Ambient Air Pollution and Stroke

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Stroke is a leading cause of death in the United States and worldwide and may lead to considerable neurological sequelae including aphasia, paraplegia, and dementia. The estimated healthcare costs of stroke in the United States exceed $36 billion per year. A large body of evidence supports the association between ambient air pollution exposure and increased cardiovascular mortality and morbidity, but only recently have several studies specifically demonstrated an association with increased stroke risk.

Background

Major sources of air pollution include traffic, power plants, and in developing countries, biomass combustion. Both particles and gases are emitted through combustion. Particulate matter with aerodynamic diameter <10 μm (PM_{10}) include ultrafine particles (PM_{0.02}), fine particles (PM_{2.5}), and coarse particles (PM_{10,2.5}). Ultrafine particles are emitted in fresh exhaust and coalesce into PM_{2.5} within a short time frame. PM_{2.5} includes both local sources from traffic emissions and domestic heating and regional sources from power plants, biogenic emissions, and traffic, whereas coarse particles are a heterogeneous mixture that include road dust, endotoxins, and suspended crustal matter. CO, NO, NO_{2}, SO_{2}, and ground-level ozone (O_{3}) are gaseous pollutants emitted as a result of combustion processes. CO is mainly attributed to mobile sources in urban environments, and NO_{x} and NO_{2} are rapidly formed in emissions from combustion sources such as traffic and power plants. The main source of SO_{2} is from fossil fuel power plants. Ground-level O_{3} is formed as a result of atmospheric reactions of NO_{x} with hydrocarbons in the presence of sunlight and is a major constituent of photochemical smog. Several of the mentioned pollutants are regulated based on evidence of adverse health effects. Possible mechanistic pathways including induction of oxidative stress, inflammation, atherosclerosis, and autonomic dysregulation have been outlined in detail and are beyond the scope of the current review.

This review aims to assess the current evidence on the association of air pollution exposure with incidence of ischemic and hemorrhagic stroke considering long-term and short-term exposure to ambient pollutants.

Long-Term Air Pollution Exposure

Most studies of long-term exposure to air pollution and stroke outcomes have used estimates of exposure at residential address in months to years as a proxy for long-term accumulated individual exposure. Exposure has then been assessed using residential distance to major roadways, measurements from closest available fixed monitor, or advanced modeling of pollutants combining fixed monitoring measurements with land-use data, emissions databases, traffic density counts, and meteorology incorporated into geographical information systems. These geographical information system models can also include population-based data such as average income level and average smoking prevalence.

Long-Term Air Pollution Exposure and Stroke Mortality

Studies considering long-term exposure to air pollution and stroke mortality have reported that living in areas with higher ambient pollution is associated with higher risk of stroke mortality (Table 1). Studies from the United Kingdom and Northwest Florida contained large administrative databases with cause of death, residence, sex, and area-based data such as socioeconomic status, urbanization, smoking prevalence, and greenness. Living near a main road, traffic sources, point sources of emissions, or higher modeled exposure to PM_{2.5}, CO, and NO_{2} were all associated with stroke mortality. Several cohort studies have also studied the association between long-term exposure to air pollution and stroke mortality. These studies have more detailed individual-level data that improve the ability to adjust for potential confounders that may influence the place of residence and the risk of stroke mortality. Strongest associations were reported in the prospective Women’s Health Initiative cohort that included well-validated outcome assessment. In the Californian residents of the American Cancer Society cohort study, associations were reported for NO_{2} and any stroke mortality and borderline significant associations for PM_{10}. In the California Teachers Study, however, higher long-term PM_{2.5} exposure was not associated with cerebrovascular mortality. In 232 rural districts of Japan, including 250 stroke

**Table 1.** Studies from the United Kingdom and Northwest Florida.

| Study | Country | Exposure Assessment | Findings |
|-------|---------|---------------------|----------|
| UK    | Regional | Residential distance | PM_{2.5}, CO, NO_{2} associated with stroke mortality |
| NC    | Administrative | Land-use data | PM_{2.5}, CO, NO_{2} associated with stroke mortality |

**Table 2.** Studies from the United States.

| Study | Region | Exposure Assessment | Findings |
|-------|--------|---------------------|----------|
| CA    | Rural  | Residential distance | PM_{2.5} not associated with cerebrovascular mortality |

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deaths, higher long-term PM\(_{10}\) exposure was not associated with stroke mortality. Specific characterization of stroke into types and subtypes was available in 2 studies: in Shizuoka, Japan\(^{13}\) and in Denmark. \(^8\) Yorifuji et al\(^{13}\) reported associations between NO\(_2\) and mortality from ischemic stroke and intracerebral hemorrhage but not subarachnoid hemorrhage. Andersen et al\(^{8}\) reported borderline significant associations between long-term NO\(_2\) exposure and ischemic stroke but not hemorrhagic strokes and did not further subtype hemorrhagic strokes.

Long-Term Air Pollution Exposure and Hospitalization for Stroke

In studies of long-term exposure to air pollution and hospitalization for stroke, higher exposure at home addresses was also associated with higher risk of admission for stroke in some studies, but results were less consistent than for stroke mortality (Table 2). Most commonly reported pollutants included long-term exposure to PM\(_{2.5}\) and PM\(_{10}\), and NO\(_2\) or NO\(_x\). Many of the cohort studies reported positive associations, whereas ecological studies\(^{6,15,19}\) and case–control studies\(^{17,18,21}\) showed mixed results. In a random-effects meta-analysis of 11 European cohorts,\(^{16}\) long-term PM\(_{2.5}\) was associated more strongly with stroke in subjects >60 years old, never-smokers, and among subjects with exposure levels <25 μg/m\(^3\) (current annual mean air quality standard in Europe). Studies that compared long-term air pollution exposure and hospital admissions according to specific stroke type reported positive associations for NO\(_2\), CO, and traffic density and admissions for both ischemic and hemorrhagic stroke\(^{19}\) in Edmonton, Canada, whereas NO\(_2\) in Denmark or NO\(_x\) in London, UK, demonstrated associations consistent with ischemic stroke but not hemorrhagic stroke. Two studies from Scania, Sweden\(^{7,14}\) only including hospital admissions for ischemic stroke observed associations between higher long-term exposure to NO\(_2\) and higher risk of hospital admission for ischemic stroke in participants with diabetes mellitus but found no association in the overall population, in smokers, or in participants with hypertension or atrial fibrillation. A recent population-based cohort study in Denmark studying long-term NO\(_2\) and traffic noise exposure and stroke incidence reported positive associations for ischemic stroke in separate analyses for both noise and NO\(_2\), but in combined analyses NO\(_2\) was only associated with fatal ischemic strokes.\(^{20}\)

**Short-Term Air Pollution Exposure**

Day-to-day differences in air pollution exposure in the days preceding stroke are used to study possible triggering effects of air pollution on stroke. In time-series analyses, daily counts of stroke deaths or admissions are compared with air pollution levels on the same day or preceding days in a study region. In case-crossover analyses, exposure levels preceding stroke mortality or hospitalization in an individual are contrasted with control periods within the same calendar month within each individual controlling for season and day of week and perfectly matching time-invariant patient characteristics by design.

