Quantification of joint relative risk from multiple pollutants

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ISGlobal Barcelona Institute for Global Health

Funded by the European Union

UBD POLICY

Outline

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1. Conceptual framework
2. Environmental burden of disease
3. Air pollution attributable mortality burden
4. HIA methodology – single and multiple pollutants
5. Technical challenges of joint RR quantification



Conceptual framework

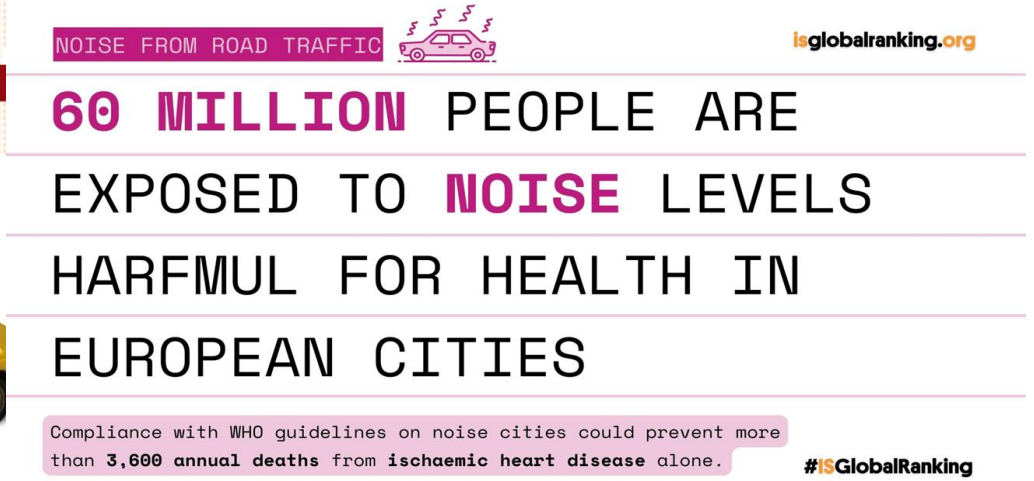
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- Relationship between urban and transport planning, environmental exposures and human health

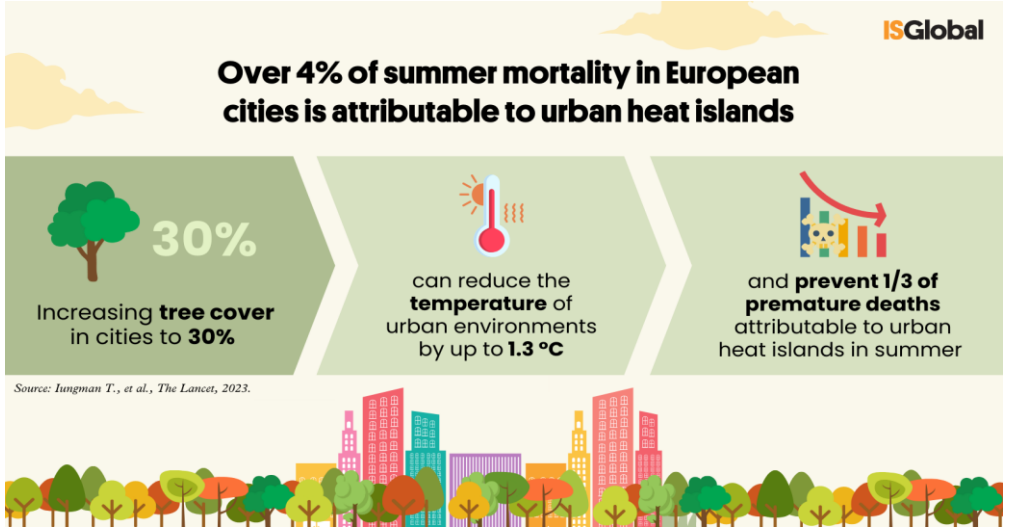


Environmental burden of disease









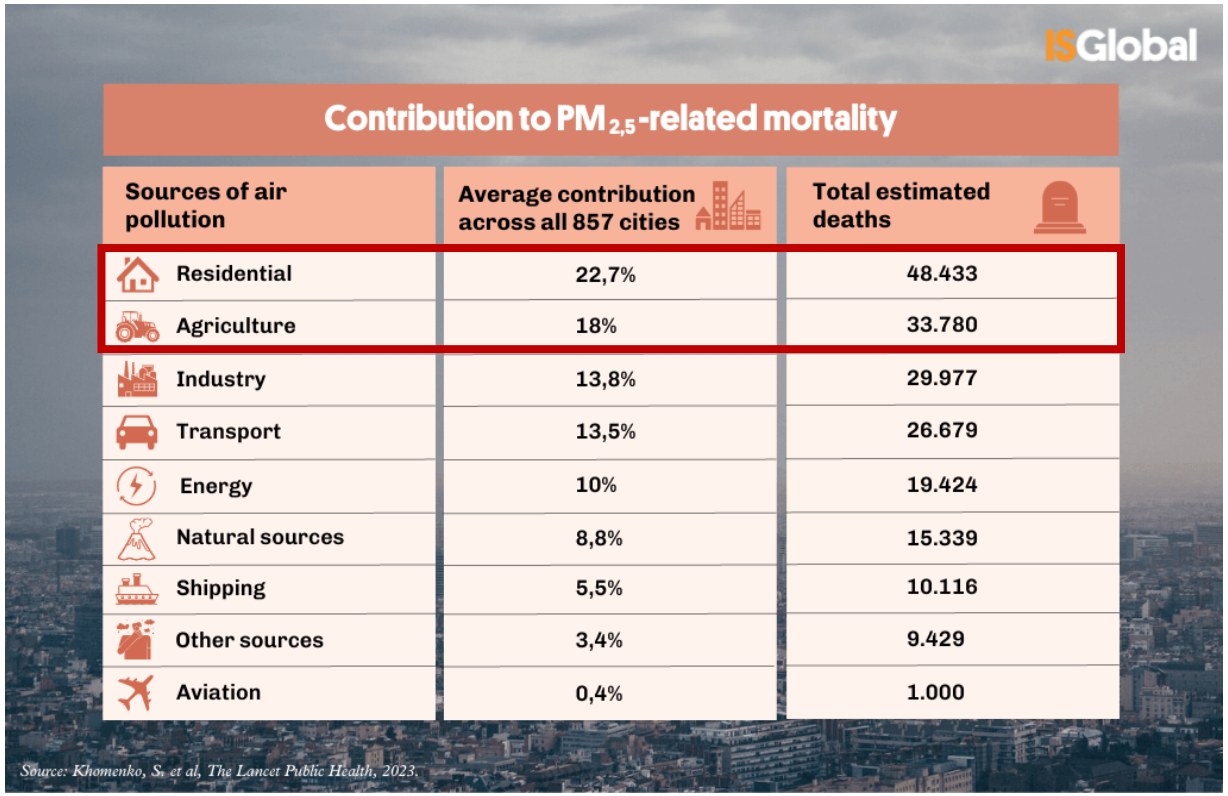
Khomenko et al., 2021 (https://doi.org/10.1016/S2542-5196(20)30272-2)
Barboza et al., 2021 (https://doi.org/10.1016/S2542-5196(21)00229-1)

