

Sex/gender in the association between ambient air pollution and cardiovascular mortality: systematic review and meta-analysis

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Supplemental Material A

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S1. Search strategy

Table 1. Search strategy in PubMed

| No. | Search query | Results |
|-----|--|--|
| #10 | Final combination | #3 AND #6 AND #8 AND #9 NOT #7 |
| #9 | Date and language | ("2000/01/01"[Date - Publication] : "2023/07/31"[Date - Publication]) AND ((English[Language]) OR (German[Language])) |
| #8 | Sex/gender terms | (sex OR gender OR female* OR male* OR women OR men) OR (sex[Mesh:NoExp] OR "gender role"[Mesh:NoExp] OR "gender identity"[Mesh:NoExp] OR female[Mesh:NoExp] OR male[Mesh:NoExp] OR women[Mesh:NoExp] OR men[Mesh:NoExp]) |
| #7 | Study population exclusions (no animals) | Mice[Mesh] OR Rats[Mesh] OR "Macaca mulatta"[Mesh] OR "disease models, animal"[Mesh] OR mice[TIAB] OR mouse[TIAB] OR rats[TIAB] OR monkey*[TIAB] OR "macaca mulatta"[TIAB] |
| #6 | Outcomes combined | #4 AND #5 |
| #5 | Outcome 2: disease | ("circulatory" OR "cardiovascular" OR ("heart" AND "disease*") OR ("cause-specific") OR ("specific cause*") OR ("specific disease*") OR ("cause of death*") OR ("death cause*")) OR "Cardiovascular Diseases/mortality"[Mesh:noexp] |
| #4 | Outcome 1: disease measure | (mortalit*[TIAB] OR death*[TIAB]) |
| #3 | Exposures, combined | #1 NOT #2 |
| #2 | Exposure, exclusions | "air pollutants, occupational"[Mesh] OR "Occupational exposure"[Mesh] OR "air pollutants, radioactive"[Mesh] OR "air pollution, radioactive"[Mesh] OR "radioactive pollutants"[Mesh] OR "air pollution, indoor"[Mesh] OR "tobacco smoke pollution"[Mesh] |
| #1 | Exposure | "particulate matter"[TIAB] OR "PM2.5"[TIAB] OR "PM25"[TIAB] OR "PM(2.5)"[TIAB] OR "PM(25)"[TIAB] OR "PM10"[TIAB] OR "PM(10)"[TIAB] OR "gaseous poll*"[TIAB] OR "ozone"[TIAB] OR "O3"[TIAB] OR "O(3)"[TIAB] OR "nitrogen dioxide"[TIAB] OR "NO2"[TIAB] OR "NO(2)"[TIAB] OR "Particulate Matter/adverse effects"[Mesh:noexp] OR "Ozone/adverse effects"[Mesh:noexp] OR "Nitrogen Dioxide/adverse effects"[Mesh:noexp] OR "Air Pollution/adverse effects"[Mesh:noexp] OR "Air Pollutants/adverse effects"[Mesh:noexp] |

Table 2. Search strategy in Web of Science

| No. | Search query | | Results |
|-----|--|---|------------|
| #10 | Final combination | #3 AND #6 AND #8 AND #9 NOT #7 | 1.019 |
| #9 | Date and language | PY=(2000-2022) AND LA=(English OR German) | 46.923.801 |
| #8 | Sex/gender terms | ALL=(sex OR gender OR female* OR male* OR women OR men) | 4.354.662 |
| #7 | Study population exclusions (no animals) | TS=(mouse OR mice OR rats OR "Macaca mulatta" OR monkey) | 3.009.932 |
| #6 | Outcomes combined | #4 AND #5 | 629.216 |
| #5 | Outcome 2: disease | ALL=(circulatory OR cardiovascular OR (heart AND disease*) OR ("cause-specific") OR (specific AND cause*) OR (specific AND disease*) OR (cause AND death*) OR (death AND cause*)) | 2.390.451 |
| #4 | Outcome 1: disease measure | TS=(mortalit* OR death*) | 1.974.818 |
| #3 | Exposures, combined | #1 NOT #2 | 304.550 |
| #2 | Exposure, exclusions | TS=(occupation* OR indoor OR radioactive) | 426.583 |
| #1 | Exposure | (TS=("particulate matter" OR "PM2.5" OR "PM25" OR "PM(2.5)" OR "PM(25)" OR "PM10" OR "PM(10)" OR "ozone" OR "O3" OR "O(3)" OR "nitrogen dioxide" OR "NO2" OR "NO(2)")) | 316.785 |

Table 3. Search strategy in Scopus

| No. | Search query | | Results |
|-----|--|--|------------|
| #10 | Final combination | #3 AND #6 AND #8 AND #9 AND NOT #7 | 3.858 |
| #9 | Date and language | LANGUAGE (english OR german) AND PUBYEAR > 2000 AND PUBYEAR < 2023 | 53.630.768 |
| #8 | Sex/gender terms | ALL(sex OR gender OR female* OR male* OR women OR men) | 23.177.538 |
| #7 | Study population exclusions (no animals) | TITLE-ABS-KEY(mouse OR mice OR rats OR "Macaca mulatta" OR monkey) | 5.004.405 |
| #6 | Outcomes combined | #4 AND #5 | 1.038.735 |
| #5 | Outcome 2: disease | ALL(circulatory OR cardiovascular OR (heart W/3 disease*) OR ("cause-specific") OR (specific W/3 cause*) OR (specific W/3 disease*) OR (cause W/3 death*) OR (death W/3 cause*)) | 5.212.334 |
| #4 | Outcome 1: disease measure | TITLE-ABS-KEY(mortalit* OR death*) | 2.902.107 |
| #3 | Exposures, combined | #1 AND NOT #2 | 572.673 |
| #2 | Exposure, exclusions | TITLE-ABS-KEY(occupation* OR indoor OR radioactive) | 1.040.551 |
| #1 | Exposure | TITLE-ABS-KEY ("particulate matter" OR "PM2.5" OR "PM25" OR "PM(2.5)" OR "PM(25)" OR "PM10" OR "PM(10)" OR "ozone" OR "O3" OR "O(3)" OR "nitrogen dioxide" OR "NO2" OR "NO(2)") | 592.243 |

S2. Formulas

S2.1 Converting units

Where concentration levels of NO₂ or ozone, respectively, were given in the unit ppb (parts per billion) we converted the unit to µg/m³ by multiplying with an air pollutant specific conversion factor (CF): µg/m³ = CF*ppb. Assuming 20°C and 1013 mbar, we used CFs of 1.91 and 2.0 for NO₂ and ozone, respectively.

S2.2 Converting estimates

Where necessary, we converted the estimates given in the studies into Odds Ratios and %-change in CVD death risk per 10 µg/m³ increase in air pollutant using following formulas shown in Table S2.1.

Table 4. Formulas used to convert estimates

| estimate given (EST _{study}) | unit | increment | Conversion formula |
|--|-------------------|---------------------------------------|--|
| %-change | ppb | INC _{ppb} | $\text{beta} = (\ln(\text{EST}_{\text{study}}/100+1))/\text{INC}_{\text{ppb}}$ $\text{sd} = (\text{beta} - (\ln(1+\text{CI}_{\text{low}}/100)))/\text{INC}_{\text{ppb}})/1.96$ $\text{OR} = \text{EXP}(\text{beta}/\text{CF}*10)$ $\text{CI} = \text{EXP}((\text{beta} \pm 1.96*\text{sd})/\text{CF}*10)$ $\% \text{-change} = (\text{EXP}(\text{beta}/\text{CF}*10) - 1)*100$ $\text{CI} = (\text{EXP}((\text{beta} \pm 1.96*\text{sd})/\text{CF}*10) - 1)*100$ |
| %-change | µg/m ³ | INC _{µg/m³} (≠10) | $\text{beta} = (\ln(\text{EST}_{\text{study}}/100+1))/\text{INC}_{\mu\text{g}/\text{m}^3}$ $\text{sd} = (\text{beta} - (\ln(1+\text{CI}_{\text{low}}/100)))/\text{INC}_{\mu\text{g}/\text{m}^3})/1.96$ $\text{OR} = \text{EXP}(\text{beta}*10)$ $\text{CI} = \text{EXP}((\text{beta} \pm 1.96*\text{sd})*10)$ $\% \text{-change} = (\text{EXP}(\text{beta}*10) - 1)*100$ $\text{CI} = (\text{EXP}((\text{beta} \pm 1.96*\text{sd})*10) - 1)*100$ |
| OR, HR, RR | ppb | INC _{ppb} | $\text{beta} = \ln(\text{EST}_{\text{study}})/\text{INC}_{\text{ppb}}$ $\text{sd} = (\text{beta} - (\ln(\text{CI}_{\text{low}})/\text{INC}_{\text{ppb}}))/1.96$ $\text{OR} = \text{EXP}(\text{beta}/\text{CF}*10)$ $\text{CI} = \text{EXP}((\text{beta} \pm 1.96*\text{sd})/\text{CF}*10)$ $\% \text{-change} = (\text{EXP}(\text{beta}/\text{CF}*10) - 1)*100$ $\text{CI} = (\text{EXP}((\text{beta} \pm 1.96*\text{sd})/\text{CF}*10) - 1)*100$ |
| OR, HR, RR | µg/m ³ | INC _{µg/m³} | $\text{beta} = \ln(\text{EST}_{\text{study}})/\text{INC}_{\mu\text{g}/\text{m}^3}$ $\text{sd} = (\text{beta} - (\ln(\text{CI}_{\text{low}})/\text{INC}_{\mu\text{g}/\text{m}^3}))/1.96$ $\text{OR} = \text{EXP}(\text{beta}*10)$ $\text{CI} = \text{EXP}((\text{beta} \pm 1.96*\text{sd})*10)$ $\% \text{-change} = (\text{EXP}(\text{beta}*10) - 1)*100$ $\text{CI} = (\text{EXP}((\text{beta} \pm 1.96*\text{sd})*10) - 1)*100$ |

CF, conversion factor (1.91 for NO₂, 2 for ozone); CI, confidence interval; CI_{low}, lower confidence interval of estimate given in study; EST_{study}, estimate given in study; HR, hazard ratio; INC, increment; OR, odds ratio; ppb, parts per billion; RR, relative risk; sd, standard deviation

