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Long-term exposure to transportation noise and air pollution in relation to incident diabetes in the SAPALDIA study

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Abstract

Background: Epidemiological studies have inconsistently linked transportation noise and air pollution (AP) with diabetes risk. Most studies have considered single noise sources and/or AP, but none has investigated their mutually independent contributions to diabetes risk.

Methods: We investigated 2631 participants of the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA), without diabetes in 2002 and without change of residence between 2002 and 2011. Using questionnaire and biomarker data, incident diabetes cases were identified in 2011. Noise and AP exposures in 2001 were assigned to participants’ residences (annual average road, railway or aircraft noise level during day-evening-night (Lden), total night number of noise events, intermittency ratio (temporal variation as proportion of event-based noise level over total noise level) and nitrogen dioxide (NO2) levels. We applied mixed Poisson regression to estimate the relative risk (RR) of diabetes and their 95% confidence intervals (CI) in mutually-adjusted models.

Results: Diabetes incidence was 4.2%. Median [interquartile range (IQR)] road, railway, aircraft noise and NO2 were 54 (10) dB, 32 (11) dB, 30 (12) dB and 21 (15) μg/m³, respectively. Lden road and aircraft were associated with incident diabetes (respective RR: 1.35; 95% CI: 1.02–1.78 and 1.86; 95% CI: 0.96–3.59 per IQR) independently of Lden railway and...
NO\textsubscript{2} (which were not associated with diabetes risk) in mutually adjusted models. We observed stronger effects of Lden road among participants reporting poor sleep quality or sleeping with open windows.

**Conclusions:** Transportation noise may be more relevant than AP in the development of diabetes, potentially acting through noise-induced sleep disturbances.

**Key words:** Noise, transportation, air pollution, diabetes mellitus, sleep

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**Key Messages**

- This study examines the mutually independent association between transportation noise and air pollution, and incidence of diabetes in 2631 Swiss adults.
- Road traffic and aircraft noise were independently associated with diabetes risk.
- Individuals who slept with open windows or had poor sleep quality were more susceptible to road traffic noise.
- Neither railway noise nor NO\textsubscript{2} was associated with diabetes risk in this study.
- The findings imply a potentially more relevant role for transportation noise than air pollution in the development of diabetes.

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**Introduction**

Transportation noise and air pollution (AP) constitute common exposures contributing to global morbidity and mortality.\textsuperscript{1,2} Transportation noise sources commonly include road traffic, aircraft and railways, whereas nitrogen dioxide (NO\textsubscript{2}) and particulate matter < 2.5 um in diameter (PM\textsubscript{2.5}) are common markers of traffic-related AP.\textsuperscript{3} Both pollutant groups have been linked to cardio-metabolic phenotypes including cardiovascular diseases,\textsuperscript{3–5} obesity,\textsuperscript{6,7} insulin resistance or diabetes.\textsuperscript{8–10} Whereas AP has been shown by experimental\textsuperscript{11,12} and epidemiological studies\textsuperscript{13–15} to induce inflammation, leading to systemic reactions that may result in insulin resistance, noise could be stress-inducing due to catecholamine dysregulation\textsuperscript{16–18} and impact on glucose homeostasis through insulin resistance.\textsuperscript{19} Noise also induces sleep disturbances,\textsuperscript{20,21} which was linked to glucose dysregulation.\textsuperscript{22}

Epidemiological evidence linking these exposures with diabetes has been mixed. Studies have shown traffic-related AP to be inconsistently associated with diabetes risk.\textsuperscript{23–31} Compared with AP, epidemiological evidence on the impact of transportation noise on diabetes risk is sparse. Exposure to road traffic noise,\textsuperscript{32,33} and aircraft noise\textsuperscript{34} but not railway noise\textsuperscript{32} increased diabetes risk. Reported road traffic intensity was also associated with incident diabetes.\textsuperscript{35}

Transportation noise and AP may occur together, may confound each other\textsuperscript{36,37} and might share pathological effect pathways.\textsuperscript{17,18} Given the need for efficient intervention strategies, it is important to better understand their respective effects on population health. Research exploring the mutually independent associations of road traffic noise and AP with diabetes is limited.\textsuperscript{32,33,38}

Thus the present study aimed to investigate the independent effects of noise (road, aircraft and railway noise and specific noise characteristics like number and temporal variation of noise events), and of NO\textsubscript{2} on diabetes incidence.