**Table 1. Studies of Long-Term Air Pollution Exposure and Stroke Mortality**

| Study                        | Location            | Study Design | Stroke Outcome | Relative Risk (95% Confidence Intervals) | Exposure                                                                 |
|------------------------------|---------------------|--------------|----------------|------------------------------------------|---------------------------------------------------------------------------|
| Maheswaran and Elliott\(^4\) | England and Wales   | Ecological   | Any stroke     | 1.05 (1.04–1.07)                          | Living within 200 m of main road compared with ≥1000 m                   |
| Maheswaran et al\(^6\)       | Sheffield, UK       | Ecological   | Any stroke     | 1.37 (1.19–1.57) PM\(_{10}\)              | Highest to lowest quintile of modeled pollutant                           |
|                              |                     |              |                | 1.26 (1.10–1.46) CO                        |                                                                            |
|                              |                     |              |                | 1.33 (1.14–1.56) NO\(_2\)                 |                                                                            |
| Hu et al\(^7\)               | Florida, USA        | Ecological   | Any stroke     | 1.09 (1.03–1.15)*                          | Per 10 000 vehicles/d within census tract                                  |
| Andersen et al\(^8\)         | Denmark             | Cohort       | Any stroke     | 1.22 (1.00–1.50)                           | Per interquartile range increase (43%) in mean modeled NO\(_2\) since 1971 |
|                              |                     |              | Ischemic       | 1.46 (0.90–2.39)                           |                                                                            |
|                              |                     |              | Hemorrhagic    | 1.00 (0.76–1.31)                           |                                                                            |
| Jerrett et al\(^9\)          | California, USA     | Cohort       | Any stroke     | 1.07 (0.99–1.15) PM\(_{2.5}\)              | Per 5.3 μg/m\(^3\) PM\(_{10}\)                                           |
|                              |                     |              |                | 1.08 (1.02–1.15) NO\(_2\)                 | Per 4.12 ppb NO\(_2\)                                                    |
|                              |                     |              |                | 1.01 (0.92–1.11) O\(_3\)                  | Per 24.2 ppb O\(_3\)                                                    |
| Lipsett et al\(^10\)         | California, USA     | Cohort       | Any stroke     | 0.99 (0.89–1.09) PM\(_{10}\)              | Per 10 μg/m\(^3\) mean PM\(_{10}\) 1996–2005 or mean PM\(_{2.5}\) 1999–2005 |
|                              |                     |              |                | 1.16 (0.92–1.46) PM\(_{2.5}\)             |                                                                            |
| Miller et al\(^11\)          | 36 US cities        | Cohort       | Any stroke     | 1.83 (1.11–3.00) PM\(_{2.5}\)             | Annual mean in 2000 at closest monitor per 10 μg/m\(^3\)                 |
| Ueda et al\(^12\)            | Japan               | Cohort       | Any stroke     | 0.86 (0.74–1.01) PM\(_{10}\)              | Per 10 μg/m\(^3\) annual mean at closest monitor                         |
| Yorifuji et al\(^13\)        | Shizuoka, Japan     | Cohort       | Any stroke     | 1.19 (1.06–1.34) PM\(_{2.5}\)             | Per 10 μg/m\(^3\) annual mean NO\(_2\)                                   |
|                              |                     |              | Ischemic       | 1.20 (1.04–1.39)                           |                                                                            |
|                              |                     |              | Hemorrhagic    | 1.28 (1.05–1.57)                           |                                                                            |

PM\(_{10}\) indicates particles with aerodynamic diameter ≤10 μm; PM\(_{2.5}\), fine particles with aerodynamic diameter ≤2.5 μm; and ppb, parts per billion.

*95% credible interval from a Bayesian analysis.
Table 2. Studies of Long-Term Air Pollution Exposure and Hospitalization for Stroke

| Study               | Location          | Study Design | Stroke Outcome | Relative Risk (95% Confidence Intervals) | Exposure                                      |
|---------------------|-------------------|--------------|----------------|-------------------------------------------|------------------------------------------------|
| Maheswaran et al6   | Sheffield, UK     | Ecological   | Any stroke     | 1.13 (0.99–1.29) PM$_{10}$                | Highest to lowest quintile of modeled pollutant |
|                     |                   |              |                | 1.11 (0.99–1.25) CO                        | Per interquartile range increase (43%) in mean modeled NO$_2$ since 1971 |
|                     |                   |              |                | 1.13 (1.04–1.27) NO$_x$                    |                                                |
| Andersen et al8     | Denmark           | Cohort       | Any stroke     | 1.05 (0.99–1.11)                            | Per 10 μg/m$^3$ annual mean pollutant at closest monitor |
|                     |                   |              | Ischemic       | 1.05 (0.95–1.17)                            |                                                |
|                     |                   |              | Hemorrhagic    | 0.93 (0.81–1.07)                            |                                                |
| Lipsett et al10     | California        | Cohort       | Any stroke     | 1.06 (1.00–1.13) PM$_{10}$                  | Per 10 μg/m$^3$ annual mean pollutant of modeled pollutant exposure |
|                     |                   |              |                | 1.14 (0.99–1.32) PM$_{2.5}$                |                                                |
| Miller et al11      | 36 US cities      | Cohort       | Any stroke     | 1.28 (1.01–1.61) PM$_{2.5}$                | Per 10 μg/m$^3$ mean of closest monitor during 2000 |
| Maheswaran et al15  | London, UK        | Ecological   | Ischemic       | 1.22 (0.77–1.93) PM$_{10}$                  | Per 10 μg/m$^3$ annual mean pollutant exposure |
|                     |                   |              | Hemorrhagic    | 1.11 (0.93–1.32) NO$_2$                    |                                                |
|                     |                   |              |                | 0.52 (0.20–1.37) PM$_{10}$                 |                                                |
|                     |                   |              |                | 0.86 (0.60–1.24) NO$_2$                    |                                                |
| Atkinson et al14    | England           | Cohort       | Any stroke     | 0.98 (0.95–1.01) PM$_{10}$                  | Per 3.0 μg/m$^3$ PM$_{10}$                     |
|                     |                   |              | Ischemic       | 0.99 (0.95–1.03) NO$_2$                    | Per 10.7 μg/m$^3$ NO$_2$                       |
|                     |                   |              | Hemorrhagic    | 1.02 (1.00–1.05) SO$_2$                    | Per 2.2 μg/m$^3$ SO$_2$                       |
|                     |                   |              |                | 1.00 (0.97–1.04) O$_3$                     | Per 3.0 μg/m$^3$ O$_3$, modeled annual mean   |
| Stafoggia et al16   | 11 cohorts, Europe| Cohort       | Any stroke     | 1.19 (0.88–1.62)                            | Per 5 μg/m$^3$ annual mean                     |
| Oudin et al17       | Scania, Sweden    | Case–control | Ischemic       | 0.99 (0.86–1.06)                            | Annual mean modeled NO$_x$ of 20–30 vs <10 μg/m$^3$ |
|                     |                   |              | Hemorrhagic    | 1.20 (1.09–1.32)                            |                                                |
| Oudin et al18       | Scania, Sweden    | Case–control | Ischemic       | 2.0 (1.2–3.4) high NO$_x$                   | High NO$_x$ ≥25 μg/m$^3$                       |
|                     |                   |              |                | 1.3 (1.1–1.6) low NO$_x$                   | Low NO$_x$ <15 μg/m$^3$                       |
|                     |                   |              | In diabetics:  | 2.0 (1.2–3.4) high NO$_x$                   | Reference: nondiabetics with low NO$_x$        |
|                     |                   |              | Modeled annual NO$_x$: | 1.3 (1.1–1.6) low NO$_x$                   |                                                |
| Johnson et al19     | Edmonton, Canada  | Ecological   | Any stroke     | 1.29 (1.16–1.43)                            | Highest (16.7–20.3 ppb) to lowest quintile (10.1–14.0 ppb) of NO$_2$ exposure |
|                     |                   |              | Nonhemorrhagic | 1.36 (1.19–1.56)                            |                                                |
|                     |                   |              | Hemorrhagic    | 1.46 (1.19–1.80)                            |                                                |
| Sørensen et al20    | Denmark           | Cohort       | Any stroke     | 1.08 (1.01–1.16)                            | Per 10 μg/m$^3$ annual mean NO$_2$             |
|                     |                   |              | Ischemic       | 1.11 (1.03–1.20)                            |                                                |
|                     |                   |              | Hemorrhagic    | 1.00 (0.80–1.24)                            |                                                |
| Johnson et al21     | Edmonton, Canada  | Case–control | Any stroke     | 1.01 (0.94–1.08)                            | Per 5 ppb NO$_2$                              |
|                     |                   |              | Ischemic       | 1.03 (0.94–1.13)                            |                                                |
|                     |                   |              | TIA            | 0.95 (0.86–1.05)                            |                                                |
|                     |                   |              | Hemorrhagic    | 1.07 (0.92–1.24)                            |                                                |

PM$_{10}$ indicates particles with aerodynamic diameter ≤10 μm; PM$_{2.5}$, fine particles with aerodynamic diameter ≤2.5 μm; ppb, parts per billion; and TIA, transient ischemic attack.
Several studies have investigated associations between short-term exposure to air pollutants including PM$_{10}$, PM$_{2.5}$, CO, NO$_2$, SO$_2$, and O$_3$ and stroke mortality or hospitalizations for stroke in many cities in North America, Europe, and East Asia. Mean levels of pollutants varied considerably between study locations from low-polluted cities such as Dijon, France (daily mean PM$_{10}$ 20 μg/m$^3$) to highly polluted cities such as Wuhan, China (daily mean PM$_{10}$ 119 μg/m$^3$).

