Air Pollution and Hypertension

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OUTLINEs

- ✓The importance of cardiovascular effects of air pollution.
- ✓ The mechanism of cardiovascular complications
- ✓Strategies to mitigate the effects

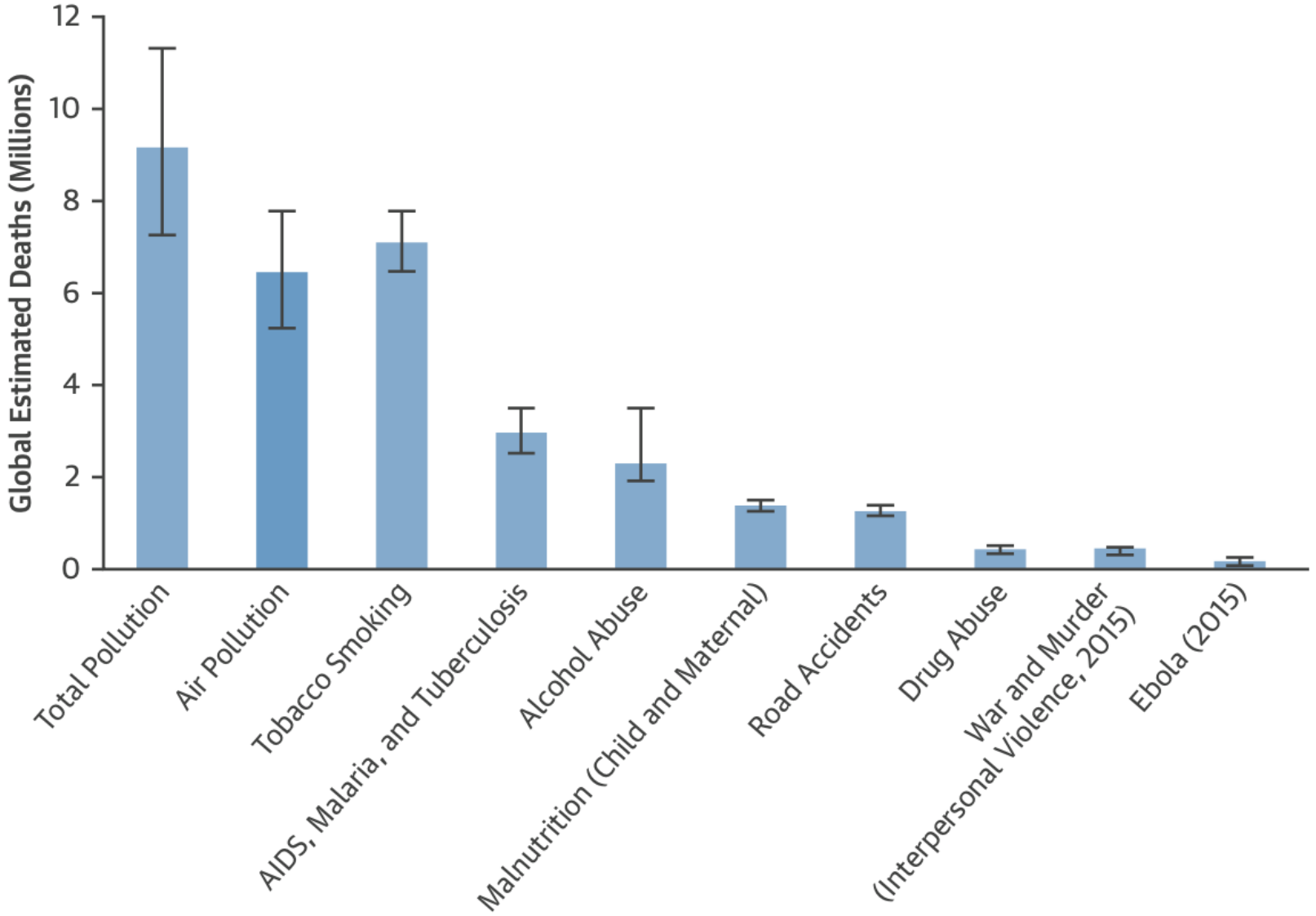
Ambient (outdoor) air pollution

- Air pollution is one of the greatest environmental risk to health. By reducing air pollution levels, countries can reduce the burden of disease from stroke, heart disease, lung cancer, and both chronic and acute respiratory diseases, including asthma.
- The lower the levels of air pollution, the better the cardiovascular and respiratory health of the population will be, both long- and short-term.
- In 2019, 99% of the world population was living in places where the WHO air quality guidelines levels were not met.

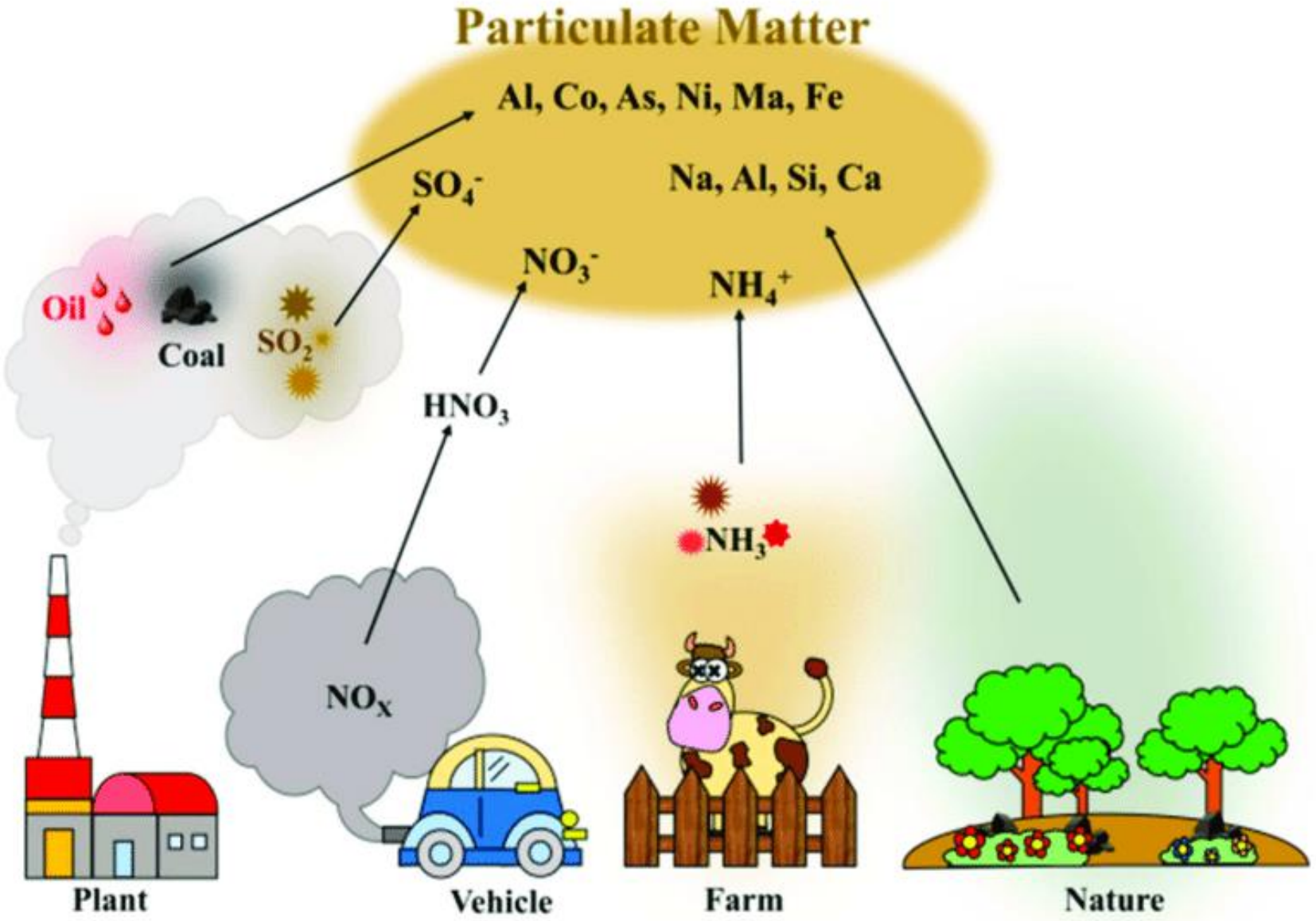
Ambient (outdoor) air pollution

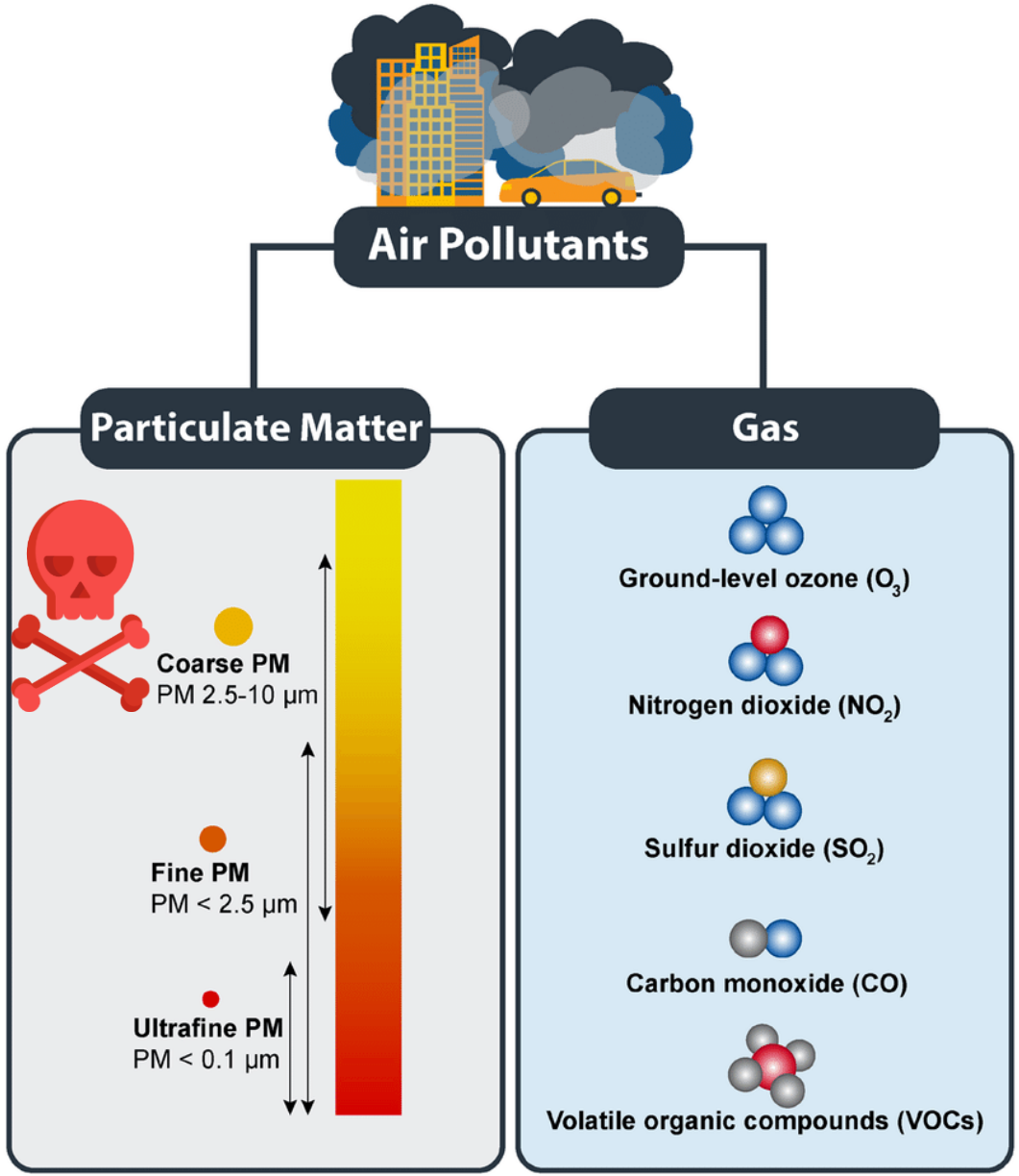
- Ambient (outdoor air pollution) in both cities and rural areas was estimated to cause 4.2 million premature deaths worldwide in 2016.
- Some 91% of those premature deaths occurred in low- and middle-income countries, and the greatest number in the WHO South-East Asia and Western Pacific regions.

