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Air Pollution Exposure Predicts ICI Outcomes in Advanced NSCLC: Geospatially-Referenced Machine-Learning Multicenter Analysis

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Nuccio A.^{1,2}, D. Zotti², F. Salomone³, A. Piva⁴, L. Mollica², L. Mazzeo⁵, G. Montelatici⁵, A. Vendittelli⁵, E. Bria⁶, E. Vita⁷, D. Signorelli⁸, A. Piemontese⁸, C. Bennati⁹, M. D'Arcangelo¹⁰, E. Caliman¹¹, L. Antonuzzo¹², G. Viscardi¹³, C.M. Della Corte¹⁴, A. Cortellini¹⁵, L. Esposito¹⁵, C. T. Saracino¹⁵, C. Sini¹⁶, R. Serra¹⁷, A. De Giglio¹⁸, C. Catania¹⁹, M. Tagliamento²⁰, C. Genova²¹, F. Verderame²², A. Ungaro²³, R. Berardi²⁴, T. Galassi²⁵, A. Servetto³, F. Colamartini²⁶, F. Biello²⁷, C. Bareggi²⁸, A. Tartarone²⁹, M.S. Cona³⁰, G. Galli³¹, A. Inno³², F.R. Ogliari³³, M.A. Reatini³⁴, G. Cattani³⁴, A. Prelaj⁵, B. Besse³⁵, R. Ferrara²

¹Gustave Roussy, Villejuif/FR; ²Univ. Vita-Salute San Raffaele, Milano; ³Univ. Federico II, Napoli; ⁴European Institute of Oncology IRCCS, Milano; ⁵Fond. IRCCS Istituto Nazionale dei Tumori, Milano; ⁶Fond. Policlinico A. Gemelli IRCCS, Roma; ⁷Comprehensive Cancer Center, Policlinico A. Gemelli IRCCS, Roma; ⁸ASST Grande Osp. Metropolitano Niguarda, Milano; ⁹Osp. S. Maria delle Croci, Ravenna; ¹⁰AUSL Romagna, Ravenna; ¹¹Univ. di Firenze; ¹²AOU Careggi, Firenze; ¹³AORN Ospedali dei Colli, Napoli; ¹⁴Univ. della Campania L. Vanvitelli, Napoli; ¹⁵Univ. Campus Bio-Medico, Roma; ¹⁶Osp. Giovanni Paolo II, Olbia; ¹⁷Univ. di Cagliari; ¹⁸Univ. di Bologna; ¹⁹Humanitas Gavazzeni, Bergamo; ²⁰Univ. di Genova; ²¹Osp. Policlinico San Martino, Genova; ²²AO Villa Sofia-Cervello, Palermo; ²³Osp. S.G. Moscati, Taranto; ²⁴Univ. Politecnica delle Marche, Ancona; ²⁵AOU delle Marche, Ancona; ²⁶Osp. S. Maria della Misericordia, Perugia; ²⁷Univ. del Piemonte Orientale, Novara; ²⁸Osp. Maggiore Policlinico, Milano; ²⁹IRCCS CROB, Rionero in Vulture; ³⁰Osp. Sacco, Milano; ³¹IRCCS Policlinico San Matteo, Pavia; ³²IRCCS Osp. Sacro Cuore Don Calabria, Negrar; ³³IRCCS San Raffaele, Milano; ³⁴ISPR, Roma; ³⁵Univ. Paris-Saclay, Gustave Roussy, Villejuif/FR

HIGHLIGHTS

PM_{2.5} exposure independently
predicted shorter PFS

Outcome-blind PM_{2.5} cutoff
stratified patients by risk

High exposure multipollutant
cluster defined a poor-outcome
phenotype

METHODS

• Retrospective multicenter cohort, APOLLO-11 consortium: 2,070 patients, advanced NSCLC, 23 Italian hospitals, first-line mono-ICI or CT-ICI between 2013 and 2024.

• Residential municipality linked to spatiotemporal exposure models; mean PM_{2.5}, PM₁₀ and NO₂ over the 3 years before treatment start
Primary endpoint PFS.

CONCLUSIONS

• Pretreatment PM_{2.5} exposure was independently associated with shorter PFS.

