II Webinar

Medical University of Bialystok
with/for EUNICE European University

LUKASZ KUŹMA, MD, MPh, PhD, FPCS, FESC

Medical University of Białystok, Białystok, Poland
PolishSmog Environmental Pollution Research Centre, Białystok, Poland (www.polishsmog.com)

e

17/12/2024

UNIVERSITY OF BIALYSTOK MEDICAL 1950

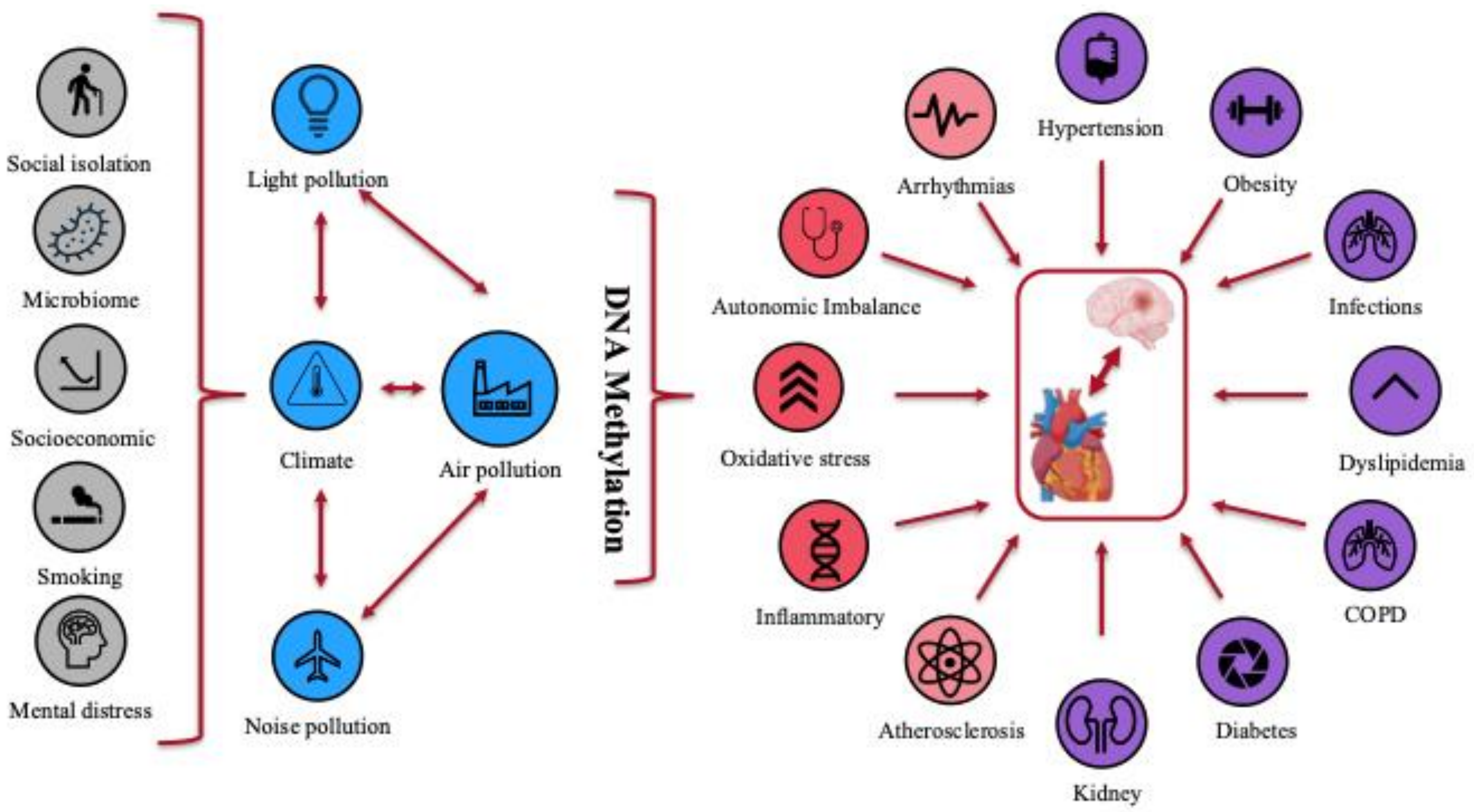
POLISH SMOG

Research centers

NO	ORGANISATION NAME
1	MEDICAL UNIVERSITY OF BIALYSTOK, POLAND (COORDINATOR)
2	UNIVERSITY OF LIVERPOOL, LIVERPOOL, UNITED KINGDOM
3	UNIVERSITY OF MURCIA, MURCIA, SPAIN
4	HARVARD UNIVERSITY, CAMBRIDGE, USA
5	UNIVERSITY OF CAMBRIDGE, CAMBRIDGE, UK
6	UTRECHT UNIVERSITY, UTRECHT, NL
7	RADBOUD UNIVERSITY, NIJMEGEN, NETHERLANDS
8	LIVERPOOL JOHN MOORES UNIVERSITY, LIVERPOOL, UNITED KINGDOM (LJMU)
9	INSTITUTE OF ENVIRONMENTAL PROTECTION – NATIONAL RESEARCH INSTITUTE, WARSAW, POLAND (IEP)

Exposome

SES-Environment   Direct & indirect impact



Key Components:

General external factors:

- ❑ Urban or rural settings.
- ❑ Socioeconomic condition
- ❑ Climate setting

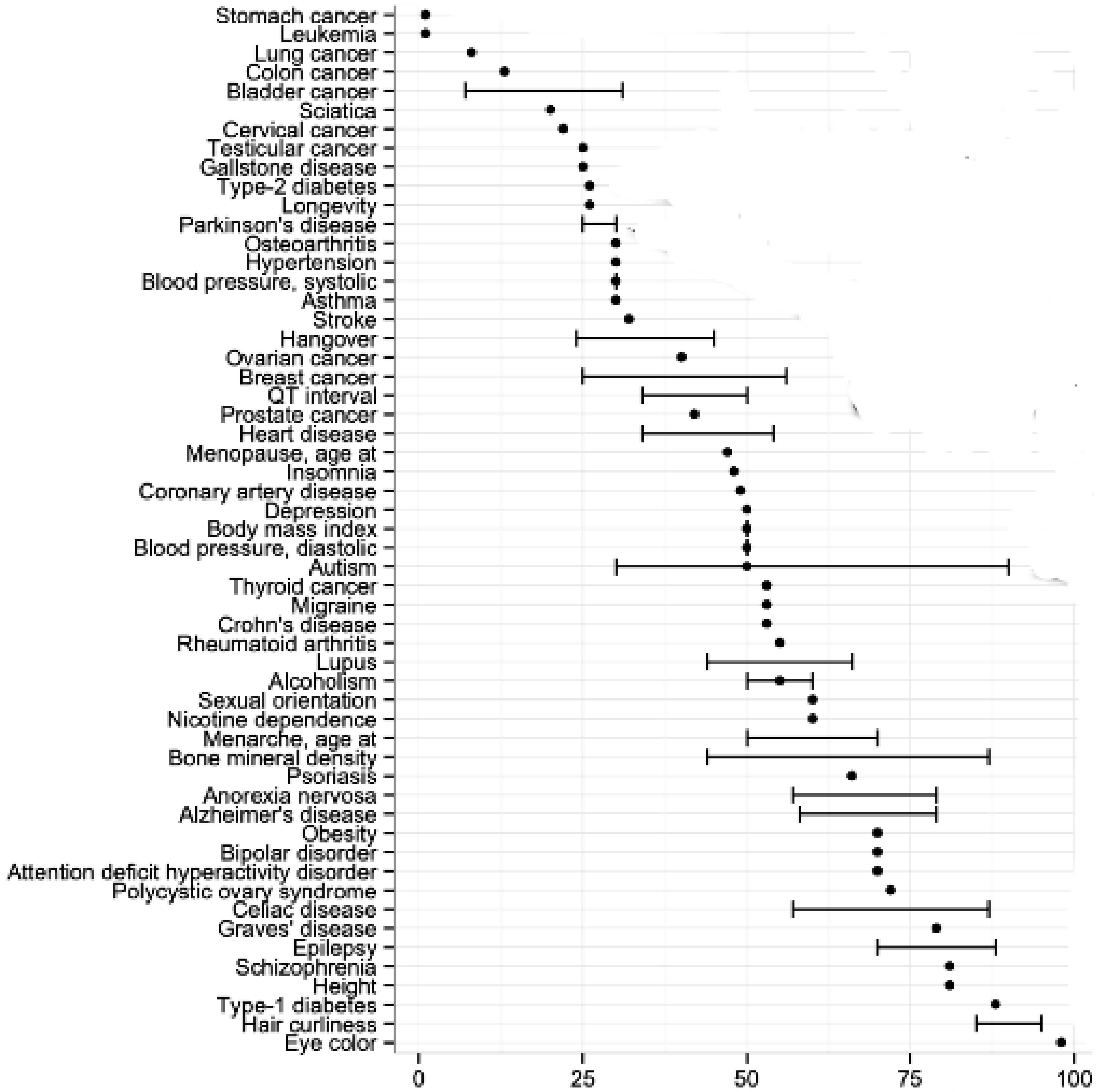
Specific external factors:

- ❑ Exposure to heatwaves, chemicals, microplastic, soil
- ❑ Air, noise & light pollution.
- ❑ Lifestyle, diet, activity, habits

Internal Factors:

- ❑ Inflammatory response, oxidative stress
- ❑ Aging
- ❑ Microbiome activity

Exposome (II)



The study of the exposome is essential because genetic burden accounts for only a small fraction of CVD disease.

Unexplained fraction

Hypertension: 65–70%

Stroke: 60–65%.

