



Exposure-Response Functions for NO₂ and COPD

Tessa Haverkate

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Funded by
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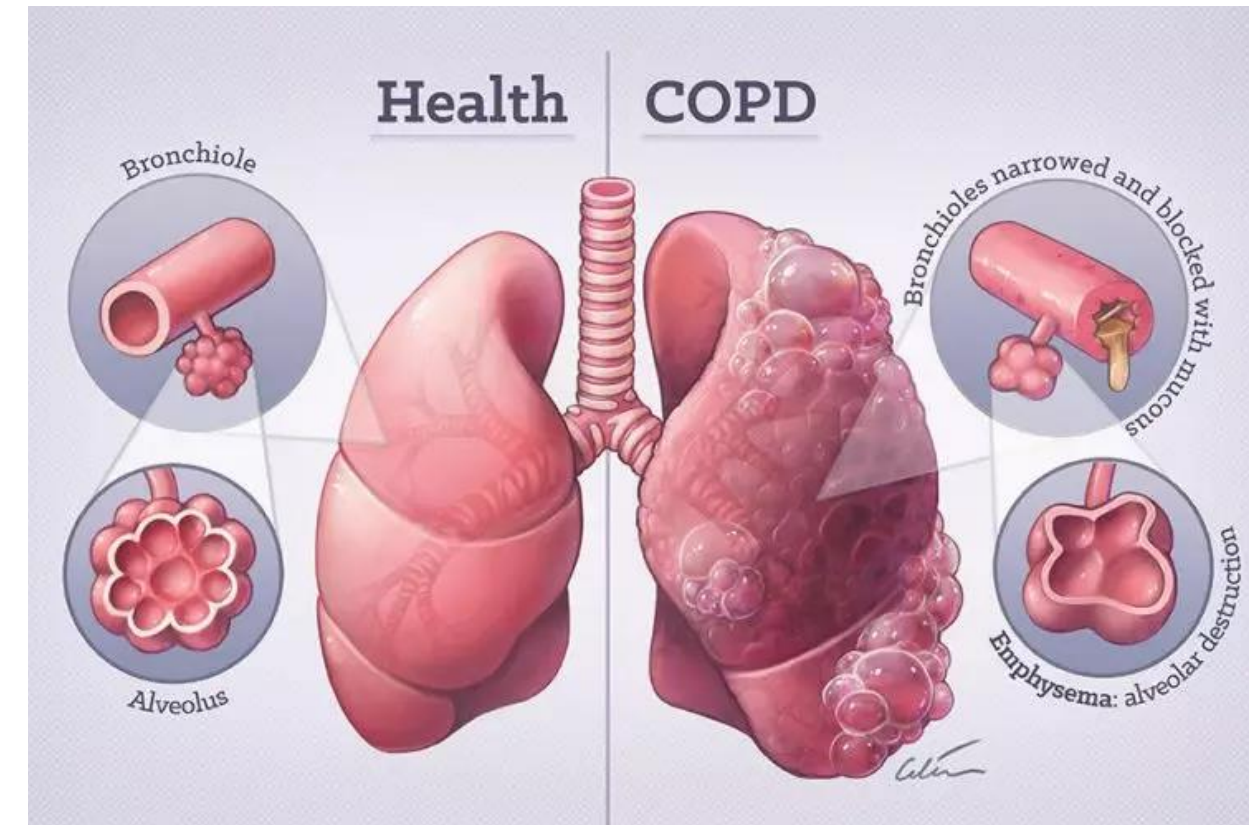
BEST-COST is funded by the European Union's Horizon Europe programme under Grant Agreement No.101095408.



COPD and NO2

Chronic Obstructive Lung Disease^{1,2}

- 4th leading cause of death in 2021
- Restricted airflow
- Breathing problems
- COPD mortality attributable to air pollution
 - 23% - ambient PM2.5
 - 13% - O3
 - ? - NO2

