Particulate matter exposure and dementia risk: a prospective cohort study in Northern Italy

Teresa Urbano, Carlotta Malagoli, Andrea Cherubini, Annalisa Chiari, Giovanna Zamboni, Manuela Tondelli, Roberta Bedin, Sofia Costanzini, Sergio Teggi, Giuseppe Maffeis, Marco Vinceti, Tommaso Filippini

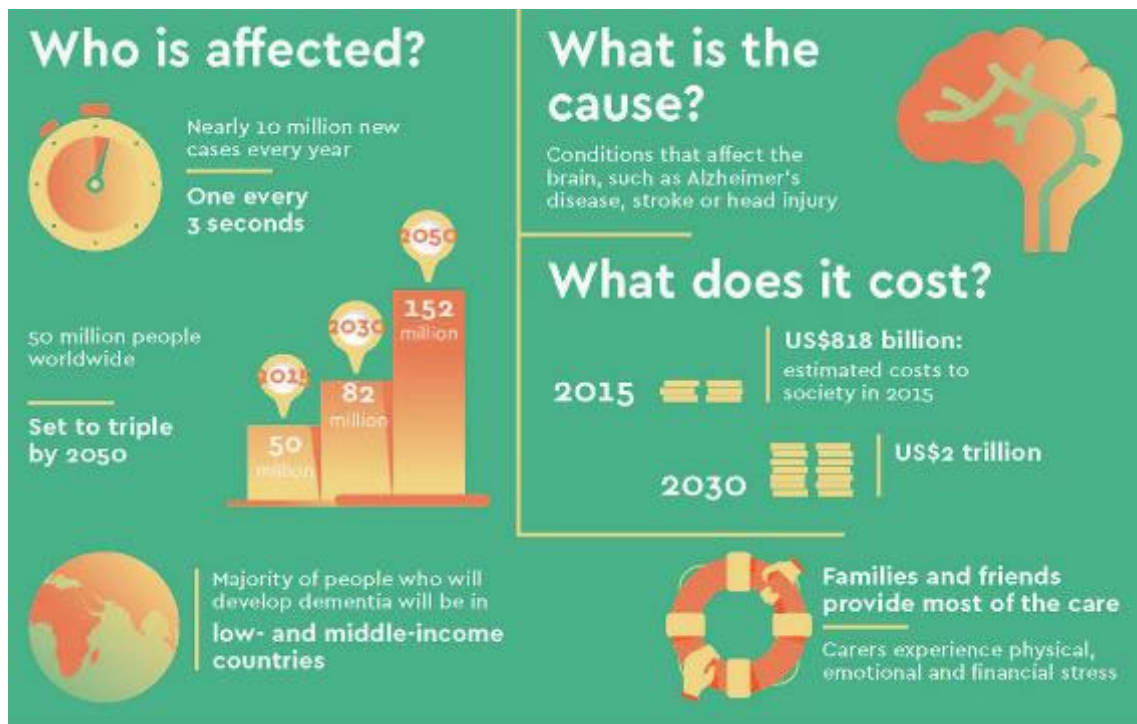Convegno Nazionale
Climate & Public Change & Health

Aula Magna Artigianelli

Università di
Modena e Reggio Emilia

Venerdì 9 giugno 2023
ore 9:30-17:30

Background: Dementia

- Incidence increased in recent decades

- Forecasted to triple by 2050

- Complex interplay between genetic and environmental risk factors

GBD Collaborators, 2021 *Global mortality from dementia: application of a new method and results from the global burden of disease study 2019* Alzheimers Dement (N Y)., 7 (2021), Article e12200, 10.1002/trc2.12200 ; WHO, Global Dementia Observatory (GDO), 2022

Background: Dementia

Modifiable + Non-modifiable risk factors

- Age
- Female sex
- Genetic factors

- Air pollutants
- Pesticides
- Electro-magnetic fields
- Dietary patterns
- Dietary intake of metals and metalloids (Al, silicon, Se)

Scheltens et al., 2021 *Alzheimer's disease* Lancet, 397 (2021), pp. 1577-1590, 10.1016/S0140-6736(20)32205-4

