occupational noise JEMs were used (FOB80, NYK-83/FOB85 and DISCO-88).[32–34] Each JEM was then attached to the cohort with the same occupational code and a noise level was derived for each occupation for each participant. Additionally, the noise level was also matched on time period, since noise levels differ within an occupation across time.

We identified participants with occupational noise exposure at baseline (recruitment date) or selected the most recent occupational exposure within 5 years preceding baseline. Only the DCH cohort had occupational exposure data during the follow-up period, which was used in separate analyses of time-varying occupational noise exposure.

Road traffic noise exposure was calculated based on each participant's address history as the equivalent continuous A-weighted sound pressure level (L_{Aeq}) at the most exposed facade for day (07:00–19:00 hours), evening (19:00–22:00 hours) and night (22:00–07:00 hours), and expressed as L_{den}.[22] Road traffic noise for all cohorts was modelled using the Nordic Prediction method.[35] This model takes into account dwelling location, screening by terrain and buildings and information on annual mean daily traffic, distribution of traffic type, travel speed and road type for all major road links. Additionally, all cohorts, barring the Stockholm cohorts, included traffic information from smaller roads and the cohorts from Denmark and Gothenburg also included information on noise barriers. Online supplemental table 2 contains further details regarding road traffic noise calculations for each respective cohort. For each participant, exposure to road traffic noise was modelled as a time-weighted mean over the 1-year period preceding baseline, taking all addresses during this period into account.

Outcome

Stroke cases were identified through linkage to national patient and mortality registries. Incident stroke cases were defined by first diagnosis of stroke using the International Classification of Diseases (ICD): ICD8 and ICD9: 431–434, 436; and ICD10: I61–I64. In subtype analyses, we defined ischaemic stroke as

ICD8: 432–434, ICD9: 433–434 or ICD10: I63, haemorrhagic stroke as ICD8: 431 and IDC9: 431–432 or ICD10: I61–I62 and unspecified stroke as ICD8 and ICD9: 436 and ICD10: I64. Subjects diagnosed with stroke before baseline were excluded.

Covariates

Covariates were selected a priori, based on availability, biological plausibility and ability to harmonise variables across cohorts, as shown by the directed acyclic graph (online supplemental figure 1).

All participants completed a baseline questionnaire on diet, lifestyle, smoking status, smoking intensity (unavailable for PPS), alcohol consumption (unavailable for PPS), physical activity and body mass index (BMI, kg/m^2). BMI was considered an intermediate factor, and therefore included in a sensitivity analysis. Marital status and education level were gathered from either questionnaire or national registries, and income at area level was obtained from registries.

Statistical methods

We applied Cox proportional hazards models with age as the underlying time scale to estimate stroke HRs for each of the five categories of occupational noise exposure with <70 dB(A) as the reference category. Participants were followed from baseline until stroke, death, emigration or loss to follow-up, or end of follow-up, whichever came first.

The proportional hazards assumption was checked by a correlation test between scaled Schoenfeld residuals and the rank order of event time. Deviations from the assumption were detected for sex, educational level and smoking, which were subsequently included as strata. All models were stratified by cohort, allowing for different baseline hazards across cohorts. The assumption of linearity of BMI was evaluated by inspection of smoothed spline with 4 df. We observed no deviation from linearity.

The association between occupational noise and stroke as well as three subtypes of stroke was assessed in three models with stepwise adjustment: model 1 with adjustment for age (underlying time scale), sex and calendar year at baseline (in 5-year categories); model 2 (main model) with additional adjustment for education level (low, medium, high), marital status (married/cohabitating, single) and area-income (in quartiles) and model 3 with the addition of smoking status (never, former, current), and physical activity (low, medium, high). In four sensitivity analyses, we further modified model 3 in the following manner: (1) adjusted for road traffic noise exposure (1-year average at baseline); (2) added BMI to model 3, since BMI is a potential mediator; (3) tested the omission of the PPS cohort, since this cohort was recruited in the early 1970s whereas the other cohorts were recruited in the 1990s and (4) tested the omission of the DCH cohort, since 56% of the cases belonged to the DCH cohort.

We assessed the concurrent effects of occupational noise and road traffic noise (1-year average at baseline) by combining categories of occupational noise (<70, 70–74, ≥75 dB(A)) and road traffic noise (<55, 55–65, ≥65 dB(A)) into nine categories, using the combination of low occupational noise and low road traffic noise as the reference category. We collapsed the five categories of occupational noise into to three to avoid limited observations in some strata. The cut point of 55 dB(A) for road traffic noise was selected to align with the Environmental Noise Directive threshold,[23] and >65 dB(A) was selected to represent very high noise levels.

In the DCH cohort, occupational history during follow-up was available for 47 310 participants. In this cohort, we calculated HRs between time-varying occupational exposure (allowing for changes in occupational exposure over time). In this analysis, we applied three different strategies to handle people outside the workforce due to unemployment or retirement: (1) taking the last recorded occupational exposure (meaning that for people with no job, eg, due to retirement, this corresponded to the noise exposure at their last job); (2) we censored all participants 5 years after they were last active in the workforce (thus 5 years since their last record of occupational noise exposure) and (3) we censored all participants 1 year after they were last active in the workforce.

Analyses were performed in SAS V.9.4 (SAS Institute, North Carolina, USA) and R (V.3.2.3).

RESULTS

Of the 104 243 eligible participants, we excluded 1123 with stroke before baseline, 19 484 with missing exposure data and 5247 with missing covariate data, resulting in 78 389 participants for the study (online supplemental figure 2). Of these, 7777 developed stroke (4401 ischaemic, 913 haemorrhagic and 2463 unspecified) during a median follow-up of 20.2 years.

Baseline characteristics across cohorts are presented in table 1.

The majority of cohorts recruited participants when they were between 50 and 60 years of age. MDC and PPS had the highest proportion of participants with low educational level. The majority of participants were married or cohabiting, 33% were current smokers and around half had low physical activity during leisure time.

Online supplemental table 3 shows the distribution of occupational noise across cohorts. Overall, 62.6% were exposed to occupational noise levels <70 dB(A), while 4.4% were exposed to levels ≥85 dB(A). PPS had the highest proportion of participants in the top exposure group. The most frequent occupations in the most exposed category were machine operators in brewery production and textile workers, blacksmiths and other metal processing workers, wood industry workers and construction workers.

In model 1, we found that occupational noise was associated with a higher risk of total strokes among those exposed to ≥70 dB(A), with HRs of 1.05–1.12 (table 2).