**Short-Term Air Pollution Exposure and Stroke Mortality**

A majority of studies investigating short-term exposure to air pollution and stroke mortality have been time-series studies,$^{22–36}$ the remainder used case-crossover design.$^{37–41}$ A qualitative summary of the studies is provided in Table 3 (for detailed estimates, see Table I in the online-only Data Supplement). Most studies do not differentiate between ischemic and hemorrhagic stroke mortality. Several studies reported associations between short-term exposure to particle matter, including several size fractions, or gases and any stroke mortality. Only a few studies further characterized stroke into ischemic and hemorrhagic stroke mortality.$^{24,33–35,38}$ Short-term exposure to particulate matter and gases was associated with both ischemic stroke and hemorrhagic stroke. In Tokyo,$^{34}$ the risk increase for subarachnoid hemorrhage mortality per 10 μg/m$^3$ PM$_{2.5}$ or NO$_2$ was roughly double the risk increase for ischemic or intracerebral

### Table 3. Studies of Short-Term Air Pollution Exposure and Stroke Mortality

| Study | Location | Study Design | Stroke Outcome | Positive Associations* | Null Associations† |
|-------|----------|--------------|----------------|------------------------|-------------------|
| Chen et al$^{22}$ | 8 Chinese cities | Time series | Any stroke | PM$_{10}$, NO$_2$, and SO$_2$ | ... |
| Hoek et al$^{23}$ | Netherlands | Time series | Any stroke | Black smoke, CO, SO$_2$, and O$_3$ | PM$_{10}$ and NO$_2$ |
| Hong et al$^{24}$ | Seoul, Korea | Time series | Ischemic | TSP, CO, NO$_2$, SO$_2$, and O$_3$ | ... |
| Hong et al$^{25}$ | Seoul, Korea | Time series | Hemorrhagic | TSP | CO$_2$, NO$_2$, SO$_2$, and O$_3$ |
| Kan et al$^{26}$ | Shanghai, China | Time series | Any stroke | PM$_{10}$, CO, NO$_2$, SO$_2$, and O$_3$ | ... |
| Kettunen et al$^{27}$ | Helsinki, Finland | Time series | Any stroke | PM$_{2.5}$ and CO in warm season | PM$_{10}$, coarse PM, PM$_{10}$, NO$_2$, and O$_3$ in warm season. |
| Li et al$^{28}$ | Tianjin, Taiwan | Time series | Any stroke | PM$_{10}$ on days with >20°C | PM$_{10}$ on days with ≤20°C |
| Qian et al$^{29}$ | Wuhan, China | Time series | Any stroke | PM$_{10}$ | ... |
| Qian et al$^{30}$ | Wuhan, China | Time series | Any stroke | NO$_2$, SO$_2$, and O$_3$ | ... |
| Qian et al$^{31}$ | Wuhan, China | Time series | Any stroke | PM$_{10}$ all days and NO$_2$, SO$_2$ on normal temperature days | O$_3$ all days and NO$_2$, SO$_2$ on high temperature days |
| Qian et al$^{32}$ | Wuhan, China | Time series | Any stroke | NO$_2$ in spring, PM$_{10}$, NO$_2$, SO$_2$ in winter | PM$_{10}$ and SO$_2$ in spring. All pollutants summer or fall |
| Turin et al$^{33}$ | Takashima, Japan | Time series | Any stroke | Ischemic NO$_2$ | Suspended PM, NO$_2$, SO$_2$, and O$_3$ |
| Yorifuji et al$^{34}$ | Tokyo, Japan | Time series | Any stroke | Ischemic PM$_{2.5}$ and NO$_2$ | Suspended PM, NO$_2$, SO$_2$, and O$_3$ |
| Yorifuji and Kashima$^{35}$ | 47 Japanese cities | Time series | Any stroke | Ischemic PM$_{10}$ | Suspended PM, NO$_2$, SO$_2$, and O$_3$ |
| Zanobetti and Schwartz$^{36}$ | 112 US cities | Time series | Any stroke | PM$_{2.5}$ and PM$_{coarse}$ | Suspended PM, NO$_2$, SO$_2$, and O$_3$ |
| Maynard et al$^{37}$ | Massachusetts, USA | Case crossover | Any stroke | Black carbon | SO$_2$ |
| Qian et al$^{38}$ | Shanghai, China | Case crossover | Any stroke | PM$_{10}$, NO$_2$, and SO$_2$ | ... |
| Ren et al$^{39}$ | Massachusetts, USA | Case crossover | Any stroke | PM$_{10}$ | ... |
| Zeka et al$^{40}$ | 20 US cities | Case crossover | Any stroke | PM$_{10}$ | ... |
| Zeka et al$^{41}$ | 20 US cities | Case crossover | Any stroke | PM$_{10}$ if pneumonia or ≥75-y old | PM$_{10}$ if no pneumonia or ≤75-y old |

PM$_{0.1}$ indicates ultrafine particles with <0.1 μm aerodynamic diameter; PM$_{10}$, particles with aerodynamic diameter ≤10 μm; PM$_{2.5}$, fine particles with aerodynamic diameter ≤2.5 μm; PM$_{coarse}$, coarse particles with aerodynamic diameter between 2.5 and 10 μm in aerodynamic diameter; and TSP, total suspended particles.

*Positive associations with confidence intervals not including the null.
†Associations with confidence intervals including the null.
### Table 4. Studies of Short-Term Exposure to Air Pollution and Hospital Admissions for Stroke

| Study | Location          | Study Design | Stroke Outcome | Positive Associations* | Null Associations† |
|-------|-------------------|--------------|----------------|------------------------|-------------------|
| Ballester et al43 | Valencia, Spain   | Time series  | Any stroke     | CO, SO₂ and O₃         |                   |
| Burnett et al44   | Toronto, Canada   | Time series  | Any stroke     | PM₁₀, PM₂·₅, and O₃    |                   |
| Chan et al45      | Taipei, Taiwan    | Time series  | Any stroke     | PM₁₀, PM₂·₅, CO, NO₂, and SO₂ |                   |
|                   |                   |              | Ischemic       | PM₁₀, PM₂·₅, CO, NO₂, SO₂, and O₃ |                   |
|                   |                   |              | Hemorrhagic    | PM₁₀, PM₂·₅, CO, NO₂, SO₂, and O₃ |                   |
| Corea et al46     | Mantua, Italy     | Case crossover | Any stroke | PM₃₂·₅, in all ischemic, large vessel, small vessel, and lacunar | PM₃₂·₅, in cardioembolic, CO, NO₂, SO₂, and O₃ |
| Jalaludin et al47 | Sydney, Australia | Time series  | Any stroke     | PM₁₀, PM₂·₅, CO, NO₂, SO₂, and O₃ |                   |
| Larrieu et al48   | 8 French cities   | Time series  | Any stroke     | PM₁₀, NO₂, and O₃      |                   |
| Le Tertre et al49 | 8 European cities | Time series  | Any stroke     | PM₁₀ and black smoke   |                   |
| Linn et al50      | Los Angeles, USA  | Time series  | Any stroke     | CO and NO₂ in spring   |                   |
| Moolgavkar51      | Los Angeles, USA  | Time series  | Any stroke     | PM₁₀, CO, NO₂, and SO₂ |                   |
| Nascimento et al52| Sao Jose Campos, Brazil | Time series | Any stroke | PM₃₂·₅, CO, NO₂, and SO₂ |                   |
| Poloniecki et al53| London, UK        | Time series  | Any stroke     | Black smoke, CO, NO₂, SO₂, and O₃ |                   |
| Pönkä and Virtanen54| Helsinki, Finland| Time series  | Any stroke     | NO₂                     |                   |
| Suryer et al55    | 7 European cities | Time series  | Any stroke     | SO₂                     |                   |
| Turin et al56     | Takashima, Japan  | Time series  | Any stroke     | PM₁₀, NO₂, SO₂, and O₃ |                   |
|                   |                   |              | Ischemic       | PM₁₀, NO₂, SO₂, and O₃ |                   |
|                   |                   |              | Hemorrhagic    | PM₁₀, SO₂               |                   |
| Villeneuve et al57| Edmonton, Canada  | Case crossover | Any stroke | PM₁₀, PM₂·₅, CO, NO₂, and SO₂ |                   |
|                   |                   |              | Ischemic       | PM₂·₅, CO, NO₂, SO₂, and O₃ |                   |
|                   |                   |              | TIA            | PM₁₀, PM₂·₅, CO, NO₂, SO₂, and O₃ |                   |
|                   |                   |              | Hemorrhagic    | PM₁₀, SO₂               |                   |
| Villeneuve et al58| Edmonton, Canada  | Case crossover | Any stroke | CO in warm season PM₂·₅, NO₂, SO₂, O₃, and CO all year |                   |
|                   |                   |              | Ischemic       | PM₂·₅, CO, NO₂, and SO₂ |                   |
|                   |                   |              | Hemorrhagic    | PM₂·₅, CO, NO₂, and SO₂ |                   |
| Wong et al59      | Hong Kong, China  | Time series  | Any stroke     | PM₁₀, PM₂·₅, NO₂, SO₂, and O₃ |                   |
| Wordley et al60   | Birmingham, UK    | Time series  | Any stroke     | PM₁₀, PM₂·₅, NO₂, SO₂, and O₃ |                   |
| Xiang et al61     | Wuhan, China      | Case crossover | Any stroke | PM₁₀ and NO₂ in cold season PM₁₀, NO₂ and SO₂ all year and in subtypes. PM₃₂·₅ and NO₂ in warm season |                   |
| Xu et al62        | Allegheny, USA    | Case crossover | Any stroke | O₃                     |                   |
| Yang et al63      | Taipei, Taiwan    | Time series  | Any stroke     | O₃                     |                   |
| Yang et al63      | Taipei, Taiwan    | Time series  | Hemorrhagic    | O₃                     |                   |
| Tsai et al64      | Kaohsiung, Taiwan | Case crossover | Ischemic | PM₁₀, NO₂, SO₂, O₃ warm days, CO all days |                   |
|                   |                   |              | Hemorrhagic    | Asian dust and intracerebral Asian dust and subarachnoidal |                   |
| Wellenius et al65 | 9 US cities       | Case crossover | Ischemic | PM₁₀, CO, NO₂, and O₃ warm days, SO₂ warm days, all pollutants cool days |                   |
| Wellenius et al65 | 9 US cities       | Case crossover | Hemorrhagic | PM₁₀, CO, NO₂, and SO₂ |                   |
| Wellenius et al65 | 9 US cities       | Case crossover | Hemorrhagic | PM₁₀, CO, NO₂, and SO₂ |                   |
| Lisabeth et al66  | Corpus Christi, USA| Time series  | Ischemic       | PM₂·₅ in diabetics and noncardioembolic |                   |
| O’Donnell et al67 | 8 Canadian cities | Case crossover | Ischemic | PM₂·₅ in ischemic strokes overall |                   |

