Residential traffic noise exposure and colorectal cancer incidence – a cohort study

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ABSTRACT

Traffic noise has become an increasing public health concern, associated with pervasive negative health effects, most likely through pathways of sleep disruption and stress. Sleep disruption and stress have both been associated with colorectal cancer (CRC). This study investigated the association between residential traffic noise and CRC incidence. Traffic noise was calculated for all residential addresses from 1987-2012 for 51,283 Danes. We used Cox Proportional Hazard Models to calculate crude and adjusted Hazard Rate Ratios (HRR) for the association between residential traffic noise 5 and 10 years before diagnosis, and incidence of CRC, and sub-types (rectal, proximal colon, distal colon). During follow-up, 1,134 CRCs developed (737 colon, 397 rectal). We found no association between road traffic noise and rectal cancer. We observed an association with distal colon cancer: HRR 1.18, 95% CI 1.00-1.40, but not proximal colon cancer: 0.99 (0.83-1.18), per 10 dB, 10 years preceding diagnosis. There was no association between railway noise and CRC, or any subtype. The present study suggested that long-term exposure to residential road traffic noise might increase the risk for distal colon cancer.

BACKGROUND

Traffic noise has become an increasing public health concern, as mounting evidence has related it to several clinical outcomes, including cardiovascular disease [1, 2], breast cancer [3], and non-Hodgkin lymphoma [4]. Publication of the World Health Organization report on night noise underscored the magnitude of the problem, and stressed specifically the detrimental consequences of night-time traffic noise [5], which has been associated with pervasive negative health effects; most likely by hampering sleep duration and quality [5-7].

A recent meta-analysis on sleep disturbances (including sleep duration, napping, and sleep quality) and cancer found sleep disturbances to be associated with a higher risk of colorectal cancer [8]. This is supported by a colonoscopy-based study, which found that individuals

sleeping less than 6 hours per night had a higher risk of colorectal adenomas, compared to those sleeping 7 or more hours/night [9]. Disrupted sleep may entail a suppression of melatonin through longer light exposure, and melatonin possesses anti-carcinogenic properties, including effects on antioxidant defense, immune response, and DNA repair [10-13]. In relation to colorectal cancer, melatonin has been found to exhibit anti-proliferative effects on intestinal cancer cells and on colon carcinogenesis in animal studies [14-16]. In human studies, colorectal cancer patients have been found to exhibit lower plasma melatonin levels compared to healthy controls [17]. Taken together, this suggests a role for sleep disturbances in the development of colorectal cancer.

Traffic noise may also function as an environmental stressor, and provoke a typical stress response by activating the hypothalamus-pituitary-adrenal (HPA) axis [18]. The effects of this stress-response have been demonstrated in a range of studies showing increased levels of cortisol, cathecolamines [19, 20], and oxidative stress, [21, 22], following noise exposure. The evidence for a role of reactive oxygen species in the carcinogenic process in general, and in colorectal carcinogenesis specifically, is comprehensive [23, 24]. Excessive production of reactive oxygen species may also entail inflammation [24], which is considered a key player in colorectal carcinogenesis [25]. Furthermore, repeated activation of the stress-response affects the circadian rhythm [26], which is extensively involved in carcinogenesis in general, as the circadian clock regulates key aspects of cell growth and survival [27], as well as in colorectal cancer particularly, where molecular and genetic data have shown that the circadian system influence the Wnt/β-catenin pathway, which is involved in the molecular biology of colorectal cancer initiation [28].

Finally, several studies have suggested an association between traffic noise exposure and obesity [29, 30] and diabetes [31]; two strong risk-factors for colorectal cancer [32, 33].

The aim of our study was to investigate the association between residential exposure to road and railway traffic noise and risk of colorectal cancer.