However, following adjustment for socioeconomic covariates (model 2), HRs remained elevated but were attenuated between 1.03 and 1.05. After further adjustment for lifestyle factors (model 3), exposure to occupational noise was no longer associated with stroke. For ischaemic stroke, we observed HRs >1 for all occupational noise categories, but with wide CIs in the high exposure groups due to a low number of cases and no consistent monotonic dose-response association. We found no association between occupational noise and haemorrhagic or unspecified strokes.

In analyses including only the Danish cohort, we observed that when investigating occupational noise exposure at the last recorded job, the fully adjusted HR for overall stroke was 1.08 (95% CI 0.95 to 1.23) among people exposed to ≥85 dB(A) (table 3).

When we censored all participants 5 years after they were last active in the workforce (thus 5 years since their last record of occupational noise exposure), we found a tendency of higher risks among those exposed to 70–74 dB(A) (HR=1.09; 95% CI 0.97 to 1.22) as well as those exposed to ≥85 dB(A) (HR=1.16; 95% CI 0.95 to 1.41). Similarly, when we censored participants

Table 1 Baseline characteristics of the study population across included cohorts

	DCH	SNAC-K	SALT	MDC	PPS	Total
Enrolment area	Copenhagen, Aarhus	Stockholm city	Stockholm county	Malmö	Gothenburg	
Total participants, N	47 310	1157	5891	19 350	4681	78 389
Recruitment period	1993–1997	2001–2004	1998–2002	1991–1996	1970–1973	
Follow-up time (years)	20.3 (6.2–22.0)	13.4 (0.9–15.3)	16.2 (3.5–18.6)	21.1 (7.8–23.2)	29.5 (15.4–39.8)	20.2 (6.2–23.7)
Stroke cases, N	4375	120	524	1672	1086	7777
Men, %	47.7	40.1	45.2	40.4	100	48.7
Age at inclusion	55.9 (50.7–64.1)	66.1 (60.2–87.6)	56.1 (44.3–78.8)	56.3 (47.1–67.1)	51.2 (47.6–54.4)	55.6 (48.3–65.6)
Educational level, %						
Low	24.7	19.3	25.3	62.7	68.8	34.0
Medium	50.3	36.9	36.3	19.4	20.2	41.8
High	25.0	43.8	38.4	18.0	11.0	24.3
Marital status, %						
Married/Cohabiting	77.1	53.4	67.8	67.7	86.2	75.1
Area-level income, %						
First quartile	33.7	2.4	6.9	20.1	25.8	28.3
Second quartile	22.5	0	10.3	19.3	22.1	20.7
Third quartile	17.0	0	18.5	27.2	24.6	19.1
Fourth quartile	26.8	97.6	64.4	33.5	27.5	32.0
Smoking status, %						
Current	35.8	18.5	20.3	28.2	39.6	33.3
Former	28.5	40.2	36.4	33.7	33.2	30.5
Never	35.7	41.4	43.4	38.1	27.2	36.3
Physical activity, %						
Low	51.1	71.8	54.3	50.8	24.9	49.8
Medium	19.9	21.9	36.6	21.8	58.8	24.3
High	29.0	6.3	9.1	27.4	16.3	25.9
BMI	25.5 (20.5–33.1)	25.3 (20.1–32.4)	24.2 (19.6–30.7)	25.0 (20.2–32.4)	25.1 (20.7–30.5)	25.3 (20.3–32.7)
Smoking intensity, g/day*†	14.9 (3.9–34.0)	7.5 (1.3–20.0)	13.0 (3.0–30.0)	15.0 (2.0–30.0)	–	14.6 (3.0–33.3)
Missing, %	1.8	1.3	0	0	–	1.5
Alcohol intake, %†						
Daily	19.9	10.2	9.0	18.7	Missing	17.3
Weekly	60.1	55.2	63.8	36.9	Missing	52.5
Seldom	17.3	29.3	24.5	30.4	Missing	19.0
Never	2.6	5.2	2.7	13.0	Missing	4.2
Missing	0.06	0	0.03	1.1	100	7.1

Median and 5–95 percentiles, unless otherwise stated.
*Among smokers.
†Only available for a subpopulation of the entire cohort.
BMI, body mass index; DCH, Diet, Cancer and Health; MDC, Malmö Diet and Cancer Study; PPS, Primary Prevention Study; SALT, Stockholm part of the Screening Across the Lifespan Twin Study; SNAC-K, Swedish National Study of Aging and Care in Kungsholmen.

1 year after they were last active in the workforce, a tendency of higher risks was observed for those exposed to 70–74 dB(A) and ≥85 dB(A) categories with HRs of 1.14 (95% CI 0.99 to 1.32) and 1.27 (95% CI 0.99 to 1.63), respectively, whereas HRs of 0.99 and 0.90 were observed for the intermediate noise exposure groups.

We found that among people exposed to ≥85 dB(A), the HR for those with medium or high education was 1.13 (95% CI 0.97 to 1.31) compared with an HR of 0.92 (95% CI 0.80 to 1.06) in the low education group (table 4).

No differences were observed in analyses stratified by sex.

Table 5 shows the results of combined exposure to occupational and road traffic noise in relation to stroke incidence.

HRs (95% CI) among people exposed to high levels of road traffic noise (≥65 dB(A)) together with intermediate (70–74 dB(A)) or high occupational noise (≥75 dB(A)) were 1.16 (1.00 to 1.34) and 1.11 (0.95 to 1.29), respectively.

Further adjustment for road traffic noise or BMI led to very small changes in risk estimates (Table S4). Overall, the exclusion of the PPS cohort resulted in small changes to risk estimates. Following omission of the DCH cohort, we observed minimal changes for overall stroke risk and an attenuation in risk estimates for ischaemic stroke in the highest exposure categories (Table S4). Lastly, the results of occupational noise and overall stroke for each cohort showed no consistent associations across cohorts (Table S5).

Table 2 Association between baseline occupational noise exposure and stroke incidence

