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## Medication use in relation to noise from aircraft and road traffic in six European countries: results of the HYENA study

Sarah Floud (1), Federica Vigna-Taglianti (2), Anna Hansell (1), Marta Blangiardo (1), Danny Houthuijs (3), Oscar Breugelmans (3), Ennio Cadum (2), Wolfgang Babisch (4), Jenny Selander (5), Goran Pershagen (5), Maria Chiara Antoniotti (6), Salvatore Pisani (8), Konstantina Dimakopoulou (7), Alexandros S Haralabidis (7), Venetia Velonakis (9), Lars Jarup (1), on behalf of the HYENA study team

1. MRC-HPA Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK
2. Environmental Epidemiologic Unit, Regional Agency for Environmental Protection (ARPA), Piedmont Region, Grugliasco, Italy
3. The National Institute of Public Health and Environmental Protection (RIVM), Bilthoven, The Netherlands
4. Department of Environment and Health at the Federal Environment Agency (UBA), Berlin, Germany
5. Institute of Environmental Medicine (IMM), Karolinska Institutet, Stockholm, Sweden
6. Department of Prevention, Local Health Unit, Novara, Italy
7. Department of Hygiene, Epidemiology and Medical Statistics, National and Kapodistrian University of Athens, Greece
8. U.O. Osservatorio Statistico-Epidemiologico, Varese, Italy
9. Laboratory of Prevention, Nurses School, University of Athens, Greece

### WHAT THIS PAPER ADDS

- There have been only a small number of studies into use of medication in relation to transport related noise exposure.
- Medication use is an objective measure of health status and as such presents an opportunity to study the possible effects of noise exposure on health.
- This is the first pan-European study of the medication use of residents living near airports.
- It has shown that exposure to aircraft noise is associated with the use of anxiolytic medication and the use of antihypertensive medication in some countries.
- These results have implications for the provision of health services and prescribing for residents living near airports.

### ABSTRACT

**Objectives** Studies on the health effects of aircraft and road traffic noise exposure suggest excess risks of hypertension, cardiovascular disease and the use of sedatives and hypnotics. Our aim was to assess the use of medication in relation to noise from aircraft and road traffic.

**Methods** This cross-sectional study measured the use of prescribed antihypertensives, antacids, anxiolytics, hypnotics, antidepressants and antasthmatics in 4,861 persons living near seven airports in six European countries (UK, Germany, the Netherlands, Sweden, Italy, and Greece). Exposure was assessed using models with 1dB resolution (5dB for UK road traffic noise) and spatial resolution of 250x250m for aircraft and 10x10m for road traffic noise. Data were analysed using multilevel logistic regression, adjusting for potential confounders.

**Results** We found marked differences between countries in the effect of aircraft noise on antihypertensive use; for night-time aircraft noise, a 10dB increase in exposure was associated with ORs of 1.34 (95% CI 1.14 to 1.57) for the UK and 1.19 (1.02 to 1.38) for the Netherlands but no significant associations were found for other countries. For day-time aircraft noise, excess risks were found for the UK (OR 1.35; CI: 1.13 to 1.60) but a risk deficit for Italy (OR 0.82; CI: 0.71 to 0.96). There was an excess risk of taking anxiolytic medication in relation to aircraft noise (OR 1.28; CI: 1.04 to 1.57 for daytime and OR 1.27; CI: 1.01 to 1.59 for night-time) which held across countries. We also found an association between exposure to 24hr road traffic noise and the use of antacids by men (OR 1.39; CI 1.11 to 1.74).

**Conclusion** Our results suggest an effect of aircraft noise on the use of antihypertensive medication, but this effect did not hold for all countries. Results were more consistent across countries for the increased use of anxiolytics in relation to aircraft noise.

## **INTRODUCTION**

Several studies have shown an association between aircraft and road traffic noise exposure and cardiovascular effects, such as hypertension and myocardial infarction. (1-6) It has also been suggested that environmental noise disturbs sleep in the short term, although it is unclear if there are long-term health consequences. (7-8) Similarly, it is a common perception that exposure to environmental noise might cause psychiatric disorders but the evidence does not support this: there have been some studies which have found links with symptoms of depression or anxiety but others have not found an association. (9-13)