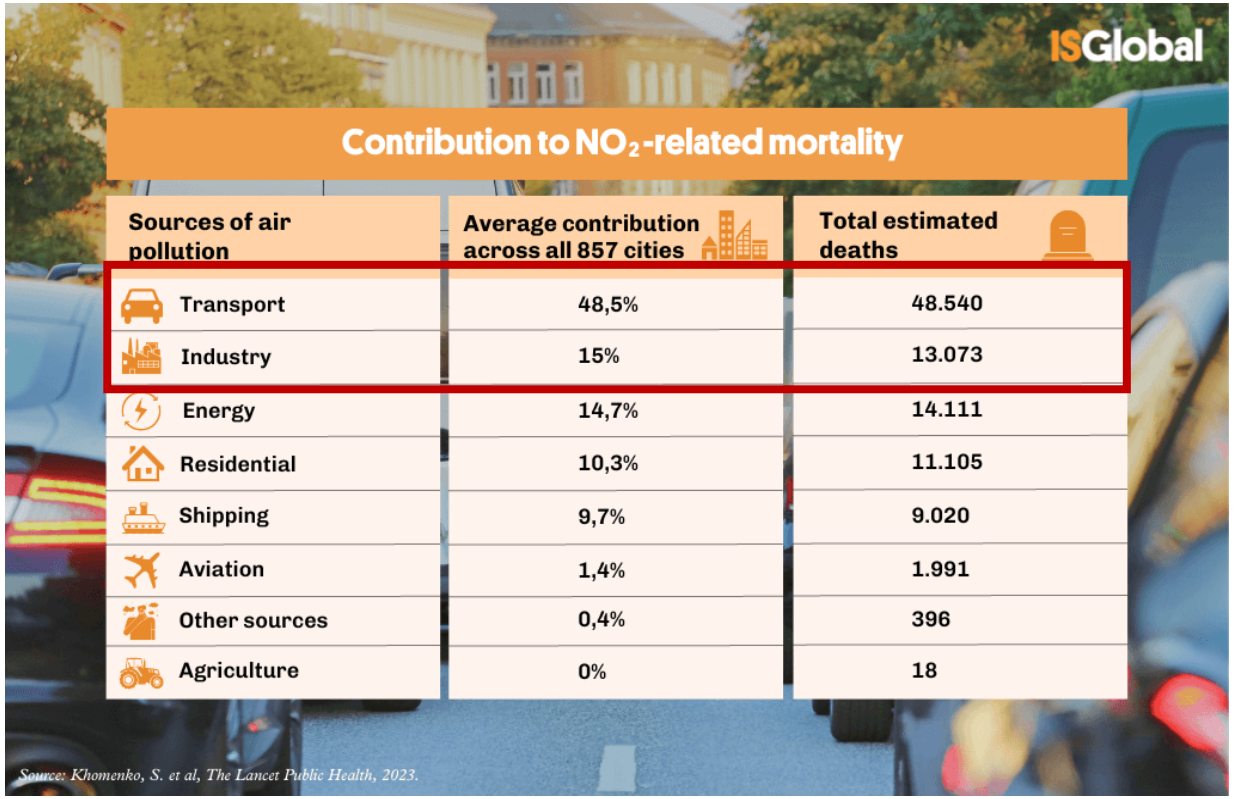
Khomenko et al., 2022 (https://doi.org/10.1016/j.envint.2022.107160)
Iungman et al., 2023 (https://doi.org/10.1016/S0140-6736(22)02585-5)

Environmental burden of disease

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- The main contributors to air pollution mortality in cities





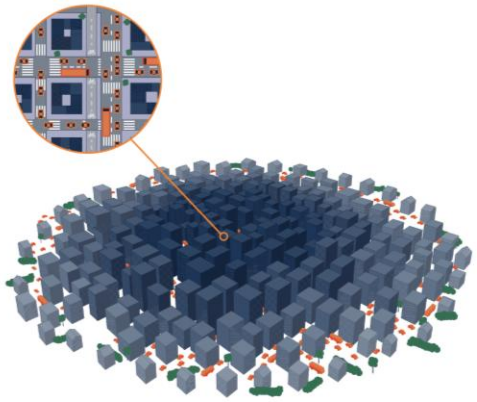
Khomenko et al., 2023 (https://doi.org/10.1016/S2468-2667(23)00106-8)

Environmental burden of disease

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Comparison of city types and environmental, climate and health impacts:

URBAN CONFIGURATION



Compact - High Density cities

Model A **(n=246)**

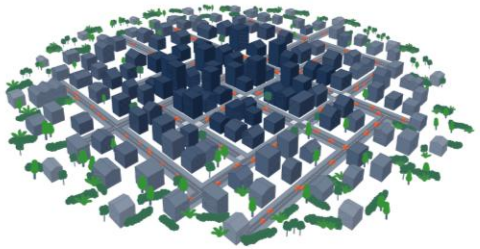
8.7% Compactness

421 Density

33 Pedestrian areas

49 Cycleways

17.3% Green space



Open Lowrise - Medium Density cities

Model B **(n=245)**

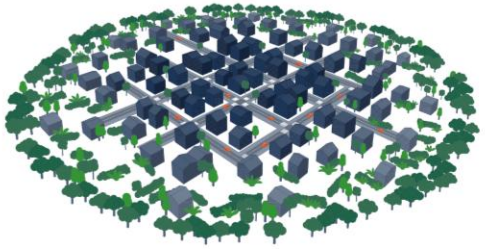
2.1% Compactness

248 Density

14 Pedestrian areas

38 Cycleways

18.5% Green space



Open Lowrise - Low Density cities

Model C **(n=261)**

1% Compactness

173 Density

9 Pedestrian areas

22 Cycleways

32.2% Green space



Green - Low Density cities

Model D **(n=167)**

1.9% Compactness

179 Density

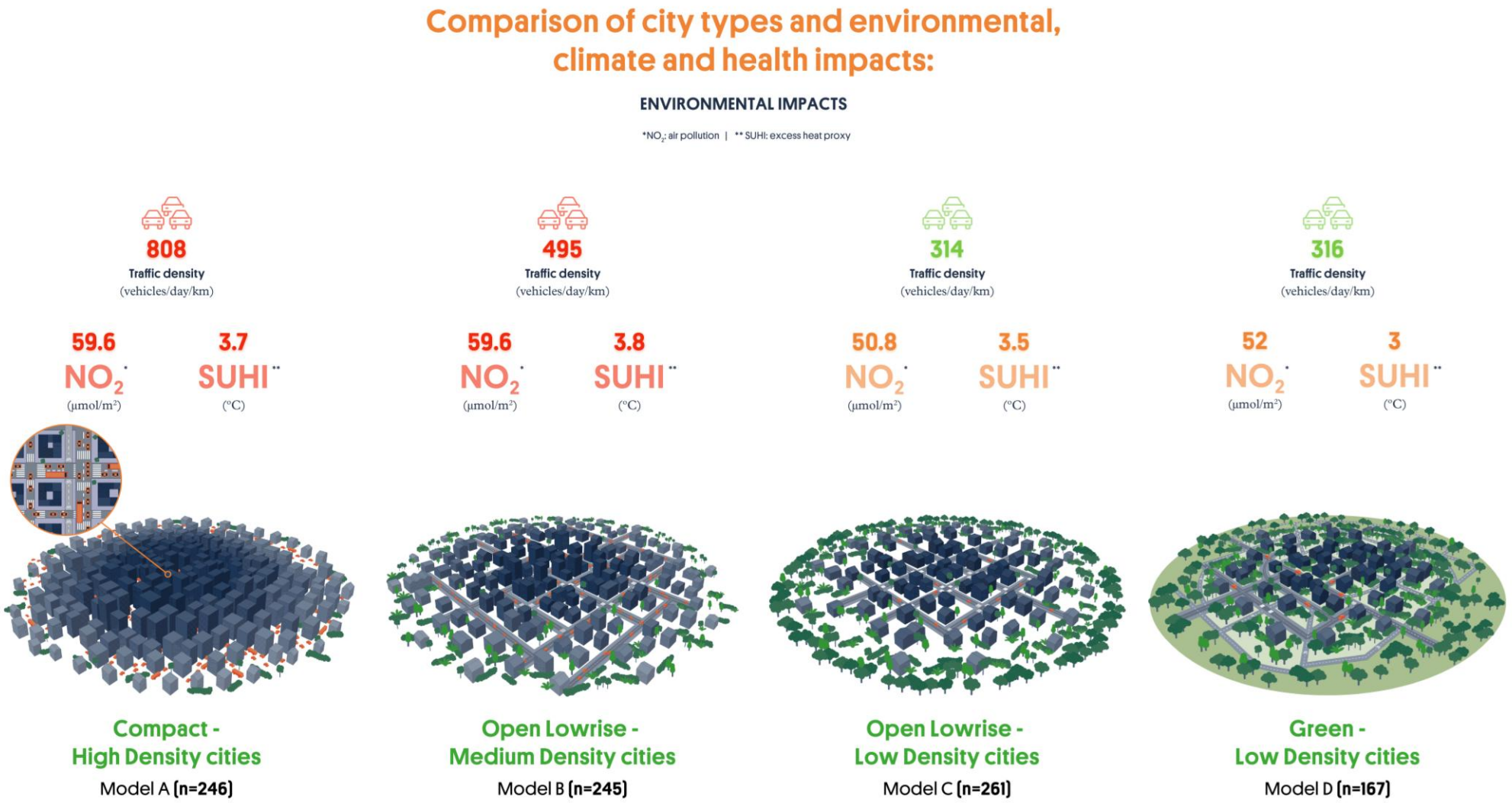
15 Pedestrian areas

118 Cycleways

38.5% Green space

Iungman & Khomenko et al., 2024 (https://doi.org/10.1016/S2542-5196(24)00120-7)

