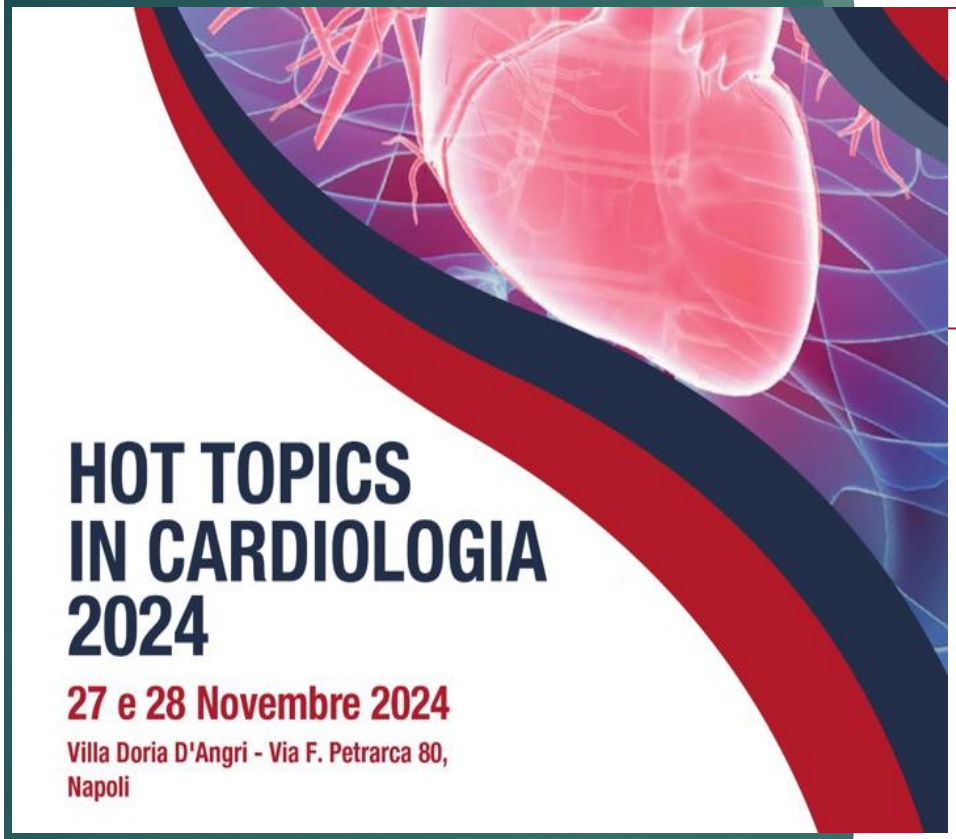


TITOLO:
New Insights in Cardiology – Fattori di rischio cardio-vascolare emergenti: le nano-plastiche -

RELATORE: Raffaele Marfella

Università degli Studi della Campania *Luigi Vanvitelli*

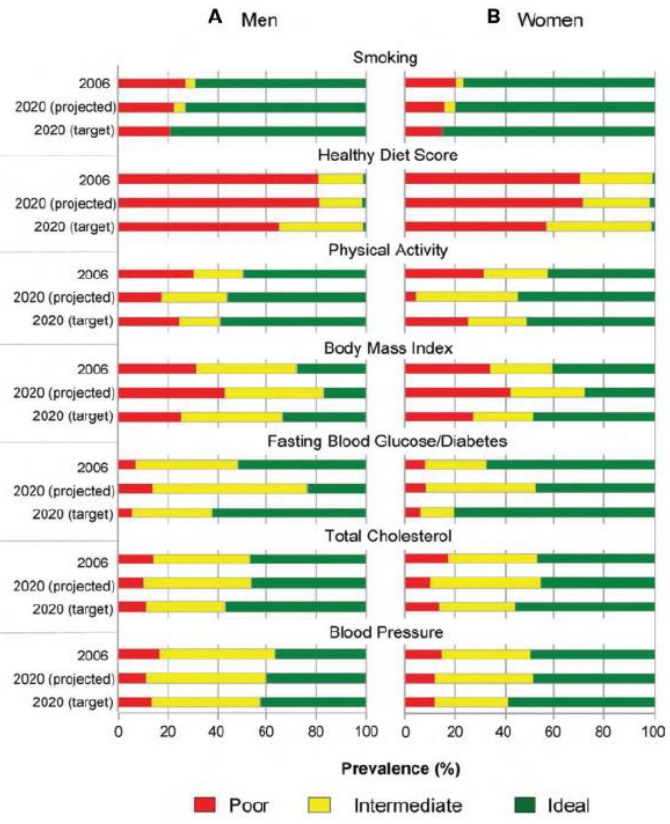
Link profitable solutions

Circulation

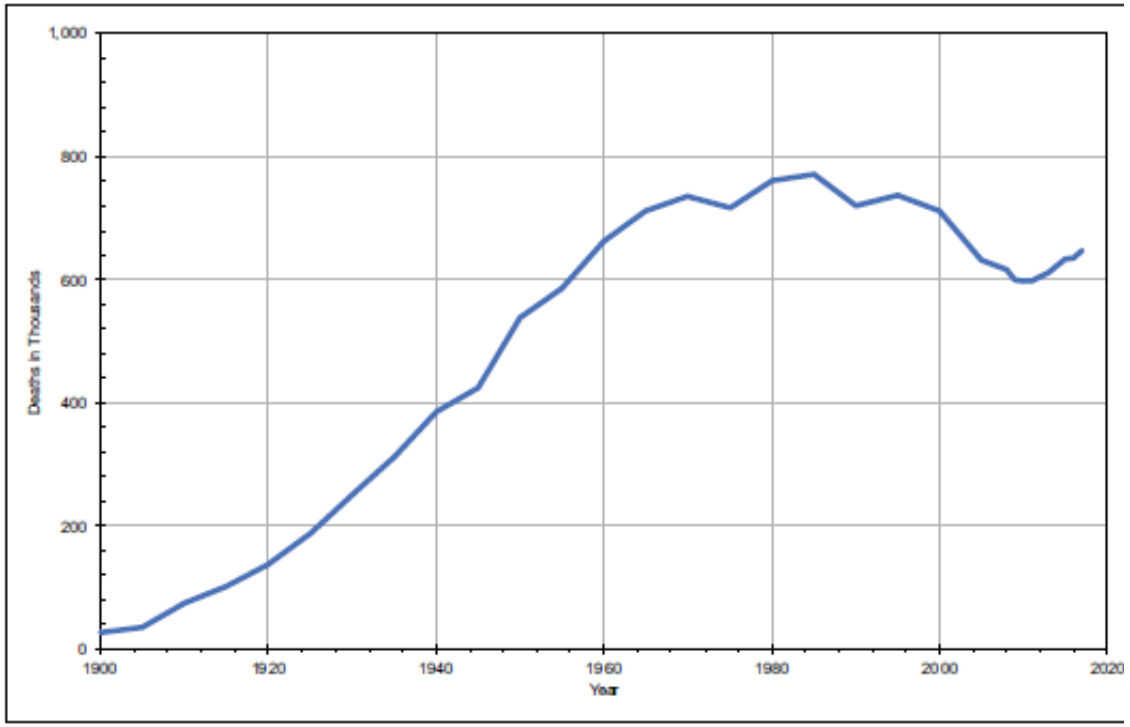
AHA STATISTICAL UPDATE

Heart Disease and Stroke Statistics—2020 Update

Circulation. 2020;141:e139–e596. DOI: 10.1161/CIR.0000000000000757



Despite good control of various risk factors, cardiovascular mortality is still very high



Exposome in ischaemic heart disease: beyond traditional risk factors

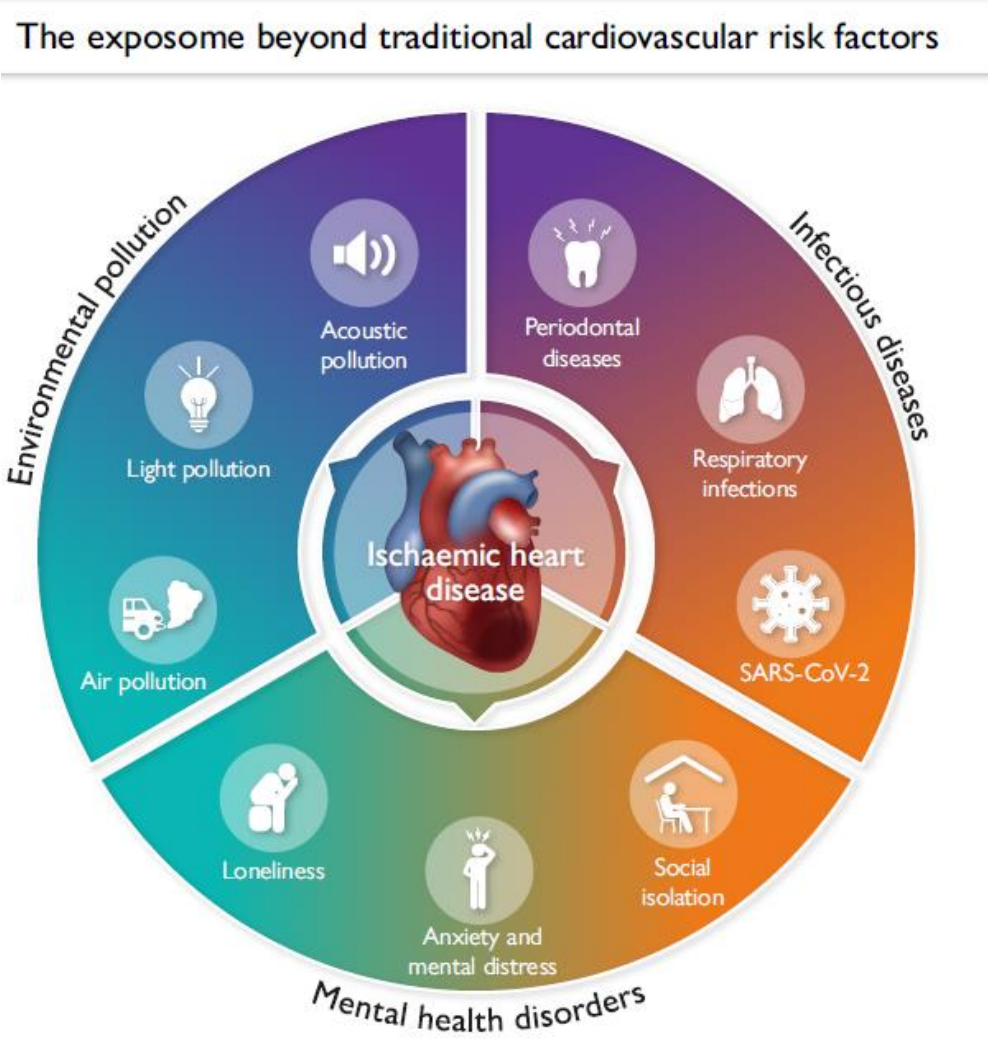
Rocco A. Montone [1*†], Massimiliano Camilli [1,2†], Camilla Calvieri[3], Giulia Magnani [4], Alice Bonanni [1], Deepak L. Bhatt [5], Sanjay Rajagopalan[6], Filippo Crea[1,2], and Giampaolo Niccoli[4]

ESC European Society of Cardiology

European Heart Journal (2024) **45**, 419–438
https://doi.org/10.1093/eurheartj/ehae001

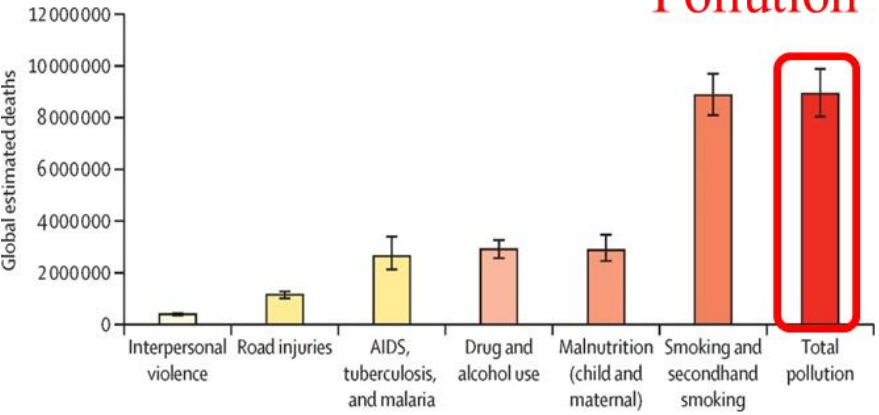
STATE OF THE ART REVIEW

Epidemiology, prevention, and health care policies




Global Burden of Disease (GBD):
in 2019 9,0 million deaths world wide were directly attributable to pollution