S2.3 Calculation of Female-to-Male Ratio (FMR) of Odds Ratios

In a first step, according to the formulas provided in S2.2, betas and standard deviations were calculated from the sex/gender-specific effect estimates and confidence intervals given in each study. The Female-to-Male Ratio (FMR) of Odds Ratios was then calculated as follows according to the method used by O'Keeffe et al. 2018 and Wang et al. 2019:

$$\text{beta}_{\text{diff}} = \text{beta}_{\text{females}} - \text{beta}_{\text{males}}$$

$$\text{stderr}_{\text{diff}} = \sqrt{(\text{stderr}_{\text{females}}^2 + \text{stderr}_{\text{males}}^2)}$$

$$\text{FMR} = \text{EXP}(\text{beta}_{\text{diff}} * 10)$$

$$\text{FMR CI} = \text{EXP}((\text{betadiff} \pm 1.96 * \text{stderrdiff}) * 10)$$

S3. PRISMA 2020 Main Checklist

Table 5. PRISMA 2020 Main Checklist

| Topic | No. | Item | Location where item is reported | |
|-----------------------------|-----|--|-------------------------------------|-------------|
| TITLE | | | Page | Line |
| Title | 1 | Identify the report as a systematic review. | 1 | 2 |
| ABSTRACT | | | | |
| Abstract | 2 | See the PRISMA 2020 for Abstracts checklist | 2 | 20ff |
| INTRODUCTION | | | | |
| Rationale | 3 | Describe the rationale for the review in the context of existing knowledge. | 3-4 (4) | 45ff (77ff) |
| Objectives | 4 | Provide an explicit statement of the objective(s) or question(s) the review addresses. | 4 | 92ff |
| METHODS | | | | |
| Eligibility criteria | 5 | Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses. | 5 | 105ff |
| Information sources | 6 | Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted. | 5 | 100ff |
| Search strategy | 7 | Ppresent the full search strategies for all databases, registers and websites, including any filters and limits used. | 5 (supplementary material A, S1) | 100ff |
| Selection process | 8 | Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process. | 5 | 105ff |
| | | | 6 | 126ff |

| Topic | No. | Item | Location where item is reported | |
|--------------------------------------|-----|--|---------------------------------|-------|
| Data collection process | 9 | Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process. | 7 | 129ff |
| | | | 7 | 131f |
| Data items | 10a | List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect. | 6 | 115ff |
| | 10b | List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information. | 7 | 129ff |
| Study risk of bias assessment | 11 | Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process. | 7 | 144ff |
| Effect measures | 12 | Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results. | 6 | 121f |
| | | | 8 | 180f |
| Synthesis methods | 13a | Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item 5)). | 6 | 112ff |

| Topic | No. | Item | Location where item is reported | |
|----------------------------------|-----|---|---------------------------------|-------------------------|
| | 13b | Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions. | 7 | 132ff |
| | 13c | Describe any methods used to tabulate or visually display results of individual studies and syntheses. | 8 | 155ff |
| | 13d | Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used. | 8 9 | 166ff 170ff 179ff |
| | 13e | Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression). | 9 | 183ff |
| | 13f | Describe any sensitivity analyses conducted to assess robustness of the synthesized results. | 9 | 187ff |
| Reporting bias assessment | 14 | Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases). | 9 | 185ff |
| Certainty assessment | 15 | Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome. | -- | -- |
| RESULTS | | | | |
| Study selection | 16a | Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram. | 10 | 199ff |
| | | | 11 | 215 |
| | 16b | Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded. | 10 | 203ff |

| Topic | No. | Item | Location where item is reported | |
|--------------------------------------|-----|--|---------------------------------|----------------|
| Study characteristics | 17 | Cite each included study and present its characteristics. | 11 supplementary material B | 218ff |
| Risk of bias in studies | 18 | Present assessments of risk of bias for each included study. | supplementary material B | -- |
| Results of individual studies | 19 | For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots. | 19ff; figures 4 to 10 | 353ff |
| Results of syntheses | 20a | For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies. | supplementary material B | |
| | 20b | Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect. | 17 19 | 322ff 353ff |
| | 20c | Present results of all investigations of possible causes of heterogeneity among study results. | 18 | 339ff |
| | 20d | Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results. | 22 | 402ff |
| Reporting biases | 21 | Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed. | 22 | 399ff |
| Certainty of evidence | 22 | Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed. | -- | -- |
| DISCUSSION | | | | |
| Discussion | 23a | Provide a general interpretation of the results in the context of other evidence. | 25 | 459ff |

| Topic | No. | Item | Location where item is reported | |
|---|-----|--|---------------------------------|-------|
| | 23b | Discuss any limitations of the evidence included in the review. | -- | -- |
| | 23c | Discuss any limitations of the review processes used. | 29 | 570ff |
| | 23d | Discuss implications of the results for practice, policy, and future research. | 30 | 588ff |
| OTHER INFORMATION | | | | |
| Registration and protocol | 24a | Provide registration information for the review, including register name and registration number, or state that the review was not registered. | 31 | 601ff |
| | 24b | Indicate where the review protocol can be accessed, or state that a protocol was not prepared. | 31 | 601ff |
| | 24c | Describe and explain any amendments to information provided at registration or in the protocol. | -- | -- |
| Support | 25 | Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review. | 31 | 616ff |
| Competing interests | 26 | Declare any competing interests of review authors. | 31 | 611 |
| Availability of data, code and other materials | 27 | Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review. | 31 | 613 |

S4. Overlaps and corresponding exclusions

Table 6. Overlaps and corresponding exclusions for short-term studies

| Study | Continent | Country | Study name | City | Study period | Outcome source | Exposure source | PM _{2.5} | PM ₁₀ | NO ₂ | O ₃ | Decision for meta-analysis |
|-------------------|-----------|---------|------------|----------|--------------|-----------------------------------|---|-------------------|------------------|-----------------|----------------|---|
| Duan et al. 2019 | Asia | China | None | Shenzhen | 2013-2017 | Shenzhen CDC | 7 state-controlled monitoring stations distributed in different administrative districts of Shenzhen, in accordance with mandatory quality assurance/quality control (QA/QC) procedures set by the State Environmental Protection Administration of China | | | no | | Exclude study, overlap with Gao et al. 2022 |
| Guo et al. 2017 | Asia | China | None | Shenzhen | 2012-2014 | Death registry system in Shenzhen | Shenzhen Environmental Monitoring Center, 10 monitors | | yes | no | yes | Exclude estimate for NO ₂ , overlap with Duan et al. 2019 & Gao et al. 2022 |
| Gao et al. 2022 | Asia | China | None | Shenzhen | 2013-2019 | Death registry system in Shenzhen | Shenzhen Environmental Monitoring Center, 10 monitors | | | yes | | Keep study, more recent analysis |
| Liu et al. 2015 | Asia | China | None | Wuhan | 2006-2009 | Hubei Provincial CDC | Municipal Environmental Protection Bureau of Wuhan, including the average daily Air Quality Index (AQI) of air pollutants, AQI levels were converted to concentration levels | | no | no | | Exclude study, overlap with Zhong et al. 2018 |
| Qian et al. 2010 | Asia | China | None | Wuhan | 2000-2004 | Wuhan CDC | Wuhan Air Automatic Monitoring System, operated by the Wuhan Environmental Monitoring Center, 7 monitors | | no | no | yes | Exclude estimates for PM ₁₀ & NO ₂ , overlap with Zhong et al. 2018 |
| Zhong et al. 2018 | Asia | China | None | Wuhan | 2002-2010 | Wuhan CDC | Wuhan Environmental Monitoring Center | | yes | yes | | Keep study, more recent analysis and longer study period |
| Cheng et al. 2019 | Asia | China | None | Hefei | 2013-2015 | Hefei CDC | Hefei Environmental Protection Bureau, 10 monitoring stations | no | | | no | Exclude study, overlap with Xu et al. 2020 |
| Sui et al. 2021 | Asia | China | None | Hefei | 2013-2018 | Hefei CDC | Hefei Environmental Protection Bureau, 10 monitoring stations | yes | | yes | | Keep study, more recent analysis |

| | | | | | | | | | | | | |
|--------------------|------|-------|------|---------------------------|----------------|-------------|--|-----|-----|-----|-----|--|
| Xu et al. 2020 | Asia | China | None | Hefei | 2006/2013-2017 | Hefei CDC | Hefei Environmental Protection Bureau, 10 monitoring stations | no | yes | no | yes | Exclude estimates for OM2.5 & NO2, overlap with Sui et al. 2021; keep estimates for PM10 and Ozone, more recent analysis |
| Zhang et al. 2017 | Asia | China | None | Hefei | 2010-2015 | Hefei CDC | Hefei Environmental Protection Bureau, 10 monitoring stations | | no | no | | Exclude study, overlap with Xu et al. 2020 and Sui et al. 2021 |
| Gong et al. 2019 | Asia | China | None | Beijing | 2006-2011 | Chinese CDC | Beijing Meteorological Bureau, 1 monitoring station located in the Haidian district | yes | | | | Keep study, more recent analysis and longer time period |
| Luo et al. 2016 | Asia | China | None | Beijing | 2008-2011 | Chinese CDC | Air quality monitoring station of the U.S. embassy, 1 monitoring station with a radius of 40km, located in the Chaoyang district | no | | | | Exclude study, overlap with Gong et al. 2019 |
| Su et al. 2015 | Asia | China | None | Beijing | May-Dez 2008 | Beijing CDC | PM2.5: obtained by a TEOM® RP1400A air sampler, located in the Haidian district | no | yes | yes | | Exclude estimate for PM _{2.5} , overlap with Gong et al. 2019 |
| Chen C et al. 2018 | Asia | China | None | nationwide (30 counties) | 2013-2015 | Chinese CDC | National Air pollution monitoring system | no | | | | Exclude study, overlap with Chen R et al. 2017, smaller study population |
| Chen C et al. 2023 | Asia | China | None | nationwide (323 counties) | 2013-2015 | Chinese CDC | National Urban Air Quality Real-Time Release Platform | | | | yes | Keep study, larger study population |
| Chen R et al. 2017 | Asia | China | None | nationwide (272 cities) | 2013-2015 | Chinese CDC | National Urban Air Quality Real-time Publishing Platform | yes | | | | Keep study, larger study population |
| Chen R et al. 2018 | Asia | China | None | nationwide (272 cities) | 2013-2015 | Chinese CDC | National Urban Air Quality Real-time Publishing Platform | | | yes | | Keep study, larger study population |
| He et al. 2020 | Asia | China | None | nationwide (42 counties) | 2013-2015 | Chinese CDC | National Air Pollution Monitoring System | | | no | | Exclude study, overlap with Chen R et al. 2018, smaller study population |
| Yin et al. 2017 | Asia | China | None | nationwide (272 cities) | 2013-2015 | Chinese CDC | China's National Urban Air Quality real-time Publishing Platform | | | | no | Exclude study, overlap with Chen C et al. 2023, smaller study population |

