



# Exposure to residential road traffic noise prior to conception and time to pregnancy



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## ABSTRACT

**Objectives:** To examine the association between residential road traffic noise and fecundity estimated by time to pregnancy (TTP).

**Design:** We identified 65,201 mothers from the Danish National Birth Cohort with self-reported information on TTP collected through computer assisted telephone interviews. Road traffic noise was modelled at all historical addresses and expressed as time-weighted means for periods corresponding to individual TTP. Associations were analyzed using logistic regression for analyses of dichotomous outcomes and ordinal logistic regression for TTP in four categories, adjusting for maternal age at conception, disposable household income, education and air pollution (NO<sub>x</sub>).

**Results:** Ordinal logistic regression showed a 10 dB increase in road traffic noise to be associated with a 8% increased risk of 6–12 month TTP (95% CI: 1.03; 1.12) whereas we found no statistically significant associations for ≥ 12 months TTP (OR = 1.04, 95% CI: 0.99; 1.09) when compared to 0–2 months TTP. Similarly, when exploring TTP as a binary outcome we found a 10 dB higher road traffic noise to be associated with a 5% higher risk of TTP of 6 months or more (95% CI: 1.01; 1.08) as compared with < 6 months TTP, whereas when the cut-point was 12 months TTP no association was found.

**Conclusion:** Road traffic noise was associated with an increased risk of 6–12 month TTP, but not with risk of longer TTP, indicating that noise may have a small impact on sub-fecundity.

## 1. Introduction

Traffic noise is an ubiquitous environmental exposure which has been associated with several adverse health problems, such as annoyance, sleep disturbances, cardiovascular disease and metabolic disease as well as overweight (Babisch, 2014; Christensen et al., 2015; Miedema and Oudshoorn, 2001; Miedema and Vos, 2007; Sorensen et al., 2013).

Exposure to traffic noise has been associated with activation of the hypothalamus-pituitary-adrenal (HPA)-axis and increased levels of cortisol (Schmidt et al., 2013; Selander et al., 2009) (Babisch et al., 2001; Griefahn and Robens, 2010; Ising and Braun, 2000; Wayne et al., 2003). Activation of the HPA-axis, with increased levels of corticotrophin-releasing hormone, may have inhibitory effects on both female and male fertility (Kalantaridou et al., 2010). A link between the HPA-axis and the hypothalamic-pituitary-gonadal (HPG) axis has been suggested (Ferin, 1999). In the HPG-axis, gonadotropin-releasing hormone

from the hypothalamus induces excretion of follicle stimulating hormone and luteinizing hormone (LH) from the anterior pituitary gland as well as estrogen and testosterone from the gonads, which regulates the uterine and ovarian cycles in women and the spermatogenesis in men (Seeley et al., 2003). Studies have indicated that activation of the HPA axis may lead to delay or inhibition of the LH surge (which triggers ovulation) (Ferin, 1999) as well as causes altered blood flow in the fallopian tubes and interrupted gamete transport (Louis et al., 2011).

Epidemiologic studies of stress and fertility vary widely in exposure measures and outcome. Some studies have found associations between self-reported perceived stress and levels of reproductive hormones, ovulatory function and overall fertility among women (Hjollund et al., 1999; Schliep et al., 2015), while others fail to find an association (Lynch et al., 2012). In men perceived stress has been associated with lower semen quality (Janevic et al., 2014). Additionally, some studies have found biomarkers of stress to be associated with longer time to pregnancy (TTP) (Louis et al., 2011).

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Sleep disturbance may be another potential pathway between noise exposure and decreased fecundity. Despite a general paucity of research in the field, sleep disturbance and dysregulation has been associated with reduced semen quality (Jensen et al., 2013) and dysregulation of reproductive hormones that negatively affects fertility in women (Kloss et al., 2015).

The aim of the present study was to examine the association between residential exposure to road traffic noise exposure while trying to conceive and TTP.

## 2. Methods

### 2.1. Study population

The Danish National Birth Cohort (DNBC) enrolled 92,274 women with a total of 104,419 pregnancies. This cross sectional study was based on all of the 84,129 women the DNBC with a planned pregnancy. Recruitment for the cohort was nationwide and performed from 1996 to 2002. General practitioners provided oral and written information about the DNBC at the first antenatal care visit. If the mother chose to participate written consent was subsequently provided. The participating women were interviewed by telephone twice during pregnancy, and twice after pregnancy when the child was 6 months and 18 months old. Approximately half of the GPs in Denmark took part in the recruitment process, and 60% of invited mothers accepted, resulting in a participation rate of ~30% of all pregnant women during the period (Nohr et al., 2006). The cohort has been described in details elsewhere (Olsen et al., 2001).