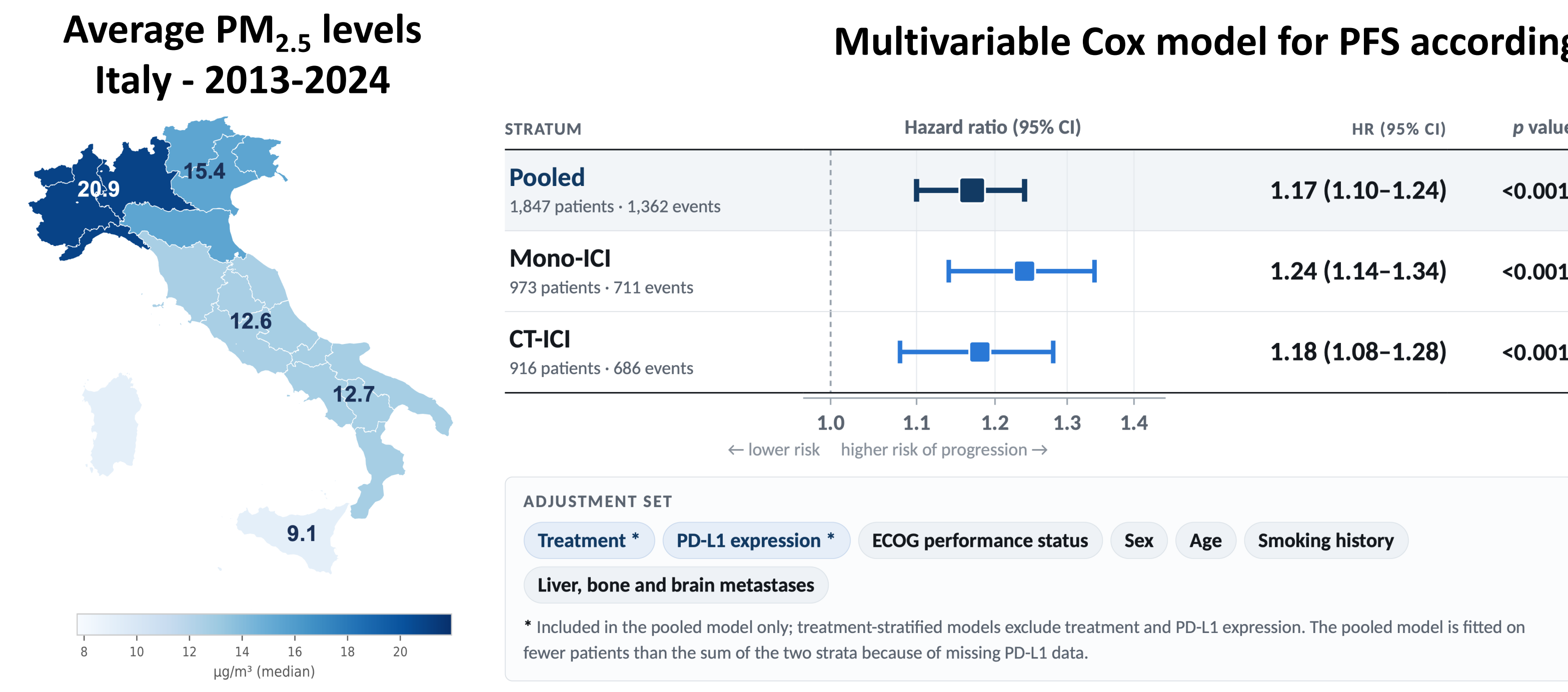
• An outcome-blind cutoff (14.59 µg/m³) was validated in an independent hold-out cohort.

• A high multipollutant exposure phenotype identified patients with worse outcomes, enriched for TP53 and KRAS mutations, PD-L1-negative tumours, and higher metastatic burden.

Air pollution may represent a measurable environmental variable to refine prognostic assessment and identify exposure-enriched populations for prospective ICI studies.

