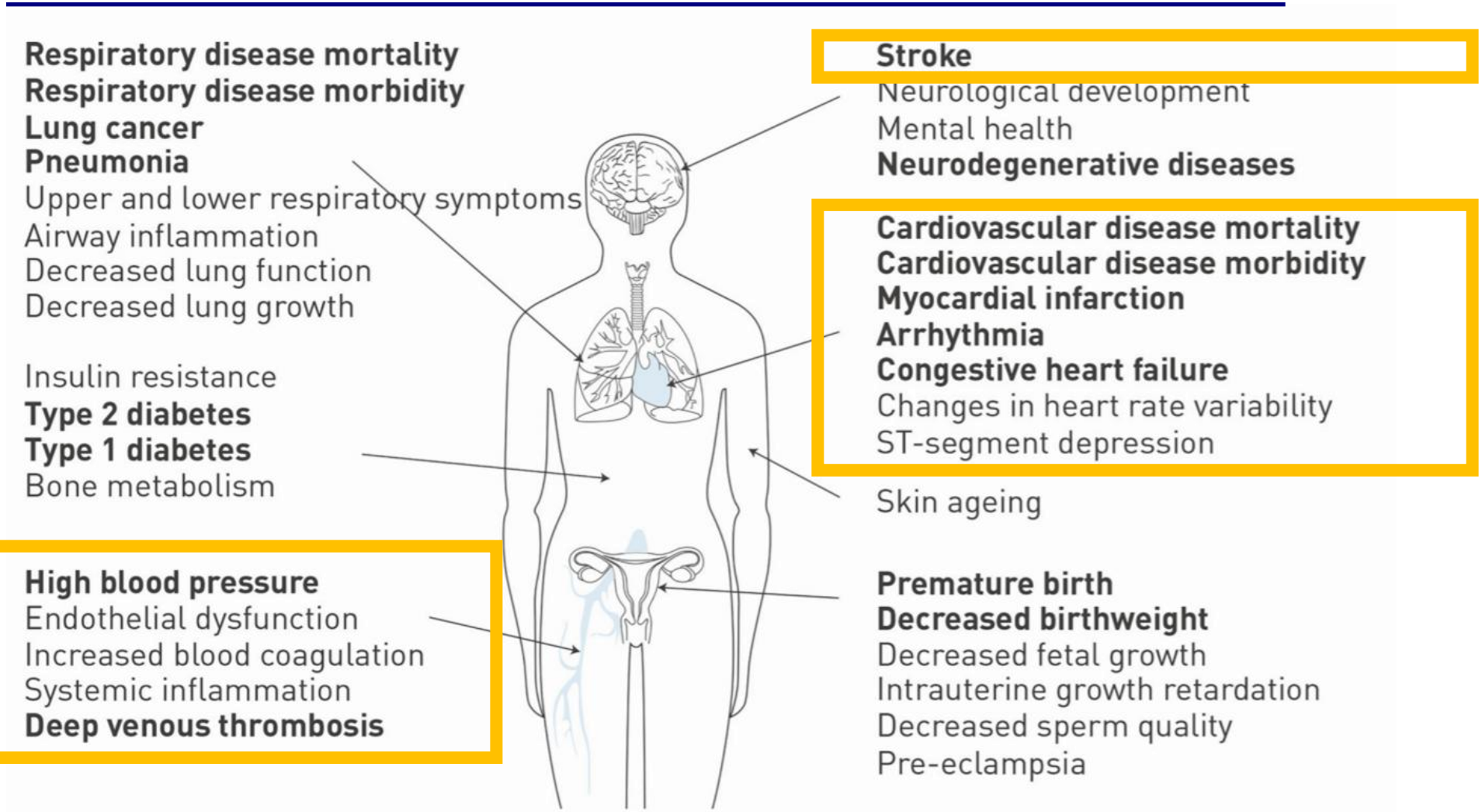
Inquinamento atmosferico e malattie cardiovascolari: dalla valutazione del rischio alle strategie di mitigazione

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Agenda

- Inquinamento atmosferico e malattie cardiovascolari: meccanismi, dati e stime di rischio
- Oltre «l'associazione»: il contributo degli studi osservazionali di popolazione
- Take-home messages

Effetti dell'inquinamento sulla salute



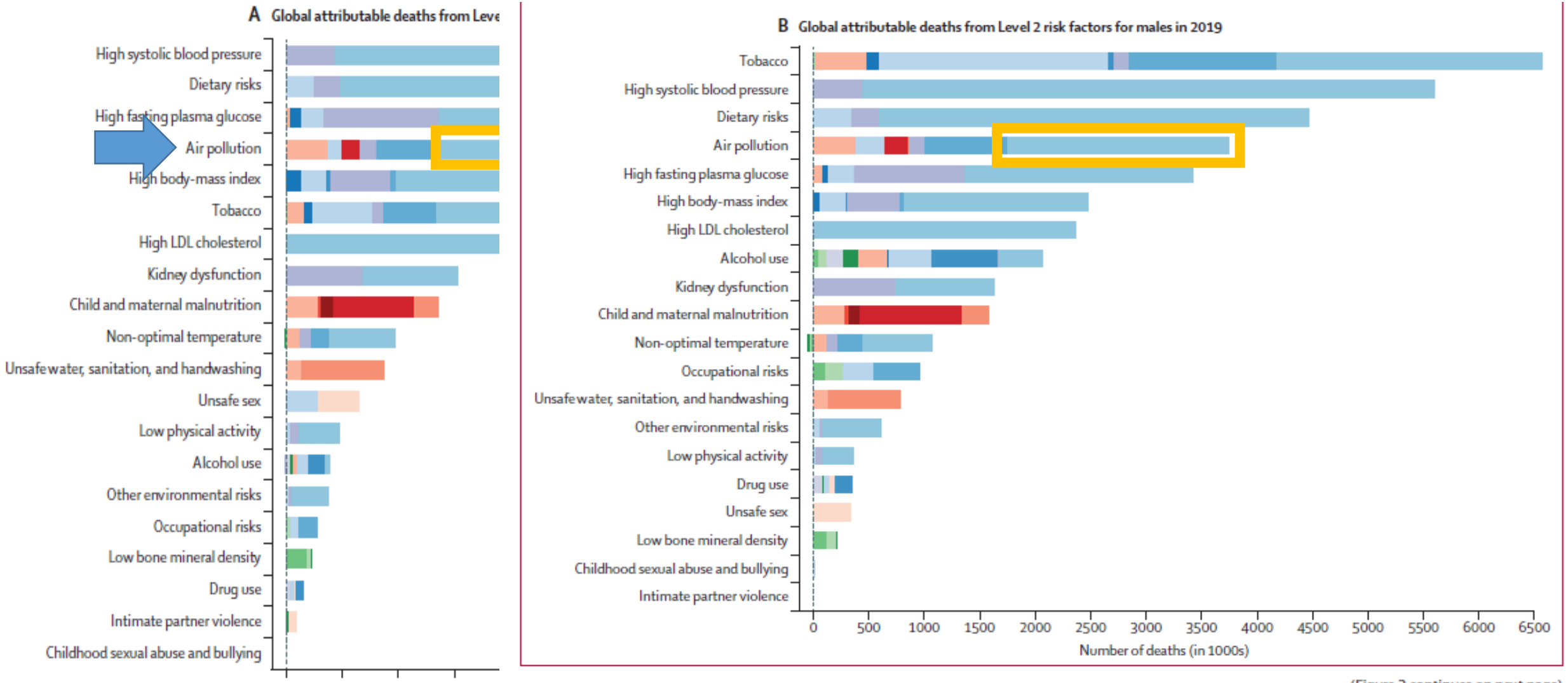
Thurston GD, Kipen H, Annesi-Maesano I, et al. A **joint ERS/ATS policy statement**: what constitutes an adverse health effect of air pollution? An analytical framework. *Eur Respir J.* 2017;49(1):1600419.

