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Title: Incident hypertension in relation to aircraft noise exposure: Results of the DEBATS longitudinal study in France

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Abstract

Background: Although several cross-sectional studies have shown that aircraft noise exposure was associated with an increased risk of hypertension, a limited number of longitudinal studies have addressed this issue. This study is part of the DEBATS (Discussion on the health effect of aircraft noise) research program and aimed to investigate the association between aircraft noise exposure and the incidence of hypertension.

Methods: In 2013, 1,244 adults living near three major French airports were included in this longitudinal study. Systolic and diastolic blood pressure, as well as demographic and lifestyle factors, were collected at baseline and after two and four years of follow-up during face-to-face interviews. Exposure to aircraft noise was estimated for each participant's home address using noise maps. Statistical analyses were performed using mixed Poisson and linear regression models adjusted for potential confounding factors.

Results: A 10 dB(A) increase in aircraft noise levels in terms of L_{den} was associated with a higher incidence of hypertension (incidence rate ratio (IRR) =1.36, 95% CI: 1.02; 1.82). The association was also significant for L_{day} (IRR=1.41, 95% CI: 1.07; 1.85) and L_{night} (IRR=1.31, 95% CI: 1.01; 1.71). Systolic and diastolic blood pressure increased with all noise indicators.

Conclusion: These results strengthen those obtained from the cross-sectional analysis of the data collected at the time of inclusion in DEBATS, as well as those from previous studies conducted in other countries. Hence, they support the hypothesis that aircraft noise exposure may be considered as a risk factor for hypertension.

Key words: epidemiology; longitudinal study; aircraft noise exposure; incident hypertension.

What this paper adds

- A growing number of cross-sectional studies have shown a significant association between aircraft noise exposure and the prevalence of hypertension. However, there is a lack of studies with a longitudinal design that have investigated the incidence of hypertension.
- The findings of the present study strengthen those obtained by two previous studies in supporting the hypothesis of a positive association between aircraft noise exposure and the incidence of hypertension.
- They also show a potential mediating role of noise annoyance and a moderating role of noise sensitivity in this association.

INTRODUCTION

According to the World Health Organization (WHO), environmental noise causes the loss of at least one million healthy life years every year in Western Europe [1]. Epidemiological studies have previously linked long-term exposure to aircraft noise to several health risks such as sleep disturbance [2–4], noise annoyance [5,6], impaired cognitive performance in children [7] and cardiovascular morbidity [8,9] including hypertension [10,11]. The association between noise exposure and hypertension has been explained by the physiological stress response that may be triggered by noise exposure, resulting in activation of the sympathetic and neuroendocrine systems, which in turn leads to increased levels of stress hormones [12]. This increase itself is associated with higher heart rate and blood pressure [13].

A growing number of cross-sectional studies have shown a significant association between exposure to aircraft noise and the prevalence of hypertension [10]. Nevertheless, after aggregating the results of nine cross-sectional studies (comprising 60,121 residents, including 9,487 cases), the review of Van Kempen et al derived a non-significant relative risk (RR) of 1.05 (95% confidence interval (CI): 0.95; 1.17) per 10 dB(A) increase in day-evening-night aircraft noise levels [10].

In addition, there is a lack of studies on the incidence of hypertension with only a few longitudinal studies that have addressed this issue. In a cohort of 4,854 participants from Stockholm County between 1992 and 2006, Pyko et al. observed an increase in the incidence of hypertension with increasing aircraft noise levels, with a hazard ratio (HR) of 1.16 (95% CI: 1.08; 1.25) per 10 dB(A) increase in day-evening-night aircraft noise levels one year prior to the event, and of 1.16, 95% CI: 1.08; 1.24) per 10-dB(A) increase in day-evening-night time-weighted average of aircraft noise levels five years preceding the event [14]. These results are consistent with those of Dimakopoulou et al. who followed the 420 HYENA (Hypertension and Exposure to Noise near Airports) participants living near the Eleftherios Venizelos airport in Athens (Greece) [15]. This cohort study reported an increased incidence of hypertension with increased exposure to aircraft noise at night (OR= 2.63, 95% CI:1.21; 5.71 per 10 dB(A) increase) [16].

Thus, in this context of insufficient longitudinal studies investigating the incidence of hypertension, this paper aimed to study the association between exposure to aircraft noise and the incidence of hypertension over four years of follow-up (2013-2017) of the French DEBATS study.

METHODS

Study population

Participants in this study were adults over 18 years of age at the time of interview. They were recruited in 2013 near three major French airports: Paris-Charles-de-Gaulle, Lyon-Saint-Exupéry, and Toulouse-Blagnac (Figure 1) [8,11]. Eligible participants were randomly selected on the basis of their home address after being stratified for aircraft noise contours which divided the study area into four aircraft noise level categories in terms of L_{den}: <50 dB(A), 50-54 dB(A), 55-59 dB(A) and >=60 dB(A). L_{den} is a day-evening-night noise indicator corresponding to an annual 24-hour average of sound pressure levels, with an additional weighting of 5 dB(A) for evening noise (18:00 to 22:00) and 10 dB(A) for night noise (22:00 to 6:00) to reflect people's sensitivity to noise [17].

A total of 1,244 participants were enrolled at baseline (Figure 2) and completed a questionnaire in a face-to-face interview at their home with a trained interviewer to collect demographic and socio-economic characteristics, anthropometric measurements, lifestyle factors (sports activities, tobacco and alcohol consumption), and personal medical history (cardiovascular disease, medication use, noise sensitivity and annoyance due to aircraft noise).

Two follow-ups were conducted two (T2 in 2015) and four (T4 in 2017) years after baseline (T0 in 2013). A total of 992 adults participated in the first follow-up visit (T2) and 811 in the second (T4), corresponding respectively to 80% and 65% of baseline participants (Figure 2). At each visit, participants completed a very similar questionnaire.

Blood pressure and incident hypertension

At each visit, participant's systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured three times, while seated, by the interviewer using a validated and automated blood pressure (BP) measuring device (Omron® M6 comfort), in accordance with recommendations of the American Heart Association [18]. The first measurement was taken after a 5-minute rest at the beginning of the interview and was followed by a second measurement 1-minute later. The average of these two BP measurements was used to define

SBP and DBP. A third reading was recorded approximately 1 hour later (at the end of the interview) and was used as a validity control to exclude, in a sensitivity analysis, 15 participants at T2 and 9 at T4 from the incident hypertension analysis on one hand, and 73 participants at T0, 75 at T2 and 43 at T4 from SBP and DBP analyses on the other hand, for whom this third reading was significantly different (±20 mm Hg) from the mean of the first two measurements (results not shown).

Participants were classified as hypertensive if their BP levels exceeded the WHO predefined threshold (SBP≥140 mm Hg or DBP≥90 mm Hg) [19], or if they reported a previous diagnosis of hypertension by a physician and the use of anti-hypertensive medication in the 12 months prior to the interview. The fact that these medications corresponded to antihypertensive medications was verified from the ATC codes. At each visit, participants with BP levels exceeding the WHO standards were recommended to visit their doctor for a possible diagnosis of hypertension.

Analyses for incident hypertension included only participants who were not classified as hypertensive at baseline (T0). Incident cases were defined as being classified as hypertensive for the first time during the study at T2 or at T4.

