

## Publication

## Long-term exposure to low-level ambient air pollution and incidence of stroke and coronary heart disease: a pooled analysis of six European cohorts within the ELAPSE project

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**BACKGROUND:** Long-term exposure to outdoor air pollution increases the risk of cardiovascular disease, but evidence is unclear on the health effects of exposure to pollutant concentrations lower than current EU and US standards and WHO guideline limits. Within the multicentre study Effects of Low-Level Air Pollution: A Study in Europe (ELAPSE), we investigated the associations of long-term exposures to fine particulate matter (PM<sub>2.5</sub>), nitrogen dioxide (NO<sub>2</sub>), black carbon, and warm-season ozone (O<sub>3</sub>) with the incidence of stroke and acute coronary heart disease. **METHODS:** We did a pooled analysis of individual data from six population-based cohort studies within ELAPSE, from Sweden, Denmark, the Netherlands, and Germany (recruited 1992-2004), and harmonised individual and area-level variables between cohorts. Participants (all adults) were followed up until migration from the study area, death, or incident stroke or coronary heart disease, or end of follow-up (2011-15). Mean 2010 air pollution concentrations from centrally developed European-wide land use regression models were assigned to participants' baseline residential addresses. We used Cox proportional hazards models with increasing levels of covariate adjustment to investigate the association of air pollution exposure with incidence of stroke and coronary heart disease. We assessed the shape of the concentration-response function and did subset analyses of participants living at pollutant concentrations lower than predefined values. **FINDINGS:** From the pooled ELAPSE cohorts, data on 137 148 participants were analysed in our fully adjusted model. During a median follow-up of 17.2 years (IQR 13.8-19.5), we observed 6950 incident events of stroke and 10 071 incident events of coronary heart disease. Incidence of stroke was associated with PM<sub>2.5</sub> (hazard ratio 1.10 [95% CI 1.01-1.21] per 5 µg/m<sup>3</sup> increase), NO<sub>2</sub> (1.08 [1.04-1.12] per 10 µg/m<sup>3</sup> increase), and black carbon (1.06 [1.02-1.10] per 0.5 10<sup>-5</sup>/m increase), whereas coronary heart disease incidence was only associated with NO<sub>2</sub> (1.04 [1.01-1.07]). Warm-season O<sub>3</sub>

was not associated with an increase in either outcome. Concentration-response curves indicated no evidence of a threshold below which air pollutant concentrations are not harmful for cardiovascular health. Effect estimates for PM<sub>2.5</sub> and NO<sub>2</sub> remained elevated even when restricting analyses to participants exposed to pollutant concentrations lower than the EU limit values of 25 µg/m<sup>3</sup> for PM<sub>2.5</sub> and 40 µg/m<sup>3</sup> for NO<sub>2</sub>. **INTERPRETATION:** Long-term air pollution exposure was associated with incidence of stroke and coronary heart disease, even at pollutant concentrations lower than current limit values. **FUNDING:** Health Effects Institute.

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