A small number of epidemiological studies have looked at the medication use of residents exposed to aircraft noise and results suggest an association with antihypertensive medication and a possible association with medications for anxiety and disturbed sleep. A study in the 1970s of pharmacists' purchasing trends near Schiphol airport found an increase in the purchase of antihypertensives, antacids, hypnotics and sedatives in relation to aircraft noise, but a study at the same time conducted near Heathrow did not find any association. (14-15) More recently, a study of the prescriptions of residents living near Cologne-Bonn airport found a higher prevalence of antihypertensive medication and a study around Schiphol airport reported an exposure-response relationship between aircraft noise and the use of antihypertensives and non-prescribed sleep medication or sedatives. (16-17) Road traffic noise may also be associated with an increased use of antihypertensives. (18-19) The use of other medication in relation to road traffic noise has been rarely studied, except for a recent study in the Netherlands which did not find an association between road traffic noise and self-reported use of sleep or tranquillising medication. (20)

In the present study, the medication use of persons living in the vicinity of airports was investigated within the wider framework of the HYENA (HYpertension and Exposure to Noise near Airports) project. (3-21) Our hypothesis was that noise acts as a non-specific stressor, which activates various pathways of the stress response. (22) An increase in morning salivary cortisol in women exposed to aircraft noise was observed in a subsample of HYENA providing some evidential support for a stress reaction induced by noise. (23) Noise, therefore, might affect prescriptions for conditions potentially affected by stress, such as blood pressure, stomach ulcers, anxiety, sleep problems, depression and asthma. Thus, we focused the study on the use of antihypertensives, antacids, anxiolytics, hypnotics, antidepressants and antasthmatics.

## **METHODS**

### **Participants**

The HYENA cross-sectional study has been described elsewhere in more detail. (3-21) It was approved by ethics committees in all six participating countries and informed written consent was obtained from each participant. Data were collected between 2004 and 2006 on 4861 adults (2404 men, 2457 women) aged 45-70 years who had lived for at least 5 years before data collection (3 years in the Greece sample) near seven European airports: London's Heathrow, Amsterdam's Schiphol, Stockholm's Arlanda and Bromma, Milan's Malpensa, Berlin's Tegel and Athens' Eleftherios Venizelos. Stratified random sampling within each country was employed to achieve contrasts in exposure to noise from both aircraft and road traffic, using noise contour maps. This ensured that there were sufficient participants who were exposed to noise greater than 60 dB and less than 50 dB. Further details of the selection process can be found elsewhere. (3-21)

## Medication

Each participant was asked, during a home visit, to provide the name of any prescribed medication which they had used in the 2 weeks preceding the interview. Participants were prompted to include prescribed sleeping pills, sedatives, tranquillisers, antidepressants and any prescribed anti-smoking remedies as well as regular medication that they were currently taking for a specific condition. Each medication was coded according to the Anatomical Therapeutic Chemical (ATC) classification system as proposed by the WHO. The medications investigated by this study are described in more detail in the online supplemental material (see table A1 showing the ATC codes).

As well as looking at the medications separately, we also combined anxiolytics and hypnotics into one group because anxiolytics can be prescribed in the short term at lower doses to relieve anxiety and at higher doses to produce hypnotic effects.

## Exposure assessment

Exposure was assessed by linking participants' home addresses to modelled aircraft and road traffic noise levels using geographical information systems (GIS) methods. (21) In the case of aircraft noise, average noise levels for the year 2002 were chosen to represent the exposure for the 5 years preceding the health assessment. All the countries, except the UK, used the Integrated Noise Model (INM). (24) The UK used their national Aircraft Noise Contour model (ANCON v 2) which is similar to the INM and meets the requirements of the European Civil Aviation Conference. (25-26) The aircraft noise maps were at 1 dB resolution (250x250 m spatial resolution). We used  $L_{Aeq,T}$ , the A-weighted equivalent continuous noise level over T hours, as the indicator of noise exposure. Two separate indicators for aircraft noise were chosen to represent daytime (16 h) and nighttime exposure:  $L_{Aeq,16h}$  (07:00-23:00 or 06:00-22:00 h according to local definition) and  $L_{night}$  (23:00-07:00 or 22:00-06:00 h) (in addition,  $L_{Aeq,24h}$  was used as a covariate in the road traffic noise model).

For road traffic noise exposure, national noise models were used and the quality of the input data was assessed using the Good Practice Guide for Strategic Noise Mapping. (3) The noise maps were at 1 dB resolution (10x10 m spatial resolution) except for the UK where only 5 dB resolution was available. Information on traffic flows at different periods of the day and night was not available for all study areas, so a 24 h indicator ( $L_{Aeq,24h}$ ) was chosen. Noise models can be inaccurate at lower levels because traffic intensities can be so low that relatively small deviations from actual flows may have large effects on the noise level. Therefore, lower cut-off values were applied to the noise levels, in order to minimise the impact of possible inaccuracies. All values lower than the cut-off values were assigned the cut-off values. For aircraft noise, the cut-off values were 35 dB for  $L_{Aeq,16h}$  and  $L_{Aeq,24h}$  and 30 dB for  $L_{night}$ . For road traffic noise, the cut-off was 45 dB.