Aircraft noise exposure assessment

Exposure to outdoor aircraft noise at each participant's place of residence was assessed in 1 dB(A) (A-weighted decibel) intervals from noise maps generated by Paris airports (Paris-Charles de Gaulle, 2013-2017) and the French Civil Aviation Authority (Lyon-Saint-Exupéry 2004, Toulouse-Blagnac, 2003) using the Integrated Noise Model (INM) [20]. The assessment was carried out by linking the participants' home addresses at each follow-up to the noise contours using Geographic Information System (GIS) technique.

In addition to L_{den}, three other noise level indicators were calculated and used in the following statistical analyses: $L_{Aeq,24h}$, L_{day} and L_{night}. $L_{Aeq,24h}$ is the A-weighted equivalent continuous noise level over a 24-hour period, L_{day} is the day-evening time indicator (6:00 to 22:00) and L_{night} is the night time indicator (22:00 to 6:00) [17]. For participants living near Paris Charles de Gaulle airport, the modelled aircraft noise levels for the years 2014 and 2016 were used for the incident hypertension analysis, while the modelled aircraft noise levels for the years 2013, 2015 and 2017 were used in SBP and DBP analyses.

Statistical analysis

The characteristics of the participants were compared by study timepoint using the Pearson chi-squared test for categorical data, and Kruskal-Wallis test for continuous data. The correlation between noise indicators was evaluated using the Spearman rank-order correlation coefficients.

Incident hypertension

Mixed Poisson regression models using the log-link function with a random intercept at the participant level were used. Those models estimate incidence rate ratios (IRR), i.e. the exponentials of the beta coefficients, with corresponding 95% confidence intervals (CI). Confounders were included in the models ensuring that they preceded the onset of hypertension [21] and the visit time indicator variable included in the models had two levels (0/2). Level 0 corresponded to the participant's hypertension information collected at T2 and the main potential confounders measured at T0. Likewise, level 2 corresponded to hypertension information collected at T4 and the main potential confounders measured at T2. All multivariable Poisson regression models included the following confounders obtained from the questionnaire: gender, age (continuous), body mass index (BMI; three categories: underweight or normal/overweight/obese), sports activities (yes/no), occupational activity (yes/no) and alcohol consumption (three categories: no/light/moderate or heavy). The selection of these a priori confounding factors was mainly based on results from a previous cross-sectional study of the baseline (T0) data in the same population [11].

Smoking was initially included in the models, but it was not included in the end as it did not contribute significantly to the models and did not modify the noise effect estimates.

Participants with missing values were excluded from the visit time for which they had missing values.

Sensitivity analyses were conducted: 1) restricting analysis to participants who had resided at their inclusion address for at least 5 years prior to the baseline interview (T0) and had not moved at the time of the follow-up visit, i.e. participants were excluded from T2 and T4 if they moved between T0 and T2 and participants were excluded from T4 if they moved between T2 and T4; 2) using at all time points the main potential confounders measured at baseline (T0); 3) restricting analysis to the participants who took part in all three visits; 4) using prevalent hypertension as an outcome instead of incident hypertension, i.e. hypertensive participants at T0 were included in this analysis.

Noise annoyance and noise sensitivity could mediate or modify the association between noise exposure and hypertension [22]. Their mediating and moderating effects were investigated following Baron and Kenny's recommendations [23]. These variables were considered in two categories in the models (highly annoyed/not highly annoyed; low or medium/high, respectively).

Systolic and diastolic blood pressure

Mixed linear regression models with a random intercept for each participant were used. The first-order autoregressive covariance structure was used to account for repeated measurements on participants. Outcomes (SBP or DBP) and a priori confounders included in these models were measured during the same visit, and the visit time indicator had three levels representing the corresponding visit. The confounders were similar to those included in the incident hypertension analyses, with the addition of anti-hypertensive medication use (yes/no). Sensitivity analyses were similar to those conducted for incident hypertension. In addition, the study population was restricted to those who did not report anti-hypertensive medication use in the same visit.

Analyses were performed using the GLIMMIX and MIXED procedures of SAS 9.4 software (SAS Institute, Cary NC). Two-sided p-values were used with a 5% statistical significance.

RESULTS

Participants' characteristics were similar over the three visits, except that anti-hypertensive medication use and the mean age of participants significantly increased with follow-up (Table 1). The mean age was 51 years at T0, 53 years at T2, and 56 years at T4 (Table1). At T0, 16% of the participants reported using anti-hypertensive medication. They were 21% at T2 and 25% at T4 (Table 1).

The distribution of participants in the four categories of L_{den} noise exposure did not vary over the follow-up period (Table 1). The mean aircraft noise exposure in terms of L_{den} was 54 dB(A) at T0, T2 and T4. The Spearman rank-order correlation coefficients between the noise indicators were significant and higher than 0.9.

The prevalence of hypertension was 34% at T0, 35 % at T2, and 38% at T4 (Table 1).

After excluding participants with hypertension (n=426) or missing hypertension status (n=14) at T0, participants lost to-follow-up (n=252, including 2 with missing hypertension status and 93 with hypertension at T0) and participants with missing hypertension status at T2 (8), the population at risk at T2 consisted of 639 participants (n=1,244-426-14-(252-2-93)-8), 80 of whom had incident hypertension at T2. Then, after excluding these 80 participants, those lost to follow-up between T2 and T4 (n=113, including 13 with incident hypertension at T2) and those with missing hypertensive status at T2 or T4 (9), the population at risk at T4 consisted of 450 (n=639-80-(113-13)-9) participants, 47 of whom had incident hypertension at T4 (Table 1 and supplementary Table 1).

The characteristics of participants with incident hypertension at T2 and T4 were relatively similar (supplementary Table 2).

Incident hypertension

Table 2 shows the IRRs for incident hypertension in relation to the main a priori confounding factors. The incidence of hypertension increased with age (IRR=1.03, 95% CI: 1.02; 1.05), and was higher in men than in women (IRR=1.72, 95% CI: 1.22; 2.41). The incidence of hypertension was also higher in overweight (IRR=1.86, 95% CI: 1.27; 2.74) and obese (IRR=2.36, 95% CI: 1.51; 3.68) participants than in those of normal weight or underweight.

Table 3 presents adjusted IRRs of the four aircraft noise indicators on incident hypertension. Higher incident hypertension was observed with a 10 dB(A) increase in aircraft noise levels in terms of L_{den} (IRR=1.36, 95% CI: 1.02; 1.82), $L_{Aeq,24h}$ (IRR=1.43, 95% CI: 1.05; 1.96), L_{day} (IRR=1.41, 95% CI: 1.07; 1.85) and L_{night} (IRR=1.31, 95% CI: 1.01; 1.71). Results of the sensitivity analyses were very similar compared with our main results (Table 3).

Higher incident hypertension was found for highly annoyed participants compared to those who were not but the association was not significant (IRR=1.24, 95% CI: 0.84; 1.83, M0 model, supplementary Table 3). When aircraft noise annoyance was included in the M2 model (also called main model in Table 3), the association between aircraft noise levels and incident hypertension became slightly lower and not significant (IRR=1.29, 95% CI 0.97–1.71, for a 10 dB(A)-increase in L_{den}) (M3 model) (supplementary Table 3).

No association was observed between noise sensitivity and incident hypertension (IRR=0.91, 95% CI: 0.70; 1.18, for high noise sensitivity versus medium or low noise sensitivity, M1 model). When noise sensitivity was included in the M2 model, the association between aircraft noise levels and incident hypertension remained similar (IRR=1.34, 95% CI 1.02–1.77, for a 10 dB(A)-increase in L_{den}) (M4 model) (supplementary Table 3).