Environmental burden of disease



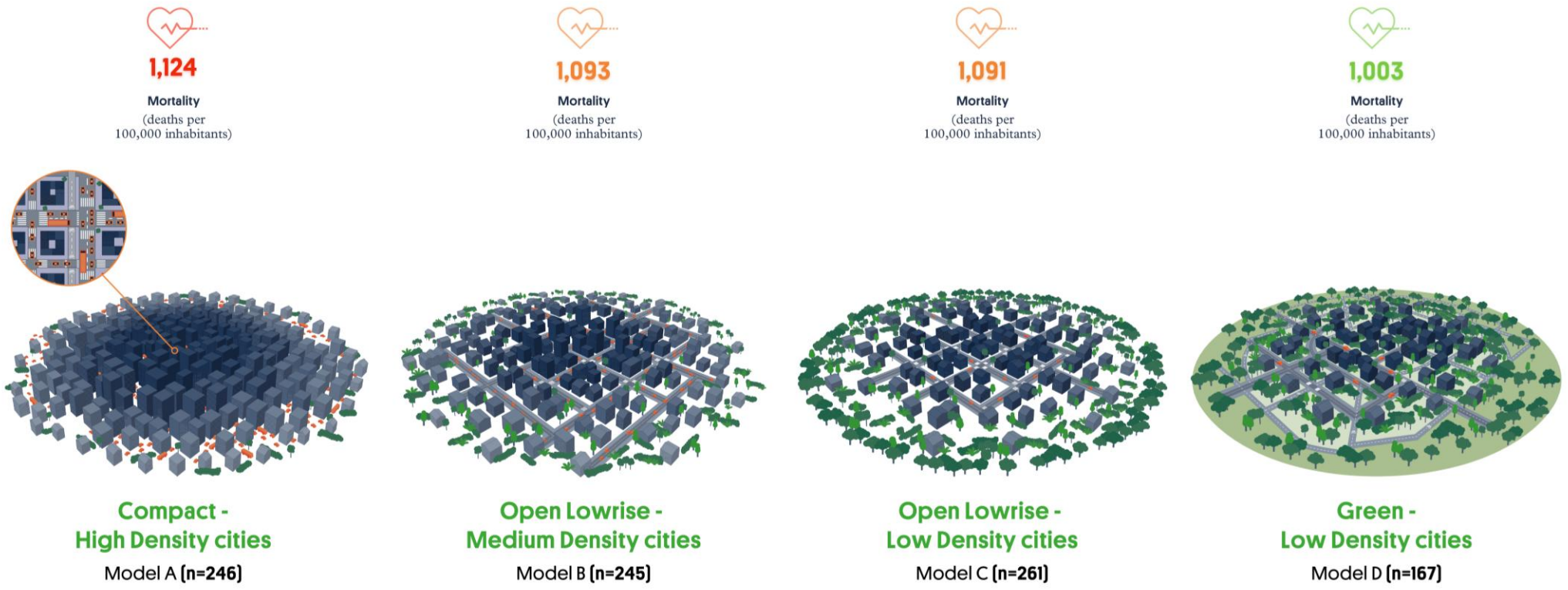
Iungman & Khomenko et al., 2024 (https://doi.org/10.1016/S2542-5196(24)00120-7)

Environmental burden of disease

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Comparison of city types and environmental, climate and health impacts:

HEALTH IMPACTS



Iungman & Khomenko et al., 2024 (https://doi.org/10.1016/S2542-5196(24)00120-7)

Air pollution attributable burden

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- Long-term exposure to ambient air pollution is the **largest environmental health risk** facing today's population



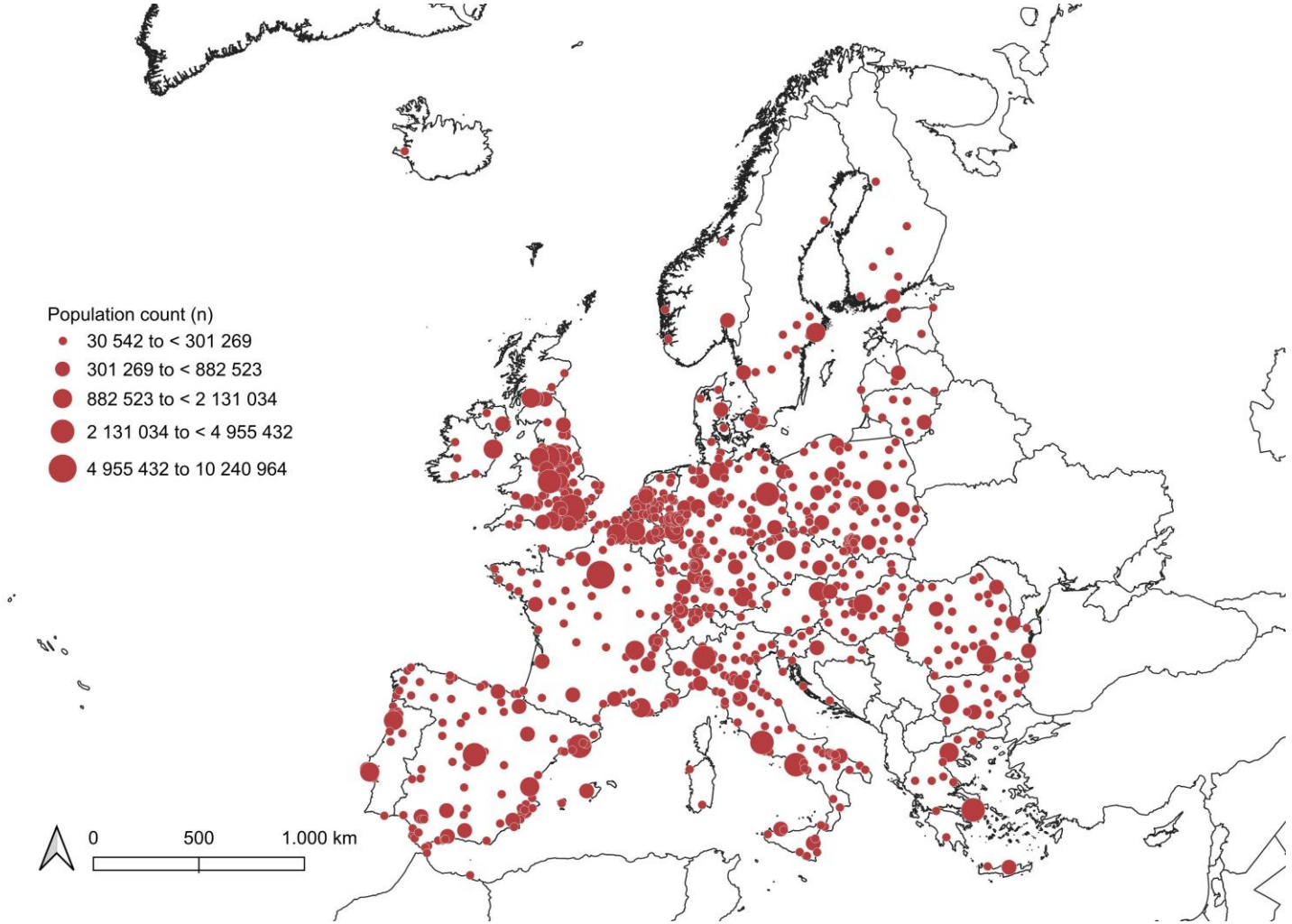
- In 2023, ambient $PM_{2.5}$ exposure contributed to 4.9 million deaths worldwide and long term NO_2 exposure was linked to 500 000 deaths in urban areas globally