The Contribution of Air Pollution Versus Other Risk Factors to Global Mortality

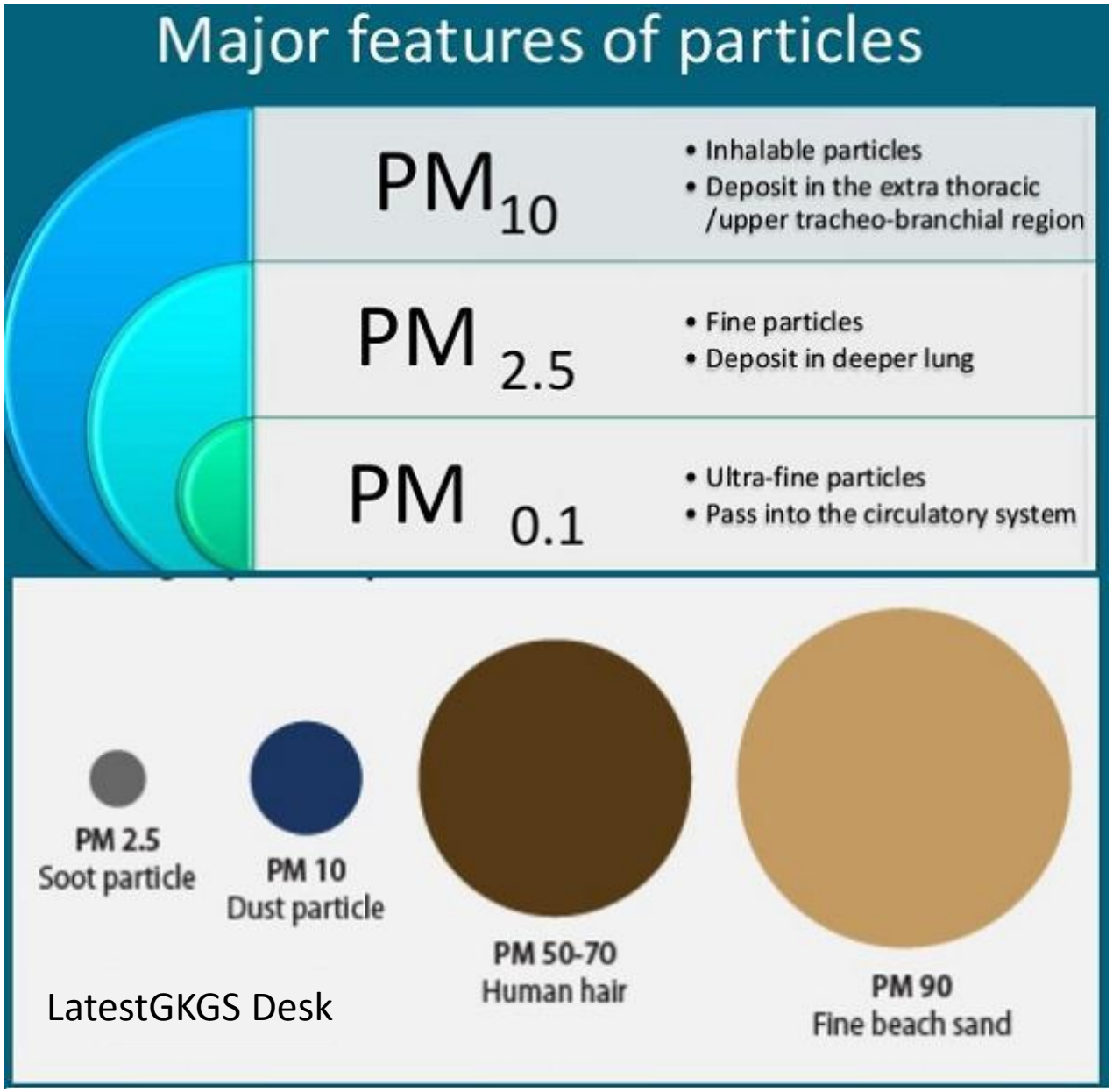


J Am Coll Cardiol 2018;72:2054-70


Particulate Matter
Al, Co, As, Ni, Ma, Fe
Na, Al, Si, Ca
SO_4^-
NO_3^-
NH_4^+
Oil
Coal
SO_2
HNO_3
NH_3
NO_X
Plant
Vehicle
Farm
Nature



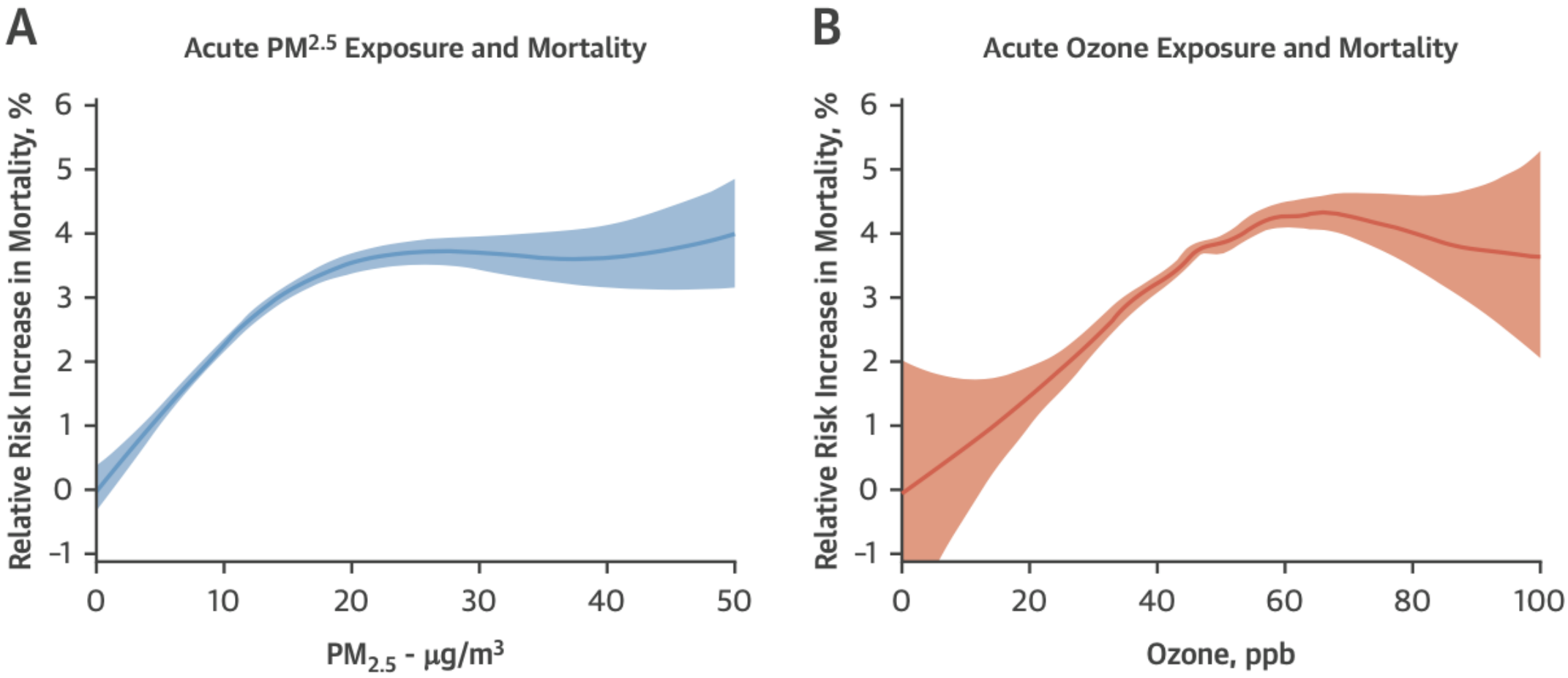
Asian Pac J Allergy Immunol DOI 10.12932/AP-100619-0579


Major features of particles
PM10
• Inhalable particles
• Deposit in the extra thoracic /upper tracheo-branchial region
PM 2.5
• Fine particles
• Deposit in deeper lung
PM 0.1
• Ultra-fine particles
• Pass into the circulatory system
PM 2.5
Soot particle
PM 10
Dust particle
PM 50-70
Human hair
PM 90
Fine beach sand
LatestGKGS Desk

- ✓Air pollution not only exacerbates the course of cardiovascular diseases, but also contributes to their development.

- ✓Increase all-cause and cardiovascular mortality.

Exposure-Response Relationship of Short- and Long-Term Effects of $PM_{2.5}$ and Ozone With Mortality



