Impact of road traffic noise on obesity measures: observational study of three European cohorts

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Highlights

- The largest study to date involving nearly 500,000 adults from three European cohorts;
- In UK Biobank, higher road-noise exposure was associated with obesity/central obesity status;
- These associations were attenuated by further adjustment for $PM_{2.5}$;
- In HUNT3, only exposure to road-noise >55dB was associated with obesity/central obesity status;
- No or negative associations were observed in the Lifelines cohort.

Key words

- Noise
- Traffic
- Central obesity
- Pollution
- Cardiometabolic risk
- Body Mass Index

Abstract

Background

Environmental stressors such as transport noise may contribute to development of obesity through increased levels of stress hormones, sleep deprivation and endocrine disruption. Epidemiological evidence supporting an association of road traffic noise with obesity markers is still relatively scant and confined to certain geographical regions. We aimed to examine the cross-sectional associations between road traffic noise and obesity markers in three large European cohorts involving nearly 500,000 individuals.

Methods

Three population-based cohorts (UK Biobank, Lifelines, HUNT3) were established between 2006-2013 in the UK, the Netherlands and Norway respectively. For all three cohorts, residential 24-hour road traffic noise (L_{den}) for 2009 was modelled from a standardised European noise assessment framework. Residential exposures to NO_2 for 2007 and $PM_{2.5}$ for 2010 were estimated from Europe-wide land use regression models. Obesity markers including body mass index and waist circumference were measured at recruitment. Obesity and central obesity status were subsequently derived. Regression models were fitted in each cohort, adjusting for a harmonised set of demographic and lifestyle covariates, with further adjustments for air pollution in the main model.

Results

The main analyses included 412,934 participants of UK Biobank, 61,032 of Lifelines and 30,305 of HUNT3, with a mean age of 43-56 years and L_{den} ranging 42-89 dB(A) across cohorts. In UK Biobank, per 10 dB(A) higher of L_{den}: BMI was higher by 0.14kg/m^2(95%CI: 0.11-0.18), waist circumference higher by 0.27cm(95%CI: 0.19-0.35), odds of obesity was 1.06(95%CI: 1.04-1.08) and of central obesity was 1.05(95%CI: 1.04-1.07).These associations were robust to most other sensitivity analyses but attenuated by further adjustment of $PM_{2.5}$ or area-level socioeconomic status. Associations were more pronounced among women, those with low physical activity, higher household income or hearing impairment. In HUNT3, associations were observed for obesity or central obesity

status among those exposed to L_{den} greater than 55dB(A). In contrast, no or negative associations were observed in the Lifelines cohort.

Conclusions

This largest study to date providing mixed findings on impacts of long-term exposure to road traffic noise on obesity, which necessitates future analyses using longitudinal data to further investigate this potentially important epidemiological link.

1. Introduction

Globally, the prevalence of obesity has tripled in both adult and children populations since 1975(1,2). Whilst diet and physical activity are pivotal in weight management, non-behavioural environmental determinants including traffic noise have been overlooked on their obesogenic potential due to scant epidemiological evidence(3). Only a small number of studies(4–11), most of which were conducted in Scandinavian countries, have investigated the associations of traffic noise with obesity markers.

The underlying biological mechanisms of associations between long-term exposure to traffic noise and obesity are generally hypothesised in two ways. First, traffic noise, as a physiological stressor, is believed to activate the hypothalamic–pituitary–adrenal(HPA) axis and the sympathetic-adrenal-medulla axis in a chronic time frame(12,13). This subsequently results in an over-production of stress hormones such as cortisol, which is then linked to increased abdominal fat distribution and food consumption(14). Second, long-term exposure to traffic noise, via sleep deprivation and endocrine disruption, may adversely affect immune functions, control of appetite, energy expenditure, and regulation of stress hormones(15–17). There may also exist a potential social mechanism as recent studies suggested that higher residential exposure to traffic noise(18), or higher level of traffic noise annoyance(19), was associated with lower levels of physical activity.

A 2018 review commissioned by the World Health Organisation reported that quality of evidence supporting an association between road traffic noise and obesity markers was graded as *very low*(20), indicating further research is urgently needed to strengthen the evidence base and inform causal inference. In view of this, we conducted this cross-sectional study to investigate the associations between road traffic noise and various markers of obesity in three large European population-based cohorts, with the largest study to date involving nearly 500,000 individuals.

2. Methods

2.1. Study populations

Three cohorts were included as parts of the BioSHaRE (Biobank Standardisation and Harmonisation for Research Excellence in the European Union) project(21).

UK Biobank is a prospective cohort study, recruiting over 500,000 men and women aged 40-69 years who lived near one of the 22 assessment centres across the UK between 2006 and 2010(22). Lifelines is a multi-disciplinary prospective population-based cohort study examining, in a unique three-generation design, the health and health-related behaviours of 167,729 persons living in the North of The Netherlands. It employs a broad range of investigative procedures in assessing the biomedical, socio-demographic, behavioural, physical and psychological factors which contribute to the health and disease of the general population, with a special focus on multi-morbidity and complex genetics. During 2006 and 2013, individuals aged between 25 and 50 years and their families were invited to participate through their general practitioners, resulting in 152,005 adult participants(23). HUNT3 is the third survey (2006-2008) of the Trøndelag Health Study, based in central Norway(24). All residents living in the Nord-Trøndelag region aged 20 years and above were eligible to participate and 50,806 out of 93,860 residents provided data. The study areas of HUNT3 consist of rural areas and small towns, and are less densely populated, as compared to those of UK Biobank and Lifelines. Our study protocol received all necessary approvals from review committees in each cohort.

2.2. Study outcomes

Weight (kg), standing height (cm), and waist circumference (cm) were measured upon recruitment by trained staff, following standard procedures in each cohort (**Supplementary-1**). Body mass index (BMI) was derived as weight (kg) divided by height squared (m^2). Additionally in UK Biobank, whole-body fat mass (kg) was measured to the nearest 0.1kg using bioelectrical impedance (Tanita BC418MA, Tokyo, Japan).

In addition to the continuous outcomes of BMI, waist circumference (WC) and whole-body fat mass, we defined three binary outcomes relating to obesity and central obesity status, with the latter using the WHO cut-off values for Europeans(25):

- *Obesity* (BMI≥30 kg/m^2);
- *WC-based central obesity* (WC≥102cm in men and ≥88cm in women);
- *WhtR-based central obesity* (waist-to-height ratio (WhtR) ≥0.55);

2.3. Study covariates

We selected *a priori* study covariates based on previous literature(4-11). Data on age, sex, smoking status and pack-years, education, employment, alcohol consumption, physical activity, daily intake of fresh vegetables and fruits, and sleep disturbance were collected at recruitment using comparable questionnaire items and have been harmonised meaningfully for this study(**Supplementary-2**). Data on household income, hearing impairment, area-level socioeconomic status (SES), and degree of urbanisation of residential areas were additionally obtained from individual cohorts, if available.

Residential annual mean concentration of nitrogen dioxide (NO_2), as a proxy for near-road traffic-related air pollution, was estimated for year 2007 through a western Europe-wide Land Use Regression (LUR) model for all three cohorts(26), with a validated model performance (explained variance (R^2) between modelled and measured exposures) ranging 46%-56%. In addition for UK Biobank and Lifelines, LUR-based annual mean concentrations of particulate matter with an aerodynamic diameter ≤2.5μm ($PM_{2.5}$) for year 2010 were estimated by the ESCAPE (European Study of Cohorts for Air Pollution Effects) project, with R^2 of 77% and 61%, respectively(27).

2.4. Exposure assessment of road traffic noise

A model based on the Common Noise Assessment Methods in European Union (CNOSSOS-EU)(28) was developed and ran for each cohort(29). This noise model used lower resolution inputs, which are usually available at a national or wider geographical scale, to enable a cross-cohort harmonised approach. Nonetheless, this model has relatively good performance on exposure ranking (Spearman ratio: 0.75) and has been used in epidemiological analyses(30,31).

Noise sound pressure level emissions were estimated for year 2009 on all roads within 500m of participant's home address at recruitment. Noise propagation was modelled with terms for distance and angle of view to source and diffraction and reflection due to buildings, and absorption due to ground cover. Road network geography, calculated hourly vehicle flows using a daily average traffic profile, building heights, land cover, and meteorological data were obtained for the respective study areas. To account for participants living on minor roads that were not captured in the national level traffic datasets, a fixed low-level baseline traffic flow (600 vehicles per day) was assigned. Traffic data were used for the year 2009 and land cover data were used for the year 2006. To facilitate comparison with previous studies, we used annual mean 24-hour A-weighted sound pressure level in decibels (dB(A)) (L_{den}, with an additional penalty of 10dB(A) and 5dB(A) added to night-time and evening noise respectively) for all participants. Given the extremely high correlation (r=0.99) between night-time noise and L_{den} in our cohorts, we did not conduct analysis using night-time noise as it would have produced almost identical results as those of L_{den}.

