

# Supplementary Materials: Air Pollution and Otitis Media in Children: A Systematic Review of Literature

## Summary of Assessed Quality of Included Studies

**Table S1.** Study quality using Newcastle-Ottawa Quality Assessment Scale for cohort studies.

| Study Name and the Author | Representativeness | Selection of Non-Exposed Cohorts | Ascertainment of Exposure | Outcome of Interest not Present at Start | Comparability <sup>†</sup> | Assessment of Outcome | Adequate Follow up Time | Adequate Follow up of Cohorts | Score/10 |
|---------------------------|--------------------|----------------------------------|---------------------------|------------------------------------------|----------------------------|-----------------------|-------------------------|-------------------------------|----------|
| Aguilera, Pedersen [1])   | *                  | *                                | *                         | *                                        | **                         | -                     | *                       | *                             | 8        |
| Brauer, Gehring [2]       | *                  | *                                | *                         | *                                        | **                         | -                     | *                       | *                             | 8        |
| Deng, Lu [3])             | *                  | *                                | -                         | *                                        | **                         | -                     | *                       | *                             | 7        |
| Deng, Lu [4])             | *                  | *                                | -                         | *                                        | **                         | -                     | *                       | *                             | 7        |
| Dostal, Prucha [5])       | *                  | *                                | -                         | *                                        | *                          | *                     | *                       | *                             | 7        |
| Jedrychowski, Galas [6])  | *                  | *                                | *                         | *                                        | **                         | -                     | *                       | *                             | 8        |
| MacIntyre, Gehring [7])   | *                  | *                                | *                         | *                                        | **                         | **                    | *                       | *                             | 9        |
| Brauer, Karr [8])         | *                  | *                                | *                         | *                                        | **                         | *                     | *                       | *                             | 9        |
| Pettigrew, Gent [9]       | *                  | *                                | -                         | *                                        | **                         | *                     | -                       | -                             | 6        |

<sup>†</sup> Key confounders identified: socio-economic status and maternal smoking.

**Table S2.** Exposure to NO<sub>2</sub>, PM<sub>2.5</sub>, PM<sub>2.5</sub> absorbance or PM<sub>10</sub> and otitis media in children – summary results of cohort studies.