J Am Coll Cardiol 2018;72:2054-70

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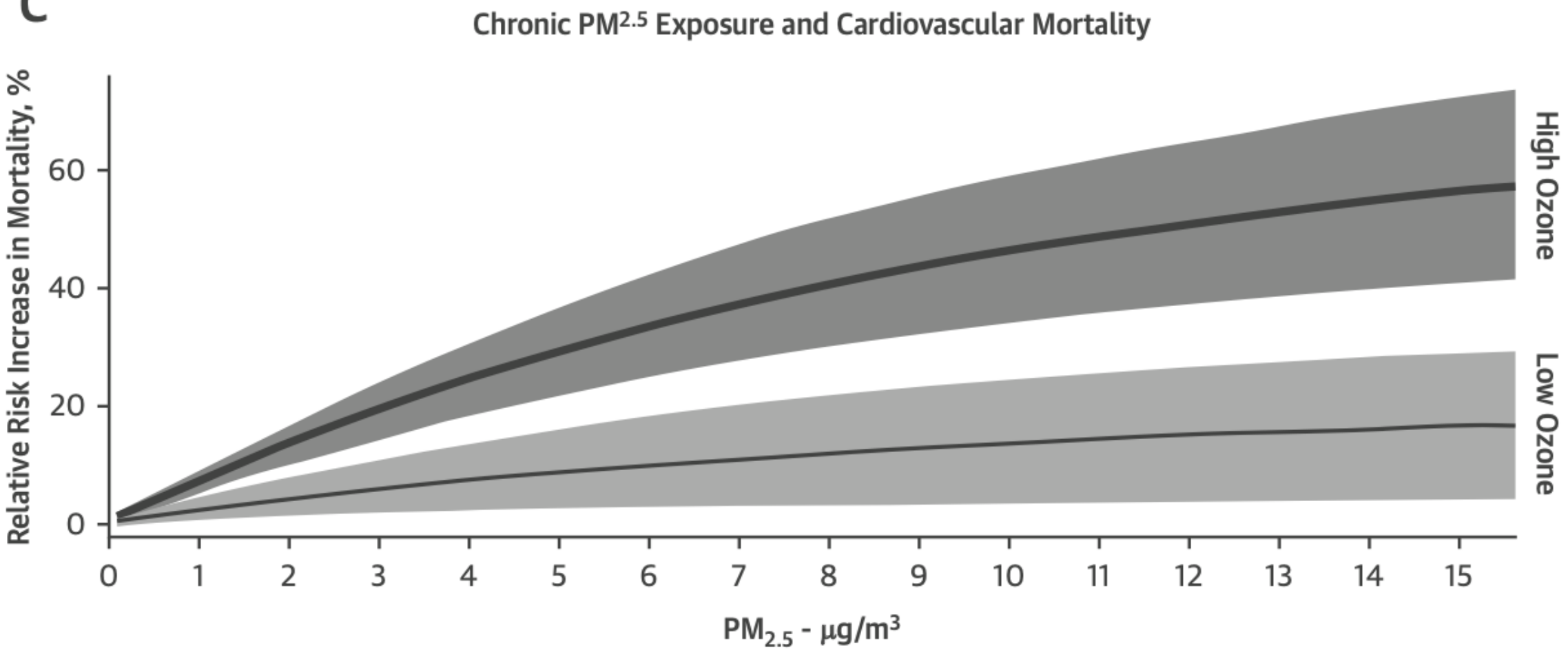
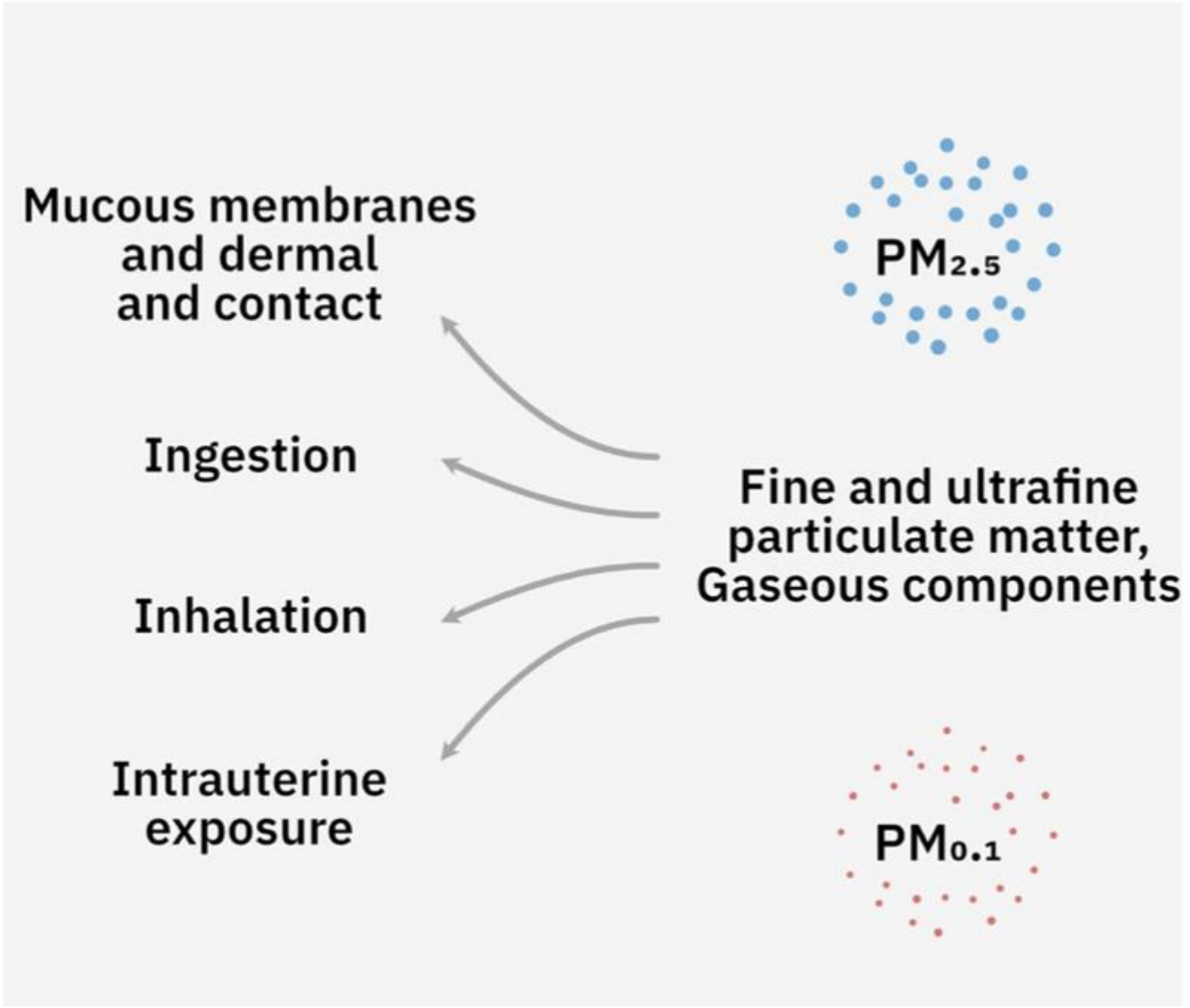


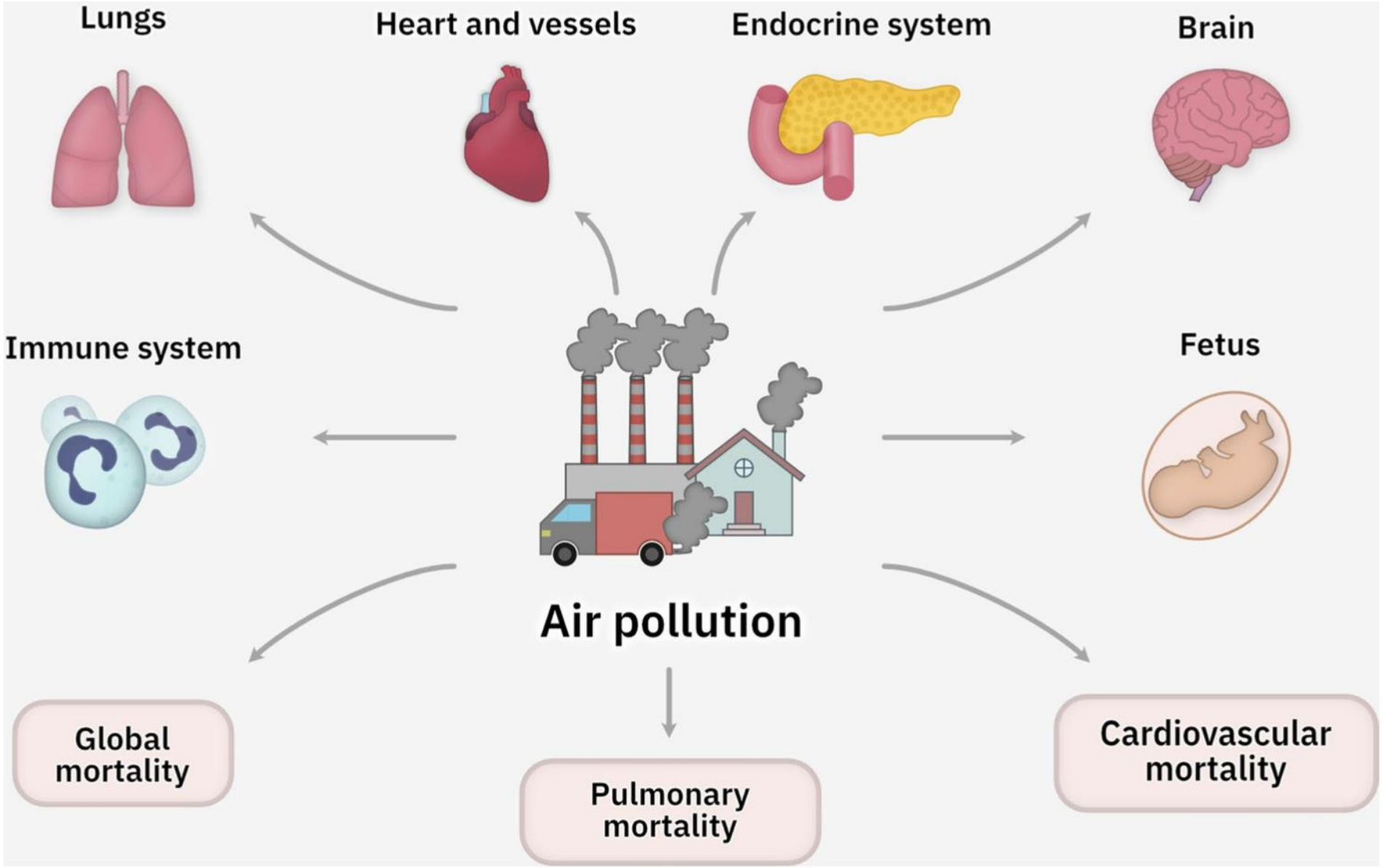
J Am Coll Cardiol 2018;72:2054-70

✓The cardiovascular response to air pollution is modulated by:

- the chemical composition of the pollutants
- exposure concentration,
- duration of exposure,
- comorbidities,
- individual vulnerability,
- changes in humidity, temperature, and ambient pressure.

