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Transportation noise exposure, noise annoyance and respiratory health in adults: A repeated-measures study



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ABSTRACT

Transportation noise leads to sleep disturbance and to psychological and physiological sustained stress reactions, which could impact respiratory health. However, epidemiologic evidence on associations of objective transportation noise exposure and also perceived noise annoyance with respiratory morbidity is limited. We investigated independent associations of transportation noise exposure and noise annoyance with prevalent respiratory symptoms and incident asthma in adults.

Using 17,138 observations (from 7049 participants) from three SAPALDIA (Swiss Cohort Study on Lung and Heart Diseases in Adults) surveys, we assessed associations of transportation noise exposure and noise annoyance with prevalent respiratory symptoms, and with incident asthma (in 10,657 nested observations from 6377 participants). Annual day-evening-night transportation noise comprising road, railway and aircraft Lden (Transportation Lden) was calculated for the most exposed façade of participants' residence using Swiss noise models. Transportation noise annoyance was assessed using an 11-point scale, and participants reported respiratory symptoms and doctor-diagnosed asthma at each survey. We estimated associations with transportation Lden (as well as source-specific Lden) and noise annoyance, independent of air pollution and other potential confounders, using mutually-adjusted mixed logistic and Poisson models and applying random intercepts at the level of the participants.

Prevalent respiratory symptoms ranged from 5% (nocturnal dyspnoea) to 23% (regular cough/phlegm). Transportation noise annoyance, but not Lden, was independently associated with respiratory symptoms and current asthma in all participants, with odds ratios (OR) and 95% confidence intervals (CI) ranging between 1.03 (95%CI: 1.01, 1.06) and 1.07 (95% CI: 1.04, 1.11) per 1-point difference in noise annoyance. Both noise annoyance and Lden showed independent associations with asthma symptoms among asthmatics, especially in those reporting adult-onset asthma [OR_{Lden}: 1.90 (95% CI: 1.25, 2.89) per 10 dB; p-value of interaction (adult-onset vs. childhood-onset): 0.03; OR_{noise annoyance}: 1.06 (95%CI: 0.97, 1.16) per 1-point difference; p-value of interaction: 0.06]. No associations were found with incident asthma.

Transportation noise level and annoyance contributed to symptom exacerbation in adult asthma. This

Abbreviations: BMI, Body mass index; CI, Confidence interval; Lden, Day-evening-night noise level; NDVI, Normalized difference vegetation index; NO₂, Nitrogen dioxide; OR, Odds ratio; PM₁₀, Particulate matter with \leq 10 μ m diameter; RR, Risk ratio; SAPALDIA, Swiss cohort study on air pollution and lung and heart diseases in adults; SEP, Socio-economic position

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suggests both psychological and physiological noise reactions on the respiratory system, and could be relevant for asthma care. More studies are needed to better understand the effects of objective and perceived noise in asthma aetiology and overall respiratory health.

1. Introduction

Transportation noise exposure could negatively impact respiratory health. Noise is thought to enhance stress response acting along the Hypothalamic-Pituitary-Adrenal axis (Recio et al., 2016) as evidenced by higher morning saliva cortisol in noise-exposed children (Ising et al., 2004). The state of stress may disrupt night-time recovery of the immune system and contribute to pro-inflammatory processes in the respiratory tract (Recio et al., 2016). Stressful life events and stress-related biomarkers, including allostatic load, were previously associated with respiratory problems and asthma incidence in children and adults (Korkeila et al., 2012; Loerbroks et al., 2009; Rod et al., 2012; van de Loo et al., 2016; Zijlmans et al., 2017) as well as worsening of symptoms in patients with asthma (Chen and Miller, 2007; Wright, 2011).

Despite these plausibility links evidencing a perceptive emotional stress reaction, the independent role of transportation noise exposure and its subjective counterpart, noise annoyance, in respiratory morbidity, have not received much attention. Short-term road traffic noise exposure was associated with increased rates of emergency service calls and hospitalizations for respiratory symptoms (Carmona et al., 2017; Tobias et al., 2001) as well as excess respiratory mortality (Recio et al., 2017; Tobias et al., 2014). Self-reported, but not modelled noise exposure was associated with health (including respiratory) symptoms in adults (Martens et al., 2018). Longer-term noise exposure was associated with neither lung function impairment in children (Franklin and Fruin, 2017) nor asthma prevalence in adults (Cai et al., 2017), but controlling for noise exposure itself strengthened the association between air pollution and these outcomes.

Air pollution is in part correlated with transportation noise, especially road traffic (Foraster, 2013) and has an established short-term effect on symptom exacerbation in patients with chronic respiratory disease, but its role in the aetiology of asthma and chronic obstructive pulmonary disease remains unclear (Doiron et al., 2017; Heinrich et al., 2005; Jacquemin et al., 2015; Schikowski et al., 2014).

None of these previous studies considered noise annoyance as a determining factor, even though it may have an independent health effect by reflecting individually-varying noise perception. To our knowledge, no study has investigated the combined association of long-term noise exposure and annoyance with respiratory symptoms and incidence of asthma. Therefore, we investigated the independent air pollution-adjusted associations of composite transportation (road, railway and aircraft) and source-specific transportation noise exposure and noise annoyance with prevalent respiratory symptoms and incident asthma in an adult population sample.

2. Materials and methods

2.1. Study population

We used data from the Swiss Cohort Study on Air Pollution and Lung and Heart Diseases in Adults (SAPALDIA) which recruited 9651 randomly-selected adults, from eight Swiss areas (Basel, Wald, Davos, Lugano, Montana, Payerne, Aarau and Geneva) in 1991 (SAP1) (Martin et al., 1997). So far, two follow-up surveys were completed in 2001/ 2002 (SAP2; 8047 participants) (Ackermann-Liebrich et al., 2005) and 2010/2011 (SAP3; 6088 participants). At each survey, participants completed questionnaires on their health and lifestyle, and had physical examination. Questions on respiratory health were covered in all three surveys, including respiratory symptoms and asthma status, as well as noise annoyance. Assignment of modelled individual-level transportation noise and air pollution exposures was also done for the three surveys. Based on participation at each survey, we had a total of 23,786 eligible observations. We excluded 6648 observations for missing covariates, thus including 17,138 observations. All included observations had data on asthma outcomes, exposures and potential confounders. Details of observation selection are presented in Supplementary Fig. S1. Ethics approvals for the SAPALDIA study were obtained from the Swiss Academy of Medical Sciences and the ethics committees of the participating cantons. All participants provided written informed consent before participating in any SAPALDIA survey.

2.2. Identification of respiratory symptoms and asthma cases

At SAP1, SAP2 and SAP3, participants answered questions on nine respiratory symptoms: regular cough/phlegm, chronic cough/phlegm, wheezing, wheezing without cold, wheezing with dyspnoea, chest tightness, nocturnal dyspnoea causing persons to wake up, diurnal dyspnoea at rest and dyspnoea after exercise. We identified participants as having a symptom based on an affirmative response to the corresponding question shown in Table 1. To enable the combined exploration of asthma-specific symptoms, we created a "current asthma" variable defined as having doctor-diagnosed asthma and having reported any of the following for the preceding 12-month period: (i) asthma attack or (ii) using asthma medication or (iii) at least three of the symptoms 'Wheezing with dyspnoea', 'chest tightness', 'nocturnal dyspnoea', 'diurnal dyspnoea at rest' and 'dyspnoea after exercise'(Boudier et al., 2013). The control group for the current asthma variable includes participants without doctor-diagnosed asthma, as well as participants with doctor-diagnosed asthma but not qualifying as having current asthma in the past 12 months (i.e. having

Table 1
Respiratory symptoms and their corresponding questions used in the study.

Respiratory symptom	Question asked at each of the three SAPALDIA surveys
Regular cough/phlegm	Do you usually cough (or bring up phlegm) first thing in the morning or during the day or at night?
Chronic cough/phlegm	Do you cough or bring up phlegm during the day or at night on most days for at least 3 months each year and since at least 2 years?
Wheezing	In the last 12 months, have you had wheezing or whistling in your chest at any time?
Wheezing without cold	Did you have this wheezing or whistling in your chest when you did not have a cold?
Wheezing with dyspnoea	Did you have trouble breathing when you had this wheezing or whistling in your chest?
Chest tightness	Have you woken up with a feeling of tightness in your chest at any time in the last 12 months?
Nocturnal dyspnoea	Have you been woken by an attack of shortness of breath at any time during the past 12 months?
Diurnal dyspnoea at rest	Have you had an attack of shortness of breath while resting at any time during the past 12 months?
Dyspnoea after exercise	Have you had an attack of shortness of breath following strenuous activity at any time during the past 12 months?