Background: Dementia

Normal aging

Mild Cognitive Impairment
- Impairment does not interfere with activities of daily living

Mild Dementia
- Reading problems; poor object recognition; poor direction sense

Moderate Dementia
- Poor judgement; impulsivity; short attention

Severe Dementia
- Impairment in two or more cognitive functions that interferes with activities of daily living

Background: PM10

Location of the study area in the Po Valley, one of the most severely polluted areas in Europe due to topographic and meteorological conditions inhibiting pollutant dispersion

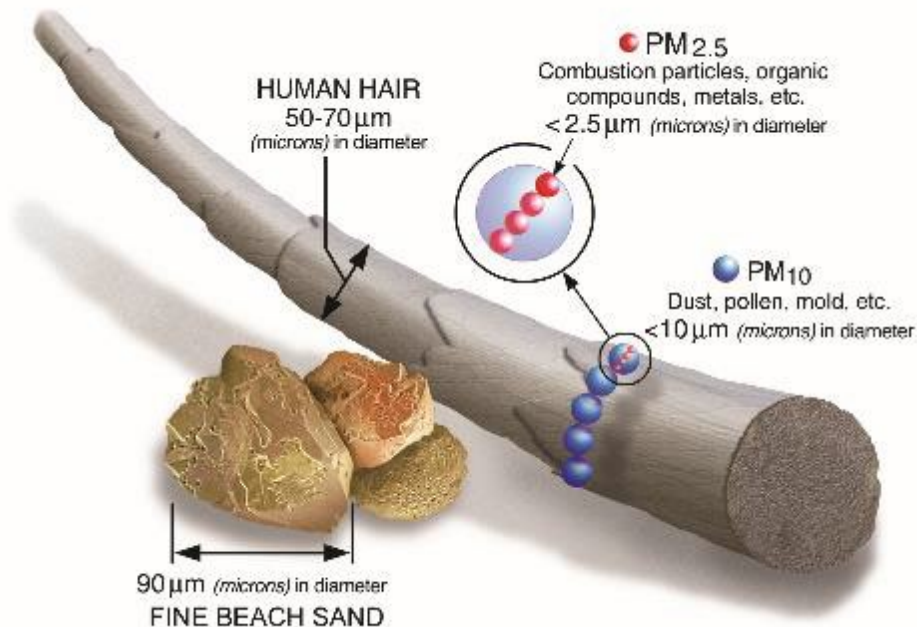| Città	Medie annuali 2022 (µg/mc)			Riduzione delle concentrazioni necessaria (%)			Variazione media annuale (%) Periodo 2011–2021	
	PM10	PM2.5	NO2	PM10	PM2.5	NO2	PM10	NO2
BOLOGNA	25	16	23	–20%	–35%	–12%	–2%	–2%
CESENA	25	–	18	–20%	–	11%	nd	nd
FERRARA	29	16	22	–30%	–38%	–8%	–2%	–4%
FORLÌ	25	14	20	–18%	–29%	2%	–3%	–3%
MODENA	33	18	27	–39%	–44%	–27%	–1%	–4%

Superamenti annuali valore limite giornaliero di PM10

	N. giornate dello sforamento soglia >50 µg/mc	Stazione di rilevamento
Modena	75	Giardni
Reggio Emilia	65	Timavo
Ferrara	62	Isonzo
Ravenna	59	Porto San Vitale

Bigi et al., 2012 *Analysis of the air pollution climate at a background site in the Po valley* J. Environ. Monit., 14 (2012), pp. 552-563, 10.1039/c1em10728c
Rapporto Mal'Aria di città 2023, Legambiente; https://www.legambiente.it/wp-content/uploads/2021/11/Rapporto_Malaria_2023.pdf

Methods

Median age of 66.3 years at recruitment

Study design: prospective cohort study

MCI subjects (n = 53) → MCI (n = 19), Dementia (n = 34)