**Methods**

**Study population**

This study includes participants of the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA) which is a population-based study that included 9651 adults in 1991 (SAP1) sampled from eight areas representing diverse characteristics of Switzerland. SAP1 focused on respiratory phenotypes, participants had interviews and health examinations\textsuperscript{39} and there was no information on participants’ diabetes status. In 2002 (SAP2), the study expanded into cardio-metabolic phenotypes, including 8047 participants who had interviews, health examination and blood sampling into a biobank for biomarkers (including glycosylated haemoglobin, HbA1c).\textsuperscript{40} In 2011 (SAP3), the study included 6088 participants and applied an extended SAP2 protocol. Ethical clearance was obtained from the ethics committees of the participating cantons and the Swiss National Ethics Committee.
Participants provided informed written consent before participating in any assessment of the SAPALDIA study. From the 6088 participants at SAP3, we excluded 309 participants with diagnosed diabetes at SAP2, defined by health questionnaire and HbA1c data. To limit misclassification in exposures and area-level covariates, we excluded 2363 participants for having changed their residence between SAP2 and SAP3 and 685 participants for lacking covariate information. We therefore included 2631 participants of SAP2 and SAP3 who were not diabetic at SAP2 and had the same residence between SAP2 and SAP3 and complete covariate data.

Identification of incident diabetes
At SAP2 and SAP3, participants answered questions concerning their health and medication use. HbA1c was measured in EDTA-buffered whole blood from both surveys using the ARK-RAY ADAMS A1c HA-8180V analyser (Menarini, Florence), based on high-performance liquid chromatography. This array performs optimally in clinical applications as it has minimal interference from alternate haemoglobin variants. HbA1c was measured in mmol/mol according to the International Federation of Clinical Chemistry and converted into percentage according to the National Glycohemoglobin Standardization Programme (NGSP). Participants were identified as incident diabetes cases if they were not diabetic at SAP2 but reported physician-diagnosed diabetes or taking diabetes medication (including insulin, metformin, thiazolidinedione, gliflozin, incretin mimetic, acarbose or their combinations) or had HbA1c ≥ 6.5%, at SAP3.

Assignment of transportation noise and AP exposures
In the framework of the SiRENE (Short and Long Term Effects of Transportation Noise Exposure) project, road traffic, aircraft and railway noise levels were calculated as annual noise levels using Swiss noise models as previously described. In 2001, exposures to road traffic, aircraft and railway noise at the most-exposed façade of the participants’ residential floors were assigned to the participants. Road noise was calculated using the SonROAD emission and Stl-86 propagation models. Aircraft noise was predicted using FLULA2 which performs a time-step simulation of individual flights, yielding maximum noise levels. Railway noise was calculated using the SonRAIL emission and SEMIBEL propagation models.

Noise exposure metrics were computed for each source including day (Lday; 07–23 h; dB), night (Lnight; 23–07 h; dB) and day-evening-night noise level with 5 dB and 10 dB penalties for evening (19–23 h) and night-time, respectively, (Lden, dB). The total number of noise events from any noise source standing out from the background noise during night-time (NEnight), and the intermittency ratio at night (IRnight; %, which is the ratio of the event-based noise level to the overall noise level for all noise sources combined) were also computed. Road, aircraft or railway noise levels were assigned respective left-truncated values of 35, 30 and 30 dB.

Annual mean residential outdoor NO2 levels were assigned to participants’ residences in 2001 using a combination of Gaussian dispersion (incorporating traffic, agricultural and industrial emission inventories) at a resolution of 200 m x 200 m, and land-use regression models (incorporating population, elevation, road length within 50- and 20-m buffers, number of apartments and buildings within 9 and 81 hectares, respectively), with the final hybrid model having an adjusted R² of 0.8. In 2010/11, using the same principle, area-specific hybrid models were used to model NO2 exposures to participants’ residences, with adjusted R² range of 0.5–0.9 across study areas. In 2000, PM2.5 was modelled to participants’ residences using similar Gaussian dispersion model as for NO2. Compared with PM2.5 which has more regional/homogeneous distribution, NO2 shows a steeper decay with distance from traffic, provides more local contrast and is therefore a better marker of near-road traffic-related air pollution. Our study therefore focused on six main exposures, namely Lden road, aircraft and railway, NEnight, IRnight, NO2, and applied PM2.5 and change in NO2 (between 2001 and 2010/11) towards sensitivity analyses.