Global burden of 87 risk factors in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019

*GBD 2019 Risk Factors Collaborators**

Lancet 2020; 396: 1223–49

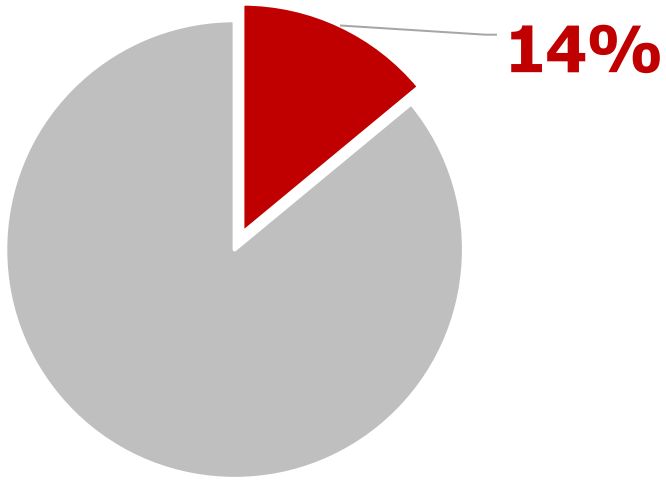
*For the list of Collaborators see
Viewpoint *Lancet* 2020;
396: 1135–59



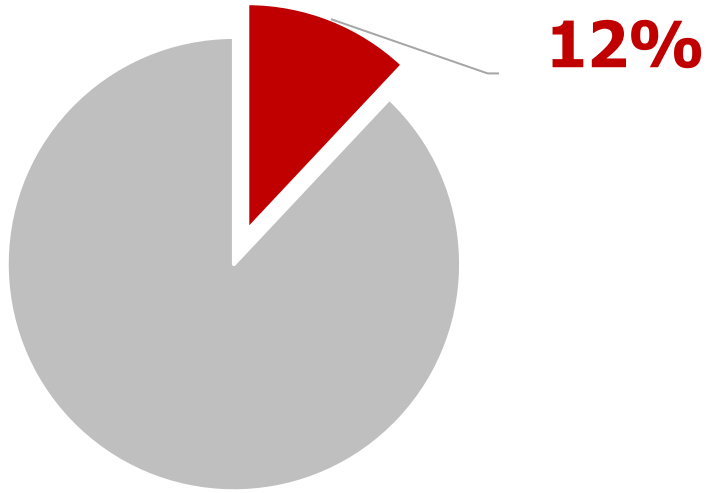
(Figure 3 continues on next page)

% mortalità attribuibile a PM, Italia 2025

Malattie ischemiche del cuore



Stroke ischemico



Health Effects Institute. 2025. State of Global Air 2025. Available: www.stateofglobalair.org [accessed: 15/10/2026].
Data source: Global Burden of Disease Study 2023. IHME, 2025.