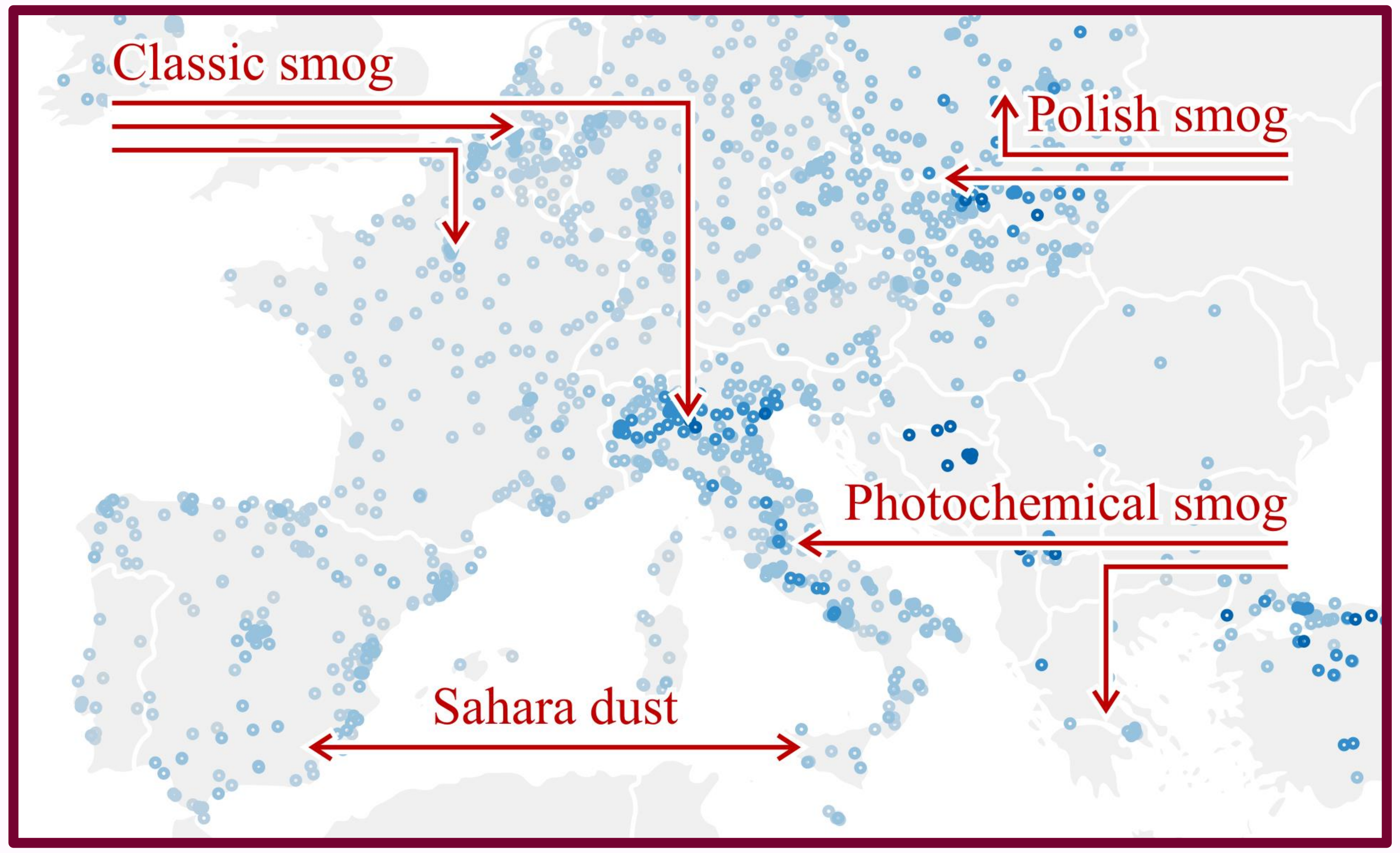
Coronary Artery Disease: 50–60%

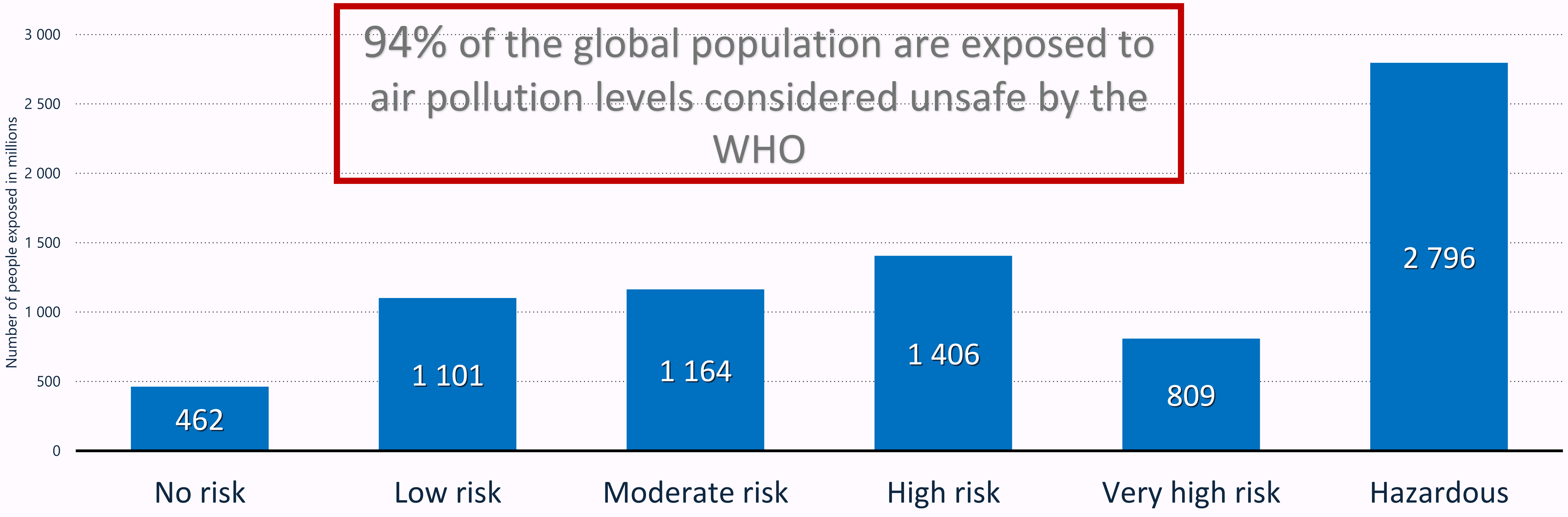
*Heritability *(H^2)* as the range of phenotypic variability attributed to genetic variability in a population

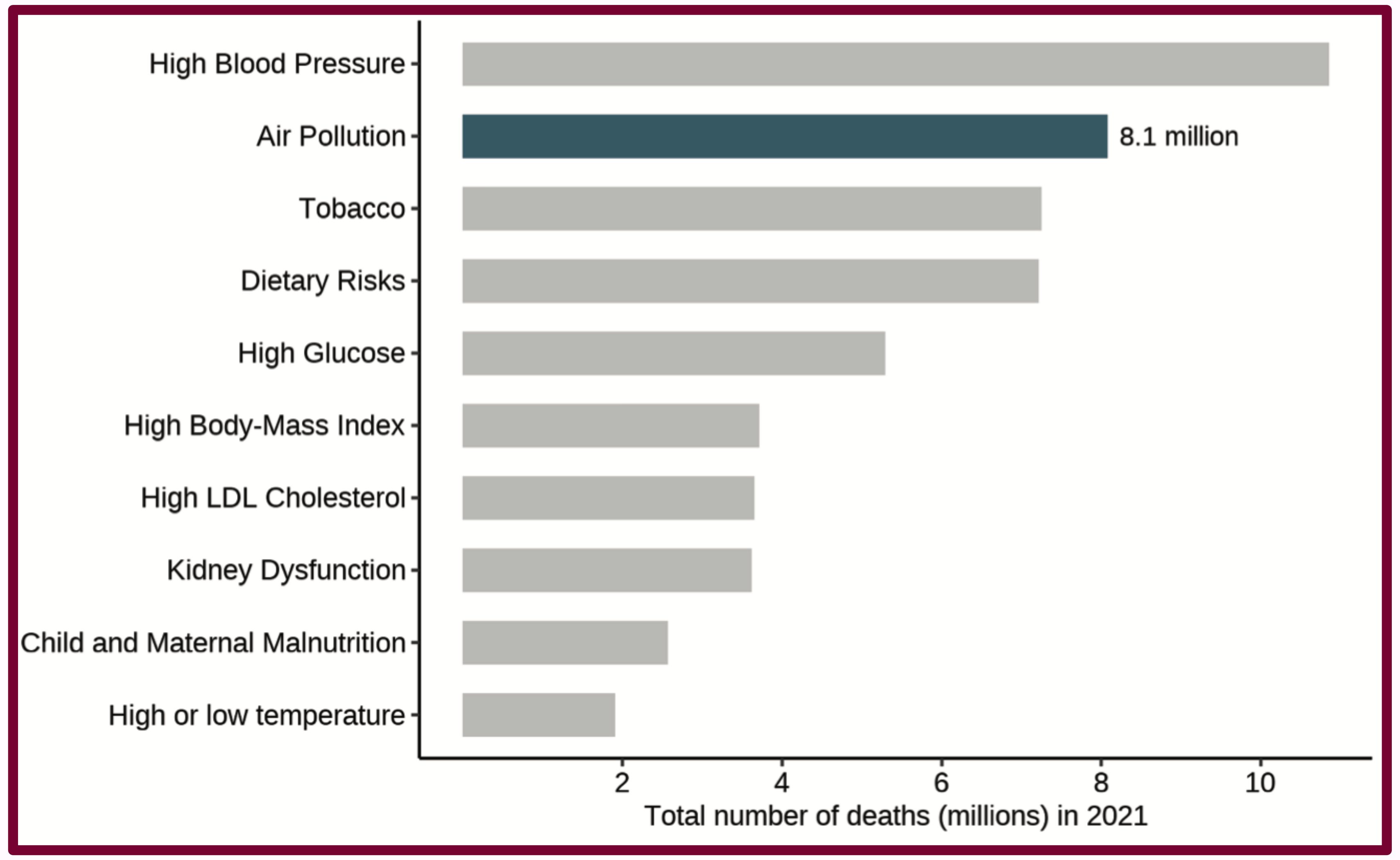
$H^2 = \sigma^2_{Genome} / \sigma^2_{Population}$

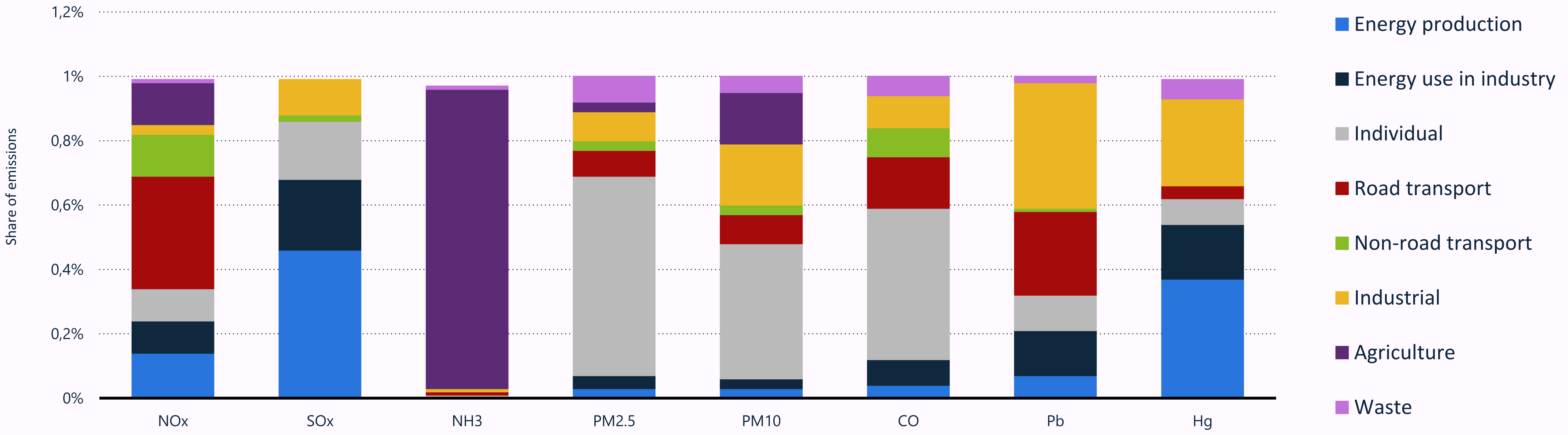
Source: SNPedia.com

Health burden









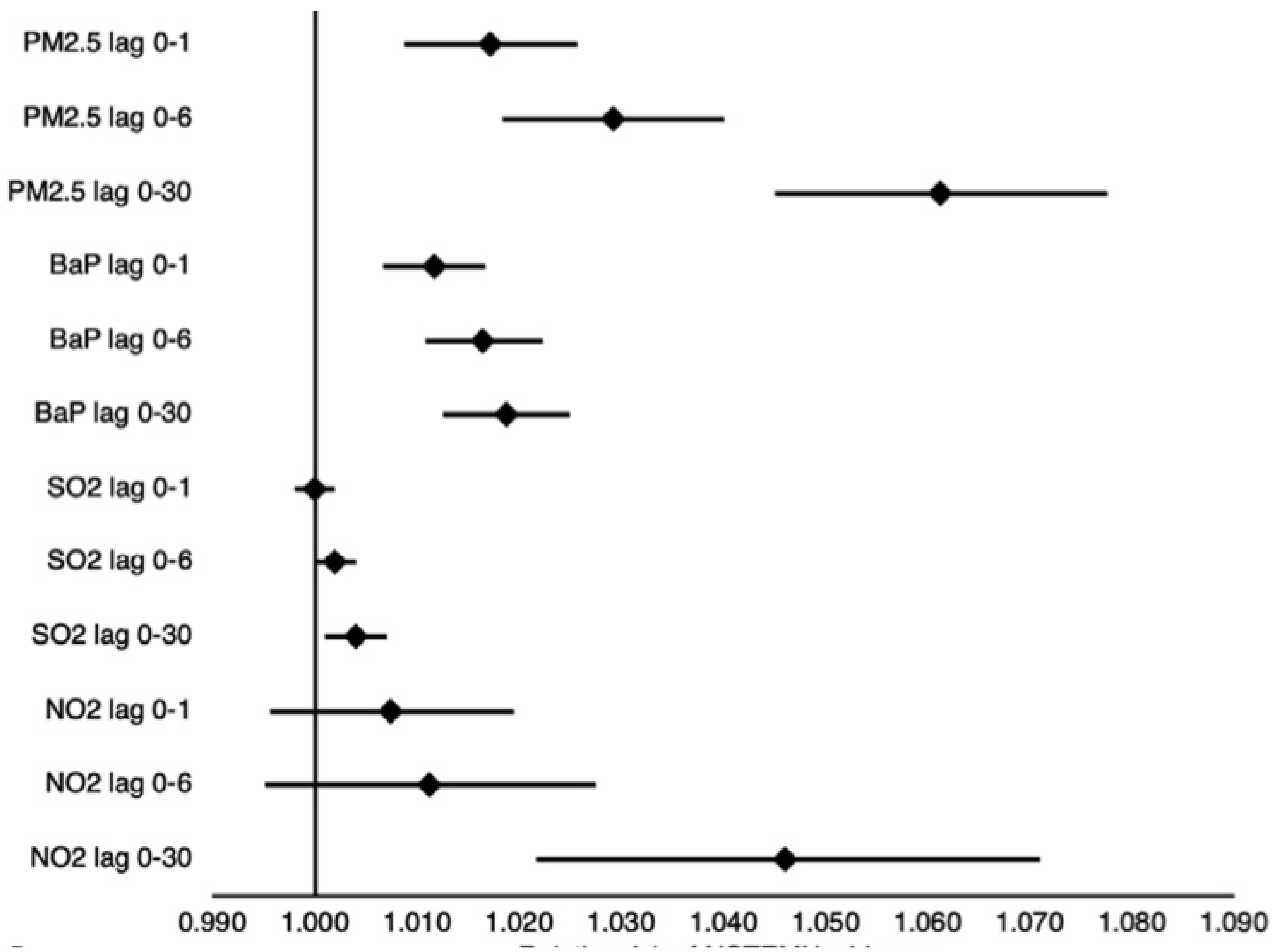
Distribution of selected air pollutant emissions in the EU-27, 2022