(Continued)
hemorrhage mortality. It is possible that these hemorrhages may have more precise temporal relationship between air pollution exposure and the timing of stroke onset leading to less exposure misclassification and more precise estimation of the association.41 Stronger associations between short-term air pollution exposure and stroke mortality were observed in elderly,23,30 women,25 and individuals with a history of diabetes mellitus41 or cardiac disease38 in some but not all studies.

**Short-Term Air Pollution Exposure and Hospitalization for Stroke**

Studies of short-term air pollution exposure and hospitalization for any stroke have reported mixed results.43–61 However, in contrast to studies investigating short-term exposure to air pollution and stroke mortality that typically use death certificate data, some studies of associations with hospital admissions for stroke have had more data on stroke type. These studies have reported associations between PM<sub>0.1</sub>62,69,70 and ischemic stroke.46,67–69 Stronger associations were reported for recurrent ischemic strokes or history of stroke,58,70 in individuals with diabetes mellitus or on diabetes mellitus medication62,70 and with ≥1 cardiovascular risk factors.69,70 A few studies reported stronger associations between O<sub>3</sub> and ischemic stroke in men than in women.52,69,72 Air pollution on warm days was more strongly associated with both hemorrhagic and ischemic stroke in Taiwan.64 Associations between air pollution and ischemic stroke were stronger in the warm season in Edmonton, Canada58 and Dijon, France30 in contrast to Wuhan41 where associations were stronger in the cold season. Differences may reflect better exposure classification because of time spent outdoors in climates such as Edmonton, Canada but may also be because of seasonal interactions between pollutants.

**Summary**

The current evidence suggests that exposure to higher levels of air pollutants related to combustion increases the risk of stroke. Studies of both long-term and short-term air pollution exposure suggest consistent evidence of increased risk of ischemic stroke and moderately consistent evidence supporting an association with hemorrhagic stroke. A few studies exploring susceptible subgroups have indicated stronger associations in individuals with several cardiovascular risk factors, diabetes mellitus, previous stroke, and of older age. A recently published meta-analysis focusing on short-term air pollution exposure and stroke incidence or mortality reported significant associations for PM<sub>10</sub>, PM<sub>2.5</sub>, SO<sub>2</sub>, CO, NO<sub>2</sub>, and O<sub>3</sub> for stroke with stronger associations for ischemic stroke.73

Because much of the existing literature is based on linkage of administrative data, an important limitation of many available studies is limited ability to classify and validate specific stroke outcomes. Ischemic stroke and hemorrhagic stroke and their subtypes have in the majority of studies been analyzed differently. Only some have separately analyzed ischemic stroke and hemorrhagic stroke and a handful have considered subtypes of ischemic stroke or hemorrhagic stroke similarly. Only a handful used thorough chart reviews and adjudicated the diagnosis and onset time of stroke. This highlights the need for high-quality validated diagnostic characterization of stroke outcome in studies of air pollution. In a study of short-term air pollution exposure and stroke specifically investigating the bias introduced through misclassification of time of event of stroke found that incorrect temporal classification caused up to 66% bias toward the null.42 This may be especially relevant in mortality studies where the date of death from death certificates is used while not accounting for the

### Table 4. Continued

| Study          | Location | Study Design | Stroke Outcome | Positive Associations* | Null Associations† |
|----------------|----------|--------------|----------------|------------------------|--------------------|
| Bedada et al<sup>72</sup> | UK       | Case crossover | Minor stroke   | NO<sub>2</sub> | CO<sub>2</sub>, NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub> |
| Wellenius et al<sup>68</sup> | Boston, USA | Case crossover | Ischemic       | PM<sub>2.5</sub>, black carbon, NO<sub>2</sub>, and PM<sub>10</sub> large and small vessel stroke | CO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub>, and PM<sub>2.5</sub> cardioembolic stroke |
| Henrotin et al<sup>69</sup> | Dijon, France | Case crossover | Ischemic       | O<sub>3</sub> in all ischemic, large vessel, and TIA | PM<sub>10</sub>, CO, NO<sub>2</sub>, and SO<sub>2</sub> |
| Henrotin et al<sup>70</sup> | Dijon, France | Case crossover | Hemorrhagic  | PM<sub>10</sub>, CO, NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub> |
| Yamazaki et al<sup>71</sup> | Japan     | Case crossover | Ischemic       | O<sub>3</sub> in recurrent stroke | O<sub>3</sub> in incident stroke |
|                 |           | Case crossover | Hemorrhagic    | PM<sub>2</sub> 2 h before intracerebral hemorrhage | PM<sub>2</sub>, NO<sub>2</sub>, and O<sub>3</sub> in 24 h averages |

PM<sub>0.1</sub> indicates ultrafine particles with less than 0.1 μm aerodynamic diameter; PM<sub>10</sub>, particles with aerodynamic diameter ≤10 μm; PM<sub>2.5</sub>, fine particles with aerodynamic diameter ≤2.5 μm; PM<sub>coarse</sub>, coarse particles with aerodynamic diameter between 2.5 and 10 μm in aerodynamic diameter; and TIA, transient ischemic attack.

*Positive associations with confidence intervals not including the null.
†Associations with confidence intervals including the null.
time between stroke onset and death. In studies of long-term exposure to air pollution, the ability to investigate associations with stroke is dependent on the validity and resolution of the spatial exposure assessment and the adequate control for confounders related to both air pollution at place of residence and the risk of stroke, in particular socioeconomic factors.

There is growing evidence to suggest that both accumulated exposure to higher air pollution during a period of years and higher mean levels during a period of days increase the risk of stroke. In addition to improving temporal classification of exposure by validating stroke onset time, future research efforts should be directed to careful characterization of stroke subtype because air pollution may variably affect the different pathophysiological pathways. Air pollution exposure and increased risk of stroke may represent a considerable public health problem and regulations have improved air quality in many countries in Europe and the United States, resulting in greater life expectancy. Yet, associations with stroke have been reported at levels in compliance with current standards, highlighting the continued importance of effective regulation and monitoring in high-income countries as well as extending efforts to address regulation in low- and middle-income countries where levels of air pollution and prevalence of stroke are on the rise.