METHODS AND MATERIAL

Study population

The study is based on the prospective Diet, Cancer and Health (DCH) cohort, which has been described in detail previously [34]. Briefly, 160,725 Danes were invited to participate from 1993-97. Inclusion criteria were 50-64 years of age, residence in the greater Copenhagen or Aarhus area, and no previous cancer diagnosis in the Danish Cancer Registry; 57,053 participants accepted the invitation and were included into the study. The Diet, Cancer and Health study was approved by the local ethical committees of Copenhagen and Frederiksberg Municipalities. All participants provided written informed consent, and the study was conducted according to the Helsinki Declaration.

Outcome

Information regarding colorectal cancers diagnosed between baseline (July 1st, 1997) and end of follow-up (February 10th, 2012) were identified by linking the unique Danish personal identification number of each cohort member to the nationwide Danish Cancer Registry (International Classification of Diseases (ICD) 10: C180-189, C19, C20) [35]. Information regarding vital status was collected by linkage to the Danish Civil Registration System [36]. In analyses of sub-sites of colorectal cancer, we defined rectal cancer as ICD-10 C20, proximal

colon cancer as ICD-10 C180-C185, and distal colon cancer as ICD10 C186-C187 or C19. As information on sub-site was not available for all cases, we included only 1,076 persons in these analyses (328 proximal colon, 351 distal colon, and 397 rectal cancers).

Exposure assessment

The assessment of traffic noise exposure for the present cohort has been described in details elsewhere [31]. Briefly, residential address histories were collected for all cohort members between July 1st, 1987 and February 10th, 2012, using the Danish Civil Registration System [36]. Road traffic noise exposure was calculated using SoundPLAN, which implements the joint Nordic prediction method for road traffic noise [37]. By use of this method, noise levels can be calculated for each address when a series of traffic and topographic parameters are known: points for noise estimation (geographical coordinate and height (floor) for each residential address), road links (information on annual average daily traffic, vehicle distribution (light/heavy), travel speed, and road type), and building polygons for all Danish buildings provided by the Danish Geodata Agency. We obtained traffic counts for all roads with more than 1,000 vehicles per day from a national road and traffic database [38]. Road traffic noise exposure was calculated for the years 1990, 1995, 2000, 2005 and 2010. Traffic noise for the year 1990 was used as a proxy for the period from July 1st 1987 – June 30th 1992, they year 1995 was used as a proxy for the period from July 1st 1992 to June 30th 1997, and so forth.

No information was available on noise barriers or road surfaces. Road traffic noise was calculated as the equivalent continuous A-weighted sound pressure level (L_{Aeq}) at the most exposed facade of the dwelling at each address for the day (L_d; 07:00–19:00 h), evening (L_e; 19:00–22:00 h) and night (L_n; 22:00–07:00 h), and was expressed as L_{den} (den = day, evening, night). A penalty of 5 and 10 dB was applied to evening and night, respectively.

Railway noise exposure was calculated for all present and historical addresses using SoundPLAN, implementing a Nordic calculation method for predicting noise propagation for railway traffic noise (NORD2000). The input variables for the noise model were: point for noise estimation (geographical coordinate and height), railway links (information on annual average daily train lengths, train types, travel speed) and building polygons for all Danish buildings. All noise barriers along the railway were included in the model. Railway traffic noise was expressed as L_{den} at the most exposed facade of the dwelling.

For the assessment of both road and railway traffic noise the terrain was assumed flat, a reasonable assumption in Denmark. Urban areas, roads, and areas with water were assumed to be hard surfaces, whereas all other areas were assumed acoustically porous.

Covariates

At baseline of the Diet, Cancer and Health study, all participants filled in a food frequency questionnaire and a lifestyle questionnaire, and anthropometric measures were collected by trained personnel. The data on diet and lifestyle factors hail from this questionnaire [34]. Information on socioeconomic variables, e.g. highest attained education, income and marital status at baseline was available from Statistics Denmark. Selection of covariates was done a priori, based on a review of existing literature, biological plausibility, and availability of data.