### 2.2. Outcomes

Information on TTP was available from the first pregnancy interview. The women were asked if their pregnancy was planned and if it was they were given the following question: “For how long did you try to become pregnant before you succeeded?” The answer categories were: a). did not try to become pregnant; b) Became pregnant immediately; c) 1–2 months; d) 3–5 months; e) 6–12 months; and f) > 12 months. Women who did not plan their pregnancy were excluded, since they did not have a TTP. Women who answered “Became pregnant immediately” or “1–2 months” were combined and categorized as having a TTP of 0–2 months. If the woman had a TTP  $\geq$  6 months she was asked whether she received fertility treatment and women who answered yes were categorized as having a TTP  $\geq$  12 months. TTP was analyzed in four categories: 0–2; 3–5; 6–12 and > 12 months and as two dichotomous outcomes with cut-points at TTP of 6 and 12 months, respectively. The cut-points reflect common definitions of subfertility (> 6 months TTP) and infertility (> 12 months TTP) (Gnoth et al., 2005).

### 2.3. Exposure assessment

Residential address history was collected for all cohort members from one year prior to conception until conception by linkage with the Danish civil registration system using the unique personal identification number (Pedersen, 2011). Exposure periods were generated using date of last menstruation together with information on TTP. If a mother had a TTP of 0–2 months, the exposure period for that mother was from 2 months prior to conception until conception. Likewise, if a mother had a TTP of 3–5 months, the exposure period was 5 months prior to conception until conception. A mother with a TTP of 6–12 months, was given an exposure period was set to 12 months prior to conception until conception. Similarly, if a mother had a TTP of > 12 months, her exposure period was 12 months prior to conception until conception, since we did not have information regarding exposure prior to this period. Residential exposure to road traffic noise was modelled using SoundPLAN ([www.soundplan.dk](http://www.soundplan.dk)), which implements the joint Nordic

prediction method for road traffic noise (Bendtsen, 1999). Equivalent noise levels were estimated for each address at the most exposed facade of the building using the following input variables: point for noise estimation (geographical coordinate and height (floor) for each residential address), building polygons for all Danish buildings (provided by the Danish Geodata Agency) and information about road links (information on annual average daily traffic, vehicle distribution, travel speed, and road type) from a national road and traffic database (Jensen et al., 2001). Traffic data was included from different sources on a ranked basis: 1) Traffic data for municipal roads, represents the period from 1995 to 1998. 2) Traffic data from a central database covering all the major state and county roads with information from 1995. 3) Traffic data for 1995–2000 for all major roads in the Greater Copenhagen Area. 4) Smoothed traffic data for 1995 for all roads based on a simple method where estimated figures for distribution of traffic by road type and by urban/rural zone were applied to the road network and subsequently calibrated against known traffic data at county level. New roads were included in the calculations from the year they opened. Road traffic noise was calculated as the equivalent continuous A-weighted sound pressure level ( $L_{Aeq}$ ) 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 5 and 10 dB penalty was added to evening and night noise respectively. For each participant we calculated time-weighted exposures taking into account all of the addresses the participants had inhabited during the relevant exposure period prior to conception, weighted by the time the participant had lived at each address. No information was available on noise barriers and 40 dB was set as a lower realistic limit for ambient noise.

### 2.4. Air pollution

Air pollution is an important potential confounder when investigating health effects of road traffic noise. The Danish AirGIS dispersion modeling system was used for calculating the concentration of nitrogen oxides ( $NO_x$ ) for the same TTP periods as for road traffic noise (2 months, 5 months and 12 months prior to conception until conception depending on the mothers' answers regarding TTP). AirGIS has been described in details elsewhere (Jensen et al., 2001). Briefly, input data for the AirGIS system included traffic data for individual road links (same input data as described for the noise modeling), emission factors for the Danish car fleet, street and building geometry, building height, and meteorological data. The AirGIS system has been applied in several studies and validated showing good performance in reproducing both temporal and geographical variation (Ketznel et al., 2011).

### 2.5. Statistical methods

The association between traffic noise and TTP was analyzed using ordinal logistic regression models for TTP in four categories and logistic regression models for dichotomous outcomes. We analyzed road traffic noise exposure both as a continuous and a categorical variable (< 55, 55–60, 60–65 and > 65 dB). Linearity trends of noise exposure were tested by fitting models including a quadratic term of the exposure. The tests were non-significant for all models ( $p > 0.05$ ) and we chose to use the non-transformed exposure variable. We included three models with increasing levels of adjustment, one crude model and two (model II and III) with adjustment for potential confounders. Potential confounders were chosen a priori and their selection was guided by directed acyclic graphs (DAG) (Greenland et al., 1999) if they were thought to potentially be associated with the exposure and outcome (see Supplemental Fig. S1). The use of DAGs suggested a model adjusted for socio economic position, maternal age and air pollution ( $NO_x$ ) (model II). Additionally we included a model adjusting for lifestyle risk factors of decreased fecundity: maternal BMI prior to pregnancy, maternal smoking (yes or no at 12 weeks pregnant), maternal alcohol

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