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SUPPLEMENTAL MATERIAL

Ambient Air Pollution and Stroke

Petter L. Ljungman, Murray A. Mittleman

Contents:
Table I. Studies of Short-term Air Pollution Exposure and Stroke Mortality: Detailed estimates.
Table II. Studies of Short-term Air Pollution Exposure and Hospitalization for Stroke: Detailed estimates.
| Study          | Location               | Stroke Outcome | Stratification | Pollutant | Averaging Period | %*  | 95% CI          |
|---------------|------------------------|----------------|----------------|-----------|-----------------|-----|-----------------|
| Chen 2013     | 8 Chinese cities       | Any stroke     | PM$_{10}$      | 2-day     | 0.5             | (0.3, 0.8) |
|               |                        |                | NO$_2$         | 2-day     | 0.8             | (0.5, 1.1) |
|               |                        |                | SO$_2$         | 2-day     | 0.3             | (0.2, 0.5) |
| Hoek 2002     | Netherlands            | Any stroke     | PM$_{10}$      | 7-day     | 0.4             | (-0.4, 1.2) |
|               |                        |                | B$_5$          | 7-day     | 4.1             | (0.7, 7.7)  |
|               |                        |                | CO             | 7-day     | 4.8             | (2.1, 7.6)  |
|               |                        |                | NO$_2$         | 7-day     | 0.9             | (-0.3, 2.1) |
|               |                        |                | SO$_2$         | 7-day     | 0.4             | (0.2, 0.7)  |
|               |                        |                | O$_3$          | Previous day 8-h max | 0.2 | (0.1, 0.4) |
| Hong 2002     | Seoul, Korea           | Ischemic stroke| TSP            | Same day  | 3.0             | (0.0, 6.0)  |
|               |                        |                | CO             | Same day  | 0.8             | (0.3, 1.2)  |
|               |                        |                | NO$_2$         | Same day  | 2.9             | (0.7, 5.0)  |
|               |                        |                | SO$_2$         | Same day  | 2.3             | (0.6, 4.0)  |
|               |                        |                | O$_3$          | 3-day lagged 8-h mean | 3.5 | (1.2, 5.8) |
|               |                        | Hemorrhagic stroke| TSP          | Same day  | 4.0             | (2.0, 7.0)  |
|               |                        |                | CO             | Same day  | NS              |               |
|               |                        |                | NO$_2$         | Same day  | NS              |               |
|               |                        |                | SO$_2$         | Same day  | NS              |               |
|               |                        |                | O$_3$          | 3-day lagged 8-h mean | NS |               |
| Hong 2002     | Seoul, Korea           | Any stroke     | PM$_{10}$      | Same day  | 0.7             | (0.6, 0.8)  |
|               |                        |                | CO             | 2-day lag | 0.7             | (0.1, 1.4)  |
|               |                        |                | NO$_2$         | 2-day lag | 3.7             | (1.3, 6.1)  |
|               |                        |                | SO$_2$         | 2-day lag | 5.1             | (1.4, 8.8)  |
|               |                        |                | O$_3$          | Same day  | 3.1             | (0.3, 5.9)  |
| Kan 2003      | Shanghai, China        | Any stroke     | PM$_{10}$      | Previous day | 0.8 | (0.0, 1.6) |
|               |                        |                | NO$_2$         | Previous day | 1.5 | (0.1, 3.0) |
|               |                        |                | SO$_2$         | Previous day | 0.6 | (-0.1, 1.3) |
| Kettunen 2007 | Helsinki, Finland      | Any stroke     | PM$_{10}$      | Previous day | -0.7 | (-2.6, 1.3) |
|               |                        |                | PM$_{2.5}$     | Previous day | -0.3 | (-1.9, 1.4) |
|               |                        |                | PM$_{10}$,lag | Previous day | -2.5 | (-7.6, 2.9) |
|               |                        |                | PM$_{10}$,lag  | Previous day | -0.8 | (-4.9, 3.3) |
|               |                        |                | CO             | Previous day | -0.3 | (-1.9, 1.4) |
|               |                        |                | NO$_2$         | Previous day | -0.7 | (-2.7, 1.8) |
|               |                        |                | O$_3$          | 8-h mean previous day | -0.2 | (-1.4, 1.2) |
|               |                        |                | PM$_{10}$      | Previous day | 8.7  | (-0.9, 19.3) |
|               |                        |                | PM$_{2.5}$     | Previous day | 13.0 | (2.3, 24.2) |
|               |                        |                | PM$_{10}$,lag | Previous day | 4.4  | (-4.3, 13.8) |
|               |                        |                | PM$_{10}$,lag  | Previous day | 8.5  | (-1.2, 19.1) |
|               |                        |                | CO             | Previous day | 3.6  | (0.3, 7.2)  |
|               |                        |                | NO$_2$         | Previous day | 1.5  | (-2.0, 5.4) |
|               |                        |                | O$_3$          | 8-h mean previous day | 1.3  | (-0.4, 3.1) |
| Li 2011       | Tianjin, Taiwan        | Any stroke     | PM$_{10}$      | Same day  | 0.1             | (-0.2, 0.5) |
|               |                        |                | PM$_{10}$      | Same day  | 0.7             | (0.0, 1.3)  |
| Qian 2007     | Wuhan, China           | Any stroke     | PM$_{10}$      | Same day  | 0.4             | (0.2, 0.7)  |
| Qian 2007     | Wuhan, China           | Any stroke     | NO$_2$         | Same day  | 0.8             | (0.0, 1.3)  |
|               |                        |                | SO$_2$         | Same day  | -0.1            | (-0.4, 0.2) |
|               |                        |                | O$_3$          | Same day  | -0.1            | (-0.3, 0.2) |
| Qian 2008     | Wuhan, China           | Any stroke     | PM$_{10}$      | 2-day     | 2.4             | (0.0, 4.8)  |
|               |                        |                | NO$_2$         | 2-day     | 2.4             | (-3.2, 8.5) |
|               |                        |                | SO$_2$         | 2-day     | -0.1            | (-3.0, 3.0) |
|               |                        |                | O$_3$          | 2-day     | 0.5             | (-0.4, 1.4) |
|               |                        |                | PM$_{10}$      | 2 day     | 0.4             | (0.1, 0.7)  |
|               |                        |                | NO$_2$         | 2-day     | 1.0             | (0.4, 1.6)  |
|               |                        |                | SO$_2$         | 2-day     | 0.4             | (0.0, 0.7)  |
|               |                        |                | O$_3$          | 2-day     | -0.1            | (-0.4, 0.1) |
| Qian 2010     | Wuhan, China           | Any stroke     | PM$_{10}$      | 2-day     | 0.1             | (-0.4, 0.7) |
|               |                        |                | NO$_2$         | 2-day     | 1.8             | (0.4, 3.3)  |
|               |                        |                | SO$_2$         | 2-day     | 0.6             | (-0.1, 1.4) |
|               |                        |                | NO$_2$         | 2-day     | 0.2             | (-0.8, 1.1) |
|               |                        |                | NO$_2$         | 2-day     | 0.9             | (-1.0, 2.9) |
### Table of Results