SAPALDIA: Swiss cohort study on air pollution and lung and heart diseases in adults.

controlled asthma symptoms).

We identified incident asthma at SAP2 and SAP3 if participants reported having doctor-diagnosed asthma or used asthma medication at SAP2 or SAP3, while having responded negatively at the previous survey. Towards sensitivity analyses, we used an alternative definition of incident asthma which excluded participants who previously qualified for incident asthma based only on having at least three of the symptoms 'Wheezing with dyspnoea', 'chest tightness', 'nocturnal dyspnoea', 'diurnal dyspnoea at rest' and 'dyspnoea after exercise' (Boudier et al., 2013).

2.3. Assignment of individual transportation noise exposure and noise annoyance

Annual average road, railway and aircraft noise were calculated at the most exposed façade of participants' residential floors for 1991, 2001 and 2011 (corresponding to SAP1, SAP2 and SAP3 respectively) using validated Swiss noise models. As described elsewhere (Karipidis et al., 2014), road traffic noise was modelled using the sonROAD emission model (Heutschi, 2004) and the StL-86 propagation model (FOEN, 1987) using input data covering bridges, noise barriers, road and hourly traffic statistics. Railway noise was modelled using the sonRAIL emission model (Thron and Hecht, 2010) and the SEMIBEL propagation model (FOEN, 1990) using input data covering railway tracks' geometry, noise barriers, train types and rail traffic statistics. Aircraft noise was modelled using FLULA2 software (Empa, 2010). Input data for aircraft noise included air traffic statistics, radar data, acoustic footprints and idealized number and timing of flights covering one military airport (Payerne) and three major civilian airports (Basel, Geneva and Zurich). These airports are located in or near the SAPALDIA areas (Wald is part of Zurich). Some participants may have moved out of the SAPALDIA areas (Supplementary Fig. S2), thus their moving history and all addresses were considered for the exposure modelling.

Input data were mostly available in good quality at the three time points for aircraft models, but road traffic and railway data in good quality were only available for 2001 and 2011. The available road traffic and railway input data before 2000 was comparably uncertain (missing data or inaccurate models) especially for minor roads and some railway lines. The nationwide average growth of road and railway traffic volumes between 1991 and 2001 amounted to 6% and 5% respectively. As these only correspond to a respective shift of the Leq of 0.2 dB, we assigned to the façade points at 1991, the exposure data for 2001 for both road traffic and railway noise (Karipidis et al., 2014). The noise assessment procedure was validated by comparison of calculated noise levels with measured levels from the field. For the noise metric Lden, the comparison revealed a mean difference of 1.6 \pm 5 dB when taking all measurements into account (Schlatter et al., 2017).

Source-specific day-evening-night noise levels (Lden; with 5 dB and 10 dB penalties for evening and night-time, respectively) were calculated, and participants without substantial source-specific noise exposures were assigned a truncated value of 35 dB for road Lden and 30 dB for railway and 30 dB for aircraft Lden values. In line with our previous studies (Eze et al., 2017a; Eze et al., 2017b; Foraster et al., 2017), these participants without substantial noise exposures were captured in the regression models using a truncation indicator (0 = non-truncated; 1 = truncated). Source-specific Ldens were then energetically summed up (whereby the loudest source dominates this energetic sum) to a composite transportation Lden using the formula:

Transportation Lden =
$$10\log_{10} \left(10^{\left(\frac{\text{Road Lden}}{10}\right)} + 10^{\left(\frac{\text{Railway Lden}}{10}\right)} + 10^{\left(\frac{\text{Aircraft Lden}}{10}\right)} \right)$$

We used transportation Lden as our main noise exposure measure,

and applied source-specific Lden in sensitivity analyses in an attempt to disentangle the source-specific contribution to observed associations, given their different reported characteristics and health effects (Guski et al., 2017; Röösli et al., 2017; van Kempen et al., 2018).

At SAP1, SAP2 and SAP3, participants also responded to a transportation noise annoyance question, "How much are you annoyed by noise from traffic in your home when the windows are open?" with a 0–10 rating scale based on the validated numerical 11-point noise annoyance scale (Fields et al., 2001). We created a categorical variable, not annoyed (noise annoyance \leq 5) and annoyed (noise annoyance \geq 5) for descriptive and interaction analyses (Foraster et al., 2016).

2.4. Potential confounders and effect modifiers

Based on plausibility and data availability, we selected the following potential confounders measured at SAP1, SAP2 and SAP3: age (continuous), sex (male/female), formal education ($\leq 9/ > 9$ years), smoking status (never/former/current) and pack years (continuous), passive smoke exposure (yes/no) and study area. Family history of asthma (yes/no) and presence of atopy (measured as response to at least one of eight inhalant allergens tested by skin-prick tests) were assessed in SAP1, and assigned to respondents at SAP2 and SAP3. Neighbourhood index of socioeconomic position (SEP), a composite score, derived from 2001 census data, and based on education, occupation of household heads, room occupancy and median rents of households (Panczak et al., 2012) was assigned to residential geo-coordinates of participants at SAP1, SAP2 and SAP3. Correlations of individual SEP levels were high across surveys (r > 0.9). Normalized difference vegetation index (NDVI), a satellite-derived indicator of greenness (30 m \times 30 m resolution) based on land surface reflectance was calculated for 2014 and assigned to participants' residential geocoordinates at SAP1, SAP2 and SAP3 (Vienneau et al., 2017). Correlations of individual NDVI levels of greenness were > 0.9 across surveys.

Nitrogen dioxide (NO2), a marker of traffic-related pollution and a potential confounder of transportation noise (Tetreault et al., 2013) was assigned to participants' residences at SAP1, SAP2 and SAP3. Annual mean levels of NO2 were modelled for 1993 and 2003 and assigned to SAP1 and SAP2 addresses, respectively. Models were derived by regressing NO2 passive sampler measurements against dispersion model estimates, land-use, traffic, seasonal and climatic variables, with respective adjusted R² of 0.9 and 0.8 (Liu et al., 2012). At SAP3, average biennial (2010/2011) levels of residential NO2 were estimated using area-specific land-use regression models, with adjusted R² of 0.5-0.9 across study areas (Eeftens et al., 2016). Particulate matter with \leq 10 μm diameter (PM₁₀) was assigned to participants' residences at SAP1, SAP2 and SAP3 using validated Gaussian dispersion modelling, with various emission inventories, at a spatial scale of 200 m \times 200 m. Emission inventories included agriculture, industrial, transport and household emissions, and these models had good PM₁₀ predictions at both traffic and non-traffic sites (FOEN, 2013; Liu et al., 2007). Spearman correlations (r) between NO2 and PM10 were 0.8 across the three surveys. Unlike NO₂ which shows a steeper decay with distance from traffic and provides more local contrast, PM has more homogeneous distribution, therefore making NO2 a better marker of nearroad traffic-related air pollution (Health Effects Institute, 2010). We therefore applied NO2 as our main marker of potential confounding by air pollution, and applied PM₁₀ towards sensitivity analyses.

For effect modification, we also included age of asthma onset (classified as childhood-onset (<16) or adult-onset (\ge 16 years) asthma (Siroux et al., 2014)) and obesity (body mass index (BMI) \ge 30 kg/m²) assessed at SAP1-SAP3. BMI at SAP1 was derived from self-reported weight and height, whereas BMI at SAP2 and SAP3 were derived from objectively-measured weight and height.

 Table 2

 Characteristics of participants included in the study.

