Original article

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The influence of environmental traffic noise exposure on breast cancer risks, especially with respect to estrogen receptor status, has scarcely been researched. We found exposure to higher levels of aircraft traffic noise was associated with increased risks of estrogen receptor negative breast cancers. Considering the prevalence of traffic-noise, a small increase in cancer risk can be of public health importance.

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Original article

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Breast cancer and exposure to aircraft, road, and railway noise: a case–control study based on health insurance records

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Objectives Aircraft, road, and rail traffic noise can cause sleep disturbances. Since night work and shorter sleep durations have been linked to increased risks of breast cancer, we examined if 24-hour, or day- or night-time traffic noise exposure may also increase the risk of breast cancer.

Methods To investigate the noise-related risks of breast cancer, the pseudonymized insurance records of three large statutory health companies (2005–2010) for women aged ≥40 years living in the region surrounding the Frankfurt international airport were analyzed with address-specific acoustic data representing aircraft, road, and rail-traffic noise. Noise exposure among women with incident breast cancer (N=6643) were compared with that of control subjects (N=471 596) using logistic regression and adjusting for age, hormone replacement therapy, education and occupation (only available for 27.9%), and a regional proportion of persons receiving long-term unemployment benefits as an ecological indicator of socioeconomic level. Analyses were also stratified according to estrogen receptor (ER) status.

Results An increased odds ratio (OR) was observed for ER negative (ER-) tumors at 24-hour aircraft noise levels 55–59 dB [OR 55–59 dB 1.41, 95% confidence interval (CI) 1.04–1.90] but not for ER positive (ER+) breast cancers (OR 55–59 dB 0.95, 95% CI 0.75–1.20). Clear associations between road and rail traffic noise were not observed.

Conclusions The results indicate increased aircraft noise may be an etiologic factor for ER- breast cancers. However, information regarding potential confounding factors was largely unattainable. Further research is required to understand how environmental noise may be involved in the pathogenesis of ER- breast cancers.

Key terms aircraft noise; road noise; breast neoplasm; environment; epidemiology; estrogen; estrogen receptor; risk; traffic noise; transportation.

According to the latest World Health Organization *World Cancer Report*, breast cancer continues to be the most frequent cancer afflicting women worldwide (1). The increased rates of breast cancer observed in more industrialized regions (2) suggests that characteristics of industrialized living, including differences in lifestyle and environmental exposures, may contribute to breast cancer risk.

One environmental risk factor for breast cancer that has been the focus of much research is exposure to light at night (LAN). Exposure to LAN reduces the production of melatonin, a hormone with oncostatic qualities that is associated with lower estrogen levels, generally secreted in the early stages of nightly sleep during the absence of light to regulate the circadian rhythm. Numerous possible mechanisms have been suggested to explain the role of melatonin in preventing or slowing tumor growth. The anti-oxidative properties of melatonin are important in metabolizing/processing the products of (oxidative) stress and experiments have shown melatonin to slow the proliferation of estrogen

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receptor positive (ER+) MCF-7 tumor cells (3, 4).

Studies of breast cancer risks among women working night shifts have examined the potential effect of exposure to LAN coupled with disruption of the circadian rhythm. Evidence from such studies led the International Agency for Research on Cancer (IARC) to declare shiftwork with circadian disruption to be "probably carcinogenic to humans (Group 2A)" (5). However, pooled breast cancer risks of female night shift workers based on meta-analyses of available studies vary and range from a 5–51% increase in risk (6–14). While an association between breast cancer and working nights may be due to the effect of LAN on melatonin levels, other aspects of working at night, such as reduced sleep may also be involved in tumor development or growth.

Studies on duration of sleep and the risk of breast cancer also report conflicting results. Some studies report increased risks for fewer average hours of sleep (15, 16), and others find no association or risks increasing with sleep duration (17–20). While poor sleep may also be associated with lowered melatonin levels, diurnal sleep itself promotes immunological processes through the production of cytokines during sleep and increased levels of white blood cells following sleep (21). Therefore, poor sleep or a lack of sleep could possibly impact the body's ability to recognize and eliminate damaged cells. As environmental aircraft, automobile, and railway transportation noise can also cause sleep disruption (22), traffic-related sleep disruptions could be associated with increased breast cancer risks.

Exposure to environmental traffic noise can also provoke stress reactions that may be immunotoxic (23). Stress-related activation of the hypothalamic–pituitary–adrenal (HPA) axis results in increased levels of corticotropin-releasing hormone and subsequently increased levels of the stress hormone cortisol. Although epidemiological studies of breast cancer risk related to stressful life events or chronic stress (eg, job strain) are inconsistent, animal models find tumor incidence and growth to be increased by stress (24). Antonova et al (24) have postulated possible mechanisms to explain how cortisol may be involved in breast cancer development and include repression of the immune system's ability to find and repair cancer cells, inhibited DNA repair, and down-regulation of breast-cancer tumor suppressor gene (BRCA1) expression.

Environmental traffic noise and malignancies

Existing research regarding a possible increased cancer risk due to environmental traffic noise exposure is limited and inconclusive (25–28). Visser and colleagues (28) first examined the incidence of cancer near the Amsterdam Schiphol airport by comparing the standardized incidence ratios (SIR) of residents living in a "core area" (defined by noise contours) exposed to increased aircraft noise and airport-related pollutants with the SIR for residents living in the less exposed surrounding areas. Incidence of hematological malignancies was especially increased in the core area of the Schiphol study and incidence of breast cancer was increased in the entire study area but slightly lower among the female residents in the core area (28).

In Germany, Greiser & Greiser (25) conducted a case–control study using health insurance claims data of residents living near the Cologne-Bonn airport to examine the risk of cancer following exposure to aircraft, road and railway traffic noise, and found an increased risk for breast cancer with increasing nightly aircraft noise. In a study of cancer-registry and resident registration data in Bremen, Greiser & Greiser (26) found non-statistically significant elevated breast cancer risks due to night-time aircraft and railway traffic noise exposure, and no increased risk for exposure to day or night-time road traffic noise.

In Denmark, Sörensen et al (27) examined the risk of breast cancer due to road and railway traffic noise exposure in a prospective study of postmenopausal women (aged 50–64 years) registered in the Danish Diet, Cancer and Health Cohort with ten years of exposure data. Although the incidence rate ratios (IRR) of all breast cancers were not related to increased traffic noise levels, stratified examination of ER status found the incidence of ER negative (ER-) cancers to be increased for each 10 dB increase in evening-night weighted (L_{den}) road [IRR 1.28, 95% confidence interval (CI) 1.04–1.56] and railway (IRR 1.38, 95% CI 1.01–1.89) traffic noise.