Air pollution

THE LANCET *Regional Health*

Effect of air pollution exposure on risk of acute coronary syndromes in Poland: a nationwide population-based study (EP-PARTICLES study)

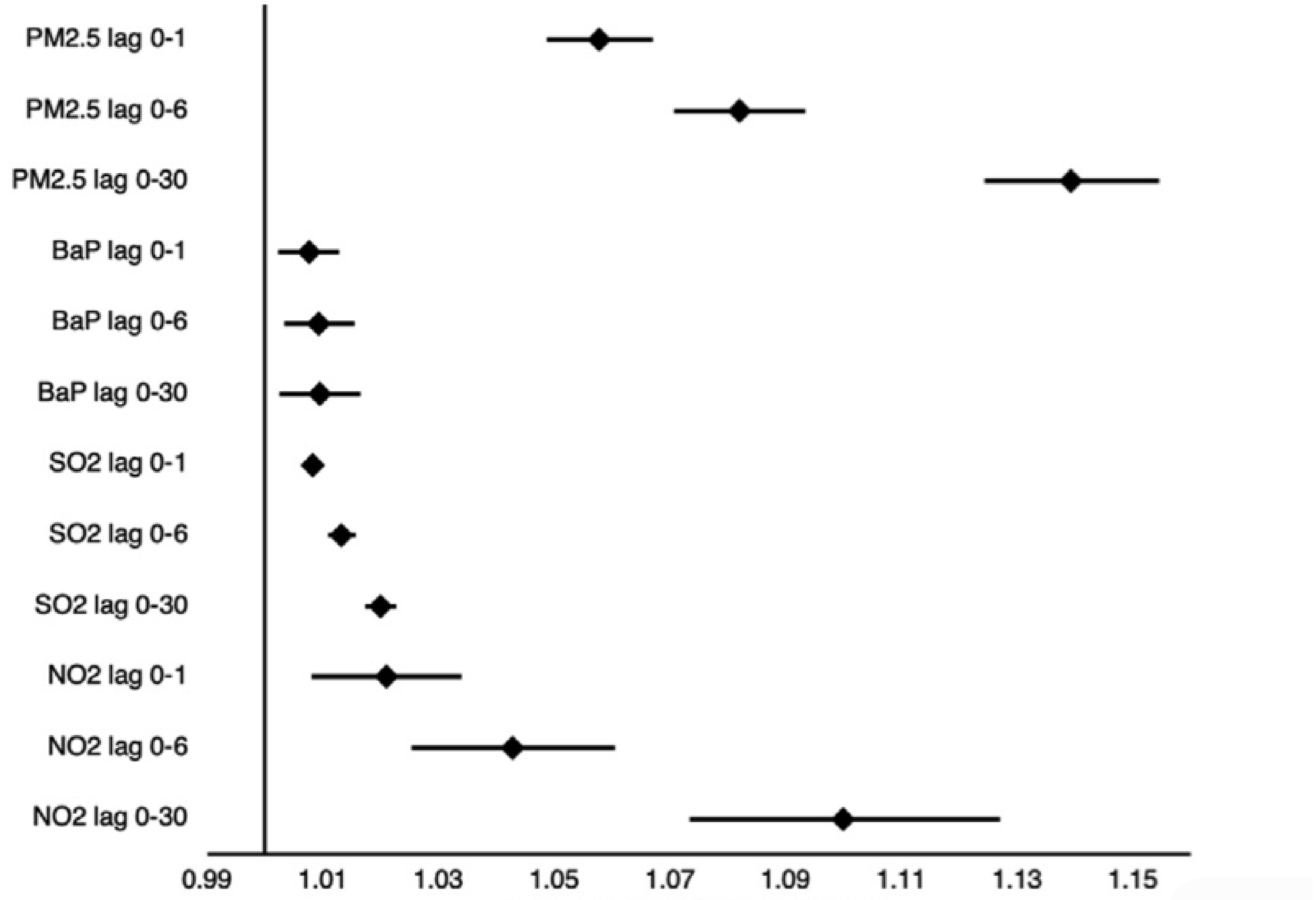
Łukasz Kuźma • Emil J. Dąbrowski • Anna Kurasz • Michał Święczkowski • Piotr Jemielita • Mariusz Kowalewski • Wojciech Wańha • Paweł Kralisz • Anna Tomaszuk-Kazberuk • Hanna Bachórzewska-Gajewska • Sławomir Dobrzycki • Gregory Y.H. Lip • Show less



POLISH SMOG
EP-PARTICLES STUDY

EP-PARTICLES Cohort

- ❑ 63,154 hospitalizations due to STEM
- ❑ 76,543 hospitalizations due to NSTEMI



No. admissions above treshold	Threshold	AC (N)	95% CI AC (N)	AF (%)	95% CI AF (%)
NSTEMI					
49,612	Daily WHO norm	641	325–953	0.85	0.43–1.26
75,531	Yearly WHO norm	2033	1045–3099	2.69	1.38–3.98
76,542	Population attributable fraction	2693	1387–3977	3.52	1.81–5.2
STEMI					
41,244	Daily WHO norm	1159	1349–1831	3.9	3.3–4.4
62,384	Yearly WHO norm	5634	4566–6150	8.6	7.3–9.9
63,154	Population attributable fraction	7029	5997–8042	11.1	9.5–12.7

AC, attributable cases; AF, attributable fraction; CI, confidence interval; NSTEMI, Non-ST-elevation myocardial infarction; STEMI, ST-elevation myocardial infarction; WHO, World Health Organization.

Table 3: **Estimated number of avoided disease cases of hospital admissions associated with the reduction of $PM_{2.5}$ air pollution levels.**

Short—and mid-term effects of air pollution
Upper on NSTEMI incidence, bottom on STEMI incidence

Air pollution (II)

POLISH SMOG
EP-PARTICLES STUDY

	Air pollutant	Rural			Urban			Ratio		
		RR	95% CI	P-value	RR	95% CI	P-value	RRR	95% CI	P-value
NSTEMI	SO_2	1.001	0.999–1.003	0.28	1.001	0.997–1.004	0.75	1.000	0.996–1.005	0.82
	$PM_{2.5}$	1.019	1.01–1.028	<0.001	1.012	0.997–1.027	0.11	1.007	0.99–1.024	0.41
	BaP	1.012	1.005–1.018	<0.001	1.008	1.002–1.015	0.02	1.003	0.994–1.013	0.50
	NO_2	1.010	0.997–1.022	0.12	1.009	0.988–1.032	0.40	1.000	0.975–1.026	0.99
STEMI	SO_2	1.009	1.007–1.011	<0.001	1.002	0.998–1.005	0.40	1.008	1.004–1.012	<0.001
	$PM_{2.5}$	1.060	1.05–1.07	<0.001	1.029	1.013–1.045	<0.001	1.03	1.012–1.049	0.001
	BaP	1.014	1.007–1.021	<0.001	0.995	0.986–1.004	0.25	1.019	1.008–1.031	0.001
	NO_2	1.022	1.008–1.035	0.001	1.012	0.988–1.036	0.33	1.010	0.983–1.037	0.49

BaP, Benzo(a)pyrene; CI, Confidence Interval; GDP, Gross domestic product per capita; NO_2, Nitrogen dioxide; NSTEMI, Non-ST Elevation Myocardial Infarction; $PM_{2.5}$, Particulate Matter with 2.5 Micrometers or Less; RR, Relative Ratio; SO_2, Sulphur Dioxide; STEMI, ST-Elevation Myocardial Infarction; RRR, Ratio of Relative Risk; SO_2, Sulphur Dioxide.

Table 1: **Impact of increased air pollution concentrations on the risk of hospitalization due to myocardial infraction in different types of areas.**

	Air pollutant	GDP < 2Q			GDP ≥ 2Q			Ratio		
		RR	95% CI	P-value	RR	95% CI	P-value	RRR	95% CI	P-value
NSTEMI	SO_2	1.002	0.999–1.004	0.21	1.000	0.998–1.003	0.7	1.001	0.998–1.005	0.49
	$PM_{2.5}$	1.022	1.011–1.034	<0.001	1.013	1.003–1.023	0.01	1.009	0.994–1.025	0.24
	BaP	1.020	1.011–1.029	<0.001	1.006	1–1.011	0.051	1.014	1.004–1.025	0.008
	NO_2	1.003	0.986–1.021	0.70	1.013	0.999–1.026	0.06	0.991	0.969–1.013	0.41
STEMI	SO_2	1.008	1.005–1.011	<0.001	1.007	1.005–1.01	<0.001	1.001	0.997–1.004	0.75
	$PM_{2.5}$	1.051	1.038–1.065	<0.001	1.051	1.04–1.061	<0.001	1.000	0.984–1.017	0.97
	BaP	1.012	1.001–1.023	0.03	1.004	0.998–1.009	0.21	1.008	0.996–1.021	0.19
	NO_2	1.016	0.997–1.037	0.10	1.019	1.005–1.034	0.007	0.997	0.973–1.021	0.81

BaP, Benzo(a)pyrene; CI, Confidence Interval; GDP, Gross domestic product per capita; NO_2, Nitrogen dioxide; NSTEMI, Non-ST Elevation Myocardial Infarction; $PM_{2.5}$, Particulate Matter with 2.5 Micrometers or Less; RR, Relative Ratio; SO_2, Sulphur Dioxide; STEMI, ST-Elevation Myocardial Infarction; RRR, Ratio of Relative Risk; SO_2, Sulphur Dioxide.