## Annoyance

The role of annoyance with aircraft noise and road traffic noise was also assessed in relation to medication use. Participants were asked to rate how much they were 'bothered, disturbed or annoyed' by a number of different potential noise sources in the daytime and night-time at home using the International Organization for Standardization (ISO) standard non-verbal 11 point scale (range: 0e10). (27) For the purposes of this analysis, participants were classified as highly annoyed if they answered  $\geq 8$  compared to not highly annoyed if they answered  $< 8$ . (28)

## Confounders

The following confounders were included in the regression models a priori, being potentially associated with medication use and with noise exposure: gender (categorical), age (continuous) and body mass index (BMI) (continuous). Alcohol intake, a continuous variable, was recorded as the number of units (1 unit=10 ml pure ethanol) consumed per week. Level of physical activity was

estimated as three categories of exercise (<once/week, 1-3 times/week and >3 times/week). Educational level was coded as quartiles of number of years in education, but standardised by country means to account for differences in education systems. Smoking (cigarettes, pipes and cigars) was coded into five categories (non-smokers, ex-smokers, 1-10 units/day, 11-20 units/day and >20 units/day).

### **Sample size**

The sample size was reduced from 4861 in the analysis because of missing values for the exposures, annoyance with aircraft noise and the following confounders: smoking, education, alcohol, physical activity and BMI. This meant that the final sample size was 4642 for the regression models for the effect of  $L_{Aeq,16h}$  aircraft noise and  $L_{Aeq,24h}$  road traffic noise and 4641 for  $L_{night}$  aircraft noise. For the effect of annoyance with aircraft noise on medication use, the final sample sizes were 4646 for annoyance with daytime noise and 4644 for night-time noise.

### **Statistical analyses**

All statistical analyses were performed using the software package Stata v 10.1. ORs and 95% CIs were calculated to show the risks per 10 dB increment in noise exposure. ORs were considered borderline positive if the lower CI was 0.99 to 1.00 or borderline negative if the upper CI was 1.01 to 1.00. For tests of independence and likelihood ratio tests (LRT), we rejected the null hypothesis if the p value was <0.05.

A hierarchical structure was specified to model possible differences between countries in prescribing using multilevel logistic regression with the medication groups as outcome variables and the exposure variables (aircraft noise ( $L_{night}$  or  $L_{Aeq,16h}$ ) or road traffic noise ( $L_{Aeq,24h}$ )) as the explanatory variables and all potential confounders as covariates. We also investigated differences between countries in the effect of noise on medication use by including in each model a random slope and performing an LRT to find the best-fitting model. If a statistically significant slope was found, then country-specific ORs were reported from the hierarchical model.

We also investigated differences between genders in the association between noise exposure and medication use, first by using the LRT to compare models with and without an interaction term. Then we calculated the ORs using stratification.

The effect of annoyance with aircraft noise on medication use was examined using a hierarchical logistic regression model with a random intercept for country (the fit of a hierarchical model with random intercept and random slope was not found to be significantly better). We investigated the degree of correlation between aircraft noise level and annoyance with aircraft noise, using Spearman's r test and treating annoyance as a scale variable. We also tested the hypothesis that the effect of noise exposure would be more pronounced in those reporting being highly annoyed by aircraft noise compared to those not highly annoyed. We used the LRT to compare models with and without an interaction term to identify significant effect modification and then we calculated the ORs using stratification. We did not investigate the effects of annoyance with road traffic noise because the noise level was measured as a 24 h average whereas annoyance was reported for day and night time separately, so a comparison between the effects of annoyance and the effects of noise level would not be meaningful.

## **RESULTS**

### **Descriptive results**

Descriptive data on the study population, stratified by exposure to aircraft noise ( $L_{Aeq,16h}$ ) are presented in table 1. Differences were detected between exposure categories for annoyance ( $p<0.001$ ) with an increasing number of highly annoyed people in the higher noise categories.

Those in the highest education category were less likely to be exposed to the highest aircraft noise levels ( $p=0.017$ ). There were differences between countries in the distribution of exposure: participants from the UK and Germany were exposed to higher aircraft noise levels than in the other countries ( $p<0.001$ ). There were also differences between exposure categories for BMI and alcohol consumption ( $p=0.009$  and  $p=0.008$ , respectively).