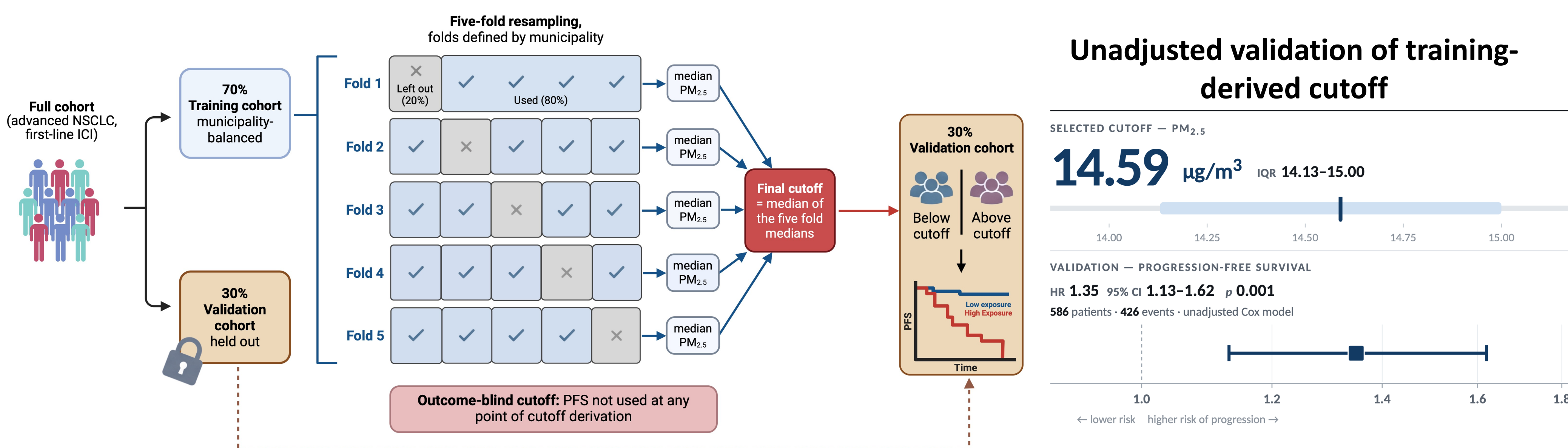
RESULTS

CONTINUOUS EXPOSURE – PM_{2.5} HR per +5µg/m³

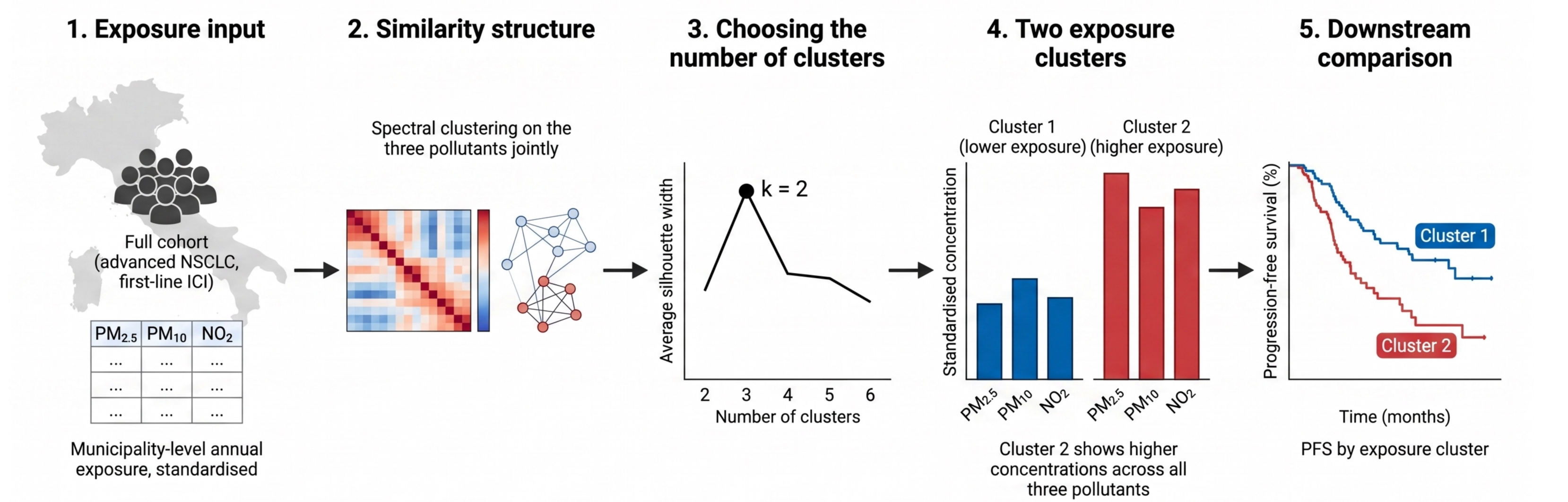


The same analyses were conducted across 2- and 5-year exposure windows and for PM₁₀ and NO₂. Findings held for the continuous and cluster analyses and were window-dependent for the cutoff-based ones, with PM₁₀ and NO₂ attenuated after adjustment.