Measurement of potential confounders/ effect modifiers
Relevant variables were extracted from data provided by the participants in both surveys. Selected potential confounders at SAP2 include: age (continuous); sex (male/female); educational attainment (≤ 9 years/> 9 years of formal education); neighbourhood socioeconomic index (SEI; continuous) derived from a principal component analysis involving educational level and income of household head, crowding and median rent of households; smoking status (never/former/current), and pack-years (continuous); passive smoke exposure (yes/no); consumption of at least one glass of alcohol (ordinal: never, rarely, 1–2 times/week, several times/week, once/day, twice/day, three or more times/day); consumption of at least one portion of fruits and vegetables (ordinal: never/seldom/from 1 to 7 days per week); at least 150 min/week of moderate physical activity defined as engagement in activities that makes one sweat or moderately out of breadth (yes/no); and body...
mass index (BMI; continuous) and change in BMI (contin-
uous) between both surveys.

Other relevant variables assessed at SAP2 include: hear-
ing problems (yes/no); noise annoyance based on 11-point
noise annoyance scale,\textsuperscript{55} and green areas within a 2-km
residential buffer, available from the European
Environment Agency hectare resolution dataset (CORINE
CLC-2006 Version 13, 02–2010). At SAP3, we measured
noise sensitivity based on the 10-item Weinstein’s noise
sensitivity 6-point score,\textsuperscript{56} self-reported sleep quality
(good/bad), sleeping with open windows (yes/no) and bed-
room orientation (street/non-street).

Statistical analyses

We summarized the participants’ characteristics based on
diabetes status and compared these characteristics between
included and excluded SAPALDIA participants. Continuous variables were summarized as medians (inter-
quartile range, IQR) and differences in medians tested using the median test, and categorical variables were sum-
marized as proportions (%) and differences in proportions
tested using the chi-squared test.

To estimate the relative risk (RR) of diabetes in relation to
transportation noise and AP exposures, we used mixed
Poisson regression models with random intercepts at the
level of study areas, and corrected for the biased variance estimates obtained by applying the Poisson model to bin-
ary data. Since our data are clustered, we could not apply
the robust sandwich estimator.\textsuperscript{53} Having only eight clus-
ters, we also could not apply the cluster-level robust vari-
ance estimator (optimal when clusters are \( \geq 50 \)) which
would lead to over-compensation of standard errors.\textsuperscript{53}
Therefore, we used a heuristic method where we adjusted
the coefficient from the mixed Poisson regression model
with the T-statistic of the corresponding mixed logistic re-
gression model, which provides unbiased standard errors and \( P \)-values:\textsuperscript{54}

\[
\text{standard error}_{\text{mixed Poisson}} = \frac{\text{coefficient}_{\text{mixed Poisson}}}{T - \text{statistic}_{\text{mixed logistic}}}
\]

The rationale behind this approach is analogous to the one underlying Miettinen’s construction of confidence intervals for odds ratios and relative risks where the 95% confidence interval for a relative risk is defined as \( RR^{1.96} / \sqrt{1.96} \) where \( t \) is the positive square root of the chi-squared statistic of the associated chi-squared test.\textsuperscript{54}

Estimation of relative risks proceeded in stages. First, we explored single exposure models for Lden road, Lden
aircraft, Lden railway and \( NO_2 \), adjusted for age, sex, edu-
cational attainment, SEI, smoking status, pack-years,

Results

Diabetes incidence was 4.2% during a median follow-up
of 8.3 years. Medians (IQR) of Lden road, aircraft, railway
noise, NEnight, IRnight and \( NO_2 \) levels were 54 (10) dB,
32 (11) dB, 30 (12) dB, 109 (160), 75 (26)% and 21 (15)
\( \mu g/m^3 \) respectively. There was a high correlation between
Lden and Lday and Lnight for road noise (\( r = 0.99 \)), and
Lden and Lday, but not Lnight, for aircraft noise
(Supplementary Table 1, available as Supplementary data
at IJE online). Road traffic noise was moderately corre-
lated with \( NO_2 \) (\( r = 0.43 \)) and NEnight (\( r = 0.62 \)). Road
traffic noise was the commonest noise exposure whereas
railway noise was the least (Lden) (Supplementary Figure
\( r = 0.99 ) \) and NEnight (in
quartiles due to its left-skewed distribution with isolated
high values) also using the main model. Next, we tested ef-
fect modification by age, sex and noise annoyance mea-
ured at SAP2, and by noise sensitivity, sleep quality, bedroom orientation and sleeping with open windows
measured at SAP3.