The distribution of sample characteristics in relation to the other noise metrics: aircraft noise at night ( $L_{\text{night}}$ ) and road traffic noise ( $L_{\text{Aeq},24\text{h}}$ ) were generally similar to those shown for daytime aircraft noise ( $L_{\text{Aeq},16\text{h}}$ ) except that participants from Germany and Italy experienced the highest road traffic noise levels (see online supplemental material A2 and A3).

The prevalence of medication use in the HYENA study population is presented in table 2. The overall prevalence of antihypertensives was 28%, whereas the prevalence of the use of the other medications was much lower. There were marked differences between countries in their use of the medications ( $p<0.001$  for all medications). The sample from Germany had the highest prevalence of antihypertensive medication use, while the UK sample had the highest prevalence of antacid use, antidepressant use, antasthmatic use and taking more than one medication. The sample from Italy had the highest use of anxiolytics.

## Regression results

When we investigated the effect of aircraft noise exposure on antihypertensive use, we found differences between countries. Table 3 shows the ORs and 95% CIs for antihypertensive use in relation to exposure to aircraft noise ( $L_{\text{Aeq},16\text{h}}$  and  $L_{\text{night}}$ ) in each country. For day-time aircraft noise, there was a significant positive association with antihypertensive use for the UK and a significant negative association for Italy. For night-time aircraft noise, significant positive associations were found for the UK and the Netherlands and a borderline negative association for Italy.

We did not find any differences between countries in the effect of road traffic noise exposure on antihypertensive use, nor did we find any differences between countries for any other medications in relation to the noise exposures. Therefore table 4 shows the ORs for medication use in relation to aircraft and road traffic noise for all HYENA participants in all six countries (excepting antihypertensive use in relation to aircraft noise as shown in table 3). Antihypertensive use did not appear to be associated with road traffic noise exposure, but there was evidence of effect modification by gender ( $p=0.02$ ): when we investigated the associations for men and women separately, we found a suggestive association for men OR (1.10; CI 0.95 to 1.25) but an opposite trend for women OR (0.89; CI 0.77 to 1.03). We did not find evidence of effect modification by gender in relation to aircraft noise exposure.

Antacid use was not significantly related to aircraft noise exposure, but the OR for the effect of road traffic noise on antacid use was elevated and borderline significant. This result was driven by the association for men OR (1.39; CI 1.11 to 1.74) because there was no association found for women OR (0.99; CI 0.78 to 1.24) ( $p=0.04$ ). For the combined group of anxiolytics or hypnotics, no significant associations were found in relation to noise. However, the use of anxiolytic medication on its own was significantly related to aircraft noise, with clearly elevated ORs for both  $L_{\text{Aeq},16\text{h}}$  and  $L_{\text{night}}$ . No associations with noise were found for the use of hypnotics, antidepressants or antasthmatics.

Associations were found between annoyance with aircraft noise and the use of medication (table 5). Reported annoyance due to aircraft noise (both day and night) was associated with the use of antihypertensives, anxiolytics or hypnotics as a group and anxiolytics on their own. Annoyance was not associated with hypnotics. Antidepressant use was also related to annoyance with aircraft noise during the day and the association between antasthmatic use and annoyance with aircraft noise during the night was borderline significant. We found moderate correlations between noise level and annoyance: Spearman's  $r=0.5$  for aircraft noise  $L_{\text{Aeq},16\text{h}}$  and  $r=0.4$  for aircraft noise  $L_{\text{night}}$  (when annoyance was measured as a scale).

We also investigated whether the association between aircraft noise level and medication use differed according to whether the subjects reported being highly annoyed with aircraft noise or not (see tables A4 and A5 in the online supplemental material). Tests for effect modification were not significant except for hypnotic use, where annoyance was a significant effect modifier of the effect of aircraft noise ( $p=0.04$  and  $p=0.03$  for  $L_{Aeq,16h}$  and  $L_{night}$ , respectively). However, after stratifying by annoyance level, higher ORs were seen for some countries in relation to antihypertensive use and for antacid, anxiolytic and hypnotic use.

## DISCUSSION

Our results suggest that exposure to aircraft noise increases the use of anxiolytic medication and of antihypertensive medication (although not in all countries). Road traffic noise exposure may also influence the use of antihypertensives and antacids by men. We also found associations between annoyance with aircraft noise and the use of antihypertensives, anxiolytics, antidepressants and antasthmatics.

