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Acute effects of military aircraft noise on sedative and analgesic drug administrations in psychiatric patients: A case-time series analysis

Benedikt Wicki [a,b,*], Danielle Vienneau [a,b], Beat Schäffer [c], Thomas J Müller [d,e], Ulrich Raub [e], Jonin Widrig [f], Charlotte Pervilhac [e,g], Martin Röösli [a,b]

[a] Swiss TPH (Swiss Tropical and Public Health Institute), Allschwil, Switzerland
[b] University of Basel, Basel, Switzerland
[c] Empa, Swiss Federal Laboratories for Materials Science and Technology, Dübendorf, Switzerland
[d] Translational Research Centre, University Hospital of Psychiatry and Psychotherapy University of Bern, Bern, Switzerland
[e] Private Clinic Meiringen, Meiringen, Switzerland
[f] University of Bern, Bern, Switzerland
[g] Institute of Psychology, Health Psychology and Behavioural Medicine, University of Bern, Bern, Switzerland

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ABSTRACT

Background: Existing evidence suggests that psychiatric patients are highly noise sensitive, and that noise exposure increases the risk for adverse mental health outcomes, such as psychiatric hospitalizations and even suicide. To investigate acute effects of noise in this vulnerable population, we assessed short-term associations between fighter jet noise and on-demand sedative and analgesic drug administrations in a psychiatric clinic located close to a military airfield in Switzerland.

Methods: We applied a case time series analysis with an hourly time resolution using distributed-lag models. Analysis was adjusted for long-term and seasonal trends, day of week, time of day, time-varying weather conditions and the week of stay. Noise exposure (hourly A-weighted equivalent continuous sound pressure levels (L_{Aeq})) was modelled using detailed flight plans and noise footprints for different fighter jet and route combinations. Outcome data were available from the clinic's records.

Outcomes: During the study period (06/2016–12/2021), 23,486 flights occurred. 5,968 clinical stays with a median length of 41 days (IQR: 28d, 50d) were recorded. The odds ratio (OR) for medication administration over the lag period of 3 hours after exposure was 1.016 (95 %CI: 1.006, 1.026) per 10 dB LAeq for sedatives and 1.032 (95 %CI: 1.016, 1.048) per 10 dB for analgesics. Effects were larger in multimorbid patients.

Interpretation: Case time series analysis is a novel method to investigate transient associations in observational data while minimizing risk of bias. Using an objectively recorded outcome measure, our results demonstrate that psychiatric patients are a vulnerable population, in which noise exposure can lead to symptom exacerbations and adverse events.

1. Introduction

Transportation noise is a widespread environmental stressor severely affecting human well-being. According to a European Environmental Agency (EEA) report from 2019, 20 % of the European population are exposed to noise levels which are considered harmful (>55 dB day-evening-night level L_{den}) at their place of residence. This exposure results in 22 million people who are highly annoyed and 6.5 million people highly sleep disturbed due to transportation noise in the European region (EEA. Environmental Noise in Europe, 2020). Among sources of transportation noise, aircraft noise and more specifically fighter jets have the biggest potential to cause annoyance (Lee et al., 2008). The odds for being highly annoyed are estimated to increase by the factor 4.8 (95 % Confidence Interval (CI): 2.3, 10.0) per 10 dB increase of aircraft noise exposure (Guski et al., 2017).

Far beyond just being a nuisance however, noise has been recognized as a health risk as well. Noise has been demonstrated to trigger physiological stress responses including activation of the autonomous nervous system and release of stress hormones, and to increase the allostatic load (Basner et al., 2014). All these factors, namely, stress, sleep

* Corresponding author.
E-mail address: benedikt.wicki@swisstph.ch (B. Wicki).

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disturbance and increased allostatic load, are well-established risk factors for the development of various mental health disorders (Freeman et al., 2020; Guidi et al., 2021; Slavich and Irwin, 2014). Besides noise contributing to risk factors for mental health disorders, since the 1970 s there has been evidence that patients suffering from psychiatric disorders are highly sensitive to noise (Barker et al., 1978; Stansfeld et al., 1985; Noise, 1992; Ghazavi et al., 2023). Additionally, noise annoyance, which is considered to be strongly correlated to noise sensitivity (Dzhambov et al., 2019;Ellermeier et al., 2020), has been shown to be more prevalent in people suffering from depression or anxiety (Beutel et al., 2016). In a study in Switzerland, noise annoyance increased the risk of depression incidence independently of noise exposure, and moderated effects of aircraft and road traffic noise exposure on depression risk (Eze et al., 2020). Most of this evidence suggesting that psychiatric patients are more noise sensitive and more vulnerable to environmental noise exposure than the general population is based on self-reported statements. However, little research has considered objectively measured outcomes such as sedative and analgesic drug administrations.