In the present study, we examined if breast cancer incidence is associated with aircraft, road, and railway traffic noise exposures among women living in the region surrounding the Frankfurt airport by linking address-specific noise exposure estimates with the health insurance claims data from three large public health insurance companies. We also examined if breast cancer risks due to environmental traffic noise exposures differ according to ER status.

Methods

Study population

The pseudonymized insurance records of three large statutory health companies from 2005–2010 served as the basis for the examinations. Altogether, the study population comprised >1 million persons (N=1 026 670) aged ≥40 years by 2010 living in the regions surrounding the Frankfurt international airport, including the Darmstadt administrative region, the cities Mainz and Worms, and

the administrative districts Mainz-Bingen and Alzey-Worms. Health insurance was available to all residents and clients were not pre-selected based on a family history of cancer or pre-existing conditions. The insurance population examined represented roughly 23% of the population >40 years of age. Only women (N=571 183) were included in the analyses of breast cancer risks as breast cancer among men is rare. The insurance records included information regarding diagnoses of inpatient and outpatient visits, procedures, prescription medications, and limited demographic information.

Definition of cases and controls

Incident breast cancer diagnoses were defined as the first main or secondary hospital discharge diagnosis of a malignant neoplasm of the breast (ICD-10: C50.-) or carcinoma in situ of the breast (ICD-10: D05.-) among women 40 years of age at the time of the diagnosis recorded within a year of one of the following corresponding breast cancer therapies: radiation [operations and procedure classification code (OPS) code 8–52], chemotherapy (OPS code 8–542), immunotherapy (OPS code 5–547) or breast operation (OPS codes 5–87; 5–88). To be considered incident, the diagnosis must have been preceded by at least one diagnosis-free year. This definition of incidence meant all identified cases of breast cancer were first diagnosed between 2006 and 2010. Control subjects were selected from all women ≥40 years of age by 2010 without any record of the above diagnoses. In order to determine if noise-induced risks differed according to estrogen status, any record of a prescription for anti-estrogens or aromatase inhibitors (anatomic therapeutic classification, ATC codes: L02BA, L02BG) was used as an indicator of ER+ tumor status.

Noise data

Address-specific acoustic data representing aircraft, road, and rail traffic noise for the years 1997–2010 were provided by the acoustic engineering company, Möhler and Partner Ingenieure AG. To ensure traffic noise exposure predated the diagnoses and would best represent noise exposure during the time period represented by the insurance data, traffic noise values for 2005 were examined. Aircraft noise was estimated for each building using STANLY track radar records obtained from the German flight safety operator (Deutsche Flugsicherung GmbH) describing aircraft type and flight path. Road traffic noise calculations were based on traffic count data provided by the municipalities, including information regarding average daily traffic volume, road type, speed limits, and proportion of vehicles weighing >3.5 tons. Rail traffic noise was calculated from data provided by the federal railway authority regarding the railway network, the number of trains traveling, train lengths, type of trains, maximum train speeds, and the proportion of disc brakes on the trains. Road and rail traffic noise levels were then modelled for the most-exposed house surface (façade) taking geographical characteristics (ie, noise reflection from neighboring buildings, noise barrier walls, and differences in elevation) into account. All noise values were calculated in accordance with current German standards using the software SoundPLAN version 7.3 (29). Equivalent continuous noise pressure (L_{pAeq}) values for each traffic noise source were available for all 24 hours, as well as daytime (06:00–22:00) and night-time (22:00–06:00) hours. L_{pAeq} for individual hours of the night and other definitions of night (ie, European night: 23:00–07:00; core night: 23:00–05:00 hours) were also available for aircraft noise. Detailed information regarding the calculation and validation of the acoustic data are published elsewhere (30).

Data handling

The ethics committee of the Faculty of Medicine at the University of Dresden reviewed the study (reference number: EK328102012; 21 February 2013 and 22 April 2014). The study design was submitted to the Federal Commissioner for Data Protection and Freedom of Information (reference number: III-320/010#0011; response dated 11 June 2012) and to the Data Protection Officers of the participating federal states of Hessen (reference number: 43.60-we; response dated 13 March 2012; amendment notification 7 February 2014) and Rhineland-Pfalz (reference number: 6.08.22.002; response dated 7 May 2012; amendment notification 4 February 2014), all of which confirmed this research project complies with data protection regulations.

Great care was taken to ensure the anonymity of the insured population was protected. Consequently, either the "trust-center" (BIPS Bremen) or the insurance company itself merged the noise-exposure data and regional socioeconomic indicators with the addresses. Matching of noise with past addresses was possible for one of the insurance companies, while the other two insurance companies could only provide the address on record at the time of the merge (February 2013). Only the exposure data and pseudonyms were made available to the department responsible for the analysis (TU Dresden) to ensure that at no time did a single entity have access to personal identifying information together with sensitive medical data. Of the insured population with available address information (N=954 986), 95.1% of the addresses could be matched with noise-exposure data.

Statistical analyses

Odds ratios (OR) and 95% CI describing the relation-

ship between transportation noise and breast cancer risks were estimated using logistic regression models. In addition to models examining all breast cancer cases, ER status subgroups were examined in separate models. All models adjusted for age, hormone replacement therapy prescriptions (ATC codes: G03C, G03D, G03F) prior to diagnosis or 2008 for controls, the regional proportion of working-aged residents collecting long-term unemployment benefits as an ecological indicator of social-economic status (quintiles) (Federal Institute for Research on Building, Urban Affairs and Spatial Development; BBSR 2012), and (when available) individual information regarding educational-level and occupation in 2005 categorized using the Blossfeld occupational classification (31). Missing values were included in the logistic regression models as separate categories. For women diagnosed with breast cancer, the age attained during the year of the diagnosis was modelled, while the age attained in 2008 (median year of all diagnoses) was used for control persons. Age was entered into the model as a 3rd degree polynomial (ie, age, age^2, age^3), since this resulted in better model fit compared to modelling age in 5-year age categories according to the Akaike information criterion (AIC). The 24-hour noise levels were modelled either in 5 dB categories or as a continuous variable (linear or 3rd degree polynomial) where traffic noise values <40 dB were set to 35 dB, since noise values <40 dB are indiscernible from typical background noise levels. Other time intervals of noise were examined only as 5 dB categories. The AIC was also used to determine the appropriateness of the linear model. A difference in AIC values of ≤5 was defined a priori as sufficient indication of adequate—albeit not necessarily better—linear model fit. Additional analyses combining all three traffic noise exposures in one model and examining only the women with available socioeconomic information were also conducted. The statistical analyses were conducted with the statistical program Stata (32) (Stata Corp, College Station, TX, USA).

