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## Supplemental Material

# Long-Term Exposure to Transportation Noise and Risk of Incident Stroke: A Pooled Study of Nine Scandinavian Cohorts

Nina Roswall, Andrei Pyko, Mikael Ögren, Anna Oudin, Annika Rosengren, Anton Lager, Aslak H. Poulsen, Charlotta Eriksson, David Segersson, Debora Rizzuto, Eva M. Andersson, Gunn Marit Aasvang, Gunnar Engström, Jeanette T. Jørgensen, Jenny Selander, Jesper H. Christensen, Jesse Thacher, Karin Leander, Kim Overvad, Kristina Eneroth, Kristoffer Mattisson, Lars Barregård, Leo Stockfelt, Maria Albin, Matthias Ketzel, Mette K. Simonsen, Mårten Spanne, Ole Raaschou-Nielsen, Patrik K.E. Magnusson, Pekka Tiittanen, Peter Molnar, Petter Ljungman, Timo Lanki, Youn-Hee Lim, Zorana J. Andersen, Göran Pershagen, and Mette Sørensen

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**Figure S2.** Association between BMI and smoking intensity and risk for incident stroke in models adjusted for age, sex, calendar-year, educational level, marital status, area-income, and other noise sources. The curves were calculated using smoothed splines with four degrees of freedom including 95% confidence intervals (dotted curves).

**Figure S3.** Distribution of exposure to road traffic noise among all (exposures <40 dB set to 40 dB) (a), railway noise among people exposed (i.e. with exposure >40 dB) (b), and aircraft noise among people exposed (i.e. with an exposure >40 dB) (c) 5 years preceding baseline. For railway noise 76% of the population were exposed to <40 dB and for aircraft noise 95% of the population were exposed to ≤40 dB.

## Supplementary files

*Supplementary tables*

**Table S1 Detailed information on the cohorts included in the present study**

| 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. End of follow-up for stroke was 31 Dec 2016. | 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 |
| **DNC** | The Danish Nurse Cohort (DNC) was initiated by sending questionnaires to the members of the Danish Nurse Organization in 1993 and 1999. Among 33,704 eligible female nurses aged 44-93 years who either worked or were retired in 1993 or 1999, 28,731 participants (85.2%) were included in the DNC. Upon enrolment, participants answered a comprehensive questionnaire on body mass index (BMI), lifestyle factors (smoking, alcohol consumption, physical activity, and dietary habits), self-reported diseases and reproductive health, and working conditions. End of follow-up for stroke was 31 Dec 2014. | Hundrup, Yrsa A., et al. Cohort profile: the Danish nurse cohort. Int J Epidemiol 2012; 41:1241-47. | The Danish Council for Independent Research (DFF-4183-00353). |
| **SDPP**[a] | The Stockholm Diabetes Preventive Program (SDPP) is a population-based prospective study aimed at investigating the aetiology of Type 2 diabetes and developing prevention strategies. It includes 7,949 subjects aged 35-54 years at recruitment 1992-1998. Study subjects resided in five municipalities in Stockholm County and were followed up 2002-2007 as well as 2014-2017. At the health examinations, extensive questionnaires were completed on lifestyle factors, health status, socioeconomic characteristics and psychosocial conditions. In addition, measurements were performed of weight, height, hip and waist circumference as well as | Eriksson AK, Ekbom A, Granath F, et al. Psychological distress and risk of pre-diabetes and Type 2 diabetes in a prospective study of Swedish middle-aged men and women. Diabet Med 2008;25:834–42. | Swedish Environmental Protection Agency, the Swedish Council for Health, Working Life and Social Research and the Swedish Heart-Lung Foundation. The SDPP cohort was additionally funded by the Stockholm County Council, the Swedish Research Council, the Swedish Diabetes Association and Novo Nordisk Scandinavia. |

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|---|---|---|---|
| | of blood pressure and oral glucose tolerance. End of follow-up for stroke was 31 Dec 2011. | | |
| **SIXTY**[a] | The SIXTY cohort is based on a random sample of every third man and woman living in Stockholm County, who were born in 1937 and 1938. A total of 4,232 subjects were recruited 1997-1999 to investigate risk factors for cardiovascular disease. People were 59-61 years at enrolment. Measurements of anthropometric indices and blood pressure were made at recruitment and fasting blood samples were collected. In addition, a comprehensive questionnaire was completed, including information on socioeconomic, medical and life-style factors. End of follow-up for stroke was 31 Dec 2016. | Wändell PE, Wajngot A, de Faire U, et al. Increased prevalence of diabetes among immigrants from non-European countries in 60-year-old men and women in Sweden. Diabetes Metab 2007;33:30–6. | Swedish Environmental Protection Agency, the Swedish Council for Health, Working Life and Social Research and the Swedish Heart-Lung Foundation. The SIXTY cohort was additionally funded by the Stockholm County Council and the Swedish Research Council. |
| **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. Those 7,043 who resided in Stockholm County at recruitment are included in the present project. People were 42-97 years at enrolment. 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. End of follow-up for stroke was 31 Dec 2017. | Lichtenstein P, Sullivan PF, Cnattingius S, et al. The Swedish Twin Registry in the third millennium: an update. Twin Res Hum Genet 2006;9:875–82. | 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. End of follow-up for stroke was 31 Dec 2016. | 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. |

