

PM₁₀ increases mortality risk in rheumatoid arthritis-associated interstitial lung disease

Soo Han Kim^{1,2}, Sun-Young Kim³, Hee-Young Yoon⁴, Jin Woo Song¹

¹Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, South Korea

²Department of Internal Medicine, Biomedical Research Institute, Pusan National University Hospital, Pusan National University School of Medicine, Busan, South Korea

³Department of Cancer AI & Digital Health, Graduate School of Cancer Science and Policy, National Cancer Center, Goyang, South Korea

⁴Division of Allergy and Respiratory Diseases, Soonchunhyang University Seoul Hospital, Seoul, South Korea

Supplemental materials

Appendix S1:

Material and methods

Individual-level exposure assessment for PM₁₀ and NO₂

On the basis of the geo-coded residential addresses, the national-scale pointwise exposure prediction model was developed in a universal kriging framework to estimate the annual average concentrations of PM₁₀ and NO₂ at any location in South Korea.^{1,2} The model uses air pollution concentration data measured at approximately 300 regular air quality monitoring sites and includes 300 geographic variables that represent plausible air pollution sources.¹ The model performance was moderately good and revealed cross-validated R² values of 0.45 and 0.82 for PM₁₀ and NO₂, respectively,¹ which were compatible with those of the previously reported national or regional models developed in Europe³ and the United States.⁴

References

1. Kim S-Y, Song I. National-scale exposure prediction for long-term concentrations of particulate matter and nitrogen dioxide in South Korea. *Environmental Pollution* 2017;226:21-9.
2. Park Y, Song I, Yi J, Yi SJ, Kim SY. Web-Based Visualization of Scientific Research Findings: National-Scale Distribution of Air Pollution in South Korea. *Int J Environ Res Public Health* 2020;17.
3. de Hoogh K, Korek M, Vienneau D, Keuken M, Kukkonen J, Nieuwenhuijsen MJ, et al. Comparing land use regression and dispersion modelling to assess residential exposure to ambient air pollution for epidemiological studies. *Environ Int* 2014;73:382-92.
4. Hart JE, Yanosky JD, Puett RC, Ryan L, Dockery DW, Smith TJ, et al. Spatial modeling of PM10 and NO2 in the continental United States, 1985-2000. *Environ Health Perspect* 2009;117:1690-6.

Table S1. Comparison of the effect of high (top 25th percentile) air pollutant concentrations on mortality in patients with RA-ILD stratified by RF*

| | | Hazard Ratio (95% Confidence Interval) | | | |
|---|--------|--|-------------------------------|-------------------------------|---------------------------------|
| | | Model 1 | Model 2 | Model 3 | Model 4 |
| Air pollutants | | | | | |
| PM ₁₀ , µg/m ³ | RF (+) | 1.16 (0.76, 1.77) p=0.495 | 1.35 (0.88, 2.09) p=0.172 | 1.46 (0.94, 2.27) p=0.091 | 1.54 (0.98, 2.42) p=0.060 |
| | RF (-) | 1.37 (0.52, 3.62) p=0.528 | 3.96 (1.07, 14.65) p=0.039 | 7.20 (1.63, 31.76) p=0.009 | 18.81 (2.91, 121.61) p=0.002 |
| NO ₂ , ppb | RF (+) | 1.04 (0.68, 1.61) p=0.845 | 0.86 (0.55, 1.34) p=0.512 | 0.89 (0.56, 1.41) p=0.610 | 0.98 (0.59, 1.62) p=0.939 |
| | RF (-) | 2.52 (1.02, 6.23) p=0.046 | 2.99 (0.79, 11.31) p=0.106 | 1.85 (0.43, 7.97) p=0.411 | 1.21 (0.14, 10.53) p=0.863 |

NO₂, nitrogen dioxide; PM₁₀, particulate matter < 10 µm; ppb, parts per billion; RA-ILD, rheumatoid arthritis–associated interstitial lung disease;

RF, rheumatoid factor. * RF (+) (n=250) versus RF (-) (n=55)

Table S2. Comparison of the effect of high (top 25th percentile) air pollutant concentrations on mortality in patients with RA-ILD stratified by ACPA*

| | | Hazard Ratio (95% Confidence Interval) | | | |
|---|----------|--|------------------------------|------------------------------|------------------------------|
| | | Model 1 | Model 2 | Model 3 | Model 4 |
| Air pollutants | | | | | |
| PM ₁₀ , µg/m ³ | ACPA (+) | 1.33 (0.86, 2.08) p=0.203 | 1.43 (0.91, 2.24) p=0.124 | 1.51 (0.96, 2.37) p=0.076 | 1.58 (0.99, 2.51) p=0.054 |
| | ACPA (-) | 0.68 (0.24, 1.90) p=0.457 | 1.23 (0.36, 4.23) p=0.741 | 1.24 (0.35, 4.41) p=0.743 | 1.55 (0.40, 6.00) p=0.524 |
| NO ₂ , ppb | ACPA (+) | 1.17 (0.75, 1.82) p=0.486 | 0.93 (0.58, 1.46) p=0.738 | 1.03 (0.64, 1.66) p=0.897 | 1.15 (0.67, 1.96) p=0.620 |
| | ACPA (-) | 0.68 (0.22, 2.08) p=0.493 | 0.85 (0.25, 2.87) p=0.794 | 0.39 (0.10, 1.48) p=0.165 | 0.42 (0.08, 2.10) p=0.290 |