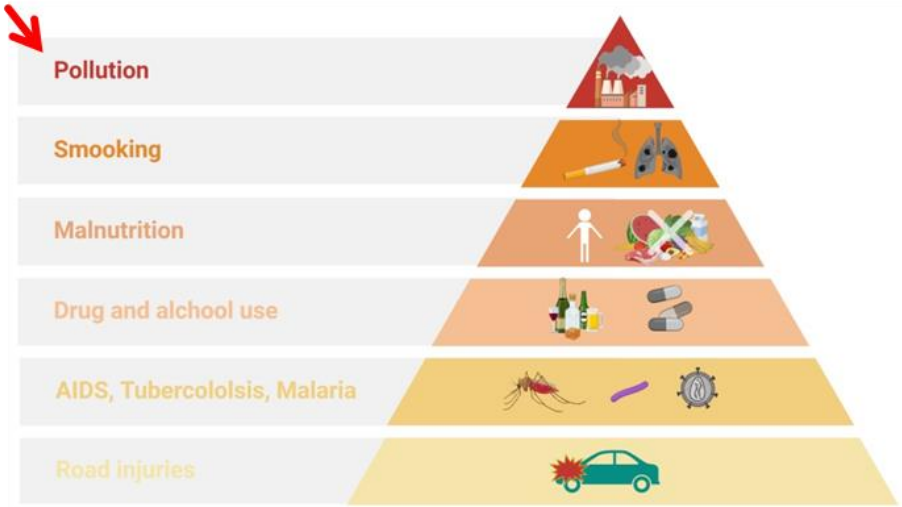
Pollution and human health

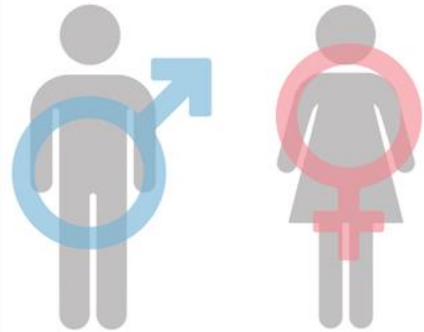


	Female	Male	Total
Total air pollution*	2·92 (2·53–3·33)	3·75 (3·31–4·25)	6·67 (5·90–7·49)
Household air†	1·13 (0·80–1·50)	1·18 (0·79–1·66)	2·31 (1·63–3·12)
Ambient particulate‡§	1·70 (1·38–2·01)	2·44 (2·02–2·83)	4·14 (3·45–4·8)
Ambient ozone‡	0·16 (0·07–0·25)	0·21 (0·09–0·33)	0·37 (0·17–0·56)
Total water pollution*	0·73 (0·40–1·26)	0·63 (0·46–0·95)	1·36 (0·96–1·96)
Unsafe sanitation†	0·40 (0·23–0·68)	0·36 (0·26–0·54)	0·76 (0·54–1·09)
Unsafe source†	0·66 (0·35–1·15)	0·57 (0·39–0·88)	1·23 (0·82–1·79)
Total occupational pollution*	0·22 (0·17–0·28)	0·65 (0·54–0·79)	0·87 (0·74–1·02)
Carcinogens‡	0·07 (0·05–0·09)	0·28 (0·22–0·35)	0·35 (0·28–0·42)
Particulates‡¶	0·15 (0·10–0·21)	0·37 (0·27–0·47)	0·52 (0·42–0·64)
Lead pollution*‡	0·35 (0·19–0·53)	0·56 (0·36–0·77)	0·90 (0·55–1·29)
Total modern pollution*	2·28 (1·86–2·67)	3·55 (3·08–4·04)	5·84 (5·03–6·61)
Total traditional pollution*	1·85 (1·39–2·42)	1·81 (1·36–2·38)	3·66 (2·82–4·63)
Total pollution*	3·92 (3·39–4·47)	5·09 (4·57–5·68)	9·01 (8·12–10·0)

Data are N in millions (95% CI). *Custom aggregate from Institute for Health Metrics and Evaluation corrected for overlap. The totals for air, water, modern, traditional, and all pollution are less than the arithmetic sum of the individual risk factors within each of these categories because their contributions overlap (eg, household air and ambient air pollution each can contribute to the same diseases). †Traditional pollution risk factor. ‡Modern pollution risk factors. §Ambient particulate matter is $PM_{2.5}$. ¶Occupational exposure to respirable, thoracic, or inhalable particulate matter.

Table: **Global estimated pollution-attributable deaths (millions) by type of pollution and sex, 2019**

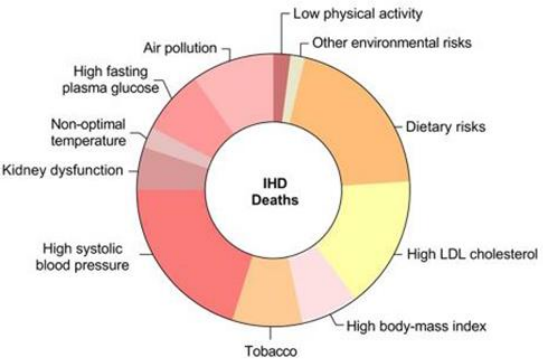


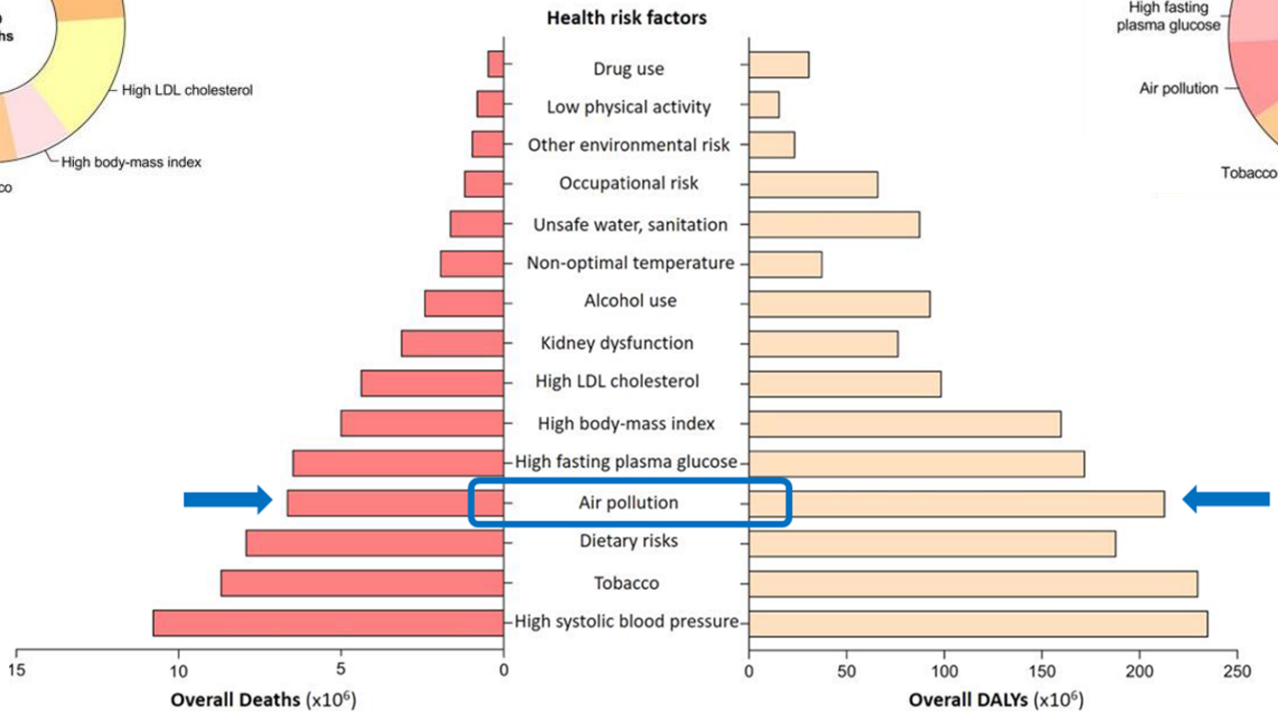


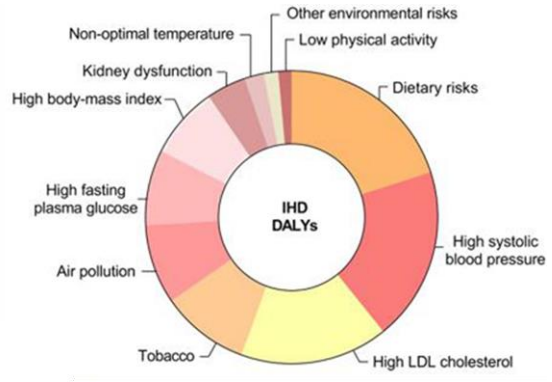
The Lancet Planetary Health Volume 6 Issue 6 Pages e535-e547 (June 2022)

Air pollution: non-traditional risk factors of CVDs

Air pollution has been shown to reduce the global average life expectancy by 2.9 years, a reduction that is more extensive when compared with traditional cardiovascular risk factors such as tobacco smoking (2.2 years)

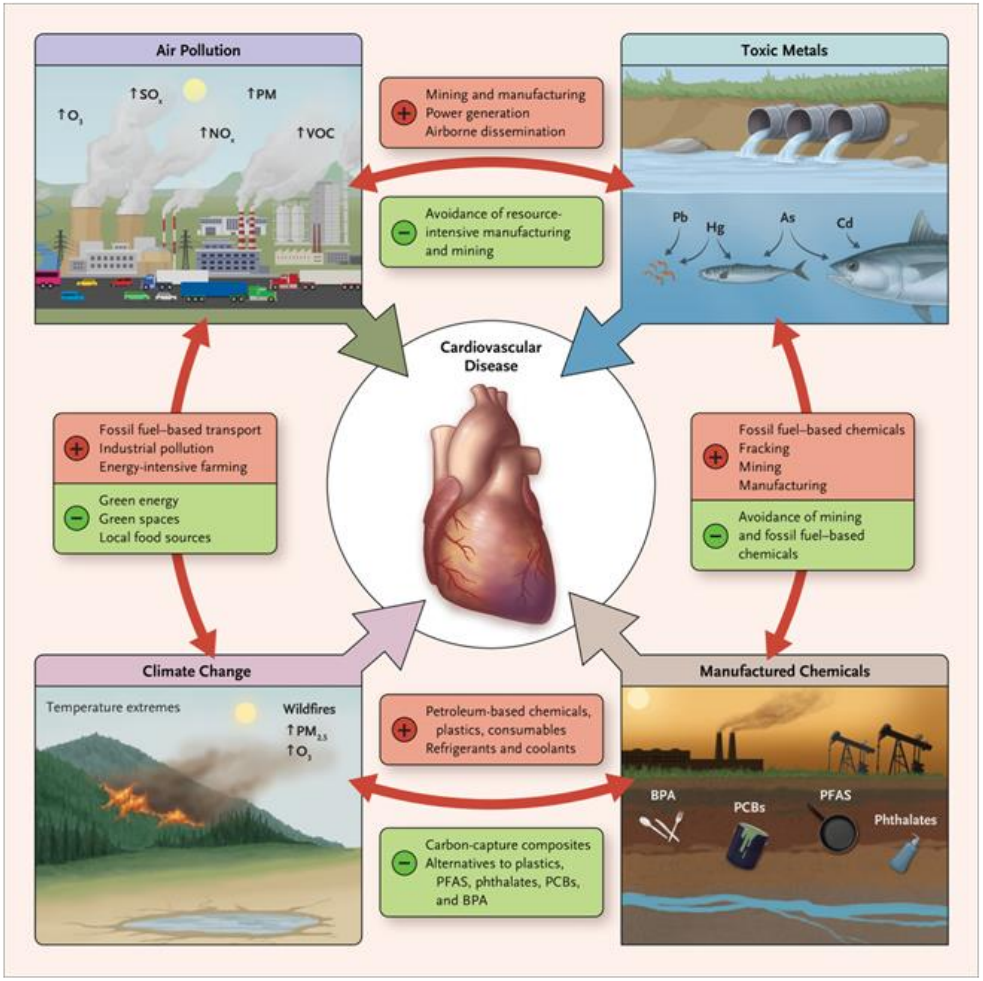






Montone RA et al., Exposome in ischaemic heart disease: beyond traditional risk factors. Eur Heart J. 2024

Pollution and cardiovascular disease



CVDs

- Ischemic heart disease
- Stroke
- Atrial fibrillation
- Ventricular arrhythmias
- Coronary-artery calcification
- Atherosclerotic plaque formation
- Left ventricular hypertrophy

Rajagopalan S. et al.,2021 N ENGL J MED Pollution and the Heart

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

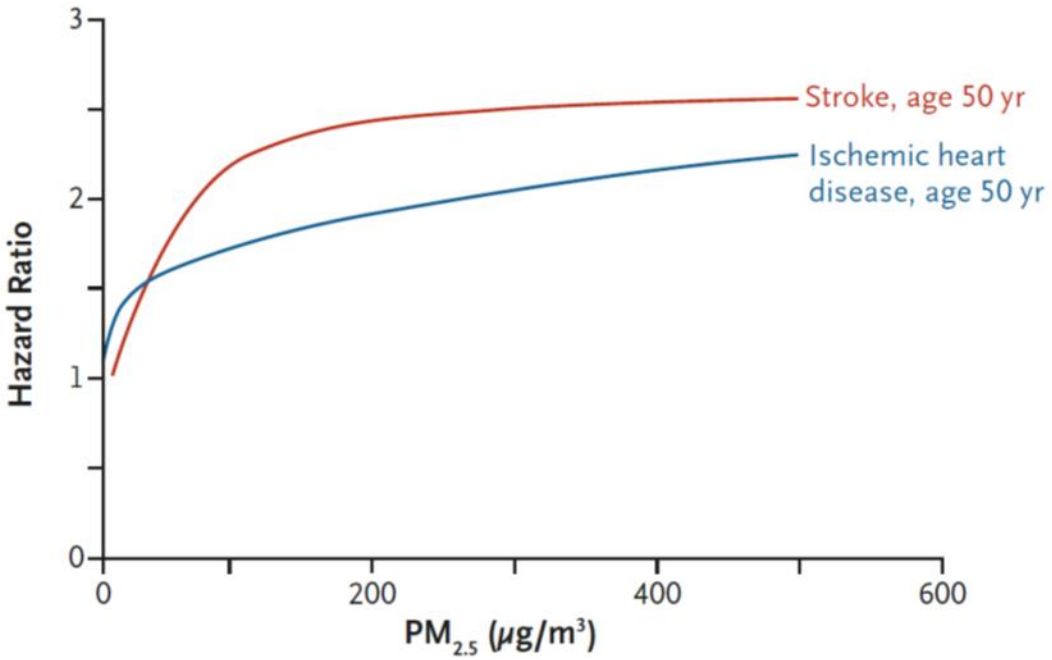
Pollution and the Heart

Sanjay Rajagopalan, M.D., and Philip J. Landrigan, M.D.