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|---|---|---|---|
| **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. People were 46-55 years at enrolment. 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 medication, psychological stress, prevalent diabetes mellitus and family history of coronary events). End of follow-up for stroke was 31 Dec 2011. | 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. |
| **GOT-MONICA** | The GOT-MONICA cohort is part of the “Multinational Monitoring of Trends and Determinants in Cardiovascular Diseases” (MONICA) project. A random selection of residents in Gothenburg aged 25–64 years at the time of inclusion were recruited in the years 1985, 1990, and 1995 (participation rates: 63%, 69%, and 72%). The participants filled out questionnaires on e.g. smoking habits, physical activity, hypertensive medication, psychological stress, marital status, and were examined by health care professionals (e.g. blood pressures, height and weight). End of follow-up for stroke was 31 Dec 2011. | Wilhelmsen L, Johansson S, Rosengren S et al. Risk factors for cardiovascular disease during the period 1985–1995 in Goteborg, Sweden. The GOT-MONICA Project. J. Intern Med, 1997;242:199-211. | The Swedish Medical Research Council, the Swedish Heart and Lung Foundation, the Ingabritt and Arne Lundberg Research Fund, the Göteborg Medical Society and the Sahlgrenska University Hospital Funds |
| **MDC** | The Malmö Diet and Cancer (MDC) study is a population based prospective cohort study. People were enrolled into the cohort 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. People were 44-73 years at enrolment. 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. End of follow-up for stroke was 31 Dec 2016. | 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<br>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 |
| **DNC** | Same method as for DCH. | |
| **CEANS (SDPP, SIXTY, 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, GOT-MONICA** | 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 Detailed information on estimation of air pollution for all participating cohorts**

| Cohort | Air pollution estimation | Key references |
|---|---|---|
| **DCH** | In the DCH cohort, we used the DEHM-UBM-AirGIS modelling system to calculate $PM_{2.5}$ and $NO_2$ at all Danish addresses for the years 2000, 2010 and 2015, which was then extrapolated to yearly means for each address, based on changes in yearly urban background levels. This multi-scale dispersion modelling system calculates air pollutants at each address as the sum of: a) $PM_{2.5}/NO_2$ from the nearest street, calculated based on traffic, car fleet emission factors, streets and building geometry, and meteorology; b) urban background, calculated based on city dimensions, emission density, and heights of buildings; and c) regional background, calculated based on all emissions in the northern hemisphere. | Khan J, Kakosimos K, Raaschou-Nielsen O, et al. Development and performance evaluation of new AirGIS – A GIS based air pollution and human exposure modelling system. Atmos Environ 2019;198:102-121.<br>Ketzel M, Berkowicz R, Hvidberg M, Jensen SS and Raaschou-Nielsen O. Evaluation of AirGIS - a GIS-based air pollution and human exposure modelling system. Int J Environ Pollution 2011;47:226–238.<br>www.au.dk/AirGIS |
| **DNC** | Same method as for DCH. | |
| **CEANS (SDPP, SIXTY, SALT, SNAC-K)** | In the Stockholm County cohorts, a high-resolution Gaussian dispersion model was used to estimate individual residential levels of $PM_{2.5}$ and $NO_x/NO_2$ using local emission inventories every fifth year from 1990 and onwards. The emission inventory contains detailed information on local emissions from road and ferry traffic, industrial areas and households. Meteorological input to the modelling includes measurements of wind velocity and direction, solar radiation and temperature. Further, a street canyon contribution is added for addresses in the most polluted street segments of the inner city of Stockholm with multi-storey houses on both sides. Annual averaged long-range contributions were added to the locally modelled concentrations based on continuous measurements at regional background monitoring stations. | Segersson D, Eneroth K, Gidhagen L, et al. Health impact of $PM_{10}$, $PM_{2.5}$ and black carbon exposure due to different source sectors in Stockholm, Gothenburg and Umea, Sweden. Int J Environ Res Public Health 2017;14:E742.<br>Ljungman PLS, Andersson N, Stockfelt L, et al. Long-Term Exposure to Particulate Air Pollution, Black Carbon, and Their Source Components in Relation to Ischemic Heart Disease and Stroke. Environ Health Perspect 2019;127:107012 |
| **PPS** | The exposure assessment was performed similarly for Gothenburg and Stockholm as part of the Swedish Clean air and Climate Research program (SCAC). For Gothenburg, high-resolution dispersion modeling of source-specific particulate matter <2.5 µm ($PM_{2.5}$), and nitrogen oxides ($NO_X$ – converted to $NO_2$) was performed over an area of 93 × 112 km for the years 1990, 2000 and 2011. Emission inventories were compiled using local and regional bottom-up inventories provided by the municipality, and supplemented to be consistent for the whole time-period. Intervening years were interpolated so that each participant could be assigned annual residential air pollutant exposures. For $NO_2$ additional data were available from dispersion modelling for the period before 1990, as described in Stockfelt et al. 2015. | Segersson D, Eneroth K, Gidhagen L et al. Health impact of $PM_{10}$, $PM_{2.5}$ and black carbon exposure due to different source sectors in Stockholm, Gothenburg and Umea, Sweden. Int J Environ Res Public Health, 2017;14:E742.<br>Stockfelt L, Andersson EM, Molnár P, et al. Long-term effects of total and source-specific particulate air pollution on incident cardiovascular disease in Gothenburg, Sweden. Environ Res. 2017;158:61-71. |
| **GOT-MONICA** | Same method as for PPS. | |

