**Multi-air pollutant exposure and amyotrophic lateral sclerosis (ALS) diagnosis in Denmark using Bayesian Hierarchical Regression Modelling**

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**Abstract**

**Background:** Amyotrophic lateral sclerosis (ALS) is a devastating and fatal neurodegenerative disease, with approximately half of patients dying within three years of symptom onset. Its aetiology remains elusive and known inherited mutated genes only account for 5–10% of the cases. There is some limited evidence to suggest ALS onset is associated with exposure to air pollution, and specifically to traffic-related pollution. However, previous smaller studies have only examined the association with relevant pollutants in separate models.

**Methods:** We used prospectively collected data from the Danish National Registers system from 4,011 ALS cases diagnosed between 1989 – 2013 and matched on age, sex, and vital status to 20,055 controls. We used predictions from a validated spatio-temporal model to assign 5-year average exposures prior to diagnosis to nitrogen oxides (NOx), carbon monoxide (CO), elemental carbon (EC), fine particles (PM2*.*5), and ozone (O3) at residential addresses of study participants. We used Bayesian Hierarchical Regression Modelling (BHRM) in a conditional logistic model to assess whether exposure to traffic- and non-traffic-related pollution is associated with ALS diagnosis, adjusting for potential confounders.

**Results:** We found that for a standard deviation (SD) increase in 5-year average concentrations, the joint effect of included traffic-related pollutants (NOx, CO, EC) was associated with an increase in odds of ALS diagnosis (XX%; 95% credible interval [CrI]:XX, XX%), with an increase in odds for elemental carbon (SD=XX µg/m3) (XX%; 95%CrI: -XX%, XX%). Overall, there was a XX% posterior probability of a positive association between the joint effect of included traffic-related pollutants and ALS diagnosis.

**Conclusions:** Our results indicate a potential positive association between ALS diagnosis and traffic-related pollution. Further work is needed to understand the role of air pollution on ALS pathogenesis and timing of onset.

**Introduction**

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**Methods**

*Data sources*

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*Statistical methods*

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We conducted statistical analyses using the R Statistical Software, version XX (Foundation for Statistical Computing, Vienna, Austria), and XX (STAN) in R-STAN, version XX. All code for analysis and visualization presented in this manuscript will be publicly available via GitHub.

**Results**

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**Discussion**

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**Contributions**

All authors contributed to study concept and interpretation of results. RMP, AB, YN and MAK organized case and control files, provided by JH. RMP, AB, YN and MAK organized the pollutant concentration data from the dataset provided by JH and MK. RMP and MAK developed the statistical model, which was implemented by RMP. RMP performed the analysis, with input from MAK. AB, YN, JH, ORN, MK, JK, MW, RV, SP and DBR assisted with interpretation of results. RMP and MAK wrote the first draft of the paper; all authors contributed to revising and finalizing the paper.

**Competing interests statement**

The authors declare no competing interests.

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**Figure 2.** XX

**Figure 3.** XX

**Figure 4**.XX

**Figure 5**. XX

**References**