6 months follow-up · 6 months follow-up · 6 months follow-up · 6 months follow-up → August, 2021
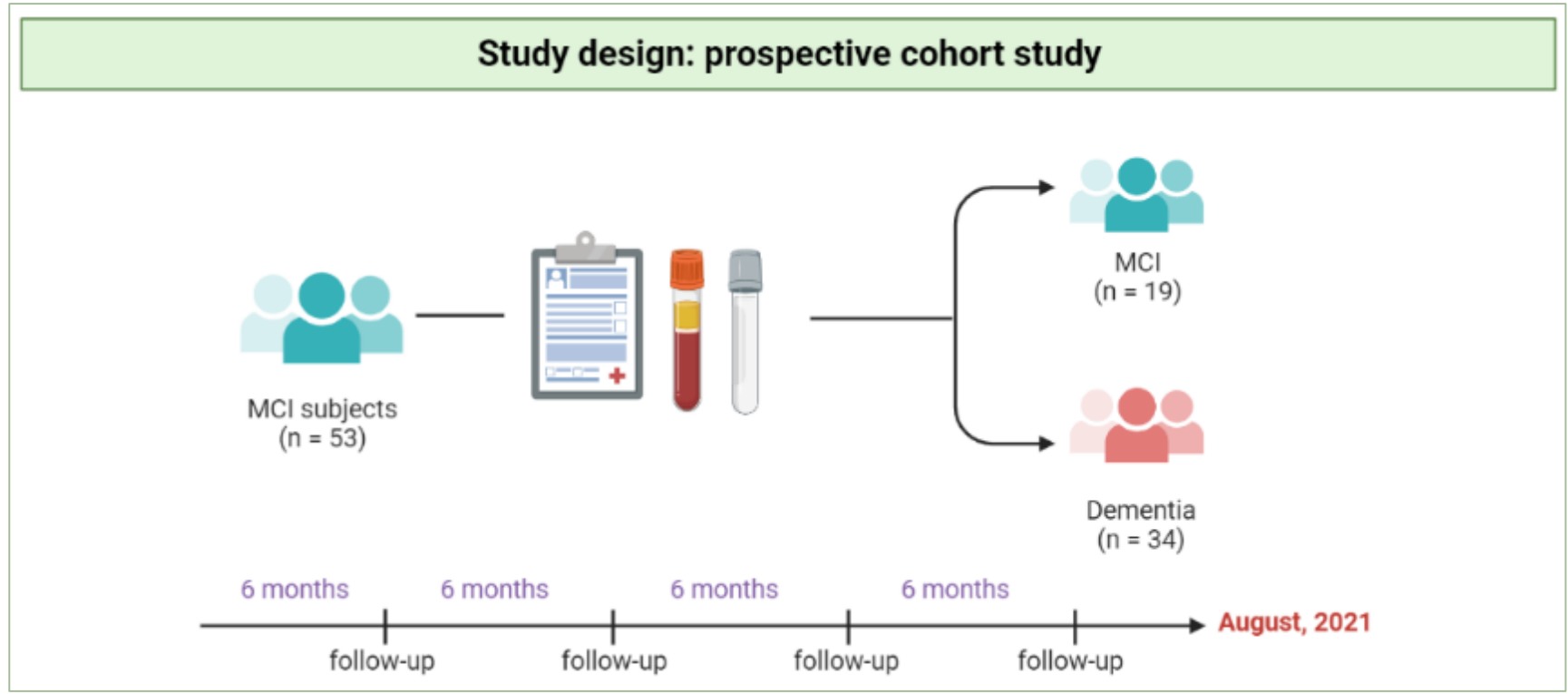
Methods
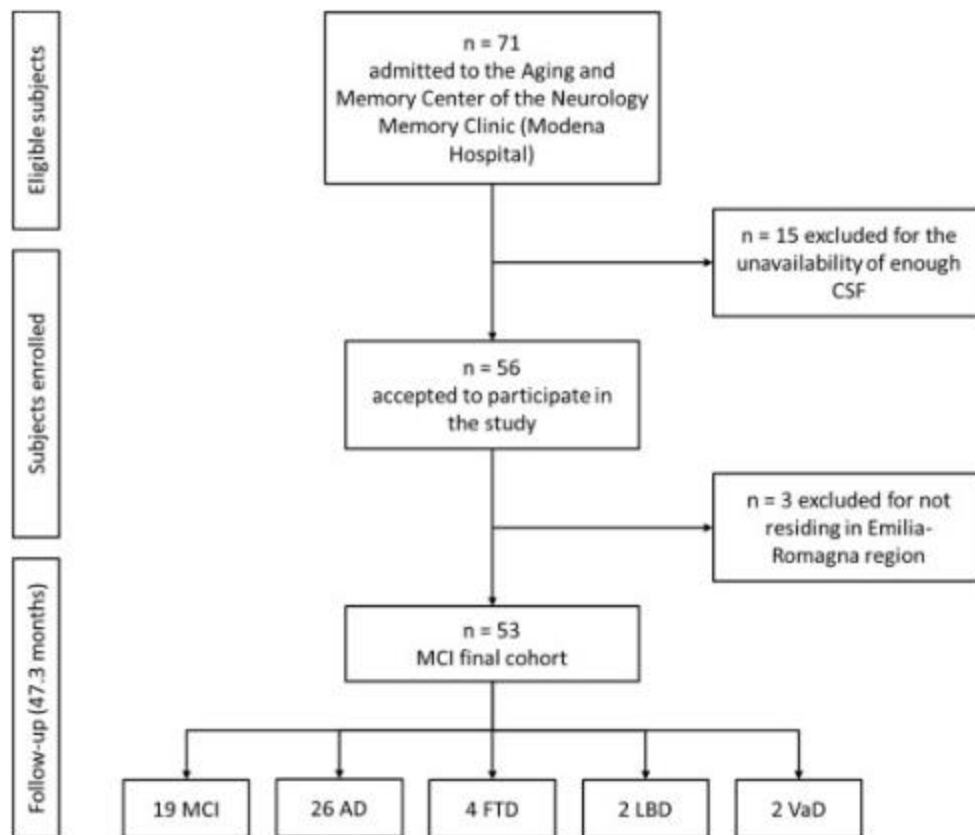
- Cohort members were followed-up at the Neurology Clinic every six months until August 2021
