Pathogen-Specific Effects of $PM_{2.5}$ in a Low-Pollution Microstate: A Population-Based Time-Series Analysis

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Background

Andorra is a high-altitude microstate (avg. elevation ~1,996 m) nestled in the Pyrenees between Spain and France, with a population of ~77,000 and ambient $PM_{2.5}$ levels consistently below WHO guideline thresholds — making it a unique natural laboratory for studying low-level pollution effects.

Interactions between air pollution and acute respiratory infections are complex, particularly where winter surges of NO_2 overlap with viral activity and chronic respiratory exacerbations. In low-pollution, high-altitude microstates, this overlap makes it challenging to separate true toxic effects from seasonal co-fluctuation.

We sought to disentangle these artefacts from pathogen-specific susceptibility by evaluating short-term environmental associations across aetiologic subgroups using complete national data from the Principality of Andorra.

Objectives

- **Disentangle seasonal confounding**
  Separate NO_2 seasonal co-fluctuation from direct pollutant toxicity in Acute Respiratory Admissions (ARA)
- **Identify pathogen-specific associations**
  Evaluate lagged $PM_{2.5}$ and NO_2 effects across microbiologically confirmed aetiologic subgroups
- **Quantify environmental vulnerability**
  Determine whether specific pathogens exhibit unique susceptibility to ambient particulate matter

Methods

Design: Retrospective, population-based time-series analysis, Andorra, January 2022 – June 2025 (**≈100% national population coverage**).

Classification

ICD-10–coded ARA; viral infections confirmed by PCR; exacerbations systematically collected

Exposures

Daily $PM_{2.5}$, PM_{10}, NO_2, temperature, humidity & precipitation from central national monitoring station

Statistics

Multivariable linear regression (LOS); time-stratified case-crossover models (lags 0–7 d); Pearson correlations (lags 0–3)

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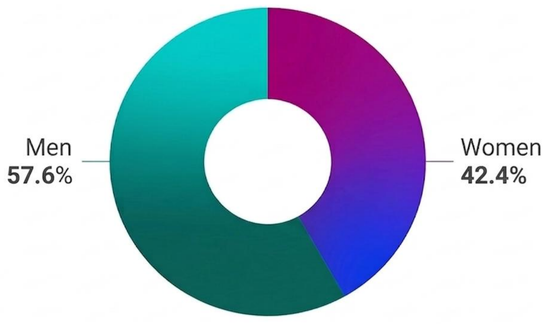
Results

1,143	62,7	8.1	8.1	25.2
Total ARAs	**Mean Age (yrs)**	**Mean LOS (days)**	**$PM_{2.5}$ µg/m³**	**NO_2 µg/m³**
Jan 2022 – Jun 2025	57.6% male	Across all aetiologies	Mean ambient level	Mean ambient level

Gender Distribution



Age Distribution of Participants

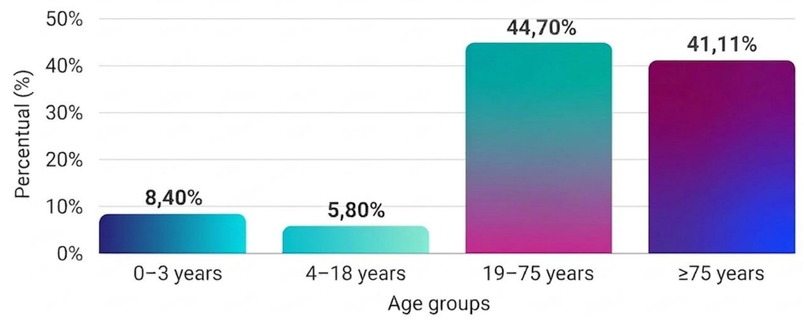
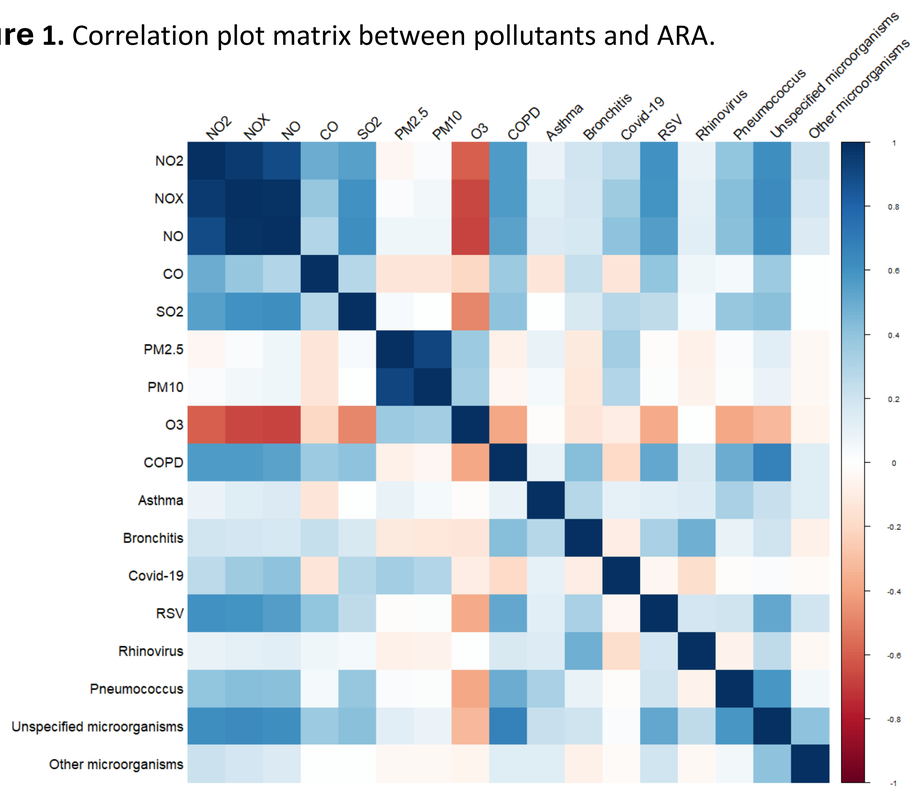