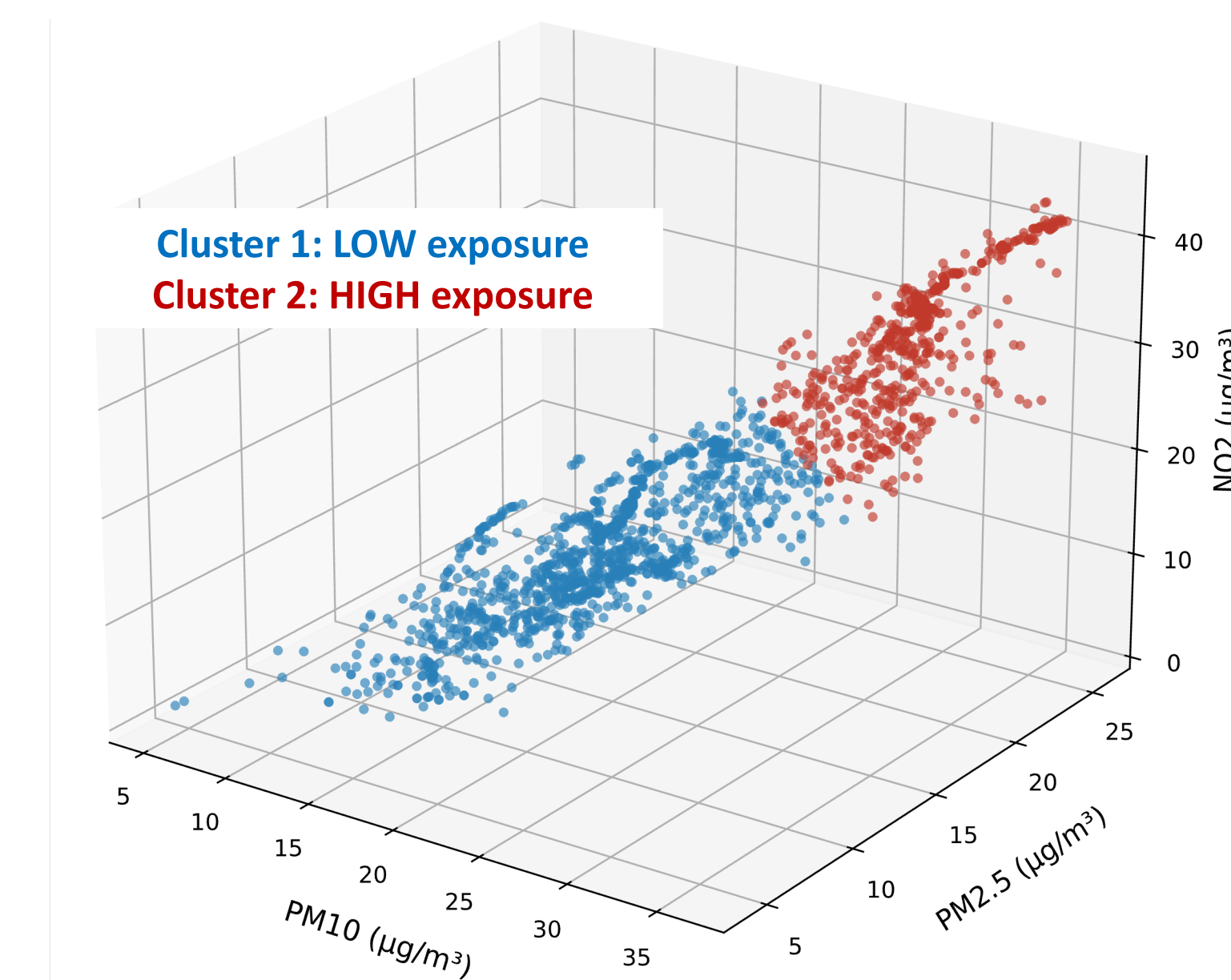
DICHOTOMISED EXPOSURE – PM_{2.5} training-derived cutoff & validation