| | | | | | | | | | | | | | |
|------------------|---------------|--------|------|---------------------|----------------|---|---|--|-----|-----|---------------------------------|---|--|
| Shin et al. 2020 | North America | Canada | None | 24 census divisions | 1984-2012 | Vital Statistics database, managed by Statistics Canada | National Air Pollution Surveillance System | | | yes | Keep study, longer study period | | |
| Shin et al. 2022 | North America | Canada | None | 24 census divisions | 2001-2012 | Vital Statistics database, managed by Statistics Canada | National Air Pollution Surveillance System | | yes | yes | no | Exclude estimate for Ozone, overlap with Shin et al. 2020 | |
| Byun et al. 2021 | Asia | Korea | None | Seoul | 1998/2001-2015 | Statistics Korea | National Institute of Environmental Research; Seoul Metropolitan Government Research Institute of Public Health and Environment; 25 monitoring stations | | | yes | | Keep study, more recent analysis; longer study period | |
| Son et al. 2012 | Asia | Korea | None | Seoul | 2000-2007 | Korean National Statistical Office | Department of Environment, Republic of Korea, 27 monitoring stations | | | no | yes | yes | Exclude estimate for PM _{2.5} , overlap with Byun et al. 2021 |
| Yi et al. 2010 | Asia | Korea | None | Seoul | 2000-2006 | Korean National Statistical Office | Korean National Institute of Environmental Research, 27 monitoring stations | | | no | | | Exclude study, overlap with Byun et al. 2021 |

Table 7. Overlaps and corresponding exclusions for long-term studies

| Study | Continent | Country | Study name | City | Study period | Outcome source | Exposure source | PM2.5 | PM ₁₀ | NO ₂ | O ₃ | Decision for meta-analysis |
|------------------------------|---------------|---------|--|--|--------------|--|---|-------|------------------|-----------------|----------------|--|
| Hvidtfeldt et al. 2019 | Europe | Denmark | Danish, Diet, Cancer & Health cohort | Kopenhagen & Aarhus | 1993-2015 | Danish Register of Causes of Death | Danish AirGIS dispersion modeling system | yes | yes | yes | | Keep study, more recent analysis, longer study period |
| Raaschou-Nielsen et al. 2012 | Europe | Denmark | Danish, Diet, Cancer & Health cohort | Kopenhagen & Aarhus | 1993-2009 | Danish Register of Causes of Death | Danish AirGIS dispersion modeling system | | | no | | Exclude study, overlap with Hvidtfeldt et al. 2019 |
| Hayes et al. 2020 | North America | USA | National Institutes of Health-AARP Diet and Health Study | 6 states (California, Florida, Louisiana, New Jersey, North Carolina, Pennsylvania) and 2 urban areas (Atlanta, Detroit) | 1995-2011 | Linkage to Social Security Administration Death Master File, cancer registries, responses to follow-up questionnaires, responses to mailings | Hybrid LUR geostatistical model, at the census tract level, based on data from the U.S. Environmental Protection Agency nationwide Air Quality System | yes | | | | Keep study, more recent analysis and longer study period |
| Thurston et al. 2016 | North America | USA | National Institutes of Health-AARP Diet and Health Study | 6 states (California, Florida, Louisiana, New Jersey, North Carolina, Pennsylvania) and 2 urban areas (Atlanta, Detroit) | 2000-2009 | Linkage to Social Security Administration Death Master File, cancer registries, responses to follow-up questionnaires, responses to mailings | Hybrid LUR geostatistical model, at the census tract level, based on data from the U.S. Environmental Protection Agency nationwide Air Quality System | no | | | | Exclude study, overlap with Hayes et al. 2020 |
| Wong et al. 2015 | Asia | China | None | Hong Kong | 1998-2011 | Linkage to death registry | Estimated from the U.S. National Aeronautics and Space Administration | no | | | | Exclude study, overlap with Yang Y et al. 2018 |

| | | | | | | | | | | | |
|--------------------|------|-------|------|-------------------------------------|-----------|----------------------------------|--|-----|-----|--|--|
| | | | | | | | (NASA) satellite data; 1kmx1km resolution | | | | |
| Yang Y et al. 2018 | Asia | China | None | Hong Kong | 1998-2011 | Linkage to death registry | LUR, precisely to home addresses | yes | | | Keep study, more recent analysis |
| Zhang et al. 2011 | Asia | China | None | Shenyang | 1998-2009 | National cause of death register | Shenyang Environmental Monitoring Center, 5 monitoring stations | no | yes | | Exclude estimate for PM ₁₀ , overlap with Zhang et al. 2014 |
| Zhang et al. 2014 | Asia | China | None | Shenyang, Tianjin, Taiyuan & Rizhao | 1998-2009 | Local CDC | Local Environmental Monitoring Centers, 5 monitoring stations in Shenyang, 7 in Tianjin, 2 in Taiyuan, 1 in Rizhao | yes | | | Keep study, more recent analysis |

S5. Assessment matrix for consideration of sex/gender

Table 8. Assessment matrix for consideration of sex/gender for short-term studies

| ID | Precise sex/gender terms used | Sex/gender in the title | Sex/gender in the abstract | Sex/gender in the rationale | Sex/gender in the objectives | Sex/gender in the hypotheses | Recruitment information described | Sex/gender specific recruitment described | Source of sex/gender information reported | Sex/gender dimensions / variability considered | Sex/gender analysis reported | Sex/gender distribution reported | Sex/gender findings reported | Sex/gender findings discussed |
|----|-------------------------------|-------------------------|----------------------------|-----------------------------|------------------------------|------------------------------|-----------------------------------|---|---|--|------------------------------|----------------------------------|------------------------------|-------------------------------|
| | a b | a b | a b c d | a b c | a b c | a b | a b | a b | a b c | a b c | a b c | a b | a b c d | a b c |
| 1 | a | a | a | a | c | a | NA | b | b | a | c | b | d | b |
| 2 | a | a | a | b | a | a | NA | b | a | a | c | b | c | a |
| 3 | a | a | a | c | a | a | NA | b | a | a | c | b | d | c |
| 4 | a | a | a | c | a | a | NA | b | b | a | c | b | c | c |
| 5 | a | a | c | b | b | a | NA | b | a | a | c | b | c | c |
| 6 | a | a | a | a | a | a | NA | b | a | a | c | b | c | b |
| 7 | a | a | a | a | a | a | NA | b | a | a | c | a | c | a |
| 8 | a | a | c | b | b | a | NA | b | a | a | c | a | c | b |
| 9 | a | a | c | c | a | a | NA | b | a | a | c | b | c | c |
| 10 | a | a | c | a | a | a | NA | b | b | a | c | b | c | c |
| 11 | a | a | a | a | b | a | NA | b | a | a | c | b | c | a |
| 12 | a | a | a | a | a | a | NA | b | a | a | c | b | c | a |
| 13 | a | a | c | a | a | a | NA | b | b | a | c | b | c | c |
| 14 | a | a | a | a | a | a | NA | a | a | a | c | b | c | a |
| 15 | a | a | c | a | c | a | NA | b | b | a | c | b | c | b |
| 16 | a | a | c | a | a | a | NA | b | b | a | c | b | c | b |
| 17 | a | a | a | a | a | a | NA | b | a | a | c | a | c | a |
| 18 | a | a | c | a | b | a | NA | b | b | a | c | b | c | c |
| 19 | a | a | c | a | b | a | NA | b | a | a | c | b | c | a |
| 20 | a | a | c | a | a | a | NA | b | b | a | c | b | c | b |
| 21 | a | a | c | a | a | a | NA | b | b | a | c | a | c | c |
| 22 | a | a | a | a | a | a | NA | b | a | a | c | b | c | c |
| 23 | a | b | c | a | c | a | NA | b | b | a | c | b | d | c |
| 24 | a | a | a | a | a | a | NA | b | a | a | c | a | c | a |
| 25 | a | a | a | a | a | a | NA | b | b | a | c | b | c | b |
| 26 | a | a | a | a | a | a | NA | b | b | a | c | a | c | c |
| 27 | a | a | a | a | b | a | NA | b | b | a | c | b | c | b |