Figure 2. Air Pollution and Cardiovascular Disease.

Panel A shows age-standardized deaths per 100,000 persons in 2019 that were attributable to $PM_{2.5}$ air pollution, according to country. Data are from the 2019 Global Burden of Disease (GBD) Study.[1] Panel B shows the numbers of deaths from pollution-related noncommunicable disease globally, according to the cause of death, in 2019. Data are from the 2019 GBD Study.[1] Panel C shows annual mean population-weighted $PM_{2.5}$ levels in the United States, China, and India from 1990 through 2019. $PM_{2.5}$ estimates were derived with the use of a blended model combining satellite observations, global chemical transport models, and ground-level data from 10,408 monitors representing urban and rural data in 116 countries. To derive population-weighted averages, $PM_{2.5}$ levels were adjusted by population size. The lavender line represents the U.S. National Ambient Air Quality Standard (NAAQS) of 12 μg per cubic millimeter, and the dashed gray line represents the World Health Organization (WHO) annual mean air-quality guideline level of 10 μg per cubic millimeter. Panel D shows exposure–response relationships between $PM_{2.5}$ air pollution and cardiovascular disease, modeled for a 50-year-old person. The response function represents a meta-regressed Bayesian, regularized, trimmed (MR-BRT) curve derived by relaxing the log-linear assumption with the use of cubic splines. Data are from the 2019 GBD Study.[1]

D Exposure–Response Relationship Between $PM_{2.5}$ Pollution and Cardiovascular Disease



JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY
VOL. 78, NO. 10, 2021

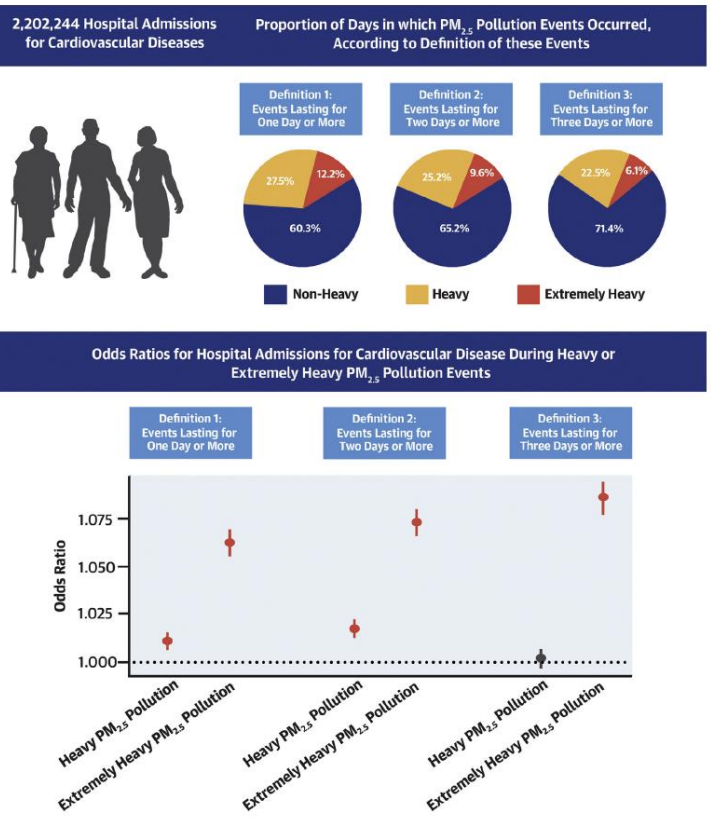
PUBLISHED BY ELSEVIER

Risk of Cardiovascular Hospital Admission After Exposure to Fine Particulate Pollution

Yi Zhang, MPH,[a] Runmei Ma, MSc,[a] Jie Ban, MD,[a] Feng Lu, PhD,[b] Moning Guo, MD,[b] Yu Zhong, MSc,[a] Ning Jiang, BSMed,[a] Chen Chen, MSc,[a] Tiantian Li, PhD,[a] Xiaoming Shi, MD[a]

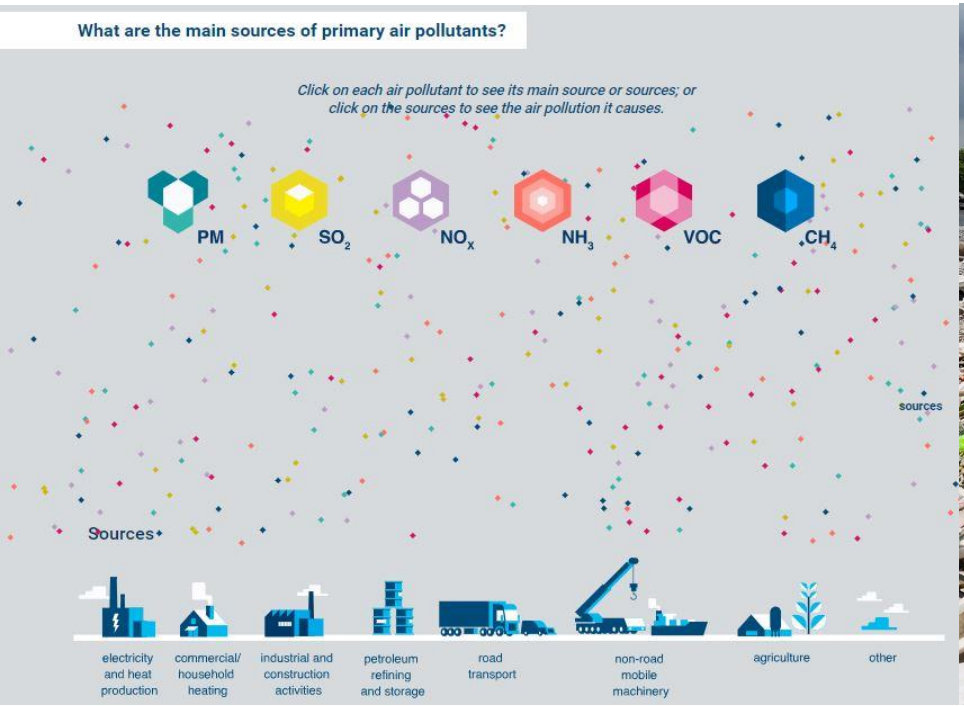
CONCLUSIONS Heavy and extremely heavy $PM_{2.5}$ pollution events resulted in substantial increased hospital admission risk for cardiovascular disease. With higher $PM_{2.5}$ concentration and longer duration of heavy $PM_{2.5}$ pollution events, a greater risk of cardiovascular hospital admission was observed. (J Am Coll Cardiol 2021;78:1015-1024) © 2021 by the American College of Cardiology Foundation.

CENTRAL ILLUSTRATION Heavy $PM_{2.5}$ Pollution Events Increased the Risks of Hospital Admission for Cardiovascular Diseases



POLLUTION

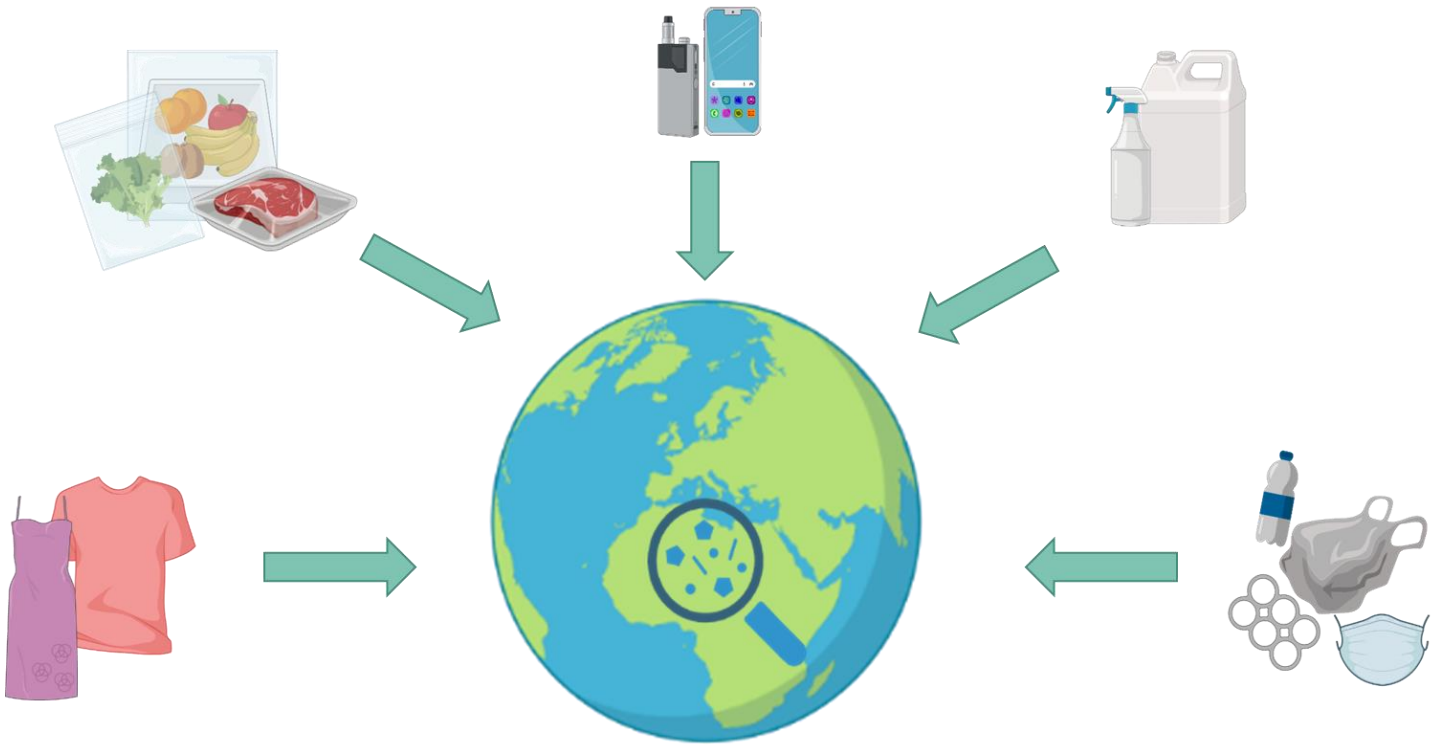
Air pollutants



Microplastics

Pollutants are substances that pollute the environment, especially gases from vehicles, poisonous chemicals and microplastics produced as waste by industrial processes.

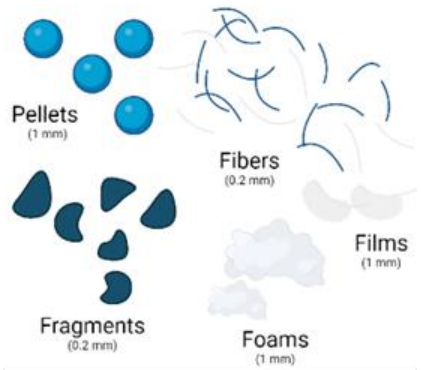
A plastics world

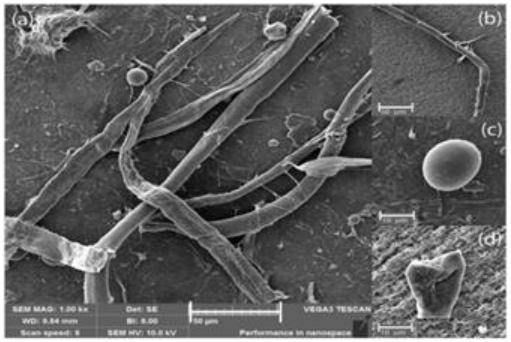


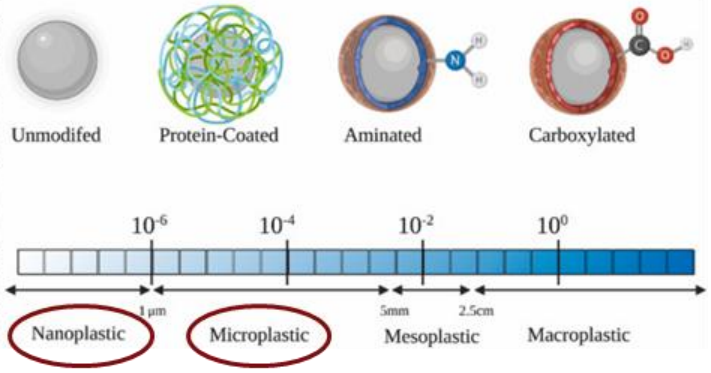
Cox, K.D., et al., Environmental Science & Technology 2019

Microplastics and nanoplastics: size, shape and composition

The production of plastics is constantly increasing, and this trajectory is set to persist until 2050. Humans are exposed to different types of fibers and particles, including **micro-nanoplastics**; the potential health effects of microplastics are largely unknown.