Results

Among the insured population with environmental noise exposure data, 6643 (1.4%) women were newly diagnosed with breast cancer in 2006–2010 according to our case definition; the control group comprised 471 596 (98.6%) women. The characteristics of the study population are depicted in table 1. Regarding ER receptor tumor status, 69.9% (N=4645) of the women with breast cancer received ancillary treatment with either anti-estrogens or aromatase inhibitors indicating an ER+ status, while 30.1% (N=1998) of the women were not prescribed these treatments during the observation period. Individual indicators of social status, ie, educational level or occupation, were available for 30% of the control subjects (N=141 612) and 25% of the women with breast cancer (N=1665). More specifically, educational level was available for 24.2% and occupational information was available for 27.9% of the entire study population.

Exposure to traffic noise

About half of the study population was exposed to aircraft or railway traffic $L_{pAeq,24h}$ levels >40 dB with exposure skewed towards lower noise levels (table 2). In comparison, road traffic noise exposure was more evenly distributed among the study population. The $L_{pAeq,24h}$ exposures ranged from <40 dB to 61.3 dB for aircraft, to 85.7 dB for road traffic, and to 83.9 dB for railway noise.

Traffic-noise and breast cancer risks

The results of the logistic regression for breast cancer risk and aircraft noise exposure are presented in table 3. For most of the exposure categories, the observed risks were close to one. The OR increased to 1.08 (95% CI 0.90–1.31) for 24-hour aircraft noise levels between 55–59 dB. Stratification according to ER receptor status showed noise-related risk for 24-hour aircraft noise was more pronounced for ER- ($OR_{55\text{-}59dB}$1.41, 95% CI 1.04–1.90) and not increased for ER+ breast cancers ($OR_{55\text{-}59dB}$ 0.95, 95% CI 0.75–1.20). This trend of greater risks for ER- cancers within the same noise-category persisted when the night- and daytime noise were considered separately. Increased cancer risks were generally detected in the highest observed night- and daytime aircraft noise exposure levels of both tumor types. Most notably, OR ranging from 2.10 for ER+ to 5.16 for ER- breast cancers were observed for the highest aircraft noise level (55–59 dB) observed during the core nighttime hours (23:00–05:00 hours). However, these estimates were based on the limited breast cases (<5).

A 4.9% increase in risk (OR 1.049, 95% CI 0.996–1.140) was observed for ER- breast cancers with each 10 dB increase in aircraft noise when aircraft noise was examined as a continuous linear variable. Risk for ER+ breast cancers, on the other hand, decreased with each 10 dB increase in noise. The AIC of the linear models were 2–4 points lower than that of the third-degree polynomial models for all three traffic noise sources, indicating adequacy of the linear model.

Similar trends were observed for road traffic noise (table 4), with increased risks generally observed in the highest exposure categories and larger increased estimated risks observed for ER- cancers. In contrast to aircraft noise, the estimated OR were slightly lower and the CI of the risk estimates always encompassed the null value.

Table 1. Population characteristics. [ER+ / ER- =estrogen receptor positive / negative.]

	Total		Control subjects		Breast cancer		ER+		ER-	
	N	%	N	%	N	%	N	%	N	%
Total	478 239	100.0	471 596	100.0	6643	100.0	4645	100.0	1998	100.0
Age (years)										
<45	67 901	14.2	67 625	14.3	276	4.2	183	3.9	93	4.7
45–49	51 466	10.8	51 002	10.8	464	7.0	315	6.8	149	7.5
50–54	47 652	10.0	47 093	10.0	559	8.4	376	8.1	183	9.2
55–59	48 592	10.2	47 893	10.2	699	10.5	484	10.4	215	10.8
60–64	43 141	9.0	42 232	9.0	909	13.7	628	13.5	281	14.1
65–69	51 981	10.9	50 852	10.8	1129	17.0	851	18.3	278	13.9
70–74	51 433	10.8	50 454	10.7	979	14.7	686	14.8	293	14.7
75–79	39 187	8.2	38 504	8.2	683	10.3	486	10.5	197	9.9
80–84	35 695	7.5	35 128	7.4	567	8.5	406	8.7	161	8.1
≥ 85	41 191	8.6	40 813	8.7	378	5.7	230	5.0	148	7.4
Insurance population										
01	278 826	58.3	275 387	58.4	3439	51.8	2401	51.7	1038	52.0
02	34 488	7.2	34 055	7.2	433	6.5	307	6.6	126	6.3
03	164 925	34.5	162 154	34.4	2771	41.7	1937	41.7	834	41.7
Education										
Primary/secondary	29 581	6.2	29 245	6.2	336	5.1	237	5.1	99	5.0
Primary/secondary with vocational training	65 864	13.8	65 024	13.8	840	12.6	560	12.1	280	14.0
High school	1822	0.4	1798	0.4	24	0.4	19	0.4	5	0.3
High school with vocational training	7628	1.6	7543	1.6	85	1.3	58	1.2	27	1.4
College	4995	1.0	4939	1.0	56	0.8	33	0.7	23	1.2
University	5614	1.2	5546	1.2	68	1.0	41	0.9	27	1.4
Unknown	362 735	75.8	357 501	75.8	5234	78.8	3697	79.6	1537	76.9
Occupational classification [a]										
Unknown	344 621	72.1	339 511	72.0	5110	76.9	3609	77.7	1501	75.1
Agricultural	509	0.1	504	0.1	5	0.1	2	0.0	3	0.2
Unskilled manual	9363	2.0	9263	2.0	100	1.5	61	1.3	39	2.0
Skilled manual	6440	1.3	6389	1.4	51	0.8	42	0.9	9	0.5
Technical	1515	0.3	1495	0.3	20	0.3	15	0.3	5	0.3
Engineering	475	0.1	473	0.1	2	0.0	0	0.0	2	0.1
Simple services	24 259	5.1	24 026	5.1	233	3.5	149	3.2	84	4.2
Qualified services	9089	1.9	8981	1.9	108	1.6	79	1.7	29	1.5
Semiprofessional	16 498	3.4	16 320	3.5	178	2.7	111	2.4	67	3.4
Professional	1254	0.3	1243	0.3	11	0.2	7	0.2	4	0.2
Simple business & administrative	19 252	4.0	19 028	4.0	224	3.4	151	3.3	73	3.7
Qualified business & administrative	39 740	8.3	39 206	8.3	534	8.0	374	8.1	160	8.0
Manager	2092	0.4	2065	0.4	27	0.4	18	0.4	9	0.5
Other	3132	0.7	3092	0.7	40	0.6	27	0.6	13	0.7
Regional proportion (%) of persons receiving unemployment benefits (2005; quintiles [b])										
≤6.7	162 012	33.9	159 737	33.9	2275	34.2	1578	34.0	697	34.9
>6.7–7.5	78 580	16.4	77 412	16.4	1168	17.6	851	18.3	317	15.9
>7.5–8.7	53 032	11.1	52 296	11.1	736	11.1	495	10.7	241	12.1
>8.7–12.7	137 471	28.7	135 616	28.8	1855	27.9	1303	28.1	552	27.6
>12.7	47 144	9.9	46 535	9.9	609	9.2	418	9.0	191	9.6