	N cases	Model 1 HR (95% CI)	**Model 2† HR (95% CI)**	Model 3‡ HR (95% CI)
Occupational noise, all strokes				
<70 dB(A)	4526	Reference	Reference	Reference
70–74 dB(A)	1455	1.05 (0.99 to 1.11)	1.03 (0.97 to 1.09)	1.01 (0.95 to 1.07)
75–79 dB(A)	818	1.08 (1.00 to 1.16)	1.03 (0.96 to 1.12)	1.02 (0.94 to 1.10)
80–84 dB(A)	517	1.10 (1.00 to 1.21)	1.04 (0.94 to 1.14)	1.00 (0.91 to 1.10)
≥85 dB(A)	461	1.12 (1.01 to 1.23)	1.05 (0.95 to 1.16)	1.01 (0.91 to 1.12)
Occupational noise, ischaemic strokes				
<70 dB(A)	2554	Reference	Reference	Reference
70–74 dB(A)	784	1.06 (0.98 to 1.15)	1.05 (0.96 to 1.14)	1.03 (0.95 to 1.12)
75–79 dB(A)	479	1.13 (1.02 to 1.25)	1.10 (0.99 to 1.22)	1.08 (0.98 to 1.20)
80–84 dB(A)	327	1.18 (1.05 to 1.33)	1.14 (1.01 to 1.29)	1.09 (0.97 to 1.24)
≥85 dB(A)	257	1.14 (1.00 to 1.30)	1.10 (0.96 to 1.26)	1.06 (0.92 to 1.21)
Occupational noise, haemorrhagic strokes				
<70 dB(A)	542	Reference	Reference	Reference
70–74 dB(A)	184	1.12 (0.95 to 1.33)	1.11 (0.94 to 1.32)	1.10 (0.93 to 1.31)
75–79 dB(A)	94	1.04 (0.84 to 1.30)	1.02 (0.81 to 1.28)	1.01 (0.80 to 1.27)
80–84 dB(A)	46	0.82 (0.60 to 1.12)	0.79 (0.57 to 1.08)	0.76 (0.56 to 1.05)
≥85 dB(A)	47	0.96 (0.71 to 1.30)	0.93 (0.68 to 1.28)	0.90 (0.66 to 1.24)
Occupational noise, unspecified strokes				
<70 dB(A)	1429	Reference	Reference	Reference
70–74 dB(A)	491	1.01 (0.91 to 1.12)	0.97 (0.87 to 1.07)	0.94 (0.84 to 1.04)
75–79 dB(A)	244	0.99 (0.87 to 1.14)	0.92 (0.80 to 1.06)	0.90 (0.78 to 1.03)
80–84 dB(A)	142	1.05 (0.88 to 1.25)	0.95 (0.79 to 1.13)	0.90 (0.75 to 1.08)
≥85 dB(A)	157	1.13 (0.95 to 1.33)	1.01 (0.85 to 1.20)	0.95 (0.80 to 1.13)

*Adjusted for age (underlying time scale), sex and calendar year at baseline (5-year periods).
†Model 1 plus adjustment for education level (low, medium, high), marital status (married/cohabiting, single), area-income (quartiles).
‡Model 2 plus adjustment for smoking status (never, former, current), and physical activity (low, medium, high).

Table 3 Association between time-varying occupational noise exposure and stroke incidence *DCH cohort only*

	N cases	Model 1* HR (95% CI)	**Model 2† HR (95% CI)**	Model 3‡ HR (95% CI)
Occupational noise (all participants)§				
<70 dB(A)	2460	Reference	Reference	Reference
70–74 dB(A)	1015	1.04 (0.97 to 1.12)	1.01 (0.94 to 1.09)	0.99 (0.92 to 1.07)
75–79 dB(A)	483	1.09 (0.99 to 1.21)	1.04 (0.94 to 1.15)	1.01 (0.91 to 1.12)
80–84 dB(A)	206	1.10 (0.95 to 1.27)	1.03 (0.90 to 1.20)	1.00 (0.86 to 1.15)
≥85 dB(A)	272	1.21 (1.06 to 1.37)	1.12 (0.99 to 1.28)	1.08 (0.95 to 1.23)
Occupational noise (up to 5 years back)¶				
<70 dB(A)	1059	Reference	Reference	Reference
70–74 dB(A)	452	1.16 (1.04 to 1.30)	1.12 (1.00 to 1.25)	1.09 (0.97 to 1.22)
75–79 dB(A)	207	1.11 (0.95 to 1.28)	1.04 (0.89 to 1.21)	1.00 (0.86 to 1.17)
80–84 dB(A)	78	1.01 (0.80 to 1.27)	0.93 (0.74 to 1.18)	0.89 (0.70 to 1.12)
≥85 dB(A)	122	1.33 (1.10 to 1.61)	1.22 (1.01 to 1.49)	1.16 (0.95 to 1.41)
Occupational noise (up to 1-year back)**				
<70 dB(A)	645	Reference	Reference	Reference
70–74 dB(A)	282	1.22 (1.06 to 1.40)	1.17 (1.01 to 1.35)	1.14 (0.99 to 1.32)
75–79 dB(A)	126	1.09 (0.90 to 1.32)	1.03 (0.84 to 1.25)	0.99 (0.81 to 1.20)
80–84 dB(A)	50	1.02 (0.77 to 1.36)	0.95 (0.71 to 1.27)	0.90 (0.67 to 1.21)
≥85 dB(A)	76	1.47 (1.15 to 1.87)	1.34 (1.05 to 1.73)	1.27 (0.99 to 1.63)

*Adjusted for age, sex and calendar year at baseline (5-year period).
†Model 1 plus adjustment for educational level (low, medium, high), marital status (married/cohabiting, single), area-income (quartiles).
‡Model 2 plus adjustment for smoking status (never, former, current), and physical activity (low, medium, high).
§Time-varying occupational noise exposure during follow-up, and handling persons outside the workforce by taking their latest occupational noise exposure.
¶Time-varying occupation noise exposure, censoring all participants 5 years after last occupation noise exposure.
**Time-varying occupation noise exposure, censoring all participants 1 year after last occupation noise exposure.
DCH, Diet, Cancer and Health.

Table 4 Association between baseline occupational noise exposure and stroke incidence stratified by education and sex

	Low education (n=29 479)		Medium/High education (n=48 910)		Males (n=38 195)		Females (n=40 194)	
	N cases	HR (95% CI)	N cases	HR (95% CI)	N cases	HR (95% CI)	N cases	HR (95% CI)
Occupational noise								
<70 dB(A)	1551	Reference	2975	Reference	2399	Reference	2127	Reference
70–74 dB(A)	718	1.02 (0.94 to 1.12)	737	0.98 (0.91 to 1.07)	869	1.04 (0.96 to 1.12)	586	0.97 (0.88 to 1.06)
75–79 dB(A)	443	0.97 (0.87 to 1.08)	375	1.07 (0.96 to 1.20)	649	1.01 (0.92 to 1.11)	169	1.07 (0.92 to 1.26)
80–84 dB(A)	345	0.97 (0.86 to 1.10)	172	1.03 (0.88 to 1.21)	439	1.03 (0.93 to 1.15)	78	0.90 (0.72 to 1.13)
≥85 dB(A)	258	0.92 (0.80 to 1.06)	203	1.13 (0.97 to 1.31)	428	1.02 (0.91 to 1.14)	33	1.05 (0.74 to 1.48)

*Adjusted for age, sex and calendar year at baseline (5-year period), marital status (married/cohabiting, single), area-income (quartiles), smoking status (never, former, current) and physical activity (low, medium, high).