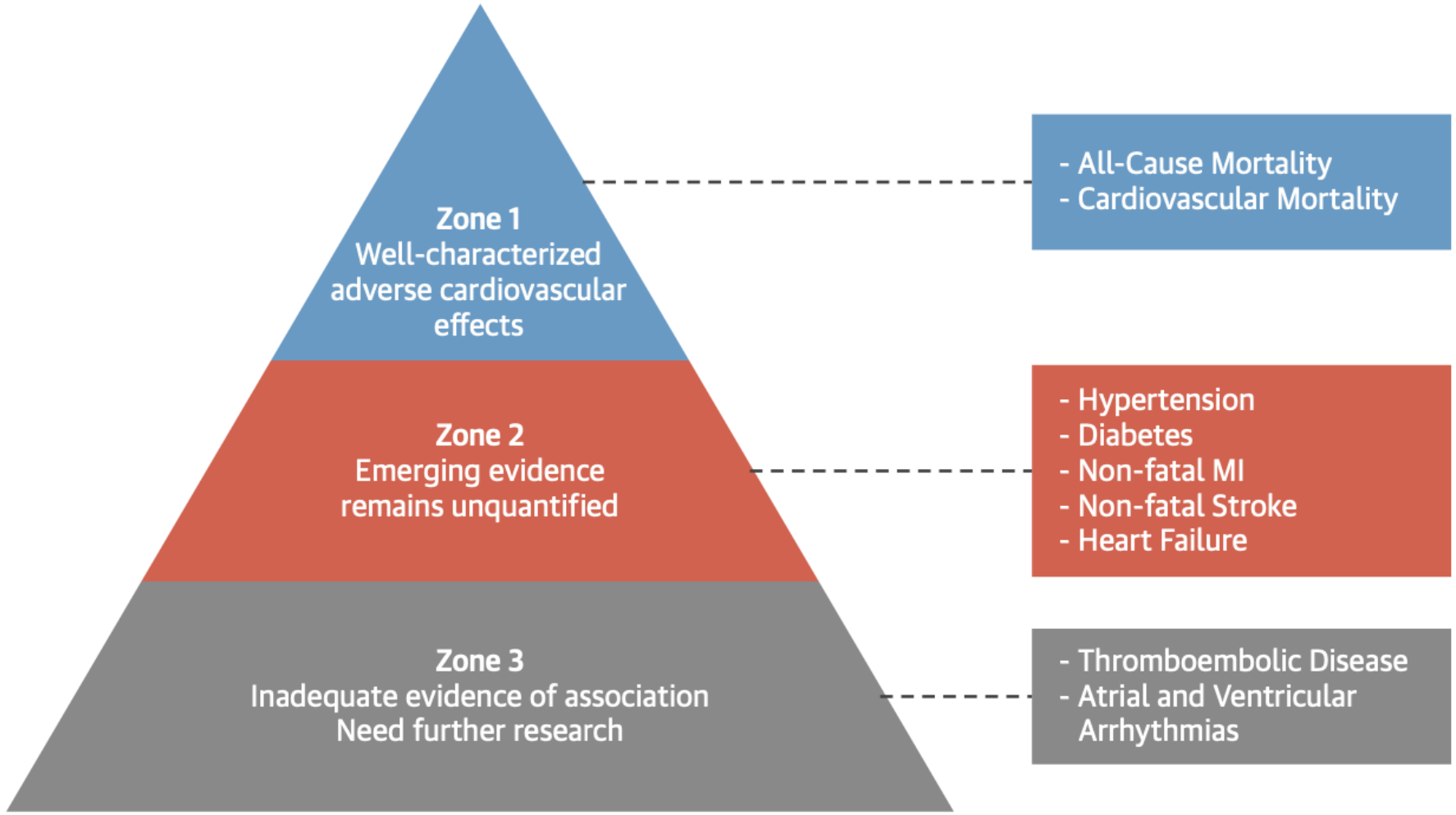


Environ Chem Lett (2022) https://doi.org/10.1007/s10311-022-01450-9



Environ Chem Lett (2022) https://doi.org/10.1007/s10311-022-01450-9

The Zones of Evidence Linking Air Pollution and CV Disease



J Am Coll Cardiol 2018;72:2054-70

Table 2. *Strength of evidence of included reviews and meta-analysis*

CVD outcomes	Exposure temporality	Strength of evidence[a]	
		PM (%)	NOx (%)
All-cause CVD mortality and morbidity	Short term	Sufficient (100)	Sufficient (100)
	Long term	Sufficient (80)	Sufficient (100)
Ischemic heart disease and myocardial infarction	Short term	Sufficient (90)	Limited (60)
	Long term	Sufficient (80)	Sufficient (100)
Atherosclerosis and arterial stiffness	Short term	No reviews	No reviews
	Long term	Limited (60)	No reviews
Blood pressure and hypertension	Short term	Sufficient (90)	Limited (60)
	Long term	Inadequate (50)	Inadequate (50)
Heart failure	Short term	Sufficient (100)	Sufficient (100)
	Long term	No reviews	No reviews
Stroke	Short term	Sufficient (80)	Sufficient (90)
	Long term	Limited (60)	No reviews
Arrhythmias, atrial fibrillation, and cardiac arrest	Short term	Sufficient (100)	Sufficient (100)
	Long term	Inadequate (50)	Inadequate (50)

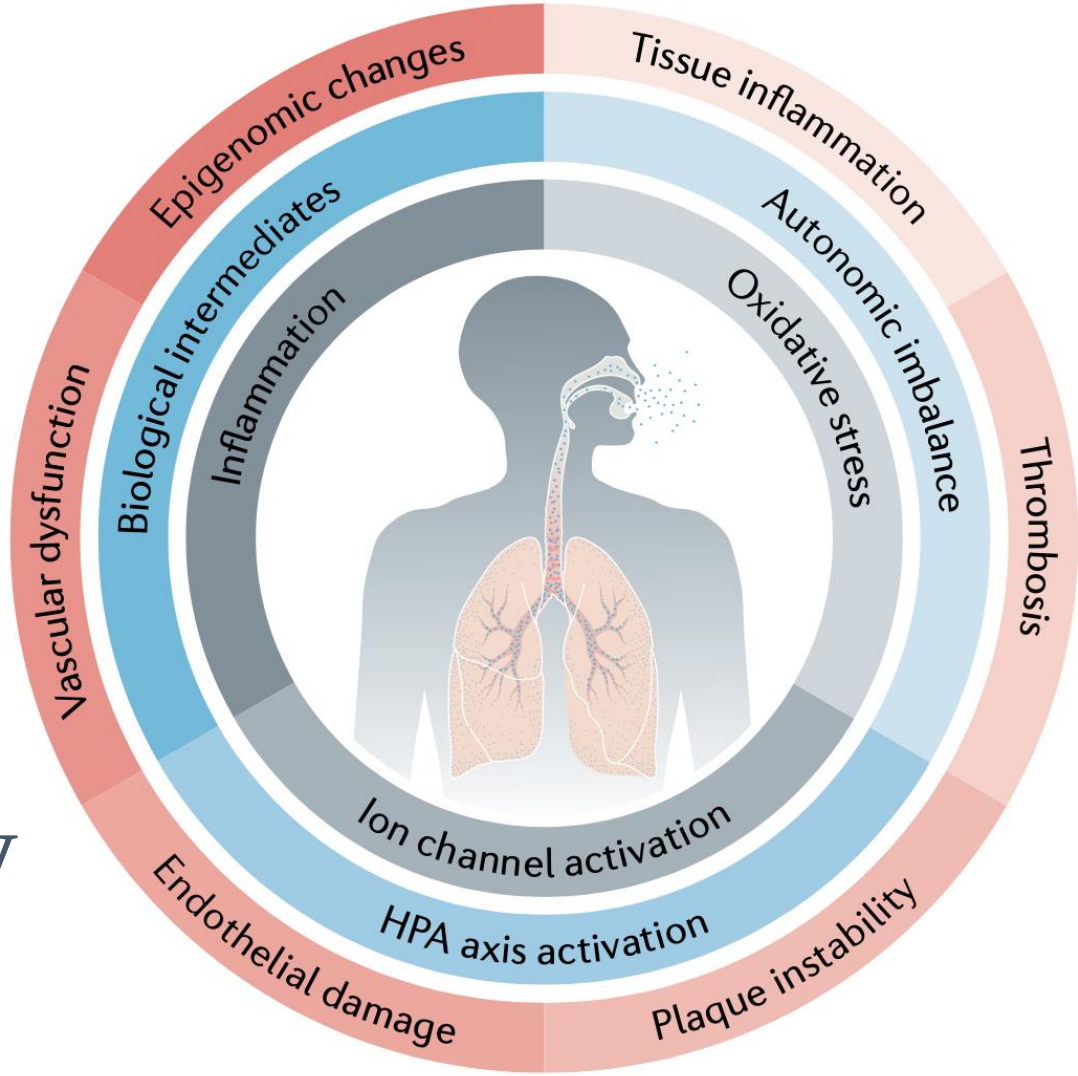
Short-term exposures ($PM_{2.5}$, NO) were consistently associated with increased risks of hypertension
Long-term exposures ($PM_{2.5}$) were largely associated with increased risk of hypertension.

Intern Med. 2022;**291:**779–800.