N 6837 5937 4364 Categorical variables n (%) n (%) n (%) n (%) χ^2 -test Female 3464 (51) 2995 (50) 2147 (49) 0.29 Formal education ≤ 9 years 983 (14) 360 (6) 227 (5) < 0.001 Current smokers 2132 (31) 1461 (25) 752 (17) < 0.001 Exposure to passive smoke 2658 (39) 1472 (25) 558 (13) < 0.001 Urban area 4418 (65) 3826 (64) 2729 (63) 0.06 Change of residence 0 (0) 3940 (58) 1763 (37) < 0.001 Exposure to passive smoke 4418 (65) 3826 (64) 2729 (63) 0.06 Change of residence 0 (0) 3940 (58) 1763 (37) < 0.001 Exposure to passive smoke 4418 (65) 3826 (64) 2729 (63) 0.06 Change of residence 0 (0) 3940 (58) 1763 (37) < 0.001 Exposure surveys Regular cough/phlegm 1450 (21) 1370 (23) 1110 (25) < 0.001 Chronic cough/phlegm 442 (6) 454 (8) 313 (7) 0.03 Wheezing 896 (13) 838 (14) 550 (13) 0.07 Wheezing without cold 487 (7) 508 (9) 324 (7) 0.01 Wheezing with dyspnoea 392 (6) 396 (7) 284 (7) 0.08 Chest tightness 926 (14) 762 (13) 488 (11) 0.001 Nocturnal dyspnoea 309 (5) 323 (5) 203 (5) 0.04 Dyspnoea after exercise 1670 (24) 1049 (18) 857 (20) < 0.001 Current asthma 456 (7) 488 (8) 342 (8) 0.003 Prevalent doctor-diagnosed 463 (7) 574 (10) 550 (13) < 0.001 asthma Incident doctor-diagnosed 463 (7) 574 (10) 550 (13) < 0.001 Atopy ^a 2355 (34) 2031 (34) 1507 (35) 0.94 Noise annoyance scale ≥ 5 2370 (35) 1562 (26) 713 (15) < 0.001 Continuous variables Mean (SD) Mean (SD) Mean (SD) Moan (SD) ANOVA Age, years 41 (11) 52 (11) 59 (11) < 0.001 Pack-years of smoking 9.7 (16) 11.7 (19) 11.7 (19) < 0.001 Pack-years of smoking 9.7 (16) 11.7 (19) 11.7 (19) < 0.001 Pack-years of smoking 9.7 (16) 11.7 (19) 11.7 (19) < 0.001 Particulate 27.5 (10) 21.1 (7) 18.6 (3) < 0.001 Particulate 37.5 (10) 21.1 (7) 18.6 (3) < 0.001 Particulate 37.5 (10) 21.1 (7) 18.6 (3) < 0.001 Particulate 37.5 (10) 25.6 (0.2) < 0.001 Particulate 37.5 (10) 26.3 (7) 55.6 (7) < 0.001 Particulate 39.6 (10) 55.7 (8) 54.9 (8) 54.7 (8) < 0.001 Particulate 50.5 (10) 55.7 (8) 54.9 (8) 54.7 (8) < 0.001	Variable	SAPALDIA1	SAPALDIA2	SAPALDIA3	p-value
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Chronic cough/phlegm 442 (6) 454 (8) 313 (7) 0.03 Wheezing 896 (13) 838 (14) 550 (13) 0.07 Wheezing without cold 487 (7) 508 (9) 324 (7) 0.01 Wheezing with dyspnoea 392 (6) 396 (7) 284 (7) 0.08 Chest tightness 926 (14) 762 (13) 488 (11) 0.001 Nocturnal dyspnoea 309 (5) 323 (5) 203 (5) 0.04 Dyspnoea at rest 375 (5) 236 (4) 171 (4) < 0.001	•	0 (0)	3940 (58)	1763 (37)	< 0.001
Wheezing without cold 896 (13) 838 (14) 550 (13) 0.07 Wheezing without cold 487 (7) 508 (9) 324 (7) 0.01 Wheezing with dyspnoea 392 (6) 396 (7) 284 (7) 0.08 Chest tightness 926 (14) 762 (13) 488 (11) 0.001 Nocturnal dyspnoea 309 (5) 323 (5) 203 (5) 0.04 Dyspnoea at rest 375 (5) 236 (4) 171 (4) < 0.001	Regular cough/phlegm	1450 (21)	1370 (23)	1110 (25)	< 0.001
Wheezing without cold 487 (7) 508 (9) 324 (7) 0.01 Wheezing with dyspnoea 392 (6) 396 (7) 284 (7) 0.08 Chest tightness 926 (14) 762 (13) 488 (11) 0.001 Nocturnal dyspnoea 309 (5) 323 (5) 203 (5) 0.04 Dyspnoea at rest 375 (5) 236 (4) 171 (4) < 0.001	Chronic cough/phlegm	442 (6)	454 (8)	313 (7)	0.03
Wheezing with dyspnoea 392 (6) 396 (7) 284 (7) 0.08 Chest tightness 926 (14) 762 (13) 488 (11) 0.001 Nocturnal dyspnoea 309 (5) 323 (5) 203 (5) 0.04 Dyspnoea at rest 375 (5) 236 (4) 171 (4) < 0.001	Wheezing	896 (13)	838 (14)	550 (13)	0.07
Chest tightness 926 (14) 762 (13) 488 (11) 0.001 Nocturnal dyspnoea 309 (5) 323 (5) 203 (5) 0.04 Dyspnoea at rest 375 (5) 236 (4) 171 (4) < 0.001	Wheezing without cold	487 (7)	508 (9)	324 (7)	0.01
Nocturnal dyspnoea 309 (5) 323 (5) 203 (5) 0.04 Dyspnoea at rest 375 (5) 236 (4) 171 (4) < 0.001 Dyspnoea at rest 1670 (24) 1049 (18) 857 (20) < 0.001 Current asthma 456 (7) 488 (8) 342 (8) 0.003 Prevalent doctor-diagnosed asthma Incident doctor-diagnosed asthma Incident doctor-diagnosed asthma Parental asthma 692 (10) 593 (10) 441 (10) 0.97 Atopy 3 2355 (34) 2031 (34) 1507 (35) 0.94 Noise annoyance scale ≥ 5 2370 (35) 1562 (26) 713 (15) < 0.001 Continuous variables Mean (8D) Nean (8D) Neighbourhood SEP index, 9.7 (16) 11.7 (19) 11.7 (19) < 0.001 Neighbourhood SEP index, 62.2 (11) 63.5 (10) 64.1 (10) < 0.001 Particulate 27.5 (10) 21.1 (7) 18.6 (3) < 0.001 Particulate 27.5 (10) 21.1 (7) 18.6 (3) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 Particulate 32.9 (3) 2.6 (3) 1.9 (2) < 0.001 P	Wheezing with dyspnoea	392 (6)	396 (7)	284 (7)	0.08
Dyspnoea at rest 375 (5) 236 (4) 171 (4) < 0.001 Dyspnoea after exercise 1670 (24) 1049 (18) 857 (20) < 0.001	Chest tightness	926 (14)	762 (13)	488 (11)	0.001
Dyspnoea after exercise 1670 (24) 1049 (18) 857 (20) < 0.001 Current asthma 456 (7) 488 (8) 342 (8) 0.003 Prevalent doctor-diagnosed asthma 463 (7) 574 (10) 550 (13) < 0.001	Nocturnal dyspnoea	309 (5)	323 (5)	203 (5)	0.04