ACPA, Anti-citrullinated protein antibodies; NO₂, nitrogen dioxide; PM₁₀, particulate matter < 10 µm; ppb, parts per billion; RA-ILD, rheumatoid arthritis-associated interstitial lung disease. * ACPA (+) (n=237) vs. ACPA (-) (n=52)

Figure S1. The correlation between the annual average concentration of PM₁₀ in 2006 and each year between 2001 and 2018 measured at regulatory monitoring sites in South Korea. The X- and Y-axes present the measured PM₁₀ in 2006 and each year during 2001–2018, respectively. The red and green lines indicate the best-fitted and identity lines, respectively. PM₁₀, particulate matter ≤ 10 μm; r, Pearson's correlation coefficient concentrations

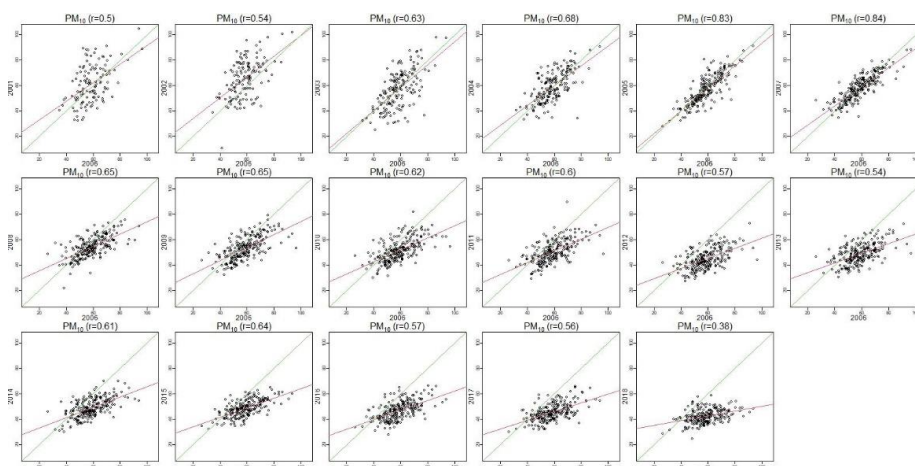


Figure S2. The correlation between the annual average concentration of NO₂ in 2006 and each year between 2001 and 2018 measured at regulatory monitoring sites in South Korea. The X- and Y-axes present the measured NO₂ in 2006 and each year during 2001–2018, respectively. The red and green lines indicate the best-fitted and identity lines, respectively. NO₂, nitrogen dioxide; r, Pearson's correlation coefficient concentrations

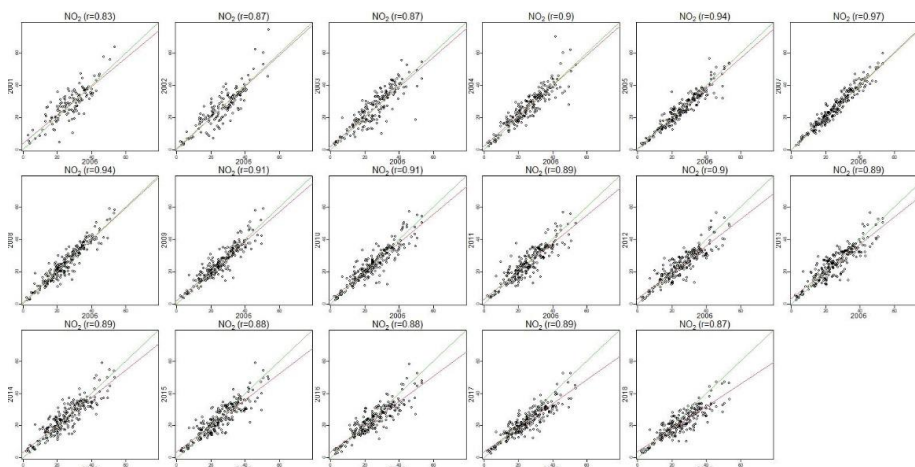
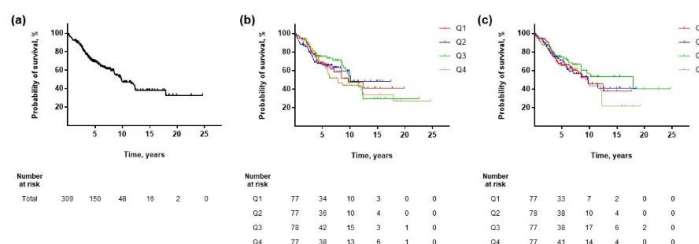