NO_x exposure was calculated with the Danish AirGIS dispersion modeling system (http://envs.au.dk/en/knowledge/air/models/airgis/) for the same years as exposure to traffic noise, for all addresses where each individual had lived, as previously described in details [39].

Statistical Methods

Cox Proportional Hazards Models, estimating hazard ratios (HR) and 95% confidence intervals (CI) were used to investigate the association between residential traffic noise exposure and colorectal cancer incidence. Age was used as the underlying time scale to ensure comparison of individuals at the same age. We used left truncation at age at July 1st, 1997 to ensure at least 10 years of exposure history for all participants, and right censoring at age of colorectal cancer diagnosis, any other cancer, death, emigration, or February 10th, 2012, whichever came first.

Exposure to road traffic noise was modelled as time-weighted averages for periods of 5 and 10 years preceding colorectal cancer diagnosis (taking all present and historical addresses in that period into account). These exposure measures were entered as time-dependent variables into the statistical model; thus exposure was estimated for all cohort members who were at risk of diagnosis at exactly the same age as each case at diagnosis. Residential road traffic noise was investigated linearly (per 10 dB) and categorically in 5 exposure groups, chosen to ensure an adequate number of cases in the reference group: < 52 dB, 52-< 57 dB, 57-<62 dB, 62-<67 dB, > 67 dB.

The assumption of linearity of road traffic noise and continuous covariates was evaluated by model control; investigating linearity. This was done by graphical evaluation using linear spline models with boundaries at the three quartiles among cases and by formal testing with linear spline models. No deviations from linearity were detected (all $p > 0.05$). The proportional hazards assumption of the Cox Models was tested by graphical inspection of the survival function versus time and the log(-log(survival) versus log(time), by using the proc lifetest procedure, which confirmed the assumption.

Estimates were adjusted for age (by design), sex (Model 1), and additionally for railway noise (at diagnosis, 0-20, >20-50, >50 dB), smoking status (never, former, current), smoking duration (linear, years), smoking intensity (linear, g/day), alcohol intake (linear, g/day), abstainers (yes, no), recreational physical activity (yes, no), education (basic, vocational, higher), whole grain cereal (linear, g/day), red meat (linear, g/day),and marital status (married/unmarried), income (household income after taxation and interest per person, adjusted for number of persons in the household and divided into tertiles based on the Danish background population) and municipal-level population density (in quartiles) at baseline.

All tests were based on the likelihood ratio test statistic. Two-sided 95% CI were calculated based on Wald's test of the Cox regression parameter, i.e. on the log ratio scale. P-values < 0.05 were considered statistically significant. The procedure PHREG in SAS, version 9.3 on a windows platform was used for all statistical analyses (SAS Institute Inc., Cary, NC).

RESULTS

Of the total cohort of 57,053 persons, we excluded 574 with a cancer diagnosis before baseline, 331 who were diagnosed with cancer, died, or emigrated before July 1st 1997, 3,071 with lacking information on exposure variables, and 1,794 with lacking information on covariates. This left a study population of 51,283 persons. Among these, 1,134 primary colorectal cancers (737 colon cancers, 397 rectal cancers) were diagnosed during a median follow-up of 14.6 years.

Distribution of the variables included in the analyses are presented in **Table 1**, for the entire cohort, for incident colorectal cancer cases, and for participants with above/below median road traffic noise exposure (57.1 dB). Cases included a higher proportion of males compared to the entire cohort (56.4 vs. 47.1 %). They were more likely to be current or former smokers and to live in municipalities with high population density, they had a higher intake of alcohol and red meat, and a higher BMI. Furthermore, they were older at baseline (median 59.7 vs. 57.6 years), less likely to engage in recreational physical activity and be in the 3rd income quartile, and they had a somewhat lower whole grain intake. Those with low road traffic exposure were more likely to be male than those with high exposure. They were less likely to have ever smoked and to live in densely populated municipalities, and more likely to participate in physical activity, be married, have a higher education, and be in the 3rd income tertile. They were also less exposed to railroad noise and air pollution. There was a very high correlation between L_{den}, L_d, L_e, and L_n road; with all Rs > 0.99.