Current asthma 456 (7) 488 (8) 342 (8) 0.003 Prevalent doctor-diagnosed asthma Incident doctor-diagnosed asthma Incident doctor-diagnosed asthma Parental asthma 692 (10) 593 (10) 441 (10) 0.97 Atopy 2355 (34) 2031 (34) 1507 (35) 0.94 Noise annoyance scale ≥ 5 2370 (35) 1562 (26) 713 (15) < 0.001 Continuous variables Mean (SD) Mean (SD) Mean (SD) ANOVA Age, years 41 (11) 52 (11) 59 (11) < 0.001 Body mass index, kg/m² 23.9 (4) 25.9 (4) 26.3 (5) < 0.001 Pack-years of smoking 9.7 (16) 11.7 (19) 11.7 (19) < 0.001 Neighbourhood SEP index, $\frac{6}{9}$ 2 (11) 63.5 (10) 64.1 (10) < 0.001 Particulate 27.5 (10) 21.1 (7) 18.6 (3) < 0.001 Particulate 27.5 (10) 21.1 (7) 18.6 (3) < 0.001 Particulate 3 (3) 2.6 (3) 1.9 (2) < 0.001 Vegetation index Noise annoyance 3.2 (3) 2.6 (3) 1.9 (2) < 0.001 Transportation Lden, dB 56.8 (7) 56.3 (7) 55.6 (7) < 0.001 Road Lden, dB 55.7 (8) 54.9 (8) 54.7 (8) <	Dyspnoea at rest	375 (5)	236 (4)	171 (4)	< 0.001
Prevalent doctor-diagnosed asthma Incident doctor-diagnosed asthma Incident doctor-diagnosed asthma Parental asthma Parental asthma Parental asthma 8	Dyspnoea after exercise	1670 (24)	1049 (18)	857 (20)	< 0.001
asthma Incident doctor-diagnosed asthma Parental asthma Pa	Current asthma	456 (7)	488 (8)	342 (8)	0.003
asthma Parental asthma ^a 692 (10) 593 (10) 441 (10) 0.97 Atopy ^a 2355 (34) 2031 (34) 1507 (35) 0.94 Noise annoyance scale ≥ 5 2370 (35) 1562 (26) 713 (15) < 0.001 Continuous variables Mean (SD) Mean (SD) Mean (SD) ANOVA Age, years 41 (11) 52 (11) 59 (11) < 0.001 Body mass index, kg/m² 23.9 (4) 25.9 (4) 26.3 (5) < 0.001 Pack-years of smoking 9.7 (16) 11.7 (19) 11.7 (19) < 0.001 Neighbourhood SEP index, 62.2 (11) 63.5 (10) 64.1 (10) < 0.001 Nitrogen dioxide, µg/m³ 34.2 (16) 22.8 (10) 18.8 (8) < 0.001 Particulate 27.5 (10) 21.1 (7) 18.6 (3) < 0.001 matter ≤ 10 µm, µg/m³ Normalized difference vegetation index° Noise annoyance 3.2 (3) 2.6 (3) 1.9 (2) < 0.001 considerance normalized (3) 2.6 (3) 1.9 (2) < 0.001 Transportation Lden, dB 56.8 (7) 56.3 (7) 55.6 (7) < 0.001 Road Lden, dB 55.7 (8) 54.9 (8) 54.7 (8) < 0.001	· ·	463 (7)	574 (10)	550 (13)	< 0.001
Atopy® 2355 (34) 2031 (34) 1507 (35) 0.94 Noise annoyance scale ≥ 5 2370 (35) 1562 (26) 713 (15) < 0.001	•	0 (0)	221 (3)	138 (3)	0.469
Noise annoyance scale ≥ 5 2370 (35) 1562 (26) 713 (15) < 0.001 Continuous variables Mean (SD) Mean (SD) Mean (SD) ANOVA Age, years 41 (11) 52 (11) 59 (11) < 0.001 Body mass index, kg/m² 23.9 (4) 25.9 (4) 26.3 (5) < 0.001 Pack-years of smoking 9.7 (16) 11.7 (19) 11.7 (19) < 0.001 Neighbourhood SEP index, $%$ 0² 62.2 (11) 63.5 (10) 64.1 (10) < 0.001 Nitrogen dioxide, $µ$ g/m³ 34.2 (16) 22.8 (10) 18.8 (8) < 0.001 Particulate 27.5 (10) 21.1 (7) 18.6 (3) < 0.001 matter ≤ 10 µm, $µ$ g/m³ 3 2.2 (0.2) 0.54 (0.2) 0.56 (0.2) < 0.001 mailized difference vegetation index² 0.52 (0.2) 0.54 (0.2) 0.56 (0.2) < 0.001 Noise annoyance 3.2 (3) 2.6 (3) 1.9 (2) < 0.001 Transportation Lden, dB 56.8 (7) 56.3 (7) 55.6 (7) < 0.001 Road Lden, dB 55.7 (8) 54.9 (8) 54.7 (8) < 0.001	Parental asthma ^a	692 (10)	593 (10)	441 (10)	0.97
Continuous variables Mean (SD) Mean (SD) Mean (SD) ANOVA Age, years 41 (11) 52 (11) 59 (11) < 0.001	Atopy ^a	2355 (34)	2031 (34)	1507 (35)	0.94
$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	Noise annoyance scale ≥ 5	2370 (35)	1562 (26)	713 (15)	< 0.001
Body mass index, kg/m² 23.9 (4) 25.9 (4) 26.3 (5) < 0.001 Pack-years of smoking 9.7 (16) 11.7 (19) 11.7 (19) < 0.001	Continuous variables	Mean (SD)	Mean (SD)	Mean (SD)	ANOVA
Pack-years of smoking 9.7 (16) 11.7 (19) 11.7 (19) < 0.001 Neighbourhood SEP index, 0 62.2 (11) 63.5 (10) 64.1 (10) < 0.001	Age, years	41 (11)	52 (11)	59 (11)	< 0.001
Neighbourhood SEP index, $000000000000000000000000000000000000$	Body mass index, kg/m ²	23.9 (4)	25.9 (4)	26.3 (5)	< 0.001
Nitrogen dioxide, μg/m³ 34.2 (16) 22.8 (10) 18.8 (8) < 0.001 Particulate 27.5 (10) 21.1 (7) 18.6 (3) < 0.001 matter $\leq 10 \mu\text{m}$, μg/m³ Normalized difference vegetation index° Noise annoyance 3.2 (3) 2.6 (3) 1.9 (2) < 0.001 Transportation Lden, dB 56.8 (7) 56.3 (7) 55.6 (7) < 0.001 Road Lden, dB 55.7 (8) 54.9 (8) 54.7 (8) < 0.001	Pack-years of smoking	9.7 (16)	11.7 (19)	11.7 (19)	< 0.001
Particulate 27.5 (10) 21.1 (7) 18.6 (3) < 0.001 matter ≤ 10 μm, μg/ m^3 Normalized difference vegetation index° Noise annoyance 3.2 (3) 2.6 (3) 1.9 (2) < 0.001 Transportation Lden, dB 56.8 (7) 56.3 (7) 55.6 (7) < 0.001 Road Lden, dB 55.7 (8) 54.9 (8) 54.7 (8) < 0.001		62.2 (11)	63.5 (10)	64.1 (10)	< 0.001
$\begin{array}{cccccccccccccccccccccccccccccccccccc$	Nitrogen dioxide, μg/m ³	34.2 (16)	22.8 (10)	18.8 (8)	< 0.001
m³ 0.52 (0.2) 0.54 (0.2) 0.56 (0.2) < 0.001	Particulate	27.5 (10)	21.1 (7)	18.6 (3)	< 0.001
vegetation index° Noise annoyance 3.2 (3) 2.6 (3) 1.9 (2) < 0.001					
Transportation Lden, dB 56.8 (7) 56.3 (7) 55.6 (7) < 0.001 Road Lden, dB 55.7 (8) 54.9 (8) 54.7 (8) < 0.001		0.52 (0.2)	0.54 (0.2)	0.56 (0.2)	< 0.001
Road Lden, dB 55.7 (8) 54.9 (8) 54.7 (8) < 0.001	Noise annoyance	3.2(3)	2.6 (3)	1.9(2)	< 0.001
Road Lden, dB 55.7 (8) 54.9 (8) 54.7 (8) < 0.001	Transportation Lden, dB	56.8 (7)	56.3 (7)	55.6 (7)	< 0.001
Railway Lden, dB 37 (9) 36.8 (9) 35.1 (8) < 0.001	Road Lden, dB	55.7 (8)	54.9 (8)		< 0.001
,,	Railway Lden, dB	37 (9)	36.8 (9)	35.1 (8)	< 0.001
Aircraft Lden, dB 35.4 (8) 35.5 (9) 35.4 (7) 0.71	Aircraft Lden, dB	35.4 (8)	35.5 (9)	35.4 (7)	0.71