Table 2: **Impact of increased air pollution concentrations on the risk of hospitalization due to myocardial infraction in areas with different gross domestic product.**

Most Vulnerable Groups:

- **Women** demonstrated a stronger association between short- and mid-term exposure to $PM_{2.5}$ and BaP with an increased risk of ACS
- **Younger individuals** exhibited a more pronounced effect of $PM_{2.5}$ and BaP, on NSTEMI risk
- **Older individuals** were more affected by pollution-induced STEMI.
- Residents with **lower SES** showed a significantly elevated risk of NSTEMI, particularly from BaP
- Individuals living in **rural areas** were more vulnerable to air pollution, with higher risks of STEMI

Air pollution (III)

POLISH SMOG
EP-PARTICLES STUDY

ESC European Society of Cardiology
European Journal of Preventive Cardiology (2024) **00**, 1–12
https://doi.org/10.1093/eurjpc/zwae301
FULL RESEARCH PAPER
Air pollution and environmental science

Association between exposure to air pollution and increased ischaemic stroke incidence: a retrospective population-based cohort study (EP-PARTICLES study)

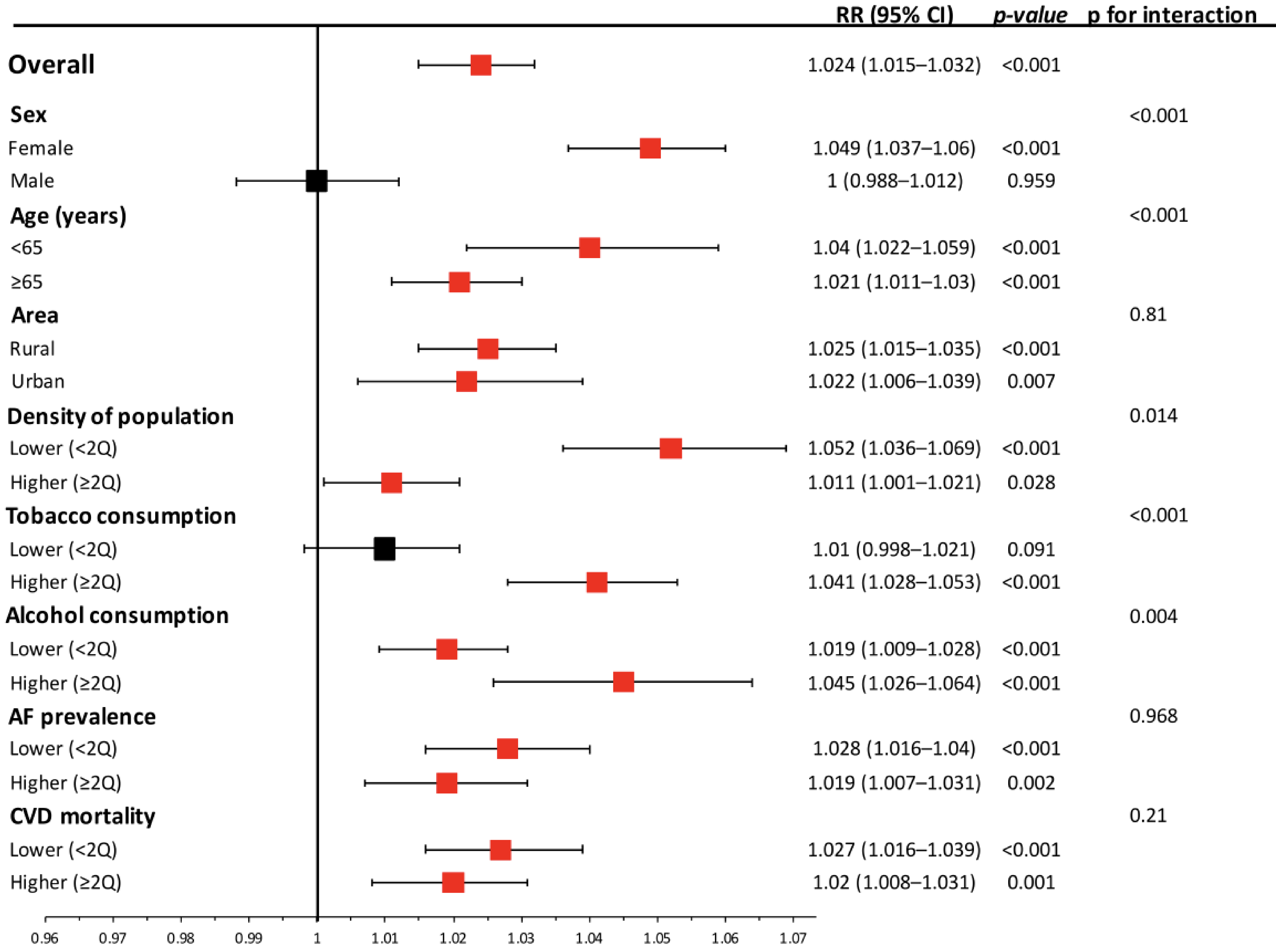
Michał Święczkowski[1]*, Gregory Y. H. Lip[2,3,4], Anna Kurasz[1], Emil J. Dąbrowski[1], Anna Tomaszuk-Kazberuk[4], Jacek W. Kamiński[5], Joanna Strużewska[5], Sławomir Dobrzycki[1], and Łukasz Kuźma[1]

Key findings:

- Exposure to air pollution, especially **$PM_{2.5}$** and **B(a)P**, is associated with an increased risk of IS
- Even **low levels of smog** can have harmful impacts, indicating that there are no ‘safe’ thresholds for air pollution exposure.
- Harmful lifestyle habits, such as **high tobacco and alcohol consumption**, may **exacerbate** the negative effects of air pollution

Most Vulnerable Groups:

- Women
- Non-elderly people
- Residents of areas with high alcohol and tobacco consumption



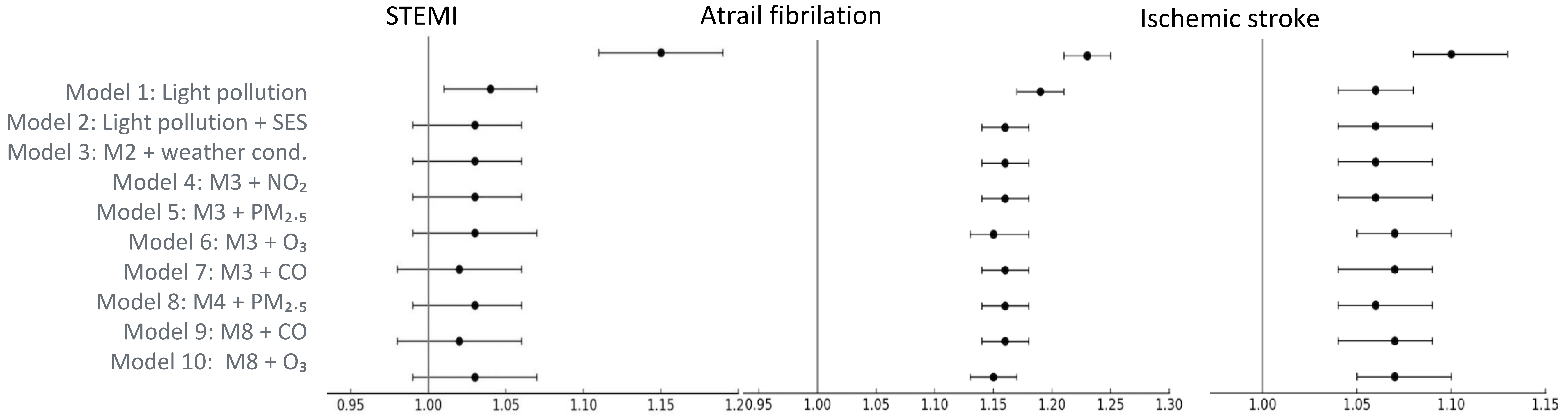
Light pollution

POLISH SMOG
EP-PARTICLES STUDY

The impact of light pollution on the number of hospitalizations due to CVD

P. Jemielita, M. Święczkowski, A. Kurasz__G.Y.H. Lip, Ł. Kuźma

Light pollution data were obtained from the Suomi NPP satellite system operated by NASA.
Between 2011 and 2020, 131,085 IS cases (51.6% women, avg. age 74), 228,410 AF cases (52.7% women, avg. age 70), and 55,081 STEMI cases (64.6% men, avg. age 67) were recorded.



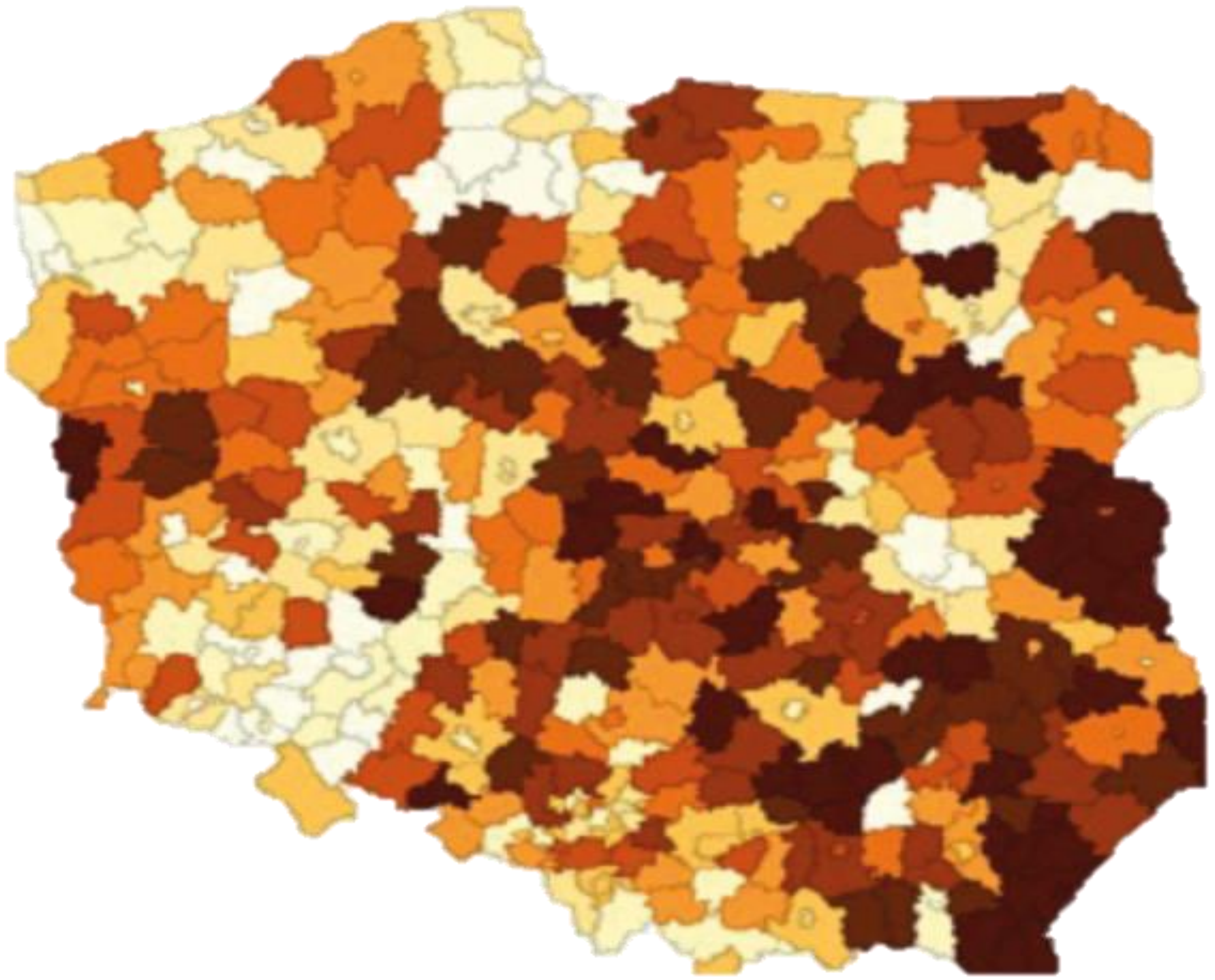
An increase in light pollution intensity by 1 interquartile range (2479.42 nW/cm²/sr) in models adjusted for SES & air pollution exposure was associated with a 15% increase in AF and a 7% increase for IS