Inquinamento e malattie CVD - meccanismi

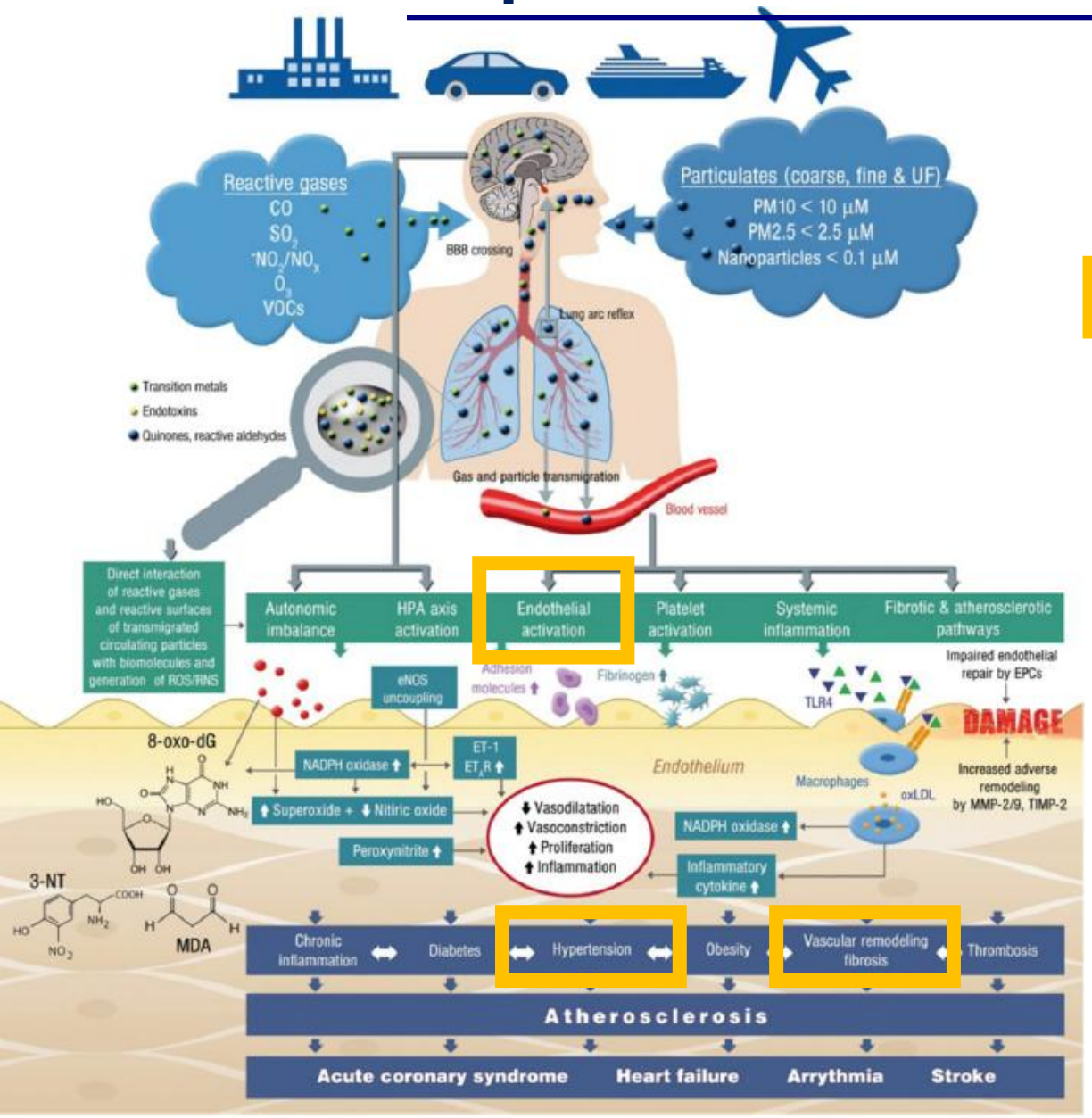


Table 3 Proposed mechanisms linking $PM_{2.5}$ exposure to cardiovascular injury

Mechanistic pathway	Description	Supporting evidence
Oxidative stress	$PM_{2.5}$ inhalation generates reactive oxygen species (ROS) in the lungs and systemic circulation, initiating oxidative damage to endothelial cells and lipids.	Brook *et al.*, 2010[1]
Systemic inflammation	Activation of pulmonary and systemic inflammatory pathways leads to elevated circulating cytokines (interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α) , C-reactive protein (CRP)), contributing to vascular inflammation and plaque	Hayes *et al.*, 2020[24]; Wang *et al.*, 2014([32]
Endothelial dysfunction	Impairment of endothelial nitric oxide bioavailability and increased endothelial apoptosis reduce vascular compliance and promote atherogenesis.	Brook *et al.*, 2010[1]; Lederer *et al.*, 2021[14]
Autonomic nervous system imbalance	$PM_{2.5}$ exposure reduces heart rate variability and enhances sympathetic activity, increasing the risk of arrhythmias and acute cardiac events.	Brook *et al.*, 2010[1]
Pro-thrombotic state	Systemic inflammation induces coagulation pathway activation, with increased fibrinogen, tissue factor expression, and platelet activation, promoting thrombosis.	Kloog *et al.*, 2015[50]; Wang *et al.*, 2014[32]
Atherosclerosis progression	Chronic exposure accelerates arterial wall thickening, plaque formation, and progression of subclinical atherosclerosis.	Brook *et al.*, 2010[1]; Hayes *et al.*, 2020[24]
Impaired endothelial repair	Specific $PM_{2.5}$ metal components impair endothelial progenitor cell function, reducing vascular repair capacity and resilience.	Lederer *et al.*, 2021[14]
Deep tissue penetration and bioavailability	$PM_{2.5}$ and ultrafine particles ($PM_{0.1}$) translocate into systemic circulation, directly impacting remote vascular and cardiac tissues.	Wang *et al.*, 2014[32]

Figura: *Eur H Journal.* 2026
Tabella: *Eur J Prev Cardiol.* 2026

Effetto di esposizioni *short-term*

ESC European Heart Journal (2026) 00, 1–25
https://doi.org/10.1093/eurheartj/ehag270
SPECIAL ARTICLE
Epidemiology, prevention, and health care policies

Environmental risk factors and cardiovascular health

A clinical consensus statement of the European Society of Cardiology

Table 1 Selected meta-analyses of short-term exposure (<1 month) to air pollutants and cardiovascular mortality and morbidity

Cardiovascular condition	Pollutant	Studies/subjects included	% increase in risk	Reference
Cardiovascular/circulatory mortality	PM_{10} $PM_{2.5}$ NO_2 O_3	196 studies, global	0.6% per 10 µg/m^3 0.9% per 10 µg/m^3 0.7% per 10 ppb 0.4% per 10 ppb	Orellano *et al.*, 2020[13]
Myocardial infarction	PM_{10} $PM_{2.5}$	33 studies, global	1.1% per 10 µg/m^3 2.4% per 10 µg/m^3	Cai *et al.*, 2016[14]
Heart failure	PM_{10} $PM_{2.5}$ NO_2 O_3	7.56 million patients	1.3% per 10 µg/m^3 1.3% per 10 µg/m^3 2.1% per 10 ppb 1.0% per 10 ppb	Yang *et al.*, 2022[15]
Stroke	PM_{10} $PM_{2.5}$ NO_2 O_3	103 studies, global	1.1% per 10 µg/m^3 0.3% per 10 µg/m^3 1.4% per 10 ppb 0.1% per 10 ppb	Shah *et al.*, 2015[16]
Arrhythmia	PM_{10} $PM_{2.5}$ NO_2 O_3	13 studies, Asia, Europe, USA	1.1% per 10 µg/m^3 1.8% per 10 µg/m^3 3.2% per 10 µg/m^3 0.5% per 10 ug/m^3	Chen *et al.*, 2021[17]
Hypertension	PM_{10}	6 studies, global	2.4% per 10 µg/m^3	Cai *et al.*, 2016[18]

Effetto di esposizioni *long-term*

ESC European Heart Journal (2026) 00, 1–25
https://doi.org/10.1093/eurheartj/ehag270
SPECIAL ARTICLE
Epidemiology, prevention, and health care policies

Environmental risk factors and cardiovascular health

A clinical consensus statement of the European Society of Cardiology

Table 2. Selected meta-analyses of long-term exposure (>1 month) to air pollutants and cardiovascular mortality and morbidity[17,19–23]

Cardiovascular condition	Pollutant	Studies/subjects included	% increase in risk	Reference
Cardiovascular/circulatory mortality	$PM_{2.5}$ PM_{10}	42 studies, global 26 studies, global	13% per 10 µg/m^3 8% per 10 µg/m^3	Orellano *et al.*, 2024[24]
Coronary artery disease	NO_2	137 148 European subjects	4% per 10 µg/m^3	Wolf *et al.*, 2021[19]
Ischaemic heart disease	$PM_{2.5}$ PM_{10}	34 studies, global 16 studies, global	14% per 10 µg/m^3 6% per 10 µg/m^3	Orellano *et al.*, 2024[24]
Myocardial infarction	$PM_{2.5}$	47 studies, global	13% per 10 µg/m^3	Forastiere *et al.*, 2024[25]
Heart failure	$PM_{2.5}$ NO_2	22 000 subjects, Denmark	1.2% per 5 µg/m^3 1.1% per 9 µg/m^3	Lim *et al.*, 2021
Stroke	$PM_{2.5}$ PM_{10} NO_2	28 studies, global 15 studies, global 137 148 European	15% per 10 µg/m^3 5% per 10 µg/m^3 8% per 10 µg/m^3	Orellano *et al.*, 2024[24] Wolf *et al.*, 2021[19]
Arrhythmia	PM_{10} $PM_{2.5}$ NO_2 O_3	6 studies, Asia, Europe, USA	3.4% per 10 µg/m^3 11.6% per 10 µg/m^3 1.7% per 10 µg/m^3 0.7% per 10 µg/m^3	Chen *et al.*, 2021[17]
Hypertension	PM_{10} $PM_{2.5}$ NO_2	53 studies, global 47 studies, global	4% per 10 µg/m^3 17% per 10 µg/m^3 No association	Qin *et al.*, 2021[21] Forastiere *et al.*, 2024[25]

Funzioni *concentrazione-risposta* per le stime di impatto

Meta-analysis

ISEE Environmental Epidemiology

OPEN

Choices of morbidity outcomes and concentration–response functions for health risk assessment of long-term exposure to air pollution

Francesco Forastiere[a,b,*], Joseph V. Spadaro[c,d], Carla Ancona[e], Zorana Jovanovic Andersen[f], Ilaria Cozzi[e], Sophie Gumy[c], Dejan Loncar[c], Pierpaolo Mudu[g], Sylvia Medina[h], Roman Perez Velasco[g], Heather Walton[b,i], Jiawei Zhang[f], Michal Krzyzanowski[b]

EMAPEC project^ on Estimating the Morbidity from Air Pollution and its Economic Costs

^: https://www.who.int/activities/estimating-the-morbidity-from-air-pollution-and-its-economic-costs

Table 1.

Causality determinations of long-term exposure according to the US EPA Integrated Science Assessments

Category	$PM_{2.5}$ [22,23]	NO_2 [24]	Ozone [25]
Reproductive and developmental effects	Suggestive	Suggestive	Suggestive
Respiratory effects	Likely	Likely	Likely
Cardiovascular diseases	Causal	Suggestive	Suggestive
Metabolic effects	Suggestive	Suggestive	Suggestive
Neurological effects	Likely		Suggestive
Cancer (lung cancer)	Likely[a]	Suggestive	Inadequate
Mortality	Causal	Suggestive	Suggestive

[a]IARC 2013: $PM_{2.5}$ and PM_{10} exposure is carcinogenic to humans (group 1).

Funzioni *concentrazione-risposta* per le stime di impatto

Table 2.