Pivokonsky, M., Cermakova, L., Novotna, K., Peer, P., Cajthaml, T., Janda, V., 2018. Occurrence of microplastics in raw and treated drinking water.

Le micro-nanoplastiche sono dannose per la salute cardiovascolare nell'uomo?

GAPs

- Le MNPs entrano nel corpo umano?
- Le MNPs alterano i processi fisiologici cellulari?
- Le MNP incidono sulla malattia cardiovascolare?

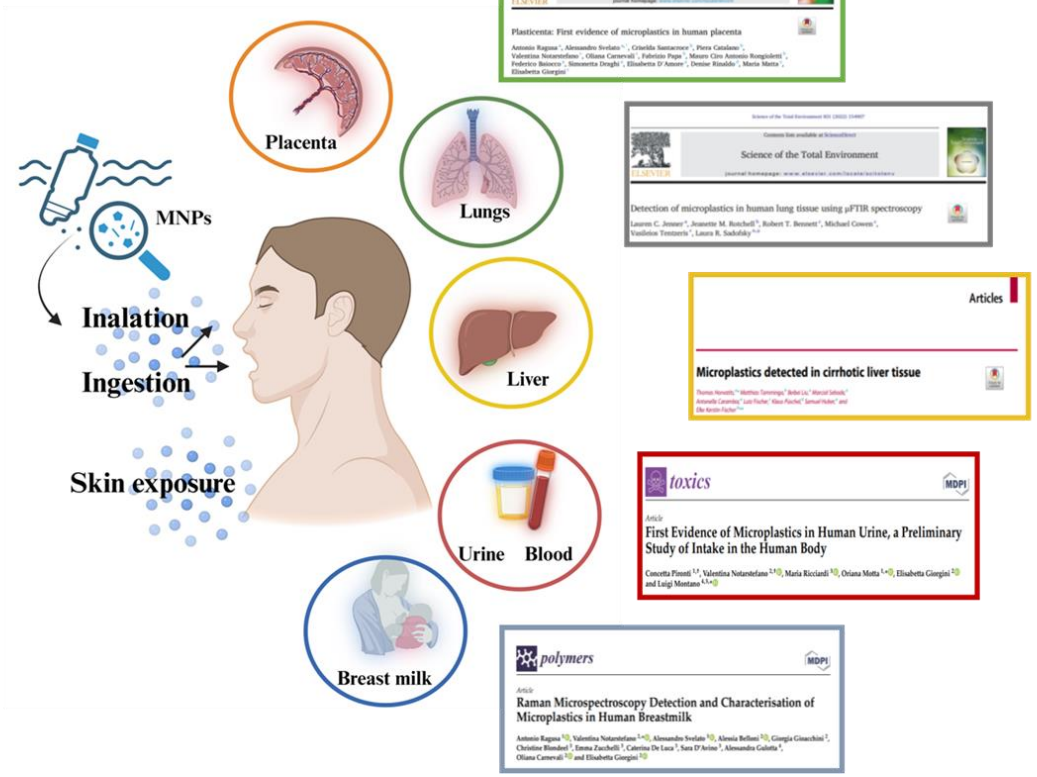
Science

Twenty years of microplastics pollution research—what have we learned?

Richard C. Thompson[1*], Winnie Courtene-Jones[1], Julien Boucher[2], Sabine Pahl[3], Karen Raubenheimer[4], Albert A. Koelmans[5]

Cite as: R. C. Thompson *et al.*, *Science* 10.1126/science.adl2746 (2024).

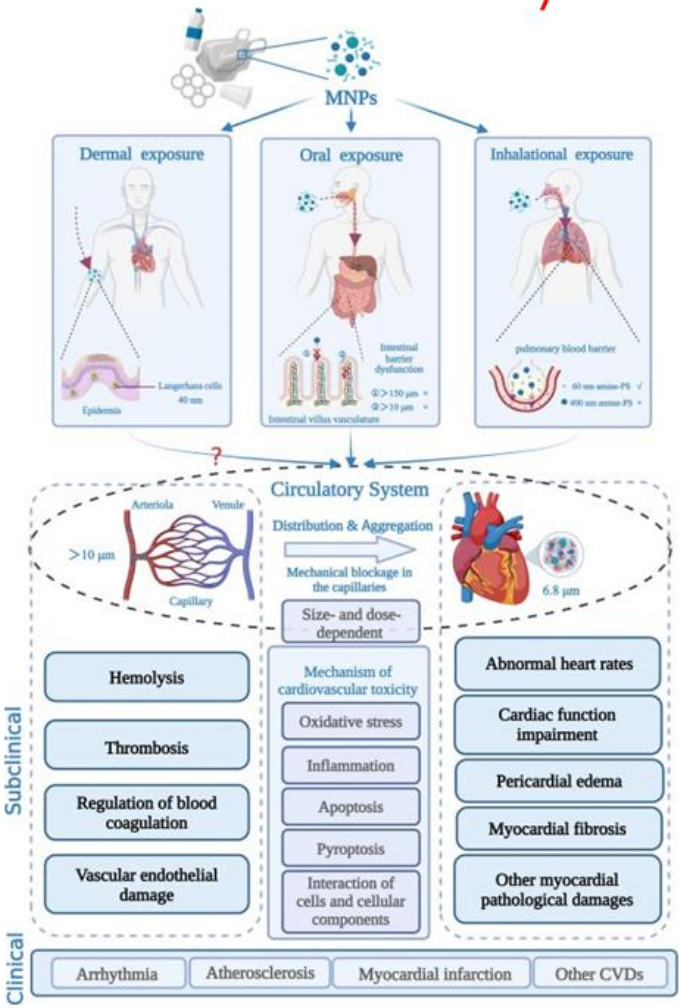
Entry and accumulation of micro-nanoplastics in human body

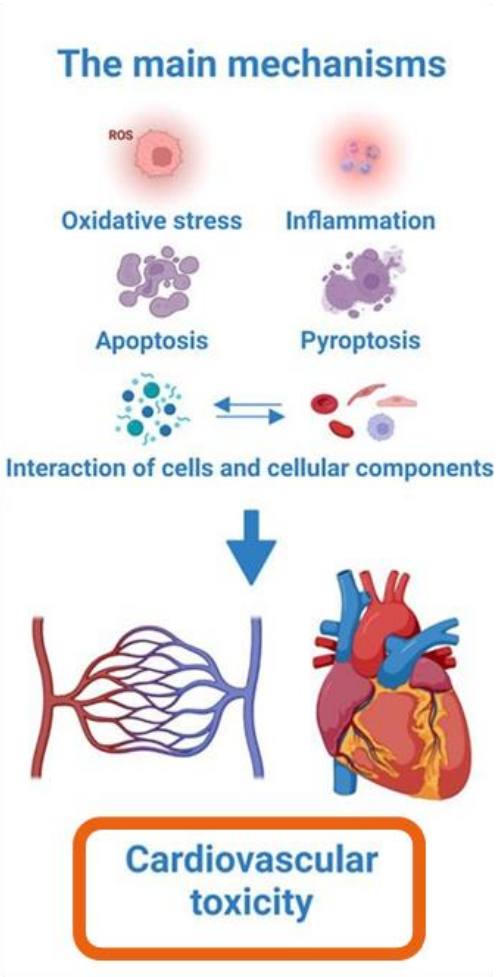


Sources of micro-nanoplastic contamination

WWF ANALYSIS INT 2019

Entry and accumulation of micro-nanoplastics in the human body: cardiovascular effects





Zhu X, et al., Micro- and nanoplastics: a new cardiovascular risk factor? Environ Int 2023;171:107662.

PLASTIC POLLUTION GAP IN CVD

- Accumulation of micro-nanoplastics in human arteries?
- Accumulation of micro-nanoplastics and CVD?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Microplastics and Nanoplastics in Atheromas and Cardiovascular Events

R. Marfella, F. Prattichizzo, C. Sardu, G. Fulgenzi, L. Graciotti, T. Spadoni, N. D'Onofrio, L. Scisciola, R. La Grotta, C. Frigé, V. Pellegrini, M. Municinò, M. Siniscalchi, F. Spinetti, G. Vigliotti, C. Vecchione, A. Carrizzo, G. Accarino, A. Squillante, G. Spaziano, D. Mirra, R. Esposito, S. Altieri, G. Falco, A. Fenti, S. Galoppo, S. Canzano, F.C. Sasso, G. Matacchione, F. Olivieri, F. Ferraraccio, I. Panarese, P. Paolisso, E. Barbato, C. Lubritto, M.L. Balestrieri, C. Mauro, A.E. Caballero, S. Rajagopalan, A. Ceriello, B. D'Agostino, P. Iovino, and G. Paolisso

N Engl J Med 2024;390:900-910.

The NEW ENGLAND JOURNAL of MEDICINE

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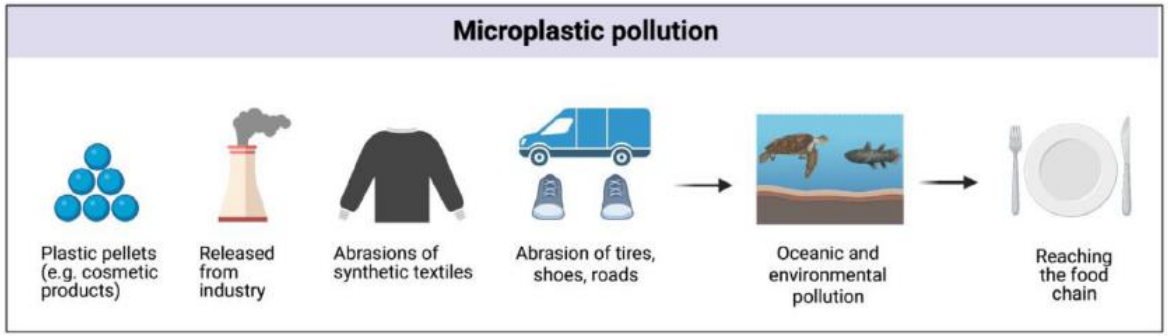
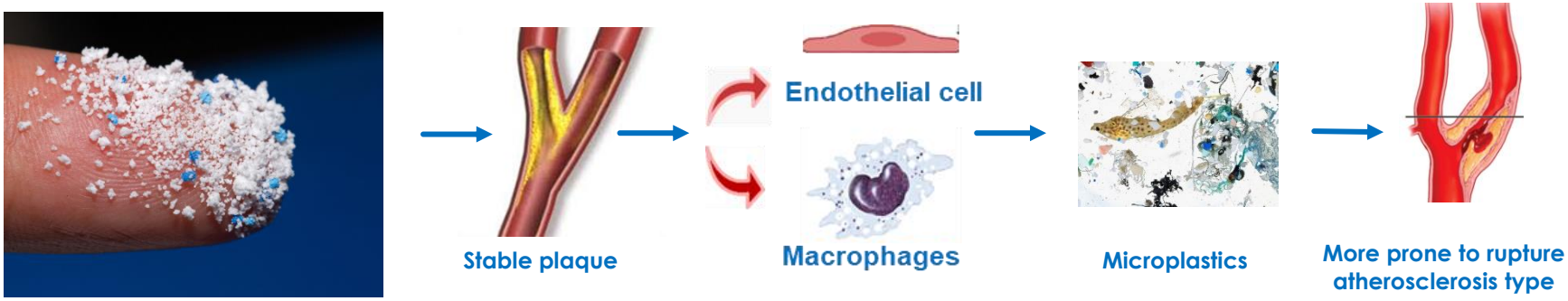
Hypothesis





N Engl J Med 2024;390:900-910.

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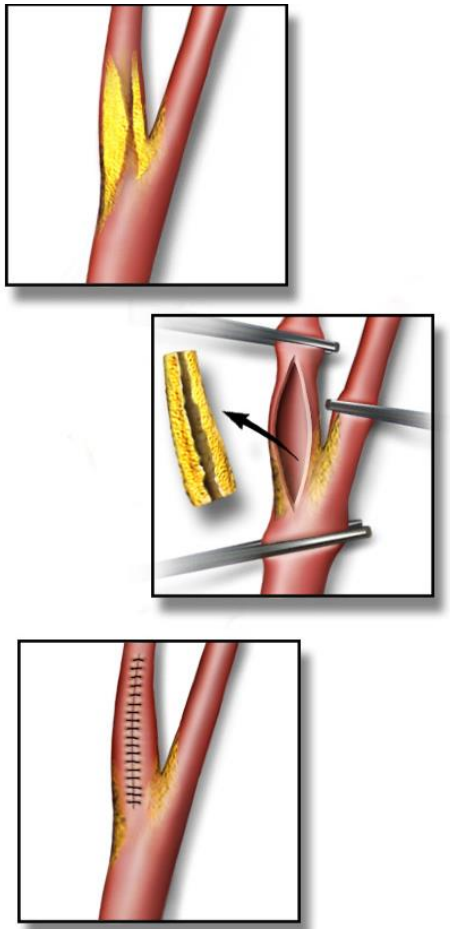
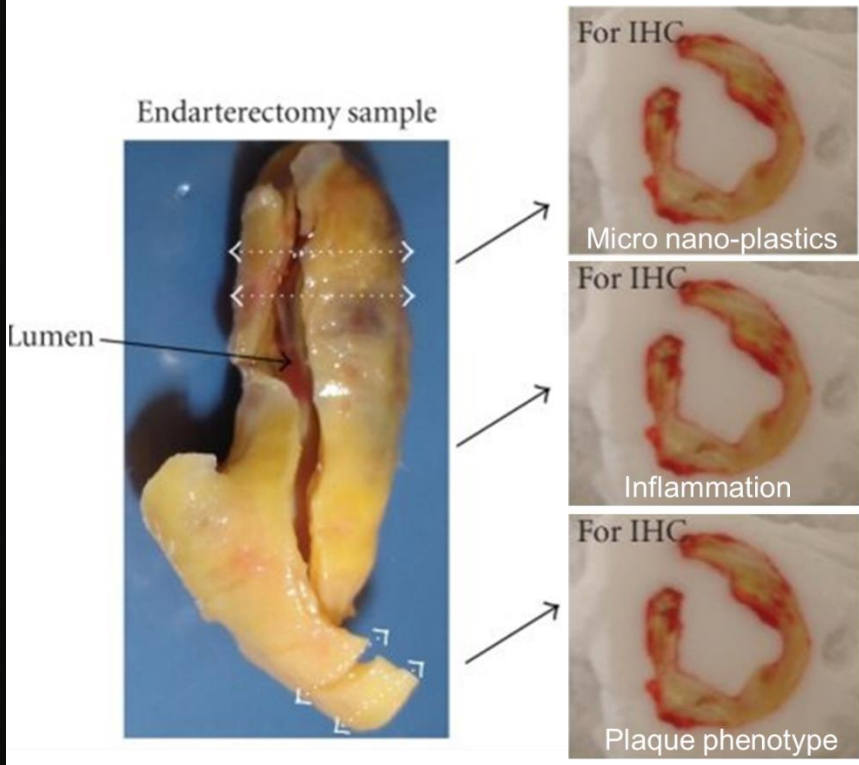
Endarterectomy





N Engl J Med 2024;390:900-910.