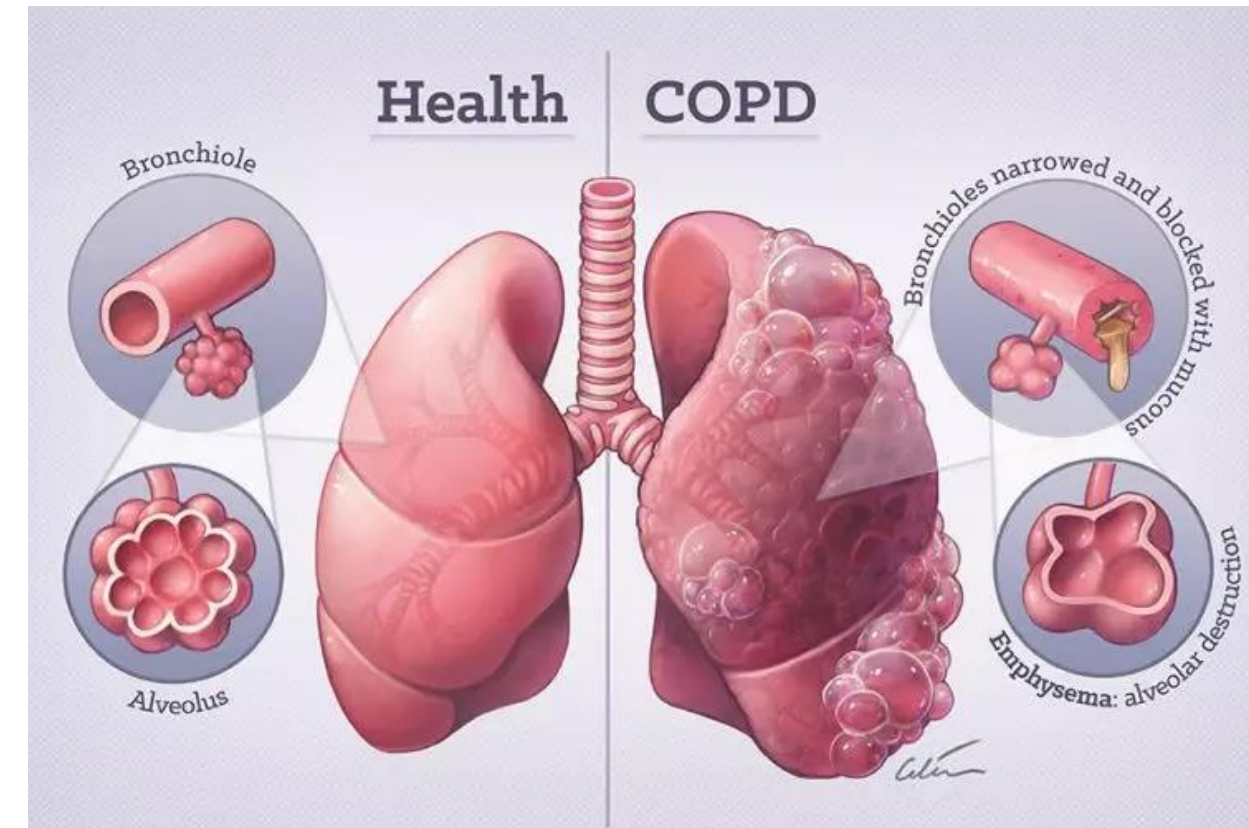




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Nitrogen dioxide (NO2)³

- Toxic, gaseous air pollutant
- Burning of fossil fuels

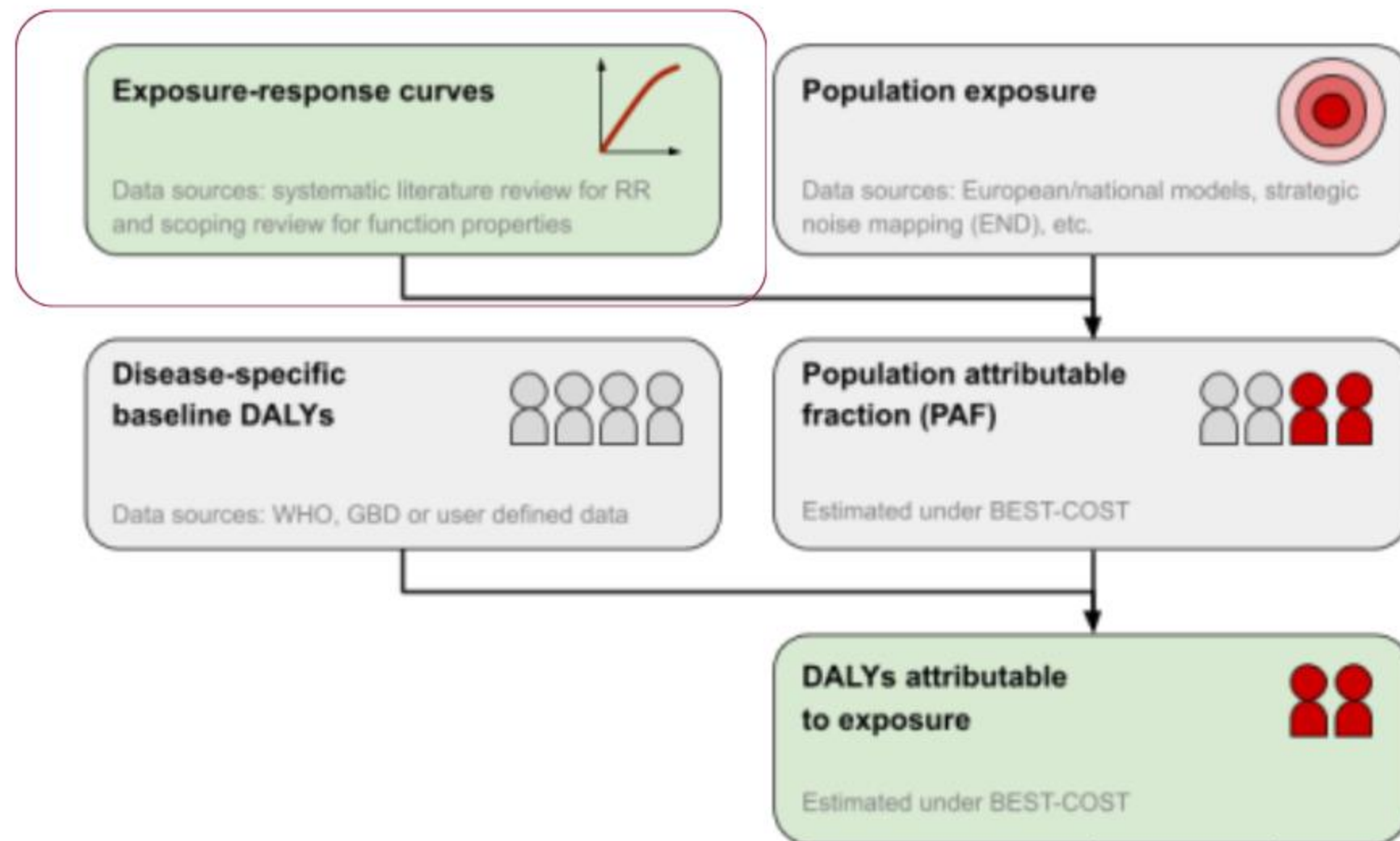




Why Exposure-Response Functions?

Essential to quantify health impact of risk factors

- Link estimates of exposure concentrations to projected response in a population





Systematic Literature Review and Meta-Analysis




1. Provide a comprehensive overview of existing evidence regarding the association between long-term exposure to ambient NO₂ and COPD incidence, prevalence, and mortality and combined COPD incidence and mortality



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a. Systematic Literature Review

- 2215 reports screened > 24 reports included
 - Mortality (n=12), incidence (n=8), prevalence (n=5)
 -  (n=12)
- Mean NO₂ exposure:
 -  12.7–68.4 µg/m³
 -  12.7–29.3 µg/m³



Systematic Literature Review and Meta-Analysis

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a. Systematic Literature Review

b. Meta-Analysis

- 10 µg/m³ increase in NO₂ & COPD incidence and mortality

 RR= **1.04**, 95%CI: **1.00–1.09**

■ I²=95.1%

 RR= **1.08**, 95%CI: **1.01–1.15**

■ I²=92.4%



Exposure Response Functions

2. Derive and compare ERFs of the NO₂-COPD association using the natural-cubic splines method and the MR-BRT approach



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Natural cubic splines

- Piecewise polynomial
- Shape: flexible

MR-BRT (Meta Regression-Bayesian Regularized Trimmed)