Pathophysiology of Injury

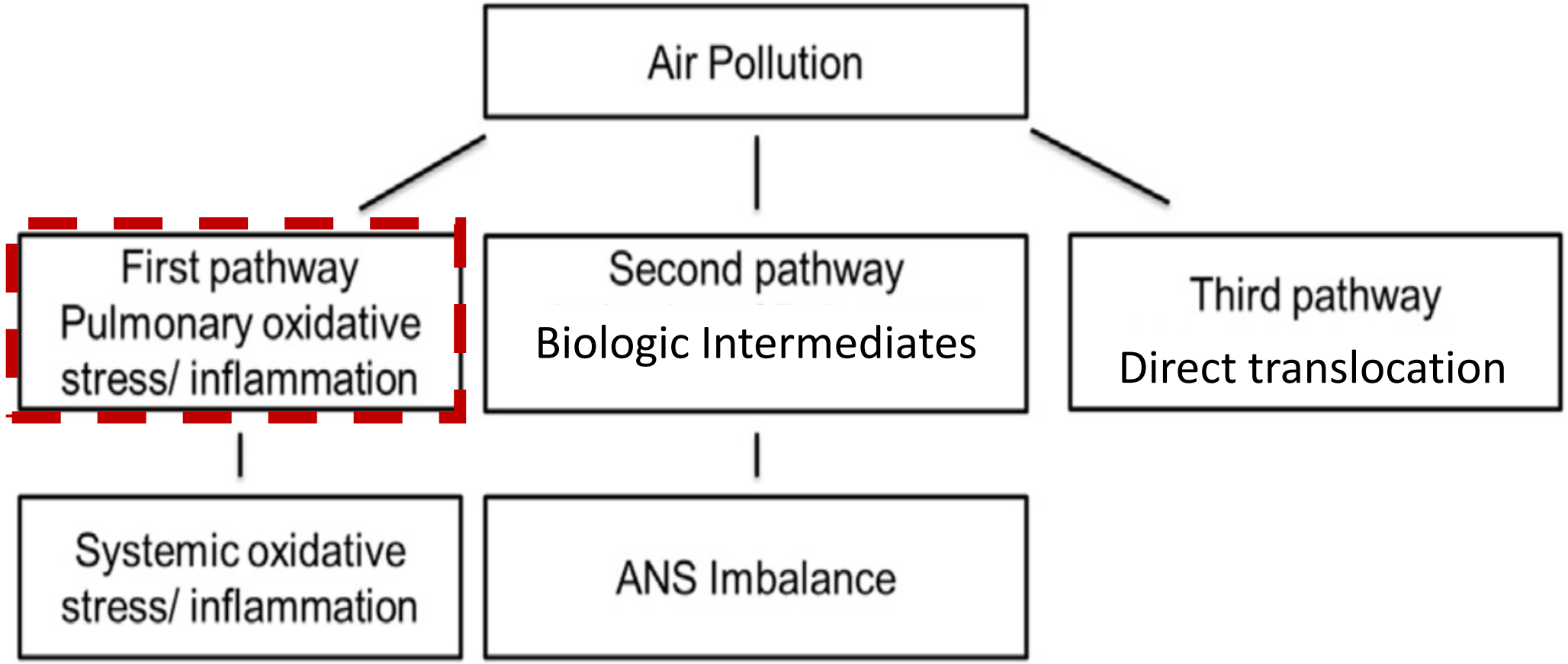
Primary initiating pathways

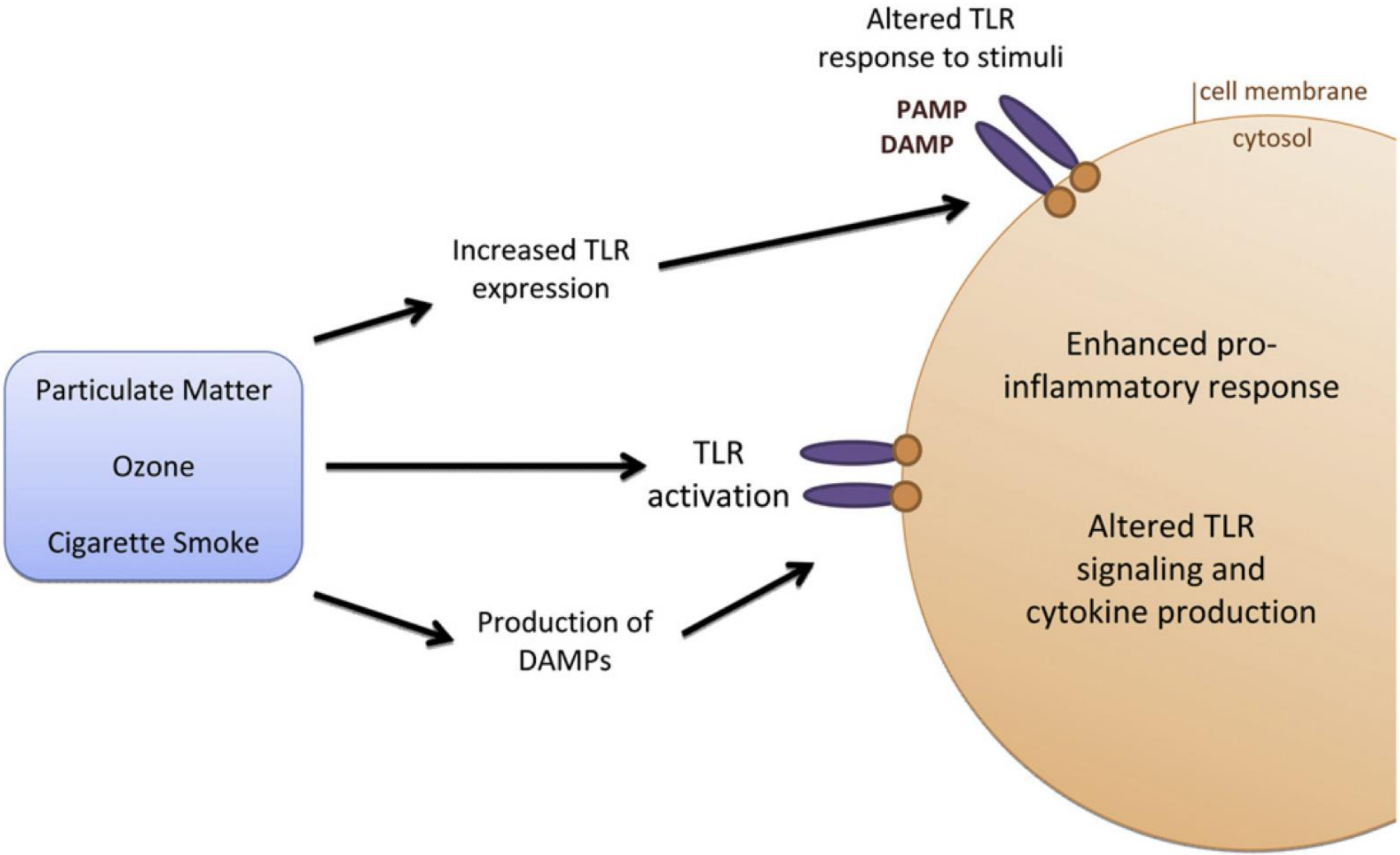
Secondary effector pathways



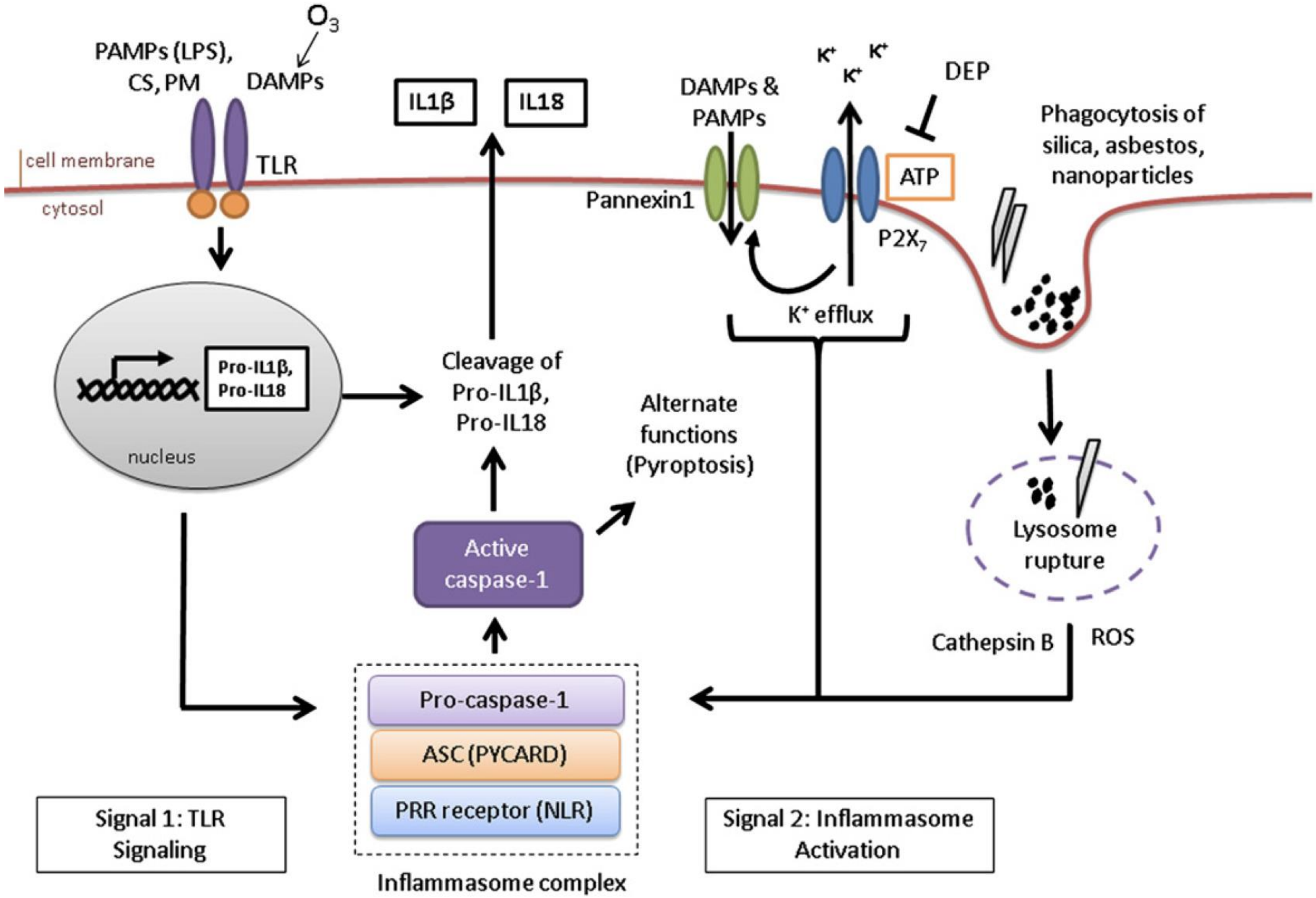
https://doi.org/10.1038/s41569-020-0371-2

Primary Initiating Pathways

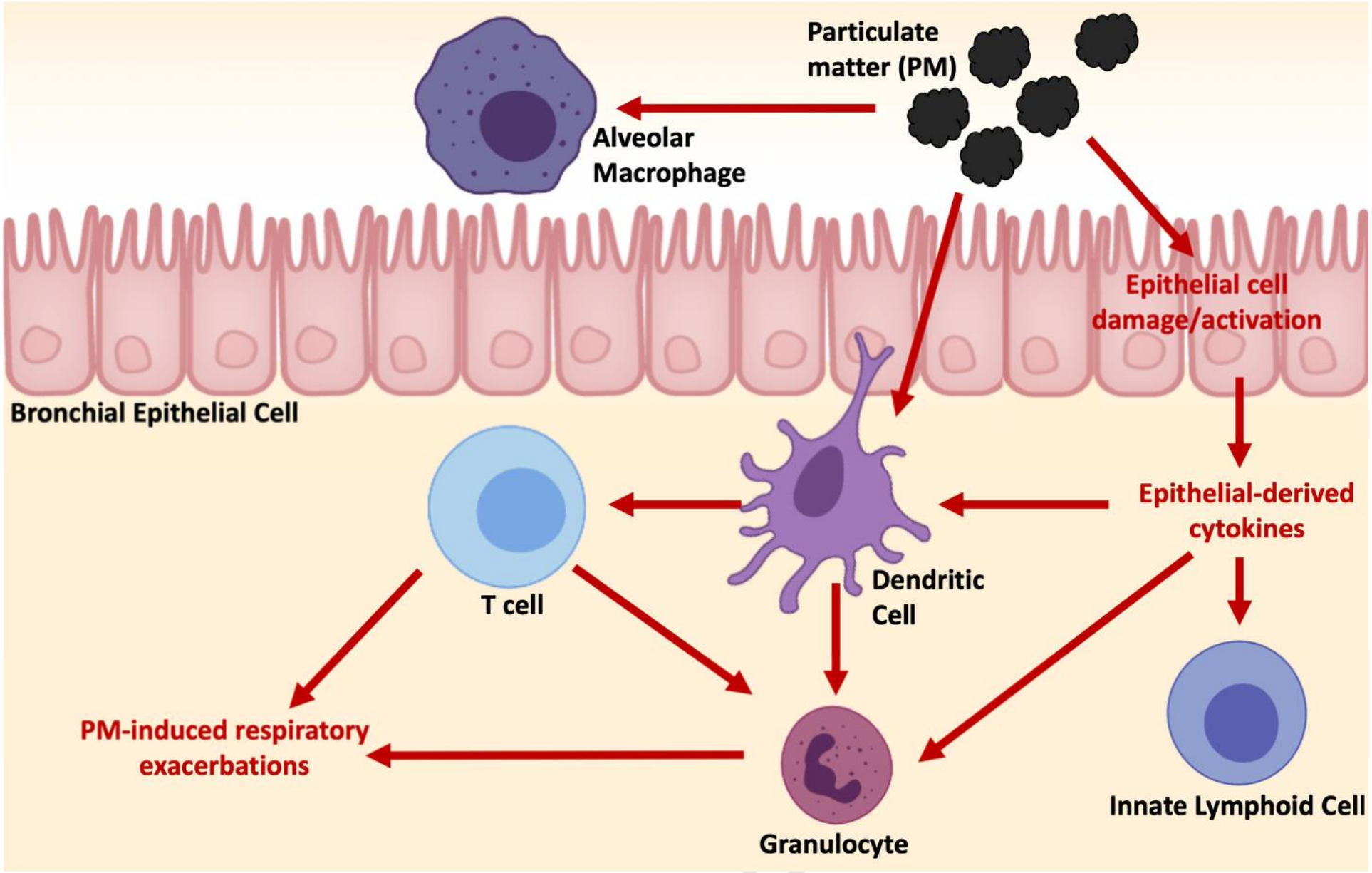




J Allergy Clin Immunol 2012;129:14-24.



J Allergy Clin Immunol 2012;129:14-24.



Free Radical Biology and Medicine (2020)

Dysregulation of Immune Tolerance

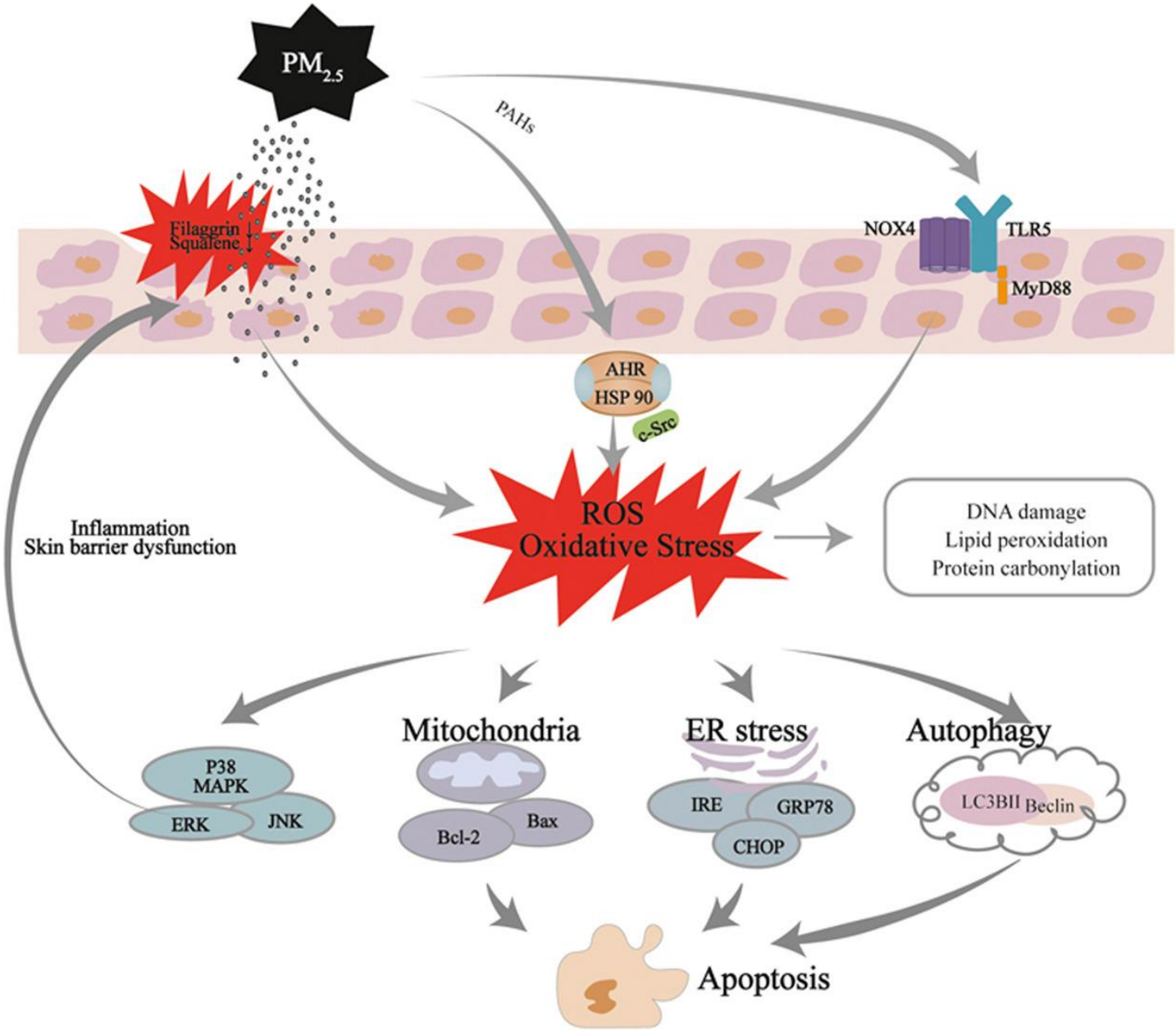
Stimulation of production of pro-inflammatory cytokines and leucocyte-attracting chemokines by epithelial cells and macrophages