2.5. Exclusions and missing data

Exclusions and missing data are outlined in flowcharts(**Supplementary-3**). Subjects with missing data on obesity markers, noise exposure and at least one covariate were excluded from analysis, leaving a final sample of at least 400,000 out of 502,642 UK Biobank participants, 61,032 out of 152,005 Lifelines participants, and at least 25,000 out of 50,806

HUNT3 participants. In Lifelines, home addresses of 56,573 participants were not geocoded as they were recruited after geocoding begun for this study. Moreover, an additional 21,703 participants had missing data on at least one covariate in the main model. In UK Biobank and HUNT3, participants were excluded mainly due to missing data on covariates.

2.6. Statistical analyses

We performed parallel harmonised statistical analyses in each cohort among participants who had complete data on the outcomes, exposures and covariates. Descriptive analyses on population characteristics and traffic noise distributions were first conducted in each cohort. Cross-sectional linear regression analyses for BMI, WC and whole-body fat mass, and logistic regression analyses for obesity and central obesity were conducted. The associations between continuous annual mean road-L_{den} at residence and each obesity marker were adjusted for: age and sex (**basic model**); and additionally for smoking status and pack-years, education, employment, alcohol consumption, physical activity, daily intake of vegetables and daily intake of fruits(**main model**). Effect estimates, odds ratios (OR) and their 95% confidence interval (CI) are presented for 10 dB increment of L_{den}, to facilitate comparison with previous studies. Assumption of linearity of the associations with continuous outcomes was evaluated by using categorical road L_{den} (<50, 50-55, ≥55 dB in HUNT3 and <55, 55-60, ≥60 dB in UK Biobank and Lifelines). The reference category is set at 50 dB(A) for HUNT3 given the distribution of noise exposure was lower than that of the other two cohorts.

Several sensitivity analyses were performed to test the robustness of the main results. Depending on data availability in each cohort, we further adjusted each of the following variables one at a time into the main model: NO_2, $PM_{2.5}$, degree of urbanisation, household income and area-level socioeconomic status (SES).

Effect modifications of the studied associations were evaluated by adding an interaction term between L_{den} and the respective potential effect modifier and by using *F-test* statistics. Selected potential modifiers included sex, physical activity level, sleep disturbance, hearing impairment and household income.

Whilst longitudinal data collection is underway and therefore data are not yet available for UK Biobank and HUNT3; for the Lifelines cohort, longitudinal associations of road L_{den} exposure at recruitment with incidence of: a) obesity, b) WC-based central obesity and c) WhtR-based central obesity were ran for 43,691 participants who participated in the follow-up visit, on average four years (ranging from one to eight years) after baseline recruitment. Analyses were conducted using multivariable Poisson regression, adjusting for covariates in the main model as with cross-sectional analyses.

Finally, in order to update the 2018 WHO review, which only included three studies published up to 2015(20), we conducted meta-analyses on the cross-sectional associations between per 10dB higher road-L_{den} and continuous BMI and waist circumference, including further studies published since 2015 and the three current studies of ours. Although random-effect (RE) model is usually chosen to conduct meta-analysis of heterogeneous studies, it however underestimates the statistical error, produces overconfident results, and penalises larger studies(32). To overcome these limitations, we used the inverse variance heterogeneity (I-Vhet) model(32). It is an estimator under the fixed-effect model assumption with a quasi-likelihood based variance structure. In contrast to the RE model, I-Vhet model favours larger studies, retains a correct coverage probability and a lower observed variance. All meta-analyses were conducted using the MetaXL software V5.3 (EpiGear International Pty Ltd, Queensland, Australia).

3. Results

In total, 504,271 participants from all three cohorts with complete data on covariates were included in the analysis **(Table 1)**. Compared to participants in the HUNT3 and UK Biobank, participants in the Lifelines cohort on average were younger (43 vs. 56 years), had lower BMI values (26 vs. 27 kg/m^2) and general obesity prevalence (15% vs. 23-24%). Prevalence of central obesity, defined by either WC or WhtR cut-off values, was highest among HUNT3 participants (53% and 48% respectively). Prevalence of WhtR-based central obesity was lowest in Lifelines (27%) among the three cohorts.

Across the three cohorts, residential road-L_{den} ranged between 42 and 89 dB(A) **(Table 2),** with the overall distribution of road-L_{den} was much lower in HUNT3 as compared to the other two cohorts. The median (interquartile range, IQR) for L_{den} in HUNT3 was 49.4 (5.9) dB(A), as compared to 54.6 (4.2) dB(A) in Lifelines and 54.9 (3.5) dB(A) in UK Biobank. In HUNT3, median(IQR) for NO_2 was 11.6 (4.8) ug/m^3 whilst in Lifelines and UK Biobank, the respective figure was 20.7 (8.7) and 28.8 (11.1) ug/m^3. Spearman correlations between L_{den} and NO_2 or $PM_{2.5}$ were low to moderate.

3.1. Cross-sectional analysis using continuous road L_{den}

Associations between continuous road-L_{den} and obesity markers varied, in terms of direction and strength, across the three cohorts in the main model **(Table 3 and 4)**. In UK Biobank, a 10dB higher annual mean road-L_{den} was associated with a higher BMI by 0.14kg/m^2 (95%CI: 0.11 to 0.18) and higher WC by 0.27cm (95%CI: 0.19 to 0.35). In contrast, negative associations were found in Lifelines for both BMI (-0.20 kg/m^2, 95%CI: -0.28 to -0.12) and WC (-0.62cm, 95%CI: -0.84 to -0.40) measures. No associations were also observed HUNT3 (**Table 3**).

In UK Biobank, each 10dB higher annual mean road-L_{den} was associated with a 6% higher prevalence in obesity (OR: 1.06, 95%CI: 1.04-1.08), with similar effect sizes also observed for WC-based central obesity (OR:1.05, 95%CI: 1.04-1.07) **(Table 4)**. In Lifelines, whilst no association was observed between L_{den} and obesity prevalence, we found a negative association with WC-based central obesity (OR: 0.92, 95%CI: 0.89 to 0.96). For all cohorts, associations between per 10 dB higher road-L_{den} and WhtR-based central obesity prevalence were observed, with an OR ranging between 1.06 and 1.08.

For both UK Biobank and Lifelines, we found that most of these associations were highly sensitive to adjustment of $PM_{2.5}$**(Table 3 and 4)**, or area-level SES, particularly in UK Biobank. In other sensitivity analyses, associations from the main model for Lifelines were sensitive to further adjustment of degree of urbanisation, with effect estimates for BMI or WC were materially reduced(**Supplementary-4.1**) while significance for WC-based or WhtR-based central obesity was lost(**Supplementary-4.2**). For both UK Biobank and HUNT3, main results persisted after further adjustment for either urbanisation degree or household income.

Significant effect modifications by the selected variables were only observed in UK Biobank but not in the other two cohorts. The associations of road-L_{den} with both BMI and WC were stronger among women, those with lower physical activity level; higher household income; or hearing impairment(**Table 5**). Across all three cohorts, we did not find evidence of effect modifications by sleep disturbance.

In the updated meta-analysis including all the currently available studies and ours, very large heterogeneity (I^2>90%) was observed across the studies. The pooled estimate from I-Vhet meta-analysis for BMI was 0.09kg/m^2 (95%CI: -0.06 to 0.25) and for WC was 0.19cm (95%CI: -0.22 to 0.60) per 10dB higher road-L_{den} (**Figure 1**).

3.2. Cross-sectional analysis using categorical road-L_{den}

In UK Biobank, associations with all obesity markers became stronger in higher exposure levels of road-L_{den}. The same pattern was also observed in HUNT3. Noteworthy, among those exposed to the highest road-L_{den} level (>55dB(A)) in HUNT3, we found associations with both obesity (OR: 1.16, 95%CI: 1.04-1.29) and central obesity status (WC-based, OR:1.11, 95%CI: 1.01-1.23; WhtR-based, OR:1.18, 95%CI:1.07-1.30) as compared to reference group (<50dB(A)) **(Table 6)**. In contrast, we observed inconsistent findings with obesity markers across L_{den} groups in Lifelines.

3.3. Longitudinal analysis in Lifelines

While no association was found between road-L_{den} and incident obesity in Lifelines, negative association was found with incident WC-based central obesity (Relative Risk: 0.89, 95%CI: 0.81-0.97), which was independent of further adjustment for $PM_{2.5}$ (**Supplementary-5**).