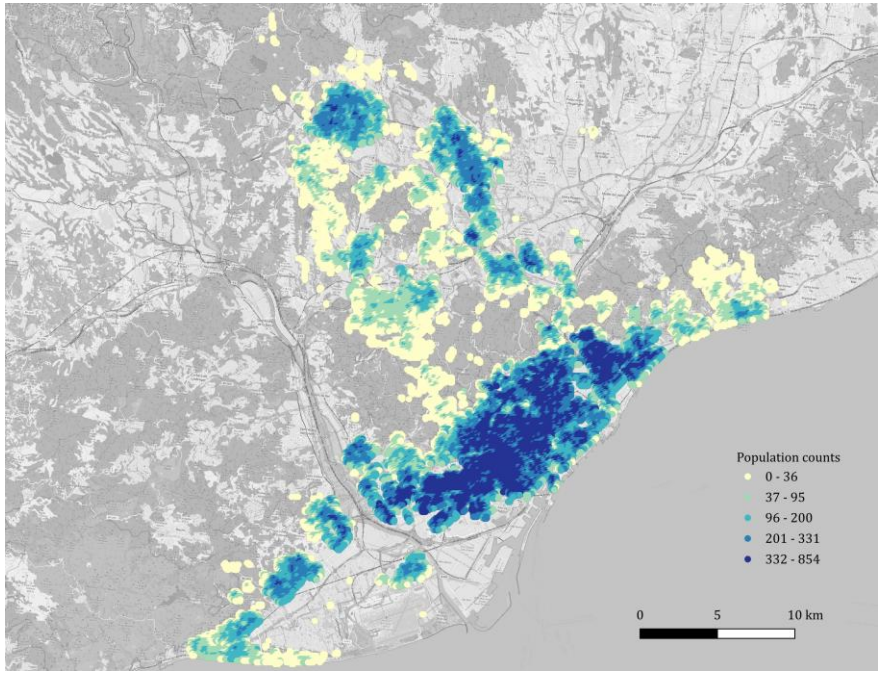
- In Europe, the effects of air pollution are concentrated in cities
  - ~75% of the European population reside in urban areas

Air pollution attributable burden

825 European cities, 29 countries



Population density data 100m-100m grid cell level

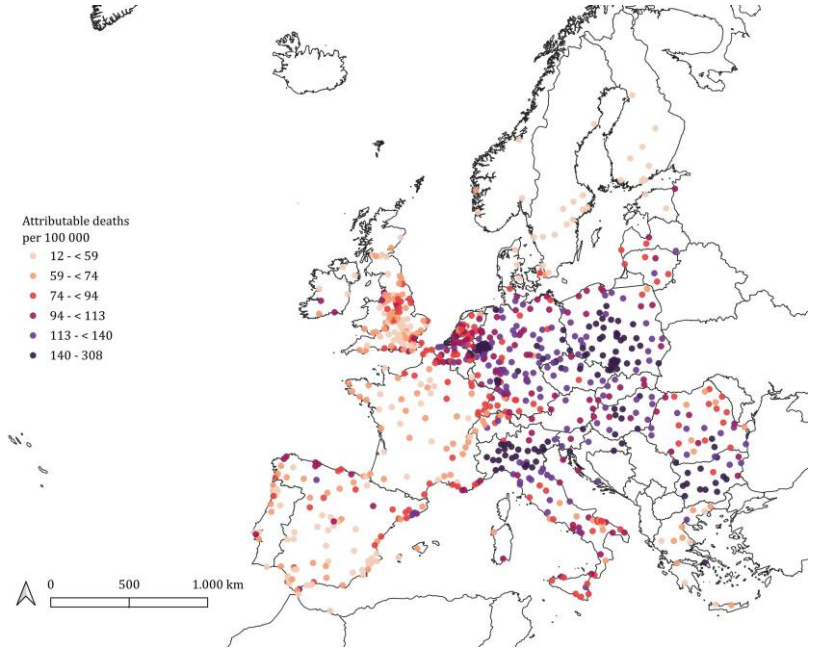


Barcelona, Spain

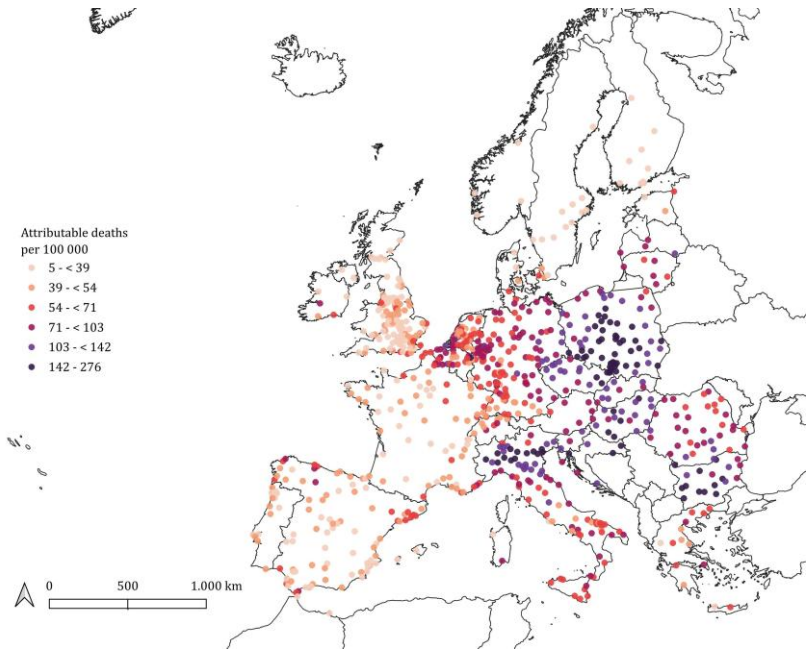
Air pollution attributable burden

Single vs. two-pollutant models

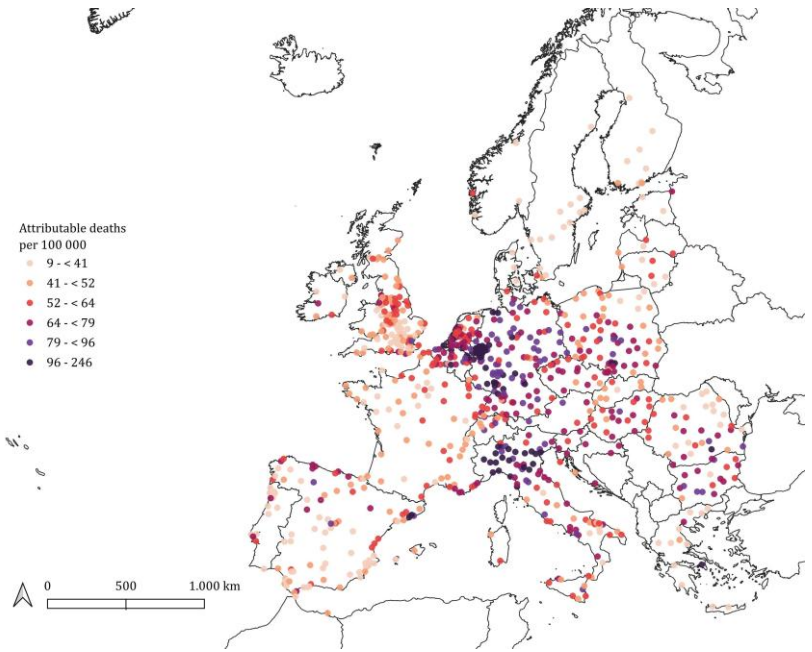
Two-pollutant attributable mortality



PM2.5 attributable mortality



NO2 attributable mortality



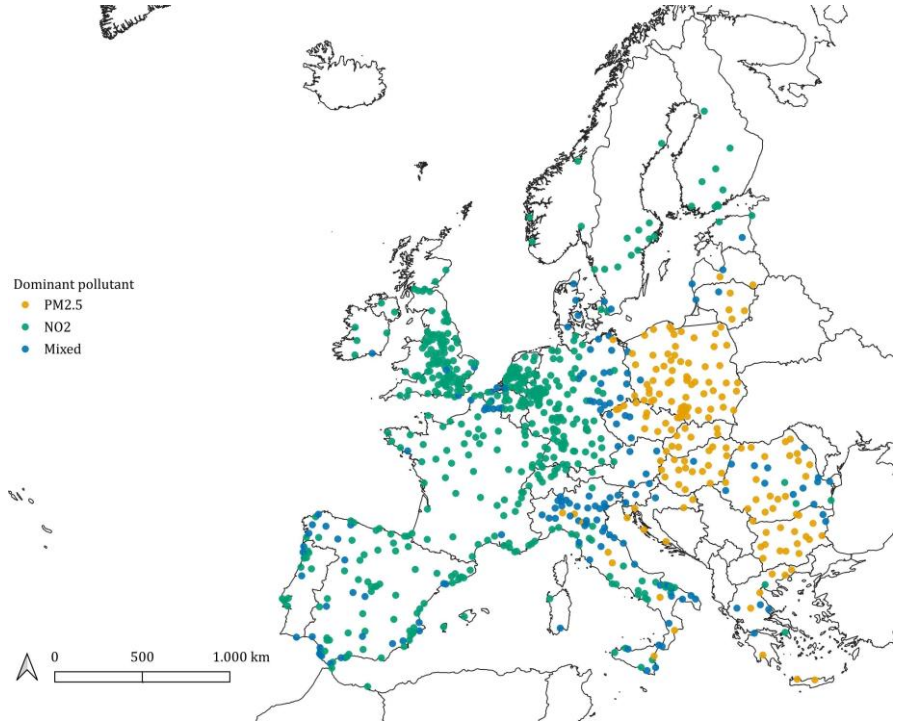
- In 2018, 213 889 deaths [95% CI: 89 224 – 344 223] attributable to PM2.5 and NO2, when quantified jointly
- Summing single pollutant attributable burden estimates → ~ 80 000 more deaths than two-pollutant attributable death estimates