SES

POLISH HEART JOURNAL

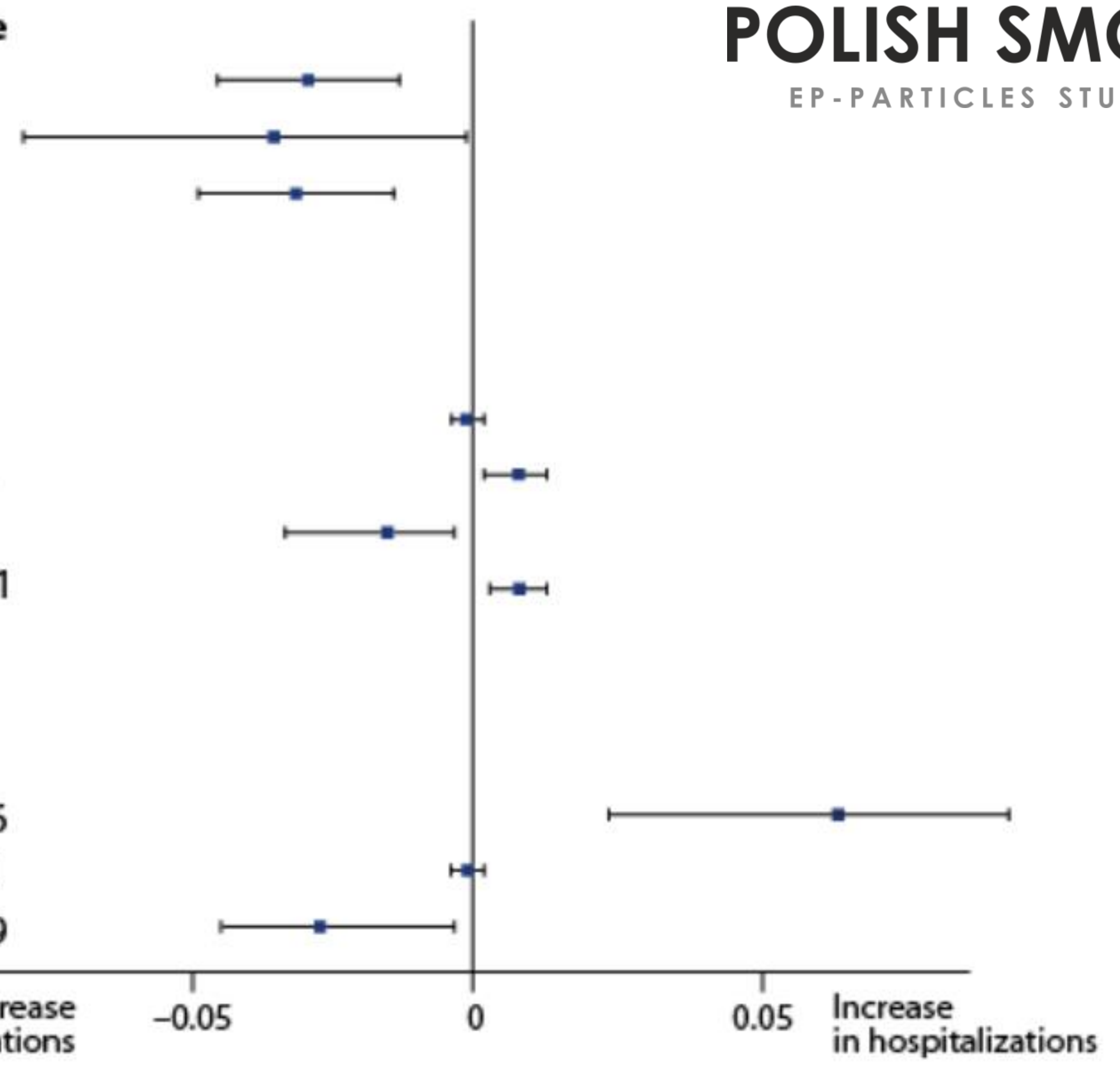
Environmental and socioeconomic determinants of heart failure

Sylwia Roszkowska[1,2], Barbara Kula[1], Natalia Pawelec[1], Michał Święczkowski[3], Anna Tomaszuk-Kazberuk[4], Hanna Bachórzewska-Gajewska[3], Sławomir Dobrzycki[3], Łukasz Kuźma[3]



Health care services

Variables	Semi-elasticity (95%CI)	*P*-value
Health expenditure (> (100 PLN per capita per year)	−0.029 (−0.04–[−0.013])	<0.001
Number of physicians (per 10/10000 population)	−0.035 (−0.06–[−0.01])	0.002
Ambulatory healthcare facility (per 10000 population)	−0.031(−0048–[−0.014])	<0.001
Socio-economic contiodions		
Gross domestic product (PLN per capita)	−0.001 (−0001–0.001)	0.15
Unemployment rate (%)	0.008 (0.001–0.011)	0.04
Working age population (per year)	−0.015 (−0033–[−0.003])	0.01
Employment in agriculture (% of total employment)	0.008 (0.006–0.01)	<0.001
Environmental contiodions		
Vehicles (per 1000 inhabitants)	0.064 (0.008–0.121)	0.026
Population density (persons per km²)	−0.001 (−0.001–0.001)	0.14
Green areas (%)	−0.027 (−0.042–[−0.01])	0.049



POL-HF Study

- 1,618,734 HF hospitalizations
- 82% > 65 y. o.

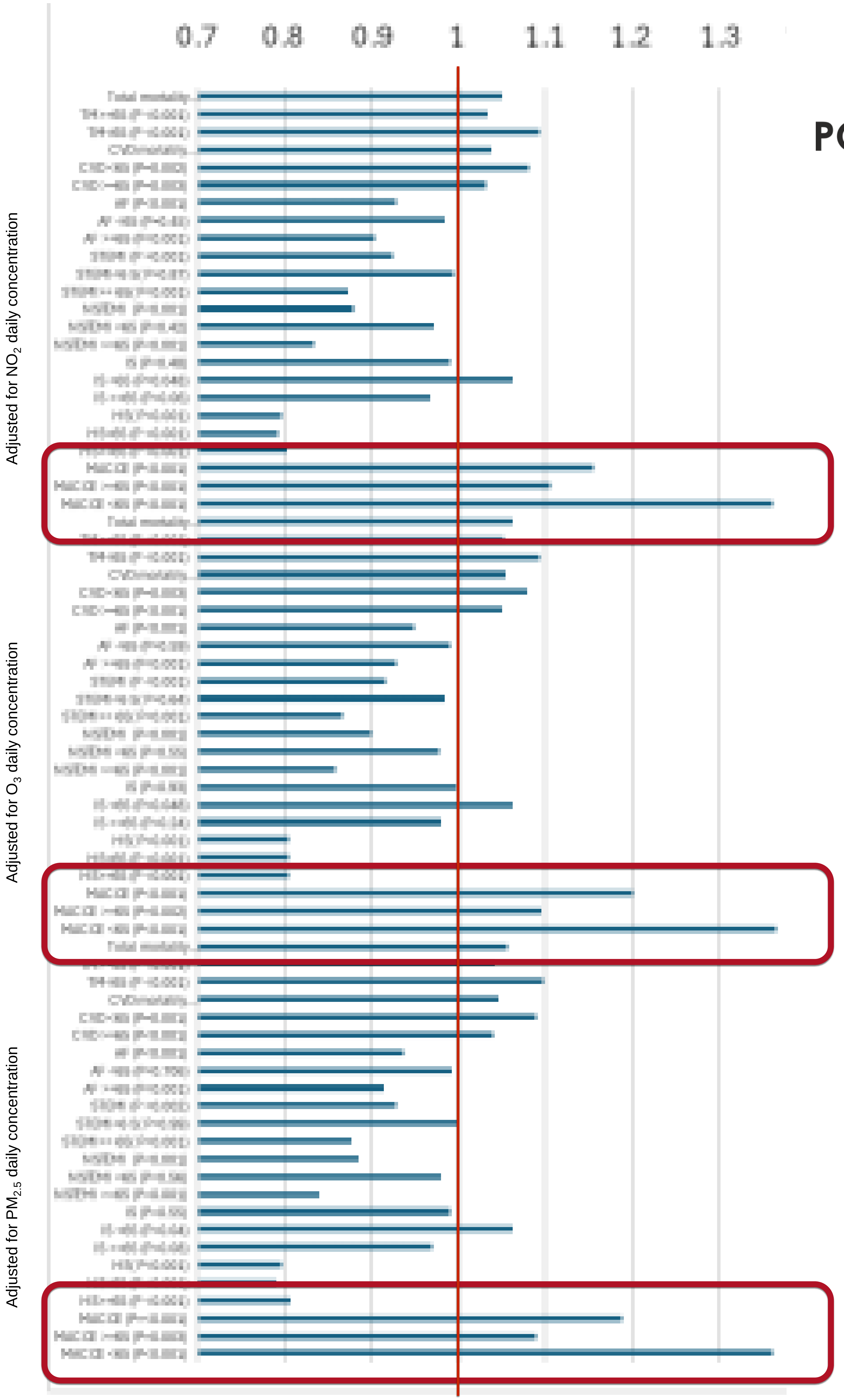
The study highlights the combination of long-term air pollution exposure with factors such as GDP per capita, unemployment rate, lack of green areas intensifies the impact of air pollution on health outcomes.

Climate changes

Title: Effect of heatwaves on daily hospital admissions and premature mortality in Poland, 2011–2020 an observational study (PL-PARTICLES Study)
Authors: Kuźma Ł, Jemielita L, Kurasz A, Święczkowski M,__ Lip G Y H on behalf of EP-PARTICLES Investigators

Key points

- ➢Heatwaves are significantly associated with increased mortality & MACCE occurrences
- ➢The observed decrease in hospitalizations for ACS and the lack of effect IS may **indicate increased pre-hospital mortality** during heatwave events.



POLISH SMOG
EP-PARTICLES STUDY

Future perspective

POLISH SMOG
EP-PARTICLES STUDY

NEW SOURCES OF DATA

- Big Data from EHRs
- RWD from Wearable Devices
- Geostationary Satellites for country level
- Low Earth Orbit Satellites for city level
- Smart City Infrastructure Sensors

NEW DIRECTIONS IN RESEARCH

- Genomics
- Randomized Controlled Trials (RCTs)
- Phenotyping
- Neuroradiology

‘ePM-years index‘

POLISH SMOG
EP-PARTICLES STUDY

Our approach to new index

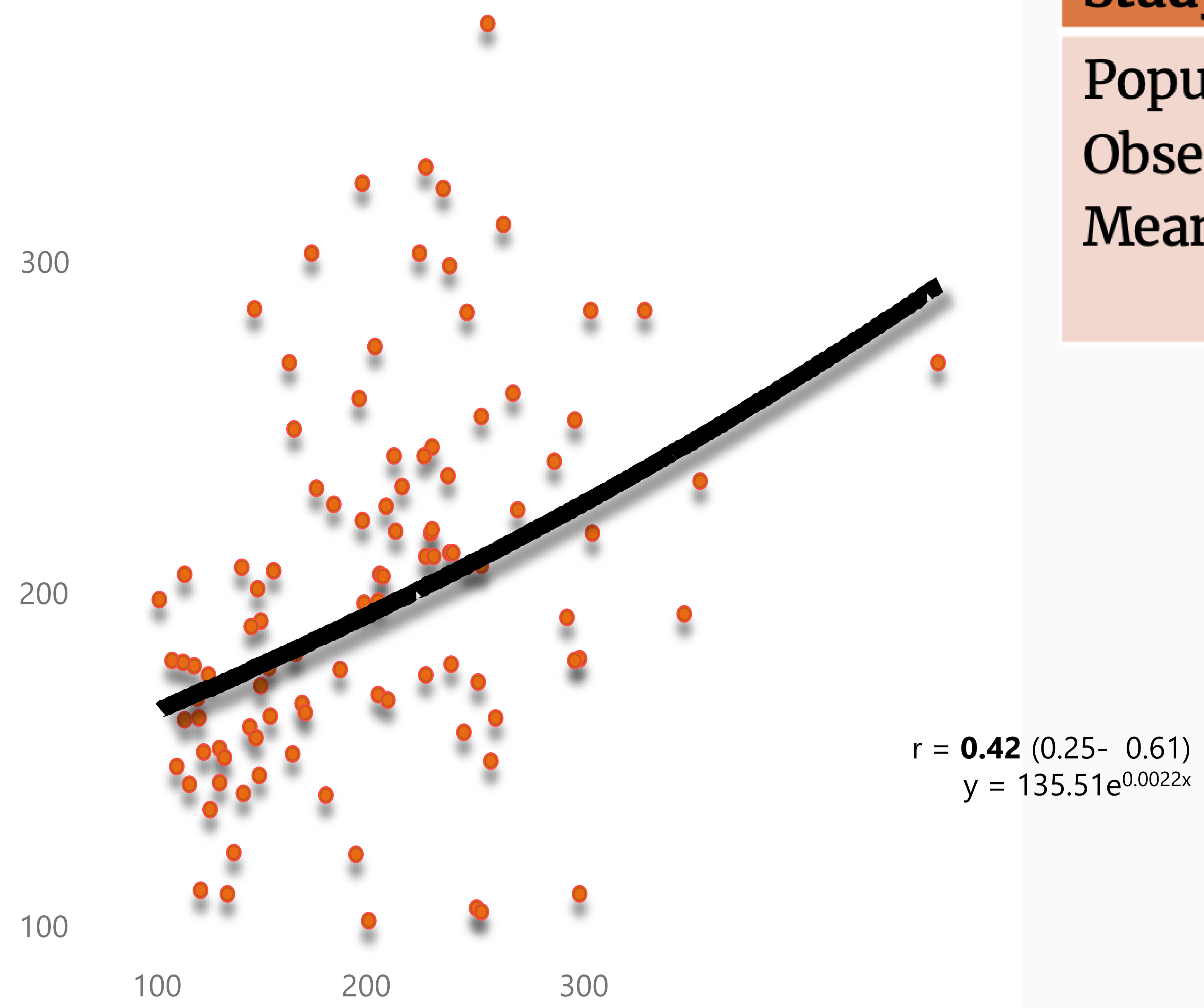
$$\text{'ePM-years index'} = \max\left(\frac{1}{c_w} \sum_{i=1}^{N} c_i - t,\ 0 \right)$$

c_i : yearly concentration for the i-th year of observation

∑ : the sum of yearly concentrations from the 1st to Nth year

c_w : WHO annual norm for $PM_{2.5}$ concentration

t : age or time of observation in years



Study area	Outcomes:
Population 8,077, 671 Observation years: 2011- 2020 Mean $PM_{2.5}$ concentration 21 μg/m³ (σ-4.8)	**2,141,213** hospitalizations due to CVD -159,952 due to IS -152,055 due to ACS **831,246** recorded deaths / **377,344** due to CVD