4. Discussion

In this largest study to date we found varied associations between road traffic noise and obesity markers across cohorts. In the largest cohort, UK Biobank, we consistently observed positive associations between long-term exposure to road-L_{den} and all adiposity markers relating to general or central obesity and body fat mass. Notably, we observed that in this cohort, women, those with a lower physical activity level, hearing impairment or higher household income were particularly susceptible to the impacts of road traffic noise on obesity. However, most effect sizes observed in UK Biobank were attenuated by further adjustment of $PM_{2.5}$ pollution or area-level socioeconomic status. In HUNT3, exposure to a road-L_{den} level greater than 55dB was associated with higher odds of obesity and central obesity. In Lifelines, we found no or negative associations with different obesity markers.

4.1. Findings in Lifelines cohort

Only follow-up data on obesity outcomes were available for the Lifelines cohort to enable a longitudinal analysis in relation to baseline road-L_{den} exposure. Partly in line with the negative association with WC-based central obesity as seen in the cross-sectional analysis, the longitudinal association was also negative but robust to $PM_{2.5}$ adjustment. Extra caution is needed to interpret this counterintuitive finding.

In the Lifelines cohort, 53% and 42% participants are living in rural and intermediate areas respectively. Although (semi)rural levels of road-L_{den} exposure were below median, these participants had a higher mean BMI or WC than that of their urban counterparts. A previous analysis in this cohort found that prevalence of metabolic syndrome was significantly higher in rural areas, as compared to that of urban areas(33), suggesting that urban residence might be a protective factor for cardiometabolic health in Lifelines. Possible reasons include that rural residents may have to rely more on cars on daily living and hence be less physically active; these more insightful data however was not specifically collected in the baseline

252 questionnaires for physical activity. Also, it has been reported that in this region of the
253 Netherlands rural residents generally have more unhealthy dietary patterns (e.g. consume
254 more on butter, sugar, meat, alcohol etc) than do their urban counterparts(34). Another
255 possible contributing factor is that exposure misclassification of road traffic noise in rural or
256 intermediate areas may be lesser as compared to urban areas, where geography (building
257 density, road network etc.) is much more complex(35).
258
259 We ran additional analyses in this particular cohort, by either further adjusting for degree of
260 urbanisation in the main model or running the main model in each strata of urbanity. In fact,
261 some of the observed negative associations were no longer statistically
262 significant**(Supplementary-4)**. These results suggested that while effects of road traffic noise
263 on adiposity markers may be negligible, it remains important to understand wider contextual
264 determinants of obesity in rural and urban populations in this particular cohort. Future studies
265 with more years of follow-up data and detailed covariates are warranted.
266
267 4.2. Findings in the UK Biobank and HUNT3 cohorts in the context of previous studies
268 Our findings in UK Biobank and HUNT3 are consistent with the small number of previous
269 studies. In the Danish Diet, Cancer, and Health Cohort, a cross-sectional study of over 50,000
270 participants found that each 10dB higher L_{den} was associated with a 0.35cm higher WC
271 (95%CI: 0.21 to 0.50) and a 0.18 kg/m^2 higher BMI (95%CI: 0.12 to 0.23)(7). After an average
272 5-year of follow-up, the effect of per 10dB higher L_{den} on change in WC was very small
273 (0.22mm/year, 95%CI: 0.02 to 0.43) and became non-significant after accounting for lifestyle
274 variables(6). In a cohort (N=5,075) from Stockholm County, a cross-sectional association was
275 reported between per 10dB higher L_{den} and WC (0.42cm, 95%CI: 0.02 to 0.82); whilst no
276 associations were found for BMI(4). This finding was later confirmed by a longitudinal analysis
277 in the same cohort which reported that each 10dB increase in L_{den} was associated with an
278 increase in WC by 0.04cm/year (95%CI: 0.02 to 0.06) and risk of incident central obesity (risk

ratio: 1.07, 95%CI: 1.00 to 1.14) during a 9-year follow-up period(5). Among the 3,796 SAPALDIA participants in Switzerland, significant positive cross-sectional associations of L_{den} with BMI, WC, % body fat, odds of obesity or central obesity were observed(9). In the longitudinal analysis, only an increased risk of incident obesity (risk ratio: 1.25, 95%CI: 1.04 to 1.51) was identified after a 10-year follow-up period whilst an association with change in continuous BMI was not observed.

Two other studies based in Oslo and Denmark observed significant positive associations only among subgroup populations, for instance, highly noise-sensitive women(8), or women with job strain or those resided in urban areas(10). More recently, a cohort study of 1,554 elderly Mexican-Americans of California reported no association between 10dB higher L_{den} and risk of abdominal obesity (hazard ratio: 0.91, 95%CI: 0.75 to 1.10)(11).

4.3. Updated meta-analysis

The 2018 WHO review based on three cross-sectional studies published up to 2015 (N=71,431) reported that for each 10dB higher of road-L_{den} within a range of 40-65dB, BMI was higher by 0.03kg/m^2(95%CI: -0.10 to 0.15), and waist circumference was higher by 0.17cm (95%CI: -0.06 to 0.40)(20). Our pooled point estimates were slightly higher than these, although the I-Vhet meta-analysis did indicate more uncertainty (i.e. a wider 95% confidence interval) around the point estimate. Nontheless, our updated meta-analysis has substantially strengthened the evidence base in terms of the number of studied individuals as well as the range of noise exposure (42-89dB). Given that large heterogeneity was found across these studies, additional studies covering more geographical regions and populations are warranted to further refine these estimates.

4.4. Confounding roles of air pollution and area-based socioeconomic status

Most previous studies included either NO_2 or nitrogen oxides (NOx), as a proxy of traffic-related pollutant, for sensitivity analyses(4,5,7–9). In line with our findings, these other studies did not observe substantial changes to the main results after adjusting for NO_2 or NOx, except in one longitudinal study(5), where the incident rate ratio for central obesity became non-significant after further adjustment of NOx.

Our study however indicated a confounding role by $PM_{2.5}$. This is supported by the observation that positive effect sizes between L_{den} and adiposity markers in UK Biobank were attenuated by >10% after further adjustment of $PM_{2.5}$. Unlike NO_2, $PM_{2.5}$ represents a mixture of particles with different chemical compositions and toxicity. Although both PM and gaseous exposures appear to be important endocrine disruptors(36), some research suggested that PM exposure may trigger a stronger innate immune response(37) in comparison to gaseous pollutants. It should be noted that associations between long-term air pollution exposure and obesity markers remain ambiguous, varying within and across study populations by different characteristics such as age, sex and physical activity level(3). Given that evidence is still relatively scant, further investigations of possible confounding role of air pollution on the relationship between road traffic noise and adiposity outcomes are needed.

Area-level socioeconomic status (SES) is a potentially important confounder in environmental health studies. Most previous studies did not consider this variable as they were geographically more confined to a city or a homogenous region where contrast of area-SES is relatively small. For example, in Lifelines cohort, further adjustment of area-SES did not affect the main findings. In UK Biobank, however, we observed attenuated associations after further adjusting for area-level SES, in a magnitude similar to that of $PM_{2.5}$ adjustment, indicating that contextual differences should be carefully considered in studies covering much wider geographical areas.

4.5. Effect modification

In UK Biobank, we found that women, participants with a lower physical activity level, or from a higher-income household were more susceptible to the adverse impacts of road traffic noise on BMI or WC. Most previous studies did not observe a significant effect modification either by sex and socioeconomic position, in part, due to insufficient statistical power. Some studies reported that higher road traffic noise exposure(18) or noise annoyance(19) was associated with less physical activity, but its role as a possible effect modifier for associations between road-L_{den} and adiposity outcomes is rarely investigated. A formal mediation analysis of physical activity is therefore recommended in future investigations. Finding of the adverse impacts of noise were more pronounced among participants with hearing impairment is counterintuitive. While the prevalence of hearing impairment increases with age, we did not detect a significant interaction between age and road traffic noise exposure. It may be possible that hearing impairment serves as a proxy of some metabolic disorders such as diabetes(38). Only one study with measured home outdoor and indoor noise estimates among 132 cardiovascular disease patients reported that the associations of nigh-time noise with adiposity outcomes were stronger among those with hearing loss(39). Sleep disturbance did not appear to be an effect modifier in our study. One previous study reported that, effects from railway noise but not road noise, were significantly modified by sleep quality on adiposity(9).