| Study               | Location          | Type                | Reference Dates | PM<sub>2.5</sub> | PM<sub>10</sub> | NO<sub>2</sub> | SO<sub>2</sub> | O<sub>3</sub> | PM<sub>10</sub> | NO<sub>2</sub> | SO<sub>2</sub> | O<sub>3</sub> |
|--------------------|-------------------|---------------------|-----------------|-----------------|-----------------|--------------|--------------|--------------|----------------|--------------|--------------|--------------|
| Turin 2012<sup>†</sup> | Takashima, Japan  | Any stroke          | 2013            | 25              | 45              | 15           | 9            | 2            | 35             | 50           | 60           | 90           |
|                    |                   | Ischemic stroke     |                 |                 |                 |              |              |              |                |              |              |              |
|                    |                   | Intracerebral stroke|                 |                 |                 |              |              |              |                |              |              |              |
|                    |                   | Subarachnoidal stroke|              |                 |                 |              |              |              |                |              |              |              |
| Yorifuji 2011<sup>†</sup> | Tokyo, Japan     | Any stroke          | 2011            | 1.3             | 1.5             | 1.4          | 1.3          | 2.3          | 4.1            | 3.4          | 2.2          | 1.1          |
|                    |                   | Ischemic stroke     |                 |                 |                 |              |              |              |                |              |              |              |
|                    |                   | Intracerebral stroke|                 |                 |                 |              |              |              |                |              |              |              |
|                    |                   | Subarachnoidal stroke|             |                 |                 |              |              |              |                |              |              |              |
| Yorifuji 2013<sup>†</sup> | 47 Japanese cities | Any stroke          | 2013            |                 | 1.4             | 1.6          | 2.0          | 1.2          | 2.6            | 3.4          |              |              |
|                    |                   | Ischemic stroke     |                 |                 |                 |              |              |              |                |              |              |              |
|                    |                   | Intracerebral stroke|                 |                 |                 |              |              |              |                |              |              |              |
|                    |                   | Subarachnoidal stroke|             |                 |                 |              |              |              |                |              |              |              |
| Zanobetti 2009<sup>†</sup> | 112 US cities    | Any stroke          | 2009            |                 | 0.8             |              |              |              | 0.8            |              |              |              |
|                    |                   | BC                  |                 |                 |                 |              |              |              |                |              |              |              |
| Maynard 2007<sup>†</sup> | Massachusetts, USA | Any stroke          | 2007            |                 | 4.4             |              |              |              |                |              |              |              |
|                    |                   | SO<sub>2</sub>      |                 |                 |                 |              |              |              |                |              |              |              |
| Qian 2013<sup>†</sup> | Shanghai, China   | Any stroke          | 2013            |                 | 0.2             |              |              |              | 0.2            |              |              |              |
|                    |                   | Ischemic stroke     |                 |                 |                 |              |              |              |                |              |              |              |
|                    |                   | Hemorrhagic stroke  |                 |                 |                 |              |              |              |                |              |              |              |
|                    |                   | Subarachnoidal stroke|             |                 |                 |              |              |              |                |              |              |              |
| Ren 2010<sup>†</sup> | Massachusetts, USA | Any stroke          | 2010            |                 | 0.4             |              |              |              |                |              |              |              |
|                    |                   | O<sub>3</sub>       |                 |                 |                 |              |              |              |                |              |              |              |
| Zeka 2005<sup>†</sup> | 20 US cities      | Any stroke          | 2005            |                 | 0.4             |              |              |              |                |              |              |              |
|                    |                   | PM<sub>10</sub>     |                 |                 |                 |              |              |              |                |              |              |              |
| Zeka 2006<sup>†</sup> | 20 US cities      | Any stroke          | 2006            |                 | 0.4             |              |              |              |                |              |              |              |
|                    |                   | O<sub>3</sub>       |                 |                 |                 |              |              |              |                |              |              |              |

**Notes:**
- Percent differences per: 10μg/cm<sup>2</sup> for PM<sub>2.5</sub>, PM<sub>10</sub>, PM<sub>2.5</sub>, 10 ppb for NO<sub>2</sub>, SO<sub>2</sub>, and O<sub>3</sub>; 0.1 ppm for CO; 52 μg/cm<sup>3</sup> for TSP; 5000 particles/cm<sup>3</sup> for PM<sub>2.5</sub>; 40μg/cm<sup>3</sup> for BS, unspecified interquartile range for BC.
- † Comparing highest to lowest quartile of air pollution
- Abbreviations: BC, Black carbon. BS, Black smoke. CI, Confidence intervals. CO, Carbon monoxide. H, hour. Max, Daily maximum. NO<sub>2</sub>, Nitrogen dioxide. NS, Non-significant associations but estimates not provided in publication. O<sub>3</sub>, Ozone. PM<sub>2.5</sub>, Particles with aerodynamic diameter ≤ 2.5μm. PM<sub>10</sub>, Fine particles with aerodynamic diameters 2.5μm. PM<sub>2.5</sub>, Coarse particles with aerodynamic diameter between 2.5 and 10 μm in aerodynamic diameter. PM<sub>10</sub>, Ultrafine particles with less than 0.1 μm aerodynamic diameter. SO<sub>2</sub>, Sulfur dioxide. SO<sub>4</sub>, Sulfate. TSP, Total suspended particles.
Table II. Studies of Short-term Air Pollution Exposure and Hospitalization for Stroke: Detailed estimates