For sensitivity analyses, we assessed the additional ef-
fect of change in \( NO_2 \) between surveys, replaced \( NO_2 \) with
PM\(_{2.5}\), and applied the in-built cluster-level robust variance
estimator. We also applied random slopes of noise vari-
ables and \( NO_2 \) at the level of study areas, excluded three
incident diabetes cases identified only through HbA1c test-
ing, excluded participants reporting hearing problems and
explored the effect of potential selection bias using inverse
probability weighting (IPW) by applying the inverse of the
probability of participation in the present analyses, derived
from SAP 1, on our main effect estimates. Analyses were
done with STATA version 14 (Stata Corporation, TX) and
R Studio version 0.99.092 (R Foundation for Statistical
Computing, Vienna). All results are presented as relative
risks of diabetes incidence per IQR of the respective expos-
ure variables.
1, available as Supplementary data at IJE online). Aircraft noise was the least observed at night (Table 1). Compared with the excluded participants, included participants were older, of higher social status, smoked less, drank less alcohol, gained less weight, had higher exposure to road traffic noise and number of events, and less green space (Table 1). Incident diabetes was comparable between included (4.2%) and excluded participants (4.7%). Incident diabetes cases were older, of lower social status and had higher BMI and reported hearing problems and poorer sleep quality, compared with participants without diabetes (Table 1). We also observed differences in their exposures to road traffic and aircraft noise (Lden and Lday) and NEnight but not with Lnight.3

In single exposure models for Lden and NO2 (Table 2), road and aircraft noise were positively associated with incident diabetes independent of traditional risk factors. Adjustment for physical activity and BMI reduced effect estimates across all exposures. Aircraft noise, which showed doubling of diabetes incidence per IQR, became more precise on accounting for noise intermittency, whereas the effects of road traffic noise remained unchanged. Noise intermittency itself was not associated with diabetes risk across single exposure models for road [relative risk (RR): 0.92; 95% CI: 0.72–1.18], aircraft (RR: 0.88; 95% CI: 0.68–1.13) and railway (RR: 0.94; 95% CI: 0.73–1.20) noise. We observed no effect of railway noise or NO2 on diabetes risk in the single exposure models.

We observed similar results with the multi-exposure models (Table 2) except for road traffic noise which became stronger and more precise (Figure 1). We observed little confounding among exposures in the multi-exposure models. Neither noise intermittency (RR: 0.83; 95% CI: 0.64–1.06), green space (RR: 0.95; 0.55–1.63) nor PM2.5 (RR: 0.99; 95% CI: 0.81–1.17) was associated with incident diabetes in the multi-exposure models. Describing the association between diabetes incidence and road and aircraft noise (Lden), by smoothing splines in multi-exposure models, showed that optimal solution was linear for both variables (Supplementary Figure 2, available as Supplementary data at IJE online). Daytime and nighttime noise effects on diabetes risk were comparable with those of Lden for road and railway noise levels (Figure 1). We observed a strong positive effect of aircraft noise on diabetes risk during the day, but not at night (Figure 1). We observed a positive trend between quartiles of NEnight and diabetes risk independent of road, railway and aircraft noise and NO2. Compared with the participants in the lowest quartile of noise events, participants in the highest quartile had more than 2-fold greater diabetes risk (Table 3). In the NEnight model, the main effects of road noise became reduced and imprecise (RR: 1.10; 95% CI: 0.81–1.50) whereas those of aircraft and railway noise remained unchanged (data not shown).

Given that we observed positive precise effects of road noise on diabetes risk, we focused our effect modification on road noise. Although the P-values of heterogeneity were > 0.05, we observed substantially increased effects of road noise among persons who reported sleeping with open windows and poor sleep quality (Table 4). Sensitivity analyses yielded robust results, and there was minimal evidence for potential selection bias (Supplementary Table 3, available as Supplementary data at IJE online).

Discussion

We have presented comprehensive evidence on the association of transportation noise and AP with diabetes risk independent of AP. Our findings suggest a strong effect of road and aircraft noise, independent of the other transportation noise sources and NO2, but no effect of railway noise or NO2. Number of noise events rather than the temporal noise variation (intermittency ratio) predicted diabetes risk.