| ID | Precise sex/gender terms used | Sex/gender in the title | Sex/gender in the abstract | Sex/gender in the rationale | Sex/gender in the objectives | Sex/gender in the hypotheses | Recruitment information described | Sex/gender specific recruitment described | Source of sex/gender information reported | Sex/gender dimensions / variability considered | Sex/gender analysis reported | Sex/gender distribution reported | Sex/gender findings reported | Sex/gender findings discussed |
|----|-------------------------------|-------------------------|----------------------------|-----------------------------|------------------------------|------------------------------|-----------------------------------|---|---|--|------------------------------|----------------------------------|------------------------------|-------------------------------|
| | a b | a b | a b c d | a b c | a b c | a b | a b | a b | a b c | a b c | a b c | a b | a b c d | a b c |
| 28 | a | a | a | a | a | a | NA | b | a | a | c | b | c | c |
| 29 | a | a | a | a | b | a | NA | b | a | a | c | b | c | c |
| 30 | a | a | c | a | a | a | NA | b | b | a | c | b | d | c |
| 31 | a | a | c | a | a | a | NA | b | b | a | c | a | c | c |
| 32 | a | a | c | b | b | a | NA | b | a | a | c | b | c | c |
| 33 | a | a | a | a | a | a | NA | b | a | a | c | b | c | c |
| 34 | a | a | c | a | a | a | NA | b | a | a | c | b | d | a |
| 35 | a | a | a | a | a | a | NA | b | a | a | c | a | c | c |
| 36 | a | a | c | a | c | a | NA | b | a | a | c | b | c | c |
| 37 | a | a | b | b | c | a | NA | b | a | a | c | b | c | b |
| 38 | a | b | c | a | c | a | NA | b | a | a | c | a | c | c |
| 39 | a | a | c | b | a | a | NA | b | a | a | c | b | c | a |
| 40 | a | a | c | c | c | a | NA | b | a | a | c | b | d | c |
| 41 | a | a | a | b | c | a | NA | b | a | a | c | b | c | c |
| 42 | a | a | b | c | a | a | NA | b | a | a | c | b | c | a |
| 43 | a | a | a | b | b | a | NA | b | a | a | c | b | c | b |
| 44 | a | a | a | a | a | a | NA | b | b | a | c | b | d | b |
| 45 | a | a | a | a | b | a | NA | b | c | a | c | b | d | b |
| 46 | a | b | d | c | c | a | NA | b | a | a | c | b | d | c |
| 47 | a | b | d | c | c | a | NA | b | b | a | c | b | d | c |
| 48 | a | a | b | b | c | a | NA | b | a | a | c | b | d | c |
| 49 | a | a | c | a | a | a | NA | b | a | a | c | b | c | c |
| 50 | a | a | c | a | a | a | NA | b | a | a | c | b | c | b |
| 51 | a | a | c | a | a | a | NA | b | b | a | c | b | d | c |
| 52 | a | a | a | a | a | a | NA | b | a | a | c | b | c | c |
| 53 | a | a | c | a | c | a | NA | b | a | a | c | b | c | c |
| 54 | a | a | c | b | b | a | NA | b | b | a | c | b | c | c |
| 55 | a | a | b | a | a | a | NA | b | a | a | c | b | c | c |
| 56 | a | a | b | a | c | a | NA | b | a | a | c | b | c | c |
| 57 | a | a | c | a | b | a | NA | b | a | a | c | b | c | a |
| 58 | a | a | c | a | c | a | NA | b | a | a | c | b | c | c |

| ID | Precise sex/gender terms used | Sex/gender in the title | Sex/gender in the abstract | Sex/gender in the rationale | Sex/gender in the objectives | Sex/gender in the hypotheses | Recruitment information described | Sex/gender specific recruitment described | Source of sex/gender information reported | Sex/gender dimensions / variability considered | Sex/gender analysis reported | Sex/gender distribution reported | Sex/gender findings reported | Sex/gender findings discussed |
|----|-------------------------------|-------------------------|----------------------------|-----------------------------|------------------------------|------------------------------|-----------------------------------|---|---|--|------------------------------|----------------------------------|------------------------------|-------------------------------|
| | a b | a b | a b c d | a b c | a b c | a b | a b | a b | a b c | a b c | a b c | a b | a b c d | a b c |
| 59 | a | a | c | a | a | a | NA | b | a | a | c | b | c | c |
| 60 | a | a | a | a | a | a | NA | b | a | a | c | b | c | c |
| 61 | a | a | c | a | a | a | NA | a | a | a | c | a | c | c |
| 62 | a | a | c | a | a | a | NA | b | b | a | c | a | c | c |
| 63 | a | a | d | c | c | a | NA | b | a | a | c | b | c | c |
| 64 | a | a | a | a | a | a | NA | a | a | a | c | a | c | a |
| 65 | a | a | b | a | a | a | NA | b | b | a | c | b | c | c |
| 66 | a | a | c | a | c | a | NA | b | b | a | c | b | d | b |
| 67 | a | a | c | c | b | a | NA | b | a | a | c | b | c | c |

1: Adebayo-Ojo et al. 2022, 2: Berger et al. 2018, 3: Bravo et al. 2016, 4: Byun et al. 2019, 5: Chen C et al. 2018, 6: Chen et al. 2010, 7: Chen et al. 2017, 8: Chen et al. 2023, 9: Chen R et al. 2018, 10: Cheng et al. 2019, 11: Dabass et al. 2013, 12: Dastoorpoor et al. 2018, 13: Duan et al. 2019, 14: Fu et al. 2020, 15: Gao et al. 2022, 16: Gariazzo et al. 2022, 17: Goldberg et al. 2001, 18: Gong et al. 2019, 19: Guo et al. 2107, 20: Han et al. 2020, 21: He et al. 2020, 22: Hůnová et al. 2013, 23: Kužma et al. 2020, 24: Lanzinger et al. 2016, 25: Li et al. 2018, 26: Li et al. 2021, 27: Li et al. 2022, 28: Liu et al. 2015, 29: Liu et al. 2019, 30: Liu et al. 2021, 31: Lu et al. 2022, 32: Luo et al. 2016, 33: Ma et al. 2011, 34: Maciejewska et al. 2020, 35: Milojevic et al. 2014, 36: Mokoena et al. 2019, 37: Ostro et al. 2008, 38: Psistaki et al. 2023, 39: Qian et al. 2010, 40: Qin et al. 2017, 41: Qu et al. 2018, 42: Raza et al. 2018, 43: Ren et al. 2010, 44: Saucy et al. 2021, 45: Shi et al. 2020, 46: Shin et al. 2020, 47: Shin et al. 2022, 48: Son et al. 2012, 49: Stojić et al. 2016, 50: Su et al. 2015, 51: Sui et al. 2021, 52: Wu et al. 2018, 53: Xu J et al. 2020, 54: Xu M et al. 2020, 55: Yang et al. 2013, 56: Yi et al. 2010, 57: Yin et al. 2017, 58: Yu et al. 2019, 59: Zhang et al. 2017, 60: Zhang et al. 2018, 61: Zhang et al. 2019, 62: Zhang et al. 2022, 63: Zhong et al. 2018, 64: Zhou et al. 2021, 65: Zhou P et al. 2022, 66: Zhou X et al. 2022, 67: Zhu et al. 2017

Table 9. Assessment matrix for consideration of sex/gender for long-term studies

| ID | Precise sex/gender terms used | Sex/gender in the title | Sex/gender in the abstract | Sex/gender in the rationale | Sex/gender in the objectives | Sex/gender in the hypotheses | Recruitment information described | Sex/gender specific recruitment described | Source of sex/gender information reported | Sex/gender dimensions/variability considered | Sex/gender analysis reported | Sex/gender distribution reported | Sex/gender findings reported | Sex/gender findings discussed |
|----|-------------------------------|-------------------------|----------------------------|-----------------------------|------------------------------|------------------------------|-----------------------------------|---|---|--|------------------------------|----------------------------------|------------------------------|-------------------------------|
| | a b | a b | a b c d | a b c | a b c | a b | a b | a b | a b c | a b c | a b c | a b | a b c d | a b c |
| 1 | a | a | b | b | c | a | NA | b | a | a | c | a | c | b |
| 2 | a | a | b | c | c | a | NA | b | b | a | c | b | c | b |
| 3 | a | a | a | a | a | a | NA | a | a | a | c | b | c | a |
| 4 | a | a | a | a | a | a | NA | a | a | a | c | b | c | a |
| 5 | a | a | b | c | c | a | NA | b | a | a | c | b | c | b |
| 6 | a | a | a | a | a | a | NA | b | a | a | c | b | c | a |
| 7 | a | a | a | a | a | a | NA | b | a | a | c | b | c | a |
| 8 | a | a | b | a | a | a | NA | a | b | a | c | b | c | a |
| 9 | a | a | a | a | a | a | NA | b | a | a | c | b | c | b |
| 10 | a | a | a | a | a | a | NA | b | a | a | c | b | c | b |
| 11 | a | a | a | a | a | a | NA | b | a | a | c | b | c | c |
| 12 | a | a | b | a | a | a | NA | b | b | a | c | b | c | a |
| 13 | a | a | a | a | a | a | NA | b | b | a | c | b | c | a |
| 14 | a | a | c | a | a | a | NA | b | b | a | c | b | c | a |
| 15 | a | a | a | a | a | a | b | b | a | a | c | b | c | a |
| 16 | a | a | a | a | a | a | NA | b | b | a | c | b | c | a |
| 17 | a | a | d | a | b | a | NA | b | b | a | c | b | c | c |
| 18 | a | a | a | a | a | a | NA | b | b | a | c | b | c | a |
| 19 | a | a | a | a | a | a | NA | b | a | a | c | b | c | a |
| 20 | a | a | a | a | a | a | NA | b | b | a | c | b | c | b |
| 21 | a | a | a | a | a | a | NA | b | b | a | c | b | d | a |
| 22 | a | a | a | a | a | a | NA | b | a | a | c | b | c | a |
| 23 | a | a | c | a | a | a | NA | b | b | a | c | b | c | a |
| 24 | a | a | a | a | a | a | NA | a | a | a | c | b | c | b |
| 25 | a | a | a | c | a | a | NA | a | b | a | c | a | c | a |
| 26 | a | a | a | a | b | a | NA | b | a | a | c | b | c | b |
| 27 | a | a | a | a | a | a | NA | b | b | a | c | b | c | c |
| 28 | a | a | c | a | a | a | NA | b | c | a | c | b | c | a |
| 29 | a | a | c | a | a | a | NA | a | b | a | c | a | d | b |
| 30 | a | a | a | a | a | a | NA | a | a | a | c | b | c | a |
| 31 | a | a | a | a | a | a | NA | a | a | a | c | b | c | a |
| 32 | a | a | c | a | c | a | NA | b | a | a | c | a | d | b |
| 33 | a | a | a | a | a | a | NA | a | a | a | c | b | c | c |

| ID | Precise sex/gender terms used | Sex/gender in the title | Sex/gender in the abstract | Sex/gender in the rationale | Sex/gender in the objectives | Sex/gender in the hypotheses | Recruitment information described | Sex/gender specific recruitment described | Source of sex/gender information reported | Sex/gender dimensions/variability considered | Sex/gender analysis reported | Sex/gender distribution reported | Sex/gender findings reported | Sex/gender findings discussed |
|----|-------------------------------|-------------------------|----------------------------|-----------------------------|------------------------------|------------------------------|-----------------------------------|---|---|--|------------------------------|----------------------------------|------------------------------|-------------------------------|
| | a b | a b | a b c d | a b c | a b c | a b | a b | a b | a b c | a b c | a b c | a b | a b c d | a b c |
| 34 | a | a | a | a | a | a | NA | a | a | a | c | b | c | b |
| 35 | a | a | a | a | a | a | NA | a | a | a | c | b | c | a |
| 36 | a | a | a | a | a | a | NA | b | b | a | c | b | c | c |
| 37 | a | a | b | b | b | a | NA | a | a | a | c | b | c | c |
| 38 | a | a | a | b | b | a | NA | b | a | a | c | b | c | b |
| 39 | a | a | a | a | b | a | NA | a | b | a | c | b | c | a |