The association between aircraft noise exposure and incident hypertension was very similar in highly annoyed and not highly annoyed people (M5 model). The association between aircraft noise exposure and incident hypertension was slightly but not significantly higher in people with high noise sensitivity (IRR=1.62, 95% CI 1.07–2.44, for a 10 dB(A)-increase in L_{den}) than in those with medium or low noise sensitivity (IRR=1.26, 95% CI 0.94–1.70, for a 10 dB(A)-increase in L_{den}) (M6 model) (supplementary Table 4).

Systolic and diastolic blood pressure

The multivariate associations between systolic and diastolic blood pressure and main a priori confounding factors are presented in supplementary Table 5.

A statistically significant increases in both SBP and DBP with increasing aircraft noise exposure levels can be seen for all noise indicators (supplementary Table 6). A 10 dB(A) increase in the day-evening-night noise level (L_{den}) was associated with a 1.93 mm Hg increase in SBP (95% CI: 0.79; 3.08,) and a 1.08 mm Hg increase in DBP (95% CI: 0.27; 1.88). Similar results were observed in sensitivity analyses (supplementary Table 6).

DISCUSSION

This study examined the longitudinal associations between exposure to aircraft noise and the incidence of hypertension using information from three visits of residents living near three major French airports.

Our results indicate that a 10 dB(A) increase in L_{den}, L_{day}, $L_{Aeq,24h}$ or L_{night} was statistically significantly associated with a higher incident hypertension. These associations were confirmed by the statistically significant increase observed in both systolic and diastolic blood pressures with increasing aircraft noise levels.

These results are consistent with those obtained in the previous cross-sectional analyses of DEBATS' baseline observations. Indeed, a significant association was found between aircraft noise exposure and the risk of hypertension in men (OR=1.34, 95% CI: 1.00; 1.97 for a 10 dB(A) increase in aircraft noise exposure at night (L_{night})), but not in women (OR=0.90, 95% CI: 0.66; 1.22) or in men and women combined (OR=1.10, 95% CI: 0.90; 1.37) [11]. When the present longitudinal analysis was conducted for men and women separately, the main model did not converge. It only converged when removing the BMI variable and using the age variable not as a continuous variable but in six categories, and gave a significant association for men but not for women. This association was slightly higher for men (IRR=1.41, 95% CI: 1.02; 1.94 for a 10 dB(A) increase in L_{night}) than for women (IRR=1.26, 95% CI: 0.81; 1.96 for a 10 dB(A) increase in L_{night}) (supplementary Table 7). Furthermore, the stronger associations found in the longitudinal analyses, for the total population, are most likely attributable to the use of incident hypertension instead of prevalent hypertension, which led to the exclusion of participants considered as hypertensive at baseline, and the use of the repeated measures approach at T0, T2 and T4 instead of a cross-sectional analysis of baseline data at T0.

Our results are in line with several previous studies showing that exposure to aircraft noise increased the risk of hypertension [24,25,15,26–28]. However, the evidence was considered to be inconclusive in a recent WHO review although the pooled estimate showed a tendency towards a positive association (RR= 1.05 per 10 dB (A) increase in L_{den}, 95% CI: 0.95; 1.17)

[10]. It should be emphasized that the majority of the reviewed studies were cross-sectional in design (nine studies out of ten) and most were judged to be at high risk of bias, mostly due to selection bias or determination of hypertension status through self-reporting only [10].

Our results are also somehow consistent with those obtained in the only two longitudinal studies that addressed this issue [14,16]. Although there were methodological differences between this study and the two cohort studies mentioned above (including in particular the different statistical methods used – Cox regression for Pyko et al, logistic regression for Dimakopoulou et al – as well as differences in the confounding factors), the findings of the three studies can still be considered consistent and support the hypothesis that exposure to aircraft noise was associated with an increase in the incidence of hypertension.

In contrast, the largest case-control study to date, around Frankfurt airport in Germany involving 137,577 cases and 355,591 controls, did not observe an association between aircraft noise and hypertension as recorded in health insurance claims data, with an OR of 0.99 (95% CI 0.98–1.01) per 10 dB(A) increase in aircraft noise levels in terms of $L_{Aeq,24h}$ [29]. Nevertheless, a significant association was found in a sub-group of newly diagnosed hypertension cases with a subsequent diagnosis of hypertensive heart disease (OR=1.14, 95% CI: 1.09; 1.19). However, one of the major limitations of this study highlighted by the authors was the lack of individual data on confounding factors.

The results of the present study remained similar in all sensitivity analyses. In particular, limiting the analysis to participants who had resided at their inclusion address for at least 5 years and had not moved at the time of visit did not change the results significantly, apart from the loss of statistical significance that could be explained by the smaller sample size. This result does not suggest any habituation to noise. This is consistent with the finding of Pyko et al. that the increased risk of hypertension was similar when considering time weighted average of aircraft noise exposure one or five years prior to the event [14].

This study showed a non-significant association between aircraft noise annoyance and incident hypertension (M0 model). When aircraft noise annoyance was included as a covariate in the M2 model, including the noise indicator together with the confounders, (M3 model), the association between aircraft noise levels and incident hypertension became slightly lower and not significant. Moreover, as aircraft noise levels were significantly associated with aircraft noise annoyance in DEBATS [5], according to Baron and Kenny [23], a potential mediating role of aircraft noise annoyance in the relationship between aircraft noise levels and incident hypertension cannot be excluded. Conversely, as no association was observed between noise sensitivity and incident hypertension, noise sensitivity would not play a mediating role in this association. Finally, no significant increase in the incidence of hypertension related to aircraft noise levels was found in participants who were highly annoyed by noise compared to those who were not highly annoyed. In contrast, the association between aircraft noise exposure and incident hypertension was slightly but not significantly higher in people with high noise sensitivity than in those with medium or low noise sensitivity. These latter results suggest that unlike noise annoyance, noise sensitivity may moderate the relationship between aircraft noise levels and the incidence of hypertension. However, further investigations using specific methodology and tools related to mediation and moderation analyses are needed to better understand this role.

The main strength of the current study certainly lies in its longitudinal design, whereas most epidemiological studies on the health effects of aircraft noise are cross-sectional and only two cohort studies to date have addressed hypertension with a longitudinal design. This design made it possible to study the incidence of hypertension and to strengthen the results previously obtained from cross-sectional studies on the prevalence of hypertension. A similar questionnaire was administered at each follow-up visit to collect information on socio-demographic characteristics and lifestyle factors. In addition, standardized questions validated in other studies were used in particular to assess participants' health status, including hypertension. A validated protocol was used to measure participants' blood pressure at their home by trained interviewers [18]. Similarly to the HYENA study in particular, we used a physician's diagnosis of hypertension and the use of anti-hypertensive medication in conjunction with blood pressure measurements to define incident cases of hypertension [15].

The fact that the medications reported by the participants corresponded to antihypertensive medications was verified from the ATC codes. As the use of these medications can only be done after a medical prescription, this was a means to verify the diagnosis of hypertension. The fact that blood pressure was measured only during visits raises the question of possible limitations in the definition of hypertension. Moreover, while there may be recall bias in the information collected on a diagnostic of hypertension and the use of anti-hypertensive medication, it is unlikely that this bias is dependent on exposure to aircraft noise. Thus, the associations observed in this study would tend to underestimate the true associations, if they exist.