In addition to these pathophysiological considerations, there is epidemiological evidence supporting an association of environmental noise exposure with ill-mental health. A *meta*-analysis from 2020 reported the risk for incidence of depression to increase by 12 % (95 %CI: 2 %, 23 %) per 10 dB L_{den} aircraft noise, while smaller effects where reported for road traffic and railway noise (Hegewald et al., 2020). Another *meta*-analysis from the same year found indications for an association of chronic exposure to transportation noise and an increased risk for anxiety disorders by 9 % per 10 dB L_{den} (95 %CI: –3%, 23 %) (Lan et al., 2020). Additionally, a cohort study from Switzerland reported an increased risk for death by suicide associated with long-term exposure to road traffic (hazard ratio (HR) = 1.040 (95 %CI: 1.015, 1.065) per 10 dB L_{den}) and railway noise (HR = 1.022 (95 % CI: 1.004, 1.041) per 10 dB L_{den}), while results for aircraft noise where inconclusive (Wicki et al., 2023). However, overall the quality of epidemiological evidence on effects of noise on mental health is low, as also noted in two previous systematic reviews (Clark et al., 2020;Clark and Paunovic, 2018).

A specific gap in the scientific literature remains how noise acutely affects patients suffering from mental or behavioral disorders outside the experimental study setting in everyday life and during treatment. Further, the longstanding awareness that these patients might be a subpopulation which is especially sensitive to noise is mostly based on self-reported sensitivity or transient physiological measures (Barker et al., 1978; Stansfeld et al., 1985; Noise, 1992). Studies using objective markers for adverse reactions to noise are rare. With an estimated prevalence of 13.4% or 970 million people affected by mental health disorders worldwide in 2019, this concerns a considerable share of the population (GBD Results, 2019). Common acute adverse events in psychiatric in-patient settings are verbal and physical agitation and aggression, as well as self-harm (Nilsson et al., 2020). Agitation is a heterogeneous phenomenon commonly involving excessive motor activity, irritability and a feeling of inner tension (Lindenmayer, 2000). These adverse events are commonly treated with on-demand administration of psychotropic medication such as benzodiazepines or atypical antipsychotics (Garriga et al., 2016). Such administrations are referred to as pro re nata (PRN= "as needed"), in contrast to scheduled administrations, and are either initiated by clinical staff or demanded by the patients themselves (Casol et al., 2023). Agitation is the most common reason for PRN administration of psychotropic drugs, while other reasons include restlessness, anxiety and insomnia (Baker et al., 2008). Besides sedatives, other commonly used medications in psychiatric care include analgesics, which are demanded by patients when they experience pain or somatization. Somatization refers to a phenomenon when psychological distress is registered and expressed as pain or other bodily sensations by patients suffering from mental health disorders (Lipowski, 1988; Fink et al., 2007).

The aim of this study was to investigate short-term effects of loud environmental noise on patients suffering from psychiatric disorders, who are suspected to be a particularly noise sensitive population. Specifically we explored short-term associations of fighter jet noise on PRN administration of sedatives and analgesics among different patient groups in a psychiatric hospital in close vicinity to a military airfield in Switzerland. We hypothesize that loud aircraft noise events can trigger inner unrest, distress, agitation and somatization, which leads to an increased probability of PRN sedative and analgesic administration in the in-patient setting.

2. Methods

2.1. Study setting

Data for this study were collected from the Privatklinik Meiringen between June 2016 and December 2021. The clinic consists of two locations approximately three kilometers apart, the main site in the valley (Meiringen,) and a specialized burnout-ward further up on a mountainside (Hasliberg / "Au Soleil" site). Both sites are located roughly 6 km from the military airfield Meiringen (see Figure S1 for a map of the area), from which flights take place according to an irregular schedule predominantly during the day only on weekdays. There is no regular aircraft noise in the Meiringen Valley, as it is far from any civil airports. The main other noise source is from road traffic, which is rather a constant noise in contrast to the irregular fighter jet noise. See supplement page 3 for more information on the airfield and flying activity.

2.2. Study sample

All stays at the Privatklinik Meiringen between June 2016 and December 2021 that were longer than three days were included in this study. As the clinic does not treat children or adolescents, this sample only included data from adult patients. No further exclusion criteria applied.

2.3. Sound exposure assessment

The noise exposure resulting from fighter jet flights was modelled using a detailed flight log provided by the Swiss Air Force in combination with aircraft noise calculations (noise footprints) done with the software FLULA2 (Krebs et al., 2004). The basic principles of our approach were adapted from procedures performed for the exposure assessment of a previous study by Saucy et al. around Zurich airport (Saucy et al., 2020). See the exposure assessment section in the supplement (page 3–4) for a detailed description of the process.

We obtained an hourly resolution time series of outdoor aircraft noise exposure at both clinic locations for the whole study period. As we did not have any detailed information on the exact whereabouts of the patients during their entire stay, we used the modelled outdoor exposure as a proxy for their actual exposure. The main noise exposure metric used was the L_{Aeq} (=equivalent continuous sound level), which is a measure for the mean hourly noise exposure. Additional exposure metrics calculated where L_{Amax} (maximum sound pressure level observed per hour), NAT55 and NAT70 (Number Above Threshold, i.e., number of events above 55 dB(A) or 70 dB(A) per hour, respectively).