DISCUSSION

In this pooled study of five Scandinavian cohorts, we observed that baseline occupational noise exposure was not associated with total incident stroke after adjustment for potential confounders. However, occupational noise seemed associated with slightly higher risk for ischaemic stroke. In a subanalysis investigating time-varying occupational noise exposure, we observed that recent occupational exposures seemed associated with higher risk of stroke compared with exposures further back in time.

To date, only three prospective studies have examined the association between occupational noise exposure and stroke, with inconclusive results.[11–13] In line with our findings of no association with total stroke, a cohort study from Denmark found no association with occupational noise exposure and overall stroke, with a risk estimate of 1.01 (95% CI 0.99 to 1.03).[11] In contrast, a Swedish study comprised men, found an indication of higher stroke risk among those exposed to occupational noise >85 dB(A) (HR 1.12 (95% CI 0.79 to 1.59)).[12] Similarly, a prospective Swedish study of male construction workers found occupational noise to be associated with a higher risk of stroke mortality (RR 1.19 (95% CI 1.03 to 1.38)).[13] One explanation could be that the Swedish studies focused on males, whereas in the present study we included both sexes. However, in the present study we observed no apparent differences in stroke risk between men and women. Moreover, one of the Swedish studies focused on construction workers, which are generally exposed to higher levels of occupational noise. Another explanation for discrepant findings could be that we assess stroke incidence while the Swedish study investigated stroke mortality.

Our results suggested that for individuals with medium to high education, occupational noise at moderate to high levels seemed associated with higher stroke risk, whereas no association was observed for persons with low education. This could be because in professions which mainly employ people of low education, such as in construction or industrial work, hearing protection is mandated, while medium to highly educated individuals with high levels of exposure, such as musicians and preschool teachers, often work in professions where hearing protection is uncommon.

Other explanations for the inconsistencies across studies could be different adjustment strategies for educational level, socioeconomic status and lifestyle factors. In the present study, we observed that the HRs approached unity following increasing levels of adjustment, particularly for lifestyle confounders. This could explain why some studies report an association and others, with a more comprehensive adjustment strategy, report no associations.

In subanalyses investigating time-varying exposure, an indication with overall stroke appeared strongest when restricting analyses to people exposed to occupational noise within the last year, suggesting that more recent exposure is potentially more crucial. In support, a Danish prospective study found that recent noise exposure (<3 years) at high levels (>80 dB(A)) suggested a higher risk of stroke (RR 1.38 (95% CI 1.10 to 1.73)).[11] One could speculate that as time passes from actual exposure to occupational noise (ie, time since retirement), any excess risk of stroke subsides, similar to other exposures such as tobacco smoking and stroke.[36] This could also explain inconsistencies across studies, as temporal proximity of exposure seems to play an important role.

Our results suggested a weak association with ischaemic stroke. Only one study previously investigated this, finding an association with haemorrhagic stroke, but not ischaemic stroke.[18] However, the study had only 13 ischaemic and 21 haemorrhagic exposed cases. Notably, studies on transportation noise have also found positive associations with ischaemic stroke (and not haemorrhagic stroke),[21 22 37] and with pathophysiological risk factors for ischaemic stroke including subclinical atherosclerosis and impaired endothelial function.[5] This suggests the involvement of noise in causing vascular damage, and may provide a pathophysiological basis to explain the higher risk of ischaemic stroke in relation to occupational noise exposure. However, CIs in the

Table 5 Associations between categories of combined exposure to baseline occupational noise and road traffic noise (1-year average) and overall stroke (n=71 628)

	Road traffic noise, L_{den}					
	L_{den} <55 dB		L_{den} 55–65 dB		L_{den} ≥65 dB	
Occupational noise	N cases	HR (95% CI)	N cases	HR (95% CI)	N cases	HR (95% CI)
<70 dB(A)	1980	Reference	1512	1.01 (0.94 to 1.08)	483	0.94 (0.85 to 1.04)
70–74 dB(A)	569	0.97 (0.88 to 1.06)	483	0.94 (0.85 to 1.04)	211	1.16 (1.00 to 1.34)
≥75 dB(A)	623	1.02 (0.93 to 1.12)	474	0.97 (0.87 to 1.08)	180	1.11 (0.95 to 1.29)

*Adjusted for age, sex and calendar year at baseline (5-year period), educational level (low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), smoking status (never, former, current) and physical activity (low, medium, high).
†All results are given as cases and HR (95% CI).

high exposure groups in the present study were wide and we cannot rule out that the tendency of higher risk estimates at high exposure was a chance finding.

When we evaluated the effect of combined exposure to occupational noise and road traffic noise, we observed that those exposed to high levels concurrently seemed to have somewhat higher stroke risk. Of note, a Swedish case-control study on concurrent occupational noise, job strain and road traffic noise in relation to myocardial infarction, found a tendency of a synergistic effect with increasing levels of multiple exposures, thus supporting that co-exposure to occupational and traffic noise is harmful to the cardiovascular system.[25] However, the indication of higher HRs in people exposed to high occupational and road traffic noise may very well be due to chance, due to low number of high exposed cases and as other exposure combinations did not indicate a consistent pattern.

It remains unclear how low levels of occupational noise could still have some adverse effects on the cardiovascular system. In general, the <70 dB(A) category is the lowest estimated level in occupational settings, and it mainly consists of office workers. Using a JEM to assess occupational noise <70 dB(A) in occupational settings is very difficult, and would require individual measurements instead of JEMs.

The main strength of our study was the use of five Scandinavian cohort studies with pooling and harmonisation of cohort data, allowing for a higher generalisability of our findings than from a single-centre study. This study also benefits from a large number of participants, information on stroke incidence through validated, national registries on hospitalisation and mortality as well as information on a number of potential socioeconomic and lifestyle confounders. The extensive JEM, covering 321 occupations and based on 145 measurement reports with a total of 569 measurements on 129 unique job families, enabled a thorough exposure classification of occupational noise exposure.[31] We were also able to assess the effects of concurrent occupational noise and road traffic noise exposure. Lastly, using the DCH cohort we were able to assess the effect of time-varying occupational noise exposure and stroke incidence. Interestingly, in the DCH cohort, 26% of individuals changed their exposure category during follow-up, which suggests that using baseline occupational exposure could be associated with some exposure misclassification. However, we found that of these 26%, 61% only changed one exposure category up or down.