[a] Blossfeld classifications.
[b] Calculation of quintiles: frequent duplication of proportions led to an uneven distribution.

The tendency for the observed risks to increase with increasing noise exposure levels and for ER- cancers that was observed with aircraft and road noise was not as evident for rail traffic noise (table 5). For example, the largest estimated OR for ER+ cancers was observed for the second highest noise level category ($OR_{65\text{-}69dB}$ 1.25, 95% CI 0.91–1.73) and exceeded the risk observed for ER- cancers in the same exposure level category ($OR_{65\text{-}69dB}$ 0.85, 95% CI 0.47–1.55).

All three traffic noise sources were also combined in one model to obtain risk estimates adjusted for the other two sources of traffic noise (see supplementary data, www.sjweh.fi/index.php?page=data-repository). Combined analysis of the three traffic noise sources resulted in negligible changes to the risk estimates observed in the separate models.

Table 2. Exposure to 24-hour environmental traffic noise (LpAeq, 24 hrs) and breast cancer status. [ER+ / ER- =estrogen receptor positive / negative.]

dB	Control subjects		Cases		ER+		ER-	
	N	%	N	%	N	%	N	%
Aircraft noise								
>40	219 066	46.5	3137	47.2	2204	47.5	933	46.7
40–44	140 231	29.7	1969	29.6	1384	29.8	585	29.3
45–49	74 346	15.8	1038	15.6	722	15.5	316	15.8
50–54	29 067	6.2	371	5.6	256	5.5	115	5.8
55–59	8786	1.9	126	1.9	77	1.7	49	2.5
≥60	100	<0.05	<5	<0.05	<5	<0.05	0	0.0
Road traffic (dB)								
<40	51 011	10.8	755	11.4	538	11.6	217	10.9
40–44	101 593	21.5	1472	22.2	1040	22.4	432	21.6
45–49	114 427	24.3	1595	24.0	1098	23.6	497	24.9
50–54	82 929	17.6	1159	17.5	812	17.5	347	17.4
55–59	51 346	10.9	720	10.8	496	10.7	224	11.2
60–64	37 865	8.0	511	7.7	357	7.7	154	7.7
65–69	25 313	5.4	327	4.9	231	5.0	96	4.8
≥70	7112	1.5	104	1.6	73	1.6	31	1.6
Railway traffic								
<40	255 215	54.1	3650	55.0	2544	54.8	1106	55.4
40–44	58 096	12.3	806	12.1	558	12.0	248	12.4
45–49	73 994	15.7	1047	15.8	734	15.8	313	15.7
50–54	51 325	10.9	697	10.5	489	10.5	208	10.4
55–59	20 184	4.3	264	4.0	185	4.0	79	4.0
60–64	7697	1.6	100	1.5	78	1.7	22	1.1
65–69	3214	0.7	49	0.7	38	0.8	11	0.6
≥70	1871	0.4	30	0.5	19	0.4	11	0.6

Discussion

Our results show some indications of increased breast cancer risks for all three sources of traffic noise at higher noise levels. However, the most compelling evidence for increased traffic-noise related risks was observed for ER- breast cancers, where the linear model indicated a 5% risk increase per 10 dB 24-hour aircraft noise, and the highest risk estimates were observed for exposures to 24-hour aircraft sound levels >55 dB and night-time aircraft sound levels >50 dB. Regarding the observed risks due to road and rail traffic noise, modest increased risk estimates were also observed in the noise exposure categories >70 dB.

In general, our findings corroborate the results reported by Sörensen et al (27) that ER- cancers appear to be more susceptible to environmental traffic noise exposure than ER+ cancers. Although the linear risks we observed for road and rail traffic noise exposure were lower than those reported for the Danish cohort, this may be due in part to the difference in exposure ranges considered. Sörensen et al (27) considered 42 dB to be the background noise level and set traffic noise beneath this level to 42 dB, while we used 40 dB as the background noise level and set lower traffic noise values to 35 dB. Differences in results may also be due to the fact that Sörensen et al were able to better adjust for potential confounding factors, such as parity and examined only postmenopausal breast cancer risks.

Table 3. Aircraft traffic noise exposure and breast cancer risk according to ER receptor status. [ER+ / ER- =estrogen receptor positive / negative; OR=odds ratio; CI=confidence interval.]