Adjuvant action of PM increases APC maturation and antigen expression

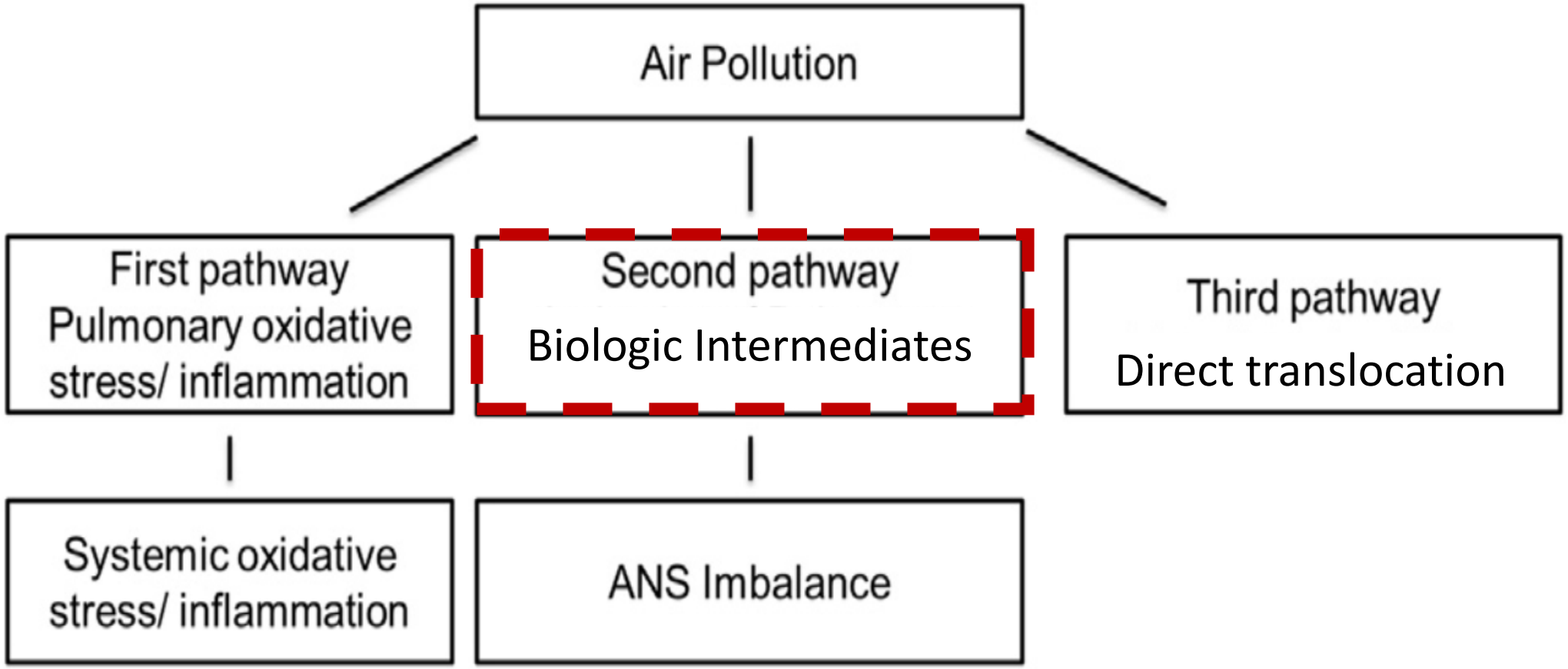
Suppression by pro-inflammatory cytokines (such as IL-6) of regulatory T cell responses

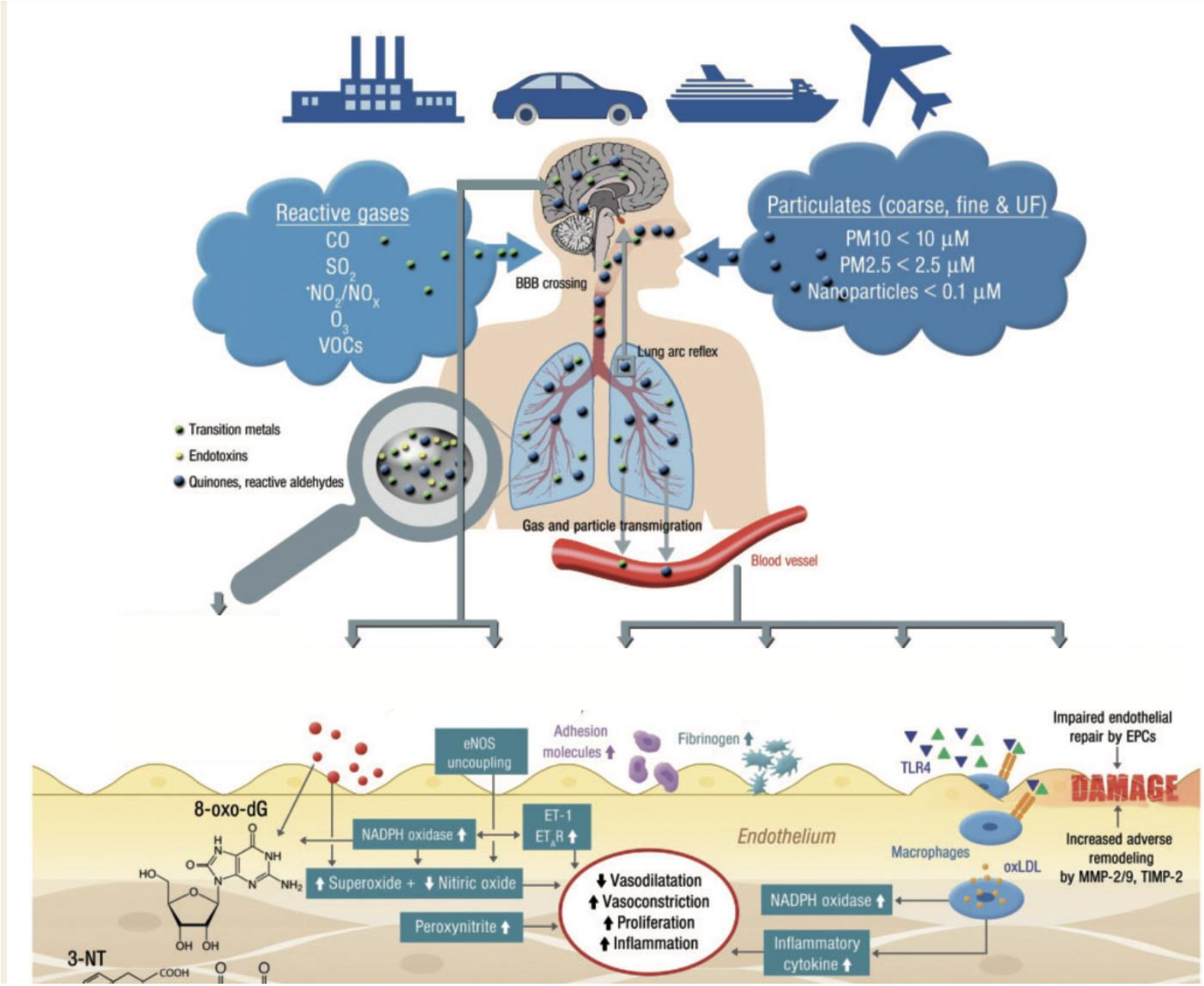
Protein oxidation leading to formation of neo-antigens

Free Radical Biology and Medicine (2020)

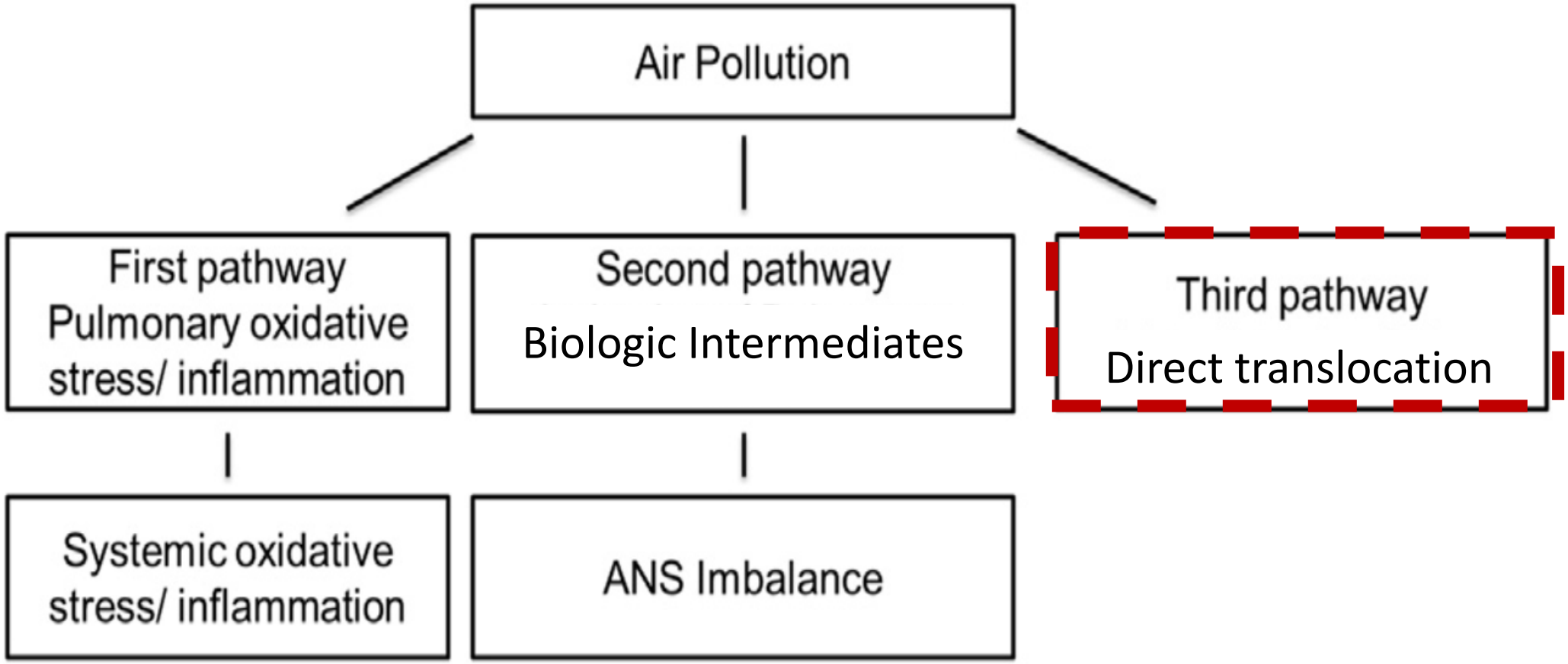


Biomedicine & Pharmacotherapy 138 (2021) 111534


Air Pollution
First pathway
Pulmonary oxidative stress/ inflammation
Second pathway
Biologic Intermediates
Third pathway
Direct translocation
Systemic oxidative stress/ inflammation
ANS Imbalance