| Study             | Location                  | Stroke Outcome | Stratification | Pollutant | Averaging Period | %*          | 95% CI        |
|-------------------|---------------------------|----------------|----------------|-----------|------------------|-------------|---------------|
| Ballester 2001**  | Valencia, Spain           | Any stroke     | BS             |          | 5-day lag        | 1.6         | (-1.4, 4.6)   |
|                   |                           |                | CO             |          | 1-h same day     | -0.1        | (-0.3, 0.09)  |
|                   |                           |                | NO₂            |          | 4-day lag        | 1.9         | (0.4, 3.5)    |
|                   |                           |                | SO₂            |          | 5-day lag        | 1.4         | (-0.6, 3.5)   |
|                   |                           |                | O₃             |          | 8-h 2-day lag    | -1.2        | (-2.6, 0.3)   |
| Burnett 1999**    | Toronto, Canada           | Any stroke     | PMₐ₁₀          | Same day | NS               |             |               |
|                   |                           |                | PMₐ₂.₅        | Same day | NS               |             |               |
|                   |                           |                | CO             |          | 2-day            | 0.1         | (-0.2, 0.4)   |
|                   |                           |                | NO₂            |          | Same day         | 0.8         | (-0.4, 2.0)   |
|                   |                           |                | SO₂            |          | Same day         | 0.1         | (-3.6, 4.5)   |
| Chan 2006**       | Taipei, Taiwan            | Any stroke     | PMₐ₁₀          | 3-day lag | 1.2              | (0.4, 1.9)  |               |
|                   |                           |                | PMₐ₂.₅        | 3-day lag | 1.1              | (0.3, 1.9)  |               |
|                   |                           |                | CO             |          | 8-h max same day | 0.4         | (-0.1, 0.8)   |
|                   |                           |                | NO₂            |          | Same day         | 3.3         | (-0.9, 7.7)   |
|                   |                           |                | SO₂            |          | Same day         | 2.6         | (-10, 15)     |
|                   |                           |                | O₃             |          | 1-h max same day | 1.0         | (0.3, 1.7)    |
| Chan 2006**       | Taipei, Taiwan            | Ischemic stroke| PMₐ₁₀          | 3-day lag | 1.7              | (-0.8, 4.1) |               |
|                   |                           |                | PMₐ₂.₅        | 3-day lag | 3.0              | (-0.8, 6.8) |               |
|                   |                           |                | CO             |          | 8-h max same day | 0.7         | (-0.2, 1.6)   |
|                   |                           |                | NO₂            |          | Same day         | 2.6         | (-4.6, 9.8)   |
|                   |                           |                | SO₂            |          | Same day         | 14          | (-11, 40)     |
|                   |                           |                | O₃             |          | 1-h max same day | 1.5         | (-0.6, 3.5)   |
| Chan 2006**       | Taipei, Taiwan            | Hemorrhagic stroke| PMₐ₁₀         | 3-day lag | -1.0             | (-3.9, 1.8) |               |
|                   |                           |                | PMₐ₂.₅        | 3-day lag | -4.0             | (-8.7, 0.6) |               |
|                   |                           |                | CO             |          | 8-h max same day | -0.2        | (-1.5, 1.0)   |
|                   |                           |                | NO₂            |          | Same day         | -3.9        | (-12, 4.4)    |
|                   |                           |                | SO₂            |          | Same day         | -27         | (-60, 6.8)    |
|                   |                           |                | O₃             |          | 1-h max same day | -0.4        | (-3.9, 3.2)   |
| Corea 2012**      | Mantua, Italy             | Any stroke     | PMₐ₁₀          | Same day | 8.0              | (0.0, 16)   |               |
|                   |                           | Ischemic stroke| PMₐ₁₀          | Same day | 8.0              | (0.0, 17)   |               |
|                   |                           | Large vessel stroke| PMₐ₁₀      | Same day | 20               | (0.0, 40)   |               |
|                   |                           |                | CO             |          | Same day         | -7.5        | (-8.6, 6.7)   |
|                   |                           |                | NO₂            |          | Same day         | 0.0         | (-32, 32)     |
|                   |                           |                | SO₂            |          | Same day         | 0.0         | (-44, 52)     |
|                   |                           |                | O₃             |          | Same day         | 9.6         | (-4.8, 29)    |
| Corea 2012**      | Mantua, Italy             | Cardioembolic stroke| PMₐ₁₀    | Same day | -10              | (-20, 10)   |               |
|                   |                           |                | CO             |          | Same day         | 9.3         | (-3.1, 48)    |
|                   |                           |                | NO₂            |          | Same day         | 0.0         | (-16, 21)     |
|                   |                           |                | SO₂            |          | Same day         | -11         | (-37, 15)     |
|                   |                           |                | O₃             |          | Same day         | -4.8        | (-14, 48)     |
| Corea 2012**      | Mantua, Italy             | Small vessel stroke| PMₐ₁₀      | Same day | 10               | (0.0, 20)   |               |
|                   |                           |                | CO             |          | Same day         | 6.9         | (-2.5, 31)    |
|                   |                           |                | NO₂            |          | Same day         | -11         | (-27, 5.3)    |
|                   |                           |                | SO₂            |          | Same day         | -11         | (-33, 7.4)    |
|                   |                           |                | O₃             |          | Same day         | 0.0         | (-9.6, 4.8)   |
| Jalaludin 2006**  | Sydney Australia          | Any stroke     | PMₐ₁₀          | Same day | -2.1             | (-4.5, 0.3) |               |
|                   |                           |                | PMₐ₂.₅        | Same day | -1.9             | (-5.0, 1.4) |               |
|                   |                           |                | CO             |          | 8-h same day     | 0.3         | (-0.02, 0.6)  |
|                   |                           |                | NO₂            |          | 1-h same day     | -1.8        | (-4.1, 0.5)   |
|                   |                           |                | SO₂            |          | Same day         | -19         | (-49, 12)     |
|                   |                           |                | O₃             |          | 1-h max same day | -1.1        | (-2.5, 0.4)   |
| Larrieu 2007**    | 8 French cities           | Any stroke     | PMₐ₁₀          | 2-day    | 0.2              | (-1.6, 1.9) |               |
|                   |                           |                | NO₂            |          | 2-day            | 0.4         | (-0.5, 1.3)   |
|                   |                           |                | O₃             |          | 2-day            | -0.2        | (-0.6, 0.1)   |
| Le Tertre 2002**  | 8 European cities         | Any stroke     | PMₐ₁₀          | 2-day    | 0.0              | (-0.3, 0.3) |               |
|                   |                           |                | BS             |          | 2-day            | -0.1        | (-0.5, 0.4)   |
| Linn 2000**       | Los Angeles, USA          | Any stroke     | PMₐ₁₀          | Same day | 0.06             | (-0.4, 0.6) |               |
|                   |                           |                | CO             |          | Same day         | 0.1         | (-0.05, 0.2)  |
|                   |                           |                | NO₂            |          | Same day         | 0.4         | (-0.4, 1.2)   |
|                   |                           |                | O₃             |          | Same day         | 0.3         | (-0.7, 1.3)   |
| Moolgavkar 2000** | Los Angeles, USA          | Any stroke     | PMₐ₁₀          | Same day | 0.6              | (0.3, 1.0)  |               |
|                   |                           |                | CO             |          | Same day         | 0.1         | (-0.1, 0.3)   |
| Study                  | Location                      | Stroke Type            | Lag Time       | Risk Estimate | 95% CI          |
|-----------------------|-------------------------------|------------------------|----------------|---------------|----------------|
| Poloniecki 1997       | London, UK                    | Any stroke             | Previous day   | -0.07         | (-0.2, 0.08)   |
|                       |                               |                        |                |               |                 |
| Poloniecki 1997       | Sao Jose Campos, Brazil       | Any stroke             | Same day       | 0.5           | (-2.1, 3.2)    |
|                       |                               |                        |                |               |                 |
| Pönkä 1996           | Helsinki, Finland             | Any stroke             | 6-day lag      | 96            | (21, 175)      |
|                       |                               |                        |                |               |                 |
| Sunyer 2003           | 7 European cities             | Any stroke             | 2-day          | 0.0           | (-0.2, 0.2)    |
|                       |                               |                        |                |               |                 |
| Turin 2012           | Takashima, Japan              | Any stroke             | Same day       | 0.5           | (-2.1, 3.2)    |
|                       |                               |                        |                |               |                 |
|                       |                               | Ischemic stroke        | 3-day          | -0.6          | (-4.4, 3.1)    |
|                       |                               |                        |                |               |                 |
|                       |                               | Intracerebral hemorrhage| 3-day         | 1.6           | (-4.3, 8.5)    |
|                       |                               |                        |                |               |                 |
|                       |                               | Subarachnoidal hemorrhage| 3-day       | 3.2           | (-5.3, 14)     |
|                       |                               |                        |                |               |                 |
| Villeneuve 2006       | Edmonton, Canada              | Any stroke             | NS             | -3.8          | (-8.1, 0.6)    |
|                       |                               |                        |                |               |                 |
|                       |                               | Ischemic stroke        | 3-day          | -6.4          | (-16, 4.8)     |
|                       |                               |                        |                |               |                 |
|                       |                               | TIA                    | 3-day          | -3.8          | (-8.1, 0.6)    |
|                       |                               |                        |                |               |                 |
|                       |                               | Hemorrhagic stroke     | 3-day          | 8.1           | (-1.2, 19)     |
|                       |                               |                        |                |               |                 |
| Villeneuve 2012       | Edmonton, Canada              | Any stroke             | Previous day   | 1.7           | (-4.5, 6.9)    |
|                       |                               |                        |                |               |                 |
|                       |                               | Ischemic stroke        | 3-day          | 1.7           | (-4.5, 6.9)    |
| Year | Location         | Stroke Type                        | Season   | Parameters | lag | Effect Size | 95% CI    |
|------|------------------|------------------------------------|----------|------------|-----|-------------|----------|
| 2003 | Kaoshiung, Taiwan| Ischemic stroke ≥20°C               |          | PM$_{2.5}$ | 3-day | 6.9         | (4.8, 9.2) |
|      |                  |                                   |          | CO         | 3-day | 7.2         | (4.8, 9.7) |
|      |                  |                                   |          | NO$_2$     | 3-day | 32.2        | (23, 42)   |
|      |                  |                                   |          | SO$_2$     | 3-day | 9.7         | (0.0, 21)  |
|      |                  |                                   |          | O$_3$      | 3-day | 7.1         | (3.3, 11)  |
|      |                  | Hemorrhagic stroke ≥20°C           |          | PM$_{2.5}$ | 3-day | 8.1         | (4.7, 12)  |
|      |                  |                                   |          | CO         | 3-day | 7.2         | (3.1, 12)  |
|      |                  |                                   |          | NO$_2$     | 3-day | 32         | (19, 49)   |
|      |                  |                                   |          | SO$_2$     | 3-day | 9.7         | (8.1, 29)  |
|      |                  |                                   |          | O$_3$      | 3-day | 9.4         | (2.8, 17)  |
|      |                  | Ischemic stroke <20°C              |          | PM$_{2.5}$ | 3-day | -0.5        | (-5.3, 3.6) |
|      |                  |                                   |          | CO         | 3-day | 27          | (11, 48)   |
|      |                  |                                   |          | NO$_2$     | 3-day | 9.4         | (-11, 40)  |
| 1999 | Hong Kong, China | Any stroke                         | Warm season | PM$_{10}$ | 2-day | 0.3         | (-0.5, 1.0) |
|      |                  |                                   |          | NO$_2$     | 2-day | 0.4         | (-0.1, 1.0) |
|      |                  |                                   |          | SO$_2$     | 3-day | -0.4        | (-0.8, 0.1) |
|      |                  |                                   |          | O$_3$      | Same day | -0.4 | (-0.8, 0.05) |
| 2013 | Wuhan, China     | Any stroke                         | 3-day    | PM$_{10}$ |           | -0.5         | (-1.5, 0.6) |
|      |                  |                                   |          | NO$_2$     | 3-day | 0.2         | (-1.2, 1.6) |
|      |                  |                                   |          | SO$_2$     | 3-day | -0.3        | (-1.0, 0.4) |
|      |                  | Ischemic stroke                    | 3-day    | PM$_{10}$ |           | 0.5         | (-1, 0.7)   |
|      |                  |                                   |          | NO$_2$     | 3-day | 0.2         | (-1.4, 1.0) |
|      |                  |                                   |          | SO$_2$     | 3-day | -0.3        | (-0.9, 0.3) |
|      |                  | Hemorrhagic stroke                 | 3-day    | PM$_{10}$ |           | -0.5        | (-1.7, 0.8) |
|      |                  |                                   |          | NO$_2$     | 3-day | 0.0         | (-1.9, 1.9) |
|      |                  |                                   |          | SO$_2$     | 3-day | -0.2        | (-1.1, 0.7) |
| 2013 | Allegheny, USA   | Any stroke                         | Same day | O$_3$     |           | 0.2         | (0.0, 0.3)  |
|      |                  | Ischemic stroke                    | Same day | O$_3$     |           | 0.2         | (0.0, 0.3)  |
|      |                  | Hemorrhagic stroke                 | Same day | O$_3$     |           | 0.0         | (0.0, 0.0)  |
| 2005 | Taipei, Taiwan   | Any stroke                         | 3-day lag post ADS | ADS | 5*         | (-1, 7) | 758 |
|      |                  | Ischemic                           | 3-day lag post ADS | ADS | 4*         | (-3, 698) |
|      |                  | Intracerebral hemorrhage           | 3-day lag post ADS | ADS | 15*        | (1, 910) |
|      |                  | Subarachnoidal hemorrhage          | 3-day lag post ADS | ADS | -19*       | (-40, 478) |
| 2003 | Kaoshiung, Taiwan| Ischemic stroke ≥20°C              |          | PM$_{2.5}$ | 3-day | 6.9         | (4.8, 9.2) |
|      |                  |                                   |          | CO         | 3-day | 7.2         | (4.8, 9.7) |
|      |                  |                                   |          | NO$_2$     | 3-day | 32.2        | (23, 42)   |
|      |                  |                                   |          | SO$_2$     | 3-day | 9.7         | (0.0, 21)  |
|      |                  |                                   |          | O$_3$      | 3-day | 7.1         | (3.3, 11)  |
|      |                  | Hemorrhagic stroke ≥20°C           |          | PM$_{2.5}$ | 3-day | 8.1         | (4.7, 12)  |
|      |                  |                                   |          | CO         | 3-day | 7.2         | (3.1, 12)  |
|      |                  |                                   |          | NO$_2$     | 3-day | 32         | (19, 49)   |
|      |                  |                                   |          | SO$_2$     | 3-day | 9.7         | (8.1, 29)  |
|      |                  |                                   |          | O$_3$      | 3-day | 9.4         | (2.8, 17)  |
|      |                  | Ischemic stroke <20°C              |          | PM$_{2.5}$ | 3-day | -0.5        | (-5.3, 3.6) |
|      |                  |                                   |          | CO         | 3-day | 27          | (11, 48)   |
|      |                  |                                   |          | NO$_2$     | 3-day | 9.4         | (-11, 40)  |
| Event                  | Stroke Type          | Location          | PM0.1 | Date          | Estimate (95% CI) |
|-----------------------|----------------------|-------------------|-------|---------------|-------------------|
| Henrotin 2007          | Ischemic stroke      | Dijon, France     | PM0.1 | Previous day  | 1.1 (-0.2, 9.4)   |
|                       |                      |                   | CO    | Previous day  | -1.8 (-2.6, 0.9)  |
|                       |                      |                   | SO2   | Previous day  | -0.8 (-5.1, 4.0)  |
|                       |                      |                   | O3    | Previous day  | 3.6 (1.1, 6.3)    |
|                       | Hemorrhagic stroke   |                   | PM0.1 | Previous day  | -9.9 (-27, 11)    |
|                       |                      |                   | CO    | Previous day  | -0.9 (-2.6, 4.4)  |
|                       |                      |                   | SO2   | Previous day  | 0.5 (-9.4, 14)    |
|                       |                      |                   | O3    | Previous day  | -1.2 (-1.1, 5.9)  |
|                       | Large vessel stroke  |                   | PM0.1 | Previous day  | -6.2 (-23, 14)    |
|                       |                      |                   | CO    | Previous day  | -1.8 (-5.2, 2.6)  |
|                       |                      |                   | SO2   | Previous day  | 3.3 (-8.0, 19)    |
|                       |                      |                   | O3    | Previous day  | 6.7 (0.6, 14)     |
|                       | Lacunar stroke       |                   | PM0.1 | Previous day  | -12 (-30, 11)     |
|                       |                      |                   | CO    | Previous day  | -2.6 (-7.0, 0.9)  |
|                       |                      |                   | SO2   | Previous day  | -6.3 (-15, 15)    |
|                       |                      |                   | O3    | Previous day  | 3.7 (-3.3, 12)    |
|                       | Cardioembolic stroke |                   | PM0.1 | Previous day  | 10 (-11, 35)      |
|                       |                      |                   | CO    | Previous day  | -0.9 (-4.4, 3.5)  |
|                       |                      |                   | SO2   | Previous day  | -1.0 (-11, 13)    |
|                       |                      |                   | O3    | Previous day  | 5.4 (-1.4, 13)    |
|                       | TIA                  |                   | PM0.1 | Previous day  | 9.5 (-17, 43)     |
|                       |                      |                   | CO    | Previous day  | -0.9 (-4.4, 3.5)  |
|                       |                      |                   | SO2   | Previous day  | -1.3 (-13, 15)    |
|                       |                      |                   | O3    | Previous day  | 9.9 (2.8, 19)     |
| Henrotin 2010          | Ischemic stroke      | Dijon, France     | O3    | 3-day lag     | -0.2 (-2.3, 1.9)  |
|                       |                      |                   | O3    | 3-day lag     | 5.5 (2.3, 10)     |
| Yamazaki 2007         | Ischemic stroke      | Japan             | PM0.1 | Same day      | 0.9 (-0.2, 2.1)   |
|                       |                      |                   | NO2   | Same day      | -0.5 (-2.9, 1.9)  |
|                       |                      |                   | O3    | Same day      | -2.5 (-4.5, 0.4)  |
|                       | Cold season          |                   | PM0.1 | Same day      | 0.2 (-0.9, 1.3)   |
|                       |                      |                   | NO2   | Same day      | 0.0 (-2.9, 1.9)   |
|                       | Hemorrhagic stroke   |                   | PM0.1 | Same day      | 1.4 (-0.5, 3.4)   |
|                       |                      |                   | NO2   | Same day      | -0.5 (-4.5, 3.7)  |
|                       |                      |                   | O3    | Same day      | -0.4 (-3.9, 3.3)  |
| Cold season | PM2.5 | Same day | 0.2 | (-1.6, 2.0) |
|-------------|-------|----------|-----|-------------|
| NO2         | Same day | 2.5     | (-2.4, 7.7) |
| O3          | Same day | 1.0     | (-5.0, 3.3) |