4.6. Strengths and limitations

A major strength is a large sample size from three cohorts (>500,000 individuals) with different populational and geographical contexts. We adopted a cross-cohort harmonised approach on exposure, health outcomes and covariates, enabling comparisons of findings across these cohorts. Another strength lies in the mutual adjustment of air pollution including both NO_2 and $PM_{2.5}$.

Several limitations are noted. First, we relied on modelling road traffic noise exposure at residential address and did not have information on exposures at places other than home;

noise modifiers including housing characteristics, window-opening habits; and use of earplugs. Exposure misclassification due to these factors is likely non-differential and therefore bias the estimates towards the null. The noise model neither specified a particular façade point, nor residential floor. Noise level usually does not decrease considerably with higher floor levels and hence the influence of residential floor on both noise exposure and its related health effects are likely non-substantial. However, by not applying façade modelling, it is likely that our estimated effects from road traffic noise may have been underestimated particularly in the urban context, as recently reported in a nationwide study in Switzerland(35). Second, the noise model used in this study tends to over-estimate noise exposures for those at low exposure levels due to the assumed national traffic flow baseline value and to under-estimate exposure for those living in areas with heavily trafficked minor roads. These scenarios may contribute to the uncertainty of continuous noise estimates and limit our ability to detect a noise effect, if present. We indeed observed some significant associations when using categorical noise exposure, for example in the HUNT3 cohort. Third, we did not have data on noise from rail, aircraft, occupation, community or wind-turbine. There is a possibility of confounding from these other environmental noise sources, although they are qualitatively different from, and not as ubiquitous as, road traffic noise. Fourth, we cannot rule out residual confounding by other unaccounted factors such as noise sensitivity. Previous studies revealed mixed evidence about the role of noise sensitivity(8,9). It should also be noted that the adjustment of dietary and lifestyle factors, was relatively crude in our analyses and may represent a potential over-adjustment issue. We nonetheless included them in the main model in order to greatly facilitate comparison with previous findings. Fifth, our analyses excluded many participants with missing data, in particular among Lifelines and HUNT3. While there were no materially differences of the obesity measures between those remained and drop-outs, there is still a potential that estimates from each cohort are likely biased **(Supplementary-6)**. Sixth, we detected many significant associations particularly in UK biobank, which may be expected in a very large sample size if the magnitude of effect is small and clinically negligible(40). While statistical significance does not necessarily imply clinical

388 importance, the large sample size in UK Biobank did offer more confidence about the true
389 effect size, i.e. it can be estimated with higher accuracy. Finally, the inherent limitation of
390 cross-sectional analyses means we were unable to investigate causal inference.
391
392 4.7. Policy implications
393 Our results contribute to an increasing body of evidence that road traffic noise could potentially
394 be a harmful risk factor for obesity in the general populations. The estimates from the updated
395 meta-analysis further strengthen the evidence base for policy-making. It is clear that effect
396 estimates at individual level are negligible for clinical implications; however, public health
397 implications should not be overlooked. In Europe, at least 100 million people are exposed to
398 a road traffic noise level greater than 55dB(41), a current threshold set by the EU. Given that
399 a) obesity is a well-established risk factor for both morbidity and mortality from diseases such
400 as CVD and diabetes(42); and b) as a population-level prevention strategy, interventions on
401 individuals' lifestyle behaviours are sometimes difficult and not always effective(43); there is
402 an opportunity to strengthen environmental policy to effectively promote a healthy built
403 environment including reducing exposures to traffic noise and many other hazards, in order to
404 maximise public health gains on a range of physical and mental health outcomes.
405
406 In conclusion, this largest study to date on 500,000 participants observing mixed findings on
407 associations between long-term exposure to road traffic noise and adiposity prevalence.
408 Future analyses with complete longitudinal follow-up data among these cohorts are warranted
409 to further investigate this potentially important epidemiological link.

Conflict of Interest

All authors declare none conflict of interest.

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Table 1 Descriptive statistics on study populations.

	HUNT3 (N=30,305)	Lifelines (N=61,032)	UK Biobank (N=412,934)
Recruitment years	2006-2008	2006-2013	2006-2010
Age at recruitment, years	56.5 (12.8)	43.0(11.5)	56.4(8.1)
Female sex	55.2%	59.0%	55.2%
Body Mass Index (BMI), kg/m^2	27.3 (4.3)	26.0(4.3)	27.4 (4.8)
Waist Circumference (WC), cm	94.1 (11.9)	89.9(12.4)	90.2 (13.5)
Obesity	23.2%	15.3%	24.5%
Central obesity (WC-based)	53.2%	34.3%	33.8%
Central obesity (WhtR-based)	48.3%	26.7%	39.2%
Smoking status			
Never smoker	47.7%	50.7%	64.5%
Former smoker	34.3%	30.0%	25.7%
Current smoker	17.9%	19.2%	9.8%
Smoking pack-years	7.9 (11.5)	5.7(9.4)	8.3 (15.7)
Education level			
Degree level and above or equivalent	24.3%	33.8%	60.2%
below degree level	75.7%	66.4%	39.8%
Work status			
Other (unemployed, student etc.)	2.7%	25.4%	8.7%
Retired	31.9%	4.5%	33.0%
Employed	65.4%	70.0%	58.3%
Physical Activity level or score			
Low or light intensity	42.4%	4315 (2665)$^+$	14.4%
Moderate or moderate intensity	39.9%	2763 (4291)$^+$	44.6%
High or high intensity	17.7%	1677 (1965)$^+$	41.0%

Alcohol drinking frequency			
Never	4.4%	17.1%	8.5%
1-3 times a month or occasional	57.2%	20.3%	23.5%
Once or twice a week	22.3%	40.8%	25.8%
3-4 times a week	13.4%	10.8%	22.5%
Daily or almost daily	2.6%	11.0%	19.7%

[+]these values represent summed physical activity scores from participants in each strata of physical activity level.

Table 2 Summary statistics of exposure distributions in each cohort.

	N	Min	5%	50%	95%	Max	Mean(SD)	IQR	Spearman correlation ratio		
L_{den}, dB(A)									L_{den}	NO_2	$PM_{2.5}$
HUNT3	25,717	42.2	42.6	49.4	59.1	69.9	49.3 (4.7)	5.9	-	-0.06	-
Lifelines	61,032	51.6	52.0	54.6	64.6	83.1	55.9 (4.0)	4.2	-	0.47	0.49
UK Biobank	406,929	51.5	51.7	54.9	66.6	89.3	56.0(4.3)	3.5	-	0.11	0.24
NO_2, ug/m^3											
HUNT3	25,715	6.6	8.1	11.6	19.1	26.8	12.5 (3.5)	4.8			
Lifelines	51,492	8.9	13.6	20.7	31.5	79.8	21.3 (5.8)	8.7			
UK Biobank	406,929	7.0	16.7	28.8	51.6	138.4	30.5 (10.5)	11.1			
$PM_{2.5}$, ug/m^3											
Lifelines	51,492	14.9	15.3	15.4	16.3	20.3	15.5 (0.36)	0.2			
UK Biobank	378,140	8.2	8.3	9.9	11.9	21.3	10.0 (1.1)	1.3			

Table 3 Cross-sectional associations (effect estimate, 95%CI)between per 10dB higher L_{den} and continuous Body Mass Index, waist circumference, and whole-body fat mass.

	N	HUNT3	N	Lifelines	N	UK Biobank
BMI, kg/m^2						
Basic model	25,661	0.10 (-0.02 to 0.22)	61,032	**-0.37(-0.45 to -0.29)**	404,863	**0.16 (0.13 to 0.20)**
Main model	25,661	0.07 (-0.05 to 0.19)	61,032	**-0.20 (-0.28 to -0.12)**	404,863	**0.14 (0.11 to 0.18)**
Main model+NO_2	25,659	0.05 (-0.07 to 0.17)	51,492	**-0.12 (-0.22 to -0.02)**	404,863	**0.16 (0.12 to 0.19)**
Main model+$PM_{2.5}$	-	-	51,492	**-0.14 (-0.24 to -0.04)**	376,171	**0.06 (0.02 to 0.10)**
Main model+ area SES	-	-	57,326	**-0.23 (-0.33 to -0.13)**	404,383	**0.06 (0.02 to 0.09)**
Waist circumference, cm						
Basic model	25,679	0.19 (-0.03 to 0.41)	61,032	**-1.11 (-1.33 to -0.89)**	405,590	**0.37 (0.28 to 0.46)**
Main model	25,679	0.09 (-0.22 to 0.40)	61,032	**-0.62 (-0.84 to -0.40)**	405,590	**0.27 (0.19 to 0.35)**
Main model+NO_2	25,677	0.05 (-0.26 to 0.36)	51,492	**-0.33 (-0.58 to -0.08)**	405,590	**0.26 (0.17 to 0.34)**
Main model+$PM2_{.5}$	-	-	51,492	**-0.39 (-0.64 to -0.14)**	376,864	0.08 (-0.02 to 0.17)
Main model+ area SES	-	-	57,326	**-0.83 (-1.07 to -0.59)**	405,105	0.06 (-0.03 to 0.14)
Whole-body fat mass, kg						
Basic model	-	-	-	-	398,587	**0.24 (0.18 to 0.31)**
Main model	-	-	-	-	398,587	**0.21 (0.14 to 0.27)**
Main model+NO_2	-	-	-	-	398,587	**0.24 (0.17 to 0.30)**
Main model+$PM_{2.5}$	-	-	-	-	370,339	**0.07 (0.00 to 0.14)**
Main model+ area SES	-	-	-	-	398,107	**0.07 (0.01 to 0.14)**

Basic model: only adjusted for age and sex; **Main model**: further adjusted for smoking status and pack-years, education, employment, alcohol consumption, physical activity, daily intake of vegetables and daily intake of fruits. SES: socioeconomic status; BOLD indicated 95%CI did not span across 0.00 (for presentation, we only kept two digits after decimals).