Figure S3. The survival probability over time in patients with RA-ILD

(a) The Kaplan–Meier survival curve for all the patients. (b) The Kaplan–Meier survival curve according to the quartiles of PM₁₀ concentrations. (c) The Kaplan–Meier survival curve according to the quartiles of NO₂ concentrations.

RA-ILD, rheumatoid arthritis–associated interstitial lung disease; PM₁₀, particulate matter \leq 10 μm ; NO₂, nitrogen dioxide; Q1, first quartile (lowest 25% of the numbers); Q2, second quartile (next lowest 25% of the numbers up to the median); Q3, third quartile (second highest 25% of the numbers above the median); Q4, fourth quartile (highest 25% of the numbers)

**Figure S4.** The effect of air pollutant concentrations on the mortality of patients with RA-ILD stratified by quartiles (Q1–Q4)

The forest plot of (a) PM₁₀ and (b) NO₂. Symbols and error bars represent hazard ratios and 95% confidence intervals, respectively.

RA-ILD, rheumatoid arthritis–associated interstitial lung disease; PM₁₀, particulate matter \leq 10 μm ; NO₂, nitrogen dioxide; Q1, first quartile (lowest 25% of the numbers); Q2, second quartile (next lowest 25% of the numbers up to the median); Q3, third quartile (second highest 25% of the numbers above the median); Q4, fourth quartile (highest 25% of the numbers)

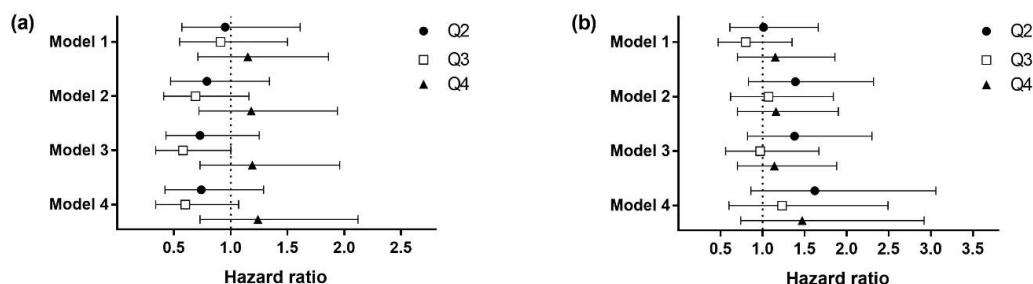


Figure S5. The effect of high (top 25th percentile) air pollutant concentrations on the mortality of patients with RA-ILD in a two-pollutant model

Symbols and error bars represent hazard ratios and 95% confidence intervals, respectively. RA-ILD, rheumatoid arthritis–associated interstitial lung disease; PM_{10} , particulate matter $\leq 10 \mu m$; NO_2 , nitrogen dioxide

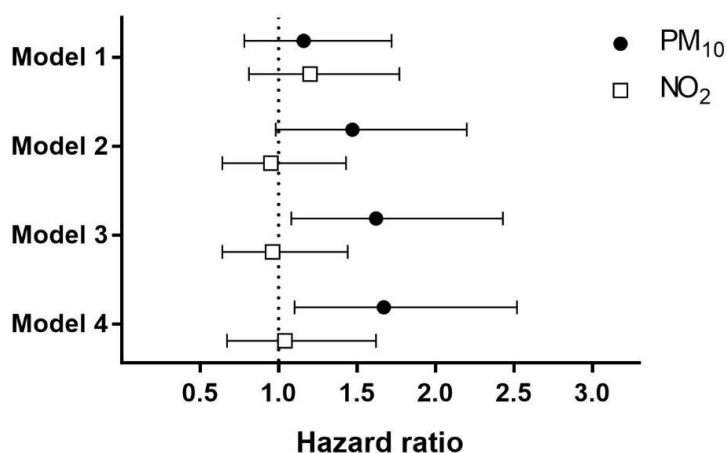


Figure S6. The effect of high (top 25th percentile) air pollutant concentrations on the mortality of patients with RA-ILD based on a single residential address (2006) for each patient

Symbols and error bars represent hazard ratios and 95% confidence intervals, respectively. RA-ILD, rheumatoid arthritis–associated interstitial lung disease; PM_{10} , particulate matter \leq

10 μm ; NO₂, nitrogen dioxide