dB	OR [a]	95% CI	ER+		ER-	
			OR [a]	95% CI	OR [a]	95% CI
24-hour (LpAeq)						
<40	1.00	Reference	1.00	Reference	1.00	Reference
40–44	1.00	0.94–1.06	1.00	0.93–1.07	1.00	0.90–1.12
45–49	1.01	0.93–1.09	0.99	0.91–1.09	1.05	0.91–1.20
50–54	0.93	0.83–1.04	0.91	0.79–1.04	0.97	0.79–1.19
55–59	1.08	0.90–1.31	0.95	0.75–1.20	1.41	1.04–1.90
≥60	.	..	.	..	.	..
linear per 10 dB	1.002	0.957–1.050	0.982	0.929–1.038	1.049	0.966–1.140
Night (LpAeq, 22:00–06:00 hrs)						
<40	1.00	Reference	1.00	Reference	1.00	Reference
40–44	0.99	0.92–1.06	0.99	0.92–1.07	0.98	0.87–1.11
45–49	0.94	0.85–1.04	0.93	0.82–1.04	0.97	0.82–1.16
50–54	1.04	0.89–1.21	0.89	0.74–1.08	1.37	1.08–1.74
55–59	1.28	0.71–2.34	1.65	0.88–3.09	.	..
≥60	.	..	.	..	.	..
European night (LpAeq, 23:00–07:00 hrs)						
<40	1.00	Reference	1.00	Reference	1.00	Reference
40–44	1.03	0.96–1.10	1.05	0.96–1.14	0.98	0.86–1.12
45–49	0.92	0.83–1.02	0.90	0.79–1.01	0.99	0.83–1.19
50–54	1.05	0.90–1.24	0.92	0.75–1.13	1.36	1.05–1.77
55–59	1.51	0.89–2.57	1.69	0.93–3.08	1.08	0.35–3.36
≥60	.	..	.	..	.	..
Core night (LpAeq, 23:00–05:00 hrs)						
<40	1.00	Reference	1.00	Reference	1.00	Reference
40–44	1.00	0.94–1.08	1.01	0.93–1.10	1.00	0.88–1.13
45–49	0.99	0.89–1.09	0.96	0.85–1.09	1.04	0.87–1.25
50–54	0.95	0.78–1.15	0.83	0.65–1.06	1.21	0.89–1.65
55–59	2.98	1.31–6.78	2.10	0.67–6.64	5.16	1.63–16.30
≥60	.	..	.	..	.	..
Day (LpAeq, 06:00–22:00 hrs)						
<40	1.00	Reference	1.00	Reference	1.00	Reference
40–44	0.97	0.91–1.03	0.93	0.86–1.00	1.08	0.97–1.21
45–49	1.00	0.93–1.08	0.98	0.89–1.07	1.07	0.93–1.23
50–54	0.95	0.86–1.05	0.94	0.83–1.06	0.96	0.80–1.16
55–59	1.06	0.90–1.25	0.89	0.73–1.10	1.48	1.13–1.93
≥60	1.17	0.64–2.13	1.32	0.68–2.56	..	..

[a] OR reported only when ≥3 cases were observed; adjusted for age (third degree polynomial), hormone replacement therapy, education and occupation (if available), regional unemployment levels.

Study strengths and limitations

Using health insurance data allowed for the examination of traffic-noise related risks in a large study population principally unaffected by selection bias. Diagnosis records are generally accurate and not subject to observational bias since the insurance claims data are collected primarily for accounting purposes. Unfortunately, a major limitation of this study is the lack of information regarding potential confounders. Other than rudimentary indicators of social status (ie, occupation and education) which were often lacking, and limited information on the use of hormone replacement therapy, information on other potential confounding factors, such as parity, alcohol consumption, and working night-shifts, could not be obtained from the health claims data. Consequently, the

Table 4. Road traffic noise exposure and breast cancer risk according to ER receptor status. [ER+ / ER- =estrogen receptor positive / negative; OR=odds ratio; CI=confidence interval.]

dB	OR [a]	95% CI	ER+		ER-	
			OR [a]	95% CI	OR [a]	95% CI
24-hour (LpAeq)						
<40	1.00	Reference	1.00	Reference	1.00	Reference
40–44	0.99	0.90–1.08	0.98	0.88–1.09	1.01	0.86–1.19
45–49	0.96	0.88–1.05	0.93	0.83–1.03	1.05	0.89–1.23
50–54	0.97	0.89–1.07	0.95	0.85–1.07	1.02	0.86–1.21
55–59	0.98	0.89–1.09	0.95	0.84–1.07	1.07	0.89–1.29
60–64	0.96	0.86–1.08	0.94	0.82–1.08	1.01	0.82–1.24
65–69	0.93	0.81–1.06	0.92	0.79–1.07	0.95	0.74–1.21
≥70	1.07	0.87–1.32	1.06	0.82–1.35	1.12	0.77–1.63
linear per 10 dB	0.992	0.964–1.020	0.982	0.950–1.016	1.015	0.965–1.067
Night (LpAeq, 22:00–06:00 hrs)						
<40	1.00	Reference	1.00	Reference	1.00	Reference
40–44	1.00	0.93–1.06	0.98	0.90–1.06	1.04	0.92–1.17
45–49	1.02	0.95–1.10	0.99	0.91–1.08	1.11	0.97–1.26
50–54	0.95	0.87–1.03	0.95	0.86–1.05	0.93	0.80–1.09
55–59	1.00	0.91–1.10	0.97	0.87–1.09	1.08	0.91–1.28
60–64	0.97	0.84–1.12	0.95	0.80–1.13	1.02	0.78–1.33
65–69	1.23	0.92–1.63	1.18	0.84–1.66	1.34	0.81–2.20
≥70	.	..	.	..	.	..
Day (LpAeq, 06:00–22:00 hrs)						
<40	1.00	Reference	1.00	Reference	1.00	Reference
40–44	0.98	0.89–1.09	0.99	0.88–1.12	0.97	0.80–1.17
45–49	0.95	0.86–1.05	0.94	0.83–1.05	0.99	0.83–1.19
50–54	1.00	0.90–1.11	0.97	0.86–1.09	1.08	0.90–1.30
55–59	0.96	0.86–1.07	0.93	0.81–1.06	1.05	0.86–1.28
60–64	0.95	0.84–1.07	0.95	0.83–1.10	0.95	0.76–1.19
65–69	1.02	0.89–1.16	0.99	0.85–1.15	1.09	0.87–1.38
≥70	0.93	0.78–1.12	0.90	0.73–1.11	1.02	0.74–1.40

[a] OR reported only when 3 or more cases were observed; adjusted for age (third degree polynomial), hormone replacement therapy, education and occupation (if available), regional unemployment levels.