Dyer et al , 2026 (https://doi.org/10.1016/j.envint.2026.110338)

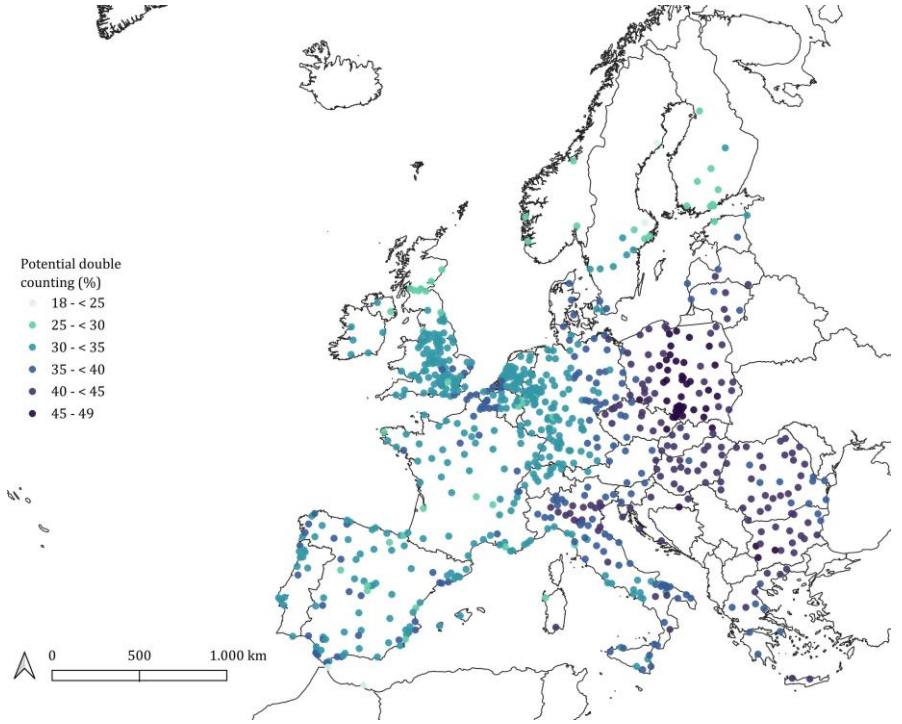
Air pollution attributable burden

Pollutant dominance and double counting

Pollutant dominance



Potential double counting from single pollutant models



$PM_{2.5}$ dominant cities:

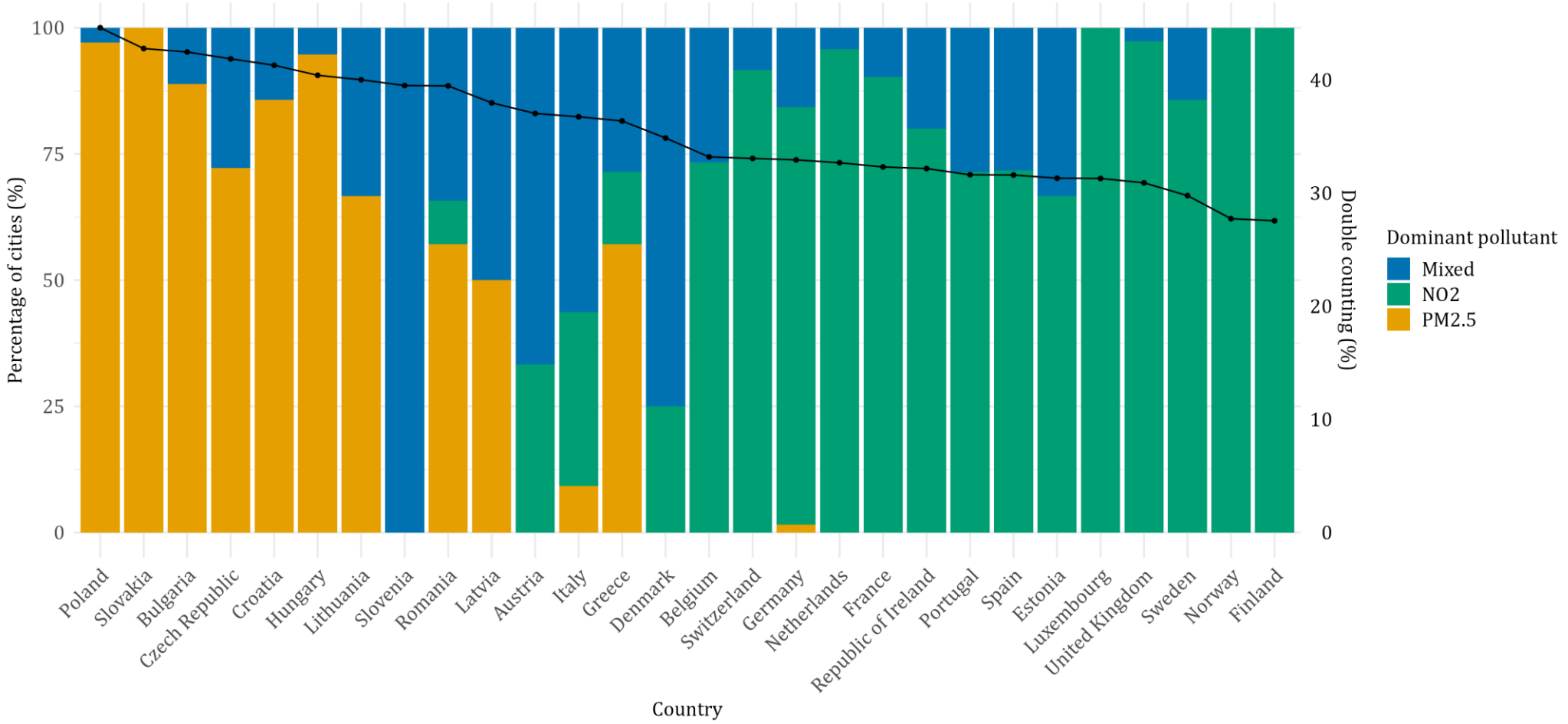
- Were amongst cities with the highest multi-pollutant attributable ASMR per 100 000 standard population
- Had a higher percentage of potential double counting

Pollutant dominance defined where one pollutant has a more prevalent health impact compared to others (≥ 55%)

Dyer et al , 2026 (https://doi.org/10.1016/j.envint.2026.110338)

Air pollution attributable burden

Pollutant dominance and double counting



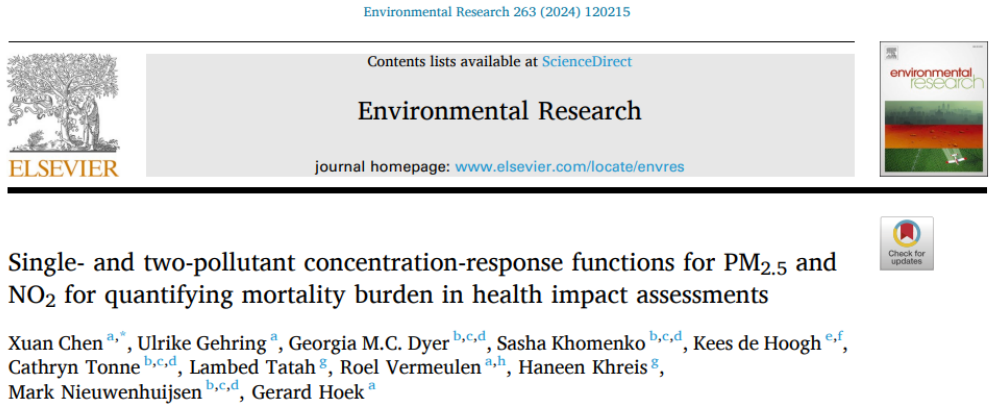
- The level of potential double counting at country-level ranged 27.5% (Finland) to 44.6% (Poland)

Dyer et al , 2026 (https://doi.org/10.1016/j.envint.2026.110338)