2.4. Outcome data

Information on drug administrations (patient & case ID, date and time, substance) were exported directly from the clinic's clinical information system. Discrimination between PRN and scheduled administrations was possible based on the time of administration, since scheduled administrations always take place at identical, pre-defined times. We included administrations of sedative psychotropics (ATC-classes N05A Antipsychotics, N05B Anxiolytics, N05C Hypnotics, N06A Antidepressants; referred to as "sedatives") and analgesics (ATC-class

N02B). Exact substances per class are listed in Table S1. Doses where summed per hour for each stay at the clinic individually, and eventually dichotomized to a binary indicator (y/n), separately for all medication classes for every hour of every stay. Additionally, sex, age, primary diagnosis, number of psychiatric diagnoses, as well as the admission and discharge dates were extracted for each stay.

2.5. Statistical analysis

To assess the short-term association between fighter jet noise and PRN drug administrations, we applied a case time series design which combines properties of traditional time series with self-matched study designs (Gasparrini, 2021). The basic principle of this design is that multiple time series with individual exposure and outcome information are combined in one model. Risk for the outcome is modelled continuously as a function of the exposure, thus taking exposed and unexposed times into account, for every participant individually. As in other self-matched designs, this accounts for time-constant, individual level confounders by design, hence limiting the risk of bias without the need for a control group (Mostofsky et al., 2018).

We defined stays at the clinic as units of the case time series, hence constructing hourly time series of medication administrations and aircraft noise for each stay at the clinic. This allowed a different baseline risk for PRN drug administration for every stay and adjusted for time constant factors, such as age and sex of the patient and primary diagnosis by design. The exposure–response relationship was modelled using distributed-lag nonlinear models (DLNM) (Gasparrini, 2011) allowing for immediate as well as delayed effects. Lag duration was set to 0–3 h.

The basic model (M0) included hourly L_{Aeq} (h) as exposure, a spline to account for long-term trends in drug administration (e.g. influence of the COVID-19 pandemic) and seasonality, the week of stay to account for treatment effects, and the day of the week and hour of the day as factors. M1 (=main model) additionally adjusted for the time-varying weather covariates temperature, daily sunshine duration and an index for foehn intensity (a warm fall wind linked to several symptoms and adverse effects on well-being (Mikutta et al., 2022). See the model specification section in the supplement (p. 5) for more detailed information. Main results are reported as OR for medication administration accumulated over the lag period of 3 hours after the exposure per 10dB L_{Aeq} increase.

Effect modification by different patient characteristics was explored by further stratifying the main analysis by sex (female or male), age (<30 y, 30–65 y, >65 y), primary diagnosis (F01-F09, F10-F19, F20-F29, F30-F39, F40-F48) and degree of multimorbidity (low: 1–2 ICD-10F-diagnoses; high: >2 ICD-10F-diagnoses). To explore differences between the two clinic locations, we conducted stratified analyses by location. Additionally, we investigated habituation to the noise by analyzing the first and second half of each stay separately.

Additional analyses were conducted using alternative noise exposure metrics (NAT50(h), NAT70(h) and L_{Amax}(h)). As sensitivity analysis, the main analysis was conducted using two alternative flight route selection processes for exposure assessment (see supplement p. 4): always using the most frequent route and random route selection for every flight. As preliminary descriptive analyses revealed higher total number of sedative administrations in the year 2020, an additional sensitivity analysis excluding stays in the year of 2020 to assess potential modification of our results by the COVID-19 Pandemic was conducted.

All analyses were conducted in the R statistical software (version 4.1.3).

3. Results

During the study period, 5968 stays that met inclusion criteria occurred at the clinic (see Table 1 for sample characteristics). Median length of stay was 41 days (IQR: 28d, 50d). During these stays, a total of 107,640 PRN sedative and 30,826 PRN analgesic administrations were recorded (Table S1). Median number of PRN doses per stay was 9 (IQR: 3, 21) for sedatives and 4 (IQR: 2, 10) for analgesics. See Figure S3 for the time distribution of PRN administrations over the time of day. Concerning exposure, median number of aircraft flyovers with a L_{Amax} above 55 dB (NAT55) per stay was 359 (IQR: 166, 607).

Table 1
Sample characteristics.

Characteristic	
Total Number of Stays	5926
Sex, N (%)	
Female	3226 (54.4 %)
Male	2700 (45.6 %)
Age, N (%)	
< 30	973 (16.4 %)
30–65	4084 (68.9 %)
> 65	869 (14.7 %)
Primary diagnosis (ICD-10), N (%)	
Mental disorders due to known physiological conditions: F01–F09	204 (3.4 %)
Mental and behavioural disorders due to psychoactive substance use: F10–F19	1089 (18.4 %)
Schizophrenia, schizotypal, delusional and other non-mood psychotic disorders: F20–F29	563 (9.5 %)
Mood (affective) disorders: F30–F39	3331 (56.2 %)
Anxiety, dissociative, stress-related, somatoform and other non-psychotic mental disorders: F40–F48	503 (8.5 %)
Other:	236 (4.0 %)
Level of psychiatric Polymorbidity, N (%)	
Low (1–2 ICD-10F-Diagnoses)	4350 (73.4 %)
High (>2 ICD-10F-Diagnoses)	1576 (26.6 %)
Length of stay, median (IQR)	41 (28; 50)
N of PRN sedative administration, median (IQR)	9 (3; 21)
N of PRN analgesic administration, median (IQR)	4 (2; 10)
NAT55 per stay, median (IQR)	359 (166; 607)