Our findings on transportation noise and risk of diabetes generally agree with other studies. Road traffic, but not railway noise, was associated with diabetes risk independent of AP exposure.32 Higher diabetes risk was reported among those living in busy traffic areas compared with those in quieter areas,35 which could relate to both road traffic noise and AP. Another study reported a positive relationship between aircraft noise and incident diabetes among those who did not change their residence during follow-up.34 A recent study reported a stronger association between road noise and prevalent diabetes compared with PM2.5 in mutually-adjusted models.33 The absence of effects from railway noise and night-time aircraft noise may be due to lower levels of exposures compared with road and daytime aircraft exposures. Most flights occur during the day and we cannot exclude the impact of night-time exposure misclassification due to flight re-routing in previous years.43 It may also be that railway noise characteristics are less detrimental for diabetes risk.

Noise may impact on diabetes risk through two major and interrelated pathways-stress and sleep disturbances.17,18 Stress responses to chronic activation of the hypothalamic-pituitary adrenal axis16 may result in metabolic impairment and insulin resistance.19,55 The impact of noise exposure on sleep is well established. Noise may impair sleep quality, leading to behavioural15 and metabolic derangements.57 Reduced sleep quantity and quality were linked to impaired glucose regulation17 and increased adiposity.58 Our finding of 2-fold stronger risk of diabetes...
Table 1. Characteristics of participants included in the study

| Characteristic                                      | Included | Excluded* |
|-----------------------------------------------------|----------|-----------|
|                                                     | Incident diabetes (%) | No incident diabetes (%) | Chi-squared test (P-value)b | n (%) | Chi-squared test (P-value)c |
|                                                     | n = 110  | n = 2521  |                        |       |                        |
| Females                                             | 50.9     | 52.8      | 0.698                  |       |                         |
| Education ≤ 9 years                                  | 11.9     | 7.0       | 0.050                  |       |                         |
| Ever-smokers                                         | 56.0     | 54.3      | 0.726                  |       |                         |
| Exposure to passive smoke                           | 46.4     | 41.2      | 0.279                  |       |                         |
| Alcohol > 1 glass/day                                | 10.1     | 8.0       | 0.439                  |       |                         |
| Fruits > 3 days/week                                 | 60.9     | 59.7      | 0.893                  |       |                         |
| Vegetables > 3 days/week                             | 69.1     | 72.5      | 0.333                  |       |                         |
| At least 150 min/week of moderate physical activity  | 52.7     | 49.4      | 0.503                  |       |                         |
| Bad sleep quality                                    | 16.4     | 10.1      | 0.034                  |       |                         |
| Hearing problems                                     | 17.3     | 9.8       | 0.011                  |       |                         |
| Bedroom facing street                                | 35.9     | 43.5      | 0.128                  |       |                         |
| Closing windows                                      | 22.1     | 21.2      | 0.826                  |       |                         |
| Area: Basel                                          | 9.1      | 13.7      | 0.212                  |       |                         |
| Wald                                                | 20.9     | 21.2      | 0.034                  |       |                         |
| Davos                                               | 4.5      | 9.2       | 0.128                  |       |                         |
| Lugano                                              | 10.9     | 11.9      | 0.778                  |       |                         |
| Montana                                              | 2.7      | 3.2       | 0.212                  |       |                         |
| Payerne                                             | 21.8     | 13.7      | 0.624                  |       |                         |
| Aarau                                               | 19.1     | 17.1      | 0.034                  |       |                         |
| Geneva                                               | 10.9     | 10.0      | 0.034                  |       |                         |
| Median (IQR)                                         | 59.2 (13.1) | 53.3 (16.1) | < 0.001               | 4715 (52.6) | 0.949 |
| Age                                                  | 28.3 (5.4) | 24.9 (5.1) | < 0.001               | 4704 (9.6) | < 0.001 |
| Body mass index (BMI)                                | 0.5 (2.7) | 0.5 (1.9) | 0.997                 | 5082 (59) | < 0.001 |
| Change in BMI                                        | 64.2 (14.7) | 65.3 (13.9) | 0.174                | 5082 (49.6) | < 0.001 |
| Neighbourhood socioeconomic index                   | 0 (16.3) | 0 (12.9) | 0.778                | 3636 (10) | 0.693 |
| Pack-years of smoking                                | 2 (4)    | 2 (5)    | 0.191                | 624 (13.2) | < 0.001 |
| 11-point noise annoyance scale                       | 31 (15) | 32 (16) | 0.414                | 782 (16.6) | 0.243 |
| Noise sensitivity score                              | 15.2 (4.5) | 16.4 (3.5) | 0.629               | 757 (16.1) | 0.014 |
| PM2.5 (μg/m³)                                        | 20.4 (15) | 21.1 (15.4) | 0.562             | 559 (11.9) | < 0.001 |
| NO2 (μg/m³)                                          | -2.8 (4.8) | -3.2 (6.7) | 0.204              | 4633 [21.5(16.8)] | 0.187 |
| Change in PM2.5 (μg/m³) between SAP2 and SAP3        | 56 (10)  | 54 (11)  | 0.031               | 5027 [55.2 (12)] | < 0.001 |
| Lden road (dB)                                       | 30 (19)  | 30 (12)  | 0.291               | 5027 [30 (12)] | 0.661 |
| Lden air (dB)                                        | 46.6 (10) | 44.8 (10.4) | 0.015              | 5027 [46 (12)] | < 0.001 |
| Lden railway (dB)                                    | 20 (3)   | 20 (3)   | 0.729               | 5027 [20 (3)] | 0.361 |
| Total intermittency ratio (IR), night                | 74 (29)  | 75 (26)  | 0.730               | 5027 [75 (26)] | 0.564 |
| Total number of events (NE), night                   | 143 (178) | 107 (157) | 0.032              | 5025 [126 (189)] | < 0.001 |
| Leq road, day (dB)                                   | 54 (10)  | 52 (11)  | 0.029               | 5027 [53 (12)] | < 0.001 |
| Leq air, day (dB)                                    | 30 (20)  | 30 (11)  | 0.267               | 5027 [30 (11)] | 0.618 |
| Leq railway, day (dB)                                | 30 (7)   | 30 (6)   | 0.756               | 5027 [30 (7)] | 0.030 |
| Green space within 2 km residential buffer (km²)     | 0.17 (0.51) | 0.17 (0.51) | 0.997             | 5027 [0.22 (0.51)] | 0.012 |