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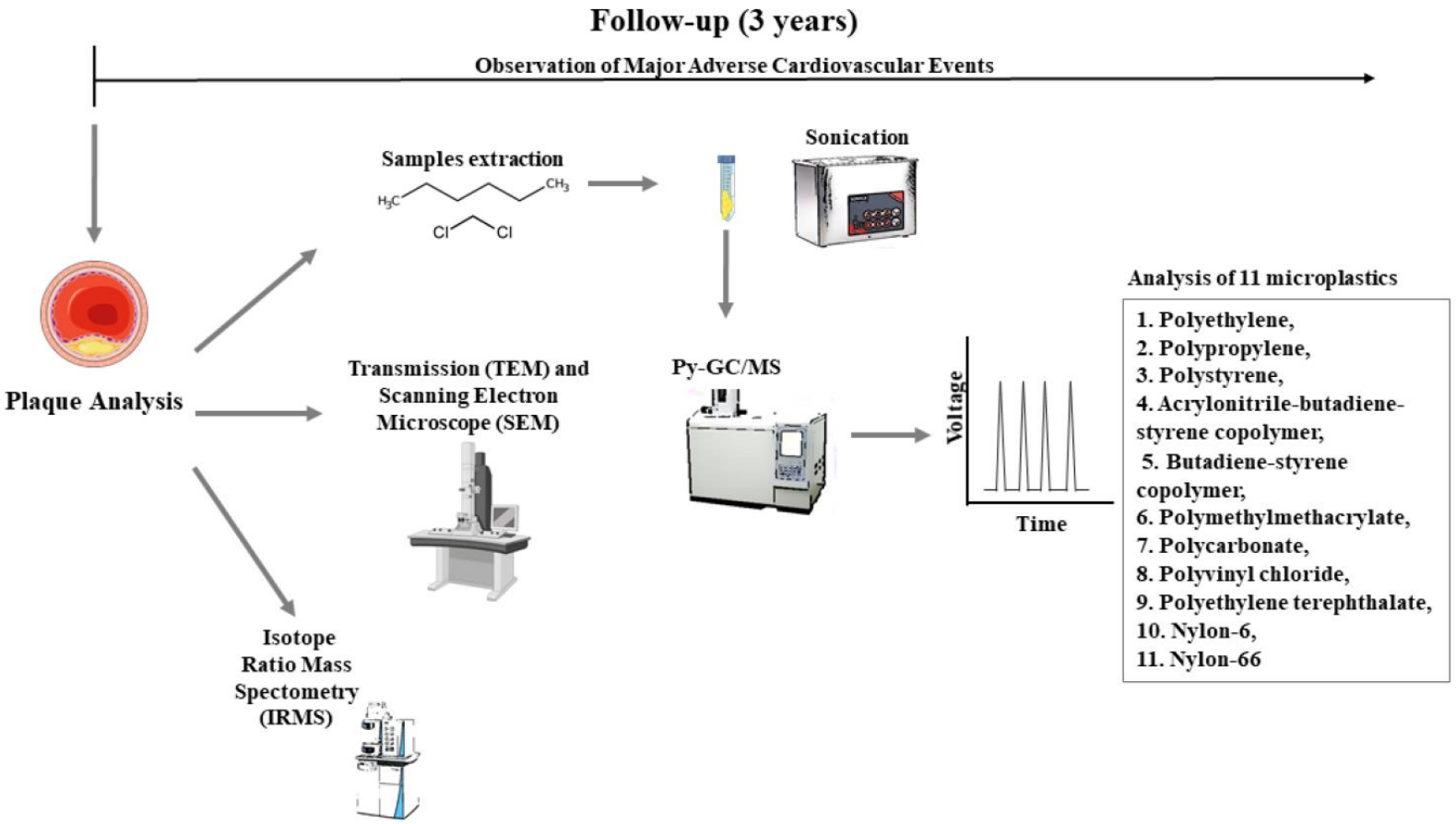

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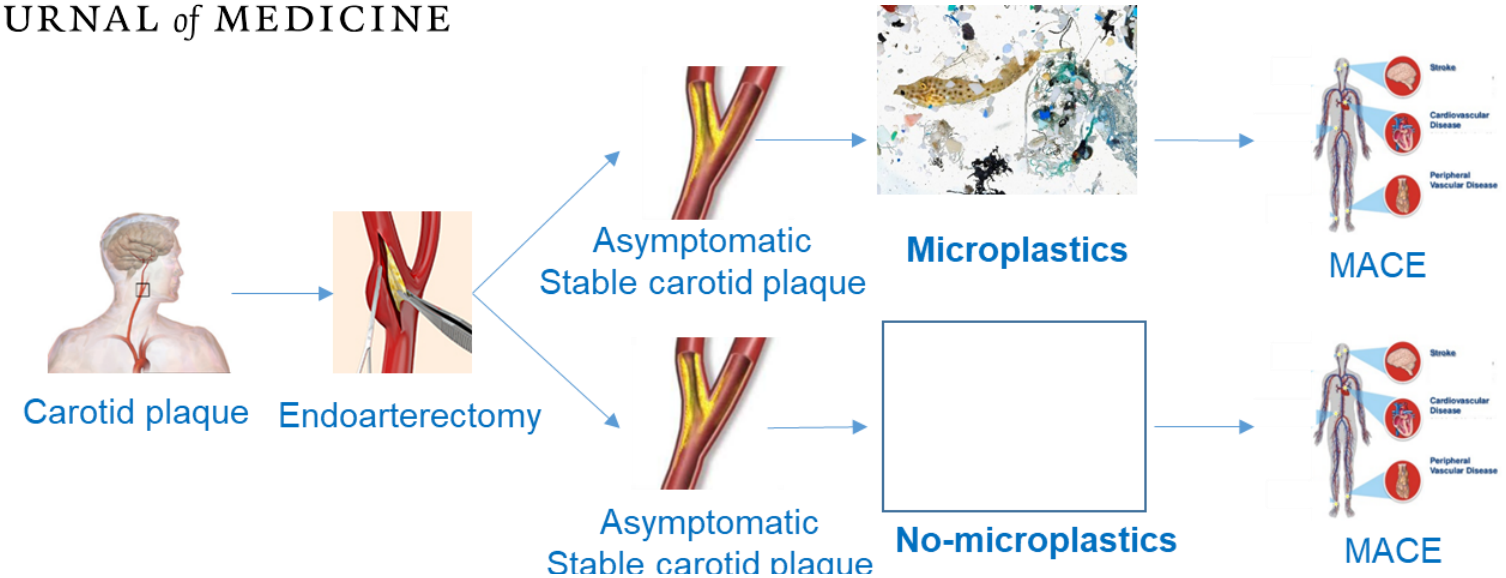

Patients without micro-nanoplastics

Patients with micro-nanoplastics

Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7
High Risk Patients	Month 6	Month 12	Month 18	Month 24	Month 30	Month 36
• Clinical evaluation • Routine analysis • Eco-doppler TSA • ECG monitoring • Echocardiography • Inclusion/Exclusion Criteria • EPCs isolation and culture • Cytokines	• Clinical evaluation • Routine analysis • Ecodoppler TSA	• Clinical evaluation • Routine analysis • ECG • Echocardiography • Eco-doppler TSA	• Clinical evaluation • Routine analysis • ECG • Echocardiography • Eco-doppler TSA	• Clinical evaluation • Routine analysis • ECG • Echocardiography • Eco-doppler TSA	• Clinical evaluation • Routine analysis • ECG • Echocardiography • Eco-doppler TSA	• Clinical evaluation • Routine analysis • Eco-doppler TSA • ECG monitoring • Echocardiography • Inclusion/Exclusion Criteria • MACE

N Engl J Med 2024;390:900-910.

Microplastics and Nanoplastics in Atheromas and Cardiovascular Events

PRIMARY ENDPOINT	SECONDARY ENDPOINT
Composite of nonfatal myocardial infarction, nonfatal stroke, or death from any cause among patients with plaque containing MNPs and patients with plaque that did not contain MNPs.	Tissue levels biomarkers interleukin-18, interleukin-1β, TNF-α, interleukin-6, CD68, CD3, and collagen in patients with evidence of MNPs as compared with those without.

R Marfella et al. N Engl J Med 2024;390:900-910.

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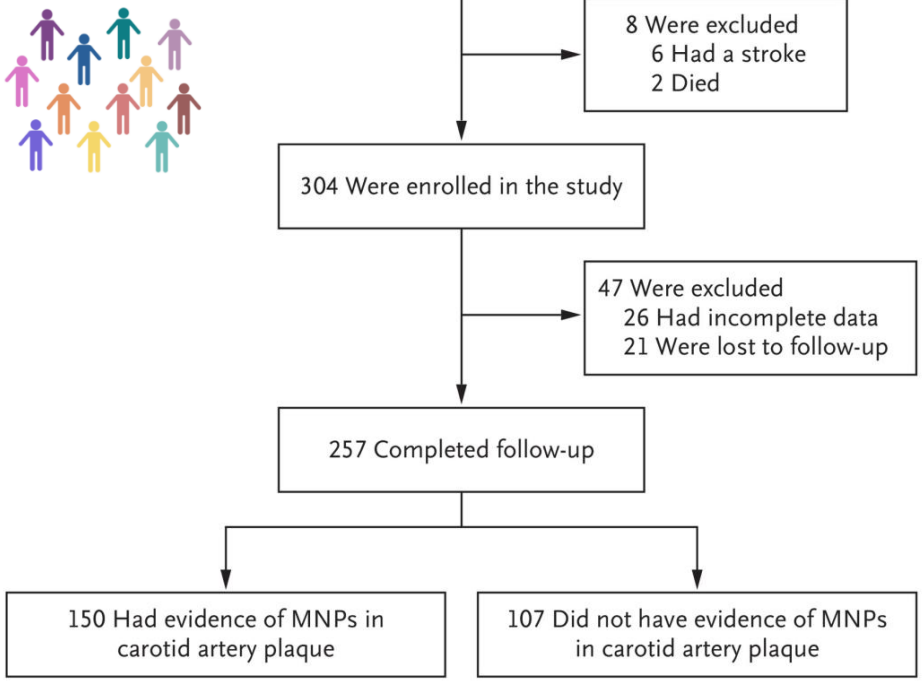
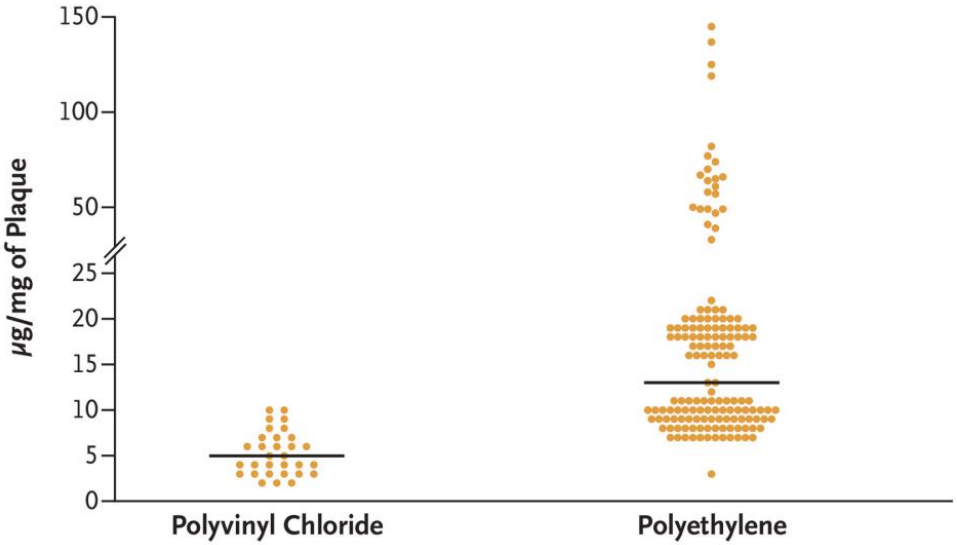
Microplastics and Nanoplastics in Atheromas and Cardiovascular Events

MNPs in Carotid Artery Plaque





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R Marfella et al. N Engl J Med 2024;390:900-910.