Our study has some limitations. In total, 56% of cases belonged to the DCH cohort. However, removing the DCH cohort resulted in only small changes in estimates. Additionally, using a JEM for exposure classification is associated with exposure misclassification within the occupational group, for example, due to varying use of hearing protection and work separated from the noise source (control rooms). This misclassification, however, is expected to be non-differential and is expected to mainly lead to an attenuation of the association, which could explain the lack of association between occupational noise and overall stroke. A previous version of the JEM has been validated by comparing classifications from the two teams of occupational hygienists creating the JEM,[31] and this found no systematic differences in classification for the average levels used in this study. When we omitted the PPS cohort, we observed slightly higher HRs in the highest exposure category. In the PPS cohort, the code system was older and misclassification larger when attaching the JEM for this cohort, despite the adaptions made to ensure a good match with the data. Another limitation is that we did not have data on working hours (night work, shift work or long working hours), all of which are important factors to consider since both are associated with occupational noise and cardiovascular outcomes,[38] including stroke.[39] Lastly, some known risk factors for stroke such as hypertension, diabetes and high cholesterol were not available for all cohorts. However, these risk factors are likely to be on the pathway from noise exposure to stroke, and thus including them as confounders would result in overadjustment.

With regard to generalisability, the cohorts included in this study were all from Scandinavia, and may not be generalisable to countries with different regulations related to occupational or environmental noise. For example, some countries could have stricter regulations regarding occupational noise levels or the use of hearing protection, as well as better sound insulated residential buildings. Therefore, generalisation of our findings to other populations outside Europe warrants caution.

In conclusion, this pooled multicentre Scandinavian study did not lend strong support to occupational noise exposure as an important risk factor for total stroke, although the indication of a potential higher risk of ischaemic stroke warrants further investigation.

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REFERENCES

1 GBD 2016 Stroke Collaborators. Global, regional, and national burden of stroke, 1990-2016: a systematic analysis for the global burden of disease study 2016. *Lancet Neurol* 2019;18:439–58.
2 Zhang S, Zhang W, Zhou G. Extended risk factors for stroke prevention. *J Natl Med Assoc* 2019;111:447–56.
3 Babisch W. The Noise/Stress concept, risk assessment and research needs. *Noise Health* 2002;4:1–11.
4 Daiber A, Kröller-Schön S, Frenis K, *et al*. Environmental noise induces the release of stress hormones and inflammatory signaling molecules leading to oxidative stress and vascular dysfunction-Signatures of the internal exposome. *Biofactors* 2019;45:495–506.
5 Münzel T, Gori T, Babisch W, *et al*. Cardiovascular effects of environmental noise exposure. *Eur Heart J* 2014;35:829–36.
6 Skogstad M, Johannessen HA, Tynes T, *et al*. Systematic review of the cardiovascular effects of occupational noise. *Occup Med* 2016;66:10–16.
7 Lin C-Y, Tsai P-J, Lin K-Y, *et al*. Will daytime occupational noise exposures induce nighttime sleep disturbance? *Sleep Med* 2018;50:87–96.
8 Clark AJ, Salo P, Lange T, *et al*. Onset of impaired sleep as a predictor of change in health-related behaviours; analysing observational data as a series of non-randomized pseudo-trials. *Int J Epidemiol* 2015;44:1027–37.
9 Torres OV, O'Dell LE. Stress is a principal factor that promotes tobacco use in females. *Prog Neuropsychopharmacol Biol Psychiatry* 2016;65:260–8.
10 Teixeira LR, Pega F, Dzhambov AM, *et al*. The effect of occupational exposure to noise on ischaemic heart disease, stroke and hypertension: a systematic review and meta-analysis from the WHO/ILO joint estimates of the work-related burden of disease and injury. *Environ Int* 2021;154:106387.
11 Stokholm ZA, Bonde JP, Christensen KL, *et al*. Occupational noise exposure and the risk of stroke. *Stroke* 2013;44:3214–6.
12 Eriksson HP, Andersson E, Schiöler L, *et al*. Longitudinal study of occupational noise exposure and joint effects with job strain and risk for coronary heart disease and stroke in Swedish men. *BMJ Open* 2018;8:e019160.
13 Pettersson H, Olsson D, Järvholm B. Occupational exposure to noise and cold environment and the risk of death due to myocardial infarction and stroke. *Int Arch Occup Environ Health* 2020;93:571–5.
14 Gopinath B, Thiagalingam A, Teber E, *et al*. Exposure to workplace noise and the risk of cardiovascular disease events and mortality among older adults. *Prev Med* 2011;53:390–4.
15 Davies HW. Exposure to occupational noise and risk of cardiovascular disease: a retrospective cohort study 2002.
16 Kerns E, Masterson EA, Themann CL, *et al*. Cardiovascular conditions, hearing difficulty, and occupational noise exposure within us industries and occupations. *Am J Ind Med* 2018;61:477–91.
17 Dzhambov AM, Dimitrova DD, Tokmakova MP. Association between self-reported occupational noise and the prevalence of stroke: secondary analysis of the National health interview survey, 2014. *Noise Control Eng J* 2016;64:779–88.
18 Fujino Y, Iso H, Tamakoshi A, *et al*. A prospective cohort study of perceived noise exposure at work and cerebrovascular diseases among male workers in Japan. *J Occup Health* 2007;49:382–8.
19 Pyko A, Andersson N, Eriksson C, *et al*. Long-Term transportation noise exposure and incidence of ischaemic heart disease and stroke: a cohort study. *Occup Environ Med* 2019;76:oemed-2018-105333–207.
20 Andersson EM, Ögren M, Molnár P, *et al*. Road traffic noise, air pollution and cardiovascular events in a Swedish cohort. *Environ Res* 2020;185:109446.
21 Héritier H, Vienneau D, Foraster M, *et al*. Transportation noise exposure and cardiovascular mortality: a nationwide cohort study from Switzerland. *Eur J Epidemiol* 2017;32:307–15.
22 Roswall N, Pyko A, Ögren M, *et al*. Long-Term exposure to transportation noise and risk of incident stroke: a pooled study of nine Scandinavian cohorts. *Environ Health Perspect*. In Press 2021;129:107002.
23 EEA. *Environmental noise in Europe — 2020 EEA Report No 22/2019*. Luxembourg: Publications Office of the European Union, 2020: European Environment Agency, 2020.
24 Parent-Thirion AB, Cabrita I, Vargas Llave O. *Sixth European working conditions survey: overview report*. Dublin: Eurofound, 2019.
25 Selander J, Bluhm G, Nilsson M, *et al*. Joint effects of job strain and road-traffic and occupational noise on myocardial infarction. *Scand J Work Environ Health* 2013;39:195–203.
26 Lagergren M, Fratiglioni L, Hallberg IR, *et al*. A longitudinal study integrating population, care and social services data. The Swedish national study on aging and care (SnAC). *Aging Clin Exp Res* 2004;16:158–68.
27 Magnusson PKE, Almqvist C, Rahman I, *et al*. The Swedish twin registry: establishment of a Biobank and other recent developments. *Twin Res Hum Genet* 2013;16:317–29.
28 Wilhelmsen L, Berglund G, Elmfeldt D, *et al*. The multifactor primary prevention trial in Göteborg, Sweden. Comparison with a previously untreated population sample. *Drugs* 1986;31 Suppl 1:47–51.
29 Berglund G, Elmstähl S, Janzon L, *et al*. The Malmo diet and cancer study. design and feasibility. *J Intern Med* 1993;233:45–51.
30 Tjønneland A, Olsen A, Boll K, *et al*. Study design, exposure variables, and socioeconomic determinants of participation in diet, cancer and health: a population-based prospective cohort study of 57,053 men and women in Denmark. *Scand J Public Health* 2007;35:432–41.
31 Sjöström M, Lewné M, Alderling M, *et al*. A job-exposure matrix for occupational noise: development and validation. *Ann Occup Hyg* 2013;57:774–83.
32 Statistics Sweden. *Folk-och bostadräkningen 1980*, 1980.
33 Arbetsmarknadsstyrelsen S. *Nordisk yrkesklassificering: svensk grundstandard*. Stockholm, Sweden: Liber, 1983.
34 Elias P. Occupational classification (ISCO-88): concepts, methods, reliability, validity and cross-national comparability 1997.
35 Bendtsen H. The Nordic prediction method for road traffic noise. *Sci Total Environ* 1999;235:331–8.
36 Wannamethee SG, Shaper AG, Whincup PH, *et al*. Smoking cessation and the risk of stroke in middle-aged men. *JAMA* 1995;274:155–60.
37 Sørensen M, Poulsen AH, Hvidtfeldt UA, *et al*. Transportation noise and risk of stroke: a nationwide prospective cohort study covering Denmark. *Int J Epidemiol* 2021;50:1147–56.
38 Brown DL, Feskanich D, Sánchez BN, *et al*. Rotating night shift work and the risk of ischemic stroke. *Am J Epidemiol* 2009;169:1370–7.
39 Pega F, Náfrádi B, Momen NC, *et al*. Global, regional, and national burdens of ischemic heart disease and stroke attributable to exposure to long working hours for 194 countries, 2000-2016: a systematic analysis from the WHO/ILO joint estimates of the work-related burden of disease and injury. *Environ Int* 2021;154:106595.