1: Al-Hamdan et al. 2018, 2: Alexeeff et al. 2023, 3: Beelen et al. 2014, 4: Bentayeb et al. 2015, 5: Cesaroni et al. 2013, 6: Chen et al. 2013, 7: Dehbi et al. 2017, 8: Eum et al. 2022, 9: Fischer et al. 2015, 10: Hayes et al. 2020, 11: Hvidtfeldt et al. 2019, 12: Hystad et al. 2020, 13: Jalali et al. 2021, 14: Kazemiparkouhi et al. 2022, 15: Kim et al. 2019, 16: Kim et al. 2020, 17: Kim et al. 2021, 18: Liang et al. 2020, 19: Lim et al. 2019, 20: Lim et al. 2020, 21: Liu et al. 2022, 22: Naess et al. 2007, 23: Niu et al. 2022, 24: Pinault et al. 2016, 25: Pope et al. 2015, 26: Raaschou-Nielsen et al. 2012, 27: Raaschou-Nielsen et al. 2020, 28: Rudolph et al. 2022, 29: Takeuchi et al. 2021, 30: Thurston et al. 2016, 31: Turner et al. 2016, 32: Wang et al. 2020, 33: Weichenthal et al. 2014, 34: Wong et al. 2015, 35: Yang et al. 2018, 36: Yu et al. 2020, 37: Zhang et al. 2011, 38: Zhang et al. 2014, 39: Zhang et al. 2021

S6. Results of meta-analysis including moderator to explore heterogeneity

Table 10. Results of meta-analysis of short-term studies including moderator to explore heterogeneity

| Air pollutant | Model | Moderator | N | I ² | QEp | QMp | R ² |
|------------------------|-------------------------------|------------------------|----|----------------|--------|-------------|----------------|
| PM _{2.5} | Random | -- | 66 | 97.0 | <.0001 | -- | -- |
| | Mixed – categorical moderator | Continent | 66 | 97.1 | 0.0000 | 0.76 | 0.1 |
| | | Study type | 66 | 93.1 | 0.0000 | 0.73 | 55.9 |
| | | Lag | 66 | 96.7 | 0.0000 | 0.00 | 14.2 |
| | Mixed – continuous moderator | CVD cases [in total] | 30 | 98.1 | <.0001 | 0.57 | 1.9 |
| | | CDV cases [daily mean] | 22 | 94.8 | <.0001 | 0.48 | 0.0 |
| | | Exposure mean | 58 | 95.8 | <.0001 | 0.00 | 30.6 |
| | | Follow up | 66 | 96.6 | <.0001 | 0.63 | 10.1 |
| | | Publication year | 66 | 97.0 | <.0001 | 0.03 | 0.0 |
| | | | | | | | |
| PM ₁₀ | Random | -- | 52 | 98.0 | <0.001 | -- | -- |
| | Mixed – categorical moderator | Continent | 52 | 95.5 | 0.0000 | 0.35 | 4.8 |
| | | Study type | 52 | 98.0 | 0.0000 | 0.43 | 0.0 |
| | | Lag | 52 | 73.9 | 0.0000 | 0.00 | 84.9 |
| | Mixed – continuous moderator | CVD cases [in total] | 26 | 97.6 | <.0001 | 0.70 | 0.0 |
| | | CDV cases [daily mean] | 20 | 90.6 | <.0001 | 0.00 | 0.0 |
| | | Exposure mean | 50 | 89.0 | <.0001 | 0.00 | 72.3 |
| | | Follow up | 52 | 94.7 | <.0001 | 0.25 | 51.0 |
| | | Publication year | 52 | 97.6 | <.0001 | 0.00 | 0.0 |
| | | | | | | | |
| NO ₂ | Random | -- | 42 | 74.4 | <0.001 | -- | -- |
| | Mixed – categorical moderator | Continent | 42 | 59.0 | 0.0000 | 0.00 | 40.9 |
| | | Study type | 42 | 66.9 | 0.0000 | 0.04 | 21.9 |
| | | Lag | 42 | 61.8 | 0.0000 | 0.00 | 38.5 |
| | Mixed – continuous moderator | CVD cases [in total] | 24 | 51.6 | 0.0023 | 0.01 | 24.6 |
| | | CDV cases [daily mean] | 18 | 61.9 | 0.0004 | 0.27 | 14.4 |
| | | Exposure mean | 38 | 68.9 | <.0001 | 0.04 | 8.0 |
| | | Follow up | 42 | 74.8 | <.0001 | 0.77 | 0.0 |
| | | Publication year | 42 | 72.7 | <.0001 | 0.12 | 5.9 |
| | | | | | | | |
| O ₃ , 8hmax | Random | -- | 18 | 71.3 | <0.001 | -- | -- |
| | Mixed – categorical moderator | Continent | 18 | 71.6 | 0.0000 | 0.99 | 0.0 |
| | | Study type | 18 | 71.8 | 0.0000 | 0.75 | 0.0 |
| | | Lag | 18 | 49.4 | 0.0223 | 0.00 | 64.8 |
| | Mixed – continuous moderator | CVD cases [in total] | 8 | 29.2 | 0.2053 | 0.03 | 57.3 |
| | | CDV cases [daily mean] | 2 | NA | NA | NA | NA |
| | | Exposure mean | 16 | 71.2 | 0.0000 | 0.81 | 7.7 |
| | | Follow up | 18 | 71.8 | 0.0000 | 0.93 | 0.0 |
| | | Publication year | 18 | 68.9 | 0.0000 | 0.79 | 6.4 |

^a estimate für mixed model with categorical moderator: %-change in CVD death risk for an increase of 10 µg/m³ in exposure; estimate für mixed model with continuous moderator: %-change of the average CVD death risk associated with air pollution exposure per unit increase in continuous moderator

CI, confidence interval, QEp, *p*-value of test for heterogeneity (in case of mixed model: test for residual heterogeneity); QMp, *p*-value of test of differences between categories of moderator (test if at least part of the moderators explain some heterogeneity); R², amount of heterogeneity accounted for

Table 11. Results of meta-analysis of long-term studies including moderator to explore heterogeneity

| Air pollutant | Model | Moderator | N | I ² | QEp | QMp | R ² |
|-------------------|-------------------------------|----------------------------|----|----------------|--------|------------------|----------------|
| PM _{2.5} | Random | -- | 42 | 87.9 | <.0001 | -- | -- |
| | Mixed – categorical moderator | Continent | 42 | 81.6 | <.0001 | <.0001 | 30.9 |
| | | Exposure assessment method | 42 | 88.0 | <.0001 | 0.43 | 55.0 |
| | Mixed – continuous moderator | Follow up | 42 | 88 | <.0001 | 0.74 | 0 |
| | | Minimum age at baseline | 24 | 78.1 | <.0001 | 0.00 | 49.5 |
| | | Population size | 32 | 81.3 | <.0001 | 0.23 | 0 |
| | | Publication year | 42 | 88.1 | <.0001 | 0.66 | 0 |
| PM ₁₀ | Random | -- | 12 | 89.1 | <0.001 | -- | -- |
| | Mixed – categorical moderator | Continent | 12 | 77.7 | <.0001 | 0.21 | 49.2 |
| | | Exposure assessment method | 12 | 74.9 | <.0001 | 0.05 | 60.5 |
| | Mixed – continuous moderator | Follow up | 12 | 84.9 | <.0001 | 0.35 | 26.3 |
| | | Minimum age at baseline | 6 | 47.8 | 0.1046 | 0.01 | 63.9 |
| | | Population size | 12 | 73.1 | <.0001 | 0.02 | 58.6 |
| | | Publication year | 12 | 89.9 | <.0001 | 0.78 | 0 |
| NO ₂ | Random | -- | 24 | 98.4 | <0.001 | -- | -- |
| | Mixed – categorical moderator | Continent | 24 | 77.2 | <.0001 | <.0001 | 93.8 |
| | | Exposure assessment method | 24 | 98.4 | <.0001 | 0.41 | 7.9 |
| | Mixed – continuous moderator | Follow up | 24 | 98.4 | <.0001 | 0.60 | 2.7 |
| | | Minimum age at baseline | 16 | 73.2 | <.0001 | 0.02 | 24.1 |
| | | Population size | 24 | 89.6 | <.0001 | 0.00 | 83.2 |
| | | Publication year | 24 | 93.4 | <.0001 | 0.02 | 73.1 |

^a estimate für mixed model with categorical moderator: %-change in CVD death risk for an increase of 10 µg/m³ in exposure; estimate für mixed model with continuous moderator: %-change of the average CVD death risk associated

CI, confidence interval, QEp, *p*-value of test for heterogeneity (in case of mixed model: test for residual heterogeneity); QMp, *p*-value of test of differences between categories of moderator (test if at least part of the moderators explain some heterogeneity); R², amount of heterogeneity accounted for

S7. Publication bias

S7.1 Funnel plots of short-term studies

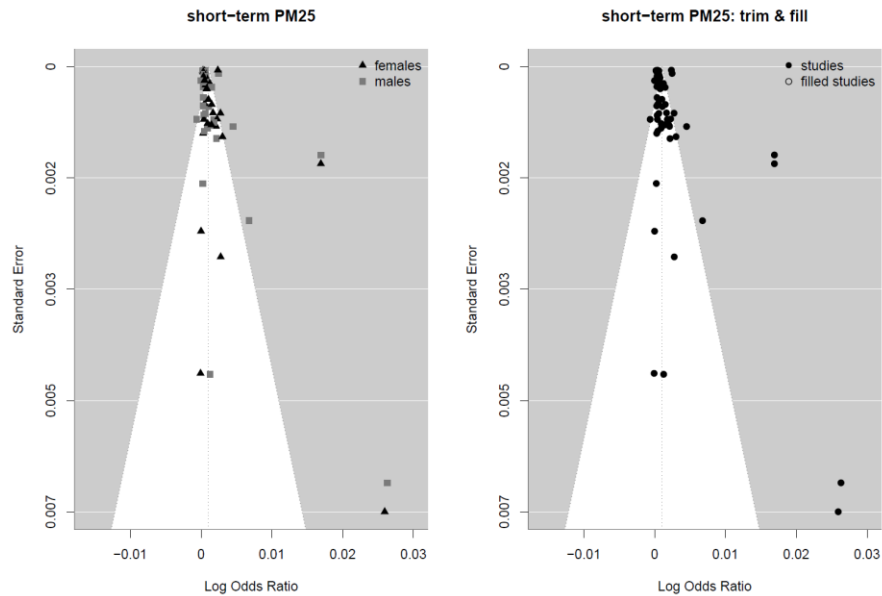


Figure 1. Funnel plots of included short-term studies on the association between PM_{2.5} and cardiovascular mortality.