Relative risk estimates for incidence of diseases from selected systematic reviews recommended for health risk assessment of $PM_{2.5}$ and NO_2

Outcome (incidence)	ICD-10 codes	Age (yrs)	List	RR (95% CI) per 10 µg/m³	Mean exposure range (µg/m³)	SR reference
Long-term exposure to $PM_{2.5}$						
Asthma in children	J45	0–18	A	1.34 (1.10, 1.63)	5–38	Khreis et al[37]
COPD	J41–J44	30+	A	1.18 (1.13, 1.23)	5–26	Park et al[38]
IHD events[a]	I21–I22	30+	A	1.13 (1.05, 1.22)[b]	5–65	Zhu et al[39]
Stroke	I60–I64	30+	A	1.16 (1.12, 1.20)[b]	5–36	Yuan et al[40]
Hypertension	I10–I11	30+	A	1.17 (1.05, 1.30)[b]	5–77	Qin et al[41]
Diabetes (type 2)	E11–E14	30+	B+	1.10 (1.03, 1.18)[b]	5–79	Yang et al[42]
Dementia	F00–F03, G30	60+	B+	1.46 (1.20, 1.78)[b]	5–25[c]	Cheng et al[43]
ASD	F84.0, F84.1, F84.5, F84.8, F84.9	2–12	B+	1.66 (1.23, 2.25)[b]	5–30[c]	Lin et al[44]
Lung cancer	C34	30+	A	1.16 (1.10, 1.23)	5–44	Yu et al[36]
Long-term exposure to NO_2						
Asthma in children	J45	0–18	A	1.10 (1.05, 1.18)	10–39	Khreis et al[37]
Asthma in adults	J45	19+	A	1.10 (1.01, 1.21)	10–40	HEI[34]
ALRI in children	J12–J18, J20–J22	0–12	A	1.09 (1.03, 1.16)	10–56	HEI[34]

[a]Acute myocardial infarction (AMI).

[b]Relative risk estimates from revised meta-analysis.

[c]Restrict applicability of the CRFs of these conditions to exposure differences not larger than 10 µg/m³ within the indicated concentration ranges (see discussion in eAppendix 2; http://links.lww.com/EE/A280).

Stimare il rischio non basta!

Montone et.al, *Eur Heart Journal* 2026

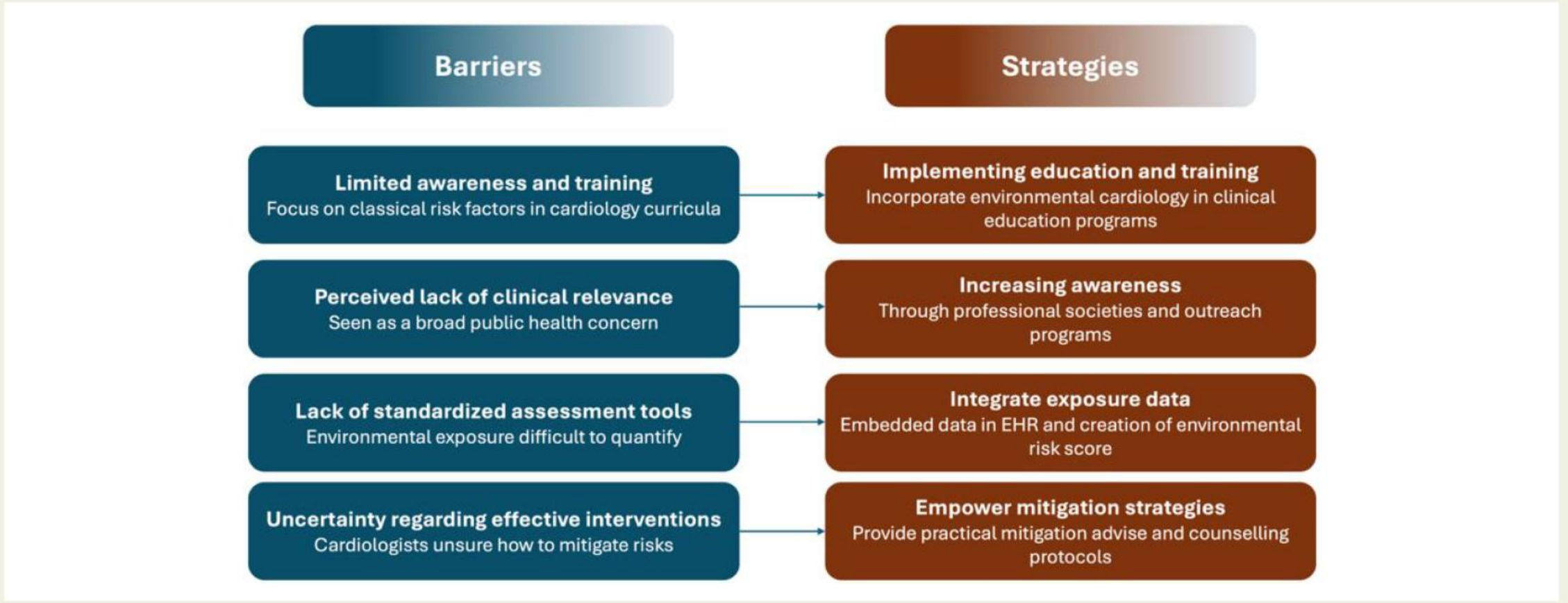


Figure 1 Barriers preventing consideration of environmental risk factors in cardiology. Key obstacles limiting the integration of environmental determinants into cardiovascular care, including limited clinician awareness, perceived low clinical relevance, lack of standardized assessment tools and risk models, restricted access to exposure data, and uncertainty about effective mitigation strategies

Oltre «l'associazione»: il contributo degli studi osservazionali

Table 6 Public health and policy recommendations to mitigate cardiovascular risks of $PM_{2.5}$ exposure

Priority area	Recommended actions	Rationale
Air quality regulation	Enforce stricter $PM_{2.5}$ limits aligned with the latest WHO guidelines (annual mean $\leq 5\ \mu g/m^3$)	Reduces baseline cardiovascular risk at a population level
Air quality monitoring infrastructure	Expand fixed-site and satellite-based air monitoring networks, particularly in LMICs and urban industrial regions	Enables timely detection of pollution spikes and chronic exposure hotspots
Targeted protections for high-risk groups	Issue public health advisories during high-pollution episodes for older adults, CVD patients, and other vulnerable groups	Prevents acute cardiovascular events in susceptible populations
Integration into cardiovascular risk assessment	Incorporate air pollution exposure history into clinical cardiovascular risk stratification tools	Allows individualized preventive advice and monitoring
Promotion of clean energy and sustainable transport	Invest in renewable energy infrastructure, emissions controls, and active/public transport systems	Reduces primary emissions sources contributing to $PM_{2.5}$ burden
Community-based health communication	Develop culturally appropriate education campaigns on air pollution health risks and protective behaviours	Increases public awareness and adoption of risk mitigation strategies
Mechanistic and epidemiologic research expansion	Fund longitudinal cohort studies, multi-pollutant modelling, and mechanistic investigations linking $PM_{2.5}$ to cardiovascular disease	Refines risk estimates, informs policy, and advances causal understanding

Tratto da: *Eur J Prev Cardiol.* 2026;33:1746-1769

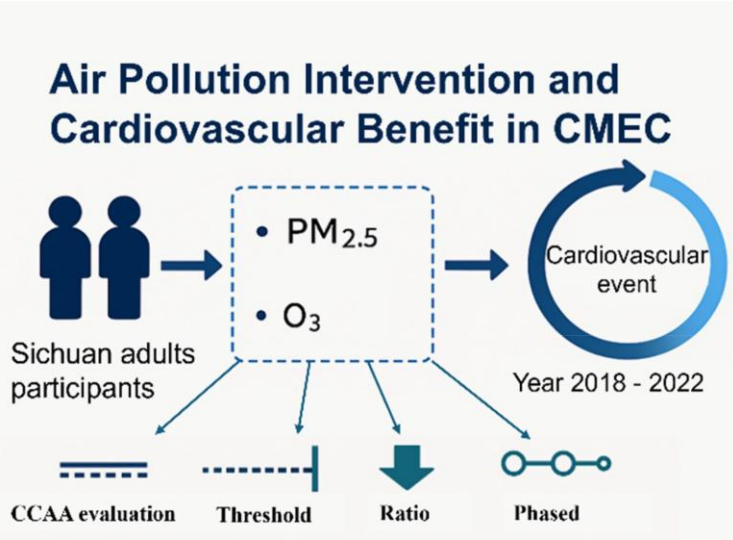
1. Stima effetto mitigazione da AQG

ESC European Journal of Preventive Cardiology (2026) 33, 1878–1890
https://doi.org/10.1093/eurjpc/zwag039