### Antihypertensive use

We found an association between aircraft noise and antihypertensive use which varied between countries: in relation to  $L_{Aeq,16h}$ , a positive association was found for the UK while a negative association was found for Italy. For  $L_{night}$ , positive associations were found for the UK and the Netherlands and a borderline negative association was found for Italy. For the other countries, the non-significant associations were mostly positive except for Sweden. We had accounted for differences between countries in the prescription of medications by specifying a hierarchical structure based on country. However, there are a number of possible explanations as to why the effect of aircraft noise on the use of antihypertensives should differ between countries; the results could reflect differences in the modelling of aircraft noise or that the personal exposure to noise (eg, in terms of housing characteristics) may differ between countries or there are other unmeasured confounders. In a previous analysis of the HYENA study population, differences between countries in the effect of aircraft noise on salivary cortisol were also found. (23) However, the previous HYENA study on hypertension did find a significant exposure-response relationship for all countries combined in relation to aircraft noise at night and hypertension (OR 1.14; CI 1.01 to 1.29), where hypertension was determined from blood pressure measurements, a doctor's diagnosis or the use of antihypertensive medication. (3) In contrast, in the current study we only looked at medication use which provided us with approximately 50% fewer cases.

We also investigated the effect of road traffic noise on the use of antihypertensives but did not find an association. However, tests for effect modification by gender did reveal differences between men and women, with a positive association for men but an opposite trend for women. Neither association was statistically significant, but they do echo the findings from Jarup et al which found excess risks of hypertension for men but not for women in relation to road traffic noise. (3) Other studies have also found associations between the use of antihypertensive medication and exposure to road traffic noise, although their results differ on whether the effect is more pronounced for men or women. A recent study in Sweden found higher relative risks for men for the use of antihypertensive medication, whereas an earlier study in Sweden found stronger associations for women for self-reported diagnosis of hypertension. (1-18) There have also been other studies which have not found effect modification by gender. (19-29)

Possible mechanisms have been proposed for how noise might affect blood pressure. It is thought that subjective annoyance with noise induces a stress reaction which activates the sympathetic and endocrine systems, leading to physiological changes. (22) It is also possible that noise induces an autonomic response through the auditory pathway, irrespective of the subjective reaction to noise. Evidence from the field study conducted as part of the HYENA programme showed that increases



in blood pressure in relation to noise events during night-time may occur at low noise levels which do not necessarily cause arousal from sleep and the HYENA study on salivary cortisol found that the effect of noise exposure on cortisol levels in women was not dependent on their degree of annoyance. (23 30)

### **Antacid use**

An effect of road traffic noise on the use of antacid medication in men was found in this study. Exposure to aircraft noise was linked to an increase in purchasing of antacids in pharmacies in the study around Schiphol airport in the 1970s, but there has been little research since then on the use of antacids in relation to noise exposure. (14) However, an effect of noise on dyspepsia is plausible given some evidence on the impact of psychological stress on the onset and course of ulcer disease. (31)

### **Anxiolytic and hypnotic use**

This study has also found an exposure-response increase in the use of anxiolytic medication in relation to aircraft noise. This could indicate an association with symptoms of anxiety. However, it could also indicate sleep disturbance because anxiolytics can be prescribed for sleep problems. We therefore also treated anxiolytics and hypnotics as one group and found that although the ORs for the relationship with exposure to noise were elevated, they were not statistically significant. The use of hypnotics was not found to be associated with noise levels.

A higher prevalence of anxiolytic use in relation to proximity to an airport has been found in a previous study of women living near Milan Malpensa airport. (32) The previously mentioned study around Schiphol looked at the use of prescribed sleep medication and sedatives (which would encompass both anxiolytics and hypnotics) in relation to aircraft noise and also found an elevated, but not statistically significant, OR of 1.25 (CI 0.93 to 1.68) per 10 dB ( $L_{den}$ ). (17) However, it is not possible to make a direct comparison with our study as the noise metrics are not identical ( $L_{den}$  is the sound level for the 24 h period, with additional weights given for evening and night). In the Schiphol study, they also found an association with non-prescribed sleep medication and sedatives. Some sleep medications are available over the counter, but as we have not investigated the association with non-prescribed medication in this study, we might not have fully captured the use of hypnotics.

### **Antidepressant use**

We did not find any evidence for an association between aircraft or road traffic noise levels and the use of antidepressants. This is consistent with the evidence from epidemiological studies on the psychological effects of noise, which indicates an effect on anxiety or depressive symptoms but not on psychiatric disorders such as depression. (33)

### **Antasthmatic use**

Antasthmatic use was also not found to be associated with exposure to noise in this study. Noise could be associated with the activation of asthma attacks by acting as a stressor, although to date, there is little evidence of a direct association between noise exposure and asthma. (34-35)