Another strength of this study is the validity of the noise maps used estimate aircraft noise exposure at each participant's place of residence. Indeed, these modelled noise levels differed by only 0.5 to 1.5 dB in terms of L_{den} from measurements from permanent stations (Aéroports de Paris, 2007) [30] or during specific campaigns [31]. Moreover, they were also very similar to those calculated from acoustic measurements carried out during one week in the homes of a sub-sample of 112 participants in DEBATS' longitudinal study, with a mean relative difference of 5% and a 95th percentile of 11% [3]. Finally, in particular, aircraft noise levels observed in our study were very consistent with those observed in the HYENA study conducted near six major European airports [32].

A main weakness of the study is that the assessment of aircraft noise exposure was based on noise maps from 2004 for Lyon-Saint-Exupéry and 2003 for Toulouse-Blagnac, while the participants were interviewed in 2013, 2015 and 2017. However, no more recent noise maps were available for these airports.

Exposure misclassification cannot be ruled out in this study. Indeed, only the exposure to aircraft noise at the participants' homes has been estimated. No information was available on their exposure outside the home, especially in the workplace. Even if exposure misclassification exists, it is probably non-differential because the exposure errors are probably not related to hypertension. It would thus have led to an underestimation of the associations observed here. On the other hand, estimating exposure to aircraft noise at night is certainly less prone to error because most people sleep at home. Here, the association between L_{night} and incident hypertension remains relatively similar to that observed for L_{den}. In addition, it was not possible to measure exposure to environmental noise from other sources than aircraft, and no estimated noise levels for sources other than aircraft were available. However, in the questionnaire, participants were asked whether they considered that they worked in a noisy environment or whether they engaged in leisure activities that exposed them to noise. As these variables did not modify the noise effect estimates, they were not included in the final models. Moreover, it was not possible to adjust the models for road noise levels. Indeed, data were not available for residents of Toulouse-Blagnac and Lyon Saint-Exupéry airports and those for residents of Paris-Charles de Gaulle airport were of considerably poorer quality than those concerning aircraft noise levels (heterogeneity of input data and methodologies used).

Another limitation is potential for selection bias. Indeed, participation rate in the study at baseline was low, about 30% (1,244 participants for 4,202 eligible individuals) (Figure 2). Nevertheless, it did not differ much from studies on the same issue conducted in Germany, Italy or the United Kingdom [15] and, it is very similar in the four noise categories (<50, 50-54, 55-59, 60 dB(A) and above) used to stratify participants' selection. In addition, a comparison of the demographic and socio-economic characteristics of the participants and those who refused to participate in the study showed only minor differences according to the four categories of noise exposure [11]. Attrition is a major issue in longitudinal studies that could lead to biased estimates but here the rate of loss to follow-up was relatively low, with 65% of the 1,244 participants recruited that participated in the last follow-up (T4). Furthermore, the loss to follow-up did not differ significantly between highly annoyed and not highly annoyed participants, nor between participants with high noise sensitivity and those with medium or low noise sensitivity. Moreover, a homogeneous distribution of participants in the four noise categories was maintained throughout the study. It should also be noted that the results remain similar when the analyses focus on the participants who took part in all three visits (Table 3).

CONCLUSION

This study is one of the very few longitudinal studies in Europe and the first in France to investigate the association between exposure to aircraft noise and the incidence of hypertension. These results strengthen those obtained by the cross-sectional analysis of the data collected at the time of inclusion in DEBATS, as well as those from previous studies conducted in other countries. Hence, the findings in this study support the hypothesis that aircraft noise exposure may be considered as a potential risk factor for hypertension. They also show a potential mediating role of noise annoyance and a moderating role of noise sensitivity in this association but these latter results deserve further investigation.

Ethics approval and consent to participate

Two national authorities in France, the French Advisory Committee for Data Processing in Health Research (CCTIRS 11-405) and the French National Commission for Data Protection and the Liberties approved the present study (DR 2012-361).
The participants signed and returned an informed consent by mail.

Competing interests

The authors declare that they have no competing interests.

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The funders had no role in the design of the study, in collection, analysis, and interpretation of data and in writing the manuscript.

Authors’ Contributions

ASE and BL with JL and PC conceived and designed the study. ASE and ML conducted the study. JL interpreted the aircraft noise data and PC interpreted the annoyance data. ML was involved in data extraction. ML, AK and LGA did data preparation. AK performed the statistical analyses, supervised by ASE, LB and LGA. The analyses were interpreted by AK with LB, LGA, ASE and BL. AK, LGA and ASE drafted the initial report. All co-authors revised the report and approved the final version. ASE is responsible for the overall content as the guarantor of this paper.

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Figure 1. DEBATS study area and DEBATS participants at baseline with and without hypertension. DEBATS, Discussion on the health effect of aircraft noise.

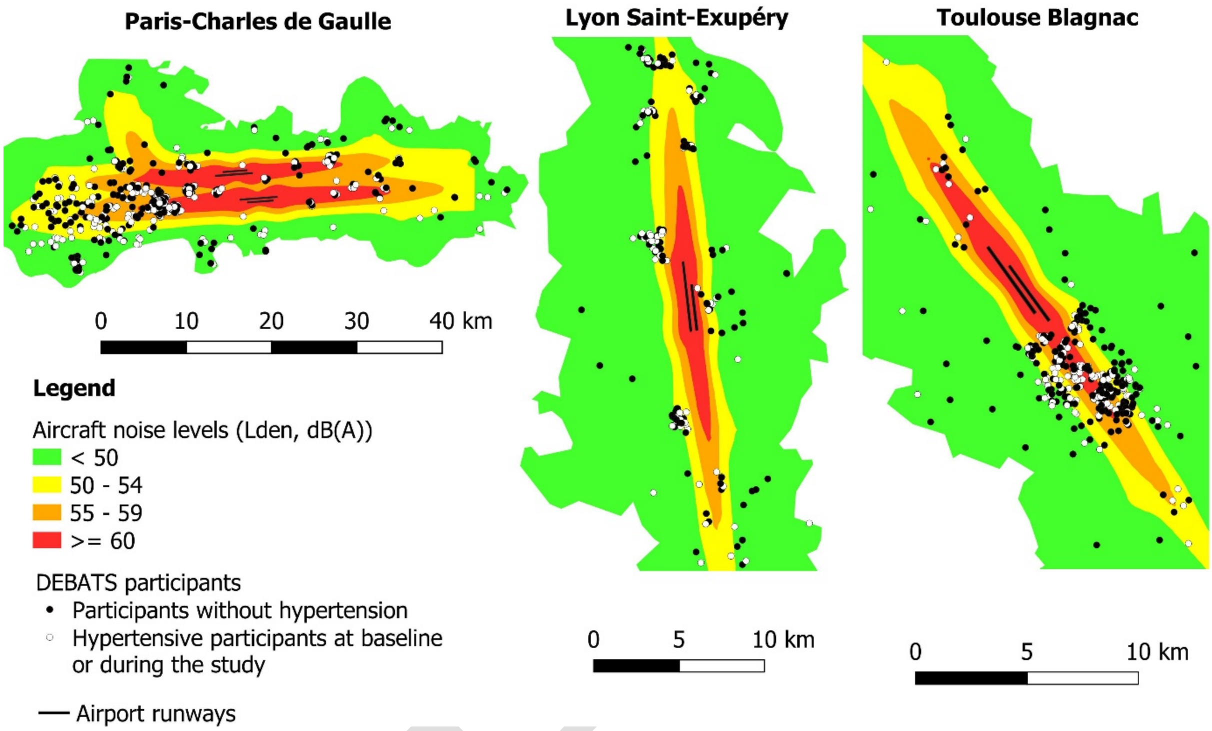

Figure 2. Flow chart of the study participants.