FULL RESEARCH PAPER
Public health

Cardiovascular disease averted by China's Clean Air Act and the potential benefit of further air pollution intervention: evidence based on the parametric G-computation

Approccio controfattuale
basato su dati reali



CVD cases averted per 100,000 people (95% CI) under CCAA	
$PM_{2.5}$	541 (184, 914)

CVD cases averted per 100,000 people (95% CI) under WHO AQG intervention	
$PM_{2.5}$	13,530 (7,400, 17,405)
O_3	6,498 (1,189, 10,840)
$PM_{2.5}$ + O_3 (joint)	15,449 (10,148, 17,998)

Among further stricter interventions, WHO AQG threshold intervention yielded the largest benefit.

CCAA: riduzione ≥18% dal valore 2015 di $PM_{2.5}$ entro il 2020 [media 2020: 33 μg/m³]

Intervento: soglia WHO di 5 μg/m³

Lay summary

This cohort study assessed the cardiovascular benefits of China's Clean Air Act (CCAA) and three further interventions strategies. Results showed that CCAA policy exhibited averted considerable cardiovascular disease cases, and WHO AQG in threshold intervention yielded the largest benefit among further interventions. Our findings suggested that air pollutant intervention policies have brought substantial benefits and there is significant room for cardiovascular health improvement if further interventions are adopted.

Coorte di popolazione di Varese

2. Strategie di mitigazione individuali: stili di vita.
Obiettivo: indagare se fumo, dieta e attività fisica [individualmente e combinati tra loro secondo approccio LS7 di AHA] possono mitigare l'eccesso di rischio CVD dovuto ad esposizione cronica a **$PM_{2.5}$** **NO_2** e **O_3**

3. Studio dei meccanismi di azione: funzionalità endoteliale
Obiettivo: quantificare il ruolo di pressione arteriosa e rigidità arteriosa come mediatori dell'effetto di esposizione cronica sul rischio CVD

- **Marcatore di rigidità arteriosa:** cfPWV [carotid-femoral Pulse-Wave Velocity]. Più è alto, e peggio è

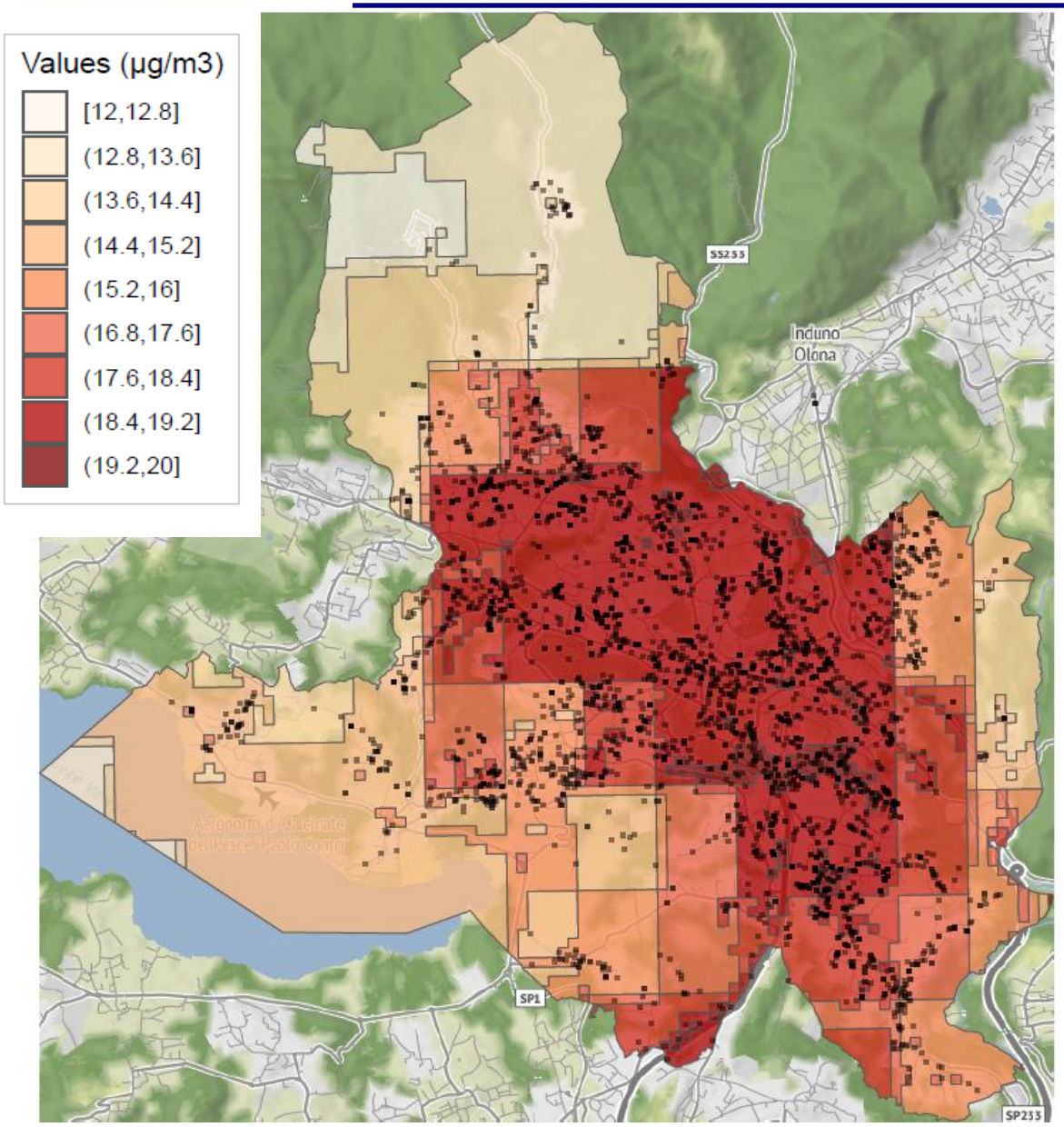
Coorte di popolazione di Varese

Studio RoCAV: campione casuale di residenti in Varese
Uomini: 50-75 anni, donne: 60-75 anni

- **Reclutamento:** giugno2013-maggio 2016
- **Partecipanti:** N=3777 (2404 men), partecipazione: 64%.
- **Protocollo:** armonizzato su standard epidemiologici internazionali per le malattie CVD (e.g., EHES, MONICA/MORGAM consortia)
- **Biobanca:** campioni di sangue a -80°C, basale e ri-esame nel 2021-22
- **Follow-up:** stato in vita/mortalità per causa & eventi cardiovascolari da RL con le banche dati sanitarie amministrative, fino al 31/12/2022

Per le analisi che seguono:
- uomini senza malattia CVD al basale **(n=2119)**
- Endpoint: prima occorrenza di evento coronarico acuto e stroke, fatale e non fatale

Coorte di popolazione di Varese



AP: da **EU-EXPANSE project** (risoluzione spaziale: 25x25mt) & link all'indirizzo di residenza al basale