SAPALDIA: Swiss cohort study on air pollution and lung and heart diseases in adults. ANOVA: Analysis of variance. Transportation Lden represents a combination of road, aircraft and railway day-evening-night noise levels. Current asthma was defined as having doctor-diagnosed asthma and having one of the following in the preceding 12 months: (i) asthma attack or (ii) using asthma medication or (iii) any three of wheezing with dyspnoea, chest tightness, nocturnal dyspnoea, diurnal dyspnoea at rest and dyspnoea after exercise (Boudier et al., 2013). SEP: socio-economic position.

- $^{\rm a}\,$ Measured at SAPALDIA1 and assigned to participants at SAPALDIA 2 and 3.
- ^b Measured at SAPALDIA2, with corresponding values assigned to participant geo-coordinates at SAPALDIA1 and 3.
- $^{\rm c}$ Measured at SAPALDIA3, with corresponding values assigned to participant geo-coordinates at SAPALDIA1 and 2.

2.5. Statistical analyses

We summarized the characteristics of included observations, stratified by survey. We compared characteristics of participants with and without incident asthma (nested within the included observations) overall and in non-movers.

Using mixed logistic regression, with random intercepts at the level of participants, we assessed cross-sectional associations (odds ratios (OR) and 95% confidence intervals (CI)) of respiratory symptoms with transportation Lden and noise annoyance: a) in crude and adjusted single exposure models; b) in mutually-adjusted models containing both transportation Lden and noise annoyance; and c) in mutually-adjusted models replacing transportation Lden with source-specific Ldens (road,

aircraft and railway). For current asthma as outcome in the mutuallyadjusted models, we a priori explored modification of effects of transportation Lden and noise annoyance by sex, obesity, atopy, parental asthma, age of asthma onset, urbanicity, transportation Lden (for noise annoyance model) and noise annoyance (for transportation Lden model). We also tested inter-area differences in associations with current asthma, based on the area-specific adjusted R² of the NO₂ models. Adjusted models included age, age-squared, sex, family history of asthma, atopy, educational level, neighbourhood SEP, smoking status and pack years, passive smoke exposure, greenness, NO2, study area, noise truncation indicator and survey. Since both BMI and physical activity which were linked to asthma (Beuther and Sutherland, 2007: Eijkemans et al., 2012) were also recently linked to noise exposure (Foraster et al., 2016; Pyko et al., 2017; Roswall et al., 2017) we excluded them from our main models, and only included BMI, which was available at all surveys, in sensitivity and effect modification analyses. These factors are more likely to be mediators than potential confounders of noise and respiratory health associations, and may therefore constitute over-adjustment when included in the primary adjusted model.

We performed sensitivity analyses which included: a) testing the linearity of observed associations with transportation Lden and noise annoyance by adding squared terms to the adjusted models; b) assessing stability of the adjusted models to additional adjustment for BMI; c) assessing stability of the adjusted models to additional adjustment for PM $_{10}$ as well as replacing NO $_{2}$ with PM $_{10}$; d) exploration for potential selection bias by comparing crude models in the included and excluded participants, as well as comparing models adjusted for variables measured at the level of geo-coordinates e.g. neighbourhood SEP, NO $_{2}$ levels and NDVI; e) limiting adjusted models of asthma-related symptoms to asthmatic participants, and excluding asthmatic participants on medication; and g) assessing the stability of the adjusted models when limited to only SAP2 and SAP3, with potentially more precise noise exposure estimates.

Using mixed Poisson regression with random intercepts at the level of participants, we assessed longitudinal associations (relative risks (RR) and 95% CI) of incident asthma with transportation Lden and noise annoyance in the same order as in the cross-sectional analyses. These analyses only included participants who did not report asthma in the baseline survey (i.e. 1991 for 2001, and 2001 for 2011). Analyses were also restricted to non-movers, in a further step. Variables used for adjustment were similar to those of the respiratory symptom models, with the exception that the survey indicator variable had two levels (SAP1 and SAP2). Here, outcomes of SAP2 and SAP3 were regressed against predictor variables of SAP1 and SAP2, respectively. We also performed sensitivity analyses using the previously-described alternative definition of incident asthma, as well as exploring the stability of our adjusted estimates to adjustment for BMI.

All results are presented as odds ratios (OR) or relative risks (RR) and their 95% confidence intervals (CI) per 10 dB difference in Lden and per 1-point difference (on a scale from 0 to 10) in noise annoyance. Results of main associations and interactions were considered statistically significant at alpha values of 0.05 and 0.1 respectively. Analyses were performed with STATA version 14 (STATA Corporation, College Station, TX) and R Studio version 0.99.092 (R Foundation for Statistical Computing, Vienna).

3. Results

3.1. Characteristics of participants

We included 17,138 observations (72%) from 7049 participants, with an average contribution of 2.4 observations per participant. For the incident asthma models, we included 10,657 nested observations (50% non-movers) from 6377 participants, with an average contribution of 1.7 observations per participant.

Prevalent asthma and BMI increased whereas average levels of air pollution, noise exposure and noise annoyance decreased across surveys. Participants tended to move to areas with higher greenness and neighbourhood SEP. While smoking prevalence decreased across surveys, smoking intensity increased among smokers (Table 2). There were no differences between incident asthma at SAP2 (3.3%) and SAP3 (3.4%). The distribution of transportation, road, aircraft and railway Ldens and noise annoyance among included participants are shown in Fig. 1 where road Lden was the predominant source of noise exposure. Transportation Lden was correlated to Road Lden across surveys (r > 0.9), and both metrics showed relatively stronger correlation with both noise annoyance ($r_{transportation} = 0.34$; $r_{road} = 0.34$) and NO_2 $(r_{transportation} = 0.34; r_{road} = 0.34)$ (Supplementary Fig. S3), compared to aircraft and railway Ldens (noise annoyance: $r_{railway} = 0.10$, $r_{aircraft} = 0.10$; NO_2 : $r_{railway} = 0.18$, $r_{aircraft} = 0.09$) (Supplementary Tables S1-S4).

Excluded observations were more likely to come from women and persons with less education, higher air pollution and noise exposures, noise annoyance and lower greenness at their homes. Although persons with excluded observations had higher prevalence of asthma risk factors and of most respiratory symptoms, they did not differ in their prevalence and incidence of asthma, from participants whose observations were included (Supplementary Table S5).

Incident asthmatics were more often female, younger, and had higher prevalence of atopy, parental asthma, and respiratory symptoms. They also had higher exposure to NO_2 and aircraft noise compared to those without incident asthma. We observed similar patterns in the distribution of variables among non-movers (Supplementary Table S6).

3.2. Transportation noise annoyance and respiratory symptoms

We consistently observed positive significant associations between transportation noise annoyance and respiratory symptoms, which remained unchanged upon adjustment for transportation Lden (Table 3). A 1-point difference in noise annoyance was associated with 3% (95% CI: 1%, 6%) to 7% (95% CI: 4%, 11%) increases in adjusted odds across the nine respiratory symptoms. Adjusted OR for having current asthma was 1.04 (95% CI: 1.01, 1.08) per 1-point difference in noise annoyance

(Table 3).

The association between noise annoyance (1-point difference) and current asthma was more pronounced in the obese participants [OR: 1.13 (95% CI: 1.05, 1.22); p-value of interaction: 0.01], non-atopic participants [OR: 1.07 (95% CI: 1.02, 1.11); p-value of interaction: 0.10] and asthmatic participants with adult-onset asthma [OR: 1.06 (95% CI: 0.97, 1.16); p-value of interaction: 0.06]. Although interactions were not significant (p-value \geq 0.2), we also found stronger and statistically significant associations between noise annoyance and current asthma among women [OR: 1.05 (95% CI: 1.01, 1.09)] and participants living in urban areas [OR: 1.05 (95% CI: 1.02, 1.09)] (Fig. 2).

3.3. Transportation Lden and respiratory symptoms

Associations with transportation (and source-specific) Lden were not statistically significant, and were sensitive to adjustments for confounders, and transportation noise annoyance in the general sample. In adjusted models without noise annoyance, we observed positive associations between transportation Lden (10 dB difference) and chest tightness [OR: 1.11 (95% CI: 1.01, 1.21)] and dyspnoea after exercise [OR: 1.09 (95% CI: 1.01, 1.19)], but these associations became weaker and statistically non-significant [chest tightness, OR: 1.06 (0.97, 1.17); dyspnoea after exercise, OR: 1.04 (95% CI: 0.96, 1.14)] following adjustment for noise annoyance (Table 3).