Occupational noise exposure and risk of incident stroke: an analysis of five Scandinavian cohorts within the NordSound project

SUPPLEMENTAL MATERIAL

Table S1. Detailed information on the cohorts.

Cohort	Detailed cohort information	Key references	Funding
DCH	The inclusion criteria for the Danish Diet Cancer and Health (DCH) cohort were age between 50 and 64 y, residing in the greater Copenhagen or Aarhus area and without a cancer diagnosis. From 1993 to 1997, 160,725 Danes were invited to participate of whom 57,053 participants accepted the invitation and were enrolled in the study. All participants completed detailed questionnaires at enrolment and trained staff members measured height, weight, and waist circumference.	Tjonneland A, Olsen A, Boll K, et al. Study design, exposure variables, and socioeconomic determinants of participation in Diet, Cancer and Health: a population-based prospective cohort study of 57,053 men and women in Denmark. Scand J Publ Health 2007;35:432-41	The Danish Cancer Society
SALT[a]	The Screening Across the Lifespan Twin Study (SALT) included a total of about 45,000 twins born 1958 and earlier from the Swedish Twin Registry who were interviewed 1998-2002. SALT participants who resided in Stockholm County at recruitment (n=7,043) are included in the present project. The interview collected data on zygosity, diseases, use of medication, occupation, education and lifestyle habits. In a subgroup of around 2,500 subjects, a clinical examination was made, including blood sampling and anthropometrics as well as blood pressure measurements.	Zagai U, Lichtenstein P, Pedersen NL, Magnusson PKE. The Swedish Twin Registry: Content and Management as a Research Infrastructure. Twin Res Hum Genet. 2019 Dec;22(6):672-680. doi: 10.1017/thg.2019.99. Epub 2019 Nov 21.	Swedish Environmental Protection Agency, the Swedish Council for Health, Working Life and Social Research and the Swedish Heart-Lung Foundation. The SALT cohort was additionally supported by NIH grant 575 AG-08724. The Swedish Twin Registry is managed by Karolinska Institutet and receives funding through the Swedish Research Council under the grant no 2017-00641.
SNAC-K[a]	The Swedish National Study of Aging and Care in Kungsholmen (SNAC-K) was established 2001-2004 and included 3,363 residents aged 60-104 years in Kungsholmen, Stockholm. The aim was to investigate the ageing process and identify possible preventive strategies to improve health and care in elderly adults. Information was collected through social interviews and clinical examinations, including assessment of physical and cognitive functioning. Follow-up investigations are performed at intervals of three to six years depending on age.	Lagergren M, Fratiglioni L, Hallberg IR, et al. A longitudinal study integrating population, care and social services data. The Swedish National study on Aging and Care (SNAC). Aging Clin Exp Res 2004;16:158–68.	Swedish Environmental Protection Agency, the Swedish Council for Health, Working Life, the Swedish Research Council and Social Research and the Swedish Heart-Lung Foundation. SNAC-K was additionally funded by the Ministry of Health and Social Affairs, Sweden, Stockholm County Council and the participating Municipalities and University Departments.
PPS	The Primary Prevention Study cohort (PPS) consists of a random third of all men in the city of Gothenburg born 1915–1925, recruited in 1970–1973 (n=7,494, participation rate 75%) to study predictors of cardiovascular disease. Participants were examined by health care professionals (e.g. height, weight, systolic and diastolic blood pressures and cholesterol levels) and filled out questionnaires on background data (e.g. occupation, smoking habits, physical activity, antihypertensive	Wilhelmsen L, Tibblin G, Werkö L. A primary preventive study in Gothenburg, Sweden. Preventive Med. 1972;1:153-60. Wilhelmsen L, Berglund G, Elmfeldt D et al. The multifactor primary prevention trial in Göteborg, Sweden. Eur Heart J. 1986;7:279-88.	The Bank of Sweden Tercentenary Fund and the Swedish Medical Research Council.

	medication, psychological stress, prevalent diabetes mellitus and family history of coronary events).		
MDC	The Malmö Diet and Cancer (MDC) study is a population based prospective cohort study. Baseline examinations were conducted between 1991 and 1996, and eligible participants were men born between 1923 and 1945 and women born between 1923 and 1950, living in the city of Malmö. Swedish reading and writing skills were required. The data collection was done both using questionnaires and interviews, including data on dietary habits, socio-economics, medical history and lifestyle factors. The total number of study subjects were 28,098.	Berglund G, Elmstahl S, Janzon L et al. The Malmö Diet and Cancer study. Design and feasibility. J Intern Med 1993;233:45–51. Manjer J, Carlsson S, Elmstahl S et al. The Malmö Diet and Cancer Study: representativity, cancer incidence and mortality in participants and non-participants. Eur J Cancer Prev, 2001, 10:489–499	Swedish Research Council (VR) Infrastructure grant, Heart-Lung Foundation.
[a]This cohort is part of The Swedish Cardiovascular Effects of Air Pollution and Noise in Stockholm (CEANS) cohort, which consists of four sub-cohorts of persons residing in Stockholm County, Sweden. Harmonisation of covariates has been conducted across the cohorts.			