Esposizione: media nei 12 mesi antecedenti alla visita basale

Performance dei modelli vs. concentrazioni misurate dalle stazioni EEA in città

- $PM_{2.5}$: ICC>85%, rRMSE 6-15%
- NO_2 : ICC 60-80%, rRMSE 9-24%
- O_3: ICC 43-95%, rRMSE 3-10%

2. Strategie di mitigazione individuali: stili di vita

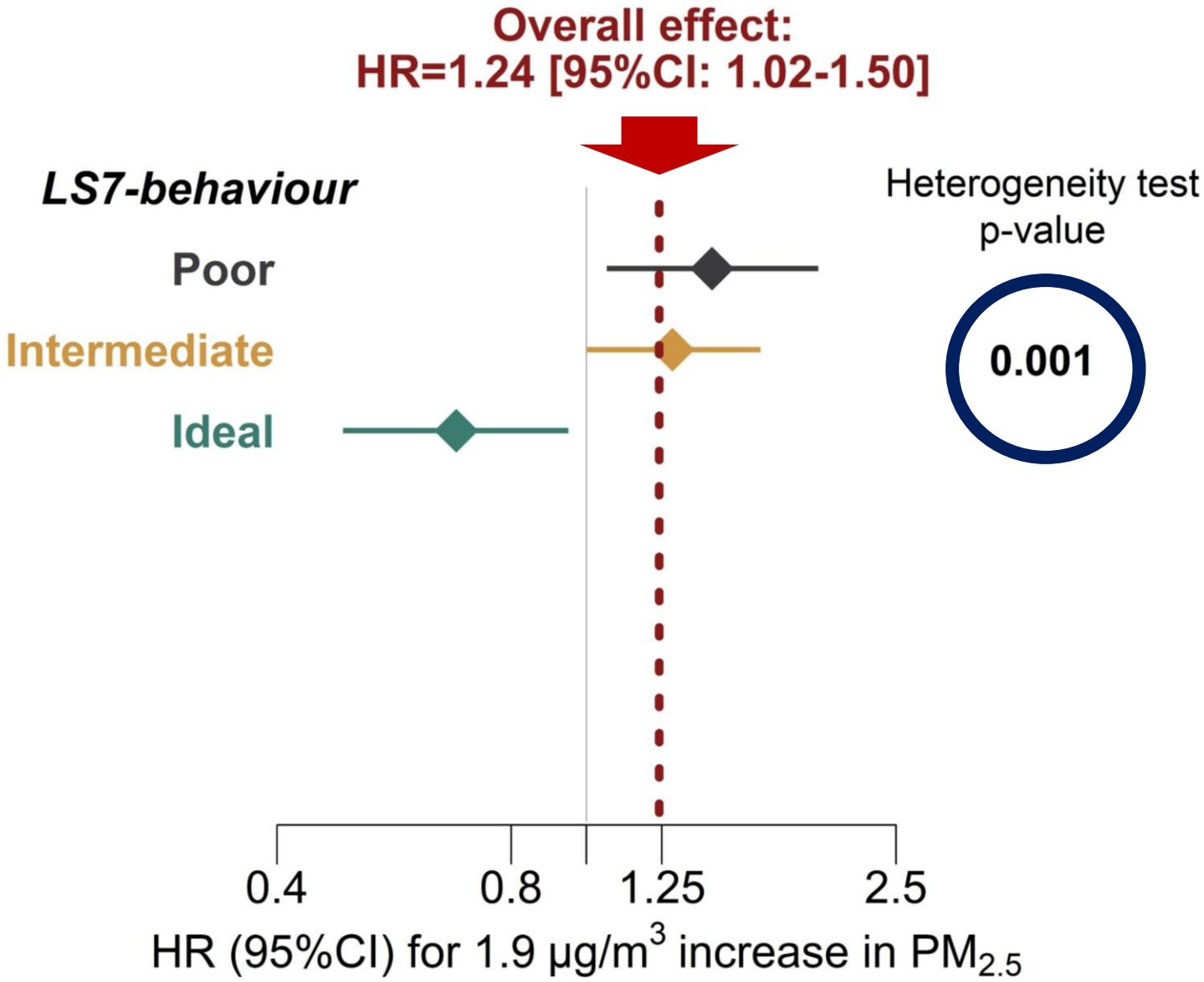
N=2119, 63.3±7.1 anni.; n=160 eventi in 7.6 anni di f-up mediano [tasso di evento: 10.4 per 1,000 p-y]

Esposizione a $PM_{2.5}$: Media±SD, 18.6±1.8 μg/m^3

Sample characteristics		Mean Difference (95%CI)	p-val
LS7 - Behavior, n (%)			
Poor (0-2 points)	**731 (34.5%)**	**0.271 (0.070; 0.471)**	
Intermediate (3-4 points)	1038 (49.0%)	**0.195 (0.013; 0.377)**	**0.03**
Ideal (5-6 points)	**350 (16.5%)**	**Ref**	
LS7 - Health factor, n (%)			
Poor (0-3 points)	494 (23.3%)	-0.115 (-0.307; 0.076)	
Intermediate (4-5 points)	1058 (49.9%)	-0.067 (-0.227; 0.094)	0.49
Ideal (6-8 points)	567 (26.8%)	Ref	

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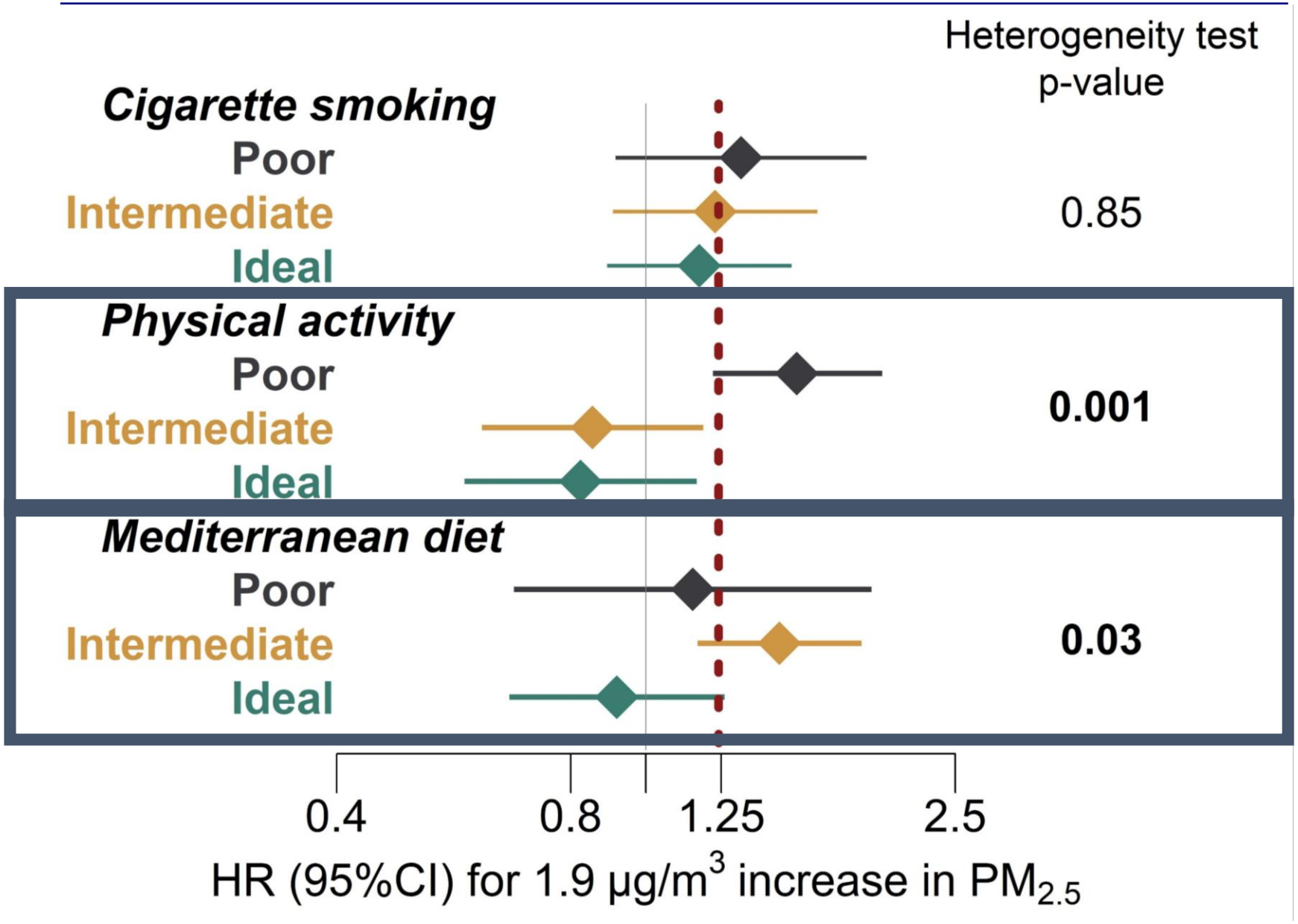
2. Strategie di mitigazione individuali: stili di vita