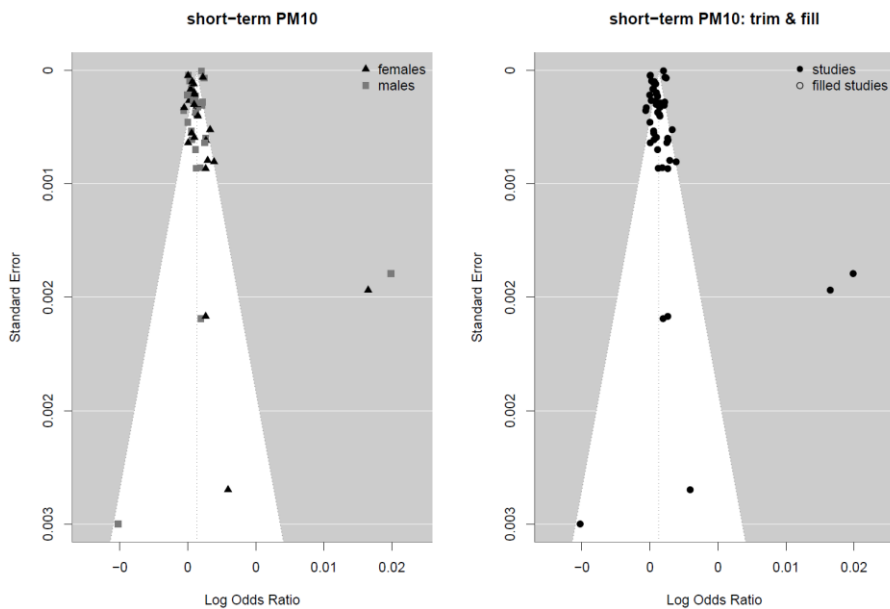


Figure 2. Funnel plots of included short-term studies on the association between PM₁₀ and cardiovascular mortality.

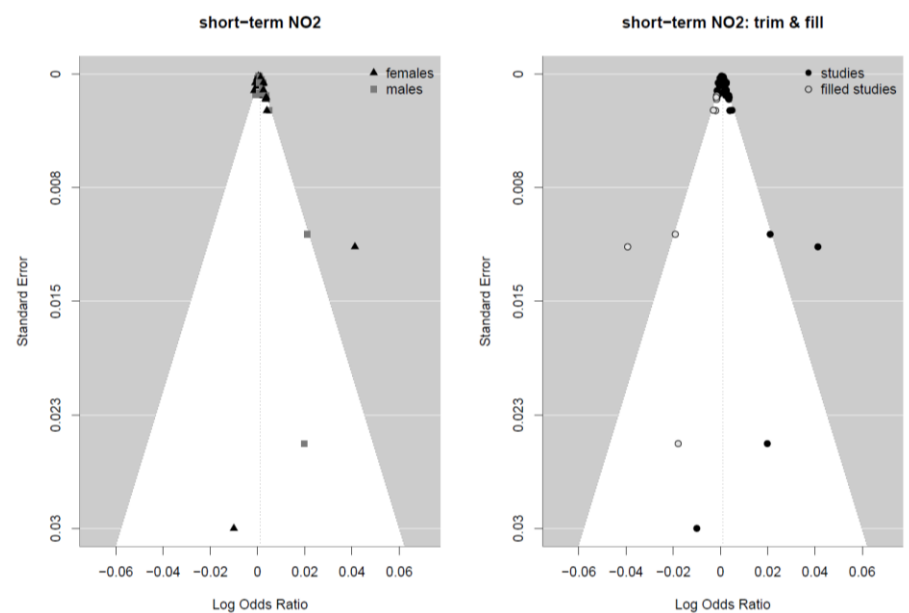


Figure 3. Funnel plots of included short-term studies on the association between NO_2 and cardiovascular mortality

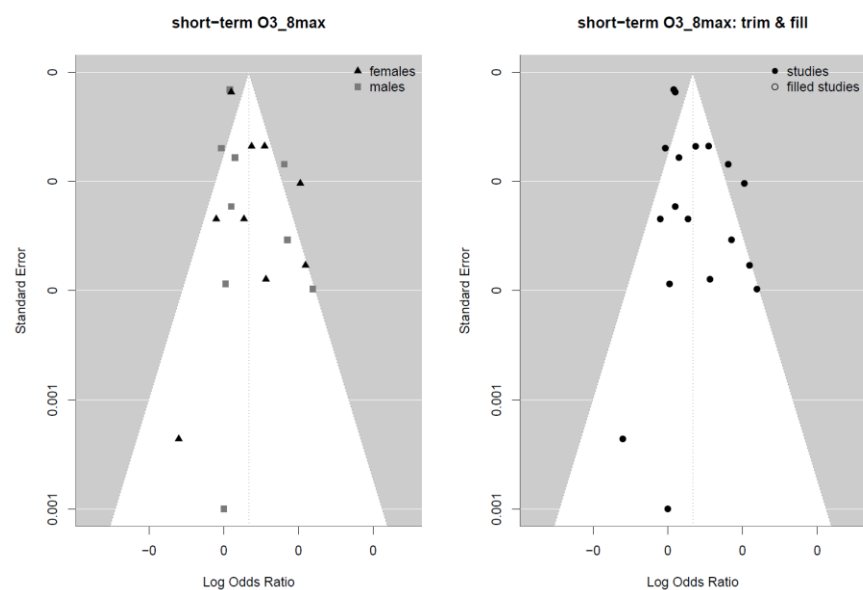


Figure 4. Funnel plots of included short-term studies on the association between $\text{Ozone}_{8\text{hmax}}$ and cardiovascular mortality

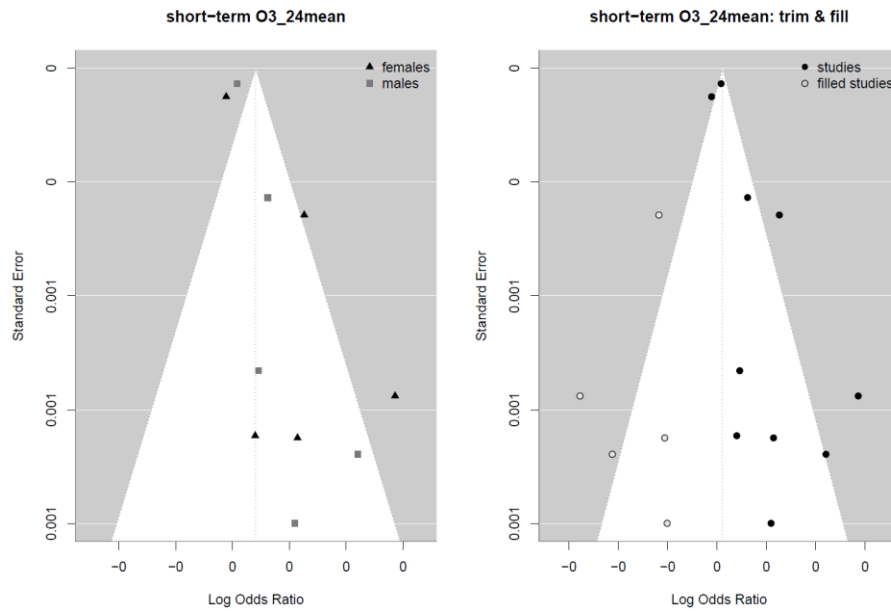


Figure 5. Funnel plots of included short-term studies on the association between Ozone_{24hmean} and cardiovascular mortality

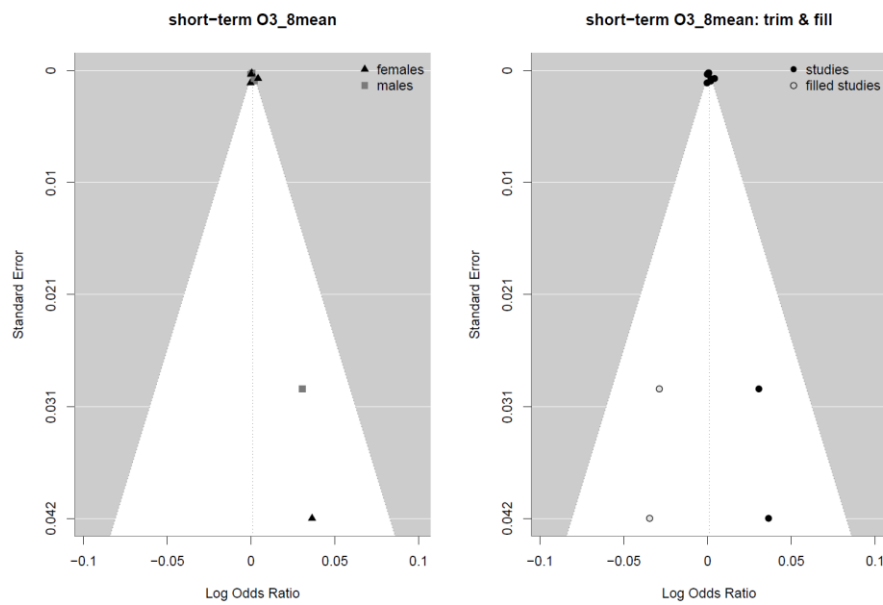


Figure 6. Funnel plots of included short-term studies on the association between Ozone_{8hmean} and cardiovascular mortality