Table 4 Cross-sectional associations (odds ratio, 95%CI) between per 10dB higher L_{den} and prevalence of obesity and central obesity.

	N	HUNT3	N	Lifelines	N	UK Biobank
Obesity						
Basic model	25,661	**1.07 (1.00 to 1.14)**	61,032	**0.90 (0.84 to 0.95)**	404,863	**1.07 (1.05 to 1.09)**
Main model	25,661	1.05 (0.97 to 1.14)	61,032	0.96 (0.91 to 1.02)	404,863	**1.06 (1.04 to 1.08)**
Main model+NO_2	25,659	1.04 (0.96 to 1.13)	51,492	0.98 (0.91 to 1.06)	404,863	**1.06 (1.04 to 1.08)**
Main model+$PM2_{.5}$	-	-	51,492	0.98 (0.91 to 1.06)	376,171	1.02 (0.99 to 1.04)
Main model+ area SES	-	-	57,326	0.93 (0.86 to 1.01)	404,383	**1.02 (1.00 to 1.04)**
Central obesity (WC-based)						
Basic model	25,679	1.06 (0.99 to 1.13)	61,032	**0.87 (0.84 to 0.90)**	405,590	**1.07 (1.05 to 1.08)**
Main model	25,679	1.03 (0.97 to 1.09)	61,032	**0.92 (0.89 to 0.96)**	405,590	**1.05 (1.04 to 1.07)**
Main model+NO_2	25,677	1.03 (0.97 to 1.09)	51,492	0.98 (0.92 to 1.04)	405,590	**1.05 (1.03 to 1.06)**
Main model+$PM2_{.5}$	-	-	51,492	0.97 (0.92 to 1.03)	376,864	**1.02 (1.00 to 1.04)**
Main model+ area SES	-	-	57,326	**0.90 (0.85 to 0.96)**	405,105	**1.02 (1.00 to 1.03)**
Central obesity (WhtR-based)						
Basic model	25,631	**1.10 (1.03 to 1.18)**	61,032	**0.89 (0.85 to 0.92)**	405,181	**1.07 (1.06 to 1.09)**
Main model	25,631	**1.08 (1.02 to 1.15)**	61,032	**1.06 (1.00 to 1.13)**	405,181	**1.06 (1.04 to 1.07)**
Main model+NO_2	25,629	**1.07 (1.01 to 1.14)**	51,492	0.94 (0.89 to 1.00)	405,181	**1.05 (1.03 to 1.06)**
Main model+$PM2_{.5}$	-	-	51,492	0.94 (0.89 to 1.00)	376,468	1.00 (0.99 to 1.02)
Main model+ area SES	-	-	57,326	**0.90 (0.84 to 0.95)**	404,699	**1.01 (1.00 to 1.03)**

Basic model: only adjusted for age and sex; **Main model**: further adjusted for smoking status and pack-years, education, employment, alcohol consumption, physical activity, daily intake of vegetables and daily intake of fruits. SES: socioeconomic status; BOLD indicated 95%CI did not span across 1.00 (for presentation, we only kept two digits after decimals).

Table 5 Effect modifications by selected variables on the cross-sectional associations (effect estimate, 95%CI) between per 10 dB higher L_{den} and continuous BMI, or waist circumference in the UK Biobank cohort: results from the main model

	N	BMI, kg/m^2	N	Waist circumference, cm
Sex				
Women	223,691	**0.19 (0.14 to 0.24)**	223,981	**0.35 (0.23 to 0.46)**
Men	181,172	**0.09 (0.04 to 0.13)**	181,609	**0.17 (0.05 to 0.29)**
P-value for interaction		0.005		0.019
Physical activity level				
Low	58,049	**0.27 (0.17 to 0.38)**	58,257	**0.52 (0.28 to 0.76)**
Moderate	180,418	**0.13 (0.07 to 0.18)**	180,744	**0.23 (0.11 to 0.36)**
High	166,396	**0.12 (0.07 to 0.17)**	166,589	**0.22 (0.10 to 0.35)**
P-value for interaction		0.005		0.046
Household income				
<£31,000	167,949	**0.10 (0.04 to 0.15)**	168,363	**0.16 (0.02 to 0.29)**
>=£31,000	181,921	**0.16 (0.11 to 0.21)**	182,092	**0.31 (0.19 to 0.43)**
P-value for interaction		0.028		0.040
Hearing impairment				
Yes	98,840	**0.22 (0.15 to 0.29)**	99,035	**0.42 (0.24 to 0.59)**
No	289,979	**0.12 (0.08 to 0.15)**	290,474	**0.21 (0.11 to 0.31)**
P-value for interaction		0.006		0.025

Main model: adjusted for age, sex, smoking status and pack-years, education, employment, alcohol consumption, physical activity, daily intake of vegetables and daily intake of fruits. BOLD indicated 95%CI did not span across 0.00 (for presentation, we only kept two digits after decimals).

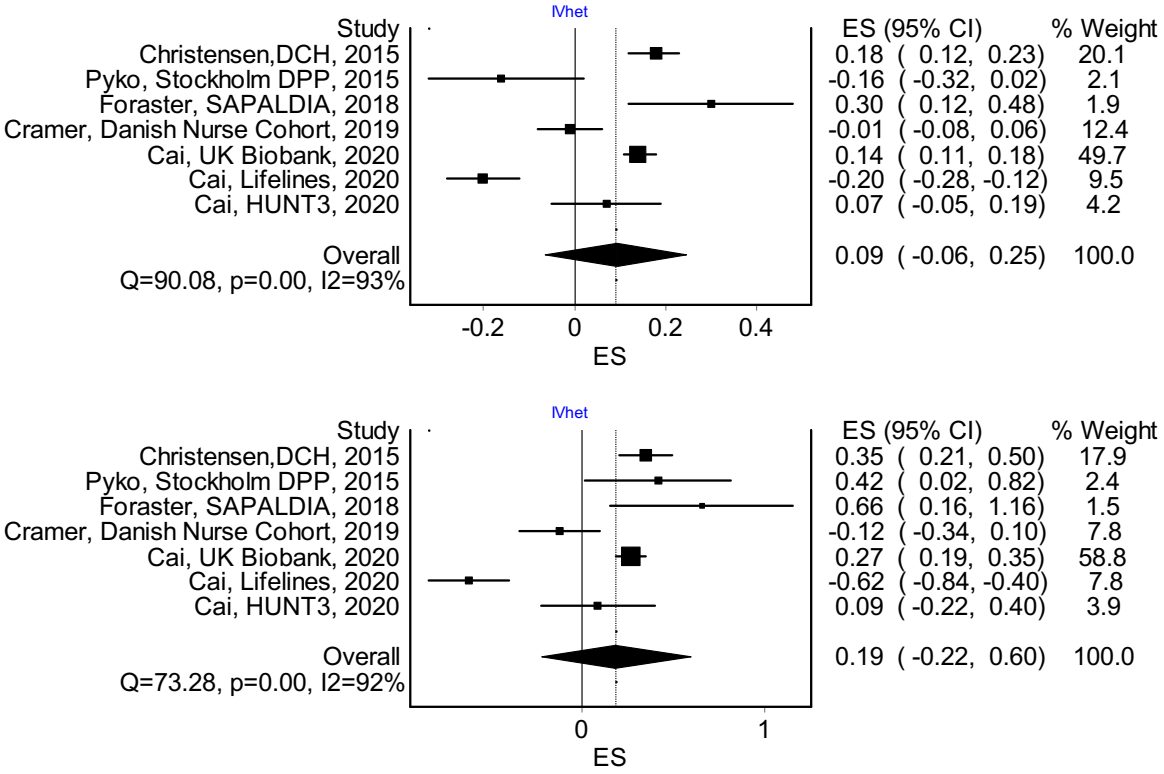
Table 6 Cross-sectional associations (effect estimate or odds ratio, 95%CI) between categorical L_{den} (dB(A)) and obesity markers in each cohort: results from main model