- Exclusion of outliers
- Shape: monotonic



Exposure Response Functions

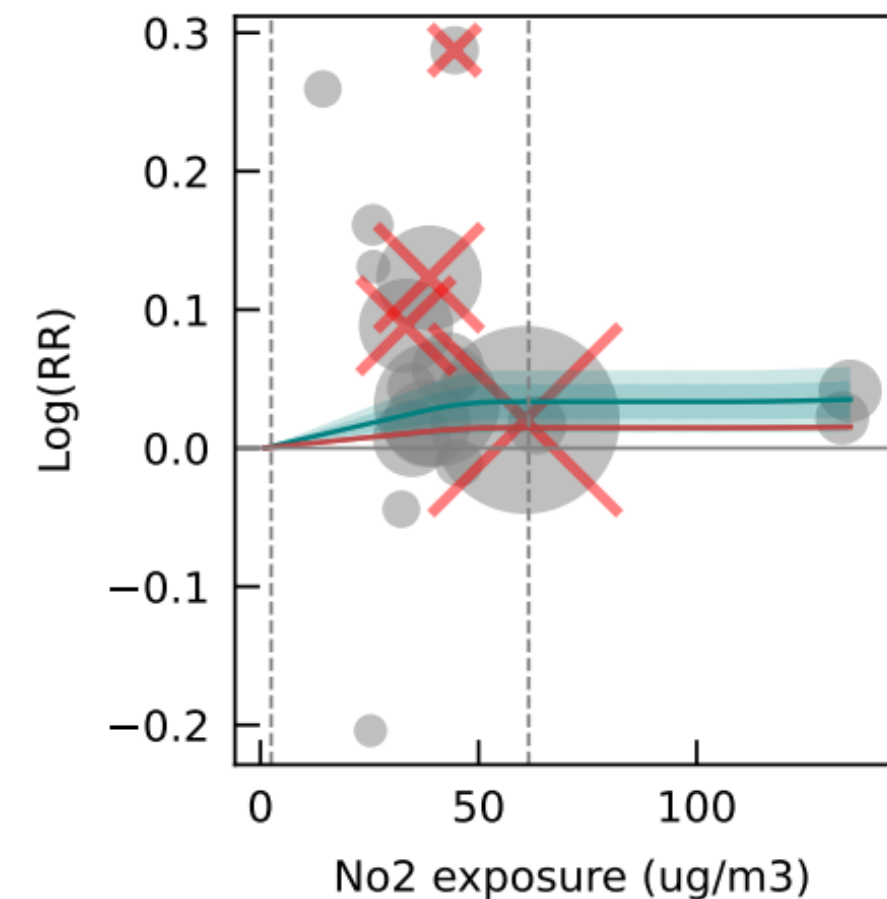