### **Effect of annoyance**

The results for the effect of annoyance on medication use echo to some extent the associations found for noise level, with significant associations found for antihypertensives and anxiolytics in relation to annoyance with aircraft noise. This might have been expected as moderate correlations were found between noise level and annoyance. Information bias may explain some of the observed

association between annoyance due to noise and medication use. Participants who are taking medication for their blood pressure, for instance, might overreport annoyance because they attribute their ill-health to external factors. (36) Indeed, analysis of the noise annoyance of the HYENA participants found an association between annoyance and hypertension if the participant had been diagnosed by a doctor or was taking medication, but a similar association was not found between clinical blood pressure measurements and noise annoyance when the participant was unaware of their medical condition. (37) Annoyance with aircraft noise was found to be associated with both antidepressant use and possibly with antasthmatic use, while no association could be found with noise level for either medication. These results could suggest an alternative explanation, where participants who are more seriously ill, as indicated by the fact that they are being treated for their conditions, are more annoyed by noise regardless of the noise level because they are more 'vulnerable'. This hypothesis was put forward by Watkins et al and might account for the discrepancy found between the results regarding noise level and those regarding annoyance. (15) It might also be the case that those with poor health are more likely to be bound to their homes and so unable to take action to avoid the noise exposure, which might result in higher annoyance levels. We hypothesised that the effect of aircraft noise on medication use would be more pronounced in those who reported being highly annoyed by aircraft noise. Tests for effect modification did not support this hypothesis, but higher ORs were seen for some countries in relation to antihypertensive use and for antacid, anxiolytic and hypnotic use. It may be that the tests for effect modification lacked sufficient power to detect significant differences.

## **Limitations**

Our results show differences in the prevalence of medication use among participating countries. This is to be expected as there are known differences across Europe in the prescription of pharmaceuticals, both in amount and in category of drug. (38) For example, the higher prevalence of anxiolytic use in Italy shown in this study has been found previously in comparisons with other European countries. (39) There are also differences in the European health systems in terms of co-payments by patients for prescriptions which could affect demand. (40) We have therefore used models with a hierarchical structure based on country in order to take into account the country-specific prescribing practices and healthcare systems which might affect the propensity to prescribe medicines. The prevalence of antihypertensive use (28%) was higher than that reported by previous studies which have looked at antihypertensive use in relation to noise. (17-19) However, our population was aged 40-75 years so this might be due to different age-sex structures of the other studies.

The use of models of noise exposure related to the participants' home address cannot capture personal noise exposure when out of their homes, at work or at leisure. This is a common problem in environmental epidemiological studies where exposure is assigned to place of residence, but we would expect it to affect night-time exposure much less than daytime exposure and to affect those aged over 60 less than the younger participants.

The cross-sectional nature of the design of this study provides a snapshot of the possible links between exposure to transportation noise and medication use. However, it does not show causation since it is not possible to know the sequence of events for exposure and medication use. It is possible that poor health and the need for medication precedes exposure to noise. There can be an impact on an area of having a major airport in the vicinity in terms of reducing house prices which might lead to an over-representation of local residents with low socioeconomic status and therefore the accompanying likelihood of poorer health. However, this study has used individual information on educational level to control for the effect on health of low socio-economic status. Conversely, people who considered themselves to be particularly vulnerable to noise may have moved out of the area, thus leading to an underestimation of the effects of noise, because the more resilient remain.

## CONCLUSION

We found an association between aircraft noise and an increased use of antihypertensives, although this effect did not hold for all countries. The results were more consistent across countries for prescriptions for other stress-related conditions, with positive associations between aircraft noise and anxiolytic use and between road traffic noise and the use of antacids by men. We did not find any associations between noise levels and hypnotics, antidepressants or antasthmatics. Our results suggest that exposure to aircraft noise may affect people's physiological and psychological health. If these results are repeated by other research studies, then measures to reduce exposure could be considered on public health grounds.

### Author footnote:

Other members of the HYENA study team are: Joy Read, Yvonne Tan, Yousouf Soogun, Marie-Louise Dudley, Pauline Savigny, Ingeburg Seiffert, Gabriele Wolke, Wim Swart, Jessica Kwekkeboom, Gösta Bluhm, Töres Theorell, Birgitta Ohlander, Eva Thunberg, Konstantina Dimakopoulou, Panayota Sourtzi, Elli Davou, Yannis Zahos, Ageliki Athanasopoulou, Federica Mathis, Claudia Preti, Raffaella Martinez, Domenico Bonarrigo, Maria Paola Ceriani, Giorgio Barbaglia, Alessandro Borgini and Matteo Giampaolo.

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### Competing interests

None.

### Ethics approval

The research undertaken by each of the HYENA partners was covered by local agreements concerning the ethical use of data and the protection of confidentiality of individuals. Ethics approvals have been obtained in all partner countries.