| | | |
|---|---|---|
| **MDC** | Air pollutants ($PM_{2.5}$, and nitrogen oxides ($NO_X$) – converted to $NO_2$) were modelled using EnviMan (Opsis AB, Sweden) by the Environmental Department, City of Malmö, using a Gaussian dispersion model (AERMOD) combined with an emission database for the county of Scania in Sweden. The 18 × 18 km modelling area covered the city of Malmö and the closest surroundings. Separate emission databases were compiled for 1992, 2000 and 2011 using existing local and regional bottom-up inventories provided by the municipality, and then supplemented to be consistent for the whole area and time-period. Yearly mean concentrations were stored as grids with a spatial resolution of 50 m × 50 m. The years in between the modelled years were interpolated linearly with adjustment for year-to-year variations in the local meteorology using a ventilation factor estimated from calculations over the whole time-period, and exposure for the years 1990 and 1991 extrapolated. Exposure data was combined with geocoded addresses to assign each participant annual residential exposures. | Hasslöf H, Molnár P, Andersson EM, et al. Long-term exposure to air pollution and atherosclerosis in the carotid arteries in the Malmö Diet and Cancer Cohort. Environ Res 2020:110095 |

**Table S4** Results from testing the proportional hazard assumption by a correlation test between scaled Schoenfeld residuals and the rank order of event time

| **Variable** | **$Chi^2$** | **p-value** |
|---|---|---|
| Road traffic noise, 5-year | 6.33 | 0.012 |
| Railway noise, 5-year | 0.66 | 0.42 |
| Aircraft noise, 5-year | 0.53 | 0.77 |
| Sex | 61.4 | <0.0001 |
| Calendar-year | 16.5 | 0.036 |
| Education | 17.6 | 0.0002 |
| Marital status | 3.69 | 0.054 |
| Area-level income | 1.44 | 0.70 |
| Smoking status | 82.6 | <0.0001 |
| Physical activity | 28.1 | <0.0001 |
| BMI < 22 $kg/m^2$ | 1.94 | 0.16 |
| BMI ≥ 22 $kg/m^2$ | 12.4 | 0.0004 |

| **Table S5** Correlation matrix between traffic noise exposures and air pollution. Pearson correlation coefficients | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | **1-year road traffic noise exposure** | **5-year road traffic noise exposure** | **1-year railway noise exposure[a]** | **5-year railway noise exposure[a]** | **1-year $PM_{2.5}$** | **5-year $PM_{2.5}$** | **1-year $NO_2$** | **5-year $NO_2$** |
| **1-year road noise exposure** | - | | | | | | | |
| **5-year road noise exposure** | 0.96 | - | | | | | | |
| **1-year railway noise exposure[a]** | 0.11 | 0.11 | - | | | | | |
| **5-year railway noise exposure[a]** | 0.11 | 0.12 | 0.95 | - | | | | |
| **1-y $PM_{2.5}$** | 0.38 | 0.37 | 0.05 | 0.05 | - | | | |
| **5-y $PM_{2.5}$** | 0.39 | 0.39 | 0.04 | 0.05 | 0.98 | - | | |
| **1-y $NO_2$** | 0.64 | 0.63 | 0.10 | 0.11 | 0.46 | 0.43 | - | |
| **5-y $NO_2$** | 0.63 | 0.65 | 0.10 | 0.11 | 0.40 | 0.39 | 0.98 | - |

[a] Among all participants, including those exposed to ≤ 40 dB

**Table S6** Categorical association between 5-year road and railway noise exposure and stroke incidence.

| | N cases | Model 1[a] HR (95% CI) | Model 2[b] HR (95% CI) | Model 3[c] HR (95% CI) | Model 4[d] HR (95% CI) |
|---|---|---|---|---|---|
| **Road traffic noise, $L_{den}$** | | | | | |
| 40-<45 dB | 1,042 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
| 45-<50 dB | 1,476 | 1.06 (0.98-1.15) | 1.06 (0.98-1.15) | 1.05 (0.97-1.14) | 1.07 (0.99-1.17) |
| 50-<55 dB | 2,347 | 1.06 (0.98-1.14) | 1.05 (0.97-1.13) | 1.05 (0.97-1.13) | 1.06 (0.97-1.14) |
| 55-<60 dB | 2,483 | 1.09 (1.01-1.17) | 1.07 (0.99-1.15) | 1.06 (0.98-1.15) | 1.07 (0.98-1.16) |
| 60-<65 dB | 2,127 | 1.15 (1.06-1.24) | 1.12 (1.03-1.21) | 1.10 (1.02-1.19) | 1.13 (1.04-1.23) |
| 65+ dB | 1,581 | 1.21 (1.11-1.31) | 1.17 (1.07-1.27) | 1.14 (1.05-1.24) | 1.19 (1.08-1.30) |
| **Railway noise, $L_{den}$** | | | | | |
| 40-<45 dB | 8,842 | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) | 1.00 (ref.) |
| 45-<50 dB | 811 | 1.05 (0.98-1.13) | 1.03 (0.96-1.11) | 1.02 (0.95-1.10) | 1.04 (0.96-1.12) |
| 50-<55 dB | 661 | 1.03 (0.95-1.12) | 1.00 (0.92-1.08) | 0.99 (0.91-1.07) | 1.01 (0.93-1.09) |
| 55-<60 dB | 399 | 0.98 (0.89-1.08) | 0.96 (0.86-1.06) | 0.95 (0.85-1.05) | 0.98 (0.88-1.09) |
| 60-<65 dB | 205 | 1.08 (0.95-1.24) | 1.05 (0.91-1.21) | 1.04 (0.90-1.20) | 1.04 (0.90-1.20) |
| 65+ dB | 138 | 1.00 (0.85-1.18) | 0.96 (0.81-1.14) | 0.95 (0.81-1.13) | 0.97 (0.81-1.15) |