S7.2 Funnel plots of long-term studies

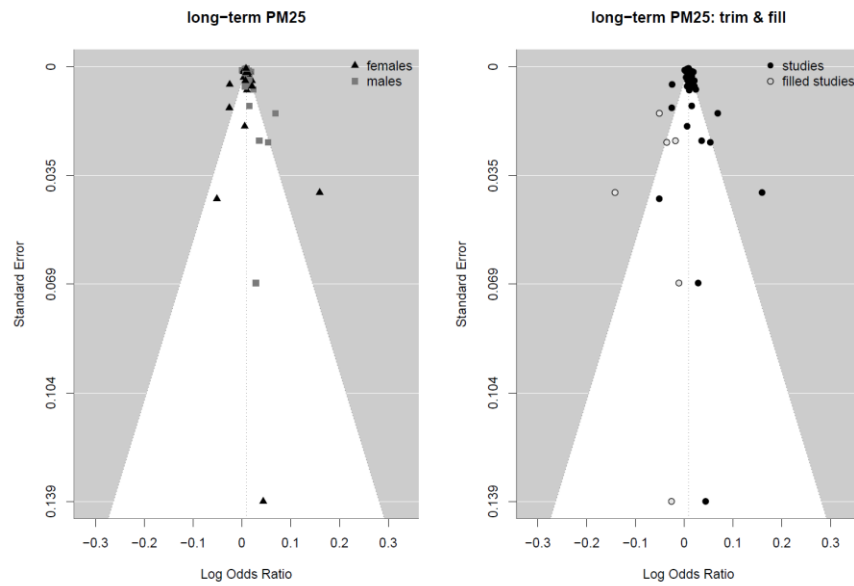


Figure 7. Funnel plots of included short-term studies on the association between $PM_{2.5}$ and cardiovascular mortality

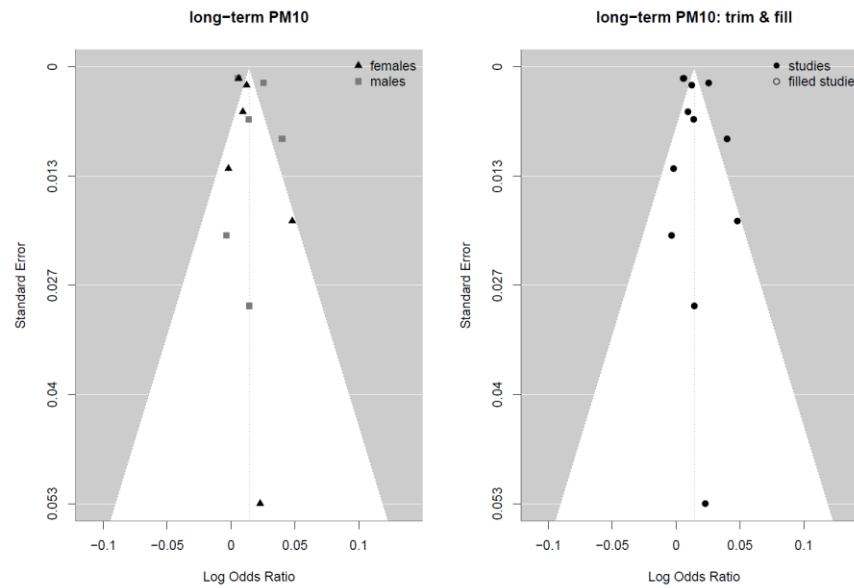


Figure 8. Funnel plots of included short-term studies on the association between PM_{10} and cardiovascular mortality

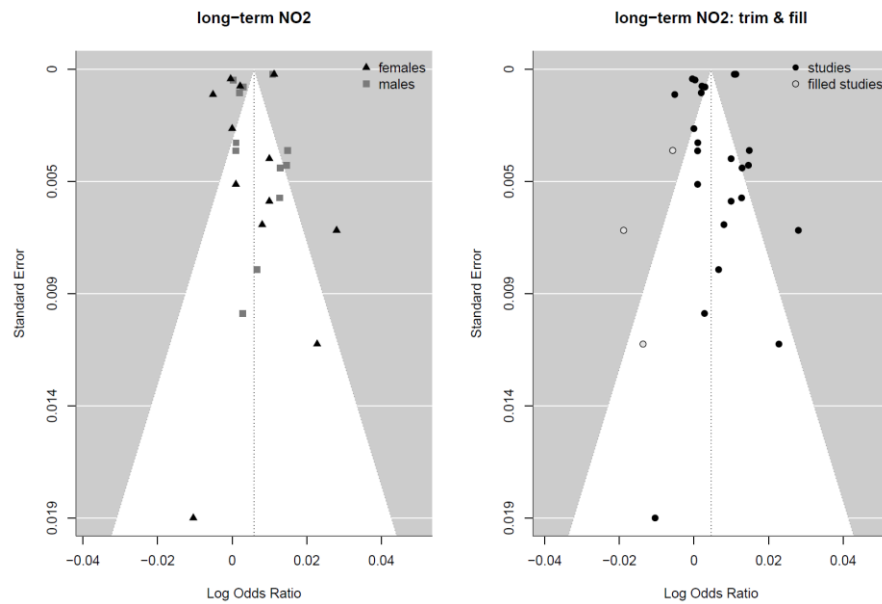


Figure 9. Funnel plots of included short-term studies on the association between NO_2 and cardiovascular mortality

S8. Sensitivity analysis

S8.1 Exclusions in moderator meta-analysis

Table 12. Exclusions in moderator meta-analysis of short-term studies

| Short-term | Model | Categories | N | I ² | QEp | QMp | R ² | %-change (CI) ^a |
|-------------------|--|------------|----|----------------|--------|------|----------------|----------------------------|
| PM _{2.5} | Main | Males | 33 | 96.9 | <0.001 | 0.52 | 0.0 | 0.99 (0.65;1.33) |
| | | Females | 33 | | | | | 1.15 (0.81;1.49) |
| | Li et al. 2022, Zhang et al. 2018 excluded | Males | 31 | 70.5 | <0.001 | 0.19 | 0.0 | 0.50 (0.36;0.64) |
| | | Females | 31 | | | | | 0.63 (0.49;0.77) |
| PM ₁₀ | Main | Males | 26 | 97.3 | <0.001 | 0.85 | 0.0 | 0.65 (0.38;0.91) |
| | | Females | 26 | | | | | 0.68 (0.42;0.95) |
| | Li et al. 2022, Zhang et al. 2018 excluded | Males | 24 | 96.6 | <0.001 | 0.74 | 14.4 | 0.50 (0.23;0.76) |
| | | Females | 24 | | | | | 0.56 (0.29;0.83) |
| Ozone (8hmax) | Main | Males | 9 | 72.2 | <0.001 | 0.59 | 0.0 | 0.31 (0.05;0.57) |
| | | Females | 9 | | | | | 0.41 (0.15;0.67) |
| | Zhang et al. 2019 excluded | Males | 8 | 53.5 | <0.001 | 0.45 | 0.0 | 0.19 (-0.03;0.41) |
| | | Females | 8 | | | | | 0.31 (0.09;0.53) |

CI, confidence interval; QEp, *p*-value of test for heterogeneity; QMp, *p*-value of test of differences between categories of moderator (tests if at least part of the moderators explains some heterogeneity); R², amount of heterogeneity accounted for

Table 13. Exclusions in moderator meta-analysis of long-term studies

| Long-term | Model | Categories | N | I ² | QEp | QMp | R ² | %-change (CI) ^a |
|-------------------|---|------------|----|----------------|--------|------|----------------|----------------------------|
| PM _{2.5} | Main | Males | 21 | 88.1 | <0.001 | 0.08 | 0.0 | 11.32 (8.76;13.95) |
| | | Females | 21 | | | | | 8.08 (5.51;10.66) |
| | Raachou-Nielsen et al. 2020 & Kazemiparkouhi et al. 2022 excluded | Males | 19 | 83.6 | <0.001 | 0.36 | 0.0 | 9.91 (7.61;12.25) |
| | | Females | 19 | | | | | 8.36 (6.05;10.72) |
| PM ₁₀ | Main | Males | 6 | 89.1 | <0.001 | 0.34 | 0.0 | 19.65 (7.56;33.10) |
| | | Females | 6 | | | | | 11.13 (-0.35;23.95) |
| | Fischer et al. 2015 excluded | Males | 5 | 40.0 | <0.001 | 0.07 | 54.4 | 26.43 (15.85;37.97) |
| | | Females | 5 | | | | | 12.42 (2.78; 22.95) |
| NO ₂ | Main | Males | 13 | 98.5 | <0.001 | 0.75 | 0.0 | 6.92 (2.09;11.99) |
| | | Females | 13 | | | | | 5.74. (0.72;11.01) |
| | Eum et al. 2022 excluded | Males | 11 | 82.8 | <0.001 | 0.19 | 0.0 | 5.15 (2.39;7.98) |
| | | Females | 11 | | | | | 2.48 (-0.37;5.41) |

CI, confidence interval; QEp, *p*-value of test for heterogeneity; QMp, *p*-value of test of differences between categories of moderator (tests if at least part of the moderators explains some heterogeneity); R², amount of heterogeneity accounted for

s8.2 Results of meta-analysis of the female-to-male ratio of Odds Ratios including Risk of Bias domains as moderator