		BMI		**Waist circumference**		**Obesity**		**Central obesity (WC-based)**		**Central obesity (WhtR-based)**
HUNT3										
<50	14,346	ref	14,352	ref	14,346	ref	14,352	ref	14,328	ref
50-55	9,293	0.06 (-0.05 to 0.16)	9,302	0.10 (-0.18 to 0.39)	9,293	1.02 (0.96 to 1.09)	9,302	1.01 (0.96 to 1.07)	9,281	1.06 (1.00 to 1.12)
>55	2,022	0.17 (-0.02 to 0.37)	2,025	0.40 (-0.12 to 0.91)	2,022	**1.16 (1.04 to 1.29)**	2,025	**1.11 (1.01 to 1.23)**	2,022	**1.18 (1.07 to 1.30)**
Lifelines										
<55	33,650	ref	33,650	ref	33,650	ref	33,650	ref	33,650	ref
55-60	19,475	**-0.12 (-0.20 to -0.05)**	19,475	**-0.58 (-0.78 to -0.39)**	19,475	1.04 (0.97 to 1.12)	19,475	**1.07 (1.01 to 1.13)**	19,475	1.06 (0.99 to 1.12)
>60	7,907	**-0.20 (-0.31 to -0.10)**	7,907	**-0.61 (-0.89 to -0.34)**	7,907	1.01 (0.94 to 1.09)	7,907	0.99 (0.93 to 1.05)	7,907	0.99 (0.93 to 1.05)
UK Biobank										
<55	208,229	ref	208,606	ref	208,229	ref	208,606	ref	208,410	ref
55-60	147,615	**0.09 (0.05 to 0.12)**	147,872	**0.18 (0.10 to 0.26)**	147,615	**1.05 (1.03 to 1.06)**	147,872	**1.02 (1.01 to 1.04)**	147,716	**1.03 (1.02 to 1.05)**
>60	49,019	**0.16 (0.11 to 0.20)**	49,112	**0.26 (0.14 to 0.37)**	49,019	**1.06 (1.04 to 1.08)**	49,112	**1.05 (1.03 to 1.07)**	49,055	**1.06 (1.04 to 1.08)**

Main model: adjusted for age, sex, smoking status and pack-years, education, employment, alcohol consumption, physical activity, daily intake of vegetables and daily intake of fruits. BOLD indicated 95%CI did not span across 0.00, or 1.00 for odds ratio (for presentation, we only kept two digits after decimals).

Figure 1 Meta-analysis of associations between per 10 dB(A) higher road-Lden and BMI (upper panel), waist circumference (lower panel) among individual-level cross-sectional studies: inverse variance heterogeneity (I-Vhet) model.

Q and I^2 are heterogeneity statistics. Cochran's Q, calculated as the weighted sum of squared differences between individual study effects and the pooled effect across studies; and I^2, variation in estimated effect attributable to heterogeneity; ES- effect size. Note, this meta-analysis excluded the null study of Oftedal (2015) as the effect estimate provided by this study could not be converted.



Supplementary materials

Impact of road traffic noise on obesity measures: observational study of three European cohorts

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Supplementary-1: Measurement of adiposity in each cohort

UK Biobank

Weight was measured to within 0.1kg, without shoes and heavy outer clothing, using the Tanita BC 418 MA body composition analyser. Standing height was measured, without shoes, using the wall-mounted SECA 202 height measure. Waist circumference at the level of the umbilicus was measured midway between lowest rib margin and iliac crest, in a horizontal plane, using a Wessex non-stretchable sprung tape measure. More details could be found http://www.ukbiobank.ac.uk/wp-content/uploads/2011/11/UK-Biobank-Protocol.pdf

HUNT3

Height and weight were measured with the participants wearing light clothes without shoes, using Jenix DS-102 Automated height and weight scale at the stationary team or Avery Berkel L115 weight scale at the mobile team. Height to the nearest centimetre and weight to the nearest half kilogram. Waist circumferences was measured with a band to the nearest centimetre, with the participant standing and with the arms hanging relaxed. The waist circumference was measured horizontally at the height of the umbilicus, using a non-stretchable measuring band (KaWe 43972). More details could be found https://hunt-db.medisin.ntnu.no/hunt-db/#/

Lifelines

Height and weight were measured with the participants wearing light clothes without shoes, using SECA222 stadiometer for height and SECA 761 scale for weight to the nearest 0.1cm and 0.1kg respectively. Waist circumference was measured to the nearest 0.1 cm, was measured twice midway between the lowest rib and the top of the iliac crest at the end of gentle expiration, using SECA200 measuring tape. More details could be found https://www.lifelines.nl

Supplementary-2: Harmonised definitions of study covariates across all cohorts

Variables	Categories/unit	Definition
Sex	0=female; 1=male	gender of the participant
Age	years	age when attending baseline assessment
Smoking status	0=never; 1=previous; 2=current;	Current smoking status at recruitment
Smoking pack-year	pack-years	smoking pack-years ; participant who never smoked was assigned a 'zero' to this variable
Education level	1= College, university, or higher professional qualifications; 2= below-degree (secondary/higher secondary school or below)	education level (derived using the highest education attained)
Employment	0=Other (unemployed, student, voluntary work, looking after family); 1=retired; 2=employed	employment status (derived in each cohort according to the categories)
Alcohol drinking frequency	0=never; 1= 1-3 times a month or special occasions only; 2= once or twice a week; 3=3-4times a week; 4=daily or almost daily	alcohol drinking frequency (derived in each cohort according to the categories)
Physical activity level	1=low; 2=moderate; 3=high	This variable was derived for UK Biobank using the IPAQ short form; In HUNT3, this variable was directly derived using

		answers to relevant questionnaire items; In Lifelines, data were grouped according to the physical activity intensity types, which were calculated by multiplying duration (minutes per week) with the MET value.
Daily intake of vegetables	0= none; 1=equal/less than 2 heaped tablespoons; 2= more than 2 heaped tablespoons (categories in UK Biobank)	daily average intake of raw and/or cooked vegetables (derived from each cohort using comparable frequency categories as with UK Biobank) For Lifelines, Intake of vegetables Never to 2-3 days/month 1 day/week to 4-5 days a week 6-7 days a week
Daily intake of fresh fruits	0= none; 1=equal/less than 2 pieces; 2= more than 2 pieces (categories in UK Biobank)	daily pieces of fresh fruits intake (derived from each cohort using comparable frequency categories as with UK Biobank) For Lifelines, Intake of fresh fruits Never to 2-3 days/month 1 day/week to 4-5 days/week 6-7 days/week
Sleep disturbance	1= never/rarely; 2= Sometimes; 3= Usually	have trouble falling asleep at night or wake up in the middle of the night

Additional data from UK Biobank, HUNT3, Lifelines

Household income:

In UK Biobank, this was derived from the questionnaire item – "What is the average total income before tax received by your household". There are five categories: <£18,000, £18,000-30,999, £31,000-51,999, £52,000-100,000, >£100,000. We defined this as binary outcome [higher/lower income], using cut-off values of £31,000, as it is close to median UK household income (£29,400 as of 2019).

In Lifelines, this was derived from questionnaire item – "What is the monthly household income after taxes?" There are eight categories: less than 750; 750–1000; 1000–1500;

1500–2000; 2000–2500; 2500– 3000; 3000–3500; more than 3500 €/month. We defined this as a binary variable (higher/lower income), using cut-off values of EUR2500.

Hearing impairment:
In UK biobank, this was derived from the questionnaire item- "do you have any difficulty with your hearing". Based on the answers, we defined this as a binary outcome [yes/no].

Area-level socioeconomic status:
In UK Biobank, Townsend deprivation index calculated immediately prior to participant joining UK Biobank. Based on the preceding national census output areas, each participant is assigned a score corresponding to the output area in which their postcode is located.