Table 1. Baseline characteristics of the study population (N=1,143)

Etiology group	N=1143	% of total ARA	Mean LOS (days)	Mean age (years)
Pneumonia – unspecified etiology	332	29.02%	8.41	62.94
COVID-19	301	26.33%	10.95	74.84
AECOPD	193	16.89%	7.76	73.63
Rhinovirus	59	5.16%	4.47	34.02
Bronchitis -unspecified etiology	55	4.81%	4.44	36.47
Asthma	54	4.72%	3.35	31.81
Streptococcus pneumoniae	53	4.64%	6.94	68.49
RSV	43	3.76%	6.28	45.00
Other microorganisms and unspecified microorganisms	53	4.64%	6.93	51

ARA: *Acute Respiratory Admissions*; LOS: *Length of Stay* ; AECOPD: *Acute Exacerbation of Chronic Obstructive Pulmonary Disease* ; RSV: *Respiratory Syncytial Virus* COVID-19: *Coronavirus Disease 2019*.

Figure 1. Correlation plot matrix between pollutants and ARA.



Pearson correlation matrix (lags 0–3). Note absence of strong positive correlations between NO_2 and any specific aetiological subgroup. $PM_{2.5}$ shows a discrete signal towards pneumococcal admissions not observed for viral or other bacterial agents.

Key Analytical Findings

$PM_{2.5}$ — Pathogen-Specific Effect on *S. pneumoniae*

Elevated $PM_{2.5}$ at **lag 5 days** was associated with significantly increased risk for pneumococcal pneumonia: **OR 1.20 µg/m³** (95% CI 1.01–1.42). Mean $PM_{2.5}$ during case periods exceeded control periods by **+0.4 µg/m³**. No significant associations were identified for other bacterial or viral aetiologies, indicating a specific rather than generalised pollutant–infection relationship.

NO_2 — Seasonal Confounding, Not Direct Toxicity

NO_2 was seasonally correlated with COPD/asthma admissions but demonstrated **no robust associations** with any specific aetiology. OR for COPD/asthma at lag_0 = **0.993** (95% CI 0.971–1.016). Risks attributed to NO_2 appear driven by co-seasonal fluctuation with viral activity rather than direct airway toxicity.

Conclusions

- In this low-pollution microstate, **NO_2-related risks appear driven by seasonal confounding, not direct toxicity.** Notably, $PM_{2.5}$ demonstrated a reproducible, **pathogen-specific effect limited to pneumococcal pneumonia** (OR 1.20 µg/m³ at lag 5 days; 95% CI 1.01–1.42), indicating unique environmental vulnerability of *Streptococcus pneumoniae* to particulate matter exposure.
- These findings underscore the imperative of **microbiological stratification** in air pollution epidemiology and support further mechanistic research into pollution–pathogen interactions.
- Even at levels well below WHO guideline thresholds, fine particulate matter may exert clinically meaningful effects on **susceptibility to bacterial pneumonia in at-risk populations.**

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