Table 5. Rail traffic noise exposure and breast cancer risk according to ER receptor status. [ER+ / ER- =estrogen receptor positive / negative; OR=odds ratio; CI=confidence interval.]

dB	OR [a]	95% CI	ER+		ER-	
			OR [a]	95% CI	OR [a]	95% CI
24-hour (LpAeq,24h)						
<40	1.00	Reference	1.00	Reference	1.00	Reference
40–44	0.99	0.91–1.07	0.98	0.89–1.07	1.01	0.88–1.16
45–49	1.02	0.95–1.09	1.02	0.93–1.11	1.02	0.89–1.16
50–54	0.97	0.89–1.05	0.96	0.87–1.06	0.97	0.84–1.13
55–59	0.93	0.82–1.06	0.93	0.80–1.08	0.95	0.75–1.19
60–64	0.94	0.77–1.15	1.05	0.84–1.32	0.70	0.46–1.06
65–69	1.13	0.85–1.51	1.25	0.91–1.73	0.85	0.47–1.55
≥70	1.15	0.80–1.65	1.03	0.66–1.63	1.43	0.79–2.59
linear per 10 dB	0.992	0.961–1.023	0.994	0.958–1.031	0.986	0.932–1.044
Night (LpAeq, 22:00–06:00 hrs)						
<40	1.00	Reference	1.00	Reference	1.00	Reference
40–44	0.99	0.91–1.07	0.96	0.87–1.06	1.05	0.91–1.21
45–49	1.02	0.95–1.10	1.02	0.94–1.12	1.02	0.89–1.17
50–54	0.98	0.91–1.07	0.97	0.87–1.07	1.03	0.89–1.19
55–59	0.94	0.84–1.06	0.95	0.83–1.09	0.93	0.74–1.16
60–64	0.90	0.73–1.10	0.95	0.75–1.20	0.77	0.51–1.14
65–69	1.06	0.81–1.40	1.13	0.82–1.56	0.90	0.52–1.55
≥70	1.21	0.87–1.67	1.22	0.83–1.78	1.19	0.66–2.16
Day (LpAeq, 06:00–22:00 hrs)						
<40	1.00	Reference	1.00	Reference	1.00	Reference
40–44	0.95	0.88–1.02	0.94	0.86–1.03	0.96	0.84–1.09
45–49	1.01	0.94–1.08	1.01	0.93–1.10	0.99	0.87–1.13
50–54	0.96	0.88–1.04	0.95	0.86–1.05	0.98	0.84–1.14
55–59	0.89	0.78–1.01	0.87	0.75–1.02	0.92	0.72–1.17
60–64	1.00	0.82–1.23	1.12	0.89–1.40	0.74	0.48–1.13
65–69	1.12	0.84–1.49	1.19	0.86–1.66	0.94	0.53–1.66
≥70	1.15	0.78–1.68	0.96	0.59–1.58	1.58	0.87–2.87

[a] Adjusted for age (third degree polynomial), hormone replacement therapy, education and occupation (if available), regional unemployment levels.

estimated risks may be subject to residual confounding. If, for example, alcohol consumption is increased in residential areas with higher traffic noise levels as a means of coping with the noise annoyance, any increased alcohol-related risk of breast cancer could appear to be due to increased traffic noise exposure. Also, despite the large study population, some of the study estimates may still be underpowered since fewer people were exposed to the highest noise levels.

Another critical limitation was the lack of individual socioeconomic information for more than two-thirds of the study population. Breast cancer incidence increases with socioeconomic status (possibly due to reproductive factors associated with socioeconomic status such as age at first birth and parity) (33), and increasing socioeconomic status often provides increasing resources to select residential areas less exposed to traffic noise. This makes socioeconomic status an important potential confounder, as well as a surrogate for socioeconomic-related risk factors. Interestingly, the results for ER+ cancers remained largely unchanged and risk estimates increased for ER- cancers when only women with available socioeconomic information were examined (supplementary data). These results do seem to indicate that residual confounding is still present in the adjusted estimates and that socioeconomic status may be a more relevant confounder for ER- cancers.

Although we had no direct information regarding the tumor receptor status, ancillary treatment should be a good indicator of ER status, and the prevalence of ER status from our derived ER status seems plausible (ER+ 69.9% / ER- 30.1%) since the proportion of ER+ tumors identified fell within the range reported for immunohistochemically assayed ER+ tumors (54%–76%) described in a systematic review of etiological hormone receptor status studies (34). However, the prevalence of ER+ cancers was lower than that reported by Sörensen et al (27) indicating a possible underreporting of ER+ cancers. This misclassification might be due in part by women first diagnosed towards the end of the observation period who had not yet received any ancillary treatment. Using the absence of ancillary treatment prescriptions as the definition for ER- cancers might also have led to over reporting of ER- cancers by including tumors of undetermined or borderline receptor status in this category. We expect that improving the accuracy of the ER status classification would provide clearer differential results.

The address-specific traffic noise estimations were matched to the addresses without knowledge of diagnoses and should therefore provide an unbiased estimate of traffic noise exposure. However, non-differential misclassification bias could not be avoided with this retrospective estimation of exposure. Information regarding if the place of residence had changed since 2005 was only available from one insurance provider and data regarding the amount of time spent in the home and noise levels at work were unattainable. This non-differential misclassification generally causes a bias towards the null, which may lead to an underestimation of actual risks. In order to examine if relocating might have influenced the overall results, we examined the subgroup of the population where noise could be matched with the yearly address records. In this subgroup, slightly more than 80% resided at the same residence for >5 years. A sensitivity analysis examining the main results for persons living at the same address for >5 years (supplementary data) showed increased risk estimates for all three types of traffic noise exposures and tended to indicate increased risks for ER- cancers and decreased risks for ER+ cancers. This was most evident for road traffic exposures. However, no dose–response relationship was observed.

Another drawback of our study was the lack of long-term exposure data estimates. Since breast cancer has an estimated latency period of approximately 16 years (35), an analysis of exposure in the 10–20 years before disease incidence would be necessary to provide compelling evidence of causality. As it is, the increased risks observed in our analysis might indicate that exposure to traffic noise may be promoting existing cancers and not acting as a causal factor. An improved long-term traffic noise exposure assessment and a comprehensive adjustment of potential confounders are necessary to determine the actual role of traffic noise exposure on breast cancer pathogenesis.

Possible biological mechanisms

The fact that traffic noise exposure appears to have more of an influence on the risk of ER- than ER+ cancers substantiates the hypothesis that the pathogenesis of these cancers differ (34, 36). However, how the biological mechanisms of ER- breast cancers are influenced by traffic noise exposure remains to be determined. One possibility may be that the stronger influence of estrogen-increasing risk factors on ER+ tumors may overshadow any weaker traffic noise-related risk contributions. Therefore, sleep arousals and diminished sleep quality caused by increased traffic noise (22) and the resulting suppression of immunological processes occurring during sleep (21) could have a greater influence on ER- cancers. A link between ER- cancers and sleep duration is supported by the work of Qian and colleagues (37), who examined the effect of sleep duration on the risk of breast cancers according to hormone receptor status using data from the prospective Breast Cancer Detection Demonstration Project. Interestingly, Qian et al found reduced sleep duration (<6 hours versus 8–≤9 hours per weekday) increased the relative risk (RR) of ER- breast cancers (RR 2.12, 95% CI 1.18–3.82) and reduced the risk of ER+ cancers (RR 0.53, 95% CI 0.33–0.86). However, other epidemiological studies found no clear association between sleep duration and ER status (18, 20).