CVD mortality (OR=**1.07**, 95%CI 1.06 - 1.08)

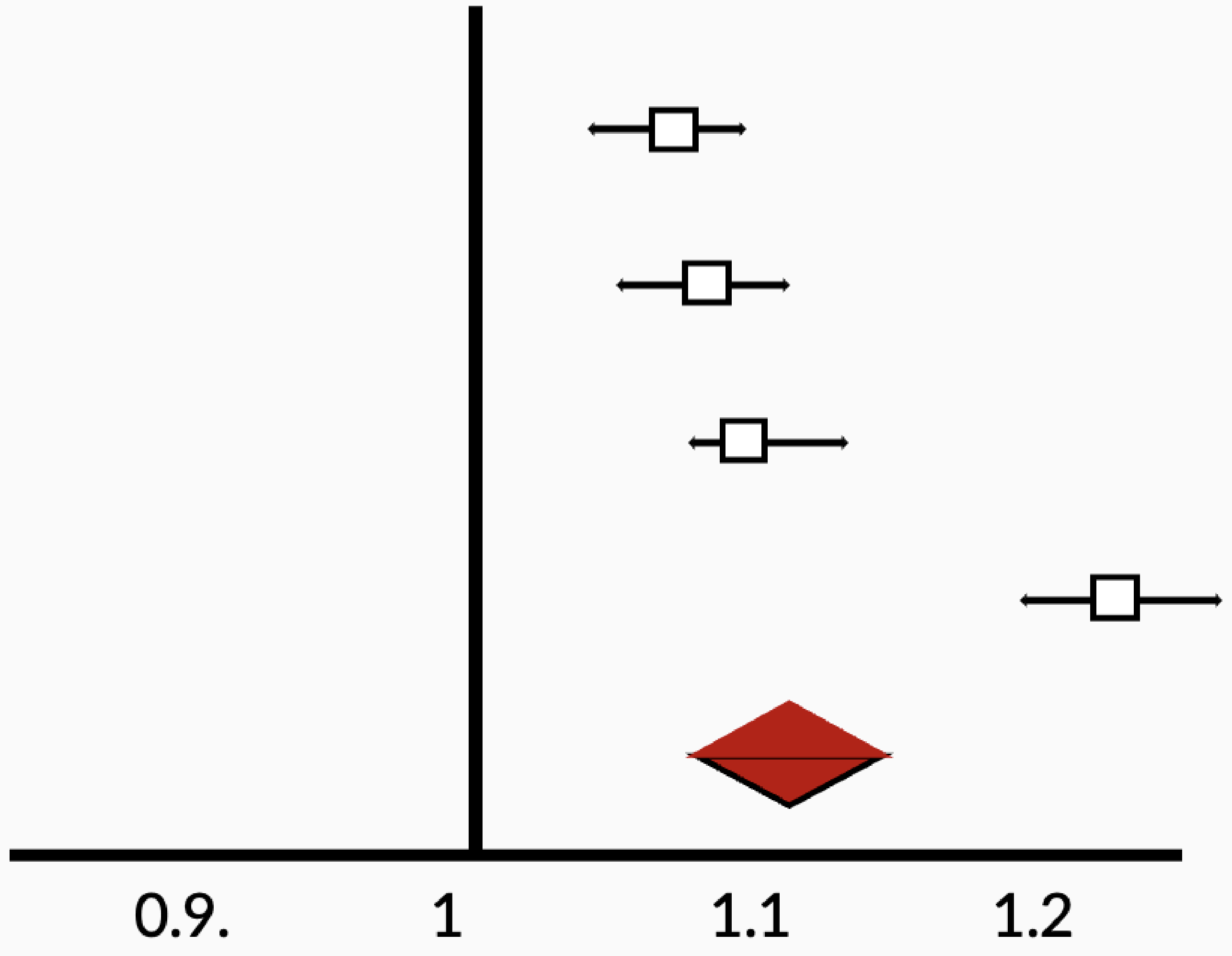
NSTEMI (OR=**1.08**, 95%CI 1.07 - 1.09)

IS (OR=**1.09**, 95%CI 1.08 - 1.101)

STEMI (OR=**1.21**, 95%CI 1.2 - 1.23)

Overall (OR=**1.11**, 95%CI 1.1 - 1.12)

per 10 ePM-years



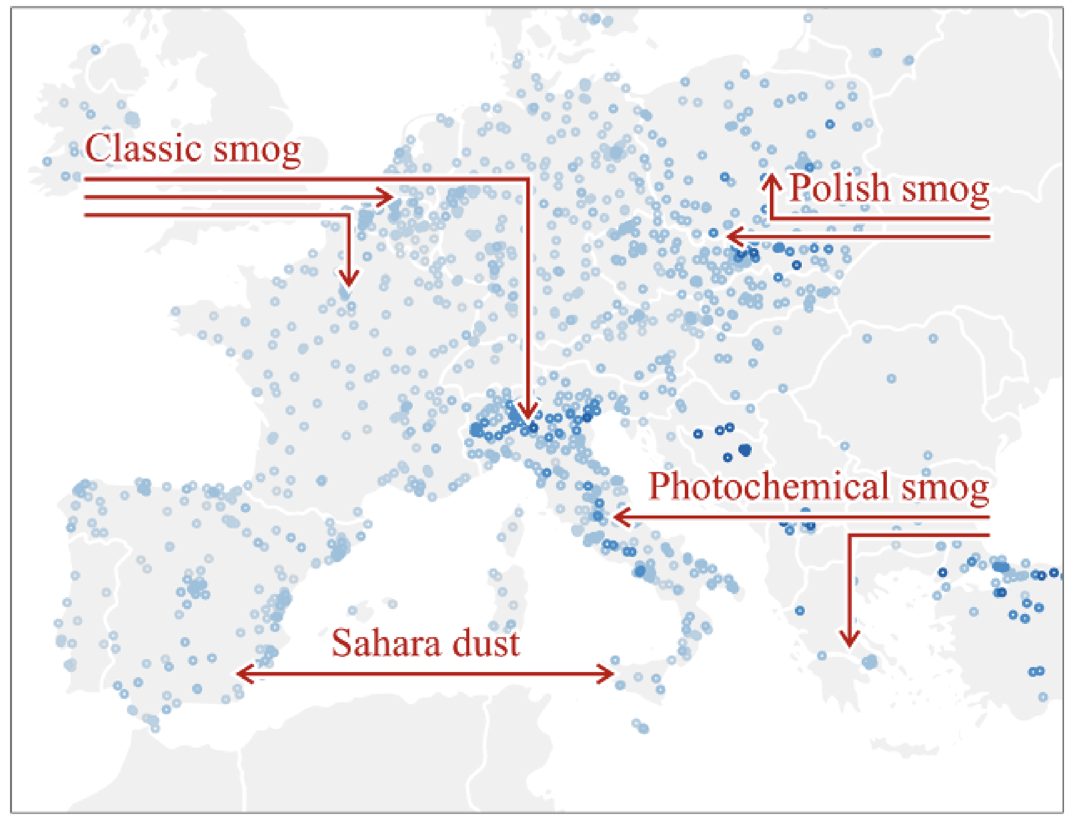
‘ePM-years index‘ (II)

POLISH SMOG
EP-PARTICLES STUDY

Purpose: To analyze the long-term predictive performance of the **‘ePM-years index’** on mortality due to heart failure in Poland

Airpocalypse:

800,000 excess deaths in Europe per year, Poland is one of the most polluted countries 50,000 excess deaths yearly due to **Polish smog**.



‘ePM-years Index’ $= \max\left(\frac{1}{c_w}\sum_{i=1}^{N} c_i - t, 0\right)$

c_i : mean yearly concentration for the i-th year of observation

$\sum$:the sum of mean yearly concentrations from the first to the N-th year of observation.

c_w : WHO annual norm for $PM_{2.5}$ concentration.

t : age or time of observation in years.

Methods:

- The data included information on gender, age, cause [according to ICD-10] codes, and place of death (municipality code - LAU -2).
- $PM_{2.5}$ concentration to calculate ‘ePM-years Index’ were obtained in partnership with the Institute of Environmental Protection – National Research Institute, we employed the GEM-AQ model for additional estimations.
- Levels of air pollutants were calculated using municipality resolution grids. In final analysis we use I50.XX ICD-10 codes for determine the HF death and zip codes of residence to connect individual exposure and outcomes.
- **The results are presented as hazard ratio (HR) and 95% confidence intervals (CI) per increase in 10 ‘ePM-years Index’.**

Results:

- We recorded all-cause **4,011,1222** deaths / CVD related deaths were **1,705,751 (34%)**
- **379,144** deaths were recorded due to exacerbation do H
- Mean age **78.3** [Median 81 (1Q=71- 3Q=87)], Female in **53.7%** (N=203,602)

Every 10 **‘ePM-years Index’** exposure → Almost **4%** increase risk od death due to HF

(HR 1.037, 95%CI 1.003-1.112, p<0.001)