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

[a]Adjusted for age (by design), cohort (strata), sex (strata) and calendar year (in 5-year periods)

[b]Model 1 plus adjustment for educational level (strata, low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), other noise sources (road/rail, continuous), railway noise (yes/no) (in models on road traffic noise only), aircraft noise (≤40 dB; 40-50 dB, >50 dB; for the 3 cohorts without aircraft noise, noise information all cohort members were assigned to the ≤40 dB group)

[c]Model 2 plus adjustment for smoking status (strata, never, former, current), leisure-time physical activity (strata, low, medium, high), BMI (kg/$m^2$, continuous)

[d]Model 2 plus adjustment for time-weighted $PM_{2.5}$ exposure (in the same time-window as noise). Due to holes in the $PM_{2.5}$ exposure history this analysis is based on the following number of cases in each of the exposure categories: road traffic noise 40-45 dB: 985 cases, 45-50 dB: 1,385 cases, 50-55 dB: 2,200 cases, 55-60 dB: 2,307 cases, 60-65 dB: 1,995 cases, >65: 1,477 cases; and railway noise 40-45 dB: 8,256 cases, 45-50 dB: 762, 50-55 dB: 625 cases, 55-60 dB: 384 cases, 60-65 dB: 192 cases, >65: 130 cases.

| **Table S7** Association between 5-year exposure to traffic noise (per 10 dB) and stroke incidence. | | | | | | |
|---|---|---|---|---|---|---|
| | Persons with information on smoking intensity and alcohol information | | Persons with information on 5-year mean exposure to $NO_2$ | | Persons with information on 5-year mean exposure to $PM_{2.5}$ | |
| | Model 3 [a] | Model 3 [a] plus adjustment for smoking intensity and alcohol [b] | Model 2 [c] | Model 2 [c] plus adjustment for $NO_2$ | Model 2 [c] | Model 4 [d] plus adjustment for $PM_{2.5}$ |
| | HR (95 % CI) | HR (95 % CI) | HR (95 % CI) | HR (95 % CI) | HR (95 % CI) | HR (95 % CI) |
| **Road traffic noise, $L_{den}$** | | | | | | |
| N, cases | 9,493 | 9,493 | 10,558 | 10,558 | 10,349 | 10,349 |
| 5-year exposure, per 10 dB | 1.04 (1.01-1.07) | 1.04 (1.01-1.07) | 1.06 (1.03-1.09) | 1.04 (1.00-1.07) | 1.06 (1.03-1.08) | 1.06 (1.03-1.09) |
| | | | | | | |
| **Railway noise, $L_{den}$** | | | | | | |
| N, cases | 9,493 | 9,493 | 10,558 | 10,558 | 10,349 | 10,349 |
| 5-year exposure, per 10 dB | 0.95 (0.91-1.00) | 0.95 (0.91-1.00) | 0.97 (0.91-1.02) | 0.97 (0.91-1.01) | 0.96 (0.91-1.01) | 0.96 (0.91-1.01) |

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

[a]Model 3: adjusted for age, cohort (strata), sex (strata), calendar year (in 5-year periods), educational level (strata, low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), other noise sources (road/rail, continuous), railway noise (yes/no), aircraft noise (≤40 dB; 40-50 dB, >50 dB; for the 3 cohorts without aircraft noise information all cohort members were assigned to the ≤40 dB group), smoking status (strata, never, former, current), physical activity (strata, low, medium, high), and BMI ($kg/m^2$, continuous)

[b]Model 3 plus adjustment for smoking intensity (g/day, continuous) and alcohol consumption (daily, weekly, seldom, never).

[c]Model 2: adjusted for age, cohort (strata), sex (strata), calendar year (5-year periods), educational level (strata, low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), and other noise source (road, railway and aircraft noise )

[d]Model 4: Model 2 plus adjustment for 5-year time-weighted $PM_{2.5}$ exposure (same HRs as shown in Table 3)

| **Table S8** Association between 5-year time-weighted traffic noise (per 10 dB) and stroke incidence, per cohort. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | **DCH** | **DNC** | **SDPP** | **Sixty** | **SNAC-K** | **SALT** | **MDC** | **PPS** | **GOT-MONICA** |
| **All strokes** | | | | | | | | | |
| Road traffic noise, $L_{den}$ Model 2[a] | | | | | | | | | |
| N cases | 5,048 | 1,381 | 157 | 344 | 384 | 587 | 2,045 | 1,012 | 98 |
| HR (95% CI), per 10 dB | 1.07 (1.03-1.11) | 1.06 (0.99-1.13) | 1.10 (0.84-1.45) | 1.11 (0.96-1.28) | 0.97 (0.83-1.13) | 0.95 (0.85-1.06) | 1.01 (0.95-1.07) | 1.07 (0.98-1.18) | 0.94 (0.71-1.24) |
| Railway noise, $L_{den}$ Model 2[a] | | | | | | | | | |
| HR (95% CI), per 10 dB | 0.99 (0.92-1.07) | 0.99 (0.84-1.16) | 0.68 (0.38-1.21) | 0.79 (0.60-1.04) | 1.00 (0.76-1.31) | 1.01 (0.85-1.19) | 0.94 (0.86-1.02) | 0.88 (0.67-1.16) | 0.75 (0.26-2.17) |
| Aircraft noise, HR (95% CI), $L_{den}$ Model 2[a] | | | | | | | | | |
| ≤ 40 dB | 1 | 1 | 1 | 1 | 1 | 1 | NA | NA | NA |
| 40.1-50 dB | 0.96 (0.66-1.41) | 1.04 (0.39-2.76) | 0.85 (0.51-1.43) | 1.06 (0.76-1.48) | 1.19 (0.90-1.58) | 1.16 (0.92-1.48) | NA | NA | NA |
| ≥ 50 dB | 1.02 (0.72-1.43) | 1.30 (0.75-2.24) | 0.92 (0.46-1.84) | 1.47 (0.86-2.53) | 0.85 (0.60-1.20) | 0.88 (0.54-1.41) | NA | NA | NA |