Reduced melatonin production due to shorter sleep duration and light exposure at night is often proposed as the possible pathway for increasing breast cancer. However, reduced melatonin levels are typically thought to increase the risks for ER+ cancers, and noise-induced arousals might need to correspond with increased ambient light exposure (ie, turning on a light or looking at an electronic device) to reduce melatonin levels. On the other hand, a controlled experiment with dim lighting exposure found exposure to 12 hours of dim light (0.2 lux) at night was enough to reduce melatonin levels and increase tamoxifen resistance of xenografted ERα + tumors in rats (3). Urban areas with more aircraft and road traffic noise are likely to be more illuminated, potentially confounding the relationship between environmental noise exposure and breast cancer incidence.

The fact that we observed increased breast cancer risks for aircraft noise at noise lower levels than road or rail noise is admittedly paradoxical since research in a laboratory setting found road noise impacted sleep patterns more than aircraft or rail noise, while aircraft and railway noise disturbed subjective assessments of sleep (eg, morning sleepiness) more (38). Therefore, our results may indicate that stress due to noise annoyance could be involved in the promotion of cancers through the activation the HPA axis and the resulting increase in cortisol levels. The international Hypertension and Exposure to Noise near Airports (HYENA) study found saliva cortisol levels increasing with aircraft sound levels among women (39), and there are indications that stressful life events may increase the risk for breast cancer, although a link between chronic stress (ie, job strain, everyday stress) is less evident (24). Clearly, further research is needed to establish the underlying biological mechanisms between traffic noise exposure and breast cancers.

In conclusion, we found exposure to higher levels of aircraft traffic noise to be associated with increased risks of ER- breast cancers, while associations between road and rail traffic noise exposure and breast cancer were less apparent. Although the results may be subject to residual confounding, they do indicate increased aircraft noise may be an etiologic or promoting factor

for estrogen negative breast cancers. Further research is needed to corroborate these findings and determine the underlying etiology in order to establish effective preventative measures.

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References

1. Stewart BW, World Health Organization. World Cancer Report 2014. Lyon: International Agency for Research in Cancer; 2014.
2. Bray F, McCarron P, Parkin DM. The changing global patterns of female breast cancer incidence and mortality. Breast Cancer Res. 2004;6(6):229–39. https://doi.org/10.1186/bcr932.
3. Dauchy RT, Xiang S, Mao L, Brimer S, Wren MA, Yuan L, et al. Circadian and melatonin disruption by exposure to light at night drives intrinsic resistance to tamoxifen therapy in breast cancer. Cancer Res. 2014 Aug 1;74(15):4099–110. https://doi.org/10.1158/0008-5472.CAN-13-3156.
4. Sanchez-Barcelo EJ, Cos S, Fernandez R, Mediavilla MD. Melatonin and mammary cancer: a short review. Endocr Relat Cancer. 2003 Jun;10(2):153–9. https://doi.org/10.1677/erc.0.0100153.
5. IARC WGotEoCRtH. Painting, firefighting, and shiftwork. IARC Monogr Eval Carcinog Risks Hum. 2010;98:9–764.
6. Erren TC, Pape HG, Reiter RJ, Piekarski C. Chronodisruption and cancer. Naturwissenschaften. 2008 May;95(5):367–82. https://doi.org/10.1007/s00114-007-0335-y.
7. He C, Anand ST, Ebell MH, Vena JE, Robb SW. Circadian disrupting exposures and breast cancer risk: a meta-analysis. Int Arch Occup Environ Health. 2015 Jul;88(5):533–47. https://doi.org/10.1007/s00420-014-0986-x.
8. Jia Y, Lu Y, Wu K, Lin Q, Shen W, Zhu M, et al. Does night work increase the risk of breast cancer? A systematic review and meta-analysis of epidemiological studies. Cancer Epidemiol. 2013 Jun;37(3):197–206. https://doi.org/10.1016/j.canep.2013.01.005.
9. Kamdar BB, Tergas AI, Mateen FJ, Bhayani NH, Oh J. Night-shift work and risk of breast cancer: a systematic review and meta-analysis. Breast Cancer Res Treat. 2013 Feb;138(1):291–301. https://doi.org/10.1007/s10549-013-2433-1.
10. Lin X, Chen W, Wei F, Ying M, Wei W, Xie X. Night-shift work increases morbidity of breast cancer and all-cause mortality: a meta-analysis of 16 prospective cohort studies. Sleep Med. 2015 Nov;16(11):1381–7. https://doi.org/10.1016/j.sleep.2015.02.543.
11. Megdal SP, Kroenke CH, Laden F, Pukkala E, Schernhammer ES. Night work and breast cancer risk: a systematic review and meta-analysis. Eur J Cancer. 2005 Sep;41(13):2023–32. https://doi.org/10.1016/j.ejca.2005.05.010.
12. Wang F, Yeung KL, Chan WC, Kwok CC, Leung SL, Wu C, et al. A meta-analysis on dose-response relationship between night shift work and the risk of breast cancer. Ann Oncol. 2013 Nov;24(11):2724–32. https://doi.org/10.1093/annonc/mdt283.
13. Yang WS, Deng Q, Fan WY, Wang WY, Wang X. Light exposure at night, sleep duration, melatonin, and breast cancer: a dose-response analysis of observational studies. Eur J Cancer Prev. 2014 Jul;23(4):269–76. https://doi.org/10.1097/CEJ.0000000000000030.
14. Ijaz S, Verbeek J, Seidler A, Lindbohm ML, Ojajarvi A, Orsini N, et al. Night-shift work and breast cancer--a systematic review and meta-analysis. Scand J Work Environ Health. 2013 Sep 1;39(5):431–47. https://doi.org/10.5271/sjweh.3371.
15. Kakizaki M, Kuriyama S, Sone T, Ohmori-Matsuda K, Hozawa A, Nakaya N, et al. Sleep duration and the risk of breast cancer: the Ohsaki Cohort Study. Br J Cancer. 2008 Nov 4;99(9):1502–5. https://doi.org/10.1038/sj.bjc.6604684.
16. Verkasalo PK, Lillberg K, Stevens RG, Hublin C, Partinen M, Koskenvuo M, et al. Sleep duration and breast cancer: a prospective cohort study. Cancer Res. 2005 Oct 15;65(20):9595–600. https://doi.org/10.1158/0008-5472.CAN-05-2138.
17. Pinheiro SP, Schernhammer ES, Tworoger SS, Michels KB. A prospective study on habitual duration of sleep and incidence of breast cancer in a large cohort of women. Cancer Res. 2006 May 15;66(10):5521–5. https://doi.org/10.1158/0008-5472.CAN-05-4652.
18. Girschik J, Heyworth J, Fritschi L. Self-reported sleep duration, sleep quality, and breast cancer risk in a population-based case-control study. Am J Epidemiol. 2013 Feb 15;177(4):316–27. https://doi.org/10.1093/aje/kws422.
19. McElroy JA, Newcomb PA, Titus-Ernstoff L, Trentham-Dietz A, Hampton JM, Egan KM. Duration of sleep and breast cancer risk in a large population-based case-control study. J Sleep Res. 2006 Sep;15(3):241–9. https://doi.org/10.1111/j.1365-2869.2006.00523.x.
20. Vogtmann E, Levitan EB, Hale L, Shikany JM, Shah NA, Endeshaw Y, et al. Association between sleep and breast cancer incidence among postmenopausal women in the Women's Health Initiative. Sleep. 2013 Oct;36(10):1437–44. https://doi.org/10.5665/sleep.3032.