Table 1: Characteristics of the Danish Diet, Cancer and Health cohort, colorectal cancer cases in the cohort, and participants categorized according to traffic noise exposure at enrollment (above/below median).

	Entire cohort **N = 51,283**	**Colorectal cancer cases** **N = 1,134**	**Exposure at enrollment < 57.1 dB** **N = 25,639**	**Exposure at enrollment ≥57.1 dB** **N = 25,644**
Male, %	47.1	56.4	48.5	45.6
Age	57.6 (51.8-65.6)	59.7 (52.3-66.2)	57.3 (51.6-65.4)	57.9 (52.0-65.8)
Smoking status, %				
Never	36.1	29.3	38.4	33.8
Former	27.5	31.0	28.6	26.4
Current	36.4	39.7	33.0	39.8
Smoking duration, years[a]	37.0 (22.0-48.0)	38.0 (23.0-48.0)	37.0 (22.0-48.0)	37.0 (23.0-48.0)
Smoking intensity, g/day	15.0 (5.0-32.0)	15.9 (5.7-35.4)	15.0 (4.8-31.8)	15.1 (5.2-32.2)
Alcohol, g/day[b]	13.2 (1.1-64.4)	15.1 (1.2-71.3)	13.2 (1.2-61.7)	13.2 (1.0-67.2)
Abstainers, %	2.3	2.8	1.9	2.6
BMI, kg/m^2	25.5 (20.4-33.4)	26.3 (20.4-34.2)	25.4 (20.5-33.0)	25.6 (20.4-33.7)
Missing, %	0.07	0.3	0.04	0.1
Recreational physical activity, %	53.8	48.5	56.7	50.9
Red meat consumption, g/day	78.2 (32.0-164.5)	83.9 (33.5-169.8)	79.3 (33.5-163.6)	77.0 (30.4-165.5)
Whole grain cereal consumption, g/day	128.1 (42.3-267.1)	123.0 (43.9-257.9)	131.6 (45.8-268.3)	124.9 (38.5-265.8)
Education, %				

Basic	27.9	28.2	25.1	30.8
Vocational	45.6	45.4	45.6	45.6
Higher	26.4	26.4	29.3	23.6
Income, %				
1st tertile	19.7	18.8	15.3	24.1
2nd tertile	30.7	33.0	28.8	32.7
3rd tertile	49.6	45.2	55.9	43.2
Municipal population density, %				
1st quartile	2.7	1.6	3.9	1.4
2nd quartile	48.7	45.8	62.4	35.0
3rd quartile	42.3	45.9	29.1	55.4
4th quartile	6.3	6.8	4.6	8.1
Married, %	71.5	71.3	77.7	65.3
Road traffic noise, dB	57.1 (49.0-70.7)	57.7 (49.3-70.8)	53.0 (47.7-56.6)	62.7 (57.6-72.8)
Railroad noise, % exposed	19.2	19.9	17.9	20.6
Air pollution, NO_x ($\mu g/m^3$)	19.2 (14.4-81.0)	19.2 (14.4-82.7)	16.9 (14.4-25.8)	25.8 (16.0-107.5)
[a] Among smokers [b] Among those drinking alcohol Median and 5-95 percentile, unless otherwise stated				

The present study design allowed estimation of associations across different exposure periods for road traffic noise. **Table 2** presents the association between time-weighted average exposure 5 and 10 years preceding diagnosis, and colorectal cancer incidence. In the continuous analyses, we found a non-significant higher risk of colorectal cancer: HR 1.05 (0.96-1.15) per 10 dB, 10 years before diagnosis. When examining residential road traffic noise categorically in five exposure groups, we observed a positive dose-response association over the first four exposure groups, which decreased for the highest exposure group.