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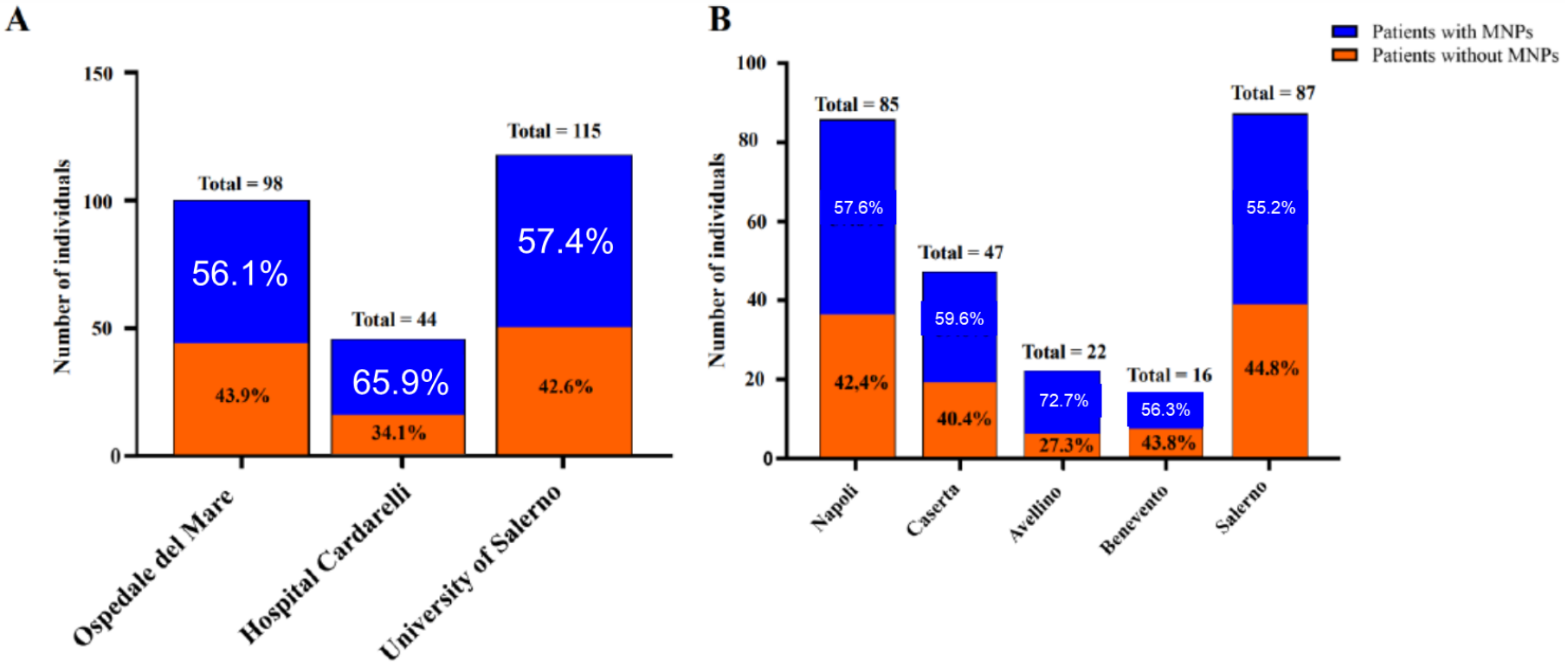
N Engl J Med 2024;390:900-910.

Figure S2. Proportion of individuals with MNPs among different centers of recruitment (A) and areas of living (B).



Microplastics and Nanoplastics in Atheromas and Cardiovascular Events

Characteristics of the Patients at Baseline

Table 1. Characteristics of the Patients at Baseline.*

Variable	MNPs Present (N=150)	MNPs Not Present (N=107)
Age (IQR) — yr	71 (65–75)	73 (67–77)
Male sex — no. (%)	116 (77.3)	79 (73.8)
Body-mass index (IQR)†	28 (27–29)	28 (26–29)
Hypertension — no. (%)	78 (52.0)	69 (64.5)
Systolic blood pressure (IQR) — mm Hg	124 (118–130)	127 (118–129)
Diastolic blood pressure (IQR) — mm Hg	78 (75–83)	77 (75–85)
Heart rate (IQR) — beats/min	85 (79–91)	81 (76–86)
Stenosis severity (IQR) — %	77 (73–83)	78 (73–83)
Diabetes — no. (%)	36 (24.0)	32 (29.9)
Cardiovascular disease — no. (%)‡	50 (33.3)	35 (32.7)
Dyslipidemia — no. (%)	55 (36.7)	40 (37.4)
Total cholesterol (IQR) — mg/dl	150 (145–158)	147 (139–158)
LDL cholesterol (IQR) — mg/dl	77 (69–84)	74 (69–82)
HDL cholesterol (IQR) — mg/dl	42 (40–43)	42 (40–44)
Triglycerides (IQR) — mg/dl	178 (165–192)	182 (163–193)
Creatinine (IQR) — mg/dl	1.00 (0.90–1.10)	0.96 (0.96–1.06)
Smoker — no. (%)	24 (16.0)	17 (15.9)
Medication use — no. (%)		
Beta-blockers	48 (32.0)	35 (32.7)
ACE inhibitors	75 (50)	53 (49.5)
ARBs	35 (23.3)	31 (29.0)
Calcium-channel blockers	13 (8.7)	8 (7.5)
Diuretics	17 (11.3)	16 (15.0)
Heparin	12 (8.0)	10 (9.3)
Antiplatelet drugs	146 (97.3)	105 (98.1)
Statin	143 (95.3)	101 (94.4)
Ezetimibe	26 (17.3)	20 (18.7)

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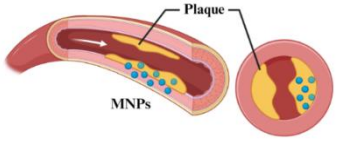
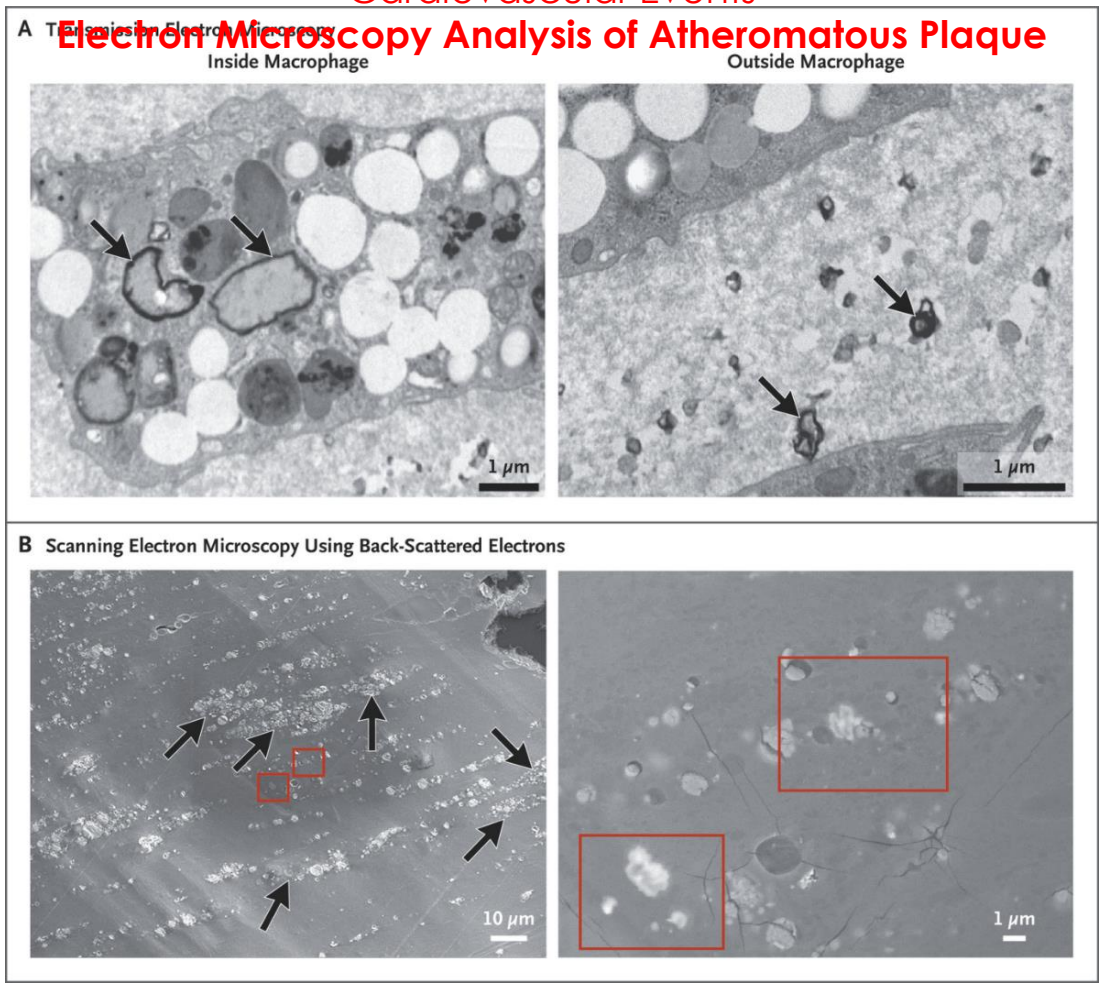
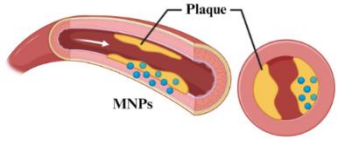
Microplastics and Nanoplastics in Atheromas and Cardiovascular Events

R Marfella et al. N Engl J Med 2024;390:900-910.



Electron Microscopy Analysis of Atheromatous Plaque





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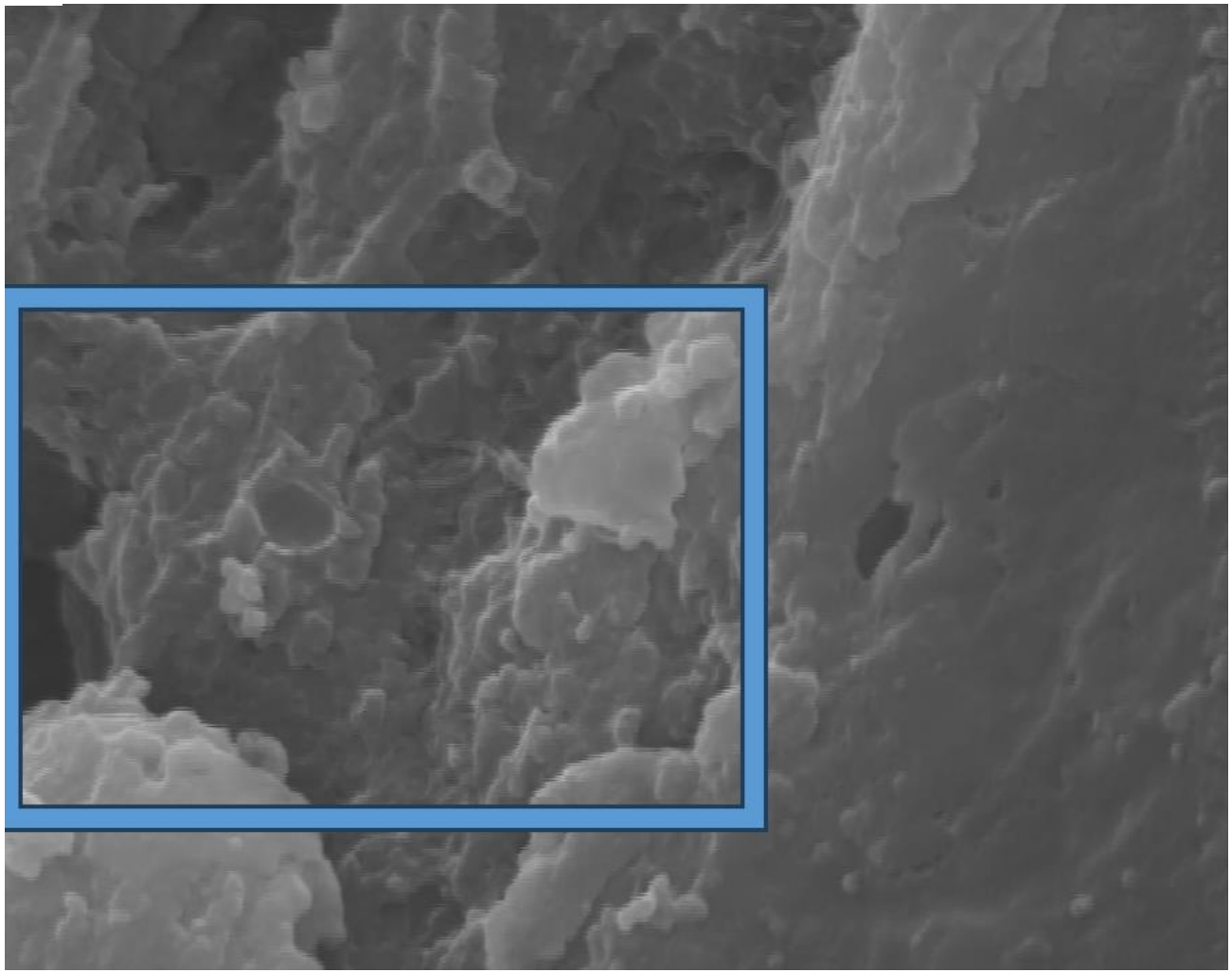