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

[a]Adjusted for age (by design), sex (strata), calendar year (in 5-year periods), educational level (strata, low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), other noise sources (road/rail, continuous), railway noise (yes/no); aircraft noise (≤40 dB; 40-50 dB, >50 dB; for the 3 cohorts without aircraft noise information all cohort members were assigned to the ≤40 dB group).

**Table S9** Association between 5-year exposure to road traffic noise (per 10 dB) and stroke incidence after one-by-one exclusion of each cohort

| Cohort excluded | N cases | Model 2[a] HR (95% CI), per 10 dB |
|---|---|---|
| DCH | 6,008 | 1.03 (1.00-1.07) |
| MKC | 9,011 | 1.06 (1.03-1.09) |
| DNC | 9,675 | 1.05 (1.03-1.08) |
| SDPP | 10,899 | 1.05 (1.03-1.08) |
| SALT | 10,469 | 1.06 (1.03-1.09) |
| SIXTY | 10,712 | 1.05 (1.03-1.08) |
| SNAC-K | 10,672 | 1.06 (1.03-1.09) |
| GOT-MONICA | 10,958 | 1.06 (1.03-1.08) |
| PPS | 10,044 | 1.05 (1.02-1.08) |

[a] Adjusted for age, cohort (strata), sex (strata), calendar-year (in 5-year periods), educational level (strata, low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), railway noise (continuous), railway noise (yes/no), aircraft noise (≤40 dB; 40-50 dB, >50 dB; for the 3 cohorts without aircraft noise information all cohort members were assigned to the ≤40 dB group)

**Table S10** Interactions between 5-year road traffic noise exposure (per 10 dB) and demographic and lifestyle-factors in relation to stroke incidence

| | Road traffic noise | | |
|---|---|---|---|
| | N cases | Model 2[a,b] HR (95% CI) | P for interaction[c] |
| **Sex** | | | |
| Male | 5,647 | 1.050 (1.014-1.087) | 0.69 |
| Female | 5,409 | 1.060 (1.024-1.097) | |
| **BMI** | | | |
| < 25 | 4,924 | 1.057 (1.023-1.093) | 0.76 |
| >= 25 | 6,132 | 1.050 (1.012-1.089) | |
| **Physical activity** | | | |
| Low | 5,454 | 1.068 (1.031-1.106) | 0.30 |
| Medium | 3,188 | 1.054 (1.008-1.102) | |
| High | 2,414 | 1.017 (0.964-1.072) | |
| **Smoking status** | | | |
| Never | 3,571 | 1.034 (0.990-1.079) | 0.21 |
| Former | 3,304 | 1.029 (0.985-1.075) | |
| Current | 4,181 | 1.078 (1.036-1.121) | |
| **Educational level** | | | |
| Low | 4,317 | 1.049 (1.009-1.091) | 0.59 |
| Medium | 5,023 | 1.049 (1.012-1.088) | |
| High | 1,716 | 1.085 (1.022-1.153) | |
| **Calendar year** | | | |
| Before 2005 | 4,410 | 1.065 (1.024-1.107) | 0.58 |
| 2005 or after | 6,646 | 1.050 (1.017-1.084) | |
| **$PM_{2.5}$ (5-year)** | | | |
| Low (<12.5 μg/m$^3$) | 5,226 | 1.035 (0.996-1.075) | 0.11 |
| High (>=12.5 μg/m$^3$) | 5,123 | 1.080 (1.041-1.120) | |