Table 14. Results of meta-analysis of the female-to-male ratio of Odds Ratios including Risk of Bias domains as moderator for short-term studies of the association between PM_{2.5} and cardiovascular mortality

| Model | RoB domain | I ² | QEp | QMp | R ² | Category | N | FMR (CI) ^a |
|-------------------------------|-------------|----------------|------|------|----------------|----------|----|-----------------------|
| Random | -- | 22.6 | 0.12 | -- | -- | -- | 35 | 1.000 (1.000;1.001) |
| Mixed – categorical moderator | Confounding | 20.2 | 0.16 | 0.86 | 0 | Low | 5 | 1.000 (0.996;1.003) |
| | | | | | | Moderate | 20 | 1.001 (0.999;1.002) |
| | | | | | | High | 8 | 1.001 (0.999;1.002) |
| | Selection | 14.97 | 0.23 | 0.33 | 0 | low | 28 | 1.001 (1.000;1.002) |
| | | | | | | moderate | 5 | 0.999 (0.997;1.002) |
| | Detection | 14.82 | 0.23 | 0.41 | 0 | low | 14 | 1.001 (1.000;1.003) |
| | | | | | | moderate | 18 | 1.000 (0.999;1.002) |
| | | | | | | high | 1 | 0.999 (0.996;1.002) |

CI, confidence interval; FMR, Female-to-Male Ratio of Odds Ratios; QEp, *p*-value of test for heterogeneity (in case of mixed model: test for residual heterogeneity); QMp, *p*-value of test of differences between categories of moderator (tests if at least part of the moderators explains some heterogeneity); RoB, Risk of Bias; R², amount of heterogeneity accounted for

Table 15. Results of meta-analysis of the female-to-male ratio of Odds Ratios including Risk of Bias domains as moderator for short-term studies of the association between PM₁₀ and cardiovascular mortality

| Model | RoB domain | I ² | QEp | QMp | R ² | Category | N | FMR (CI) ^a |
|-------------------------------|-------------|----------------|------|-------|----------------|----------|----|-----------------------|
| Random | -- | 34.4 | 0.04 | | | | 26 | 1.000 (0.999;1.001) |
| Mixed – categorical moderator | Confounding | 75.5 | 0.36 | 0.003 | 81.3 | low | 5 | 0.997 (0.995;1.000) |
| | | | | | | moderate | 17 | 1.000 (0.999;1.001) |
| | | | | | | high | 4 | 1.002 (1.000;1.004) |
| | Selection | 36.9 | 0.03 | 0.76 | 0 | low | 23 | 1.000 (0.999;1.001) |
| | | | | | | moderate | 3 | 1.002 (0.991;1.012) |
| | Detection | 33.1 | 0.06 | 0.32 | 0 | low | 8 | 1.002 (0.999;1.004) |
| | | | | | | moderate | 17 | 1.000 (0.998;1.001) |
| | | | | | | high | 1 | 0.999 (0.995;1.003) |

CI, confidence interval; FMR, Female-to-Male Ratio of Odds Ratios; QEp, *p*-value of test for heterogeneity (in case of mixed model: test for residual heterogeneity); QMp, *p*-value of test of differences between categories of moderator (tests if at least part of the moderators explains some heterogeneity); RoB, Risk of Bias; R², amount of heterogeneity accounted for

Table 16. Results of meta-analysis of the female-to-male ratio of Odds Ratios including Risk of Bias domains as moderator for short-term studies of the association between NO₂ and cardiovascular mortality

| Model | RoB domain | I ² | QEp | QMp | R ² | Category | N | FMR (CI) ^a |
|-------------------------------|-------------|----------------|------|-------|----------------|----------|----|-----------------------|
| Random | -- | 32.5 | 0.08 | 0.77 | -- | -- | 21 | 1.000 (0.997;1.004) |
| Mixed – categorical moderator | Confounding | 0.0 | 0.94 | <.001 | 100 | low | 4 | 0.985 (0.975;0.994) |
| | | | | | | moderate | 13 | 0.999 (0.996;1.001) |
| | | | | | | high | 4 | 1.005 (1.002;1.008) |
| | Selection | 34.8 | 0.06 | 0.47 | 0 | low | 19 | 1.000 (0.997;1.004) |
| | | | | | | moderate | 2 | 1.016 (0.974;1.059) |
| | Detection | 18.4 | 0.23 | 0.01 | 49.5 | low | 9 | 0.995 (0.990;1.000) |
| | | | | | | moderate | 12 | 1.003 (1.000;1.007) |

CI, confidence interval; FMR, Female-to-Male Ratio of Odds Ratios; QEp, *p*-value of test for heterogeneity (in case of mixed model: test for residual heterogeneity); QMp, *p*-value of test of differences between categories of moderator (tests if at least part of the moderators explains some heterogeneity); RoB, Risk of Bias; R², amount of heterogeneity accounted for

Table 17. Results of meta-analysis of the female-to-male ratio of Odds Ratios including Risk of Bias domains as moderator for short-term studies of the association between Ozone_{8hmax} and cardiovascular mortality

| Model | RoB domain | I ² | QEp | QMp | R ² | Category | N | FMR (CI) ^a |
|-------------------------------|-------------|----------------|------|------|----------------|----------|---|-----------------------|
| Random | -- | 71.7 | 0.38 | 0.25 | | | 9 | 1.000 (0.999;1.002) |
| Mixed – categorical moderator | Confounding | 26.4 | 0.23 | 0.61 | 0.0 | low | 2 | 1.002 (0.993;1.011) |
| | | | | | | moderate | 4 | 1.002 (0.999;1.004) |
| | | | | | | high | 3 | 0.999 (0.995;1.004) |
| | Selection | NA | NA | NA | NA | low | 9 | NA |
| | Detection | 14.3 | 0.32 | 0.94 | 0.0 | low | 5 | 1.001 (0.998;1.005) |
| | | | | | | moderate | 4 | 1.001 (0.999;1.003) |

CI, confidence interval; FMR, Female-to-Male Ratio of Odds Ratios; QEp, *p*-value of test for heterogeneity (in case of mixed model: test for residual heterogeneity); QMp, *p*-value of test of differences between categories of moderator (tests if at least part of the moderators explains some heterogeneity); RoB, Risk of Bias; R², amount of heterogeneity accounted for

Table 18. Results of meta-analysis of the female-to-male ratio of Odds Ratios including Risk of Bias domains as moderator for long-term studies of the association between PM_{2.5} and cardiovascular mortality

| Model | RoB domain | I ² | QEp | QMp | R ² | Category | N | FMR (CI) ^a |
|-------------------------------|-------------|----------------|-------|------|----------------|----------|----|-----------------------|
| Random | -- | 72.5 | <.001 | | | | 22 | 0.979 (0.957;1.002) |
| Mixed – categorical moderator | Confounding | 74.8 | <.001 | 0.41 | 0.0 | low | 3 | 1.066 (0.905;1.256) |
| | | | | | | moderate | 11 | 0.986 (0.952;1.021) |
| | | | | | | high | 7 | 0.965 (0.930;1.001) |
| | Selection | 71.1 | <.001 | 0.47 | 0.0 | low | 18 | 0.975 (0.950;1.001) |
| | | | | | | moderate | 3 | 0.998 (0.942;1.057) |
| | Detection | 74.9 | <.001 | 0.83 | 0.0 | low | 16 | 0.972 (0.941;1.004) |
| | | | | | | moderate | 4 | 0.990 (0.942;1.041) |
| | | | | | | high | 1 | 0.977 (0.889;1.072) |

CI, confidence interval; FMR, Female-to-Male Ratio of Odds Ratios; QEp, *p*-value of test for heterogeneity (in case of mixed model: test for residual heterogeneity); QMp, *p*-value of test of differences between categories of moderator (tests if at least part of the moderators explains some heterogeneity); RoB, Risk of Bias; R², amount of heterogeneity accounted for

Table 19. Results of meta-analysis of the female-to-male ratio of Odds Ratios including Risk of Bias domains as moderator for long-term studies of the association between PM₁₀ and cardiovascular mortality

| Model | RoB domain | I ² | QEp | QMp | R ² | Category | N | FMR (CI) ^a |
|-------------------------------|-------------|----------------|-------|------|----------------|----------|---|-----------------------|
| Random | -- | 80.3 | <.001 | | | | 6 | 0.930 (0.957;1.002) |
| Mixed – categorical moderator | Confounding | 84.0 | <.001 | 0.23 | 0 | moderate | 3 | 0.889 (0.769;1.028) |
| | | | | | | high | 3 | 1.058 (0.830;1.348) |
| | Selection | 79.0 | <.001 | 0.04 | 23.3 | low | 5 | 0.965 (0.863;1.080) |
| | | | | | | moderate | 1 | 0.658 (0.465;0.930) |
| | Detection | 83.1 | <.001 | 0.26 | 0 | low | 2 | 0.839 (0.676;1.041) |
| | | | | | | moderate | 4 | 0.976 (0.843;1.131) |

CI, confidence interval; FMR, Female-to-Male Ratio of Odds Ratios; QEp, *p*-value of test for heterogeneity (in case of mixed model: test for residual heterogeneity); QMp, *p*-value of test of differences between categories of moderator (tests if at least part of the moderators explains some heterogeneity); RoB, Risk of Bias; R², amount of heterogeneity accounted for

Table 20. Results of meta-analysis of the female-to-male ratio of Odds Ratios including Risk of Bias domains as moderator for long-term studies of the association between NO₂ and cardiovascular mortality

| Model | RoB domain | I ² | QEp | QMp | R ² | Category | N | FMR (CI) ^a |
|-------------------------------|-------------|----------------|-------|------|----------------|----------|----|-----------------------|
| Random | -- | 74.7 | <.001 | | | | 12 | 0.987 (0.966;1.007) |
| Mixed – categorical moderator | Confounding | 71.2 | <.001 | 0.49 | 0.0 | low | 2 | 1.043 (0.941;1.156) |
| | | | | | | moderate | 5 | 0.982 (0.925;1.042) |
| | | | | | | high | 4 | 0.969 (0.907;1.035) |
| | Selection | 68.8 | <.001 | 0.06 | 13.4 | low | 10 | 0.989 (0.960;1.019) |
| | | | | | | moderate | 1 | 0.871 (0.765;0.991) |
| | Detection | 76.5 | <.001 | 0.24 | 0.0 | low | 7 | 0.983 (0.961;1.005) |
| | | | | | | moderate | 5 | 1.028 (0.957;1.105) |

CI, confidence interval; FMR, Female-to-Male Ratio of Odds Ratios; QEp, *p*-value of test for heterogeneity (in case of mixed model: test for residual heterogeneity); QMp, *p*-value of test of differences between categories of moderator (tests if at least part of the moderators explains some heterogeneity); RoB, Risk of Bias; R², amount of heterogeneity accounted for

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