*Number of participants excluded due to missing data, change of residence or having diabetes at baseline for each variable, and their corresponding summary measure (proportion or median). SAP2 and SAP3 refer to the first and second follow-up surveys of the SAPALDIA (Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults) study.

bP-value of difference in proportions or medians between participants with and without incident diabetes.

cP-value of difference in proportions or medians between included and excluded participants.

Lden; day-evening-night noise levels with 5dB and 10dB penalties for evening and night-time respectively.
related to road traffic noise among participants reporting poor sleep quality agrees with the metabolic complications of noise exposure. In fact, exploratory analyses showed that railway noise was only positively associated with diabetes risk among participants reporting poor sleep quality [(RR: 1.28; 95% CI: 0.80–2.05) vs (RR: 0.83; 95% CI: 0.60–1.16 for good sleep quality)]. Noise annoyance represents a cognitive pathway through which noise may impact on health outcomes.59,60 Although effect modification by noise annoyance and/or sensitivity has been reported with hypertension61 and obesity,62 we could not find any modification by these attributes. However, we cannot discard the conscious pathway of the noise effects on diabetes, given our observation of daytime road and aircraft noise effects.

Although we found stronger effect among participants who slept with open windows, we did not replicate this trend among participants whose bedrooms faced the street. Participants with sleeping rooms away from the street were more likely to sleep with open windows (84% vs 73%), thus increasing their noise exposure. Evidence on the relevance of number of noise events and intermittency in understanding the health impacts of noise has been limited to sleep studies.63,64 We did not observe any main effect with noise intermittency on diabetes risk. Experimental mouse models showed that chronic intermittent noise did not affect pancreatic function.65 Although we observed positive association with noise events, the main effect of road traffic noise was lost due to the high correlation between both parameters. Therefore, number of events may capture some road noise effects. Further exploration of