| Study and Sample Size                                                                      | Exposure Window     | Level of Exposure NO <sub>2</sub> | OR/RR and 95% CI NO <sub>2</sub> | Level of Exposure PM <sub>2.5</sub> | OR/RR and 95% CI PM <sub>2.5</sub> | Level of Exposure PM <sub>2.5</sub> Absorbance | OR/RR and 95% CI PM <sub>2.5</sub> Absorbance | Level of Exposure PM <sub>10</sub> Absorbance | OR/RR and 95% CI PM <sub>10</sub> Absorbance |
|--------------------------------------------------------------------------------------------|---------------------|-----------------------------------|----------------------------------|-------------------------------------|------------------------------------|------------------------------------------------|-----------------------------------------------|-----------------------------------------------|----------------------------------------------|
| Aguilera, Pedersen (1)<br>INMA <i>n</i> = 2199 *                                           | Entire prenatal     | 10 µg/m <sup>3</sup>              | 1.18 (0.98, 1.41)                | N/A                                 | N/A                                | N/A                                            |                                               | N/A                                           | N/A                                          |
|                                                                                            | 1st trimester       | 10 µg/m <sup>3</sup>              | 1.11 (0.99, 1.24)                | N/A                                 | N/A                                | N/A                                            |                                               | N/A                                           | N/A                                          |
|                                                                                            | 2nd trimester       | 10 µg/m <sup>3</sup>              | 1.16 (0.98, 1.37)                | N/A                                 | N/A                                | N/A                                            |                                               | N/A                                           | N/A                                          |
|                                                                                            | 3rd trimester       | 10 µg/m <sup>3</sup>              | 1.12 (0.98, 1.29)                | N/A                                 | N/A                                | N/A                                            |                                               | N/A                                           | N/A                                          |
|                                                                                            | 1st year of life    | 10 µg/m <sup>3</sup>              | 1.15 (1.01, 1.31)                | N/A                                 | N/A                                | N/A                                            |                                               | N/A                                           | N/A                                          |
| Brauer, Gehring (2)<br>PIAMA<br><i>n</i> = 2984 (1 st year)<br><i>n</i> = 2970 (2 nd year) | 1st year of life    | 3 µg/m <sup>3</sup>               | 1.17 (1.03,1.34)                 | 10 µg/m <sup>3</sup>                | 1.13 (0.98, 1.32)                  | 0.5 µg/m <sup>3</sup>                          | 1.11 (0.98, 1.26)                             | N/A                                           | N/A                                          |
|                                                                                            | 1st 2 years of life | 3 µg/m <sup>3</sup>               | 1.14 (1.03,1.27)                 | 10 µg/m <sup>3</sup>                | 1.13 (1.00, 1.27)                  | 0.5 µg/m <sup>3</sup>                          | 1.10 (1.00, 1.22)                             | N/A                                           | N/A                                          |
| Brauer, Gehring (2)<br>LISA<br><i>n</i> = 620 (1 st year)<br><i>n</i> = 605 (2 nd year)    | 1st year of life    | 3 µg/m <sup>3</sup>               | 1.09 (0.78,1.54)                 | 10 µg/m <sup>3</sup>                | 1.19 (0.73, 1.92)                  | 0.5 µg/m <sup>3</sup>                          | 1.12 (0.83, 1.51)                             | N/A                                           | N/A                                          |
|                                                                                            | 1st 2 years of life | 3 µg/m <sup>3</sup>               | 1.14 (0.87,1.49)                 | 10 µg/m <sup>3</sup>                | 1.24 (0.84, 1.83)                  | 0.5 µg/m <sup>3</sup>                          | 1.10 (0.86, 1.41)                             | N/A                                           | N/A                                          |
| Deng, Lu (3) <i>n</i> = 1617                                                               | prenatal            | 12 µg/m <sup>3</sup>              | 1.10 (0.76, 1.60)                | N/A                                 | N/A                                | N/A                                            | N/A                                           | 7 µg/m <sup>3</sup>                           | 0.95 (0.73, 1.23)                            |
|                                                                                            | postnatal           | 13 µg/m <sup>3</sup>              | 1.16 (0.73, 1.83)                | N/A                                 | N/A                                | N/A                                            | N/A                                           | 6 µg/m <sup>3</sup>                           | 1.36 (0.95, 1.94)                            |
| Deng, Lu (4) <i>n</i> = 1617                                                               | 1st trimester       | 17 µg/m <sup>3</sup>              | 0.89 (0.57, 1.37)                | N/A                                 | N/A                                | N/A                                            | N/A                                           | 15 µg/m <sup>3</sup>                          | 0.91 (0.67, 1.26)                            |
|                                                                                            | 2nd trimester       | 15 µg/m <sup>3</sup>              | 1.20 (0.83, 1.74)                | N/A                                 | N/A                                | N/A                                            | N/A                                           | 14 µg/m <sup>3</sup>                          | 1.03 (0.77, 1.39)                            |
|                                                                                            | 3rd trimester       | 14 µg/m <sup>3</sup>              | 1.10 (0.77, 1.56)                | N/A                                 | N/A                                | N/A                                            | N/A                                           | 16 µg/m <sup>3</sup>                          | 0.89 (0.65, 1.22)                            |
| MacIntyre, Karr (10)<br>British Colombia<br><i>n</i> = 45,513                              | During birth        | 10 µg/m <sup>3</sup>              | 1.09 (1.07, 1.12)                | 1.8 µg/m <sup>3</sup>               | 0.91 (0.89, 0.93)                  | 1.1 µg/m <sup>3</sup>                          | 0.94 (0.93, 0.96)                             | N/A                                           | N/A                                          |
| MacIntyre, Gehring (7)<br>BAMSE, <i>n</i> = 3,821                                          | During birth        | 10 µg/m <sup>3</sup>              | 1.01 (0.81, 1.27)                | 5 µg/m <sup>3</sup>                 | 0.95 (0.66, 1.38)                  | 1 unit                                         | 1.19 (0.63, 2.21)                             | 10 µg/m <sup>3</sup>                          | 0.94 (0.78, 1.14)                            |
| GASPII, <i>n</i> = 678                                                                     | During birth        | 10 µg/m <sup>3</sup>              | 1.02 (0.84, 1.23)                | 5 µg/m <sup>3</sup>                 | 0.75 (0.46, 1.22)                  | 1 unit                                         | 0.79 (0.55, 1.12)                             | 10 µg/m <sup>3</sup>                          | 0.84 (0.59, 1.2)                             |
| INMA Asturias,<br><i>n</i> = 360                                                           | During birth        | 10 µg/m <sup>3</sup>              | 1.1 (0.89, 1.36)                 | N/A                                 | N/A                                | N/A                                            | N/A                                           | N/A                                           | N/A                                          |
| INMA Gipuzkoa,<br><i>n</i> = 437                                                           | During birth        | 10 µg/m <sup>3</sup>              | 1.64 (1.03, 2.63)                | N/A                                 | N/A                                | N/A                                            | N/A                                           | N/A                                           | N/A                                          |
| INMA Sabadell,<br><i>n</i> = 402                                                           | During birth        | 10 µg/m <sup>3</sup>              | 0.94 (0.76, 1.15)                | 5 µg/m <sup>3</sup>                 | 0.8 (0.34, 1.87)                   | 1 unit                                         | 0.87 (0.53, 1.43)                             | 10 µg/m <sup>3</sup>                          | 1.06 (0.56, 1.98)                            |
| INMA Valencia, <i>n</i> = 559                                                              | During birth        | 10 µg/m <sup>3</sup>              | 1.13 (0.95, 1.34)                | N/A                                 | N/A                                | N/A                                            | N/A                                           | N/A                                           | N/A                                          |
| LISA South, <i>n</i> = 3,321                                                               | During birth        | 10 µg/m <sup>3</sup>              | 1.05 (0.86, 1.29)                | 5 µg/m <sup>3</sup>                 | 1.06 (0.58, 1.94)                  | 1 unit                                         | 1.08 (0.63, 1.87)                             | 10 µg/m <sup>3</sup>                          | 1.23 (0.73, 2.07)                            |
| LISA North, <i>n</i> = 2,460                                                               | During birth        | 10 µg/m <sup>3</sup>              | 0.9 (0.33, 2.44)                 | 5 µg/m <sup>3</sup>                 | 0.85 (0.13, 5.42)                  | 1 unit                                         | 2.47 (0.51, 12)                               | 10 µg/m <sup>3</sup>                          | 1.21 (0.11, 14)                              |
| PIAMA, <i>n</i> = 3,475                                                                    | During birth        | 10 µg/m <sup>3</sup>              | 1.15 (1.03, 1.29)                | 5 µg/m <sup>3</sup>                 | 2.06 (1.25, 3.39)                  | 1 unit                                         | 1.42 (1.06, 1.91)                             | 10 µg/m <sup>3</sup>                          | 1.61 (0.86, 3.01)                            |
| Combined                                                                                   | During birth        | 10 µg/m <sup>3</sup>              | 1.09 (1.02, 1.16)                | 5 µg/m <sup>3</sup>                 | 1.06 (0.75, 1.49)                  | 1 unit                                         | 1.08 (0.83, 1.39)                             | 10 µg/m <sup>3</sup>                          | 0.98 (0.84, 1.14)                            |