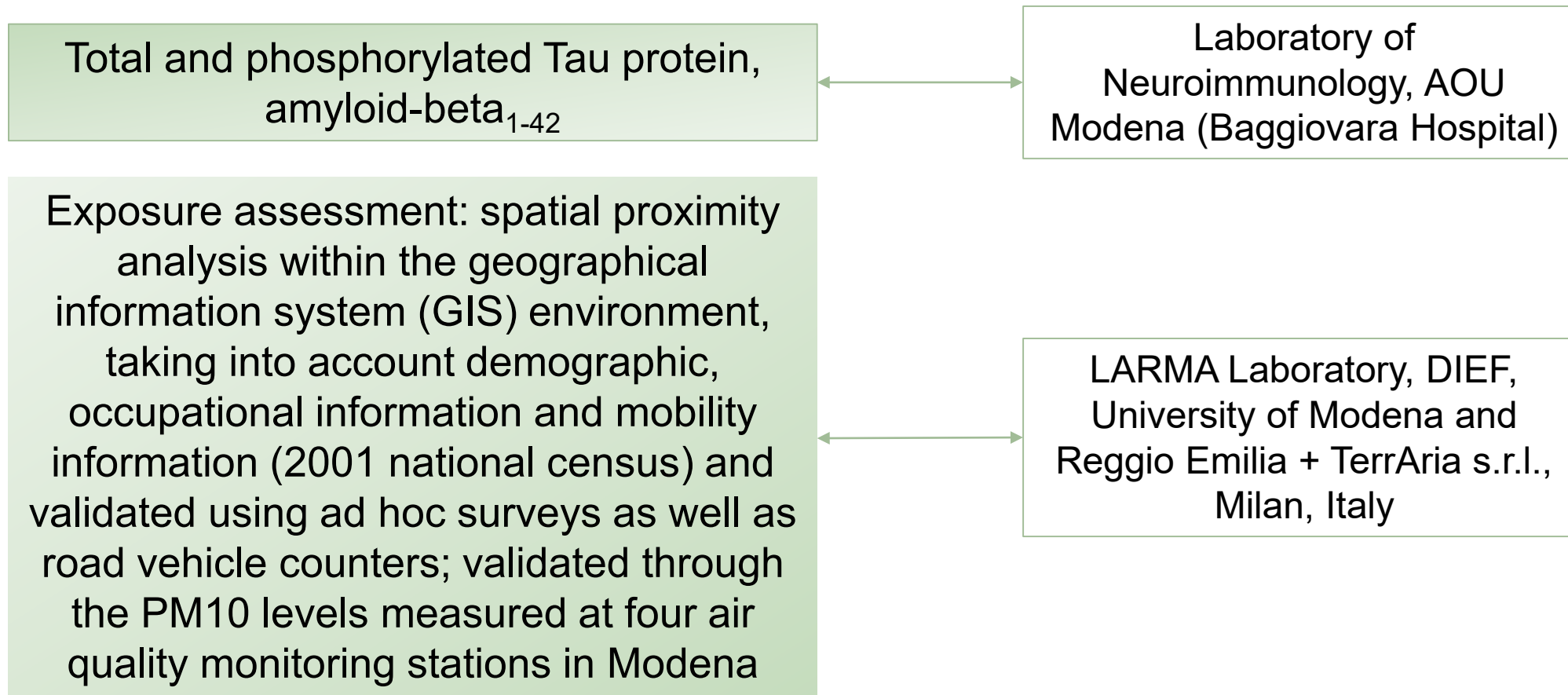
- During each follow up visit each patient was classified as stable (i.e., **confirmed MCI**), or as a converter to dementia (any form, i.e., **AD**, frontotemporal dementia (**FTD**), Lewy-body dementia (**LBD**) or **vascular dementia**)