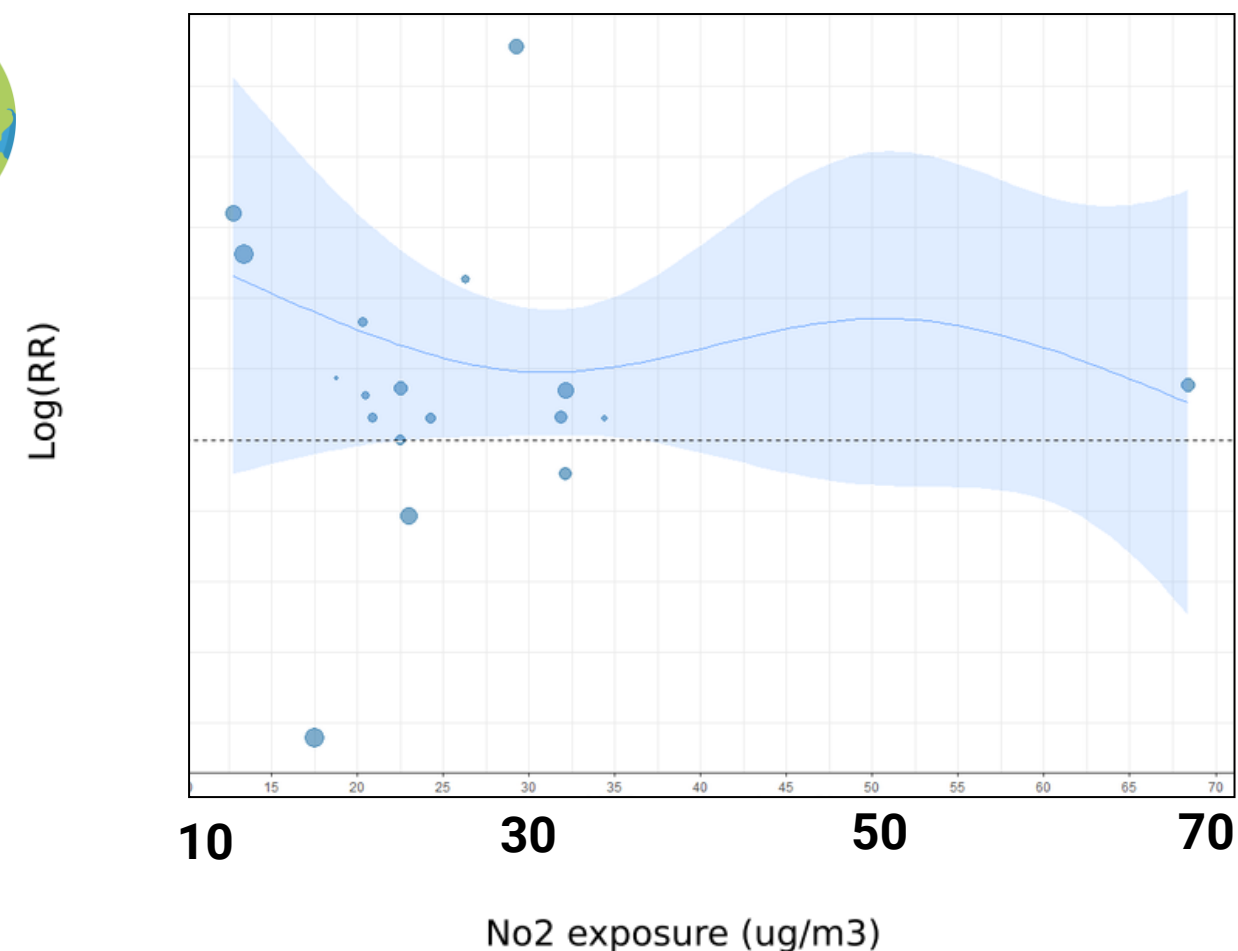
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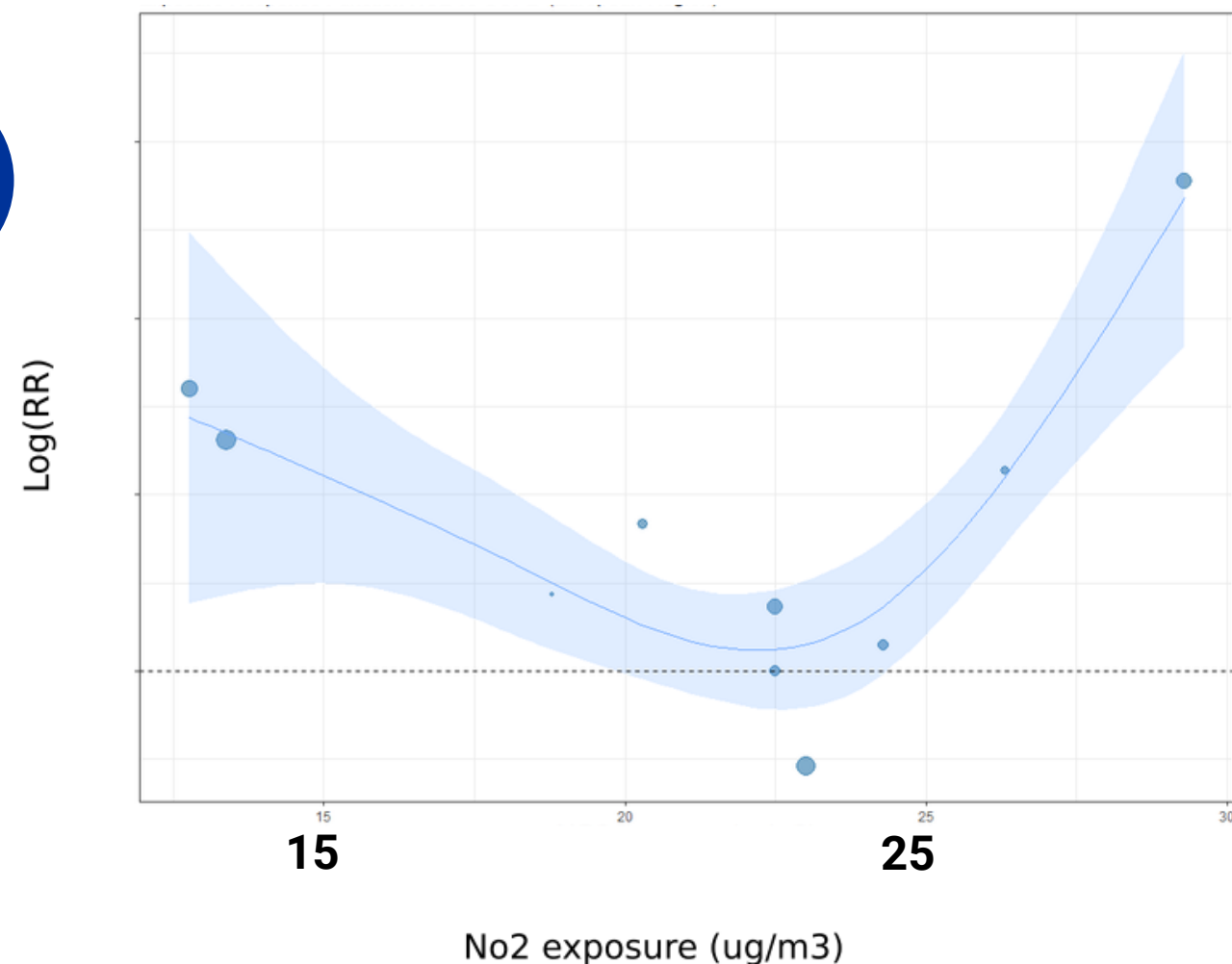