HIA methodology – single and multiple pollutants

- Health impact assessments (HIAs) of air pollution traditionally rely on single-pollutant models
  - Insufficient number of epidemiological studies incorporating multiple pollutants
  - Single-pollutant ERFs do not account for the potential confounding effect from other pollutants
    - Non-additive → potential double counting

- Recent methodological advancement now makes it possible to conduct a multi-pollutant quantitative HIA



Environmental Research 263 (2024) 120215

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Single- and two-pollutant concentration-response functions for $PM_{2.5}$ and NO_2 for quantifying mortality burden in health impact assessments

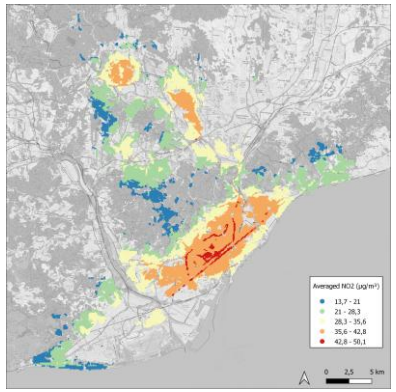
Xuan Chen [a,*], Ulrike Gehring [a], Georgia M.C. Dyer [b,c,d], Sasha Khomenko [b,c,d], Kees de Hoogh [e,f], Cathryn Tonne [b,c,d], Lambed Tatah [g], Roel Vermeulen [a,h], Haneen Khreis [g], Mark Nieuwenhuijsen [b,c,d], Gerard Hoek [a]

- Offers to mitigate double counting from summing single pollutant burdens
  - Provides one interpretable estimate related to air pollution exposure

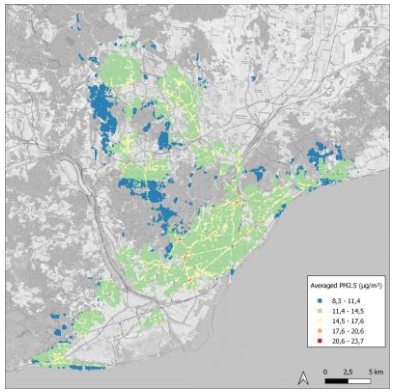
HIA methodology – single and multiple pollutants

Single pollutant comparative risk assessment

Barcelona pollutant concentrations grid-cell-level



NO2 (µg/m^3)

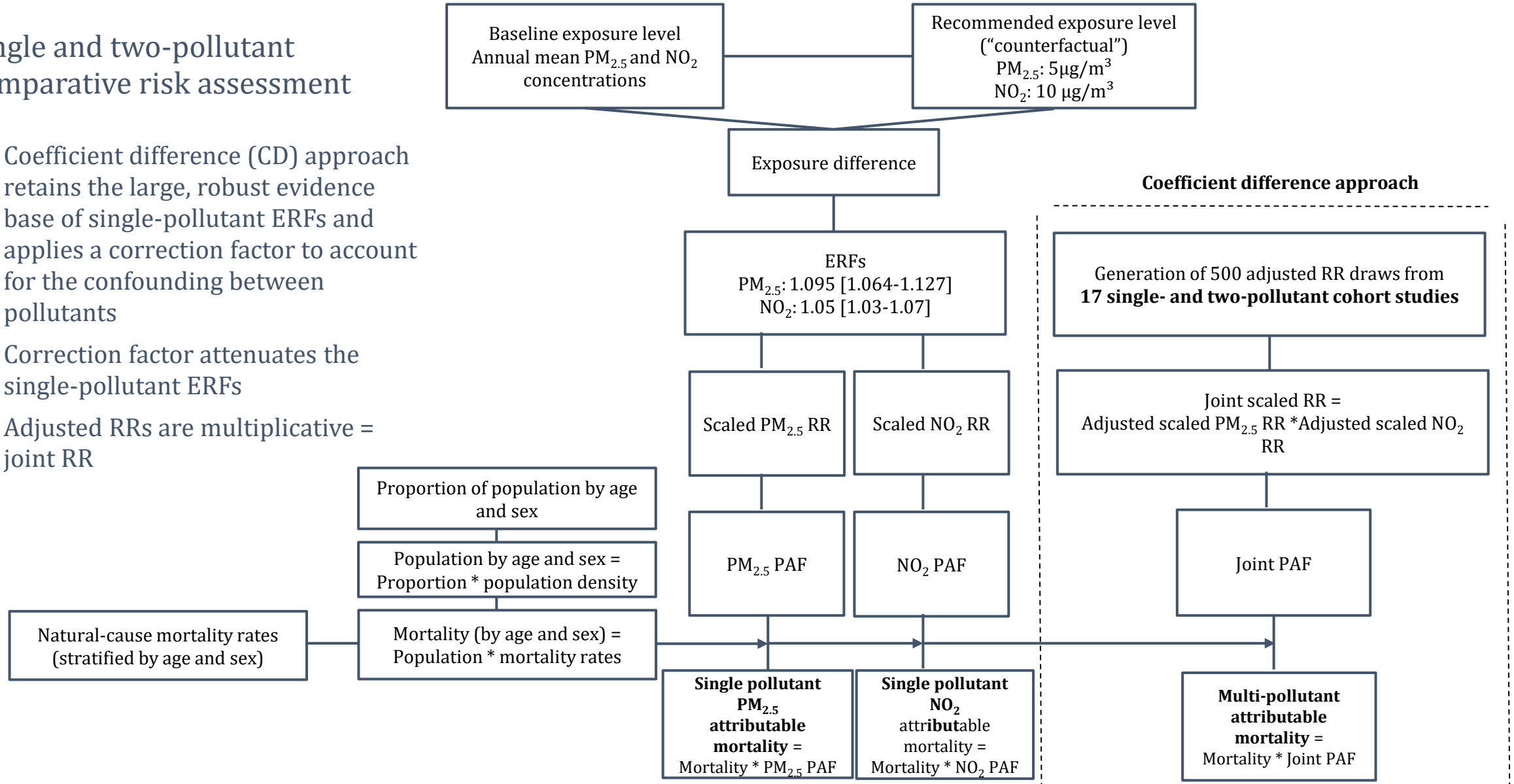


PM2.5 (µg/m^3)

HIA methodology – single and multiple pollutants

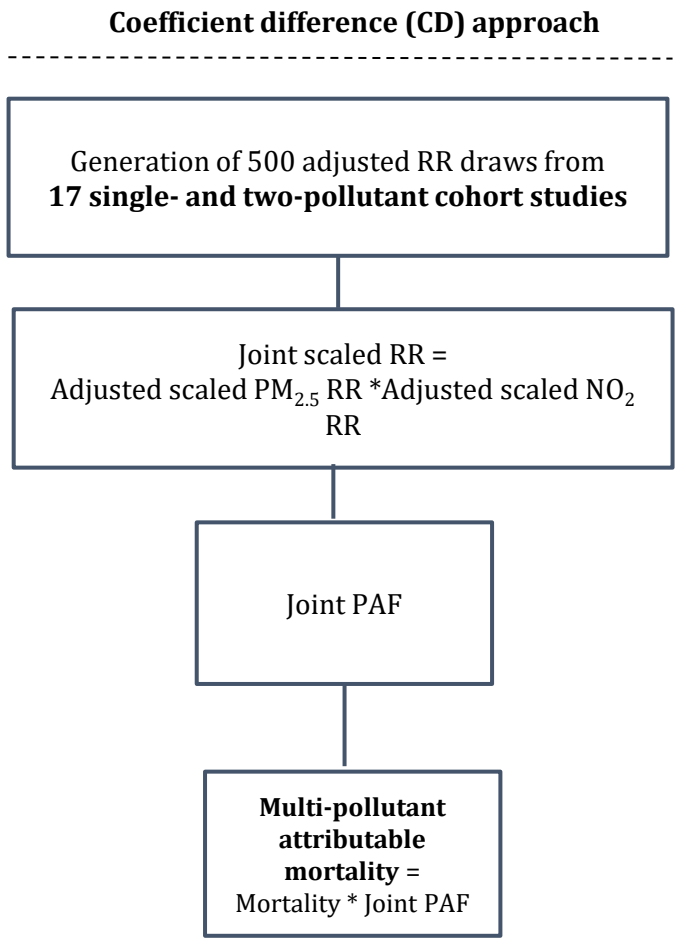
Single and two-pollutant comparative risk assessment

- Coefficient difference (CD) approach retains the large, robust evidence base of single-pollutant ERFs and applies a correction factor to account for the confounding between pollutants
- Correction factor attenuates the single-pollutant ERFs
- Adjusted RRs are multiplicative = joint RR