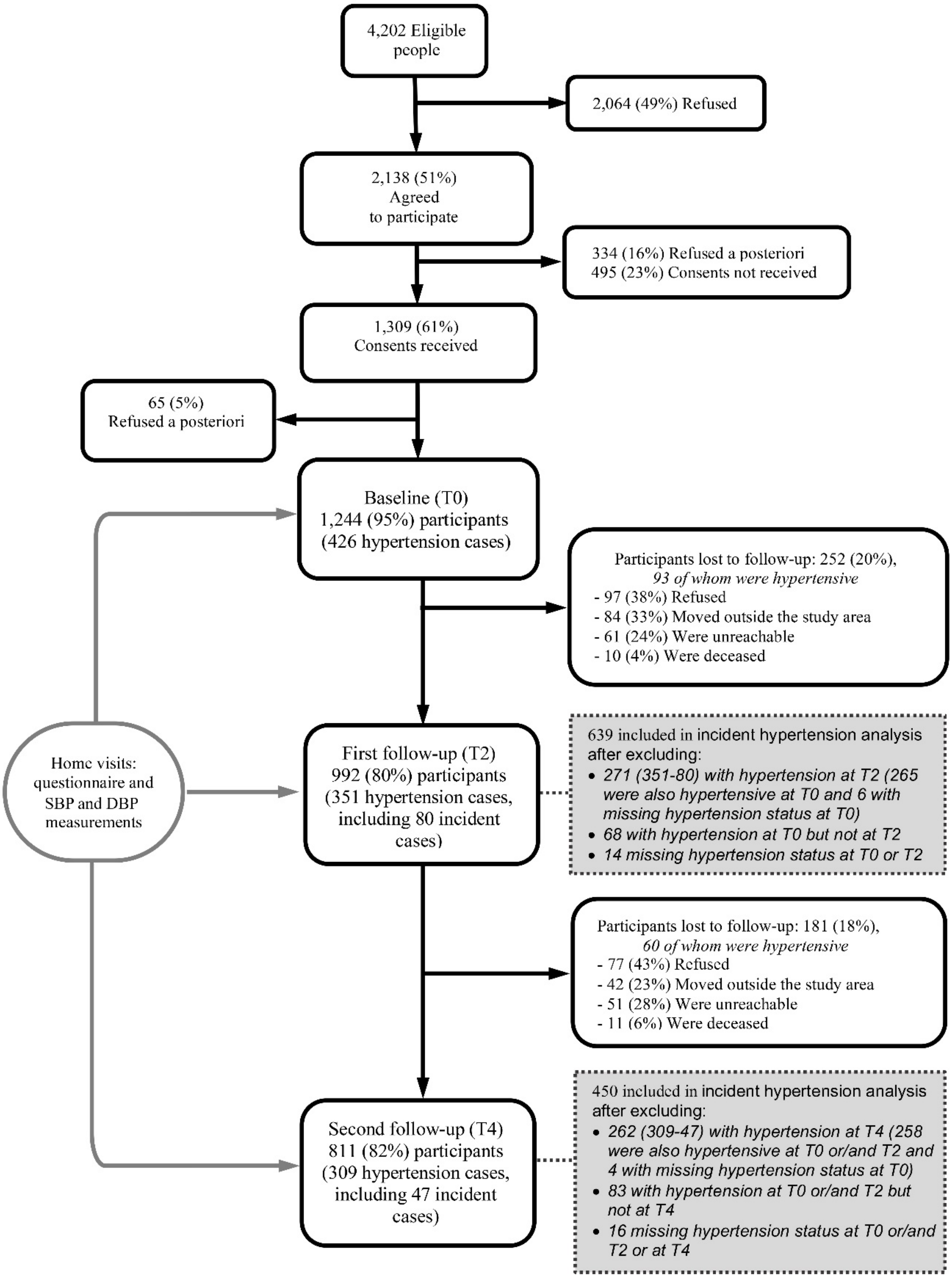

Table 1. Characteristics of the study population at each visit (T0, T2 and T4)

	T0 (N=1244)		T2 (N=992)		T4 (N=811)		
Variable	**n**	**(%)**	**n**	**(%)**	**n**	**(%)**	**p-value [a]**
Gender							0.71
Women	695	(56)	549	(55)	438	(54)	
Men	549	(44)	443	(45)	373	(46)	
Age (years)							<0.01
18-34	226	(18)	125	(13)	67	(8)	
35-44	236	(19)	178	(18)	122	(15)	
45-54	266	(21)	222	(22)	201	(25)	
55-64	260	(21)	223	(22)	177	(22)	
65-74	185	(15)	176	(18)	170	(21)	
≥75	71	(6)	68	(7)	74	(9)	
Body mass index							0.91
Underweight or normal weight	562	(45)	454	(46)	367	(45)	
Overweight	424	(34)	346	(35)	292	(36)	
Obese	249	(20)	192	(19)	151	(19)	
Missing values	9	(1)	0	(0)	1	(0.1)	
Alcohol consumption							0.90
No	348	(28)	292	(29)	245	(30)	
Light	637	(51)	509	(51)	409	(50)	
Moderate or heavy	247	(20)	191	(19)	156	(19)	
Missing values	12	(1)	0	(0)	1	(0.1)	
Sports activities							0.14
No	587	(47)	458	(46)	347	(43)	
Yes	657	(53)	534	(54)	464	(57)	

Variable	T0 (N=1244) n	(%)	T2 (N=992) n	(%)	T4 (N=811) n	(%)	p-value [a]
Occupational activity							0.46
No	499	(40)	415	(42)	347	(43)	
Yes	745	(60)	577	(58)	464	(57)	
Study area							0.39
Paris	620	(50)	469	(47)	369	(46)	
Lyon	213	(17)	184	(19)	156	(19)	
Toulouse	411	(33)	339	(34)	286	(35)	
Noise level, L_{den} (dB(A))							0.14
<50	297	(24)	280	(28)	232	(29)	
50-54	332	(27)	256	(26)	217	(27)	
55-59	293	(24)	210	(21)	161	(20)	
≥60	322	(26)	246	(25)	201	(25)	
Prevalent hypertension							0.23
No	804	(65)	633	(64)	497	(61)	
Yes	426	(34)	351	(35)	309	(38)	
							<0.01
A. Diagnosis and treatment*	111	(9)	134	(14)	128	(16)	
B. SBP≥140 or DBP≥90 mm Hg	223	(18)	151	(15)	117	(15)	
Both A & B	92	(7)	66	(7)	64	(8)	
Missing values	14	(1)	8	(1)	5	(1)	
Anti-hypertensive medication use							<0.01
No	1041	(84)	787	(79)	610	(75)	
Yes	203	(16)	205	(21)	201	(25)	

Variable	T0 (N=1244) n	(%)	T2 (N=992) n	(%)	T4 (N=811) n	(%)	p-value [a]
Incident hypertension cases	-	-	80	(8)	47	(6)	0.29
							0.16
A. Diagnosis and treatment*	-	-	20	(2)	6	(1)	
B. SBP≥140 or DBP≥90 mm Hg	-	-	54	(5)	39	(5)	
Both A & B	-	-	6	(1)	2	(0.2)	
	Mean	**(SD)**	**Mean**	**(SD)**	**Mean**	**(SD)**	
Systolic BP (mm Hg) [b]	123	(18)	123	(17)	123	(17)	0.59
Diastolic BP (mm Hg) [b]	80	(11)	79	(11)	79	(10)	0.07