However, we observed positive associations between transportation Lden and asthma-related symptoms in models limited to asthmatics, independent of NO₂ and noise annoyance. Adjusted odds of wheezing, wheezing without cold, wheezing with dyspnoea, chest tightness and dyspnoea after exercise respectively increased by 29% (95% CI: 1%, 65%), 50% (95% CI: 16%, 93%), 29% (95% CI: -1%, 68%), 28% (95% CI: 1%, 63%) and 26% (95% CI: 1%, 56%) per 10 dB increase in transportation Lden. Adjusted odds of having current asthma increased by 33% (95%CI: 2%, 74%) per 10 dB increase in transportation Lden (Table 3). Associations between transportation Lden and current asthma were pronounced in participants who were non-atopic [OR: 1.13 (95% CI: 0.93, 1.37); p-value of interaction: 0.02] or asthmatic participants who reported adult-onset of asthma [OR: 1.90 (95% CI: 1.25, 2.89); p-value of interaction: 0.03]. We observed no sex

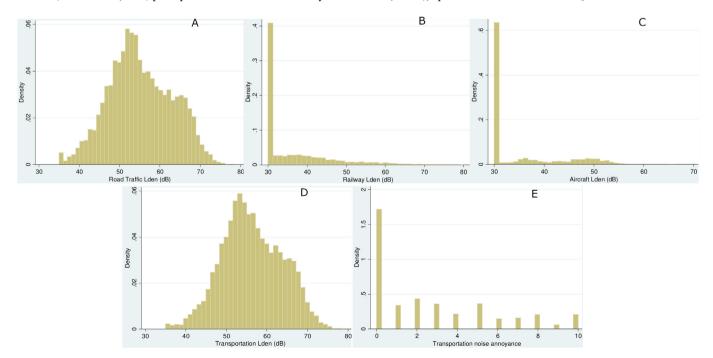


Fig. 1. Distribution of source-specific and combined 24-hour transportation noise exposure levels and noise annoyance in the present study. A: Road traffic noise level; B: Railway noise level; C: Aircraft noise level; D: Transportation noise level; E: Transportation noise annoyance.

Repeated-measures associations (odds ratios and 95% confidence intervals) of respiratory symptoms with one-year mean transportation noise (Lden) and noise annoyance. Table 3

Model	Regular cough/	Chronic cough/	Wheezing	Wheezing without	Wheezing with	Chest tightness	Nocturnal dyspnea	Diurnal dyspnea at	Dyspnea after	Current asthma
Model 1 Lden	1.15 (1.07, 1.25)*	1.22 (1.09, 1.37)*	1.17 (1.06, 1.29)*	1.15 (1.02, 1.29)*	1.07 (0.94, 1.22)	1.12 (1.02,	1.15 (1.01, 1.30)*	1.28 (1.12, 1.45)*	1.28 (1.18, 1.38)*	1.04 (0.91, 1.19)
Noise annoyance	Noise annoyance 1.05 (1.03, 1.06)*	1.06 (1.04, 1.09)*	1.04 (1.02, 1.06)*	1.04 (1.01, 1.07)*	1.04 (1.01, 1.07)*	1.22)* 1.04 (1.02, 1.06)*	1.07 (1.04, 1.10)*	1.10 (1.07, 1.13)*	1.06 (1.04, 1.08)*	1.04 (1.01, 1.07)*
Model 2 Lden	1.00 (0.92, 1.09)	1.03 (0.91, 1.16)	1.07 (0.97, 1.19)	1.07 (0.95, 1.22)	1.03 (0.89, 1.18)	1.11 (1.01,	1.07 (0.94, 1.25)	1.08 (0.94, 1.24)	1.09 (1.01, 1.19)*	1.01 (0.87, 1.16)
Noise annoyance	Noise annoyance 1.04 (1.02, 1.05)*	1.05 (1.02, 1.07)*	1.04 (1.01, 1.06)*	1.04 (1.01, 1.07)*	1.04 (1.01, 1.08)*	1.05 (1.03, 1.07)*	1.06 (1.03, 1.09)*	1.07 (1.04, 1.10)*	1.05 (1.03, 1.07)*	1.04 (1.01, 1.07)*
Model 3 Lden Noise annoyance	0.97 (0.89, 1.05) 1.04 (1.02, 1.06)*	0.98 (0.86, 1.11) 1.05 (1.02, 1.08)*	1.04 (0.93, 1.16) 1.03 (1.01, 1.06)*	1.04 (0.91, 1.18) 1.04 (1.01, 1.07)*	0.98 (0.85, 1.14) 1.04 (1.01, 1.08)*	1.06 (0.97, 1.17) 1.04 (1.02, 1.07)*	1.02 (0.88, 1.18) 1.06 (1.03, 1.09)*	1.00 (0.86, 1.15) 1.07 (1.04, 1.11)*	1.04 (0.96, 1.14)	0.97 (0.84, 1.12) 1.04 (1.01, 1.08)*
Model 4 Road Lden Railway Lden Aircraft Lden Noise annoyance	0.95 (0.88, 1.03) 1.03 (0.95, 1.12) 1.08 (0.90, 1.30) 1.04 (1.02, 1.06)*	0.92 (0.82, 1.04) 1.09 (0.98, 1.22) 0.86 (0.66, 1.12) 1.05 (1.02, 1.08)*	1.03 (0.93, 1.14) 1.00 (0.90, 1.11) 0.90 (0.72, 1.13) 1.03 (1.01, 1.06)*	1.03 (0.91, 1.16) 1.01 (0.90, 1.14) 0.94 (0.72, 1.22) 1.04 (1.01, 1.07)*	1.00 (0.86, 1.15) 0.94 (0.82, 1.08) 0.90 (0.67, 1.21) 1.04 (1.01, 1.08)*	1.04 (0.95, 1.14) 1.01 (0.93, 1.11) 0.90 (0.73, 1.09) 1.04 (1.02, 1.07)*	0.98 (0.85, 1.12) 1.05 (0.92, 1.20) 0.90 (0.66, 1.22) 1.06 (1.03, 1.09)*	1.02 (0.89, 1.17) 0.96 (0.85, 1.10) 1.27 (0.95, 1.69) 1.07 (1.04, 1.10)*	1.03 (0.95, 1.11) 0.96 (0.89, 1.04) 0.68 (0.57, 0.81) 1.05 (1.03, 1.07)*	0.96 (0.83, 1.10) 0.94 (0.81, 1.08) 0.85 (0.63, 0.14) 1.04 (1.01, 1.08)*
Model 3 in asthmatic participants Lden 0.84 (0.66, 1.0	atic participants 0.84 (0.66, 1.08)	0.99 (0.72, 1.35)	1.29 (1.01, 1.65)*	1.50 (1.16, 1.93)*	$1.29~(0.99,1.68)^{\dagger}$	1.28 (1.01, 1.63)*	1.25 (0.93, 1.67)	0.96 (0.73, 1.28)	1.26 (1.01, 1.56)*	1.33 (1.02, 1.74)*
Noise annoyance	Noise annoyance 1.04 (0.99, 1.10)	1.04 (0.97, 1.11)	1.00 (0.95, 1.06)	1.00 (0.95, 1.06)	1.01 (0.96, 1.07)	0.97, 1.07)	1.05 (0.98, 1.12)	1.03 (0.97, 1.10)	0.99 (0.94, 1.04)	1.02 (0.96, 1.08)
Model 3 in asthma Lden	Model 3 in asthmatic participants without medication Lden 0.71 (0.52, 0.96) 0.69 (0.46, 1	ut medication 0.69 (0.46, 1.03)	1.10 (0.82, 1.48)	1.32 (0.95, 1.83)	1.26 (0.90, 1.77)	1.58 (1.16,	1.28 (0.84, 1.95)	1.13 (0.78, 1.65)	$1.27~(0.97,1.66)^{\dagger}$	1.18 (0.86, 1.61)
Noise annoyance	Noise annoyance $1.06~(0.99,1.14)^{\dagger}$	$1.08 \ (0.99, \ 1.17)^{\dagger}$	1.03 (0.97, 1.10)	1.05 (0.97, 1.12)	1.05 (0.98, 1.13)	0.96, 1.09)	$1.09\ (0.99,\ 1.19)^{\dagger}$	1.02 (0.94, 1.10)	1.01 (0.95, 1.07)	1.04 (0.97, 1.12)

All results per 10 dB of noise exposure and per 1 point of the 11-point noise annoyance scale. Lden (unless specified otherwise) represents a combination of road, aircraft and railway Ldens. Road, aircraft and railway effect estimates are from adjusted multi-noise exposure models. All mixed logistic models were adjusted for survey, and random intercepts were placed at the levels of the participants. Model 1: Crude; Model 2: Model 2: Model 1 + age, age-squared, sex, formal education, neighbourhood socio-economic status, atopy, parental asthma, smoking status and pack-years, exposure to passive smoke, study area, residential nitrogen dioxide levels, greenness, noise truncation indicators. Model 3: Model 2+ noise annoyance/Lden; Model 4: Model 3 using source-specific Lden. Current asthma was defined as having doctor-diagnosed asthma and having one of the following in the preceding 12 months: (i) asthma attack or (ii) using asthma medication or (iii) any three of wheezing with dyspnoea, chest tightness, nocturnal dyspnoea, diurnal dyspnoea at rest and dyspnoea after exercise (Boudier et al., 2013).

kercise (Boudier et al.,
 p-value < 0.05.</pre>

 $^{^{\}dagger}$ p-value < 0.1.