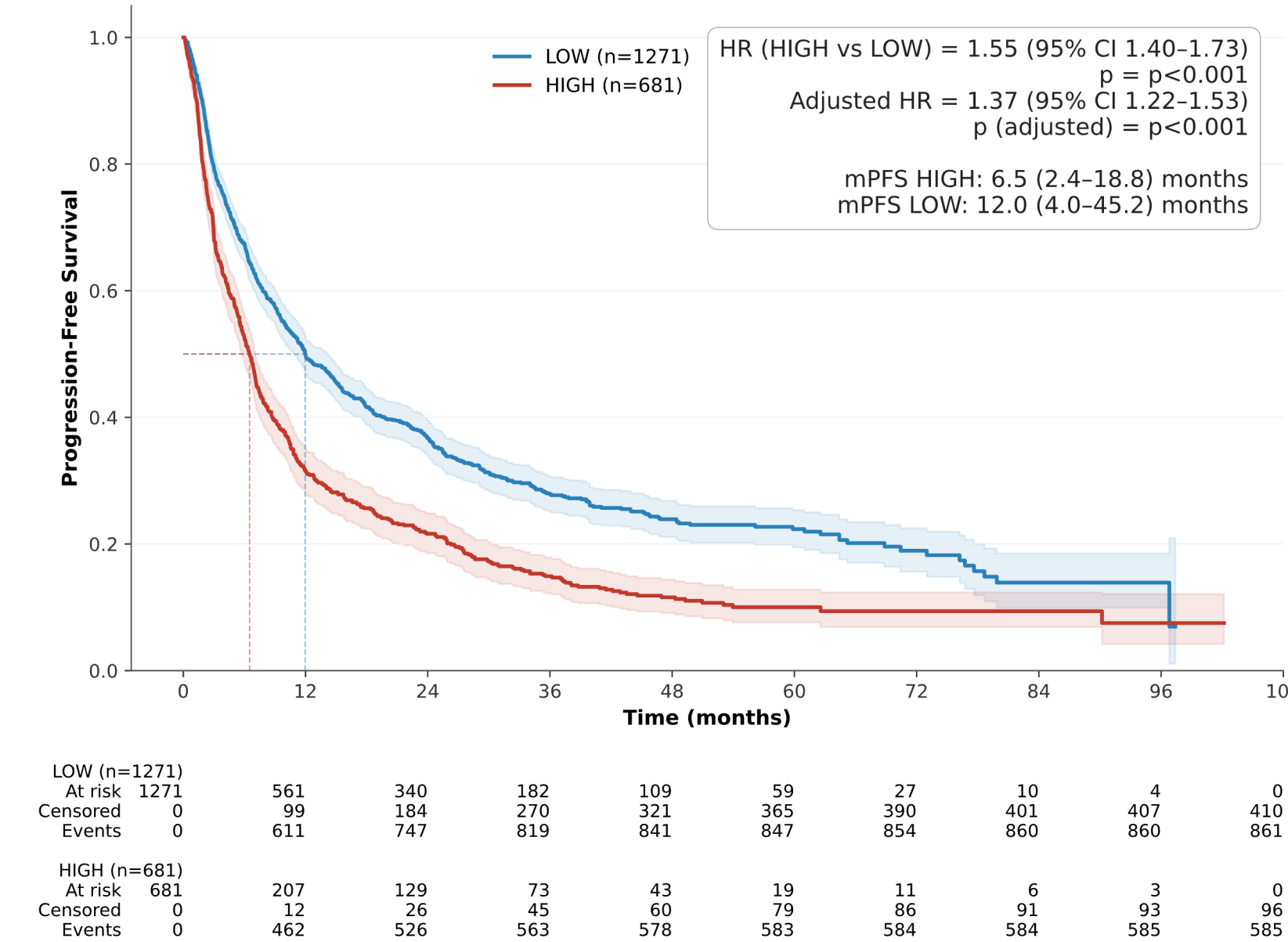
MULTIPOLLUTANT CLUSTERING – PM_{2.5} + PM₁₀ + NO₂