Table 2: Crude and adjusted associations between residential road traffic noise exposure (L_{den}) and colorectal cancer incidence. Linear estimates per 10 dB, and categorical estimates.

	Cases	***Model 1[a]*** **HR (95% CI)**	***Model 2[b]*** **HR (95% CI)**
Average L_{den} 5 years before diagnosis			
Linear estimate	1134	1.07 (0.98-1.16)	1.05 (0.96-1.15)
Categorical estimate			
< 52 dB	152	1.00 (ref.)	1.00 (ref.)
52-57 dB	314	1.10 (0.91-1.34)	1.11 (0.91-1.35)
57-62 dB	318	1.20 (0.99-1.47)	1.20 (0.98-1.48)

62-67 dB	207	1.24 (1.00-1.53)	1.23 (0.99-1.53)
>67 dB	143	1.14 (0.91-1.43)	1.13 (0.89-1.43)
p for trend		0.16	0.28
Average L_{den} 10 years before diagnosis			
Linear estimate	1134	1.07 (0.98-1.16)	1.05 (0.96-1.15)
Categorical estimate			
< 52 dB	150	1.00 (ref.)	1.00 (ref.)
52-57 dB	323	1.12 (0.92-1.36)	1.12 (0.92-1.37)
57-62 dB	313	1.19 (0.97-1.45)	1.18 (0.96-1.45)
62-67 dB	213	1.29 (1.05-1.59)	1.27 (1.02-1.58)
>67 dB	135	1.11 (0.88-1.40)	1.10 (0.86-1.40)
p for trend		0.16	0.30

[a] Adjusted for age (by design), and sex

[b] Adjusted as model 1, and for train noise (0-20, >20-50, >50 dB), smoking (never, former, current), smoking duration (linear, years), smoking intensity (linear, g/day), alcohol intake (linear, g/day), abstainers (yes, no), recreational physical activity (yes, no), education (basic, vocational, higher), red meat (linear, g/day), wholegrain cereal intake (linear, g/day), marital status (married/unmarried), income (tertiles), municipal population density (quartiles)

When examining sub-types of colorectal cancer, we found no association between residential road traffic noise and rectal cancer: the linear estimate was HR 0.98, 95% CI 0.84-1.16, per 10 dB over the 10 years preceding diagnosis, and the categorical estimates did not suggest an association either. For colon cancer, we found that the association with residential road traffic noise was carried primarily by a borderline higher risk of distal colon cancer: HR 1.18, 95% CI 1.00-1.40, per 10 dB over the 10 years preceding diagnosis, whereas for proximal colon cancer, the corresponding estimate was weak: 0.99, 95% CI: 0.83-1.18. The categorical estimates suggested a positive dose-response association over the first four exposure groups, with a leveling off in the highest exposure group (**Table 3**).

Table 3: Crude and adjusted associations between average residential road traffic noise exposure (L_{den}) 10 years before diagnosis and proximal and distal colon cancer and rectal cancer incidence. Linear estimates per 10 dB, and categorical estimates.

	Proximal colon cancer			***Distal colon cancer***			***Rectal cancer***		
	Cases	***Model 1[a]*** **HR (95% CI)**	***Model 2[b]*** **HR (95% CI)**	**Cases**	***Model 1[a]*** **HR (95% CI)**	***Model 2[b]*** **HR (95% CI)**	**Cases**	***Model 1[a]*** **HR (95% CI)**	***Model 2[b]*** **HR (95% CI)**
Linear estimate	328	1.04 (0.88-1.22)	0.99 (0.83-1.18)	351	1.18 (1.01-1.31)	1.18 (1.00-1.40)	397	0.99 (0.85-1.15)	0.98 (0.84-1.16)
Categorical estimate									
< 52 dB	46	1.00 (ref.)	1.00 (ref.)	39	1.00 (ref.)	1.00 (ref.)	56	1.00 (ref.)	1.00 (ref.)
52-57 dB	89	0.99	0.97	96	1.25	1.28	123	1.18	1.19