### Provenance and peer review

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**Table 1** HYENA study population characteristics stratified by exposure to daytime aircraft noise ( $L_{Aeq,16h}$ )

	$L_{Aeq,16h}$ Aircraft (dB)				Total
	35–44.9	45–54.9	55–64.9	≥65	
<b>Population characteristics</b>					
N	1132	1266	2022	222	4642
Females (%)	52.2	50.2	50.0	45.1	50.3
Age (mean ±SD)	57.9 ±7.1	57.9 ±7.2	57.4 ±7.0	58.4 ±7.0	57.7 ±7.1
Body mass index (mean ±SD)	27.2 ±4.9	26.9 ±4.4	27.0 ±4.5	28.1 ±4.8	27.1 ±4.6
Alcohol units/week (mean ±SD)	6.8 ±9.0	6.8 ±9.0	5.9 ±8.4	6.2 ±9.7	6.4 ±9.1
Physical activity <once a week (%)	35.3	29.9	30.6	39.2	31.9
Education highest quartile (%)	25.4	27.4	22.7	13.5	24.2
Non-smokers (%)	39.8	40.6	40.3	47.3	40.6
Highly annoyed by aircraft noise in day (%)	4.0	26.1	41.4	53.2	28.7
<b>Country (% within each exposure band)</b>					
UK (%)	7.1	8.9	13.5	53.6	12.6
Germany (%)	34.5	13.6	16.3	34.2	20.9
Netherlands (%)	3.8	30.3	21.1	8.1	18.8
Sweden (%)	17.3	18.7	27.5	0.9	21.4
Greece (%)	11.0	17.5	13.1	1.4	13.3
Italy (%)	26.2	11.0	8.5	1.8	13.2
Total (%)	99.9	100.0	100.0	100.0	100.2

Percentages are calculated within each band of exposure.

**Table 2** Prevalence of medication use in the HYENA study population overall and by country

		UK	Germany	Netherlands	Sweden	Greece	Italy	Overall
Medication group								
Antihypertensives	(N)	181	315	199	221	187	180	1283
	(%)	31.0	32.5	22.9	22.3	30.4	29.4	27.6
Antacids	(N)	62	78	83	38	29	35	325
	(%)	10.6	8.1	9.5	3.8	4.7	5.7	7.0
Anxiolytics or hypnotics	(N)	19	14	70	37	27	64	231
	(%)	3.3	1.4	8.0	3.7	4.4	10.5	5.0
Anxiolytics	(N)	6	5	42	11	26	55	145
	(%)	1.0	0.5	4.8	1.1	4.2	9.0	3.1
Hypnotics	(N)	13	10	31	30	1	12	97
	(%)	2.2	1.0	3.6	3.0	0.2	2.0	2.1
Antidepressants	(N)	37	29	48	53	7	18	192
	(%)	6.3	3.0	5.5	5.4	1.1	2.9	4.1
Antasthmatics	(N)	50	43	44	50	19	10	216
	(%)	8.6	4.4	5.1	5.1	3.1	1.6	4.7
>1 medication*	(N)	70	68	99	68	36	56	397
	(%)	12.0	7.0	11.4	6.9	5.9	9.2	8.6
No medication†	(N)	322	569	551	668	393	365	2868
	(%)	55.1	58.7	63.3	67.4	63.9	59.6	61.8
Total	(N)	584	969	871	991	615	612	4642

\*Participants taking more than one of the medication groups investigated in this study.

†Participants taking none of the medications investigated in this study.

**Table 3** Country-specific ORs (95% CIs) of antihypertensive use related to aircraft noise per 10 dB

Medication group	Noise source	Country	OR (95% CI)	N
Antihypertensives	L <sub>Aeq,16h</sub> Aircraft	UK	1.35 (1.13 to 1.60)	584
		Germany	1.08 (0.95 to 1.23)	969
		Netherlands	1.12 (0.91 to 1.39)	871
		Sweden	0.89 (0.76 to 1.04)	991
		Greece	1.09 (0.89 to 1.34)	615
		Italy	0.82 (0.71 to 0.96)	612
		L <sub>night</sub> Aircraft	UK	1.34 (1.14 to 1.57)
	Germany	1.05 (0.93 to 1.19)	969	
	Netherlands	1.19 (1.02 to 1.38)	871	
	Sweden	1.05 (0.91 to 1.22)	990	
	Greece	1.03 (0.83 to 1.28)	615	
	Italy	0.85 (0.73 to 1.00)	612	

The hierarchical structure of each logistic regression model assumed a random intercept that accounts for differences in the use of medication between countries and a random slope to account for differences between countries in the effect of aircraft noise on medication use, and adjustment was made for age, sex, BMI, alcohol intake, education, exercise and smoking status.