In Lifelines, the % of low-income households per postal code area is used for year 2013. All household with available income data were ranked and the lowest 40% was then defined as a low-income household. Data were available from Statistics Netherlands.
http://www.cbs.nl/nl-NL/menu/themas/dossiers/nederland-regionaal/cijfers/incidenteel/maatwerk/wijk-buurtstatistieken/kwb-recent/default.htm

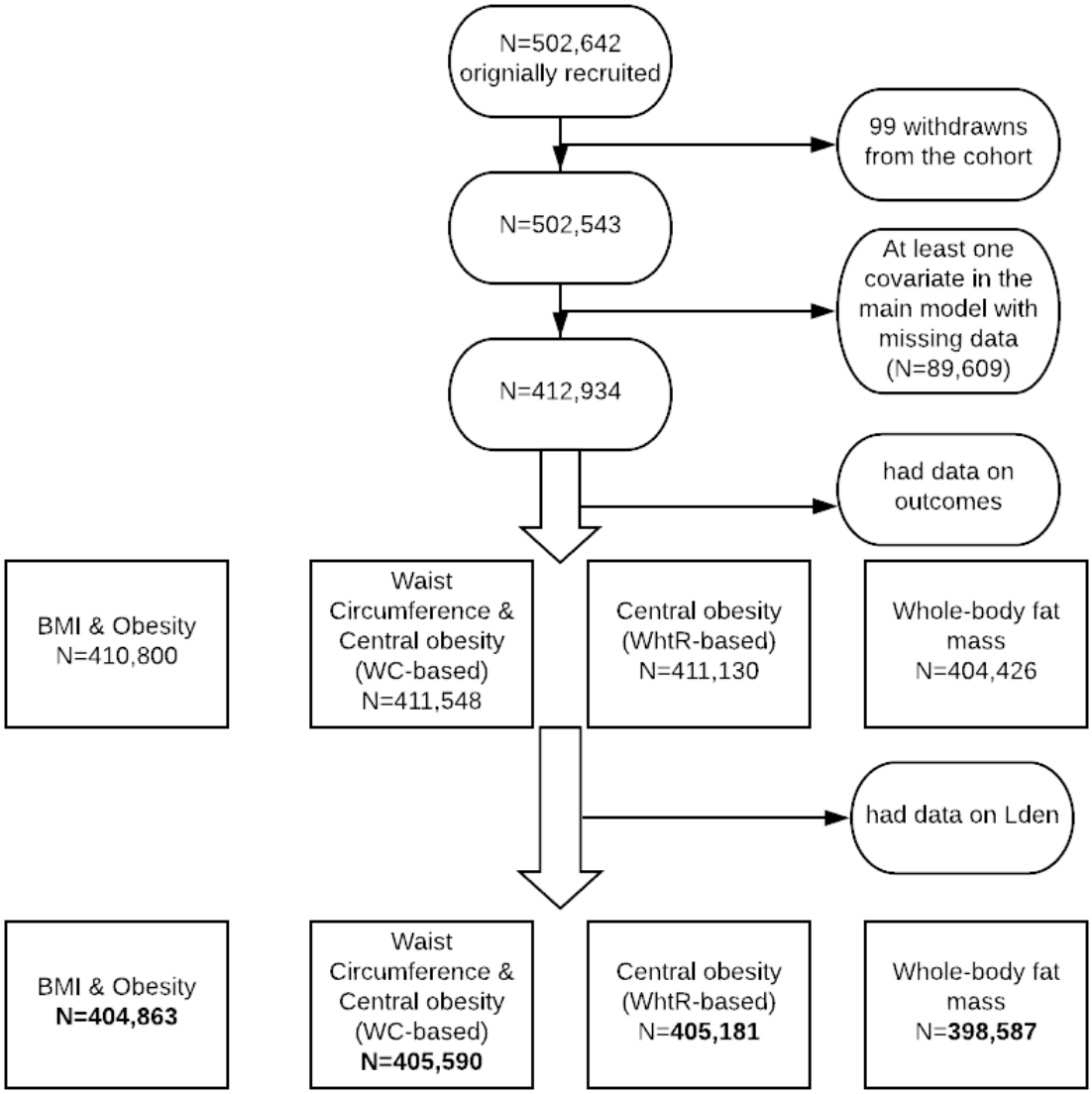
Urbanisation degree:
In UK Biobank, classification of urbanisation degree is based on the home area population density from the 2001 census from the Office of National Statistics. We derived this from the variable (20118) in UK Biobank, those resided in England/Wales (urban/sparse, urban/less sparse) and in Scotland (large urban area/ other urban area) were classified as 'urban residents', those resided in any other areas were classified as 'rural residents' (including small, rural, remote rural, very remote rural town/villages).

In Lifelines, classification of urbanisation degree is based on the average address density per km^2 per postal code area for year 2013. Data were available from Statistics Netherlands.
http://www.cbs.nl/nl-NL/menu/themas/dossiers/nederland-regionaal/cijfers/incidenteel/maatwerk/wijk-buurtstatistieken/kwb-recent/default.htm

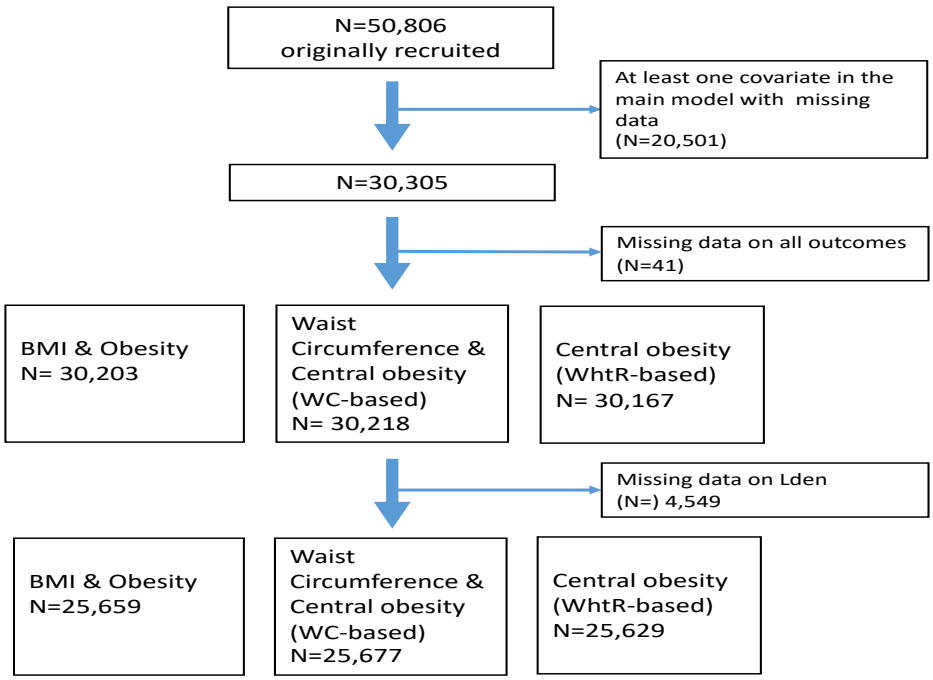
In HUNT3, classification of urbanisation degree is based on how much the municipalities in the Nord-Trøndelag region are densely populated. Five of the municipalities have status as towns and are considered densely populated urban areas and were coded as "Urban". The remaining municipalities are sparsely populated rural areas and were coded as "Rural".
https://hunt-db.medisin.ntnu.no/hunt-db/#/variable/403

Supplementary-3: Flowcharts of data exclusion in each cohort

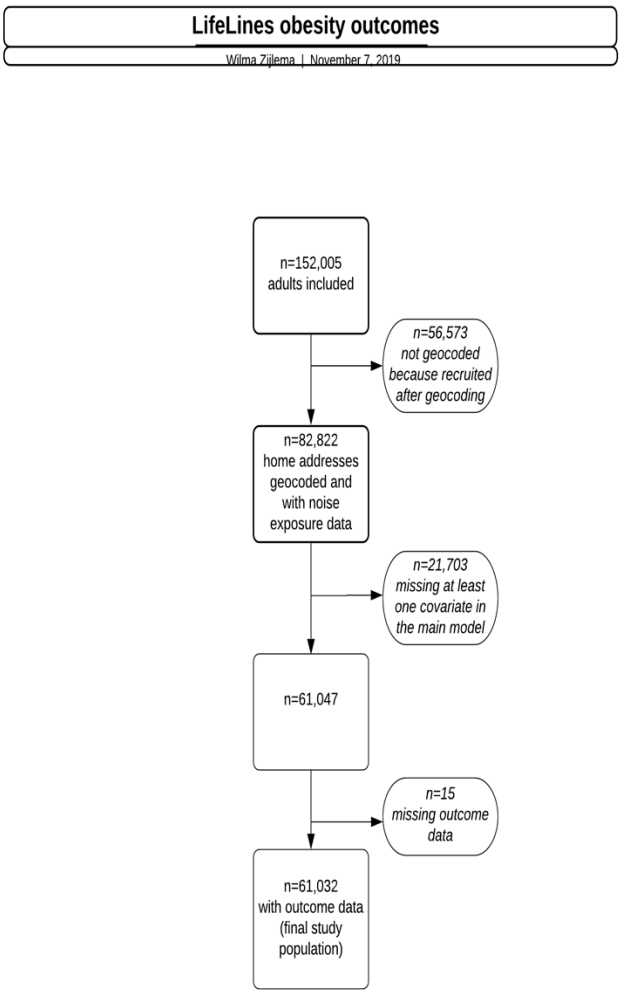
UK Biobank



HUNT3


N=50,806
originally recruited
At least one covariate in the main model with missing data
(N=20,501)
N=30,305
Missing data on all outcomes
(N=41)
BMI & Obesity
N= 30,203
Waist Circumference & Central obesity (WC-based)
N= 30,218
Central obesity (WhtR-based)
N= 30,167
Missing data on Lden
(N=) 4,549
BMI & Obesity
N=25,659
Waist Circumference & Central obesity (WC-based)
N=25,677
Central obesity (WhtR-based)
N=25,629