Methods

Total and phosphorylated Tau protein, amyloid-beta$_{1-42}$

Laboratory of Neuroimmunology, AOU Modena (Baggiovara Hospital)

Exposure assessment: spatial proximity analysis within the geographical information system (GIS) environment, taking into account demographic, occupational information and mobility information (2001 national census) and validated using ad hoc surveys as well as road vehicle counters; validated through the PM10 levels measured at four air quality monitoring stations in Modena

LARMA Laboratory, DIEF, University of Modena and Reggio Emilia + TerrAria s.r.l., Milan, Italy

Results

| Study population	Mean PM$_{10}$ (μg/m^3)	Maximum PM$_{10}$ (μg/m^3)
All subjects (n = 53)	8.17 (5.13–13.10)	23.64 (14.73–34.52)

Figure 3: Percentage of reporting monitoring stations registering PM$_{10}$ concentrations above the EU limit values and the WHO guideline levels in 2021 and 2022

PM$_{10}$	EU daily limit value of 50 μg/m³	WHO daily guideline level of 45 μg/m³	EU annual limit value of 40 μg/m³	WHO annual guideline level of 15 μg/m³
2021 validated	15%	71%	4%	71%
2022 preliminary	10%	65%	1%	73%
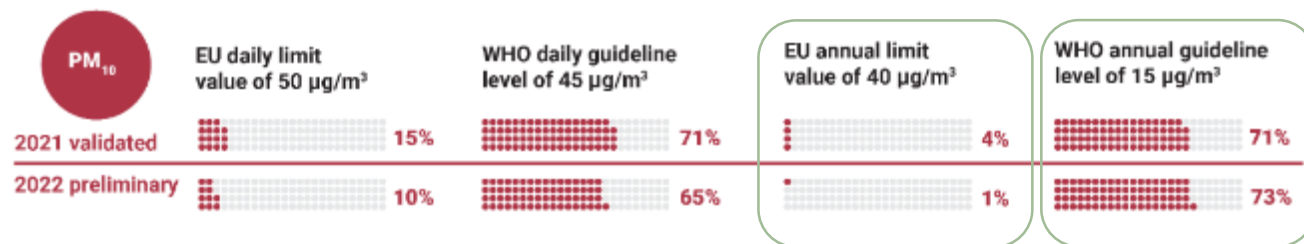
| Any dementia	N	HR	95% CI	Alzheimer's dementia	N	HR	95% CI
PM$_{10}$ (mean) (μg/m^3)				**PM$_{10}$ (mean) (μg/m^3)**			
≤5	12	1.00	–	≤5	5	1.00	–
>5-≤10	18	1.39	0.50–3.86	>5-≤10	9	0.66	0.21–2.06
>10-≤20	19	1.19	0.43–3.31	>10-≤20	8	0.75	0.20–2.73
>20	4	2.77	0.61–12.47	>20	4	3.10	0.64–14.93
PM$_{10}$ (max) (μg/m^3)				**PM$_{10}$ (max) (μg/m^3)**			
≤20	23	1.00	–	≤20	9	1.00	–
>20-≤50	26	1.37	0.63–2.99	>20-≤50	13	0.73	0.28–1.92
>50	4	2.96	0.70–12.47	>50	4	3.34	0.74–15.02