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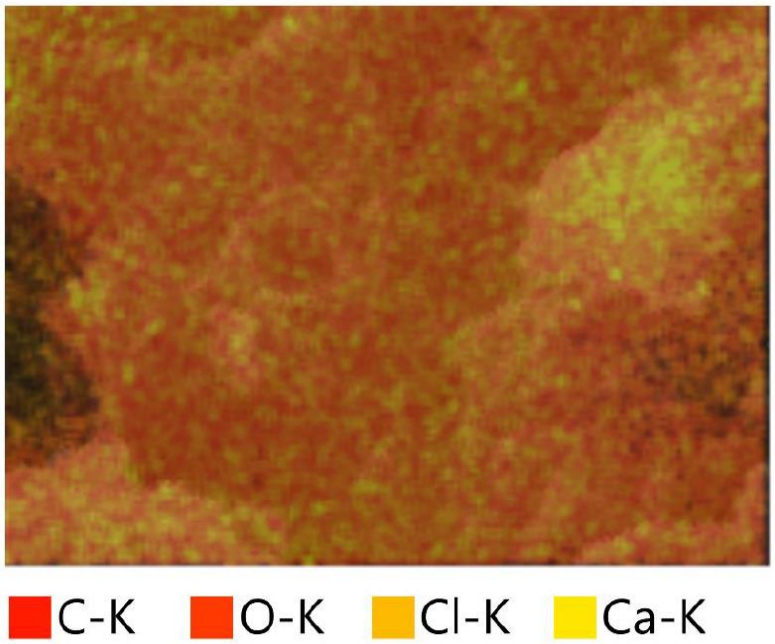

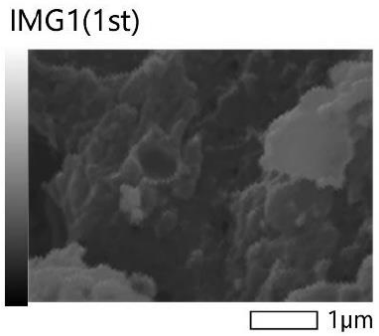

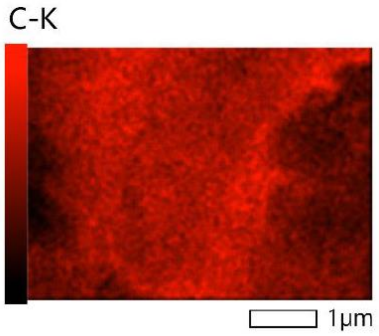

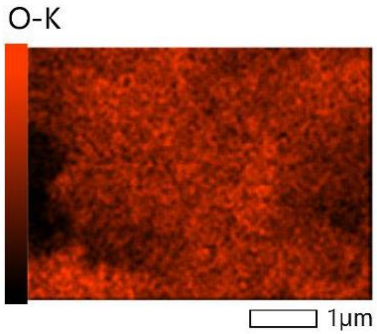

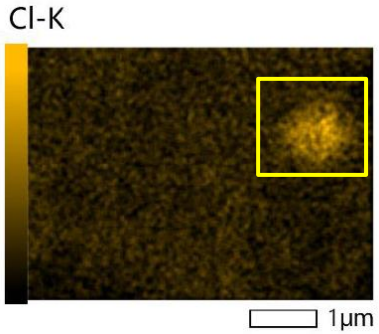

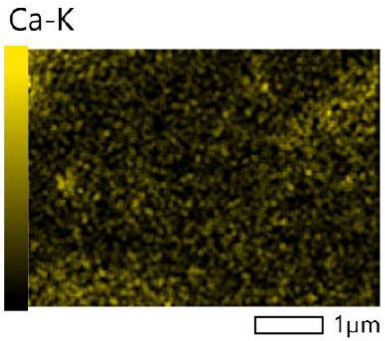

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Microplastics and Nanoplastics in Atheromas and Cardiovascular Events

Inflammatory Markers in plaque sample

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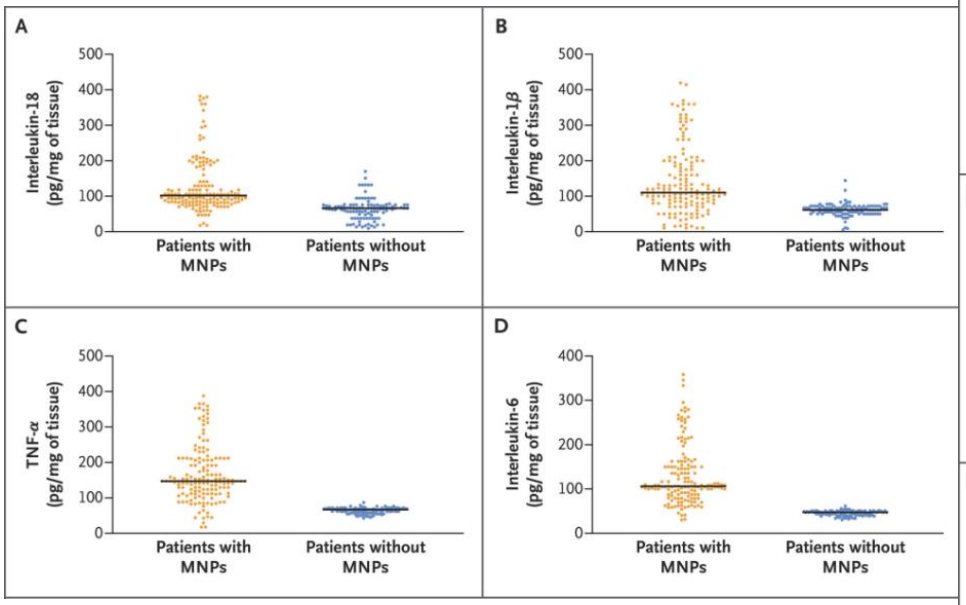

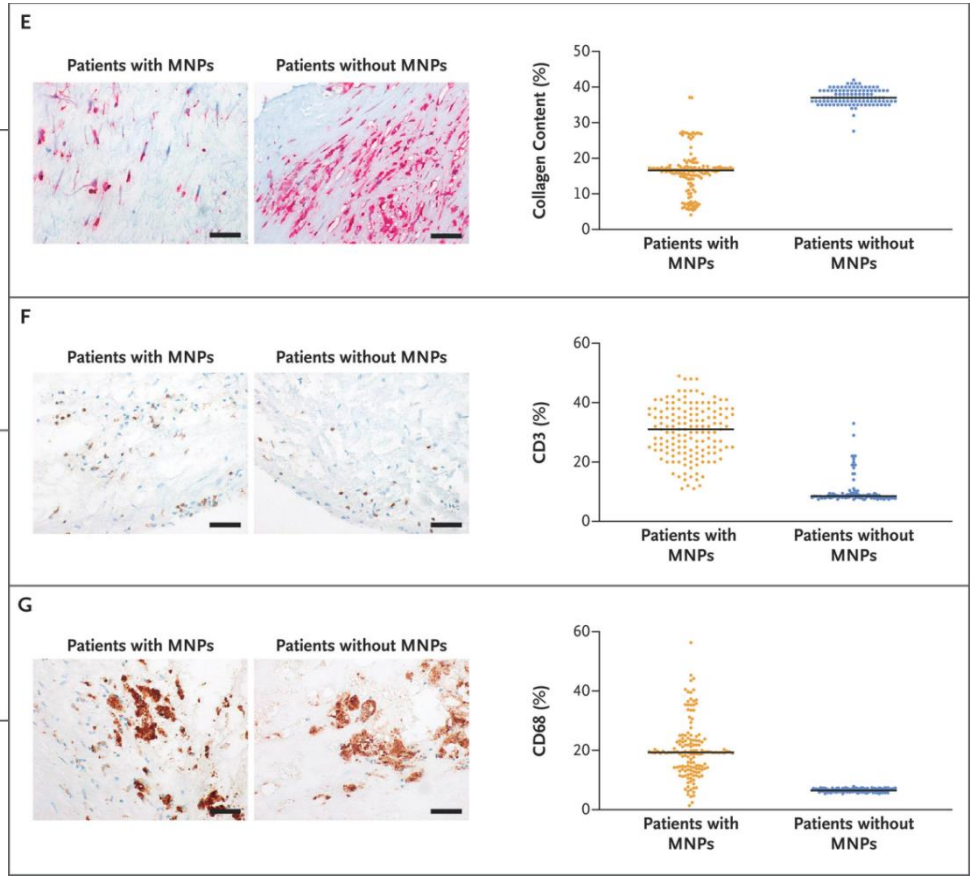

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ORIGINAL ARTICLE

Microplastics and Nanoplastics in Atheromas and Cardiovascular Events

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Published March 6, 2024 | N Engl J Med 2024;390:900-910 | DOI: 10.1056/NEJMoa2309822 | VOL. 390 NO. 10

comments on PubPeer (by: Cortinarius Sanguineus, Cylindrospermopsis Philippinensis)

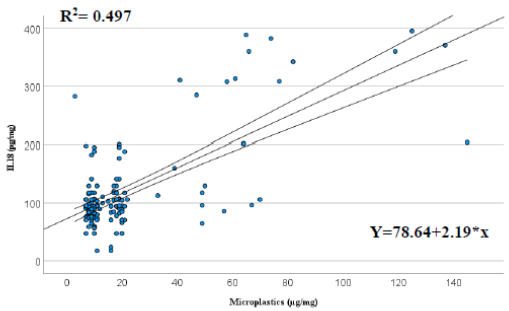
Abstract

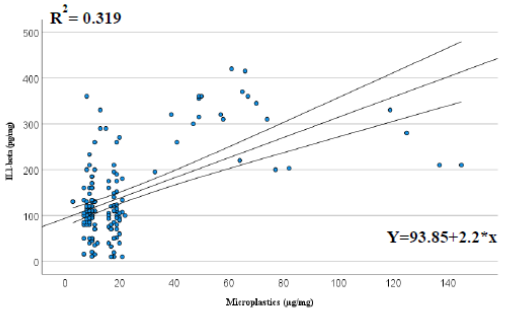
BACKGROUND

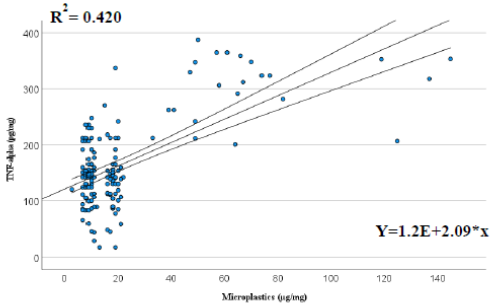
Microplastics and nanoplastics (MNPs) are emerging as a potential risk factor for cardiovascular disease in preclinical studies. Direct evidence that this risk extends to humans is lacking.

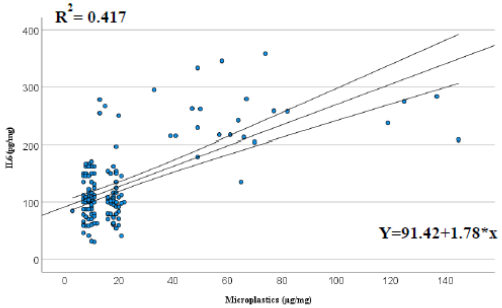
METHODS

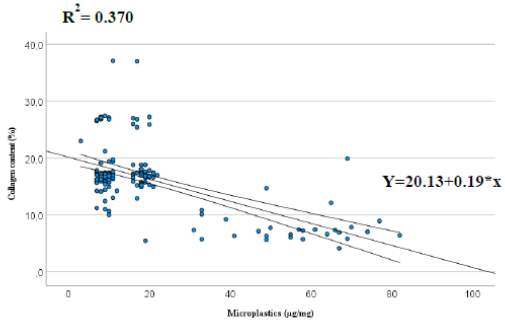
We conducted a prospective, multicenter, observational study involving patients who were undergoing carotid endarterectomy for asymptomatic carotid artery disease. The excised carotid plaque specimens were analyzed for the presence of MNPs with the use of pyrolysis–gas chromatography–mass spectrometry, stable isotope analysis, and electron microscopy. Inflammatory biomarkers were assessed with enzyme-linked immunosorbent assay and immunohistochemical assay. The primary end point was a composite of myocardial infarction, stroke, or death from any cause among patients who had evidence of MNPs in plaque as compared with patients with plaque that showed no evidence of MNPs

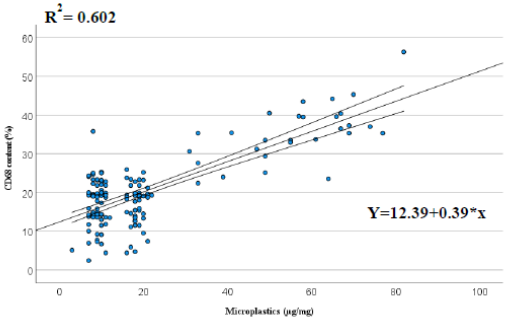












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Microplastics and Nanoplastics in Atheromas and Cardiovascular Events:

Associations between the presence of MNPs and cardiovascular events

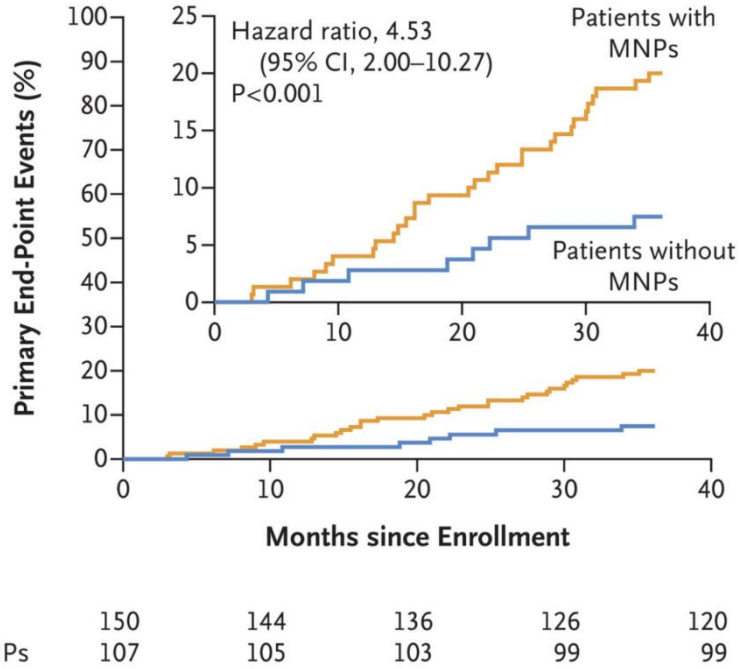

Table S3. Cox regression analysis for the primary outcome.