* Reported a diagnosis by a physician and the use of anti-hypertensive medication in the questionnaire

[a] p-value calculated using χ2 test for categorical variables and Kruskal-Wallis test for continuous variables

[b] 16 missing values at T0, 15 at T2 and 11 at T4

Table 2. Adjusted estimates and 95% confidence intervals (CIs) for incident hypertension in relation to the main a priori confounding factors

	Hypertension N= (T2: 630[a]; T4: 450)	
Variable	**IRR[b] (95% CI)**	**p-value**
Gender		<0.01
Women	1.00	
Men	1.72 (1.22; 2.41)	
Age	1.03 (1.02; 1.05)	<0.01
Body mass index		<0.01
Underweight or normal weight	1.00	
Overweight	1.86 (1.27; 2.74)	
Obese	2.36 (1.51; 3.68)	
Alcohol consumption		0.52
No	1.00	
Light	0.84 (0.57; 1.26)	
Moderate or heavy	0.75 (0.46; 1.24)	
Sports activities		0.62
No	1.00	
Yes	1.09 (0.78; 1.53)	
Occupational activity		0.07
No	1.00	
Yes	0.68 (0.44; 1.04)	

[a] 9 participants with missing data for alcohol consumption or BMI at T0 were excluded at T2

	Hypertension N= (T2: 630[a]; T4: 450)	
Variable	**IRR[b] (95% CI)**	**p-value**
[b] Model was adjusted for age, gender, BMI, sports activities, alcohol consumption and occupational activity and visit time indicator. Confounders (age, gender, BMI, sports activities, alcohol consumption and occupational activity) measured at the previous time visit		

Table 3. Adjusted estimates of the effects of various aircraft noise indicators* on incident hypertension

	N of cases/N total		
	Noise indicator dB(A)	**IRR (95% CI)**	**p-value**
Main model [b]	N^a = (T2: 79/630; T4: 47/450)		
	L_{den}	1.36 (1.02; 1.82)	0.04
	$L_{Aeq,24h}$	1.43 (1.05; 1.96)	0.03
	L_{day}	1.41 (1.07; 1.85)	0.02
	L_{night}	1.31 (1.01; 1.71)	0.04
Sensitivity analysis			
Participants who had resided at their inclusion address for at least 5 years and had not moved at the time of visit [b]	N^a = (T2: 70/494; T4: 42/336)		
	L_{den}	1.30 (0.95; 1.77)	0.10
	$L_{Aeq,24h}$	1.38 (0.99; 1.93)	0.06
	L_{day}	1.32 (0.98; 1.79)	0.07
	L_{night}	1.24 (0.93; 1.65)	0.15
Inclusion of the main potential confounding factors measured at baseline (T0) for all the time points	N^a = (T2: 79/630; T4: 47/444)		
	L_{den}	1.28 (0.96; 1.70)	0.09
	$L_{Aeq,24h}$	1.36 (1.00; 1.86)	0.05
	L_{day}	1.32 (1.00; 1.75)	0.05
	L_{night}	1.26 (0.97; 1.64)	0.09
Participants who took part in all three visits [b,c]	N^a = (T2: 66/510; T4: 47/450)		
	L_{night}	1.35 (1.04; 1.76)	0.03
		RR[d] (95% CI)	**p-value**
Using prevalent hypertension as an outcome	N^a = (T0: 419/1,210; T2: 351/984; T4: 308/804)		
	L_{den}	1.22 (1.05; 1.41)	0.01
	$L_{Aeq,24h}$	1.26 (1.06; 1.49)	0.01
	L_{day}	1.19 (1.04; 1.36)	0.01

	N of cases/N total		
	Noise indicator dB(A)	IRR (95% CI)	p-value
	L_{night}	1.19 (1.04; 1.35)	0.01

All models were adjusted for age, gender, BMI, sports activities, alcohol consumption, occupational activity and visit time indicator

[*] Per 10 dB(A) increase in aircraft noise exposure

[a] Number of participants included in the analysis, after excluding those with missing values for confounders

[b] Adjusted for confounders measured at the previous time visit

[c] Models did not converge for L_{den}, $L_{Aeq,24h}$ and L_{day}

[d] Relative risk. Model adjusted for confounders measured at the same time visit.

Supplementary Table 1. Characteristics of the participants included in the incident hypertension analysis at each visit (T2 and T4), after excluding hypertensive participants at T0

	T2 (N=639)		T4 (N=450)		
Variable	**n**	**(%)**	**n**	**(%)**	**p-value ***
Incident hypertension					0.29
No	559	(87)	403	(90)	
Yes	80	(13)	47	(10)	
Gender					0.97
Women	377	(59)	265	(59)	
Men	262	(41)	185	(41)	
Age (years)					0.12
18-34	111	(17)	54	(12)	
35-44	147	(23)	101	(22)	
45-54	155	(24)	131	(29)	
55-64	123	(19)	81	(18)	
65-74	83	(13)	64	(14)	
≥75	20	(3)	19	(4)	
Body mass index					0.67
Underweight or normal weight	337	(53)	243	(54)	
Overweight	206	(32)	148	(33)	
Obese	96	(15)	59	(13)	

Alcohol consumption					0.83
No	203	(32)	137	(30)	
Light	328	(51)	239	(53)	
Moderate or heavy	108	(17)	73	(16)	
Missing values	0	(0)	1	(0.2)	
Sports activities					0.16
No	276	(43)	175	(39)	
Yes	363	(57)	275	(61)	
Occupational activity					0.12
No	220	(34)	135	(30)	
Yes	419	(66)	315	(70)	
Study area					0.62
Paris	280	(44)	186	(41)	
Lyon	134	(21)	104	(23)	
Toulouse	225	(35)	160	(36)	
Noise level, L_{den} (dB(A))					0.98
<50	201	(31)	146	(32)	
50-54	178	(28)	126	(28)	
55-59	136	(21)	92	(20)	
≥60	124	(19)	86	(19)	
Anti-hypertensive medication use					0.03
No	26	(4)	8	(2)	

Yes	613	(96)	442	(98)	
	Mean	**(SD)**	**Mean**	**(SD)**	
Systolic BP (mm Hg)	116	(13)	116	(14)	0.60
Diastolic BP (mm Hg)	76	(9)	76	(9)	0.91

* p-value calculated using $\chi 2$ test for categorical variables and Kruskal-Wallis test for continuous variables

Supplementary Table 2. Characteristics of incident cases of hypertension at T2 and T4

	T2 (N=80)		**T4** (N=47)		
Variable	**n**	**(%)**	**n**	**(%)**	**p-value ***
Gender					0.74
Women	35	(44)	22	(47)	
Men	45	(56)	25	(53)	
Age (years)					0.96
18-34	4	(5)	3	(6)	
35-44	10	(13)	5	(11)	
45-54	16	(20)	12	(26)	
55-64	20	(25)	9	(19)	
65-74	25	(31)	15	(32)	
≥75	5	(6)	3	(6)	
Body mass index					0.25
Underweight or normal weight	22	(28)	18	(38)	
Overweight	35	(44)	21	(45)	
Obese	23	(29)	8	(17)	
Alcohol consumption					0.85
No	25	(31)	17	(36)	
Light	38	(48)	21	(45)	
Moderate or heavy	17	(21)	9	(19)	