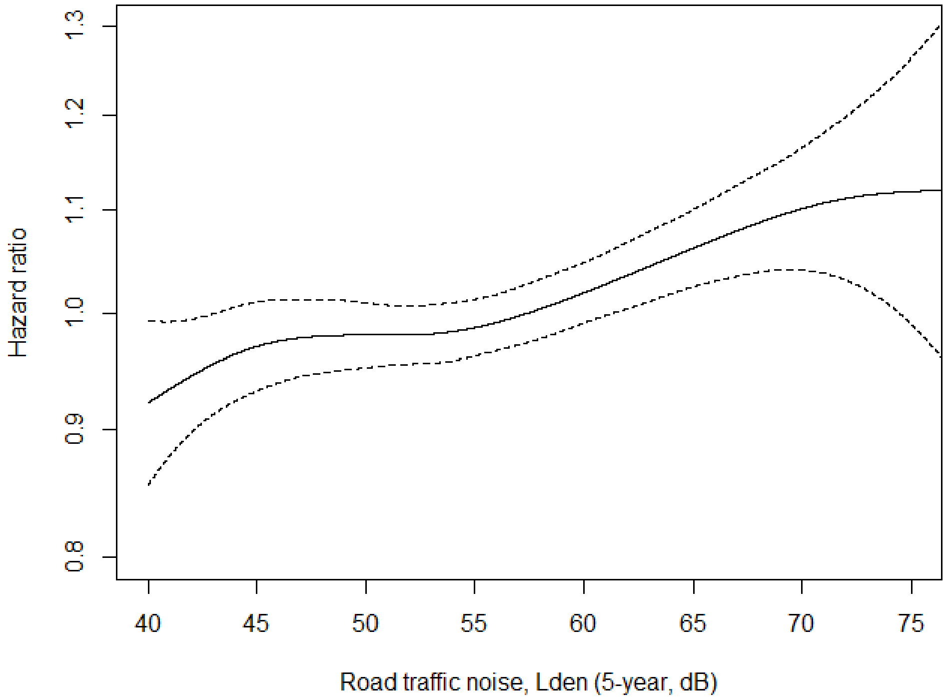
[a] Adjusted for age, cohort (strata), sex (strata) and calendar year (in 5-year periods), educational level (strata; low, medium, high), marital status (married/cohabiting, single), area-income (quartiles), and other noise sources (road and rail (continuous), railway noise (yes/no), aircraft noise (≤40 dB; 40-50 dB, >50 dB, for the 3 cohorts without aircraft noise information all cohort members were assigned to the ≤40 dB group)

[b] All analyses included an interaction term between the potential effect modifiers and the 5-year mean noise exposure

[c] Interaction tested by Wald test

*Supplementary figures*

**Figure S1** Association between 5-year road traffic and railway noise exposure and risk for incident stroke in models adjusted for age, sex, calendar-year, educational level, marital status, area-income, and other noise sources. The curves were calculated using smoothed splines with four degrees of freedom including 95% confidence intervals (dotted curves).



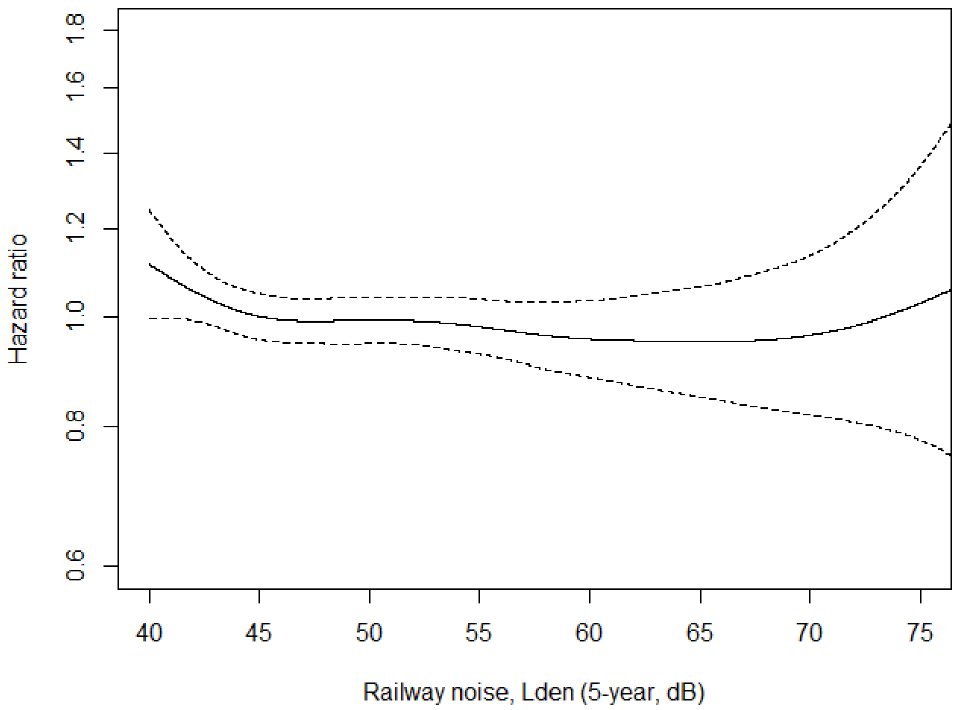



**Figure S2** Association between BMI and smoking intensity and risk for incident stroke in models adjusted for age, sex, calendar-year, educational level, marital status, area-income, and other noise sources. The curves were calculated using smoothed splines with four degrees of freedom including 95% confidence intervals (dotted curves).