**Table S3.** Study quality using Newcastle-Ottawa Quality Assessment Scale for case-control and case-crossover studies.

| Study Name and the Author            | Adequate Case Definition | Representativeness of Cases | Selection of Controls | Definition of Controls | Comparability <sup>†</sup> | Assessment of Exposure | Method of Ascertainment | Nonresponse Rate | Score/10 |
|--------------------------------------|--------------------------|-----------------------------|-----------------------|------------------------|----------------------------|------------------------|-------------------------|------------------|----------|
| Daigler, Markello [11] <sup>†</sup>  | *                        | -                           | *                     | *                      | -                          | -                      | *                       | *                | 5        |
| da Costa, Navarro [12] <sup>†</sup>  | *                        | *                           | *                     | *                      | -                          | -                      | *                       | *                | 5        |
| Xiao, Liu [13] <sup>†</sup>          | *                        | *                           | *                     | *                      | **                         | *                      | *                       | *                | 9        |
| Kousha and Castner[14] <sup>†</sup>  | *                        | *                           | *                     | *                      | **                         | *                      | *                       | *                | 9        |
| Strickland, Hao [15] <sup>†</sup>    | *                        | *                           | *                     | *                      | **                         | *                      | *                       | *                | 9        |
| Zemek, Szyszkowicz [16] <sup>†</sup> | *                        | *                           | *                     | *                      | **                         | *                      | *                       | *                | 7        |