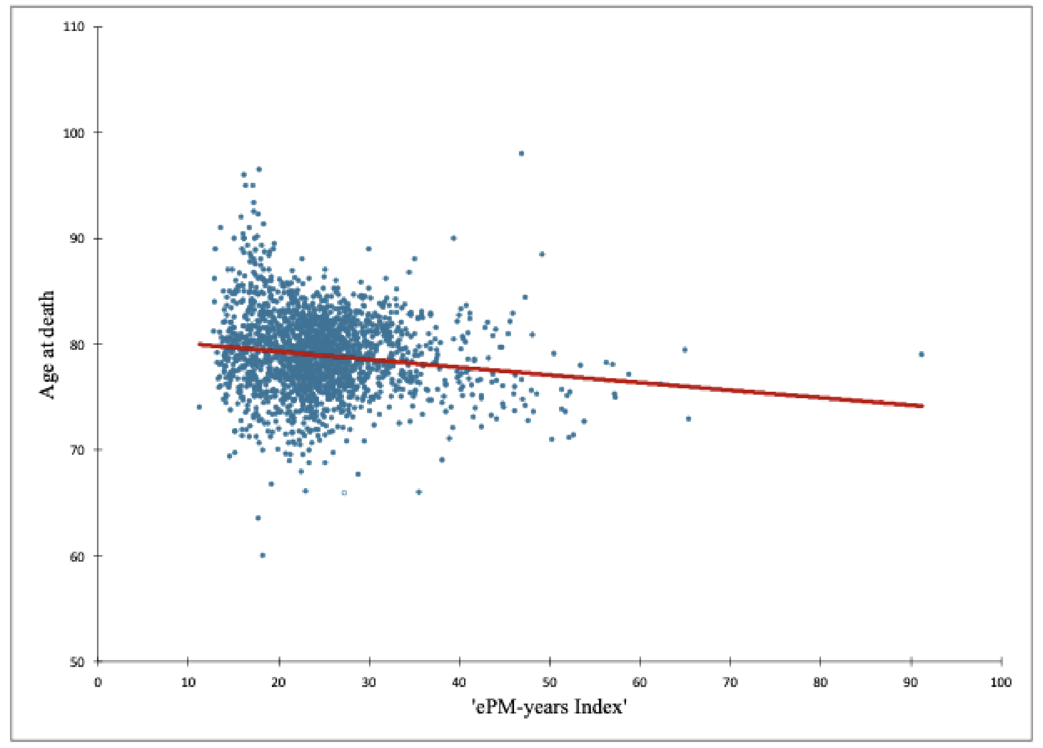


Fig 1. Correlation between 'ePM-years Index' exposure and age at deaths

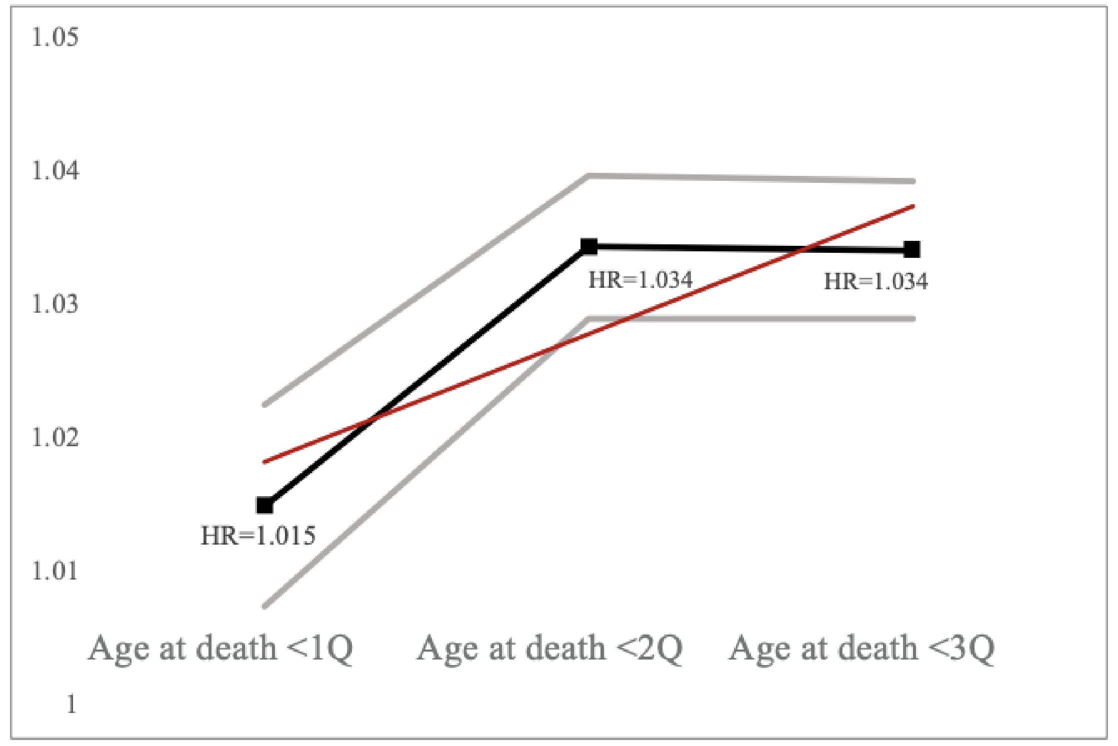


Fig 2. Differences in 'ePM-years Index' impact depend age at deaths

Clinicial implinactions:

The 'ePM-years Index'

- is an independent predictor of HF mortality.
- can be used as a tool for risk stratification for patients
- can be incorporated into prediction models to improve efficacy in primary & secondary prevention

Analysis of an Effect of ‘ePM-years Index’ on Heart Failure Mortality in Poland (EP-PARTICLES Study) Ł. Kuźma__G.Y.H. Lip: In publication.

‘ePM-years index‘ (III)

Machine learning to improve cardiovascular disease mortality risk prediction due to air pollution: Insights into the ‘exposome’ from the EP-PARTICLES project

A. M. Wijata, G. Y.H. Lip, A Kurasz. M Swięczkowski,
P. Jemielita__Łukasz Kuźma (In revison)

‘AF-CAD’ Cohort

6,935 participants

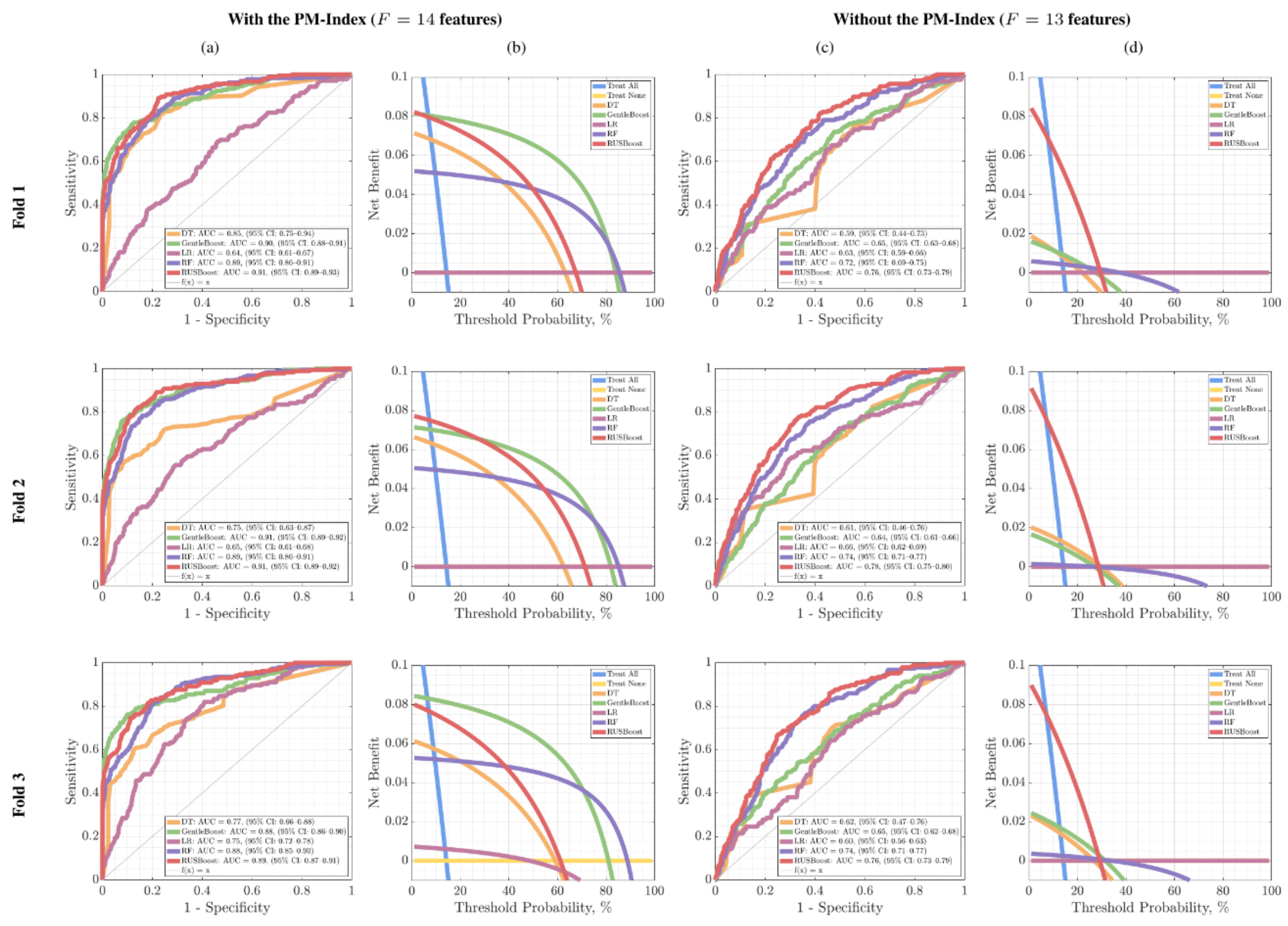
Media age 66 (58-73)

10 years of observation

Primary outcome: CVD death

Key points:

- Question: Does integrating environmental risk factors into CVD risk scores improve their predictive value?
- Findings: In this prospective cohort-based study of 6935 patients adding ‘ePM-years index’ to ML models improved correct classification of CVD risk **from 72.59% to 92.75% of patients.**
- Meaning: ML incorporating AP demonstrated greater predictive abilities and clinical utility



Future perspective

POLISH SMOG
EP-PARTICLES STUDY

DTs models for evidence generation

Mechanistic modelling

- Simulations of CVD outcomes based on multi-omics profiles & pollution exposure
- Impact of pollutants on cardiovascular mechanics and structure
- Multi-omics models integrating demographic and clinical characteristics

Deduction

Induction

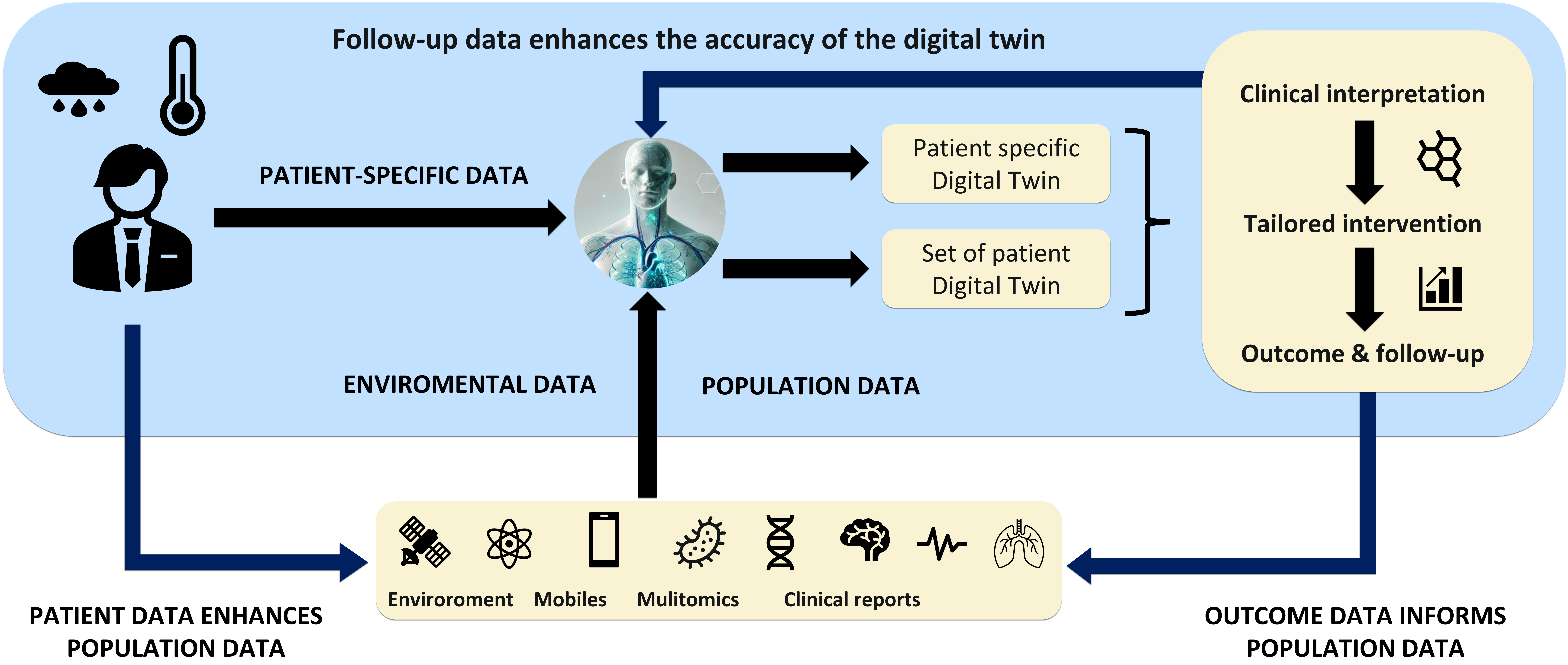
Statistical modelling

- Definition of multi-omics, demographic, clinical predictors related to air pollution exposure
- Extraction of multi-omics biomarkers related to CVD effects of air pollution
- Predictive modelling of CVD events related to environmental pollution exposure

Interpretation of multi-omics phenotypes → **Insight** ← Identification of multi-omics phenotypes

Future perspective

DTs as controls for pollution exposure scenarios
DTs for translation of pollution impact across diverse populations