		(0.70-1.42)	(0.67-1.39)		(0.86-1.81)	(0.88-1.86)		(0.85-1.63)	(0.86-1.65)
57-62 dB	95	1.09 (0.76-1.57)	1.04 (0.71-1.50)	97	1.36 (0.93-1.98)	1.39 (0.94-2.04)	103	1.13 (0.81-1.59)	1.14 (0.81-1.61)
62-67 dB	61	1.15 (0.78-1.68)	1.07 (0.72-1.59)	71	1.63 (1.10-2.39)	1.64 (1.10-2.45)	75	1.26 (0.89-1.79)	1.25 (0.87-1.79)
>67 dB	37	0.99 (0.65-1.51)	0.90 (0.58-1.41)	48	1.44 (0.94-2.18)	1.46 (0.94-2.26)	40	0.98 (0.66-1.46)	0.98 (0.64-1.48)
p for trend		0.68	0.90		0.04	0.05		0.93	0.84

[a] Adjusted for age (by design) and sex

[b] Adjusted as model 1, and for railway noise (0-20, >20-50, >50 dB), smoking (never, former, current), smoking duration (linear, years), smoking intensity (linear, g/day), alcohol intake (linear, g/day), abstainers (yes, no), recreational physical activity (yes, no), education (basic, vocational, higher), red meat (linear, g/day), wholegrain cereal intake (linear, g/day), marital status (married/unmarried), income (tertiles), municipal population density (quartiles)

We found no association between residential railway traffic noise and colorectal cancer or colorectal cancer subtypes (Results not shown).

We investigated the effect of adjustment for BMI, a known risk-factor for colorectal cancer, in the analyses, but found that the estimates were similar in models with and without BMI adjustment, for all outcomes investigated (results not shown).

We did not find a positive association between NO_x and colorectal cancer (results not shown). When adjusting the association between residential road traffic noise and our outcomes of interest for NO_x, the estimates were higher: Colorectal cancer: HR 1.21, 95% CI: 1.08-1.35, and distal colon cancer HR 1.26, 95% CI: 1.03-1.54, per 10 dB over the 10 years preceding diagnosis. The correlation ($R_{Spearman}$) between road traffic noise and NO_x at time of enrollment was 0.62. The correlation was 0.03 between road traffic and railway noise.

DISCUSSION

In the present study, we found a borderline significant positive association between modelled road traffic noise at the residence and distal colon cancer. Railway noise was not associated with colorectal cancer.

The strengths of the study include the large cohort size, and the long follow-up time, which allowed accumulation of a relatively large number of colorectal cancer cases. Furthermore, we were able to follow up all participants through validated Danish registries on cancer and vital status, and access to detailed address history over the entire study period, which allowed calculation of average exposure over different time-windows. The modelling of exposure over time is an important study strength, as colorectal carcinogenesis is a lengthy, multistep process, which usually evolves over decades [40]. Thus, it seems plausible, that the historic exposure is of larger relevance than exposure at time of diagnosis. This is supported by our finding that the IRR for an association between traffic noise exposure at time of diagnosis in the present study was weaker than the longitudinal estimates: 1.03, 95% CI: 0.95-1.13 (all colorectal cancer cases). The Nordic Prediction Model, which was used to calculate exposure, has been the standard method for estimation of traffic noise in the Nordic countries for many years [37]. A validation of the model, based on a number of outdoor measurements in up to

300 m from the road, found the average difference between measurements and calculations to be 0.2 dB (noise from road traffic is typically within the range of 40-80 dB), showing that the model is very accurate [41].