<sup>†</sup> Key confounders identified: socio-economic status and maternal smoking

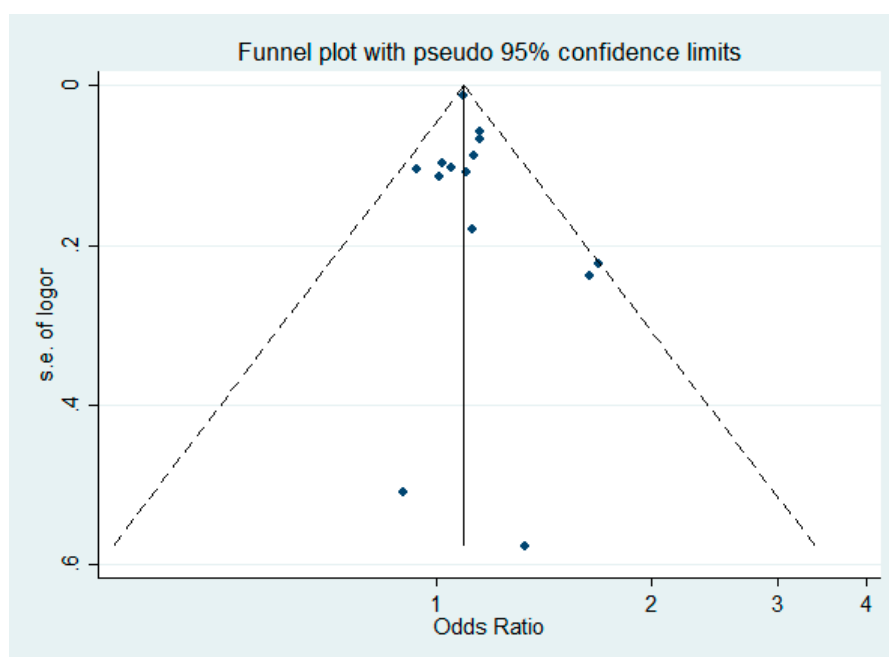
**Table S4.** Study quality of time series studies using quality assessment tool adapted from Zaza et al (Maximum score in brackets).

| Study Name and the Author | Study Design (7) | Population Eligibility and Sampling Described (4) | Valid and Reliable Exposure Measures (2) | Valid and Reliable Outcome Measures (2) | Appropriate Statistical Methods (3) | Multilevel Analyses (2) | Interpretation (1) | Confounding and Bias Addressed (3) | Score/23 |
|---------------------------|------------------|---------------------------------------------------|------------------------------------------|-----------------------------------------|-------------------------------------|-------------------------|--------------------|------------------------------------|----------|
| Gestro, Condemni [17]     | 2                | 4                                                 | 2                                        | 2                                       | 3                                   | 2                       | 1                  | 3                                  | 19       |

**Table S5.** Study quality using Newcastle-Ottawa Quality Assessment Scale for cross-sectional studies.

| Study Name and the Author      | Representativeness | Sample Size | Non-Respondents | Ascertainment of Exposure | Comparability <sup>†</sup> | Assessment of Outcome | Statistical Test | Score/10 |
|--------------------------------|--------------------|-------------|-----------------|---------------------------|----------------------------|-----------------------|------------------|----------|
| Harvey [18]                    | *                  | -           | -               | -                         | -                          | **                    | -                | 3        |
| Bhattacharyya and Shapiro [19] | *                  | *           | -               | *                         | -                          | *                     | *                | 5        |
| Bhopal, Phillimore [20]        | *                  | *           | -               | *                         | -                          | -                     | *                | 4        |
| Heinrich, Hoelscher [21]       | *                  | *           | -               | *                         | **                         | -                     | *                | 6        |
| Heinrich, Hoelscher [22]       | *                  | *           | -               | *                         | **                         | -                     | *                | 6        |
| Sprem and Branica [23]         | -                  | -           | -               | *                         | -                          | **                    | -                | 3        |
| Ribeiro and Cardoso [24]       | *                  | -           | *               | *                         | -                          | -                     | *                | 4        |
| Holtby, Elliott [25]           | *                  | *           | *               | -                         | -                          | *                     | -                | 4        |

<sup>†</sup> Key confounders identified: socio-economic status and maternal smoking



**Figure S1.** Funnel plot for the studies investigating associations between birth or first year of life NO<sub>2</sub> exposure and subsequent otitis media in children.

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