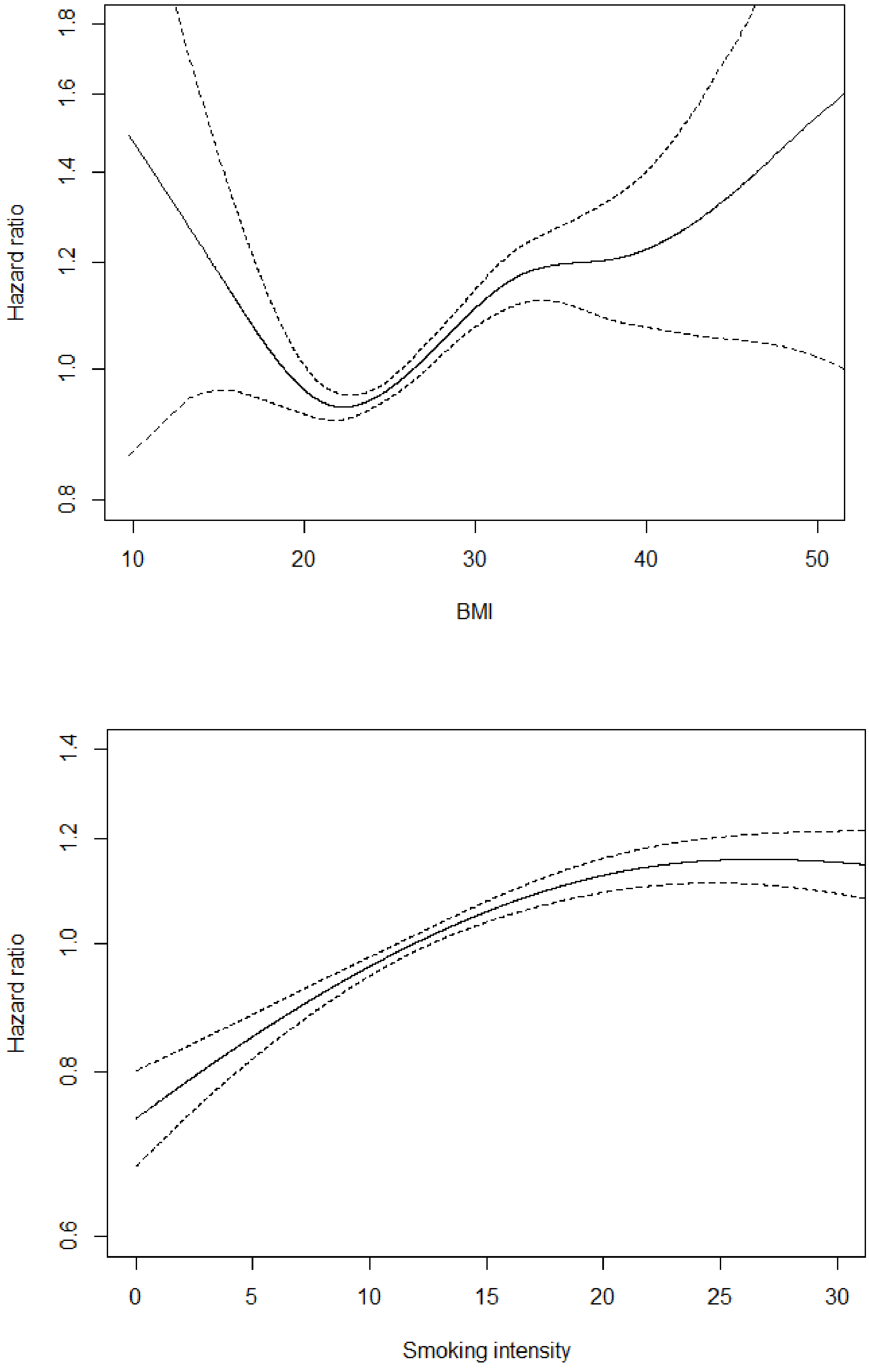
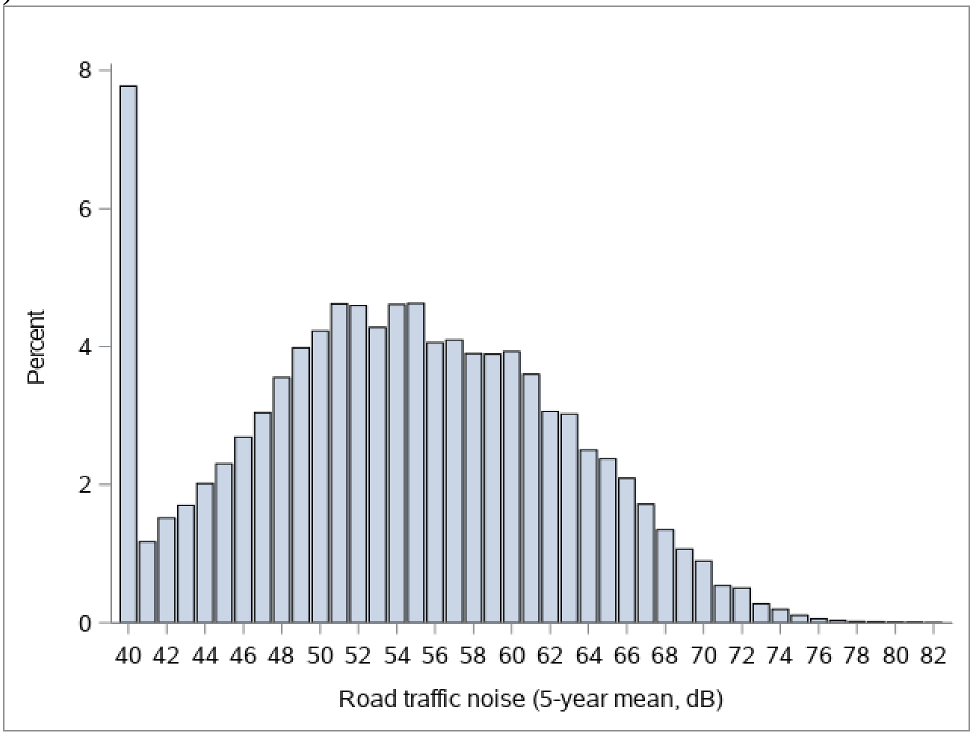
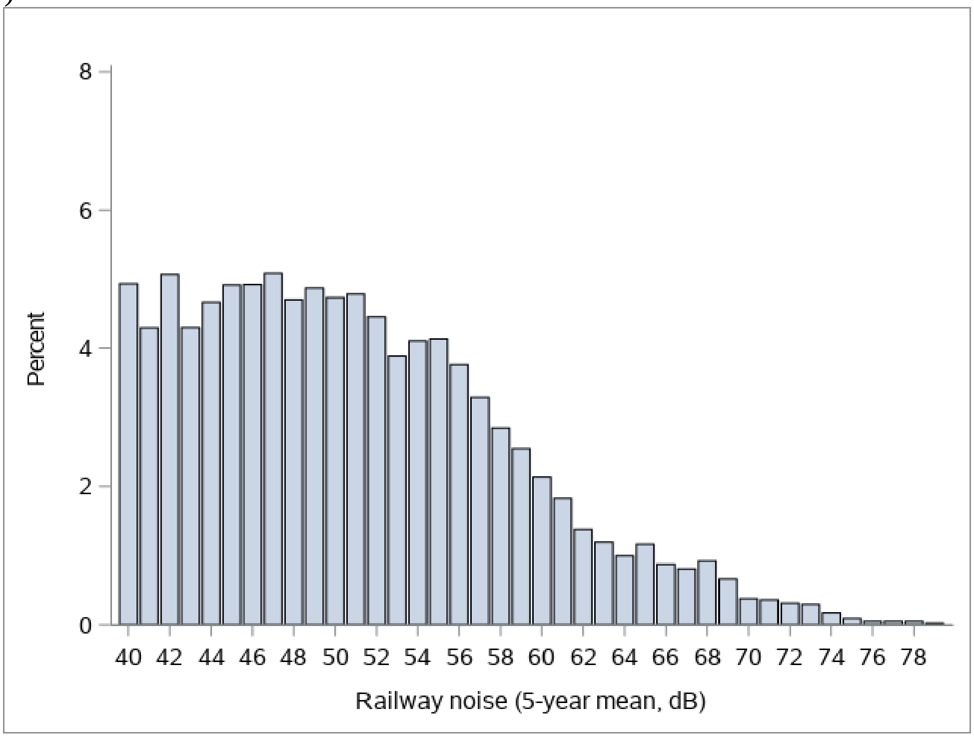