	T2 (N=80)		T4 (N=47)		
Variable	**n**	**(%)**	**n**	**(%)**	**p-value ***
Sports activities					0.07
No	37	(46)	14	(30)	
Yes	43	(54)	33	(70)	
Occupational activity					0.92
No	45	(56)	26	(55)	
Yes	35	(44)	21	(45)	
Study area					0.70
Paris	33	(41)	23	(49)	
Lyon	13	(16)	7	(15)	
Toulouse	34	(43)	17	(36)	
Noise level, L_{den} (dB(A))					0.56
<50	19	(24)	13	(28)	
50-54	23	(29)	9	(19)	
55-59	19	(24)	10	(21)	
≥60	19	(24)	15	(32)	
Anti-hypertensive medication use					0.06
No	26	(33)	8	(17)	
Yes	54	(68)	39	(83)	
	Mean	**(SD)**	**Mean**	**(SD)**	

	T2 (N=80)		T4 (N=47)		
Variable	**n**	**(%)**	**n**	**(%)**	**p-value ***
Systolic BP (mm Hg)	134	(15)	137	(11)	0.31
Diastolic BP (mm Hg)	86	(12)	90	(8)	0.06

* p-value calculated using χ2 test for categorical variables and Kruskal-Wallis test for continuous variables

Supplementary Table 3. Adjusted estimates of the effects of various aircraft noise indicators, noise annoyance and noise sensitivity on incident hypertension

Noise indicator	Model	Variable	Incident hypertension	
			IRR (95% CI)	p-value
None	M0	Highly annoyed vs. not highly annoyed	1.24 (0.84; 1.83)	0.29
	M1	High noise sensitivity vs. medium or low noise sensitivity	0.91 (0.70; 1.18)	0.45
L_{den}	M2	L_{den}	1.36 (1.02; 1.82) *	0.04
	M3	L_{den}	1.29 (0.97; 1.71) *	0.07
		Highly annoyed vs. not highly annoyed	1.25 (0.93; 1.68)	0.14
	M4	L_{den}	1.34 (1.02; 1.77) *	0.03
		High noise sensitivity vs. medium or low noise sensitivity	0.92 (0.71; 1.20)	0.53
$L_{Aeq,24h}$	M2	$L_{Aeq,24h}$	1.43 (1.05; 1.96) *	0.03
	M3	$L_{Aeq,24h}$	1.34 (0.98; 1.83) *	0.07
		Highly annoyed vs. not highly annoyed	1.25 (0.93; 1.68)	0.14
	M4	$L_{Aeq,24h}$	1.40 (1.03; 1.90) *	0.03
		High noise sensitivity vs. medium or low noise sensitivity	0.92 (0.71; 1.19)	0.51
L_{day}	M2	L_{day}	1.41 (1.07; 1.85) *	0.02
	M3	L_{day}	1.34 (1.03; 1.75) *	0.03
		Highly annoyed vs. not highly annoyed	1.23 (0.92; 1.66)	0.16
	M4	L_{day}	1.39 (1.07; 1.80) *	0.01
		High noise sensitivity vs. medium or low noise sensitivity	0.92 (0.71; 1.20)	0.53
L_{night}	M2	L_{night}	1.31 (1.01; 1.71) *	0.04
	M3	L_{night}	1.24 (0.96; 1.60) *	0.10
		Highly annoyed vs. not highly annoyed	1.26 (0.93; 1.70)	0.13
	M4	L_{night}	1.28 (1.00; 1.65) *	0.05

	High noise sensitivity vs. medium or low noise sensitivity	0.92 (0.71; 1.20)	0.56

* Per 10 dB(A) increase in aircraft noise exposure

M0 = aircraft noise annoyance + confounding factors; M1 = noise sensitivity + confounding factors; M2 = noise indicator dB(A) + confounding factors; M3 model = noise indicator dB(A) + aircraft noise annoyance + confounding factors; M4 model = noise indicator dB(A) + noise sensitivity + confounding factors

All models were adjusted for age, gender, BMI, sports activities, alcohol consumption, occupational activity and visit time indicator

Supplementary Table 4. Adjusted estimates of the effects of various aircraft noise indicators on incident hypertension in highly annoyed/sensitive to noise participants compared to those who are not

	M5 model			***M6 model***		
	Not highly annoyed	**Highly annoyed**	**$p_{(interaction)}$ [a]**	**High noise sensitivity**	**Medium or low noise sensitivity**	**$p_{(interaction)}$ [b]**
	IRR * (95% CI)	**IRR * (95% CI)**		**IRR * (95% CI)**	**IRR * (95% CI)**	
L_{den}	1.31 (0.95; 1.82)	1.41 (0.72; 2.78)	0.85	1.26 (0.94; 1.70)	1.62 (1.07; 2.44)	0.26
$L_{Aeq,24h}$	1.35 (0.94; 1.94)	1.64 (0.80; 3.34)	0.63	1.28 (0.92; 1.79)	1.75 (1.13; 2.71)	0.18
L_{day}	1.35 (0.99; 1.85)	1.53 (0.78; 2.99)	0.74	1.31 (0.99; 1.34)	1.60 (1.10; 2.34)	0.31
L_{night}	1.28 (0.95; 1.73)	1.30 (0.69; 2.43)	0.98	1.20 (0.91; 1.57)	1.56 (1.07; 2.29)	0.18

* Per 10 dB(A) increase in aircraft noise exposure

M5 and M6 models included age, gender, BMI, sports activities, alcohol consumption, occupational activity and visit time indicator

[a] p-value for the interaction between noise indicator and aircraft noise annoyance

[b] p-value for the interaction between noise indicator and noise sensitivity

Supplementary Table 5. Adjusted estimates* and 95% confidence intervals (CIs) for blood pressure (BP) in relation to the main a priori confounding factors

	Systolic BP N[a] = (T0: 1,208; T2: 977; T4: 798)		Diastolic BP N[a] = (T0: 1,208; T2: 977; T4: 798)	
Variable	**β (95% CI)**	**p-value**	**β (95% CI)**	**p-value**
Gender		<0.01		<0.01
Women	1.00		1.00	
Men	9.05 (7.57; 10.54)		1.80 (0.75; 2.84)	
Age	0.42 (0.37; 0.48)	<0.01	0.14 (0.10; 0.17)	<0.01
Body mass index		<0.01		<0.01
Underweight or normal weight	1.00		1.00	
Overweight	2.24 (0.93; 3.55)		2.03 (1.11; 2.94)	
Obese	4.45 (2.72; 6.19)		4.32 (3.10; 5.53)	
Alcohol consumption		0.04		0.20

	Systolic BP N[a] = (T0: 1,208; T2: 977; T4: 798)		Diastolic BP N[a] = (T0: 1,208; T2: 977; T4: 798)	
Variable	**β (95% CI)**	**p-value**	**β (95% CI)**	**p-value**
No	1.00		1.00	
Light	0.93 (-0.26; 2.13)		0.38 (-0.45; 1.21)	
Moderate or heavy	2.02 (0.44; 3.60)		1.00 (-0.10; 2.10)	
Sports activities		0.09		0.01
No	1.00		1.00	
Yes	-0.91 (-1.97; 0.16)		-0.93 (-1.67; -0.18)	
Occupational activity		0.94		<0.01
No	1.00		1.00	
Yes	0.05 (-1.33; 1.44)		2.06 (1.10; 3.03)	
Anti-hypertensive medication use		<0.01		0.75
No	1.00		1.00	