A total of 23,486 flights occurred during the study period. See Table S2 for descriptive statistics on the estimated noise exposure (L_{AE} and L_{Amax}) per flight and Figure S4 for an overview of the distribution of aircraft noise over the time of day. Hourly L_{Aeq} (h) values at the two locations ranged from 20 dB (=censoring value) to 68.9 dB for Meiringen and to 77.5dB for Hasliberg. For 87 % of the L_{Aeq} (h) no aircraft noise occurred. The 50th percentile of L_{Aeq} (h) values in hours with flights was 50 dB (Figure S5). Comparison of metrics at the two locations showed that L_{Aeq} (h) depends more on the highest observed noise level (L_{Amax}(h)) than on the number of loud flights per hour (NAT55(h)) (Figure S6). This means that one loud flight (e.g. $L_{\mathrm{Amax}} = 80$ dB) results in a higher L_{Aeq} (h) than several moderately loud flights (e.g. 15 flights with $L_{\mathrm{Amax}} = 60$ dB).

We found that higher fighter jet noise levels were associated with an increased probability for PRN administration of sedatives and analgesics. The odds ratio (OR) for any PRN sedative administration over the lag period of 3 hours after exposure was 1.016 (95% Confidence Interval (CI): 1.006, 1.026) per 10 dB increase of L_{Aeq} (Table 2). This corresponds to an OR of 1.048 (95% CI: 1.017, 1.079) following hours with median fighter jet noise exposure (=50dB L_{Aeq}) compared to hours with no flights (See Table S3). Results were robust to adjustment for meteorological covariates (Table S4). Concerning sedative sub-classes (Table 2), significant associations were observed for hypnotics (OR = 1.025 (95% CI: 1.005, 1.046) per 10 dB) and antipsychotics (OR = 1.017 (95% CI: 1.005, 1.03) per 10 dB), while a strong yet not statistically significant association was seen for antidepressants (OR = 1.040 (95% CI: 0.976, 1.108) per 10 dB). No association was observed with anxiolytics (OR = 0.990 (95% CI: 0.964, 1.017) per 10 dB). For analgesics, the effect was larger than for all sedatives with an OR of 1.032 (95% CI: 1.016, 1.048)

Table 2
Odds ratios (OR) and 95 % confidence interval for medication administration per 10 dB $L_{Aeq}(h)$.

	All Sedatives	*Antidepressants*	*Antipsychotics*	*Anxiolytics*	*Hypnotics*	Analgesics
All (N = 5926)	1.016 (1.006, 1.026)	1.040 (0.976, 1.108)	1.017 (1.005, 1.030)	0.990 (0.964, 1.017)	1.025 (1.005, 1.046)	1.032 (1.016, 1.048)
Sex						
Male (N = 2700)	1.022 (1.006, 1.038)	1.035 (0.935, 1.146)	1.027 (1.007, 1.047)	0.990 (0.952, 1.030)	1.040 (1.006, 1.076)	1.082 (1.051, 1.114)
Female (N = 3226)	1.013 (1.000, 1.026)	1.053 (0.970, 1.142)	1.012 (0.996, 1.028)	0.984 (0.948, 1.021)	1.013 (0.988, 1.038)	1.013 (0.994, 1.032)
Age						
< 30y (N = 973)	1.028 (1.006, 1.051)	*NA*	1.021 (0.994, 1.050)	0.988 (0.934, 1.045)	1.079 (1.033, 1.128)	1.027 (0.978, 1.078)
30-65y (N = 4084)	1.019 (1.006, 1.031)	*NA*	1.021 (1.005, 1.037)	0.999 (0.965, 1.033)	1.015 (0.991, 1.039)	1.039 (1.020, 1.057)
> 65y (N = 869)	0.976 (0.951, 1.002)	*NA*	0.981 (0.950, 1.012)	0.928 (0.860, 1.002)	0.963 (0.905, 1.024)	0.972 (0.923, 1.024)
Primary Diagnosis (by ICD-10 Group)						
F01 – 09 (N = 204)	0.975 (0.933, 1.020)	*NA*	1.011 (0.963, 1.062)	0.954 (0.809, 1.125)	0.893 (0.780, 1.023)	1.001 (0.910, 1.101)
F10 – 19 (N = 1089)	1.038 (1.013, 1.063)	*NA*	1.051 (1.022, 1.082)	0.998 (0.949, 1.049)	0.943 (0.846, 1.051)	1.089 (1.049, 1.131)
F20 – 29 (N = 563)	1.026 (1.000, 1.053)	*NA*	1.029 (0.997, 1.062)	0.995 (0.936, 1.057)	1.034 (0.972, 1.099)	1.019 (0.979, 1.061)
F30 – 39 (N = 3331)	1.014 (1.000, 1.029)	*NA*	1.008 (0.989, 1.027)	0.987 (0.944, 1.032)	1.030 (1.005, 1.056)	1.020 (0.998, 1.043)
F40 – 48 (N = 503)	0.986 (0.954, 1.019)	*NA*	0.986 (0.944, 1.030)	0.986 (0.875, 1.111)	1.009 (0.955, 1.067)	1.049 (0.993, 1.107)
Level of Comorbidity (Low: 1–2 ICD-10 F-Diagnoses; High: >2 ICD-10 F-Diagnoses)						
Low (N = 4350)	1.009 (0.997, 1.022)	1.050 (0.974, 1.131)	1.012 (0.996, 1.027)	0.968 (0.933, 1.003)	1.017 (0.994, 1.041)	1.024 (1.005, 1.043)
High (N = 1576)	1.041 (1.023, 1.059)	1.086 (0.959, 1.231)	1.040 (1.017, 1.062)	1.010 (0.967, 1.054)	1.062 (1.022, 1.104)	1.056 (1.024, 1.088)
Half of Stay						
First half	1.007 (0.993, 1.021)	1.032 (0.942, 1.130)	1.005 (0.987, 1.023)	0.992 (0.958, 1.028)	1.022 (0.994, 1.050)	1.032 (1.008, 1.057)
Second half	1.017 (1.001, 1.034)	1.031 (0.932, 1.139)	1.031 (1.011, 1.051)	0.963 (0.916, 1.013)	0.998 (0.966, 1.032)	1.042 (1.017, 1.066)
Location						
Meiringen (N = 5329)	1.019 (1.009, 1.030)	1.053 (0.970, 1.142)	1.019 (1.007, 1.033)	0.992 (0.965, 1.020)	1.027 (1.007, 1.049)	1.037 (1.020, 1.055)
Hasliberg (N = 597)	0.963 (0.922, 1.006)	1.036 (0.935, 1.148)	0.948 (0.893, 1.008)	NA	0.962 (0.884, 1.047)	0.968 (0.918, 1.021)