Despite using a well-validated noise exposure model and high-quality input data, a limitation of the study is potential exposure misclassification due to e.g. lack of information on bedroom orientation, time spent at home, window opening habits, noise from neighbors, and hearing impairment, which may all affect the actual, individual noise exposure. However, this misclassification was most likely unrelated to our outcome of interest, and it is thus expected to be non-differential; drawing the estimates towards the null. Furthermore, the study participants are not representative of the general Danish population: Only 35 % of those originally invited into the cohort chose to participate, and participants had a higher socioeconomic position, compared to non-participants. They were selected primarily from the two largest urban areas of Denmark; Copenhagen and Aarhus, and are therefore also not representative of the entire Danish population with regards to residential noise exposure [34]. Findings should thus be generalized with caution.

We have not identified any previous prospective cohort studies examining the association between residential traffic noise exposure and colorectal cancer. A study of differences in cancer incidence rates around the Schiphol Airport examined all gastrointestinal cancers in combination, but found no association with this overall group [42]. Few studies have examined nightshift work, which may, as traffic noise, be a marker for circadian disruption, in relation to colorectal cancer, but a review of these suggested, that there was insufficient evidence for an association between nightshift work and colon cancer [43].

We found that the indicated association between road traffic noise and colorectal cancer was confined to distal colon cancer. It is increasingly acknowledged, that proximal and distal colon cancer are separate disease entities, with different embryologic origin, including different blood supply [44], which may explain the differences in epidemiology, biology, and clinical responses [45, 46]. Notably, they are found to develop through two distinctly different molecular pathways of carcinogenesis; microsatellite instability, and chromosomal instability [44, 47, 48], with the first being dominant in proximal colon cancers, and the second in distal colon cancers [47]. Interestingly, tumors with microsatellite instability have been suggested related to methylating carcinogens, whereas tumors with chromosomal instability have been related to bulky-adduct-forming carcinogens, including, among others, reactive oxygen species [48], which may be produced as a result of noise exposure [21, 22].

The finding of a dose-response relation between road traffic noise exposure and distal colon cancer, which levels off for the quintile of highest exposed (> 67 dB), is not exclusive: A similar shape of association has been found in a study of traffic noise and diabetes [31]. A potential explanation for this could be, that persons living in very high-exposure areas may have put up noise-barriers, and insulated windows to a higher extend that people living in less-exposed areas. Their actual noise exposure will thus be reduced, and the health consequences may be similarly reduced. We have no information on such individual actions to limit noise exposure.

The lack of an association between railway noise exposure and colorectal cancer may be explained by the limited power to investigate this association, as less than 20% of participants were exposed to railway traffic noise, and of those exposed, only 55 % were exposed to more than 50 dB. Furthermore, a study modelling the association between transportation noise exposure and annoyance showed, that railway noise was generally experienced as less

annoying than road traffic noise [49], suggesting that it may not produce physiological effects of a magnitude strong enough to affect a clinically relevant response.

As the association between traffic noise and obesity has been described in several studies [29, 30], and obesity furthermore is a well-known factor for colorectal cancer [33], we did not adjust the models in the present study for obesity, as we would hereby remove a potential pathway through which traffic noise affect colorectal cancer risk. However, as a sensitivity analysis, we tried adjusting the models for linear BMI, and found that this resulted in associations of similar magnitude as models without adjustment.

We did not include NO_x as a covariate in the present study, as it showed strong collinearity with road traffic noise and further adjustment for NO_x resulted in higher estimates for an association with road traffic noise. Furthermore, exposure to NO_x in itself did not result in higher risk for colorectal cancer in the present study, which is supported by a previous study on air pollution and cancer incidence in the DCH cohort, showing no association with colon or rectal cancer [50]. A number of studies investigating combined effects of noise and air pollution in relation to health, have found largely independent effects, which may be explained by the fact that the two exposures operate through diverse pathways in their effect on health [51].

In conclusion, the present study based on a large, prospective cohort of middle-aged Danes suggested that long-term exposure to residential road traffic noise might be associated with a higher risk of distal colon cancer. As this is the first study to examine traffic noise and colorectal cancer, further studies are warranted.

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