Table S2. Detailed information on estimation of road traffic noise for all participating cohorts.

Cohort	Road traffic noise estimation	Key references
DCH	Calculations were conducted for the years 1995, 2000, 2005, 2010, and 2015 using the Nordic prediction method implemented in SoundPLAN (version 8.0). Various input variables were used in the model, most importantly geocode and height (floor) for each address; information on travel speed, light/heavy vehicle distributions, road type, annual average daily traffic for all Danish road links (Jensen et al 2019) and 3D information on all Danish buildings. Screening effects from buildings, terrain, and noise barriers were included. All road traffic sources within 1500 m from the receivers were included. The parameter setting were set to allow 2 reflections.	Thacher JD, Poulsen AH, Raaschou-Nielsen O, et al. High-resolution assessment of road traffic noise exposure in Denmark. Environ Res 2019; 182:109051 Jensen SS, Plejdrup MS, Hillig K. GIS-based National Road and Traffic Database 1960-2020. Aarhus University, Danish Centre for Environment and Energy 2019; Report 151
CEANS (SALT, SNAC-K)	To assess long-term individual transportation noise exposure a noise database for Stockholm County was developed representing the period from 1990 and onwards, with detailed estimation every fifth year. The database includes 3D terrain data as well as information on ground surface, road net, daily traffic flows, speed limits and percentage of heavy vehicles. To calculate noise levels for road traffic a modification of the Nordic prediction method was used, where possible reflection and shielding were taken into account by a Ground Space Index based on building density. The methodology has been developed from the one described by Ögren and Barregard (2016), which was validated against the full Nordic prediction method modelled with SoundPlan and showed coherent estimates.	Ögren M, Barregard L. Road traffic noise exposure in Gothenburg1975-2010. PLoS One. 2016;11:e015532.
PPS	Yearly average road traffic flows, speed and percentage of heavy vehicles were obtained from the environmental office of the municipality of Gothenburg and the traffic office of the municipality of Mölndal. The traffic flow estimations were based on measurements for all major and medium links but used a standard default flow for very small streets. Terrain data and building footprints were obtained from Lantmäteriet and road links from the Swedish National Traffic Administration. Noise barriers of at least 2 m height and 100 m length were also included, and earth berms were included in the terrain model. To save calculation time and reduce demands on detailed input data a simplified methodology was used for multiple reflections in dense urban areas.	Ögren M, Barregard L. Road traffic noise exposure in Gothenburg1975-2010. PLoS One. 2016;11:e015532.
MDC	Estimated for the years 1990, 2000 and 2010, using the Nordic Prediction Method implemented in SoundPLAN (version 8.0, SoundPLAN Nord ApS). Input variables included geocode, information on annual average daily traffic for all road links in Malmö municipality, distribution of light/heavy traffic, signposted travel speed and road type and polygons for all buildings in Malmö. All road traffic sources within 1000m from the receivers were included. Traffic data were retrieved from a regional emission database (Rittner et al. 2020). The screening effects from buildings were included and ground softness considered. The parameter setting in the models were set to allow 2 reflections and receivers placed at 2m height.	Rittner R, Gustafsson S, Spanne M, Malmqvist E. Particle concentrations, dispersion modelling and evaluation in southern Sweden, SN Applied Sciences 2020;2:1013.

Table S3. Distribution of baseline categorical occupational noise exposure.

	Noise category				
Cohort	**<70 dB(A) n/(%)**	**70-74 dB(A) n/(%)**	**75-79 dB(A) n/(%)**	**80-84 dB(A) n/(%)**	**≥85 dB(A) n/(%)**
DCH	28,794 (60.9)	10,419 (22.0)	4,183 (8.8)	1,827 (3.9)	2,087 (4.4)
SNAC-K	916 (79.2)	129 (11.2)	68 (5.9)	39 (3.4)	5 (0.4)
SALT	3,959 (67.2)	831 (14.1)	505 (8.6)	541 (9.2)	55 (0.9)
MDC	13,448 (69.5)	2,733 (14.1)	1617 (8.4)	927 (4.8)	625 (3.2)
PPS	1,928 (41.2)	615 (13.1)	692 (14.8)	811 (17.3)	635 (13.6)
TOTAL	49,045 (62.6)	14,727 (18.7)	7,065 (9.1)	4,145 (5.3)	3,407 (4.4)

Table S4. Association between baseline occupational noise exposure and stroke incidence with additional adjustments.

	Model 3[a]	Model 3[b] plus road traffic noise	Model 3[c] plus BMI	Model 3[d] removal of PPS cohort	Model 3[d] removal of DCH cohort
		HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Occupational noise, all strokes					
<70 dB(A)	Reference	Reference	Reference	Reference	Reference
70-74 dB(A)	1.01 (0.95-1.07)	0.98 (0.92-1.05)	1.00 (0.94-1.06)	0.99 (0.93-1.05)	1.07 (0.96-1.18)
75-79 dB(A)	1.02 (0.94-1.10)	1.00 (0.91-1.09)	1.01 (0.93-1.09)	1.02 (0.94-1.11)	1.02 (0.91-1.15)
80-84 dB(A)	1.00 (0.91-1.10)	0.96 (0.85-1.08)	0.99 (0.90-1.09)	1.00 (0.89-1.12)	0.97 (0.86-1.11)
≥85 dB(A)	1.01 (0.91-1.12)	1.04 (0.92-1.17)	1.00 (0.90-1.10)	1.07 (0.95-1.20)	0.94 (0.80-1.09)
Occupational noise, ischaemic strokes					
<70 dB(A)	Reference	Reference	Reference	Reference	Reference
70-74 dB(A)	1.03 (0.95-1.12)	1.01 (0.92-1.10)	1.02 (0.94-1.11)	1.00 (0.92-1.10)	1.10 (0.98-1.23)
75-79 dB(A)	1.08 (0.98-1.20)	1.08 (0.96-1.21)	1.07 (0.97-1.19)	1.08 (0.96-1.20)	1.11 (0.97-1.27)
80-84 dB(A)	1.09 (0.97-1.24)	1.09 (0.94-1.26)	1.08 (0.95-1.22)	1.10 (0.95-1.27)	1.04 (0.90-1.21)
≥85 dB(A)	1.06 (0.92-1.21)	1.09 (0.92-1.28)	1.04 (0.91-1.19)	1.11 (0.94-1.30)	1.04 (0.87-1.25)

HR: Hazard Ratio; 95% CI: 95% Confidence Interval.