### Table 2. Association between 1-year mean transportation noise levels, NO2 and incident diabetes

|                          | Lden road RR (95% CI) | Lden aircraft RR (95% CI) | Lden railway RR (95% CI) | NO2 RR (95% CI) |
|--------------------------|-----------------------|--------------------------|--------------------------|----------------|
| **Single exposure**      |                       |                          |                          |                |
| Model 1                  | 1.29 (1.00, 1.67)     | 1.83 (1.03, 3.28)        | 0.96 (0.71, 1.28)        | 0.94 (0.68, 1.30) |
| Model 2                  | 1.21 (0.94, 1.57)     | 1.80 (0.97, 3.35)        | 0.90 (0.68, 1.19)        | 0.88 (0.65, 1.20) |
| Model 3                  | 1.20 (0.92, 1.56)     | 1.75 (0.96, 3.19)        | 0.94 (0.72, 1.22)        | 0.92 (0.67, 1.26) |
| Model 4                  | 1.20 (0.93, 1.55)     | 1.86 (1.01, 3.40)        | 0.95 (0.73, 1.24)        | 0.89 (0.64, 1.23) |
| Model 5                  | 1.17 (0.88, 1.53)     | 1.92 (1.04, 3.55)        | 0.94 (0.72, 1.22)        | 0.87 (0.62, 1.21) |
| **Multi-exposure**       |                       |                          |                          |                |
| Model 1                  | 1.41 (1.07, 1.87)     | 1.86 (1.00, 3.45)        | 0.94 (0.71, 1.26)        | 0.84 (0.59, 1.20) |
| Model 2                  | 1.38 (1.03, 1.83)     | 1.82 (0.93, 3.56)        | 0.90 (0.68, 1.20)        | 0.81 (0.56, 1.15) |
| Model 3                  | 1.35 (1.02, 1.78)     | 1.86 (0.96, 3.59)        | 0.94 (0.71, 1.24)        | 0.86 (0.61, 1.22) |
| Model 4                  | 1.40 (1.05, 1.86)     | 1.95 (1.01, 3.77)        | 0.98 (0.74, 1.29)        | 0.79 (0.55, 1.15) |
| Model 5                  | 1.31 (0.98, 1.75)     | 1.96 (1.00, 3.81)        | 0.94 (0.72, 1.24)        | 0.86 (0.60, 1.22) |
| Model 6                  | 1.35 (1.02, 1.78)     | 1.87 (0.96, 3.62)        | 0.94 (0.71, 1.24)        | 0.87 (0.60, 1.22) |

All RRs are per IQR of respective noise metric (road: 10 dB; aircraft: 12 dB; rail: 11 dB; NO2: 15 µg/m³). Single exposure models included one exposure at a time whereas multi-exposure models considered all exposure metrics at the same time. Random intercepts were applied at the level of the study areas in all models.

Model 1: unadjusted model. Unadjusted model for multi-exposure models include road, aircraft and railway traffic noise, noise truncation indicator and NO2.

Model 2: Model 1 + age, sex, educational level, neighbourhood socioeconomic index, smoking status and pack-years, consumption of alcohol, fruits and vegetables.

Model 3: Model 2 + physical activity, body mass index and change in body mass index.

Model 4: Model 3 + noise intermittency.

Model 5: Model 3 + traffic noise annoyance.

Model 6: Model 3 + green space.

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![Figure 1. Relationship between transportation noise and risk of diabetes. All effect estimates are per inter-quar-tile range of respective noise metric (Lden/Lday/Lnight road: 10 dB; Lden/Lday aircraft: 12 dB; Lden/ Lday/Lnight railway: 11 dB). Leq: noise level. Lden: day-evening-night noise level. All estimates are from multi-exposure models adjusted for age, sex, educational level, neighborhood socio-economic index, smoking status and pack years, consumption of alcohol, fruits and vegetables, nitrogen dioxide, physical activity, body mass index and change in body mass index. Random intercepts were applied at the level of the study areas in the all models.](image-url)
these noise attributes are needed to better understand the
health impacts of noise exposure.

Despite the plausibility of a link between air pollutants
and diabetes risk, and previous observation of a positive
association between NO$_2$ and prevalent diabetes in
SAPALDIA$^{6,6}$ and other studies,$^8$ we could not replicate
those findings in this study. This may be due to our few in-
cident diabetes cases and relatively short follow-up time.
In addition, mean NO$_2$ levels, which comprised our meas-
ure of contrasts in long-term exposure to AP, were much
lower at the first follow-up survey (22.6 g/m$^3$) compared
with the previous 10-year mean (27 g/m$^3$) used in our pre-
vious studies.$^{10,6}$ NO$_2$ levels further decreased between
surveys (Table 1), and this change was not associated with
incident diabetes (RR: 0.90; 0.71–1.15). Furthermore, we
did not observe any associations with PM$_{2.5}$, corroborating
the findings of recent studies where no association was
observed between both pollutants and incident diabetes.$^{2,8–}
30$ Our observation of stronger noise effects among partici-
pants with lower NO$_2$ exposures during follow-up may re-
fect less NO$_2$ exposure misclassification and therefore
residual confounding by NO$_2$ in this group.