Results from Model 1: Case Time Series with stays as observational unit, hourly L_{Aeq} (h) as exposure, adjusted for long-term trends and seasonality (spline with 6 df/year), week of stay, day of the week, hour of the day, temperature, daily sunshine duration and foehn intensity index. Exposure-Response was modelled using a DLNM with linear exposure–response and natural spline lag-response with 1df and a lag of 0–3 h. Results are reported as OR for medication administration accumulated over the lag period of 3 hours after the exposure per 10dB L_{Aeq} increase
NAs: For Antidepressants and Anxiolytics, there were not enough administrations to conduct analyses in all subgroupgs.

per 10 dB. Stratified analysis by sex revealed that odds for PRN administrations of all investigated medication groups where higher in males than in females, with the exception of antidepressants where the effect was larger in females. In terms of effect modification by age, no effects were observed in the age group above 65 years. Concerning primary diagnosis, the largest effects on sedative administrations were observed in patients with disorders due to psychoactive substance use (ICD-10: F10, OR = 1.038 (95% CI: 1.013, 1.063) per 10 dB) followed by patients with schizophrenia and psychotic disorders (ICD-10: F20, OR = 1.026 (95% CI: 1.000, 1.053) per 10 dB). No effects where observed in patients with disorders due to physiological conditions (ICD-10: F00) or anxiety, stress-related or somatoform disorders (ICD-10: F40) as primary diagnosis. Concerning analgesics, the observed effect was also largest in patients with an F10 diagnosis (OR = 1.089 (95% CI: 1.049, 1.131) per 10 dB), while again no effect was observed in patients with a primary F00 diagnosis (Table 2, Fig. 1). Stratification by level of comorbidity