Results
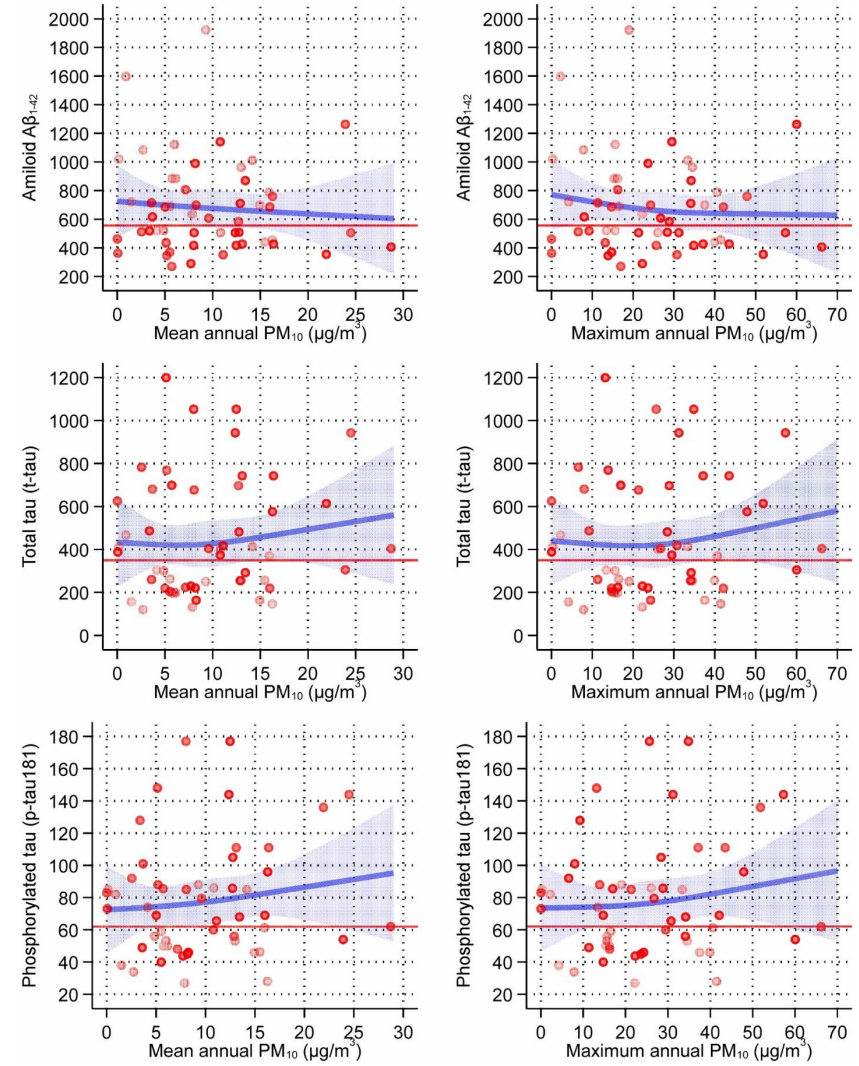
- Both annual mean and maximum PM10 levels were **negatively correlated with Aβ1-42**, and **positively**, though not linearly, **associated with t-tau and p-tau181** concentrations