Exposure Response Functions

3. Derive region-specific curves for Europe

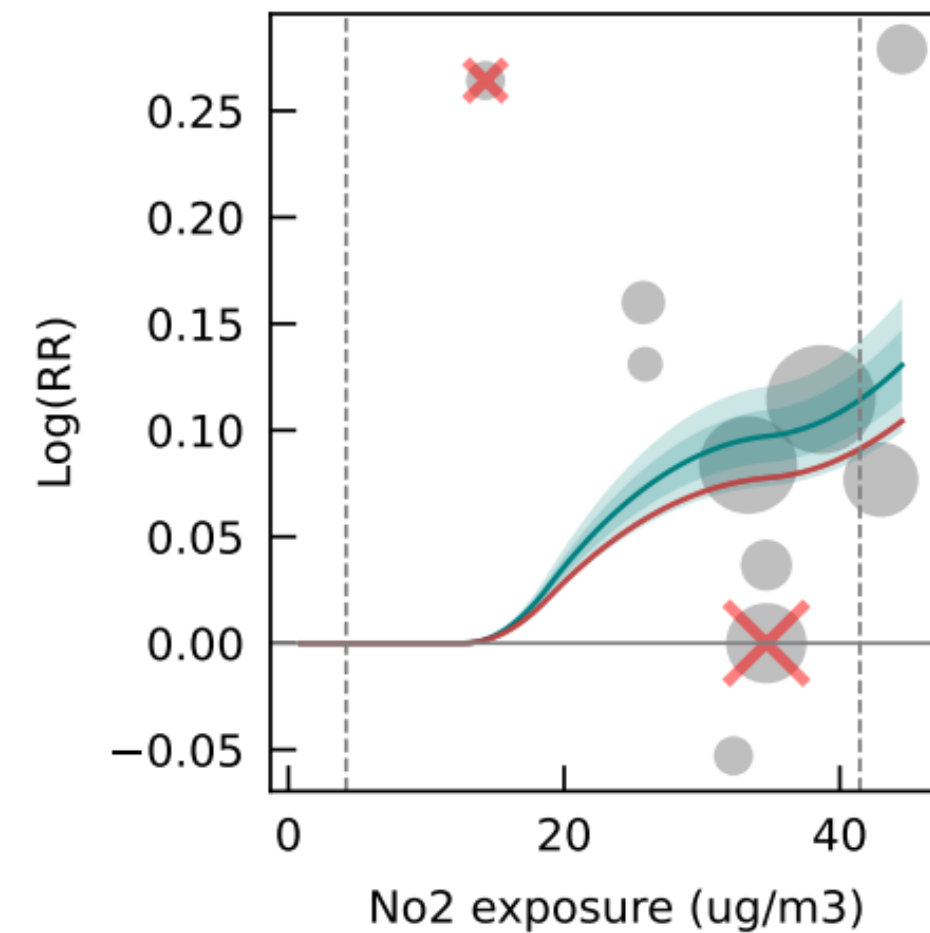
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Complexity Establishing COPD-NO₂ Relationship

- **Considerable heterogeneity**
 - Inconsistent COPD definitions, exposure assessments, and unaccounted confounding factors
- **Methodological assumptions can influence interpretations of COPD-NO₂ relationship**
 - Implications for disease burden assessments
- **Regional differences were evident**
 - Need for tailored ERFs



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- **To improve relevance and applicability of ERFs, methodological choices should align with...:**
 - Available exposure data;
 - Regional exposure patterns;
 - Expected shape of the exposure-response relationship;
 - Objective of the analysis.

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3. Stavrakou, T., Müller, JF., Bauwens, M. et al. Satellite evidence for changes in the NO₂ weekly cycle over large cities. *Sci Rep* 10, 10066 (2020). <https://doi.org/10.1038/s41598-020-66891-0>