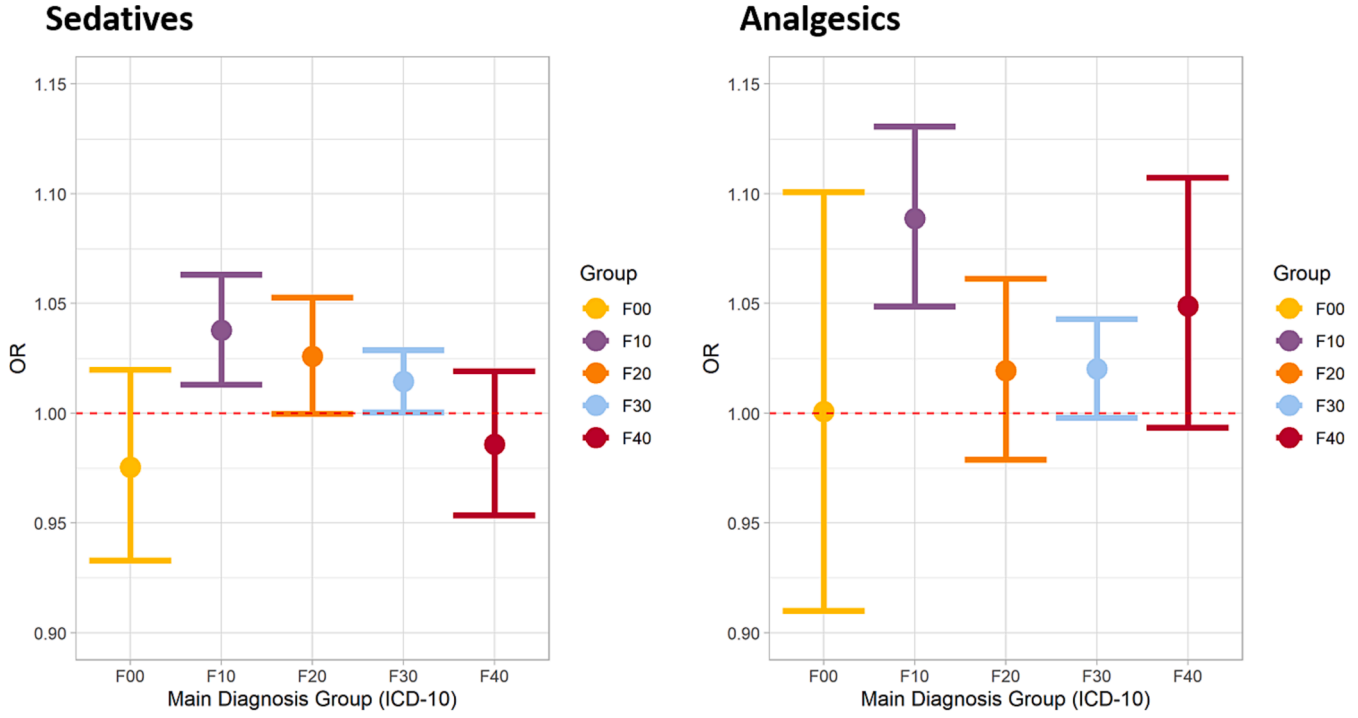

Fig. 1. Effect modification of the effect of fighter jet noise on PRN administration of sedatives or analgesics by primary diagnosis. Points indicate OR for administration accumulated over the lag period of 3 hours after the exposure per 10 dB LAeq(h), whiskers indicate 95 %CIs.

revealed that the observed associations on sedative administrations were larger in patients with high comorbidity (>2 ICD-10 F-diagnoses, OR = 1.041 (95% CI: 1.023, 1.059) per 10 dB) than in patients with low comorbidity (1–2 ICD-10 F-diagnoses, OR = 1.009 (95% CI: 0.997, 1.022) per 10 dB). The same pattern was observed for antipsychotic, antidepressant, hypnotic and analgesic administrations (Table 2, Figure S7). Separate investigation of the effect of fighter jet noise during the first and second half of each stay did not show an indication of a habituation effect (Table 2, Figure S8). Regarding the different clinic locations, no effects of fighter jet noise on drug administrations were observed in the burnout-ward / Hasliberg site, with the exception of antidepressants (Table 2).

The exposure-lag-response structure showed that for both all sedatives and analgesics the odds for drug administrations peaked at lag 1 h and then quickly dropped back towards the null after 3 h. Antipsychotics followed the same pattern. Antidepressants, anxiolytics and hypnotics, however, followed a different lag structure of immediate low risk only starting to increase after a couple of hours, and not reaching a peak at the end of the 3-hour lag period (Fig. 2).

Results from models using L_{Amax}(h) as exposure were smaller than results using L_{Aeq} when expressed as per 10 dB changes (Table S5). When using either NAT55(h) or NAT70(h), we only observed weak, non-significant associations of the exposures with sedative administrations. Concerning analgesic administrations, in contrast, strong associations were also observed when using these latter event based exposure metrics (table S5).

Sensitivity analysis excluding stays from the year 2020 revealed virtually unchanged effect estimates (OR for sedative administration per 10 dB = 1.013 (95% CI: 1.002, 1.025)) as the main analysis.

Exposure metrics derived with alternative exposure assessment approaches were strongly correlated to values used in the main analysis (Figure S9). Sensitivity analysis using these different assumptions for exposure assessment revealed very similar effect estimates as the main analysis (supplemental table S6).

4. Discussion

In this study, we found that fighter jet noise increases the short-term probability for PRN administration of both sedatives and analgesics in a psychiatric clinic in Switzerland. Given that sedatives in inpatient psychiatry are mainly used to treat acute agitation, anxiety, strong feelings of distress and inner unrest (Baker et al., 2008), these findings suggest that loud noise events can trigger such emotions. Similarly, the increased probability of analgesic consumption following high noise exposure is an indication that noise can cause somatization, which is also an expression of psychological distress (Lipowski, 1988). In line with previous research, these results suggest that noise can have relevant effects on patients suffering from mental health disorders, potentially exacerbating symptoms and contributing to adverse outcomes. Additionally, we saw larger effects in patients with psychiatric multimorbidity, supporting previous evidence that poorer mental health is associated with an increased sensitivity to noise.