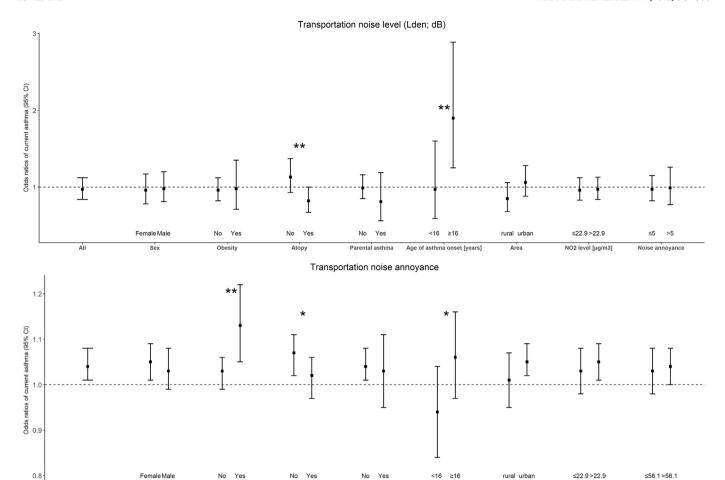


Fig. 2. Modification of the association of current asthma in adults with transportation noise exposure and noise annoyance.

Lden: Day-evening-night noise level. All results are per 10 dB of noise exposure and per 1 point of the 11-point noise annoyance scale. All mixed logistic models were adjusted for age, age-squared, sex, formal education, neighbourhood socio-economic status, atopy, parental asthma, smoking status and pack-years, exposure to passive smoke, residential nitrogen dioxide levels, greenness, noise truncation indicators, study area and survey. Random intercepts at the level of participants were included in all models. Current asthma was defined as having doctor-diagnosed asthma and having one of the following in the preceding 12 months: (i) asthma attack or (ii) using asthma medication or (iii) any three of wheezing with dyspnoea, chest tightness, nocturnal dyspnoea, diurnal dyspnoea at rest and dyspnoea after exercise (Boudier et al., 2013). *p < 0.1; **p < 0.05

Parental asthma

Age of asthma onset [years]

differences in the association between transportation Lden and current asthma (Fig. 2).

Obesity

3.4. Sensitivity analyses

Associations of respiratory symptoms with transportation Lden and noise annoyance were stable across sensitivity analyses. Associations between noise annoyance and respiratory symptoms were close to linear, as indicated by positive estimates of the squared terms of noise annoyance. Adjusted estimates of transportation Lden and noise annovance were stable to additional adjustment for BMI, PM₁₀ and also in models replacing NO₂ with PM₁₀. We observed similar unadjusted estimates of associations between the included and excluded participants. We also observed similar estimates of associations between included and excluded participants when we adjusted for covariates defined at the level of geo-coordinates. Estimates of association of Lden and noise annoyance with respiratory symptoms limited to SAP2 and SAP3 were very similar to those reported for SAP1-SAP3 (Supplementary Table S7). Adjusted effect estimates also remained in size, in models limited to asthmatic participants, after excluding those on asthma medication, but became mostly statistically non-significant (Table 3). We did not observe considerable inter-area differences in associations of Lden and noise annoyance on current asthma (Supplementary Table S8).

3.5. Transportation Lden, noise annoyance and incident asthma

We did not observe any associations of incident asthma with transportation Lden and noise annoyance in crude, adjusted and mutually-adjusted models (Table 4). Adjusted relative risks of incident asthma were 0.98 (95% CI: 0.84, 1.14) per 10 dB of transportation Lden and 1.01 (95% CI: 0.97, 1.04) per 1-point difference in noise annoyance. Mutually-adjusted relative risks of incident asthma were 0.97 (95% CI: 0.83, 1.14) per 10 dB of transportation Lden and 1.01 (95% CI: 0.98, 1.04) per 1-point difference in noise annoyance These estimates remained stable upon adjustment for BMI, in models limited to nonmovers, and in models using an alternative definition of incident asthma (Table 4).

NO2 level [µg/m3]

Noise level [dB]

4. Discussion

To our knowledge, this is the first study examining associations of transportation noise and noise annoyance with both current respiratory and asthma symptoms, as well as with incident asthma in an adult population. Our results showed that noise annoyance was associated with respiratory symptoms and prevalent asthma in a general adult population. Both noise level and annoyance were independently associated with exacerbation of asthma, but not with incidence of asthma,

Table 4
Repeated-measures associations (relative risks and 95% confidence intervals) of incidence of asthma with transportation noise exposure and noise annoyance.

		Repeated incident asthr	na	Repeated incident asthma	(clean controls) ^a
Model	Exposure	All	Non-movers	All	Non-movers
N		10,657	5378	10,112	5121
Model 1	Lden	1.05 (0.92, 1.21)	0.97 (0.79, 1.20)	0.97 (0.84, 1.13)	0.87 (0.69, 1.09)
	Noise annoyance	1.02 (0.99, 1.06)	1.03 (0.98, 1.07)	1.01 (0.98, 1.05)	1.01 (0.96, 1.07)
Model 2	Lden	0.98 (0.84, 1.14)	0.90 (0.71, 1.14)	0.91 (0.77, 1.07)	0.82 (0.63, 1.06)
	Noise annoyance	1.01 (0.97, 1.04)	1.02 (0.97, 1.07)	1.00 (0.96, 1.04)	1.01 (0.95, 1.06)
Model 3	Lden	0.97 (0.83, 1.14)	0.88 (0.69, 1.12)	0.91 (0.77, 1.07)	0.80 (0.61, 1.04)
	Noise annoyance	1.01 (0.98, 1.04)	1.02 (0.97, 1.07)	1.00 (0.97, 1.04)	1.02 (0.96, 1.08)
Model 4	Road Lden	0.98 (0.85, 1.14)	0.91 (0.73, 1.14)	0.93 (0.79, 1.09)	0.83 (0.65, 1.07)
	Railway Lden	1.07 (0.93, 1.22)	0.97 (0.79, 1.20)	1.06 (0.92, 1.22)	0.97 (0.78, 1.22)
	Aircraft Lden	1.24 (0.89, 1.72)	0.87 (0.50, 1.52)	1.24 (0.86, 1.78)	0.85 (0.45, 1.59)
	Noise annoyance	1.01 (0.97, 1.04)	1.02 (0.97, 1.07)	1.00 (0.97, 1.04)	1.02 (0.96, 1.08)
Model 3 + BMI	Lden	0.96 (0.82, 1.13)	0.87 (0.68, 1.11)	0.90 (0.76, 1.07)	0.79 (0.61, 1.04)
	Noise annoyance	1.01 (0.98, 1.04)	1.02 (0.97, 1.07)	1.01 (0.97, 1.04)	1.02 (0.96, 1.08)

All results per 10 dB of noise exposure and per 1 point of the 11-point noise annoyance scale. SAPALDIA: Swiss cohort study on air pollution and lung and heart diseases in adults. BMI: body mass index. Lden (unless specified otherwise) represents a combination of road, aircraft and railway day-evening-night noise levels. Road, aircraft and railway effect estimates are from adjusted multi-noise exposure models. All mixed Poisson models were adjusted for survey, and random intercepts were placed at the levels of the participants.