Variables	Hazard Ratio (95% Confidence Interval)
Presence of MNPs	4.53 (2.00 – 10.27)
Age	1.04 (0.98 – 1.09)
Sex	0.55 (0.26 – 2.00)
Body-mass index*	0.82 (0.68 – 0.97)
Diabetes	4.76 (2.35 – 9.60)
Hypertension	1.37 (0.69 – 2.72)
Cardiovascular diseases+	1.65 (0.80 – 3.41)
Total cholesterol	1.01 (0.97 – 1.04)
LDL cholesterol	0.96 (0.93 – 1.00)
HDL cholesterol	0.97 (0.86 – 1.09)
Triglycerides	1.01 (1.00 – 1.03)
Creatinine	0.30 (0.04 – 2.46)

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ESC European Society of Cardiology

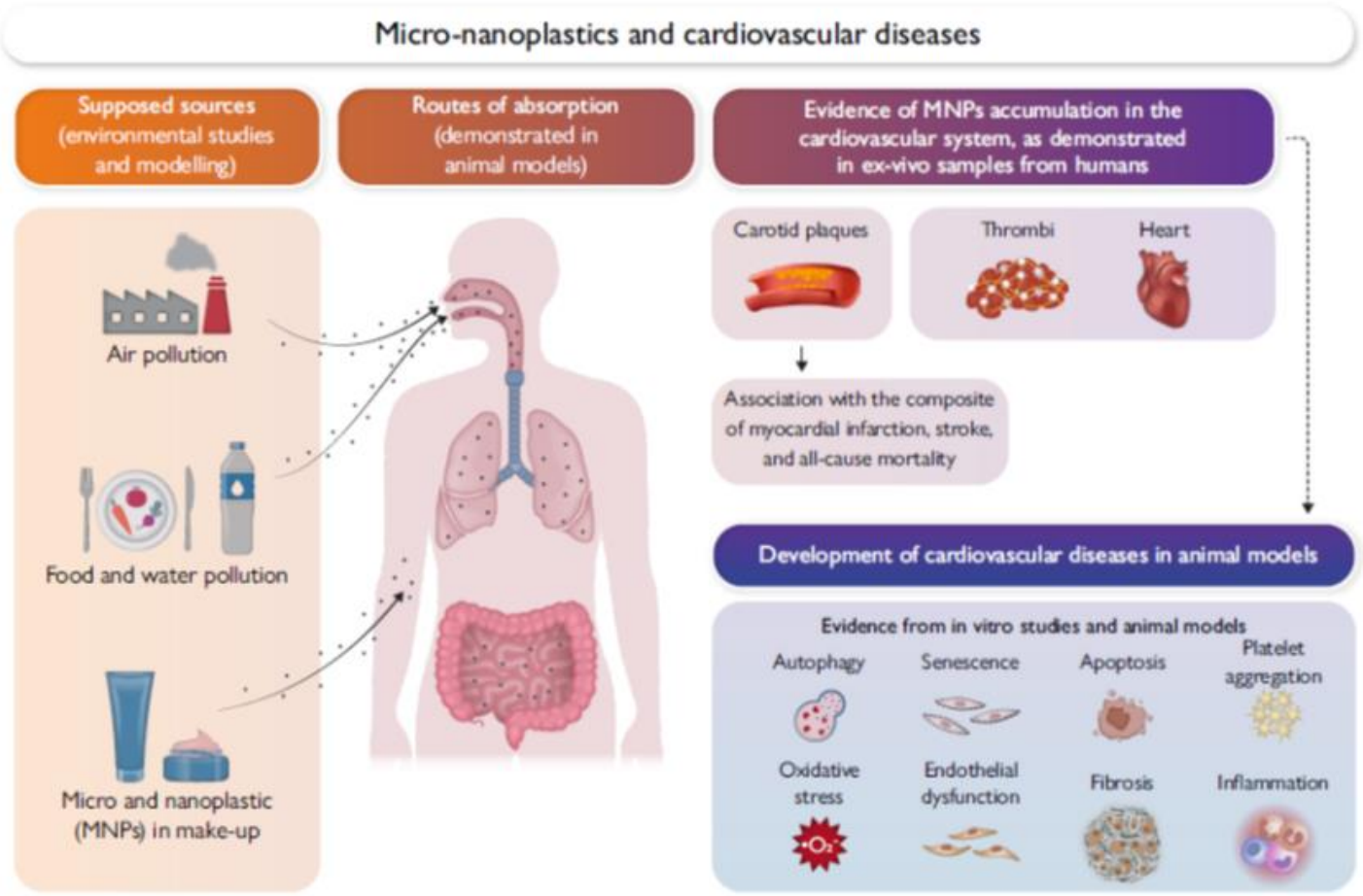
European Heart Journal (2024) **00**, 1–12
https://doi.org/10.1093/eurheartj/ehae552

STATE OF THE ART REVIEW

Epidemiology, prevention, and health care policies

Micro-nanoplastics and cardiovascular diseases: evidence and perspectives

Francesco Prattichizzo [1]*, Antonio Ceriello[1]*, Valeria Pellegrini[1], Rosalba La Grotta[1], Laura Graciotti[2], Fabiola Olivieri[3,4], Pasquale Paolisso [5], Bruno D'Agostino[6], Pasquale Iovino[6], Maria Luisa Balestrieri[7], Sanjay Rajagopalan[8], Philip J. Landrigan[9,10], Raffaele Marfella[11]†, and Giuseppe Paolisso[11,12]†



Prevention

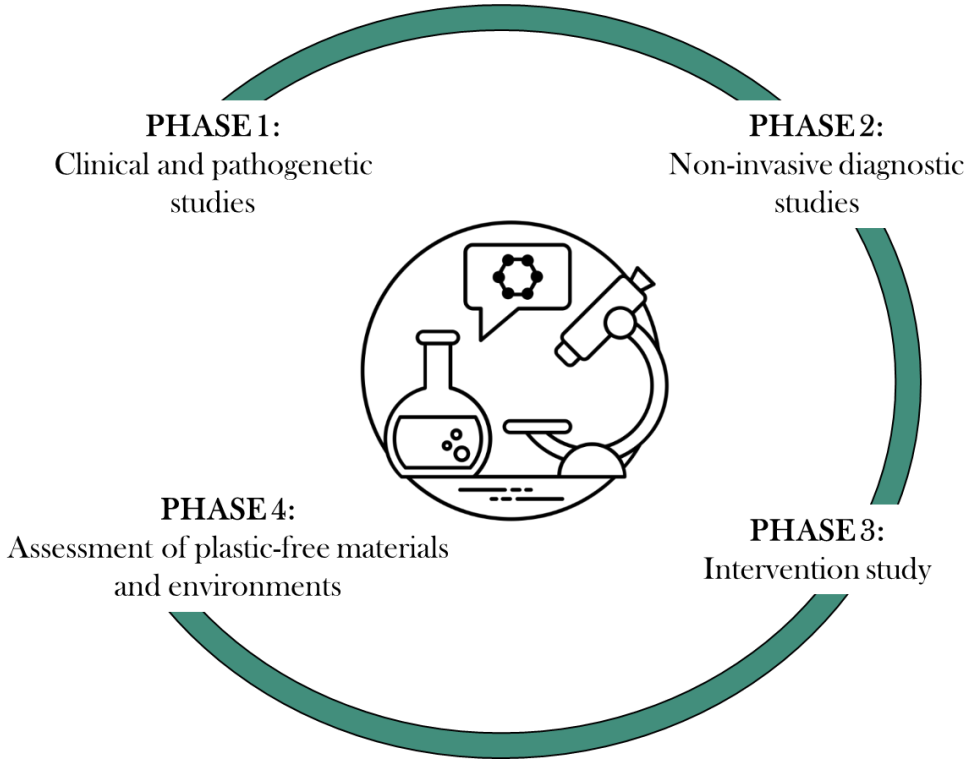

What can we do?
• Reducing the use of single-use plastics
• Ensuring plastics are recycled properly
• Using eco-friendly alternative plastic products, such as reusable water bottles, reusable bags, and stainless steel or wooden cutlery.
• Avoiding products containing microplastics, such as some laundry detergents, facial exfoliants, and cosmetics containing plastic microbeads.

What can we do now to reduce the MNP's effects on health?

MNPs Vanvitelli Research Center

Università
degli Studi
della Campania
Luigi Vanvitelli

Scuola di Medicina e Chirurgia
Dipartimento di Scienze Mediche e Chirurgiche Avanzate



THE FACTS

10 MILLION

TONS OF PLASTIC ARE DUMPED IN OUR OCEANS ANNUALLY. THAT'S EQUAL TO MORE THAN A GARBAGE TRUCK LOAD EVERY MINUTE!

50%

OF ALL PLASTIC PRODUCED (380 MILLION TONS PER YEAR) IS FOR SINGLE-USE PURPOSES - USED FOR JUST MINUTES AND THEN THROWN AWAY

100%

OF MUSSELS TESTED HAVE CONTAINED MICROPLASTICS

1 MILLION

MARINE ANIMALS ARE KILLED BY PLASTIC POLLUTION EVERY YEAR

LESS THAN

9%

OF ALL PLASTIC GETS RECYCLED

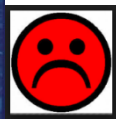
HUMANS EAT OVER

40 POUNDS

OF PLASTIC IN THEIR LIFETIME

"THERE WILL BE MORE PLASTIC IN OUR OCEANS THAN FISH BY 2050."

The Ellen MacArthur Foundation



NewScientist

Health

Microplastics linked to a greater risk of heart attack and stroke

People with artery plaques containing microplastics were about four times as likely to have a heart attack or stroke as those with plastic-free plaques

By Grace Wade

6 March 2024

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Environment

Microscopic plastics could raise risk of stroke and heart attack, study says

Scientists link tiny particles in blood vessels with substantially higher risk of death

Ian Sample *Science editor*

@iansample

Wed 6 Mar 2024 23.00 CET

REUTERS

Healthcare & Pharmaceuticals

Plastic lodged in arteries may be linked to higher risk of heart disease and death

By Nancy Lapid

March 6, 2024 11:30 PM GMT+1 · Updated 11 hours ago

March 6 (Reuters) - Minuscule pieces of plastic lodged in the fatty deposits that line human arteries may be linked with higher risks for heart disease, strokes, and death, Italian researchers reported on Wednesday.

Among 304 patients who underwent procedures to clear a major artery in the neck, 58% were found to have microscopic and nanoscopic "jagged-edged" pieces of plastic in the plaque lining the blood vessel, including polyethylene and polyvinyl chloride containing chlorine, Dr. Raffaele Marfella at the University of Campania in Naples and colleagues reported.

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What is a microplastic?

Arab News Network • Source: Oman News Agency

Editorial | AE | Mar 07 · 11:59 PM

Study Links Nanoplastics to Heart Attack, Stroke, Early Death

A groundbreaking study published in the *New England Journal of Medicine* reveals a significant association between *microplastic* and ...

New England Journal of Medicine,microplastic,Marfella

NBC NEWS

HEALTH NEWS

Doctors found tiny nanoplastics in people's arteries. Their presence was tied to a higher risk of heart disease.

The new research is the first to associate such plastics inside the body with heart attack, stroke or death.

Salute

Microplastiche nelle placche delle arterie: più che raddoppiato il rischio di infarto e ictus, lo studio italiano

IL MATTINO

Microplastiche, provati per la prima volta i danni causati alle arterie: raddoppia il rischio di infarto e ictus. «Scoperta rivoluzionaria»

Lo studio, ideato e coordinato dall'Università della Campania 'Luigi Vanvitelli' è pubblicato su The New England Journal of Medicine

The New York Times

Business Arts Lifestyle Opinion Audio Games Cooking Wirecutter

Microplastics Are a Big Problem, a New Film Warns

At SXSW, a documentary traces the arc of plastics in our lives, and highlights evolving research of the potential harm of its presence in our bodies.

Share full article 19

Microplastic nurdles, or virgin plastic beads, found discharged in waterways near Point Comfort, Texas. Plastic People: The Hidden Crisis of Microplastics