European Heart Journal (2018) **39**, 3543–3550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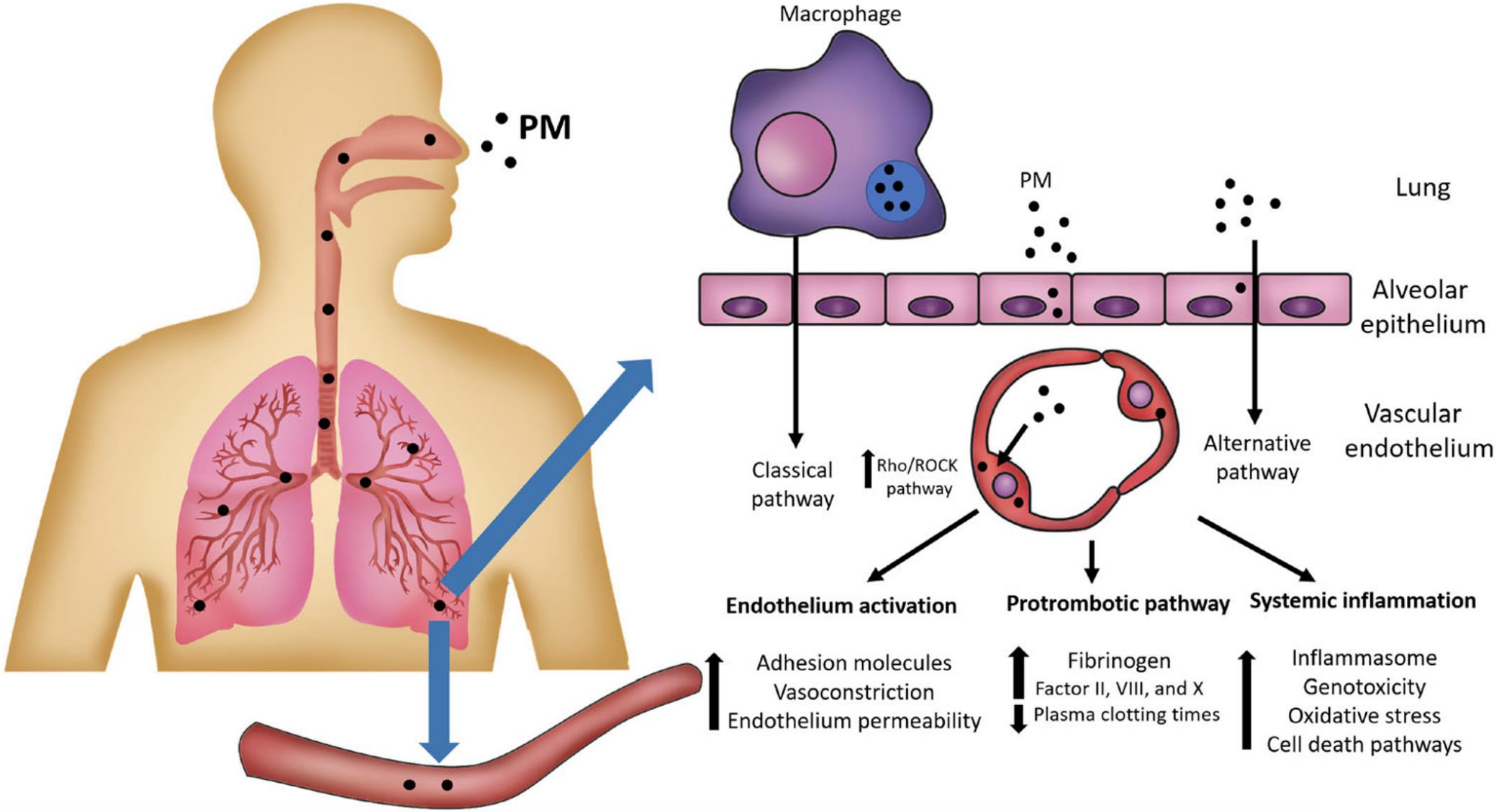
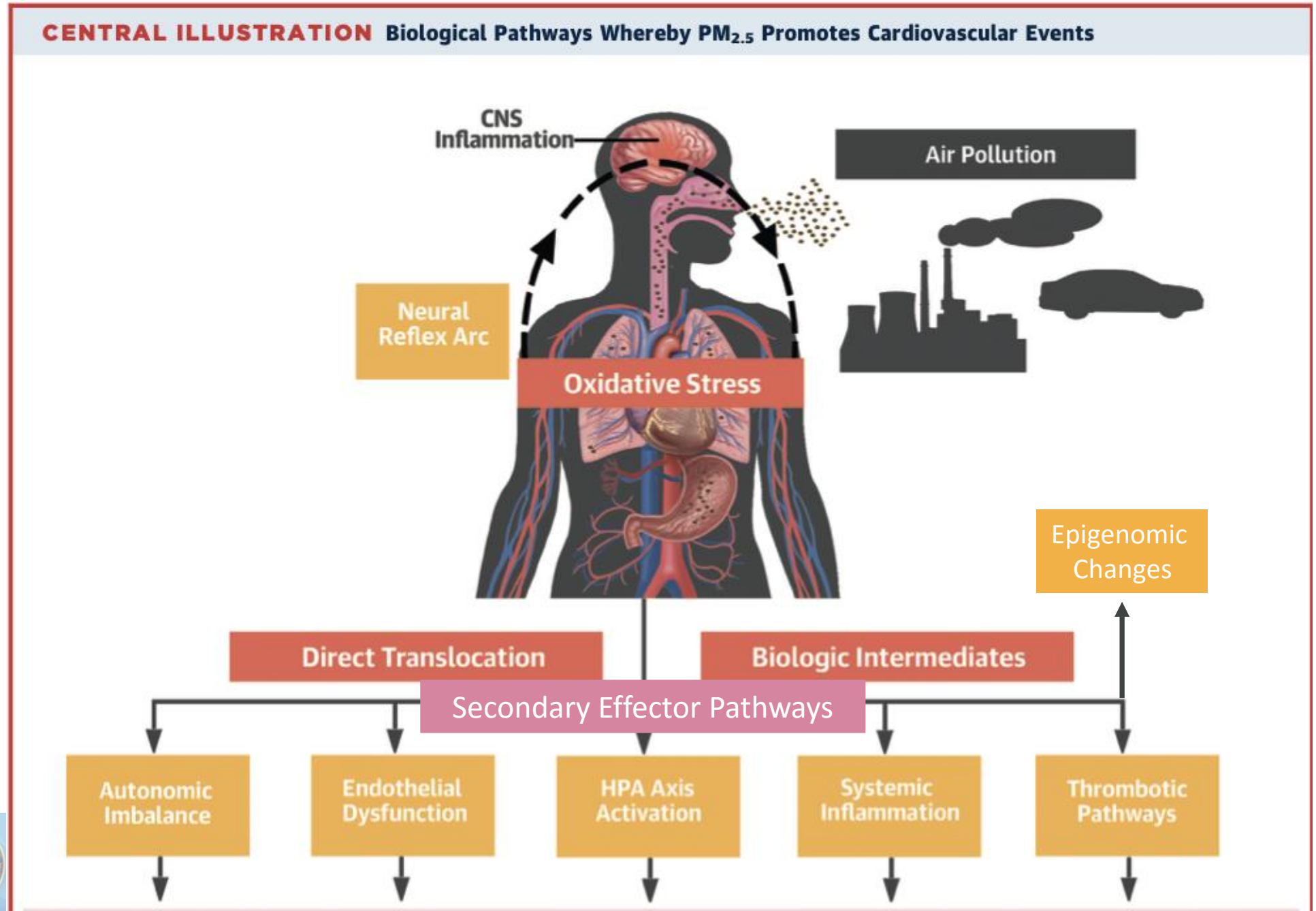
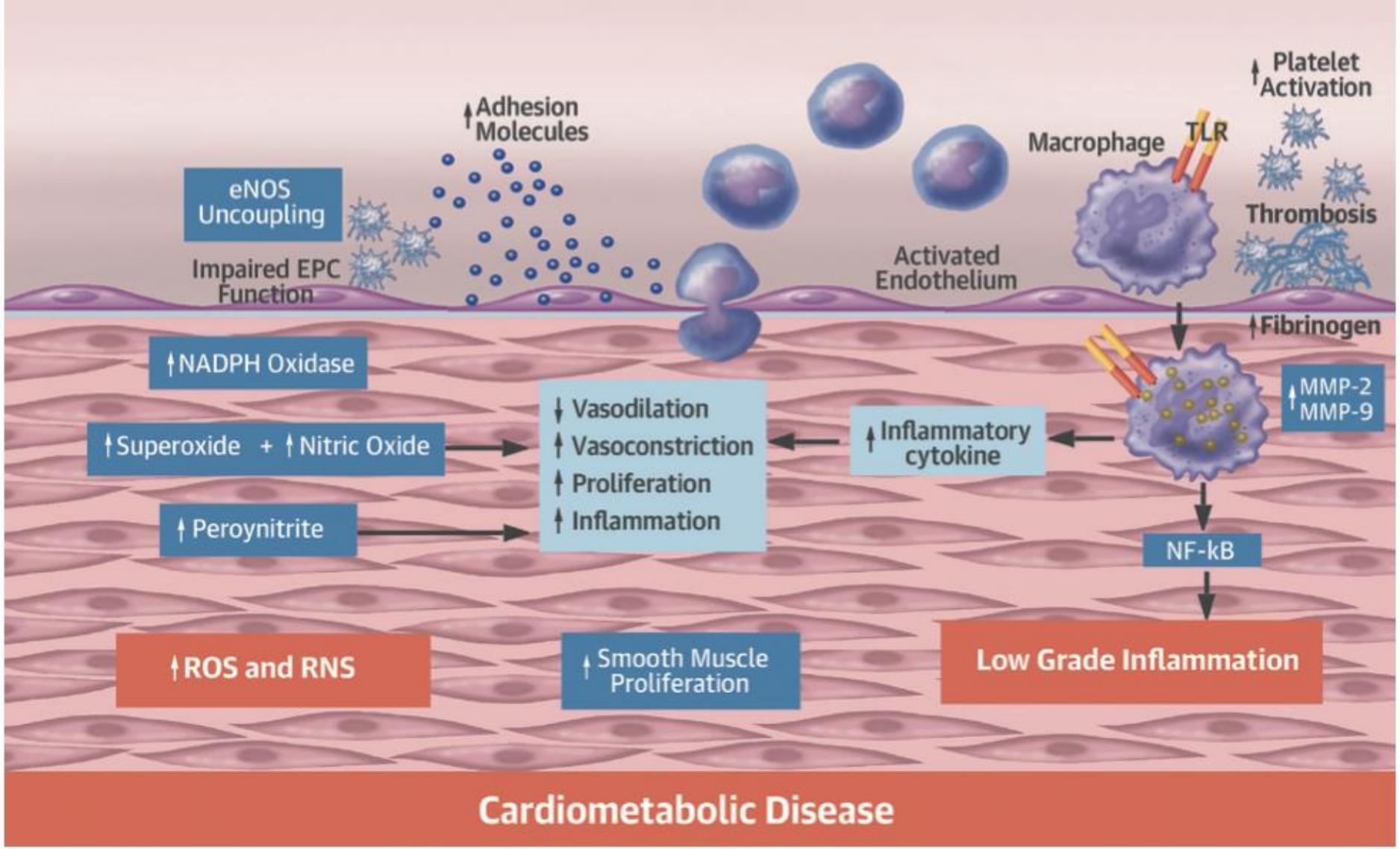
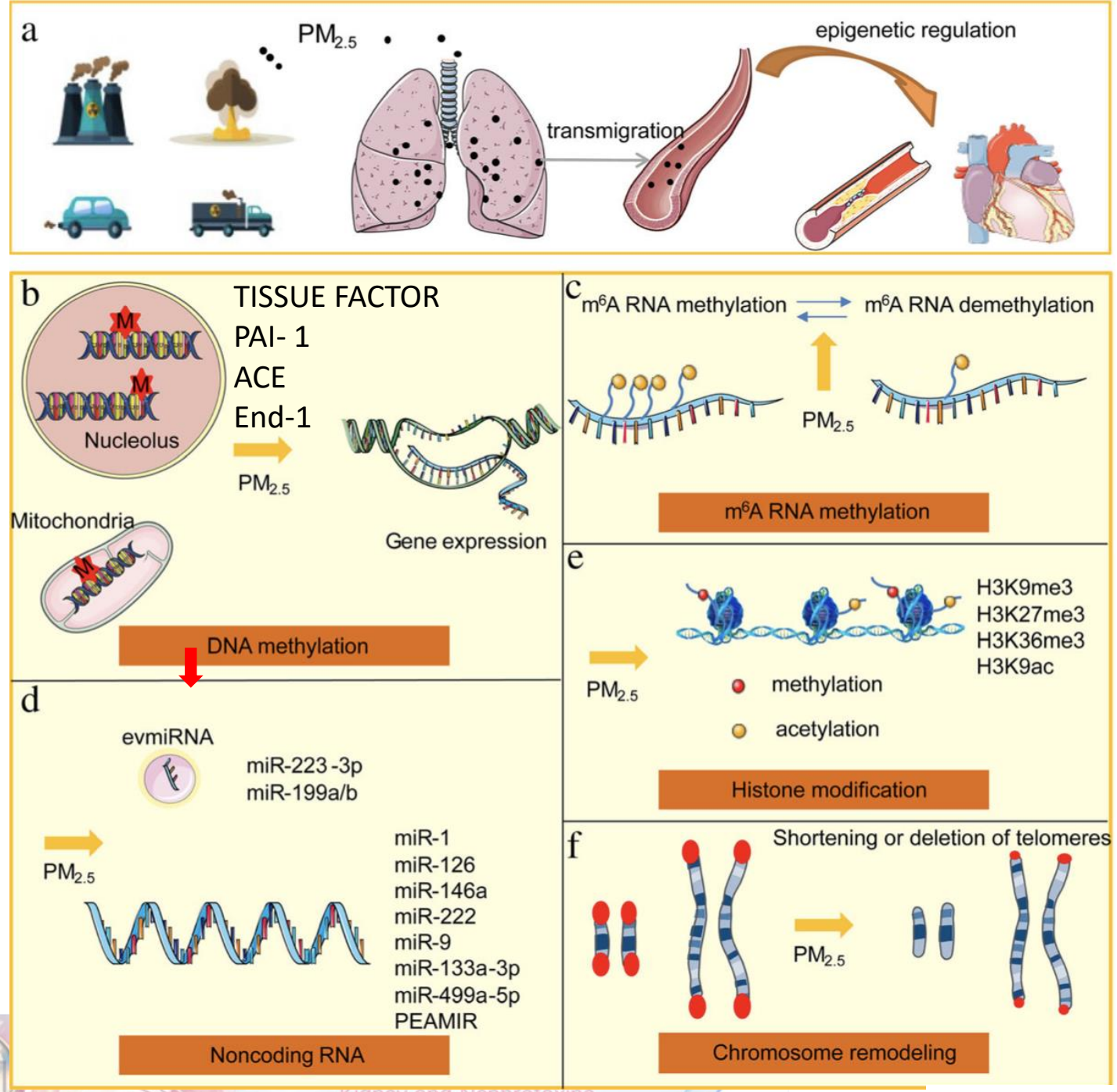