HIA methodology – single and multiple pollutants

Two-pollutant comparative risk assessment



Coefficient difference (CD) = log HR from single-pollutant model minus log HR from two-pollutant model

For each of the 17 studies:

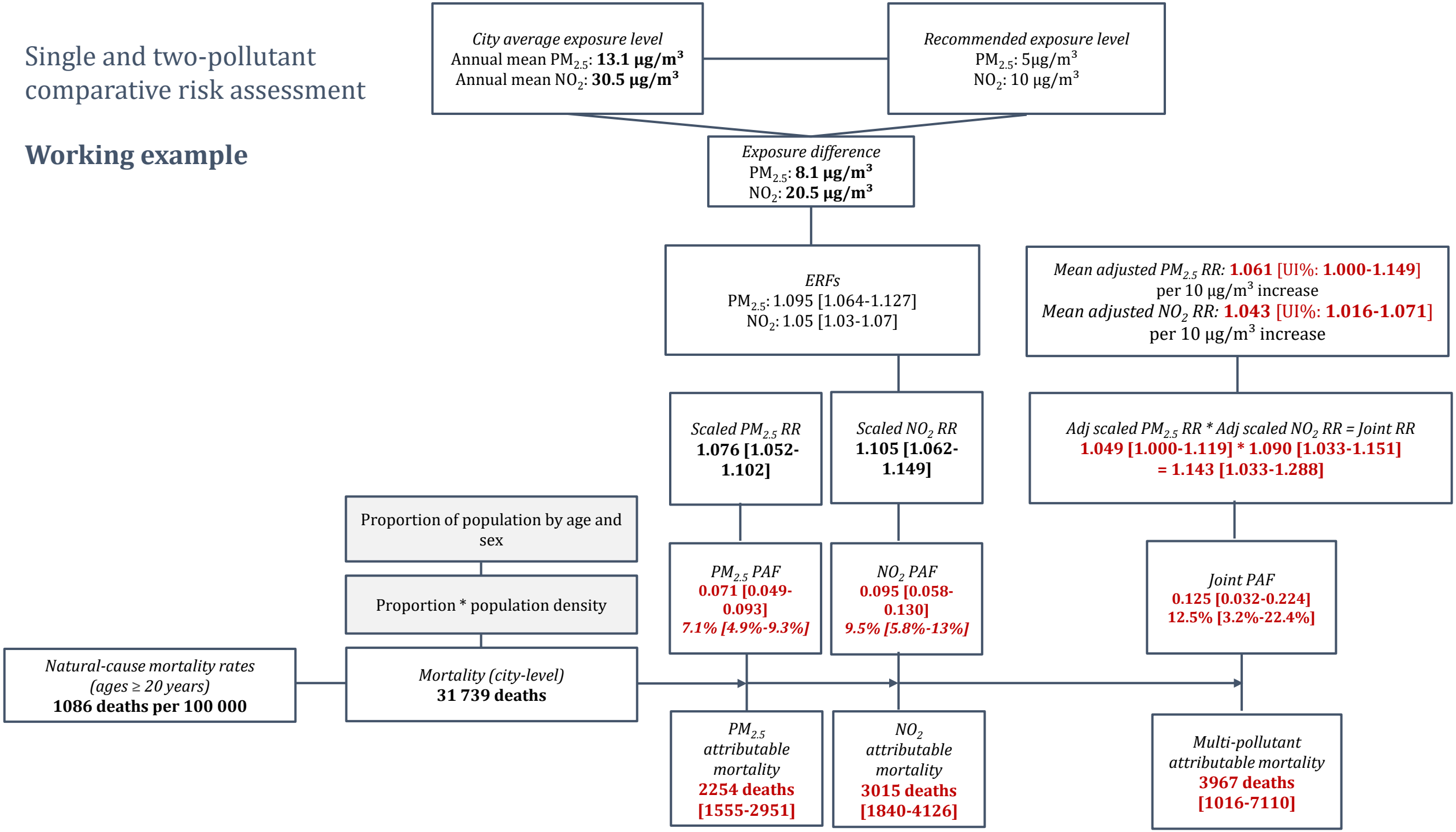
- CD calculated by: $CD_i = \log(HR_{single,i}) - \log(HR_{two-poll,i})$
- Variance calculated by: $Var(CD_i) = SE^2_{\log(HR_{single,i})} + SE^2_{\log(HR_{two-poll,i})}$

Obtained pooled mean CD and uncertainty in CD:

1) Fitted separate random-effects meta-analyses for PM2.5 and NO2 to obtain:
   - Pooled mean coefficient difference (CD)
   - Uncertainty in the pooled mean
   - Between-study heterogeneity
2) Monte Caro simulation of 500 iterations → 500 PM2.5 and NO2 adjusted RR
3) Imputed adjusted RR into the CRA, scaled to the exposure difference for each grid cell

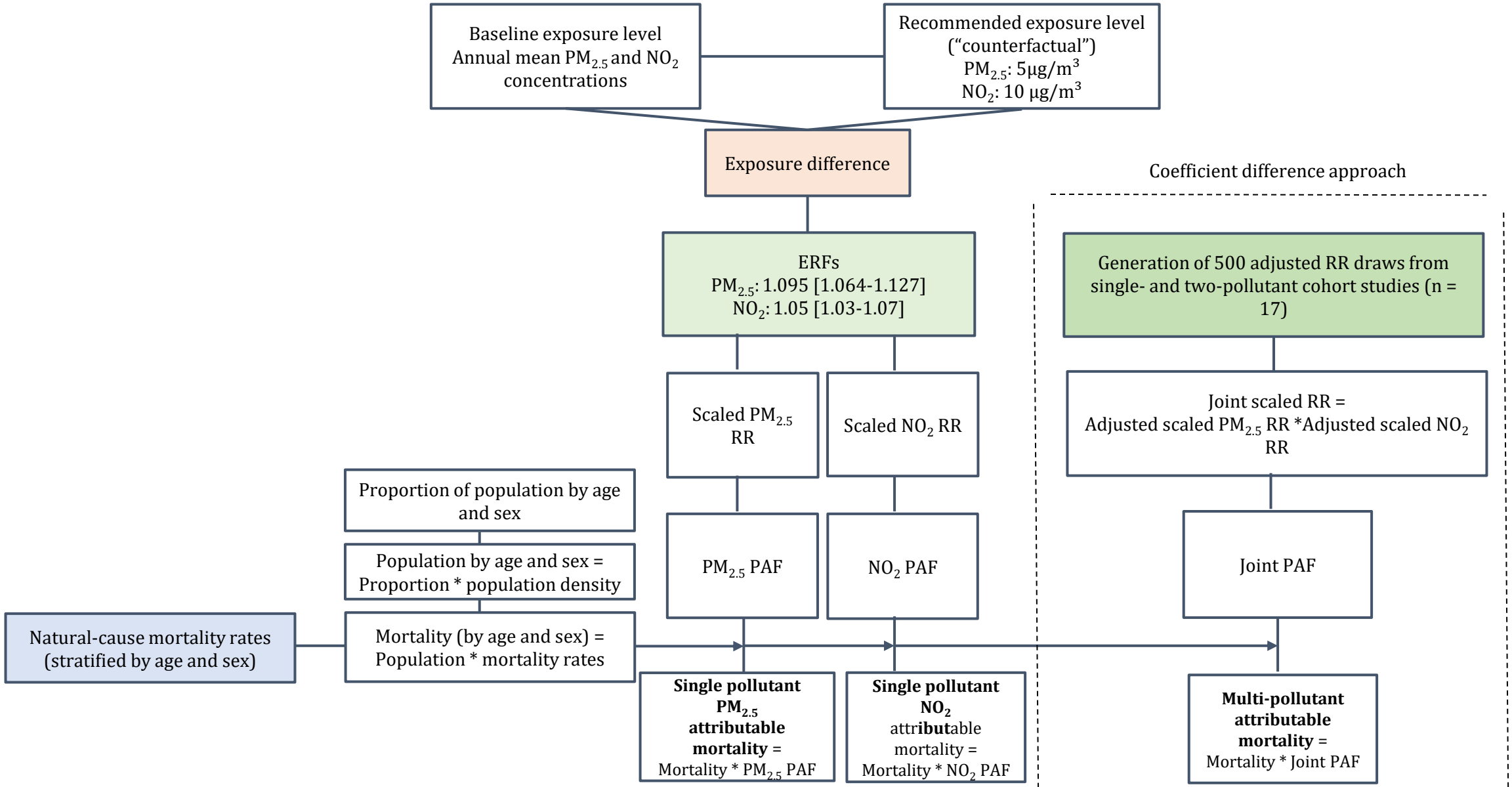
Single and two-pollutant comparative risk assessment