For each of the aircraft noise models (L<sub>Aeq,16h</sub> and L<sub>night</sub>), adjustment was made for exposure to road traffic noise (L<sub>Aeq,24h</sub>).

**Table 4** ORs (95% CIs) of medication use related to aircraft and road traffic noise per 10 dB

Medication group	Noise source	OR (95% CI)	N
Antihypertensives	L <sub>Aeq,24h</sub> Road traffic	0.98 (0.89 to 1.08)	4642
Antacids	L <sub>Aeq,16h</sub> Aircraft	1.01 (0.89 to 1.15)	4642
	L <sub>night</sub> Aircraft	1.10 (0.96 to 1.25)	4641
	L <sub>Aeq,24h</sub> Road traffic	1.16 (0.99 to 1.36)	4642
Anxiolytics or hypnotics	L <sub>Aeq,16h</sub> Aircraft	1.14 (0.97 to 1.34)	4642
	L <sub>night</sub> Aircraft	1.10 (0.93 to 1.31)	4641
	L <sub>Aeq,24h</sub> Road traffic	1.11 (0.92 to 1.34)	4642
Anxiolytics	L <sub>Aeq,16h</sub> Aircraft	1.28 (1.04 to 1.57)	4642
	L <sub>night</sub> Aircraft	1.27 (1.01 to 1.59)	4641
	L <sub>Aeq,24h</sub> Road traffic	1.06 (0.84 to 1.33)	4642
Hypnotics	L <sub>Aeq,16h</sub> Aircraft	0.96 (0.76 to 1.22)	4642
	L <sub>night</sub> Aircraft	0.90 (0.70 to 1.14)	4641
	L <sub>Aeq,24h</sub> Road traffic	1.28 (0.96 to 1.71)	4642
Antidepressants	L <sub>Aeq,16h</sub> Aircraft	1.07 (0.90 to 1.26)	4642
	L <sub>night</sub> Aircraft	0.96 (0.81 to 1.13)	4641
	L <sub>Aeq,24h</sub> Road traffic	0.97 (0.78 to 1.21)	4642
Antasthmatics	L <sub>Aeq,16h</sub> Aircraft	1.05 (0.90 to 1.23)	4642
	L <sub>night</sub> Aircraft	1.03 (0.88 to 1.21)	4641
	L <sub>Aeq,24h</sub> Road traffic	1.01 (0.82 to 1.24)	4642

The hierarchical structure of each logistic regression model assumed a random intercept accounting for differences in the use of medication between countries and adjustment was made for age, sex, BMI, alcohol intake, education, exercise and smoking status.

For each of the aircraft noise models (L<sub>Aeq,16h</sub> and L<sub>night</sub>), adjustment was made for exposure to road traffic noise (L<sub>Aeq,24h</sub>); and for the road traffic noise models, adjustment was made for exposure to aircraft noise (L<sub>Aeq,24h</sub>).

**Table 5** ORs (95% CIs) for the association between annoyance due to aircraft noise (day and night) and medication use

Medication group	Annoyance	OR (95% CI)	N
Antihypertensives	Annoyed by aircraft noise in day	1.34 (1.15 to 1.56)	4646
	Annoyed by aircraft noise at night	1.34 (1.12 to 1.60)	4644
Antacids	Annoyed by aircraft noise in day	1.08 (0.83 to 1.40)	4646
	Annoyed by aircraft noise at night	1.16 (0.86 to 1.55)	4644
Anxiolytics or hypnotics	Annoyed by aircraft noise in day	1.74 (1.30 to 2.34)	4646
	Annoyed by aircraft noise at night	1.70 (1.22 to 2.36)	4644
Anxiolytics	Annoyed by aircraft noise in day	1.79 (1.24 to 2.59)	4646
	Annoyed by aircraft noise at night	1.74 (1.16 to 2.61)	4644
Hypnotics	Annoyed by aircraft noise in day	1.47 (0.94 to 2.29)	4646
	Annoyed by aircraft noise at night	1.40 (0.82 to 2.38)	4644
Antidepressants	Annoyed by aircraft noise in day	1.59 (1.16 to 2.18)	4646
	Annoyed by aircraft noise at night	1.00 (0.67 to 1.50)	4644
Antasthmatics	Annoyed by aircraft noise in day	1.10 (0.80 to 1.48)	4646
	Annoyed by aircraft noise at night	1.39 (0.99 to 1.95)	4644

The hierarchical structure of each logistic regression model assumed a random intercept that accounts for differences in the use of medication between countries and adjustment was made for age, sex, BMI, alcohol intake, education, exercise and smoking status.