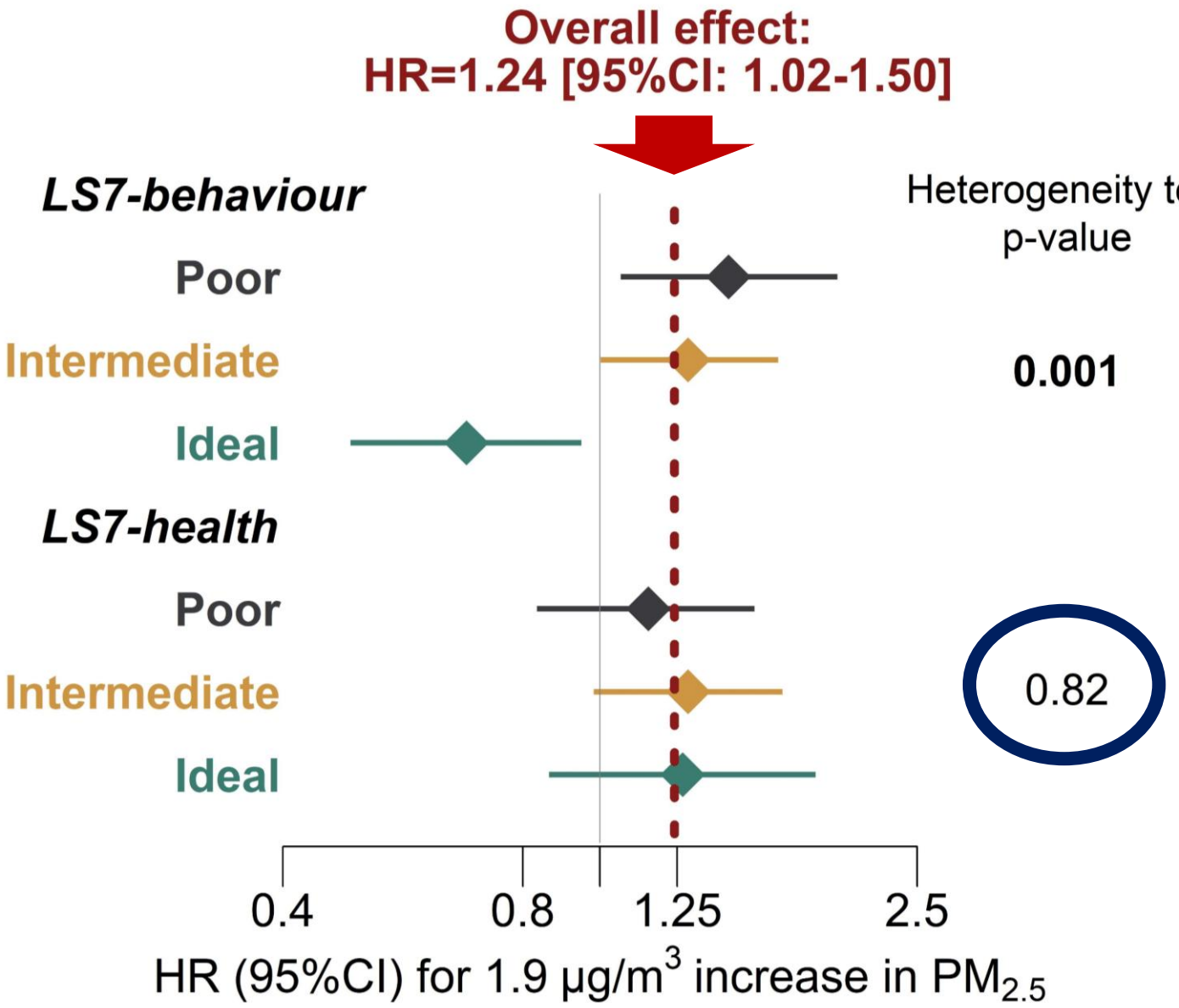
Numero di casi aggiuntivi dovuti all'interazione:
7.7 [2.8-12.5] per 1,000 p-y

Veronesi G et al. *Environment International* 2026

2. Strategie di mitigazione individuali: stili di vita



2. Strategie di mitigazione individuali: stili di vita



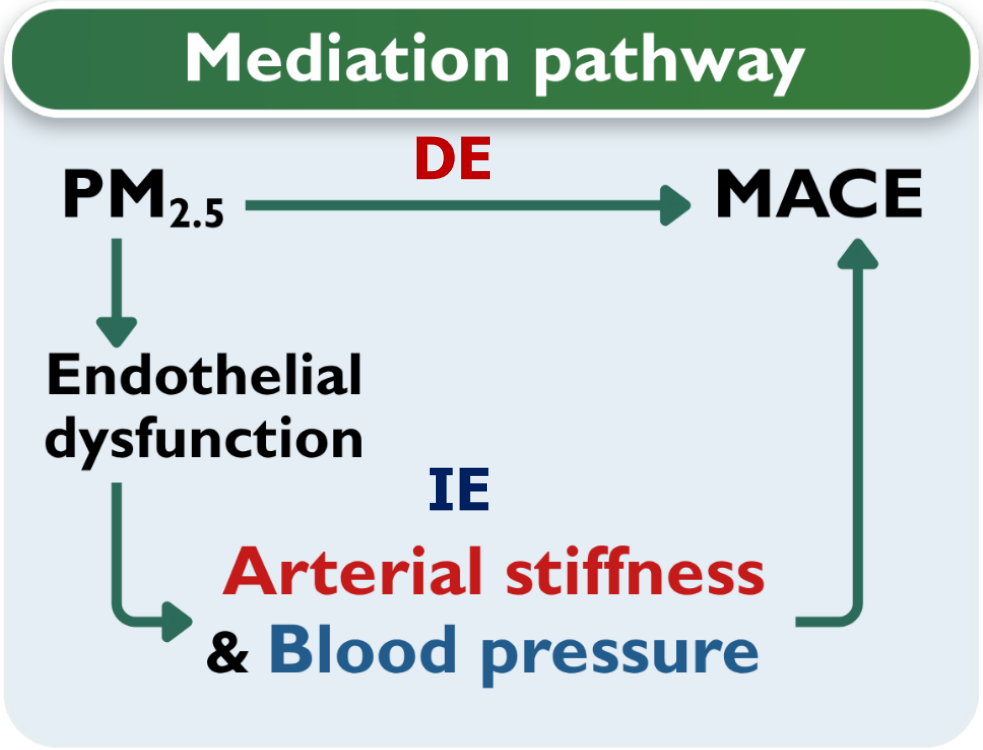
Nessuna evidenza di interazione con fattori "clinici" [BP, colesterolo, obesità, glicemia] – ruolo dei trattamenti?