As epidemiological studies on acute effects of loud noise events specifically on patients with mental health disorders are still rather scarce, direct comparison of our results to the existing literature is difficult. An ecological time series study from Madrid, Spain reported a short term risk increase for emergency hospital mental health admissions associated with higher transportation noise levels (Gómez González et al., 2023). The authors used daily values from a city wide noise monitoring network and daily emergency admissions from the

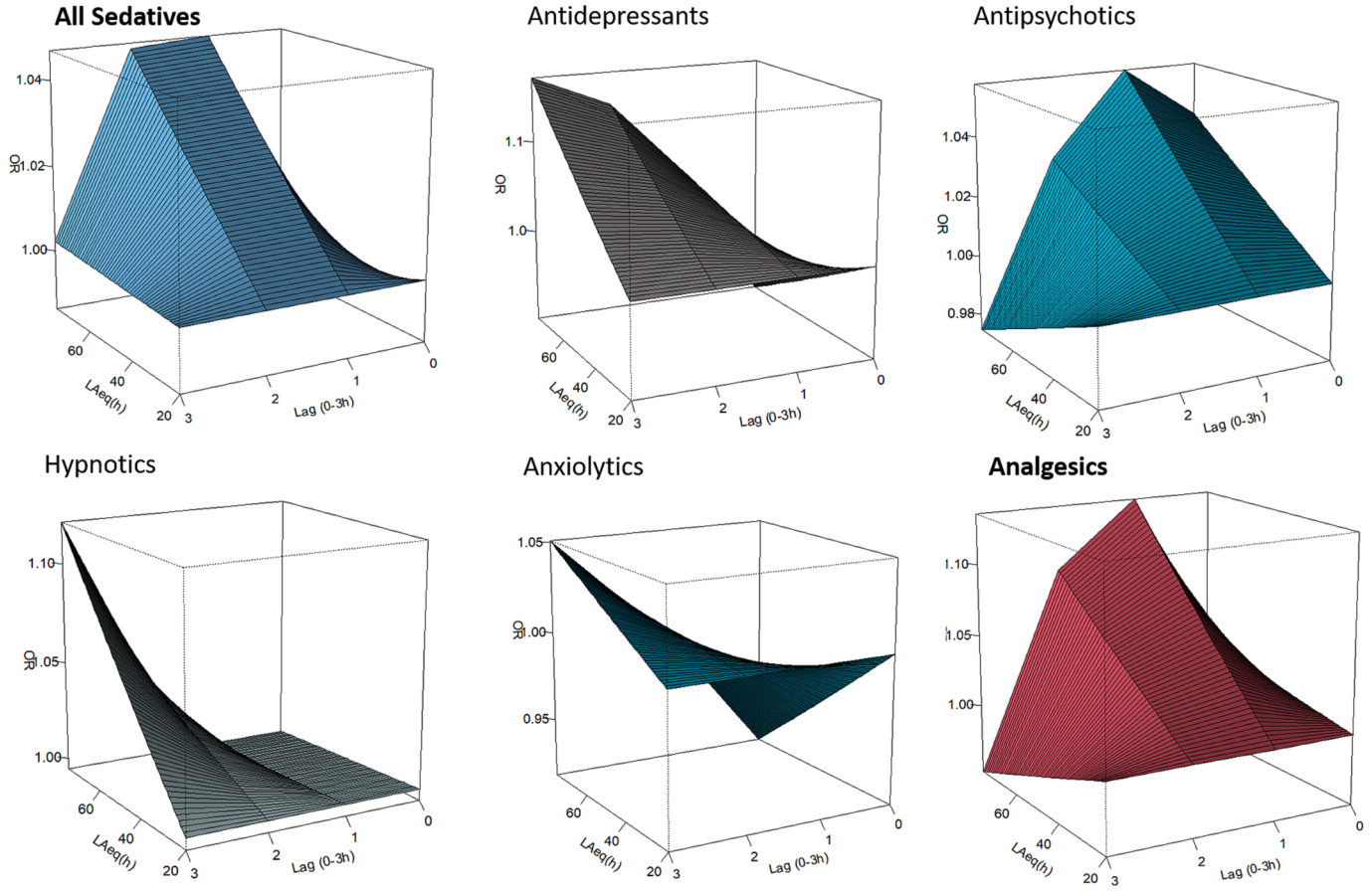

Fig. 2. Exposure-lag-risk surface for the association between hourly fighter jet noise exposure (L_{Aeq} (h) [dB(A)]) and PRN medication administration over a lag of 0–3 h.

years 2013–2018, and estimated that 5.5 % of all psychiatric emergency admissions in their study sample had been attributable to environmental noise. An earlier study using similar data and methodology had already reported an association between same day transportation noise and risk for emergency hospital admission due to depression (risk ratio RR per 1 dB L_{day} at lag = day 0: 1.11 (95% CI: 1.06, 1.16)) and anxiety (RR per 1 dB L_{day} at lag = day 0: 1.20 (95% CI: 1.14; 1.26)), and also between previous day noise levels and suicides (RR per 1 dB L_{day} at lag = day 1: 1.17 (95% CI: 1.05, 1.30)) (Díaz et al., 2020). However, due to the imprecise exposure assessment and low variability in noise levels, these results are subject to a substantial risk of bias and confounding. Nonetheless, our study is in line with these findings, even though we observed smaller effects ranging between ORs of 1.016 and 1.040 per 10 dB in the full sample. Relative risks depends on the baseline risk. PRN administration are relatively common in our study population and accordingly, the observed relative risks still mean considerable absolute risk increases. Further, the observed effect sizes are similar to long-term mental health effects (Wicki et al., 2023). Additionally, as our use of modelled outdoor noise levels is subject to some random exposure misclassification, we may also have underestimated the true effect size. Nonetheless, given the consistent observed effects, also in subgroup analyses, we argue that our findings can be interpreted as a "proof of concept" that loud environmental noise acutely affects psychiatric patients, with higher vulnerability in more severe cases. This is very much in support of a substantial body of evidence stating that patients suffering from mental disorders are more sensitive to noise (Stansfeld, 1992;Dzhambov et al., 2019).