Apart from being the first study exploring the simultan-
eous impact of all three types of transportation noise,
including number of events and intermittency, and AP, our
study has other strengths. It was a longitudinal study with
at least 8-year follow-up time. We identified undiagnosed
diabetes using National Glycohemoglobin Standardization
Program (NGSP)-certified methods. The SAPALDIA study
provided an extensive database of lifestyle characteristics
which enabled the exploration of potential confounding
and susceptibility. Our noise exposures were derived from
validated and detailed Swiss noise models, and noise ex-
posure characteristics were assigned individually to facades
on participants’ residential floors. Our AP estimates as-
signed to participants’ residences also derive from vali-
dated models with high spatial resolution. This study
focused on non-movers, further reducing exposure
misclassification.

This study was mainly limited by the sample size and
the number of diabetes cases which precluded detailed ex-
ploration of susceptibilities, especially for aircraft noise
where only about 40% was exposed. Some exposure mis-
classification could have occurred due to data errors,
building characteristics and daytime mobility of partici-
ants, which is most likely non-systematic, leading to bias
towards null. Sleep quality was subjectively assessed by the
participants. Bias from loss to follow-up due to noise-
related death from cardiovascular causes may have led to
underestimating the observed noise effects on diabetes.
Although IPW showed minimal evidence for potential se-
lection bias, some bias may still persist, given that road
noise effects were weaker among participants excluded due
to missing data (Supplementary Table 3). Finally, distinc-
tion of type 2 diabetes from type 1 diabetes cases was not
possible, but we expect only < 10% to be incident type 1
diabetes.$^{6,7}$

**Conclusion**

We found positive associations of road and aircraft noise,
but not traffic-related AP, with incidence of diabetes.
Window opening pattern and sleep disturbance may mod-
yfy the susceptibility to road traffic noise. Larger longitudi-
nal studies are needed to confirm these findings and
consider indoor and non-transportation noise.
Table 4. Modification of the association between 1-year mean Lden road and diabetes risk

| Characteristics                  | n   | RR (95% CI) |
|----------------------------------|-----|-------------|
| Sex                              |     |             |
| Males                            | 1244| 1.66 (1.08, 2.55) |
| Females                          | 1387| 1.17 (0.77, 1.77) |
| P-value of interaction           |     | 0.259       |
| Age groups                       |     |             |
| ≤ 54                             | 1316| 1.10 (0.67, 1.82) |
| > 54                             | 1315| 1.46 (1.04, 2.04) |
| P-value of interaction           |     | 0.344       |
| Sleep quality                    |     |             |
| Good                             | 2359| 1.28 (0.95, 1.72)  |
| Bad                              | 272 | 2.05 (1.02, 4.12)  |
| P-value of interaction           |     | 0.228       |
| Noise annoyance                  |     |             |
| ≤ P50                            | 1533| 1.21 (0.83, 1.78)  |
| > P50                            | 1095| 1.27 (0.85, 1.91)  |
| P-value of interaction           |     | 0.872       |
| Noise sensitivity score          |     |             |
| ≤ P50                            | 1144| 1.20 (0.75, 1.92)  |
| > P50                            | 1091| 1.19 (0.69, 2.06)  |
| P-value of interaction           |     | 0.935       |
| Bedroom orientation had to be   |     |             |
| Non-street                       | 1108| 1.61 (1.11, 2.35)  |
| Street                           | 1457| 1.08 (0.64, 1.83)  |
| P-value of interaction           |     | 0.341       |
| Sleeping with open windows       |     |             |
| Yes                              | 2016| 1.44 (1.02, 2.03)  |
| No                               | 544 | 0.64 (0.34, 1.19)  |
| P-value of interaction           |     | 0.083       |
| Noise intermittency              |     |             |
| ≤ P50                            | 1312| 1.28 (0.88, 1.86)  |
| > P50                            | 1319| 1.35 (0.90, 2.02)  |
| P-value of interaction           |     | 0.839       |
| Residential NO2 level            |     |             |
| ≤ P50                            | 1316| 1.30 (0.89, 1.92)  |
| > P50                            | 1315| 1.42 (0.94, 2.15)  |
| P-value of interaction           |     | 0.852       |
| Decline in NO2 level             |     |             |
| ≤ P50                            | 1315| 1.72 (1.13, 1.92)  |
| > P50                            | 1314| 1.11 (0.76, 1.62)  |
| P-value of interaction           |     | 0.096       |

All RRs are per 10 dB of road traffic noise. P50 represents the median level of each variable. All estimates are from multi-exposure models adjusted for age, sex, educational level, neighbourhood socioeconomic index, smoking status and pack-years, consumption of alcohol, fruits and vegetables, physical activity, body mass index and change in body mass index. Random intercepts were applied at the level of the study areas in all models.

Supplementary Data

Supplementary data are available at IJE online.

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