| Bedada 2012 | Manchester, UK | Minor stroke/ TIA | PM10 | 3-day lag | 13 | (-1.1, 29) |
|-------------|----------------|------------------|------|----------|-----|----------------|
|              |                 |                  | CO   | 3-day lag | 4.7 | (0.6, 11)     |
|              |                 |                  | NO2  | 3-day lag | 4.1 | (-2.4, 12)    |
|              |                 |                  | SO2  | 3-day lag | 3.7 | (-14, 23)     |
|              |                 |                  | O3   | 3-day lag | -2.9 | (-6.5, 1.6)  |
|              |                 |                  | PM10 | 3-day lag | -5.9 | (-20, 9.4)   |
|              |                 |                  | CO   | 3-day lag | -8.7 | (1.5, 3.5)   |
|              |                 |                  | NO2  | 3-day lag | -3.3 | (-9.2, 4.0)  |
|              |                 |                  | SO2  | 3-day lag | -1.9 | (-16, 11)    |
|              |                 |                  | O3   | 3-day lag | 3.5  | (-10, 9.2)   |

| Liverpool, UK | Minor stroke/TIA | PM10 | 3-day lag | -5.9 | (-20, 9.4) |
|----------------|------------------|------|----------|-----|-------------|
|                 |                  | CO   | 3-day lag | -8.7 | (1.5, 3.5) |
|                 |                  | NO2  | 3-day lag | -3.3 | (-9.2, 4.0) |
|                 |                  | SO2  | 3-day lag | -1.9 | (-16, 11)  |
|                 |                  | O3   | 3-day lag | 3.5  | (-10, 9.2) |

*Percent differences per: 10µg/cm³ for BS, PM₁₀, PM₁₅, PM₂.₅; 10 ppb for NO₂, SO₂, and O₃; 0.1ppm for CO; 1 µg/cm³ for TSP; 0.5 µg/cm³ for BC.
† Comparing risk of stroke admission on third day after an Asian dust storm with the risk of stroke admission on non-Asian dust storm days.

Abbreviations: ADS, Asian dust storm episodes. BC, Black carbon. BS, Black smoke. CO, Carbon monoxide. NO₂, Nitrogen dioxide. NS, Non-significant associations but estimates not provided in publication. O₃, Ozone. PM₁₀, Particles with aerodynamic diameter ≤10µm. PM₁₅, Fine particles with aerodynamic diameters 2.5µm. PM₂.₅, Coarse particles with aerodynamic diameter between 2.5 and 10 µm in aerodynamic diameter. PM₁₀, Ultradefine particles with less than 0.1 µm aerodynamic diameter. SO₂, Sulfur dioxide. SO₄, Sulfate. TSP, Total suspended particles.

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