Working example



Technical challenges of joint RR quantification

Propagating uncertainty in two-pollutant estimates



Technical challenges of joint RR quantification

Propagating uncertainty in two-pollutant estimates

Exposure difference

- Relative root mean square error of pollutant data
  - $PM_{2.5}$ = 2.31
  - NO_2 = 6.33

Single-pollutant RRs (unadjusted)

- Standard error of the log-relative risk

Adjusted RRs

- Monte Carlo simulation of 500 iterations, combined uncertainty in:
  - Unadjusted RR
  - Coefficient difference distribution: uncertainty in pooled CD and between-study heterogeneity

Natural-cause mortality rates

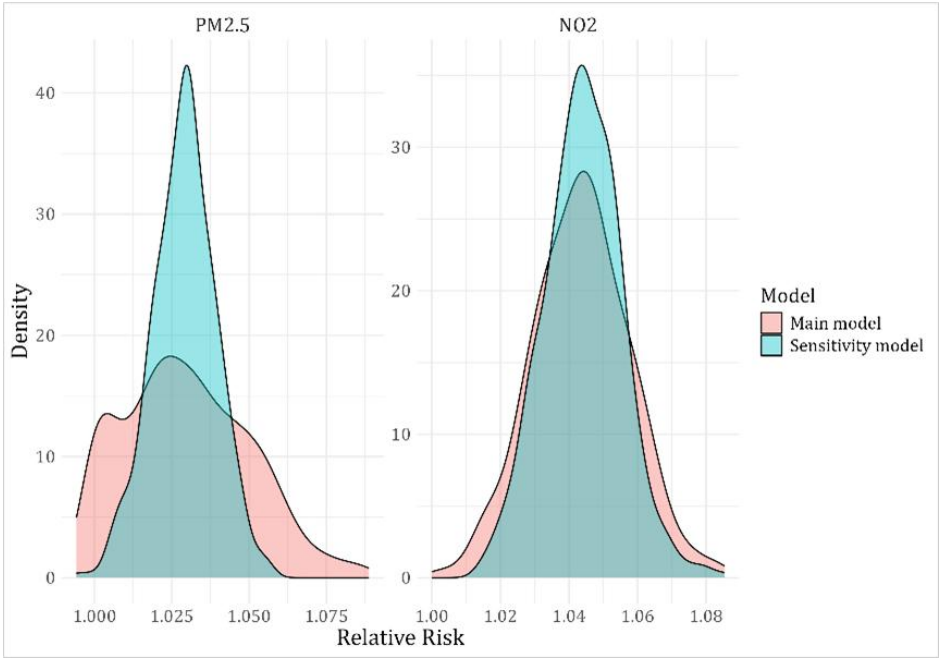
- Fitted linear-mixed effects models with natural cubic splines to fill for missing city mortality or population data
- Model residual standard deviation imputed into monte carlo simulations → uncertainty bounds of mortality rates

Technical challenges of joint RR quantification

Propagating uncertainty in two-pollutant estimates

Sensitivity analysis for propagation of uncertainty in pooled CD

- Main analysis: SE of pooled mean and between-study heterogeneity
- Sensitivity analysis: only SE of pooled mean



$PM_{2.5}$

- Sensitivity model produced narrower uncertainty distribution, similar central estimates
  - Wide uncertainty interval in main model primarily driven by between-study heterogeneity

NO_2

- Less heterogeneity between studies
- Traffic is the dominant source of NO_2 across study settings
  → Less variability

Technical challenges of joint RR quantification

1. **No interaction term**
   Effects of PM2.5 and NO2 are assumed to combine independently on the multiplicative scale

2. **Approximation of covariance**
   Covariance between single- and two-pollutant models is not known or reported

3. **Correlation of pollutants**
   PM2.5 and NO2 coefficients are correlated, but independence is assumed uniformly

4. **Cannot perform city-specific CD adjustment**
   Pollutant correlation varies by city

Technical challenges of joint RR quantification

ASSUMPTION

No interaction term: the RR for PM2.5 is assumed constant regardless of NO2's concentration (and vice versa)

CONSEQUENCE

- Co-exposure can amplify or dampen risk — neither can be detected with the CD approach
- Direction of bias is unknown (under- vs over-estimation of joint effects)

Net effect: possible unquantified bias

Technical challenges of joint RR quantification

ASSUMPTION

Covariance between the single- and two-pollutant models is not known (in any of the 17 cohort studies) and approximated

Despite risk effect estimates coming from the same regression (as two-pollutant model is the single-pollutant model plus a covariate)

CONSEQUENCE

- CD variance was approximated as the sum of the squared SEs of the single- and two-pollutant HRs
- If the true covariance were positive, this overestimates the true variance of the CD

Net effect: wider, more conservative confidence intervals

Technical challenges of joint RR quantification

OBSERVATIONS

PM2.5–NO2 correlation varied by city

PM2.5's coefficient change is more strongly correlated with NO2's effect (r = 0.79) than NO2's is with PM2.5's (r = 0.44)

IMPLICATION from varied correlation

- In high-correlation cities the omitted interaction is more likely to matter
- Collinearity inflates the variance of each pollutant's independent effect

IMPLICATION from PM2.5 absorbing more shared signal

- $PM_{2.5}$ likely reflects a broader mixture of sources, so a considerable share of its health effect may capture shared variance with traffic-related NO_2
- Harder to isolate $PM_{2.5}$ pollutant-specific effect

Net effect: pollutant coefficients are less precisely estimated + possible unquantified bias

Summary of quantifying joint RR using CD approach

Advantages:

- Minimises double counting single-pollutant effect estimates
- Offers to better capture population exposure to multiple pollutants
- Provides one interpretable burden estimate for policy makers
- Allows identification of pollutant dominance

Limitations:

Assumption	Consequence
No interaction term assumed (effects combine independently, multiplicative scale)	Can't detect amplified/dampened joint risk; direction of bias unknown
Covariance not reported between single- and two-pollutant models	CD variance approximated (sum of squared SEs): wider, more conservative CIs
Independence assumed uniformly across cities, despite PM2.5–NO2 correlation varying by city	Unquantified bias risk + collinearity-driven imprecision in high-correlation cities
$PM_{2.5}$ effect more strongly correlated with NO_2 adjustment than the reverse (r = 0.79 vs 0.44)	$PM_{2.5}$ estimates likely capture shared/traffic-related signal; harder to isolate pollutant-specific effect

Related publications

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Single- and two-pollutant concentration-response functions for $PM_{2.5}$ and NO_2 for quantifying mortality burden in health impact assessments

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Environment International 202 (2025) 109645

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Full length article

Exposure-response functions of the correlated environmental exposures green space, noise, and air pollution for quantifying mortality burden in health impact assessment

Xuan Chen [a,*], Ulrike Gehring [a], Georgia M.C. Dyer [b,c,d], Kees de Hoogh [e,f], Sasha Khomenko [b,c,d], Haneen Khreis [g,h], Natalie Mueller [b,c,d], Roel Vermeulen [a,i], Harry Williams [g], Belen Zapata-Diomedi [g], Mark Nieuwenhuijsen [b,c,d], Gerard Hoek [a]

European Journal of Public Health, 2026, **36**(5), ckag155
https://doi.org/10.1093/eurpub/ckag155
Original Manuscript

Improving mortality rate estimation in 825 European cities: a linear mixed-effects modelling approach using Urban Audit data

Georgia M.C. Dyer[1,2,3], Pierre Masselot[4], Marta Cirach[1,2,3], Sasha Khomenko[1,2,3], Xuan Chen[5], Ulrike Gehring[5], Kees de Hoogh[5,6,7], Sandra Márquez[1,2,3], Noé Moreno[8], Cathryn Tonne[1,2,3], Xavier Basagaña[1,2,3], Mark Nieuwenhuijsen[1,2,3,*]

Environment International 213 (2026) 110338

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Full length article

The use of single and multiple pollutant models in health impact assessment of air pollution: What difference does it make and where?

Georgia M.C. Dyer [a,b,c], Sasha Khomenko [a,b,c], Xuan Chen [d], Marta Cirach [a,b,c], Benjamin Flückiger [e,f], Ulrike Gehring [d], Gerard Hoek [d], Kees de Hoogh [d,e,f], Tamara Iungman [a,b,c], Natalie Mueller [a,b,c], Mark Nieuwenhuijsen [a,b,c,*]

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Thank you