*Adjusted for age, sex, and education

Results
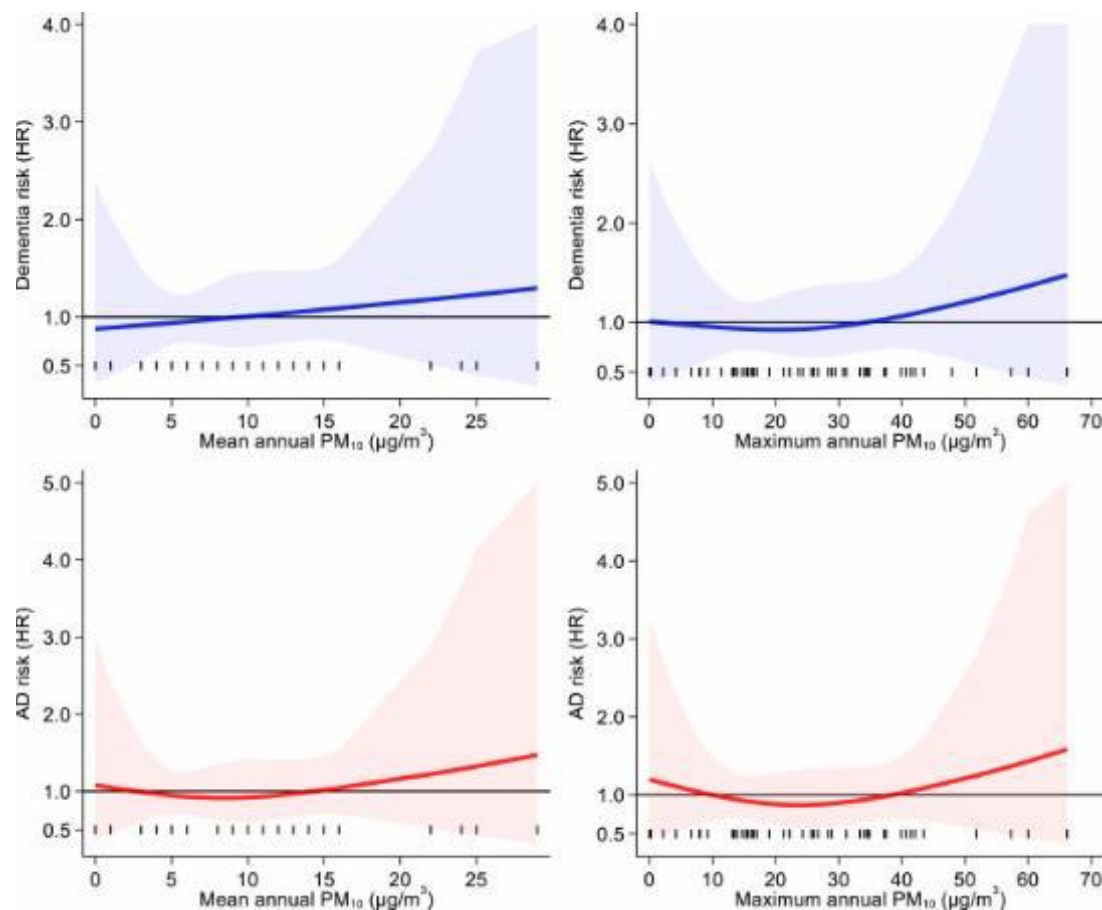
*Adjusted for age, sex, and education

- Increased risk of overall dementia for **mean PM10 levels above 10 μg/m3** and for **maximum PM10 levels above 35 μg/m3.** At **70 μg/m3** of PM10, **risk increased by 50%**

- For AD as specific outcome, **non-linearly increased risk above 15 μg/m3 of mean PM10** levels. For maximum PM10 levels, a trend emerged towards a U-shaped association with AD risk, with a **turning point at around 25 μg/m3**

Conclusions

- First prospective cohort study of an Italian population indicating that relatively, but not exceedingly high, levels of **traffic-related PM10** levels were associated with **increased risk of MCI conversion to dementia**

- Higher **PM10 levels positively associated** also to the baseline levels of CSF neurodegeneration biomarkers, namely **t-tau and p-tau181**, as well as (**inversely**) with CSF **amyloid levels**, another hallmark of AD

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Particulate matter exposure from motorized traffic and risk of conversion from mild cognitive impairment to dementia: An Italian prospective cohort study

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- All the co-authors

- Patients and family members

Thank you for the attention