The evidence base on reasons for PRN administrations is very thin. We only found descriptive studies reporting what are the most common reasons for PRN administrations (Casol et al., 2023;Baker et al., 2008 ; Martin et al., 2017), but no evidence on the risk due to different triggering factors. Hence, we cannot tell how the fighter jet noise compares to other triggers in terms of relevance. This is an important gap in the literature, which future research should address.

Our results warrant some reflection about possible effects outside the psychiatric in-patient setting. Outside of psychiatric care, loud noise events may also lead to acute exacerbation of symptoms possibly resulting in emergency admissions or self-harm. The physiological mechanism behind this assumption is that persons with preexisting mental health disorders already have a high allostatic load (Juster et al., 2018). As has been previously reported, noise can further increase this allostatic load (Basner et al., 2014), leading to an acute allostatic overload, eventually resulting in adverse events. Furthermore, self-medication using alcohol or tobacco is common in the outpatient setting among individuals suffering from mental or behavioral disorders (Turner et al., 2018), but also in the general population as a pathological mechanism to cope with stress (Creswell and Bachrach, 2020). Hence, we speculate that exposure to loud noise events might lead to a short-term increase in alcohol and tobacco consumption when sedatives are not available. Besides the increase in allostatic load, this could be a part of the mechanism behind the reported increased risk for the incidence of depression, anxiety disorders and even suicide associated with chronic exposure to transportation noise in other studies (Hegewald et al., 2020; Lan et al., 2020; Wicki et al., 2023). More research focusing on the effects of noise in this vulnerable population is needed to elucidate the exact pathway of adverse effects and find ways to prevent them.

We saw slightly larger effects of noise on both sedative and analgesic administration in the second compared to the first half of stays (Figure S8), suggesting that there is no habituation to the noise. An alternative explanation for this could be that patients receive higher fixed medication doses at the beginning of their stays that are then consecutively lowered, hence possibly resulting in a higher vulnerability in the second half of stays.

The main strengths of our study is the unique setting of the psychiatric clinic in close vicinity to the military airfield with its irregular jet flights. This enabled us to apply the novel case-time-series design, in order to adjust for time-constant, individual level confounders by design without the need for a control group. This makes our observational study very robust in terms of causality by limiting the risk for bias, confounding and reverse causality. Since military flights are logged, we could precisely estimate noise exposure with hourly resolution matching the time resolution of drug prescription. The large dataset of almost 6,000 stays with over 130,000 PRN administrations over more than five years yielded to high statistical power.

A limitation of the study design is that one cannot resolve whether noise exposure generally increases sedative and analgesic drug consumption or just advances PRN administrations, which would have occurred later anyway. Second, given that we did not have information on the exact flight routes, we had to use some approximations in the exposure assessment. However, sensitivity analyses do not indicate that resulting exposure misclassification is critical. Additionally, the modelled outdoor noise exposure is only a proxy for the actual exposure the patients experienced, also resulting in non-differential exposure misclassification. Any such exposure error might have led to an underestimation of the true effect size. Third, we did not have information on the exact indication of individual medication administrations. Some studies suggest that administrations are sometimes rather driven by the staff than by the patient, especially with regards to PRN sedative use in psychiatric care (Usher et al., 2001). Hence, we consistently refer to drug administrations rather than drug use, as the latter would imply a proactive role of the patient in all events. Strikingly however, we found much larger effects on PRN analgesic use than sedative use, which we suspect to be administered more commonly due to patient requests.

5. Conclusions

This study applied a novel design to investigate acute effects of exposure to loud noise events on objectively recorded mental health outcomes in patients affected by mental health disorders in a natural experiment setting with a highly irregular noise exposure. The study adds to the existing evidence that mental and behavioral disorders are associated with vulnerability to noise exposure, suggesting that noise can lead to symptom exacerbations and adverse mental health outcomes in psychiatric patients. Further, the findings support previous results suggesting that chronic noise exposure can contribute to the development of mental health disorders or worsening of preexisting conditions.

CRediT authorship contribution statement

Benedikt Wicki: Writing – review & editing, Writing – original draft, Visualization, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Danielle Vienneau:** Writing – review & editing, Writing – original draft, Supervision, Data curation, Conceptualization. **Beat Schäffer:** Data curation, Supervision, Writing – review & editing. **Thomas J Müller:** Writing – review & editing, Data curation, Conceptualization. **Ulrich Raub:** Data curation. **Jonin Widrig:** Data curation. **Charlotte Pervilhac:** Writing – review & editing, Conceptualization. **Martin Röösli:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.envint.2024.108501.

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