NO_2: stesso pattern di interazione, più debole

Sensitivity analyses: conferma dei risultati principali

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3. Meccanismi di azione: analisi di mediazione

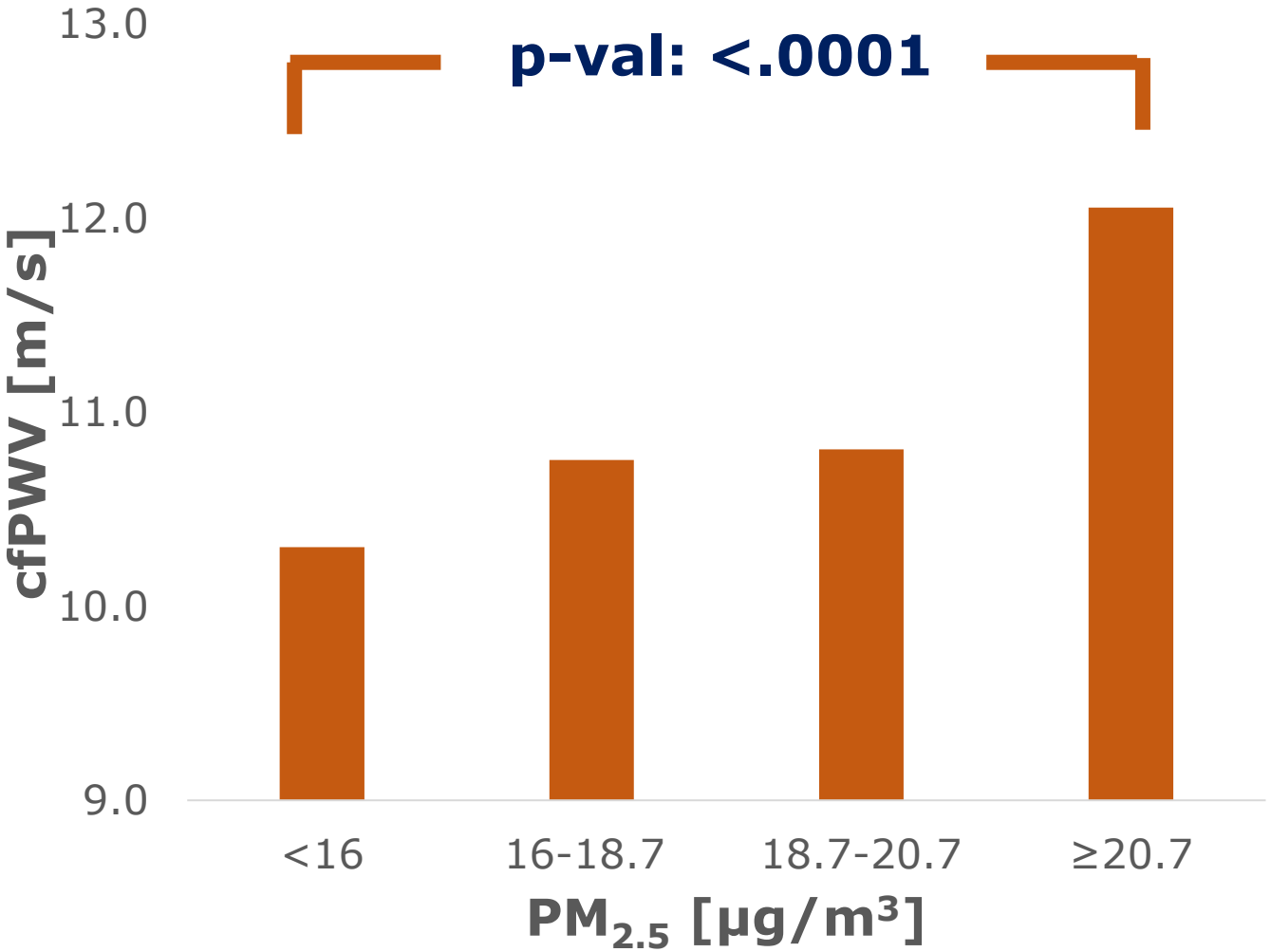


- **Natural Direct Effect (DE):** effetto di $PM_{2.5}$ su rischio CVD che non dipende dal mediatore [BP/arterial stiffness]
- **Natural Indirect Effect (IE):** effetto di $PM_{2.5}$ su rischio CVD mediato da BP/arterial stiffness
- **Total effect: TE=DE+IE:** numero di eventi CVD per 100,000 py dovuti a incremento in esposizione di 1 $\mu g/m^3$ $PM_{2.5}$
- **Mediated proportion%: 100*IE/TE**

Confondenti:

- Individuali: età, educazione, fumo, dieta, attività fisica, trattamento anti-ipertensivo, IMC, glicemia, colesterolo LDL;
- Area-based: indice di deprivazione, area censuale

3. Meccanismi di azione: analisi di mediazione



Rischio di evento CVD per incremento di 1-SD in cfPWV:

HR [95%CI] = 1.45 [1.21 to 1.74]

Veronesi G et al.
Confidential, unpublished results
Please do not disseminate

3. Meccanismi di azione: analisi di mediazione

Incremento di 1 µg/m³ in $PM_{2.5}$ sul numero di eventi CVD per 100,000 py:

Mediator	Direct	Indirect (IE)	Total (TE)	IE/TE %
Systolic BP	119 (-12 to 250)	23 (-4 to 50)	**142 (6 to 278)**	16%
Brachial PP	114 (-16 to 244)	26 (-2 to 53)	**140 (4 to 275)**	18%
cfPWV	103 (-21 to 227)	**48 (17 to 79)**	**151 (21 to 282)**	32%
cfPWV > 12 m/s	100 (-30 to 230)	**36 (7 to 66)**	**136 (1 to 271)**	27%

Mediazione tramite cfPWV: maggiore in soggetti con elevato glucosio e con elevato colesterolo LDL

Brachial PP: difference between systolic and diastolic BP

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Take-home (1)

Ruolo di inquinamento atmosferico su malattie CVD:

- **Effetti sia acuti che cronici**
- **Evidenze solide [«causali»]** per malattie coronariche, stroke, AF e HF; **da consolidare** per pathway trombotico venoso (es. trombo-embolismo venoso, VTE)
- Funzioni concentrazione-risposta **per valutazione complessiva del rischio CVD** in contesti di *risk assessment* – anche se con approccio «one-size»
- Primi lavori che **stimano impatto di politiche di riduzione/contenimento** degli inquinanti – ancora senza **valutazioni di fattibilità e dei co-benefici**

Take-home (2)

Suscettibilità individuale & studio meccanismi:

- Identificazione di sottopopolazioni che hanno più da perdere da ritardi nell'implementazione delle **EU Air Quality Guidelines**
- Promozione di **politiche di promozione di stili di vita sani nella pianificazione urbana hanno «doppio impatto»** sulla riduzione del numero assoluto di eventi CVD:
  - **Mitigazione del rischio individuale**
  - **Riduzione della prevalenza di suscettibili nella popolazione**
- Forniscono indicazioni utili per una **maggiore integrazione tra strategie di prevenzione cardiovascolare e rischio ambientale – es. cosa monitorare e in quali soggetti**

Take-home (3)

Integrazione tra studi osservazionali di popolazione e modellistica ambientale: strumento privilegiato per azioni di pianificazione e monitoraggio per molteplici stakeholders:

- **Policy-makers**
- **Clinici**
- **Comunità scientifica**
- **Singoli individui/cittadini**
- **…**

Grazie per l'attenzione!

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