[a] Adjusted for age, sex, and calendar year at baseline (5-year periods), educational level (low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), smoking status (never, former, current), and physical activity (low, medium, high).

[b] Adjusted for age, sex, and calendar year at baseline (5-year periods), educational level (low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), smoking status (never, former, current), physical activity (low, medium, high), and adjustment for road traffic noise (1 year-average) among those with no missing address/exposure history (N=71,628).

[c] Adjusted for age, sex, and calendar year at baseline (5-year periods), educational level (low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), smoking status (never, former, current), physical activity (low, medium, high), and BMI.

[d] Adjusted for age, sex, and calendar year at baseline (5-year periods), educational level (low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), smoking status (never, former, current), and physical activity (low, medium, high).

Table S5. Association between baseline occupational noise exposure and stroke incidence in each cohort.

	DCH		SNAC-K		SALT		MDC		PPS	
	N cases	Model 3[a] HR (95% CI)	N cases	Model 3[a] HR (95% CI)	N cases	Model 3[a] HR (95% CI)	N cases	Model 3[a] HR (95% CI)	N cases	Model 3[a] HR (95% CI)
Occupational noise, all strokes										
<70 dB(A)	2568	Reference	96	Reference	351	Reference	1072	Reference	439	Reference
70-74 dB(A)	936	0.97 (0.89-1.04)	12	0.78 (0.42-1.46)	69	0.91 (0.70-1.19)	272	1.07 (0.93-1.23)	166	1.19 (0.99-1.43)
75-79 dB(A)	437	1.00 (0.90-1.11)	9	1.66 (0.81-3.40)	60	0.92 (0.69-1.22)	153	1.05 (0.88-1.26)	159	1.03 (0.84-1.25)
≥80 dB(A)	434	1.05 (0.94-1.16)	3	0.50 (0.15-1.65)	44	0.68 (0.49-0.95)	175	1.10 (0.92-1.31)	322	0.98 (0.83-1.15)

HR: Hazard Ratio; 95% CI: 95% Confidence Interval.

[a] Adjusted for age, sex, and calendar year at baseline (5-year periods), education level (low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), smoking status (never, former, current), and physical activity (low, medium, high).

Figure S1. Directed acyclic graph on covariates for assessment of the direct effect of occupational noise for development of stroke.

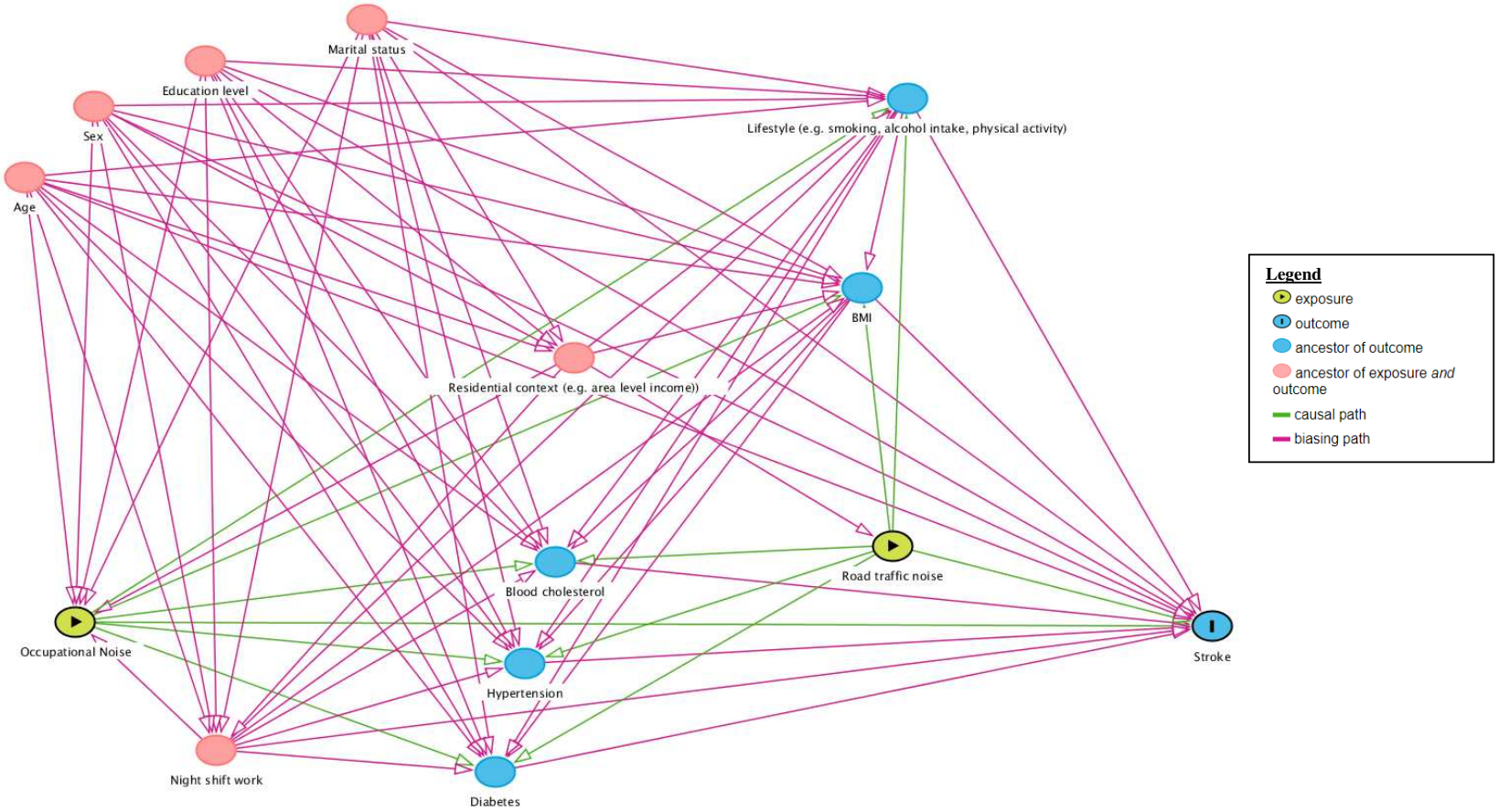

Figure S2. Selection of cohort participants.