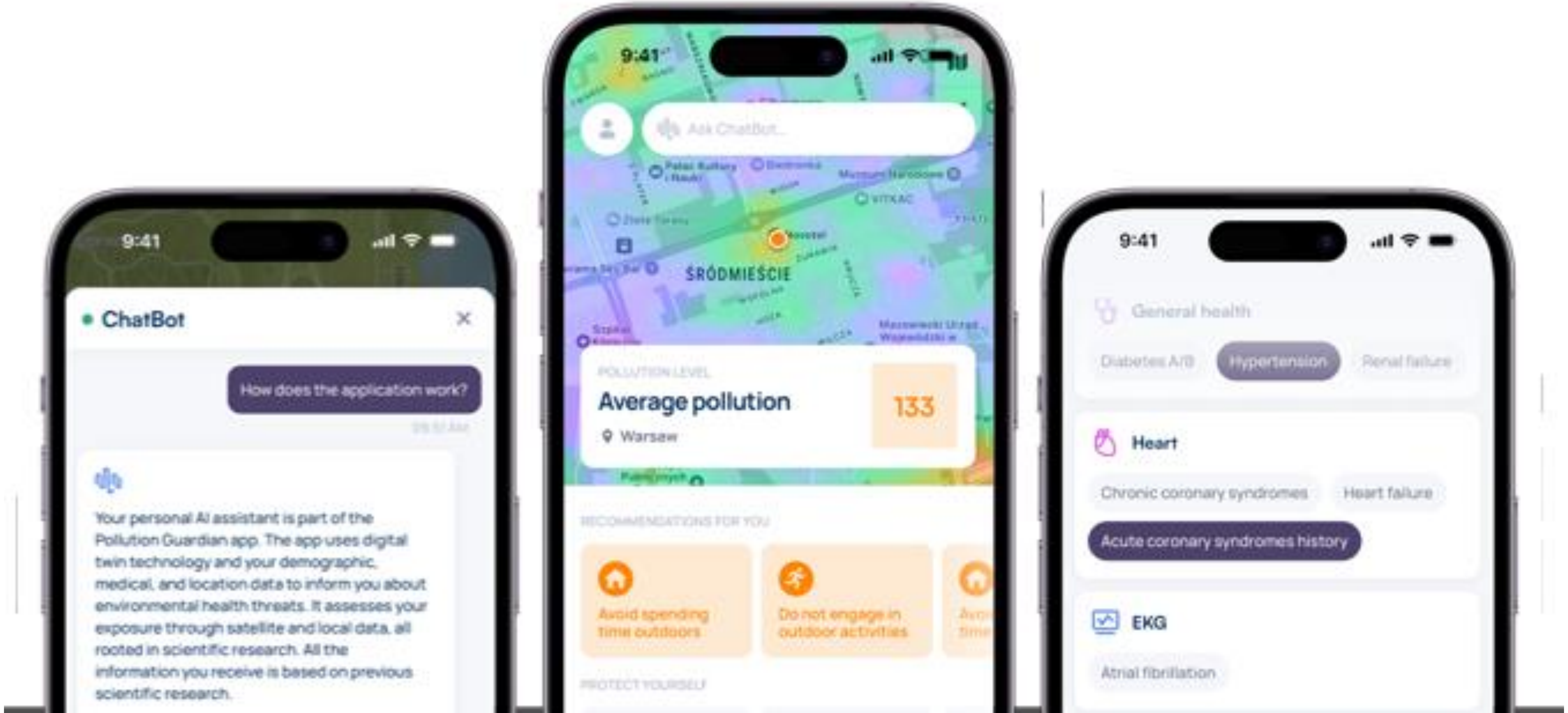


POLISH SMOG
EP-PARTICLES STUDY

Future perspective

‘Pollution Guardian’

Real-time reporting on environmental risks tailored to planned activities, your health condition, and risk factors



Future perspective

'Pollution Guardian' scenario

POLISH SMOG
EP-PARTICLES STUDY

Mr. X, a 65-year-old man with HFpEF, PAF, obesity **is exercising outdoors**

Wearable device have recorded episodes of atrial tachycardia.

The temperature is 25°C, PMs & NO_x levels are very high, triggering analysis.

LLM models analyse the EHR, and transfer data to the DT

The DT, based on knowledge from previous studies, guidelines, comparison with other DTs, Mr. X's current activity and forecast of the PMs levels

concluding that Mr. X is likely to experience an episode of AF.

The Digital Twin model provides recommendation and information for:

Mr. X, regarding the **optimal duration and intensity of exercise that aligns with health benefits while minimizing risks**

Mr. X's physician regarding the occurrence of AT and needs for further test

Future perspective

’ePM-years index’

Our approach to new index

$$\text{'ePM-years index'} = \max\left(\frac{1}{c_w}\sum_{i=1}^{N} c_i - t,\ 0\right)$$

c_i : yearly concentration for the i-th year of observation

$\sum$: the sum of yearly concentrations from the 1^{st} to N^{th} year

c_w : WHO annual norm for $PM_{2.5}$ concentration

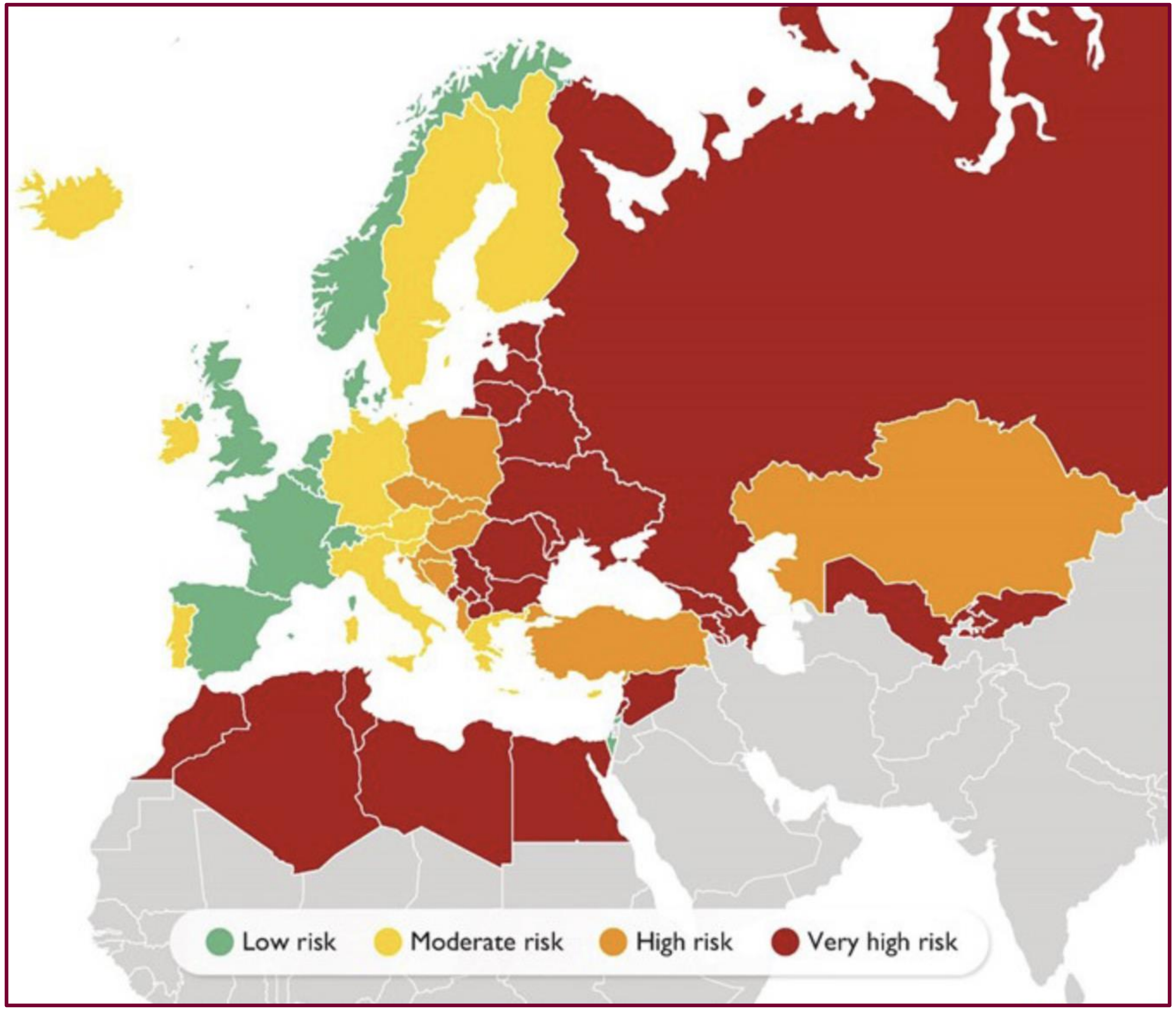
t : age or time of observation in years

EP-SCORE

- ✓ Enhanced risk stratification, showing differences within each risk region
- ✓ CVD risk reclassification, identifies the cohorts at high risk
- ✓ More information & role in decision-making for those at "intermediate" risk
- ✓ Allows for modification of intensity of monitoring & preventive strategies

Future perspective

EP-SCORE



Development Process

⇩

Original SCORE2 algorithms:
Predictors: age, sex, smoking, SBP, total & HDL cholesterol

⇩

Calibrated to predict CVD risk in:
Low, moderate, high, and very high-risk regions of Europe

⇩

Creating an 'ePM-years index' **map for Poland**
High resolution data at LAU2

⇩

Adaptation of EP-SCORE for individuals
Added predictors: 'ePM-years index' according to postal code & age

⇩

Validation of EP-SCORE
In low, moderate, high, and **very high-risk** regions of Europe

Future perspective

EP-SCORE scenario

52 y.o., male,
smoker, SPB 120 mmHg,
TC 250 mg/dl, HDL 60 mg/dl

SCORE2

	Men							
Age	Non-smoking				Smoking			
65 - 69	17	18	20	22	25	28	30	32
	14	15	16	18	21	23	25	27
	11	12	13	15	17	19	20	22
	9	10	11	12	14	15	17	18
60 - 64	13	14	16	18	20	23	25	28
	10	11	13	14	16	18	20	23
	8	9	10	11	13	15	16	18
	6	7	8	9	10	12	13	15
55 - 59	9	11	12	14	16	19	21	24
	7	8	10	11	13	15	17	19
	6	6	7	9	10	11	13	15
	4	5	6	7	8	9	10	12
50 - 54	7	8	10	11	13	15	18	21
	5	6	7	9	10	12	14	16
	4	5	5	6	7	9	10	12
	3	3	4	5	6	7	8	9
45 - 49	5	6	8	9	10	13	15	18
	4	5	6	7	8	9	11	14
	3	3	4	5	6	7	8	10
	2	2	3	4	4	5	6	7
40 - 44	4	5	6	7	8	10	13	16
	3	3	4	5	6	7	9	11
	2	2	3	4	4	5	7	8
	1	2	2	3	3	4	5	6
	3.0-3.9	4.0-4.9	5.0-5.9	6.0-6.9	3.0-3.9	4.0-4.9	5.0-5.9	6.0-6.9

MURCIA
LIVERPOOL
5.2%

ATHENS
MILAN
6.8%

BIALYSTOK
KRAKOW
7.2%

BELGRAD
VILNIUS
13.2%

	BIALYSTOK	RZESZÓW
SCORE2	7.2%	7.2%

+ ’ePM-years index’

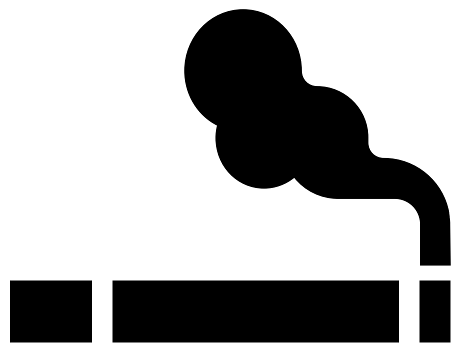
EP-SCORE	4.9%	11.2%
	5% for low-risk region	13% for very high-risk region

Take home message

POLISH SMOG
EP-PARTICLES STUDY

Health = *f* (Exposome; Genome)

$PM_{2.5}$ >



Thank you

lukasz.kuzma@umb.edu.pl
@LukaszKuzma
www.polishsmog.com