Lifelines


LifeLines obesity outcomes
Wilma Zijlema | November 7, 2019
n=152,005 adults included
n=56,573 not geocoded because recruited after geocoding
n=82,822 home addresses geocoded and with noise exposure data
n=21,703 missing at least one covariate in the main model
n=61,047
n=15 missing outcome data
n=61,032 with outcome data (final study population)

Supplementary-4.1: Sensitivity analyses to the main model in each cohort, as per 10 dB higher of Lden: continuous measures

	N	HUNT3	N	Lifelines	N	UK Biobank
BMI, kg/m^2						
Main model	25,661	0.07 (-0.05 to 0.19)	61,032	**-0.20 (-0.28 to -0.12)**	404,863	**0.14 (0.11 to 0.18)**
Main model+ household income	-	-	42,120	**-0.23 (-0.33 to -0.13)**	349,870	**0.13 (0.09 to 0.17)**
Main model+ urbanisation	25,012	0.07 (-0.05 to 0.19)	58,894	**-0.10 (-0.19 to -0.01)**	401,090	**0.15 (0.12 to 0.18)**
Waist circumference, cm						
Main model	25,679	0.09 (-0.22 to 0.40)	61,032	**-0.62 (-0.84 to -0.40)**	405,590	**0.27 (0.19 to 0.35)**
Main model+ household income	-	-	42,120	**-0.69 (-0.96 to -0.42)**	350,455	**0.23 (0.14 to 0.32)**
Main model+ urbanisation	25,025	0.12 (-0.19 to 0.43)	58,894	**-0.42 (-0.66 to -0.18)**	401,806	**0.28 (0.20 to 0.37)**
Whole-body fat mass, kg						
Main model	-	-	-	-	398,587	**0.21 (0.14 to 0.27)**
Main model+ household income	-	-	-	-	344,600	**0.19 (0.12 to 0.26)**
Main model+ urbanisation	-	-	-	-	394,871	**0.22 (0.15 to 0.28)**

Supplementary-4.2: Sensitivity analyses to the main model in each cohort, as per 10 dB higher of Lden: binary measures

	N	HUNT3	N	Lifelines	N	UK Biobank
Obesity						
Main model	25,661	1.05 (0.97 to 1.14)	61,032	0.96 (0.91 to 1.02)	404,863	**1.06 (1.04 to 1.08)**
Main model+ household income	-	-	42,120	**0.93 (0.88 to 0.99)**	349,870	**1.05 (1.03 to 1.07)**
Main model+ urbanisation	25,012	1.05 (0.97 to 1.14)	58,894	1.00 (0.94 to 1.06)	401,090	**1.06 (1.04 to 1.08)**
Central obesity (WC-based)						
Main model	25,679	1.03 (0.97 to 1.09)	61,032	**0.92 (0.89 to 0.96)**	405,590	**1.05 (1.04 to 1.07)**
Main model+ household income	-	-	42,120	**0.90 (0.85 to 0.96)**	350,455	**1.05 (1.03 to 1.07)**
Main model+ urbanisation	25,025	1.04 (0.98 to 1.10)	58,894	0.97 (0.94 to 1.06)	401,806	**1.05 (1.04 to 1.07)**
Central obesity (WhtR-based)						
Main model	25,631	**1.08 (1.02 to 1.15)**	61,032	**1.06 (1.00 to 1.13)**	405,181	**1.06 (1.04 to 1.07)**
Main model+ household income	-	-	42,120	**0.91 (0.86 to 0.97)**	350,130	**1.05 (1.03 to 1.06)**
Main model+ urbanisation	24,982	**1.08 (1.02 to 1.15)**	58,894	0.97 (0.94 to 1.06)	401,405	**1.06 (1.04 to 1.08)**

Supplementary-4.3: Subgroup analyses to the main model by degree of urbanisation of the Lifelines cohort participants' residential areas, as per 10 dB higher of Lden association with BMI or waist circumference

Degree of Urbanisation	N	BMI	N	Waist circumference
rural	31,012	-0.04 (-0.20 to 0.12)	31,012	-0.35 (-0.77 to 0.07)
intermediate	23,946	-0.07 (-0.20 to 0.05)	23,946	**-0.42 (-0.76 to -0.08)**
urban	3,936	-0.06 (-0.29 to 0.18)	3,936	0.01 (-0.62 to 0.63)
P-value for interaction		0.003		0.139

Main model: adjusted for age, sex, smoking status and pack-years, education, employment, alcohol consumption, physical activity, daily intake of vegetables and daily intake of fruits.

Supplementary-5: Longitudinal associations between per 10dB higher exposure of Lden at baseline and incident obesity and central obesity: the Lifelines cohort

	N	Main model	N	Main model +NO_2	N	Main model +$PM_{2.5}$
Incident obesity	37,362	1.02 (0.90 to 1.16)	31,587	0.98 (0.84 to 1.14)	31,587	1.09 (0.94 to 1.27)
Incident Central obesity (WC-based)	28,672	**0.89 (0.81 to 0.97)**	24,684	0.90 (0.81 to 1.01)	24,684	**0.88 (0.79 to 0.98)**
Incident Central obesity (WhtR-based)	32,114	0.97 (0.88 to 1.07)	27,560	0.99 (0.89 to 1.10)	27,560	0.95 (0.85 to 1.07)

Main model: adjusted for age, sex, smoking status and pack-years, education, employment, alcohol consumption, physical activity, daily intake of vegetables and daily intake of fruits.

Supplementary-6 Comparisons of obesity markers and noise exposure (if data available) between subjects who were included in the analysis and those excluded from the analyses.

HUNT3

	All data on covariates from main model					Missing at least one covariates from main model						
	N		Mean	Median	Std. Deviation	N		Mean	Median	Std. Deviation	P-value	Effect-size index#
	Valid	Missing				Valid	Missing					
BMI	30203	102	27.3	26.8	4.3	20204	297	26.9	26.4	4.6	<0.001	0.093
Waist	30218	87	94.1	94.0	11.9	20142	359	92.8	92.0	12.9	<0.001	0.109
L_{den}	25748	4557	49.3	49.4	4.3	15567	4934	49.3	49.5	4.4	0.28	0

UK Biobank

	All data on covariates from main model. N=412,934			Missing at least one covariates from main model, N=89,609			p-value	Effect size index#
	N	Mean	SD	N	Mean	SD		
BMI	410,800	27.4	4.8	88,638	27.4	4.7	0.49	0
Waist	411,548	90.2	13.5	88,835	90.9	13.4	<0.001	0.052
lden	406,929	56.0	4.3	88,233	56.1	4.4	<0.001	0.023

Lifelines

	Geocoded	Non-geocoded	Had data on Lden and all covariates	Had data on Lden and at least one covariate was missing	Effect size index#
	82,822*	56,573	61,032	21,718	
BMI, mean (SD)	26.0 (4.37)	26.1 (4.32)	26.0 (4.33)	26.2 (4.46)	0.046
Waist, mean (SD)	90.2 (12.5)	90.1 (12.6)	89.9 (12.4)	90.9 (12.6)	0.080

Lden, mean (SD)	NA	NA	55.9 (3.99)	55.7 (3.86)	

*In Lifelines, 95,432 participants' addresses were geocoded, but only 82,822 addresses were assigned a value of Lden. #Effect size index was computed by the difference between the two means divided by the standard deviation of the datasets with complete information. Benchmark values of effect size index: small <0.20, medium 0.20-0.50, large >0.50 (Reference: doi: 10.1111/j.1471-6712.2012.01052.x). .