# eAppendix

## Supplemental Methods

### *Exposure assessment*

Individual exposure to air pollution was assigned based on a methodology described by Hoek et al,[1] and further refined and described in detail by Beelen et al.[2] Long-term exposure to ambient $NO_2$, $PM_{2.5}$, black smoke and $SO_2$ was characterised as the sum of a regional, an urban and a local traffic component. The home addresses of the participants at baseline were geocoded into standard Dutch geographical coordinates (Address Coordinates Netherlands (ACN); unpublished data). Hourly ($NO_2$ and $SO_2$), and daily ($PM_{10}$ and black smoke) concentrations measured at regional background and urban sites of the National Air Quality Monitoring Network (NAQMN) were averaged for the year 2000. One black smoke monitoring site was excluded from the assessment as it exceeded the predefined cut-off of having more than 25% missing values. The regional component was estimated using inverse distance squared weighted interpolation.

To estimate the urban component for each of the four pollutants at the participants´ home addresses, separate regression models were developed using a manual forward selection process. The dependent variable was the monitoring site residual concentrations, calculated as the measured minus the interpolated regional concentrations. Potential predictor variables were determined for 300, 1000 and 5000-m buffers around each NAQMN monitoring station and each home address, and included the number of inhabitants (from a 1995 database), and 10 land cover variables from the 2000 CORINE database (Co-ordination of Information on the Environment, Copenhagen, Denmark). Estimated regional and urban concentrations were summed to obtain a distinct “background” exposure variable. Since $PM_{2.5}$ was not measured during 2000, $PM_{10}$ concentrations were converted into $PM_{2.5}$ concentrations using the formula $PM_{2.5} = 0.6739*PM_{10}–0.1038$ to allow overall $PM_{2.5}$ concentrations to be derived.[3]

Contributions from traffic on roads nearby to the home address were estimated for $NO_2$, $PM_{2.5}$ and black smoke by developing regression models based on traffic intensity data from two studies[4, 5] and GIS derived distances. $SO_2$ was not estimated since traffic is not a primary determinant of this pollutant. This local component was characterised as the sum of traffic intensities in a 100-m buffer

excluding motorway contributions, in addition to the added effect of truck traffic on motorways and distance to this motorway (<100 m and 100-300 m versus the reference, 300-500 m), for those participants living within 500 m of a motorway (n=66, 11%).[2]

A separate exposure assessment was performed to calculate background $NO_2$ and $SO_2$ concentrations for the childhood home addresses, making use of air pollution data and urban predictor data from the year 1978.

**References**


**1.** Hoek G, Fischer P, Van Den Brandt P, Goldbohm S, Brunekreef B. Estimation of long-term average exposure to outdoor air pollution for a cohort study on mortality. *J Expo Anal Environ Epidemiol.* 2001;11:459-469.

**2.** Beelen R, Hoek G, Fischer P, Brandt PAvd, Brunekreef B. Estimated long-term outdoor air pollution concentrations in a cohort study. *Atmos Environ.* 2007;41:1343-1358.

**3.** Cyrys J, Heinrich J, Hoek G, Meliefste K, Lewné M, Gehring U, Bellander T, Fischer P, van Vliet P, Brauer M. Comparison between different traffic-related particle indicators: Elemental carbon (EC), PM 2.5 mass, and absorbance. *J Expo Anal Env Epidemiol.* 2003;13:134-143.

**4.** Janssen N, van Vliet P, Aarts F, Harssema H, Brunekreef B. Assessment of exposure to traffic related air pollution of children attending schools near motorways. *Atmos Environ.* 2001;35:3875-3884.

**5.** Brauer M, Hoek G, van Vliet P, Meliefste K, Fischer P, Gehring U, Heinrich J, Cyrys J, Bellander T, Lewne M. Estimating Long-Term Average Particulate Air Pollution Concentrations: Application of Traffic Indicators and Geographic Information Systems. *Epidemiology.* 2003;14:228-239.

eTable 1: Correlations between overall air pollution exposure estimates per pollutant in 2000 (n=745)

| | BS | $PM_{2.5}$ | $SO_2$ |
|---|---|---|---|
| $NO_2$ | 0.59 | 0.70 | 0.09 |
| BS | | 0.84 | 0.10 |
| $PM_{2.5}$ | | | 0.12 |

eTable 2: Correlations between overall air pollution exposure estimates and traffic intensities in 2000 (n=745)

| | 100 m buffer | Nearest road | Nearest major road |
|---|---|---|---|
| $NO_2$ | 0.59 | -0.07 | -0.15 |
| BS | 0.94 | 0.04 | 0.05 |
| $PM_{2.5}$ | 0.86 | -0.04 | -0.26 |
| $SO_2$ | 0.06 | -0.06 | -0.03 |