21. Besedovsky L, Lange T, Born J. Sleep and immune function. Pflugers Arch. 2012 Jan;463(1):121–37. https://doi.org/10.1007/s00424-011-1044-0.

22. Hume KI, Brink M, Basner M. Effects of environmental noise on sleep. Noise Health. 2012 Nov-Dec;14(61):297–302. https://doi.org/10.4103/1463-1741.104897.

23. Prasher D. Is there evidence that environmental noise is immunotoxic? Noise and Health. 2009;11(44):151. https://doi.org/10.4103/1463-1741.53361.

24. Antonova L, Aronson K, Mueller CR. Stress and breast cancer: from epidemiology to molecular biology. Breast Cancer Res. 2011;13(2):208. https://doi.org/10.1186/bcr2836.

25. Greiser E, Greiser C. Bösartige Neubildungen und Fluglärm Abschlussbericht über eine Fall-Kontroll-Studie im Umkreis des Flughafens Köln-Bonn (Malignant neoplasms and aircraft noise- a report on a case-control study in the vicinity of the Cologne-Bonn Airport). Musweiler: Epi.Consult GmbH, 2009. Available from: http://www.fluglaermhalleost.de/untersites/download/Fluglaerm_und_Malignome_Greiser.pdf. (Accessed: 13 March 2017).

26. Greiser E, Greiser C. Umgebungslärm und Gesundheit am Beispiel Bremen Forschungskennzahl 3710 61 170 (UBA-FB 002168) (Environmental noise and health in Bremen, Research Identification Number 3710 61 170 (UBA-FB 002168)). Umweltbundesamt 2016 Decemeber 2015. Report No.: Contract No.: 101/2015. Available from: https://www.umweltbundesamt.de/sites/default/files/medien/378/publikationen/texte_105_2015_umgebungslaerm_und_gesundheit_am_beispiel_bremen.pdf. (Accessed: 13 March 2017).

27. Sörensen M, Ketzel M, Overvad K, Tjonneland A, Raaschou-Nielsen O. Exposure to road traffic and railway noise and postmenopausal breast cancer: A cohort study. Int J Cancer. 2014 Jun 1;134(11):2691–8. https://doi.org/10.1002/ijc.28592.

28. Visser O, van Wijnen JH, van Leeuwen FE. Incidence of cancer in the area around Amsterdam Airport Schiphol in 1988-2003: a population-based ecological study. BMC Public Health. 2005;5:127. https://doi.org/10.1186/1471-2458-5-127.

29. Braunstein & Berndt GmbH. SoundPLAN. 7.3 ed. Backnang, Germany; 2013.

30. Möhler U, Liepert M, Mühlbacher M, Klatte M, Vogelsang B, Thomann G. The acoustic basis of the NORAH field studies. 45th International Congress on Noise Control Engineering (INTER-NOISE); Hamburg, Germany; 2016.

31. Blossfeld H-P. Bildungsexpansion und Berufschancen: empirische Analysen zur Lage der Berufsanfänger in der Bundesrepublik (Educational Expansions and Career Opportunities: Empirical Analysis of the Situation of Beginners in the Federal Republic of Germany): Campus; 1985.

32. StataCorp. Stata Statistical Software. College Station, TX: StataCorp LP; 2015.

33. Lundqvist A, Andersson E, Ahlberg I, Nilbert M, Gerdtham U. Socioeconomic inequalities in breast cancer incidence and mortality in Europe-a systematic review and meta-analysis. Eur J Public Health. 2016 Oct;26(5):804–13. https://doi.org/10.1093/eurpub/ckw070.

34. Althuis MD, Fergenbaum JH, Garcia-Closas M, Brinton LA, Madigan MP, Sherman ME. Etiology of hormone receptor-defined breast cancer: a systematic review of the literature. Cancer Epidemiol Biomarkers Prev. 2004 Oct;13(10):1558–68.

35. Nadler DL, Zurbenko IG. Estimating Cancer Latency Times Using a Weibull Model. Advances in Epidemiology. 2014;2014:8.

36. Chen WY, Colditz GA. Risk factors and hormone-receptor status: epidemiology, risk-prediction models and treatment implications for breast cancer. Nat Clin Pract Oncol. 2007 Jul;4(7):415–23. https://doi.org/10.1038/ncponc0851.

37. Qian X, Brinton LA, Schairer C, Matthews CE. Sleep duration and breast cancer risk in the Breast Cancer Detection Demonstration Project follow-up cohort. Br J Cancer. 2015 Feb 3;112(3):567–71. https://doi.org/10.1038/bjc.2014.600.

38. Basner M, Muller U, Elmenhorst EM. Single and combined effects of air, road, and rail traffic noise on sleep and recuperation. Sleep. 2011 Jan;34(1):11–23. https://doi.org/10.1093/sleep/34.1.11.

39. Selander J, Bluhm G, Theorell T, Pershagen G, Babisch W, Seiffert I, et al. Saliva cortisol and exposure to aircraft noise in six European countries. Environ Health Perspect. 2009 Nov;117(11):1713–7. https://doi.org/10.1289/ehp.0900933.

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