**Figure S3** Distribution of exposure to road traffic noise among all (exposures <40 dB set to 40 dB) (a), railway noise among people exposed (i.e. with exposure >40 dB) (b), and aircraft noise among people exposed (i.e. with an exposure >40 dB) (c) 5 years preceding baseline. For railway noise 76% of the population were exposed to <40 dB and for aircraft noise 95% of the population were exposed to ≤40 dB.

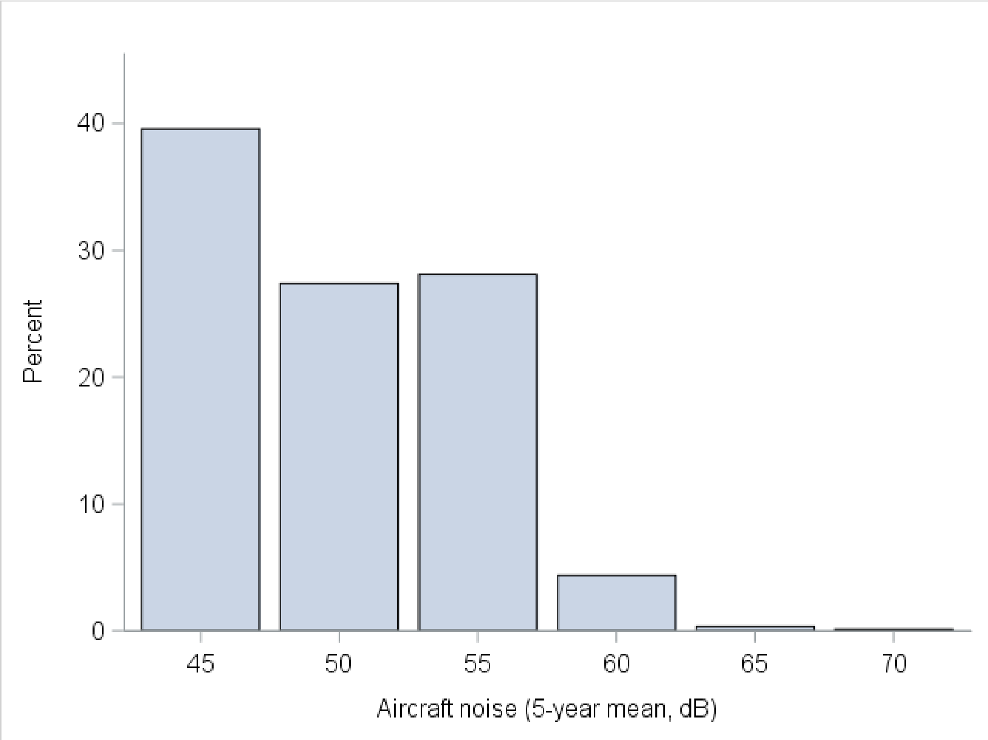
a)




b)



c)



40
30
20
10
0
Percent
45
50
55
60
65
70
Aircraft noise (5-year mean, dB)