	Systolic BP N[a] = (T0: 1,208; T2: 977; T4: 798)		Diastolic BP N[a] = (T0: 1,208; T2: 977; T4: 798)	
Variable	**β (95% CI)**	**p-value**	**β (95% CI)**	**p-value**
Yes	2.79 (1.06; 4.53)		0.19 (-1.02; 141)	

Both models were adjusted for age, gender, BMI, sports activities, alcohol consumption, occupational activity, anti-hypertensive medication use and visit time indicator

* In 1 mm Hg per 10 dB(A) increase in aircraft noise exposure

[a] Number of participants included in the analysis, after excluding those with missing values for confounders

Supplementary Table 6. Adjusted estimates of the effects of various aircraft noise indicators* on blood pressure (BP)

		Systolic BP		Diastolic BP	
	Noise indicator dB(A)	**β (95% CI)**	**p-value**	**β (95% CI)**	**p-value**
		N[a] = (T0: 1,208; T2: 977; T4: 798)		N[a] = (T0: 1,208; T2: 977; T4: 798)	
Main models	L_{den}	1.93 (0.79; 3.08)	<0.01	1.08 (0.27; 1.88)	0.01
	$L_{Aeq,24h}$	2.25 (0.95; 3.55)	<0.01	1.30 (0.39; 2.22)	0.01
	L_{day}	1.85 (0.80; 2.90)	<0.01	1.02 (0.28; 1.76)	0.01
	L_{night}	1.61 (0.61; 2.61)	<0.01	0.83 (0.13; 1.53)	0.02
Sensitivity analysis					
		N[a] = (T0: 960; T2: 763; T4: 618)		N[a] = (T0: 960; T2: 763; T4: 618)	
Participants who had resided at their inclusion address for at least 5 years and had not moved at the time of visit	L_{den}	1.83 (0.38; 3.29)	0.01	1.01 (0.02; 2.01)	0.05
	$L_{Aeq,24h}$	2.08 (0.48; 3.69)	0.01	1.28 (0. 18; 2.38)	0.02
	L_{day}	1.90 (0.48; 3.31)	0.01	0.95 (-0.02; 1.91)	0.06
	L_{night}	1.69 (0.36; 3.02)	0.01	0.83 (-0.08; 1.74)	0.07

	Noise indicator dB(A)	Systolic BP β (95% CI)	Systolic BP p-value	Diastolic BP β (95% CI)	Diastolic BP p-value
Inclusion of the main potential confounding factors measured at baseline (T0) for all time points		N[a] = (T0: 1,208; T2: 963; T4: 789)		N[a] = (T0: 1,208; T2: 963; T4: 789)	
	L_{den}	1.97 (0.71; 3.23)	<0.01	1.18 (0.29; 2.07)	0.01
	$L_{Aeq,24h}$	2.21 (0.81; 3.62)	<0.01	1.41 (0.43; 2.40)	0.01
	L_{day}	2.01 (0.79; 3.23)	<0.01	1.16 (0.30; 2.02)	0.01
	L_{night}	1.71 (0.57; 2.85)	<0.01	0.95 (0.14; 1.75)	0.02
Participants who took part in all three visits [b]		N[a] = (T0: 768; T2: 768; T4: 768)		N[a] = (T0: 768; T2: 768; T4: 768)	
	L_{den}	2.06 (0.70; 3.41)	<0.01	0.98 (0.02; 1.93)	0.04
	$L_{Aeq,24h}$	2.40 (0.86; 3.93)	<0.01	1.19 (0.11; 2.27)	0.03
	L_{day}	1.89 (0.66; 3.12)	<0.01	0.89 (0.02; 1.75)	0.04
	L_{night}	1.70 (0.53; 2.87)	<0.01	0.73 (-0.10; 1.55)	0.08
		N[a] = (T0: 1,012; T2: 779; T4: 604)		N[a] = (T0: 1,012; T2: 779; T4: 604)	
	L_{den}	1.87 (0.69; 3.05)	<0.01	1.11 (0.27; 1.96)	0.01

		Systolic BP		Diastolic BP	
	Noise indicator dB(A)	β (95% CI)	p-value	β (95% CI)	p-value
Participants who did not report the use of anti-hypertensive medication in the same visit [c]	$L_{Aeq,24h}$	2.15 (0.81; 3.50)	<0.01	1.32 (0.36; 2.28)	0.01
	L_{day}	1.78 (0.71; 2.84)	<0.01	1.05 (0.29; 1.82)	0.01
	L_{night}	1.54 (0.52; 2.56)	<0.01	0.85 (0.12; 1.58)	0.02

All models were adjusted for age, gender, BMI, sports activities, alcohol consumption, occupational activity, anti-hypertensive medication use and visit time indicator

* In 1 mm Hg per 10 dB(A) increase in aircraft noise exposure

[a] Number of participants included in the analysis, after excluding those with missing values for confounders

[b] Participants with missing data at any visit time were excluded from all 3 visit times

[c] Participants were excluded from the time visit if they reported the use of anti-hypertensive medication for the corresponding visit

Supplementary Table 7. Adjusted estimates of the effects of various aircraft noise indicators* on incident hypertension in men and women separately

	N of cases/N total		
	Noise indicator dB(A)	IRR (95% CI)	p-value
	N^a = (T2: 79/630; T4: 47/450)		
Main model [b]	L_{den}	1.36 (1.02; 1.82)	0.04
	$L_{Aeq,24h}$	1.43 (1.05; 1.96)	0.03
	L_{day}	1.41 (1.07; 1.85)	0.02
	L_{night}	1.31 (1.01; 1.71)	0.04
	N^a = (T2: 79/631; T4: 47/450)		
Total study population [c]	L_{den}	1.36 (1.02; 1.83)	0.04
	$L_{Aeq,24h}$	1.41 (1.02; 1.95)	0.03
	L_{day}	1.41 (1.08; 1.84)	0.01
	L_{night}	1.31 (1.02; 1.69)	0.04
	N^a = (T2: 44/257; T4: 25/185)		
Among men [d]	L_{den}	1.48 (1.03; 2.12)	0.03
	$L_{Aeq,24h}$	1.52 (1.01; 2.28)	0.04
	L_{day}	1.51 (1.08; 2.10)	0.02
	L_{night}	1.41 (1.02; 1.94)	0.04
	N^a = (T2: 35/374; T4: 22/265)		
Among women [d]	L_{den}	1.28 (0.79; 2.09)	0.31
	$L_{Aeq,24h}$	1.32 (0.78; 2.22)	0.29

	N of cases/N total		
	Noise indicator dB(A)	IRR (95% CI)	p-value
	L_{day}	1.32 (0.82; 2.10)	0.25
	L_{night}	1.26 (0.81; 1.96)	0.31

[*] Per 10 dB(A) increase in aircraft noise exposure

[a] Number of participants included in the analysis, after excluding those with missing values for alcohol consumption

[b] Adjusted for age, gender, BMI, sports activities, alcohol consumption, occupational activity and visit time indicator

[c] Adjusted for age (in six categories), gender, sports activities, alcohol consumption, occupational activity and visit time indicator

[d] Adjusted for age (in six categories), sports activities, alcohol consumption, occupational activity and visit time indicator