Model 1: Crude model. Model 2: age, age-squared, sex, formal education, neighbourhood socio-economic status, atopy, parental asthma, smoking status and pack-years, exposure to passive smoke, residential nitrogen dioxide levels, greenness, study area, noise truncation indicators. Model 3: Model 2 + noise annoyance/Lden. Model 4: Model 3 using source-specific Lden. Analyses combined incident asthma at first and second follow-up with predictor variables from baseline and first follow-up surveys respectively.

a Incident asthma excluding from the controls, participants who reported having any three of (i) wheezing with dyspnoea, (ii) chest tightness on waking up, (iii) nocturnal dyspnoea, (iv) diurnal dyspnoea at rest or (v) dyspnoea following exercise, but did not report doctor-diagnosed asthma at both baseline and follow-up study time points.

regardless of air pollution and other respiratory disease risk factors. Associations with noise level and respiratory symptoms were explained to an extent, by noise annoyance, whereas those with annoyance were not explained by noise levels.

Noise levels in our study were comparatively lower than observed in a similar study (Cai et al., 2017), and even further reduced over followup. The reduction in transportation noise level could be explained by the increased construction of noise barriers over highways and rail lines since 2000, improvements in the rolling stock of freight trains, reduction and re-routing of aircrafts to reduce night-time exposures in Switzerland (Karipidis et al., 2014). Participants additionally tended to move to quieter areas across surveys. Correspondingly, noise annoyance also reduced, given their positive significant correlations (Supplementary Fig. S3). However, the magnitude of correlation between transportation noise level and annoyance was only modest, implying that noise level may not be the only determining factor for noise annoyance. Interestingly, noise sensitivity was recently shown to be a stronger determinant of noise annoyance than noise level (Sung et al., 2017). Thus, noise annoyance may not only capture noise exposure of participants, but also their noise sensitivity or susceptibility to stressors

Noise annoyance is thought to reflect perceived stress due to noise. Our observation of associations of respiratory symptoms with noise annoyance is not surprising, given that unpleasant emotional states were associated with decline in lung function in both healthy and asthmatic individuals (Ritz and Kullowatz, 2005). In addition, annoyance due to noise exposure may encompass the activation of the Hypothalamic-Pituitary Axis and lead to increased production of stress hormones (Babisch et al., 2001; Recio et al., 2016) and inflammatory processes as a possible pathway to respiratory symptoms. Our finding of associations with noise annoyance, but not noise level in the whole sample agrees with a recent study from the Netherlands where perceived but not modelled noise exposure was associated with respiratory and other health symptoms in adults (Martens et al., 2018). Although the self-reported noise exposure in (Martens et al., 2018) may not directly capture annoyance, people might be more likely to report higher exposures if they are more sensitive or annoyed by noise, regardless of the actual level, thus supporting the comparability of our findings. These therefore suggest that for respiratory symptoms in adults, the perceptive stress pathway with an emotional response might be more relevant than objective noise level, which would relate more to the non-perceptive physiological response (Foraster et al., 2016; Ndrepepa and Twardella, 2011).

Similar to a previous study which reported exposure to traffic intensity, a proxy marker for both traffic-related air pollution and noise exposures, to be associated with non-allergic respiratory symptoms (Heinrich et al., 2005), we found higher effects of noise levels on current asthma in the non-atopic asthmatics. Our observation of positive associations of noise level with respiratory symptoms in asthmatics may indicate their higher vulnerability to stressors (Ritz et al., 2000). Asthmatics may be more sensitive to chronic stress-induced immune system dysfunction (Schmid-Ott et al., 2001) and smooth-muscle reactivity (Isenberg et al., 1992). More so, associations were stronger in asthmatics on medication given the weakening of associations on their exclusion, showing increased effects with disease severity. Our observation of stronger associations of noise annovance with asthma exacerbation in adult-onset asthma are somewhat consistent with the similar findings among the obese and non-atopic, which are more frequent among persons with adult-onset asthma than persons with childhood-onset asthma (Beuther and Sutherland, 2007; de Nijs et al., 2013). Furthermore, our finding of stronger noise annoyance effects in the obese asthmatics corroborates the previous finding on noise annoyance and reduced physical activity in the SAPALDIA population (Foraster et al., 2016), evidencing the potential negative impact of noise annoyance to allostasis. While asthmatics are prone to allostatic load (Bahreinian et al., 2013; Loerbroks et al., 2009) including obesity (Jeong et al., 2017; Mohanan et al., 2014), physical activity reduces their accumulation by counteracting obesity and other states of subclinical inflammation (Gay et al., 2015).

In line with a previous study (Cai et al., 2017), we did not find any associations between noise levels and prevalent and incident asthma, except for a higher prevalence of symptoms in asthmatic participants. Exposure to traffic intensity was also not associated with prevalent asthma (Heinrich et al., 2005). Unlike other studies which linked stress

to incident adult asthma (Korkeila et al., 2012; Loerbroks et al., 2009; Loerbroks et al., 2010; Rod et al., 2012), our results do not support an association between noise annoyance and incident asthma. This might be due to the low incident asthma rate in our study, or because both noise and annoyance might not play a role in the development of asthma among adults. More studies are needed to confirm and better understand these findings.

Strengths of our study include its novelty in concurrently investigating the relationship of transportation noise exposure and annovance with respiratory health, particularly taking into account concurrent exposure to air pollution. This study is also comprehensive in consideration of respiratory symptoms as well as risk of adult asthma. using multiple measurements, in a cohort followed for about 20 years. We had composite and high-quality individually-assigned long-term noise exposure variables covering the main transportation noise sources, and could do several sensitivity analyses enabled by the detailed phenotypic and exposure characteristics of the SAPALDIA study population. We could control for traffic-related air pollution, better captured by NO₂ than PM₁₀ in our study. Although both pollutants were correlated (r = 0.8), Lden correlated better with NO₂ (r = 0.34) than with PM_{10} (r = 0.20). The better correlation of NO_2 , in addition to its known decay properties with distance from traffic, made it a better potential confounder of transportation noise in our study. With data from three repeated assessments, we could include a large number of observations, increasing our power to detect associations. Our findings could be generalized to the entire SAPALDIA population since there was no indication of sizable selection bias.

Our study is mainly limited by the low rate of incident asthma. We could not explore the modifying effect of stress or sleep-related variables due to their non-availability across all three surveys. Our noise exposure estimates might have been prone to misclassification due to input data errors such as missing noise barriers and buildings, inaccuracies of buildings and infrastructure geometries. But this misclassification is likely non-differential as evidenced by our observation of similar results in sensitivity analyses limited to the two follow-up surveys with less error in input data. Moreover, we applied detailed individual noise exposure assessment, considering participant mobility history and based again on the sensitivity analyses, we did not observe exposure misclassification due to mobility. We did not have fine particulate matter (PM_{2.5}) at the three time-points, which might have stronger confounding respiratory effect than PM10, limiting further exploration by this pollutant. But PM2.5 was highly correlated with PM_{10} and NO_2 both at SAP2 (respective r = 0.9 and 0.8) and SAP3 (respective r = 0.9 and 0.6) therefore we would expect similar results with consideration of PM2.5 in our study. Participants with respiratory problems may have over-reported being annoyed by noise as they might be more susceptible to environmental stressors. In addition, recall bias may have affected the responses to the respiratory symptoms, but we expect this bias to be minimal, especially in asthmatic participants. Finally, our estimates may also have been affected by residual confounding by unmeasured factors which may influence respiratory symptom or asthma severity such as ozone, temperature, pollen exposure or seasonality and other potential stressors. But susceptibility to these factors is influenced by allergy and genetic factors, therefore our adjustment for atopic status and family history of asthma should have limited residual confounding due to these factors.

5. Conclusion

Our novel findings indicate that noise annoyance may influence the occurrence of respiratory symptoms, and that noise annoyance and noise level, may both independently exacerbate asthma in adults. Our findings suggest that both psychological and physiological noise reactions could impact the respiratory system and therefore could be relevant for asthma management. More studies are therefore needed to confirm these novel findings, as well as to further disentangle the

effects of objective and perceived transportation noise exposure on respiratory health.

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Declarations of interest

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2018.10.006.

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