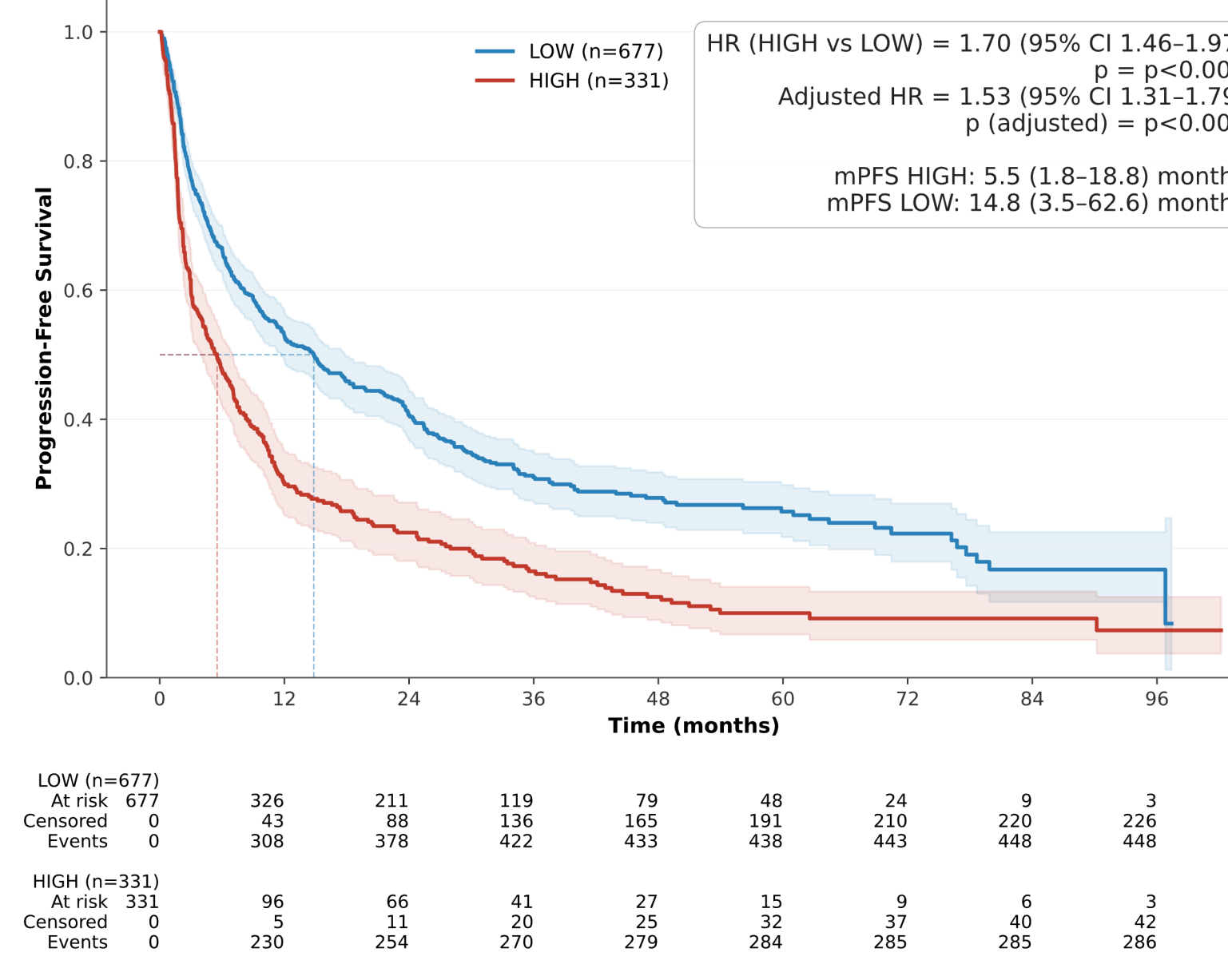
Cluster 3D scatter plot



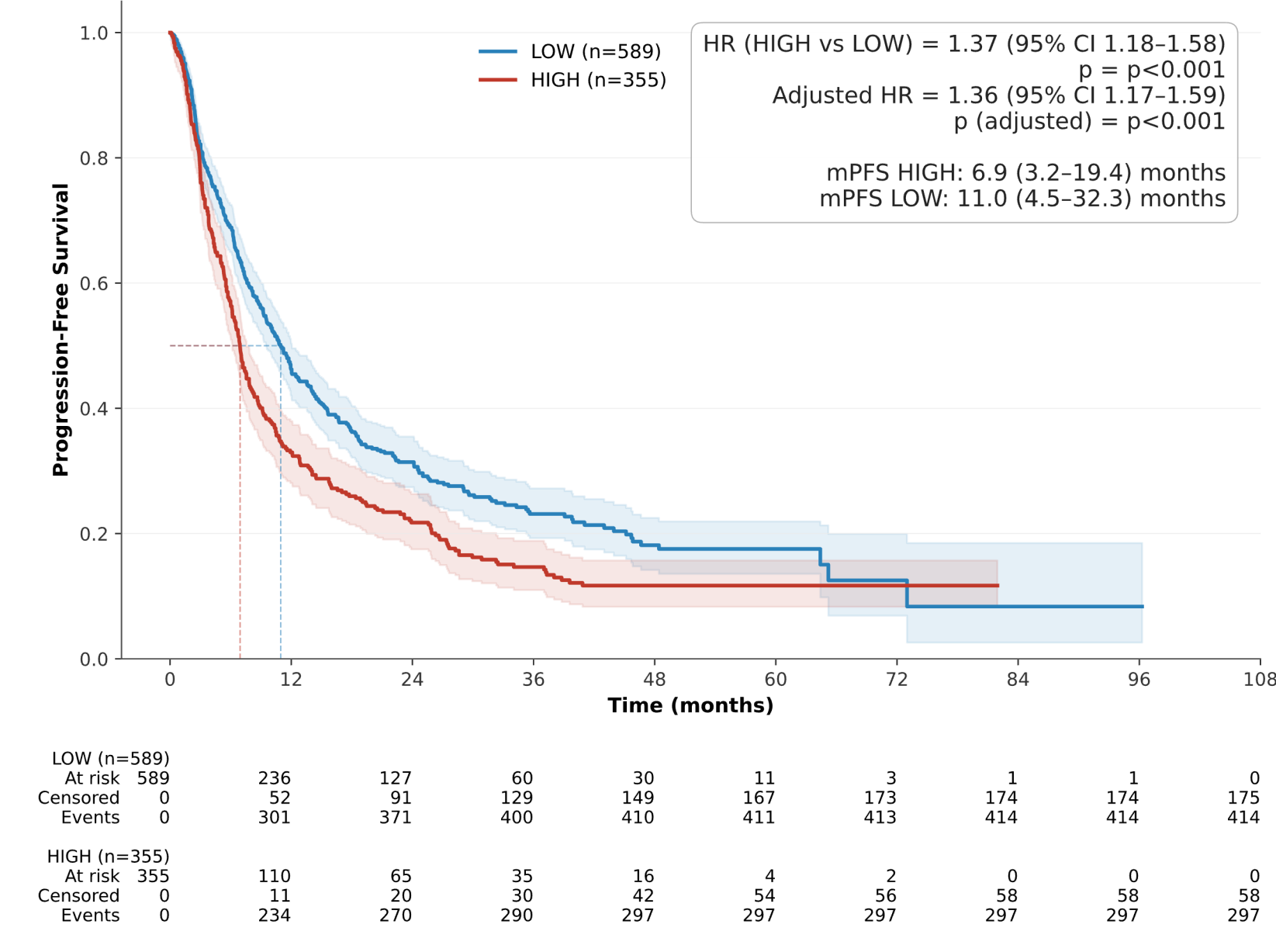
Overall population



Mono-ICI population



CT-ICI population



Variables significantly associated with the exposure

METASTATIC BURDEN		GENOMIC ALTERATIONS		PD-L1 EXPRESSION		
Oligometastatic disease	Bone metastasis	TP53 mutation	KRAS mutation	PD-L1 <1%	PD-L1 1-49%	PD-L1 ≥50%
62.3% 778/1,249	31.9% 417/1,309	23.8% 181/762	31.7% 353/1,115	19.3% 250/1,297	32.2% 418/1,297	48.5% 629/1,297
54.8% 242/442	37.7% 257/682	54.0% 176/326	39.2% 227/579	27.5% 179/652	31.0% 202/652	41.6% 271/652
χ ² 7.44 p 0.006	χ ² 6.54 p 0.011	χ ² 93.31 p <0.001	χ ² 9.31 p 0.002	χ ² 17.91 p <0.001		

AI was used to improve the visual presentation of the figures