Environmental Science and Pollution Research
https://doi.org/10.1007/s11356-020-10574-w


CENTRAL ILLUSTRATION Biological Pathways Whereby $PM_{2.5}$ Promotes Cardiovascular Events
CNS Inflammation
Air Pollution
Neural Reflex Arc
Oxidative Stress
Epigenomic Changes
Direct Translocation
Biologic Intermediates
Secondary Effector Pathways
Autonomic Imbalance
Endothelial Dysfunction
HPA Axis Activation
Systemic Inflammation
Thrombotic Pathways



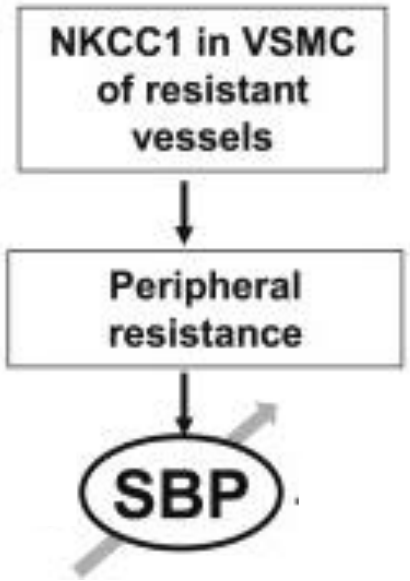
Rajagopalan, S. et al. J Am Coll Cardiol. 2018;72(17):2054-70.



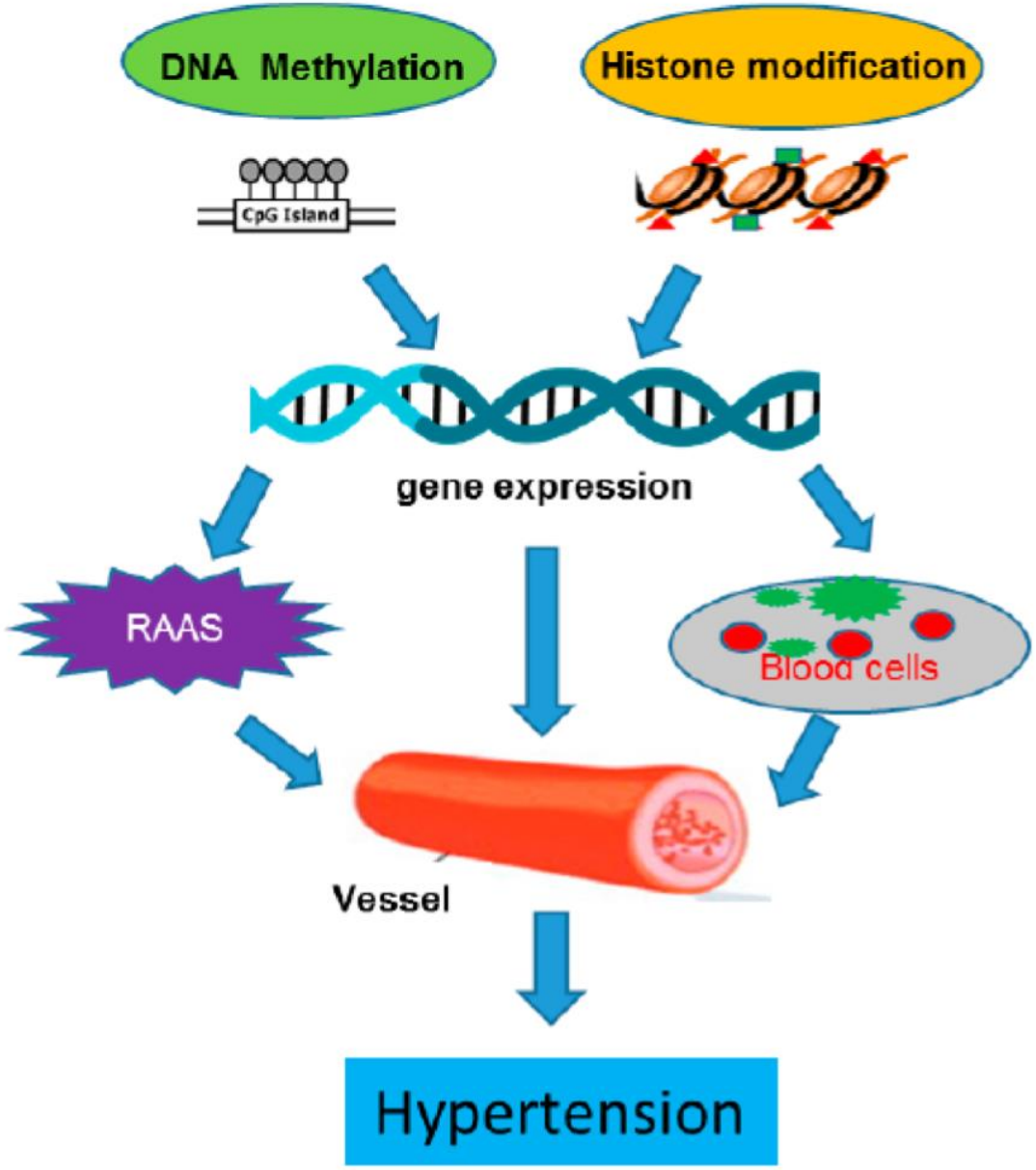
Sun *et al. Genes and Environment* (2021) 43:47

Table 1. DNA methylation and histone modification associated with hypertension.

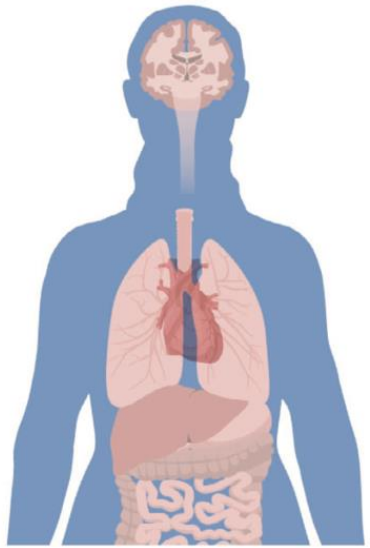
Genes	Mark	Status	Species	Models	Tissues/Cells	Function	Ref
DNA methylation							
Atgr1α	5mC	Hypo	Rat	SHR	Aorta and mesentery artery	Increased expression of receptor and effect of RAAS	[6]
Atgr1β	5mC	Hypo	Rat	Maternal low protein rat		RAAS	
Ace-1	5mC	Hypo	Mice	Maternal protein deficient mice		RAAS	
HSD11B2	5mC	Hyper	Human	Glucocorticoid treatment	Human PBMCs	Renal sodium balance	
Sslc12a2 **(NKCC1)**	5mC	Hypo	Rat	SHR	Aorta and heart	Ionic balance	



Genes	Mark	Status	Species	Models	Tissues/Cells	Function	Ref
Histone modification							
Ace1	H3Ac, H3K4me3, H3K9me2	Hyper, Hyper, Hypo	Rat	SHR	Heart, kidney	RAAS	[19]
SM22	H3Ac	Hyper	Mouse		10T1/2 cells	Contractile phenotype	[20]
Nlrp3	H3K9Ac	Hyper	Rat	SHR	VSMCs	Chronic inflammation	[21]
NOS3 (eNOS)	H3K9Ac, H4K12 H3K4 me2, H3K4me3	Hyper	Human		Cell culture; HUVEC, HMVEC, VSMC, HEPG2, HeLa, JEG-3	Vasodilation in endothelial cells	[22]
Slc12a2 (NKCC1)	H3Ac H3K27me3	Hyper, Hypo	Rat	Angiotensin II delivery	Aorta	Ionic balance	[23]



Int. J. Mol. Sci. **2018**, *19*, 1174

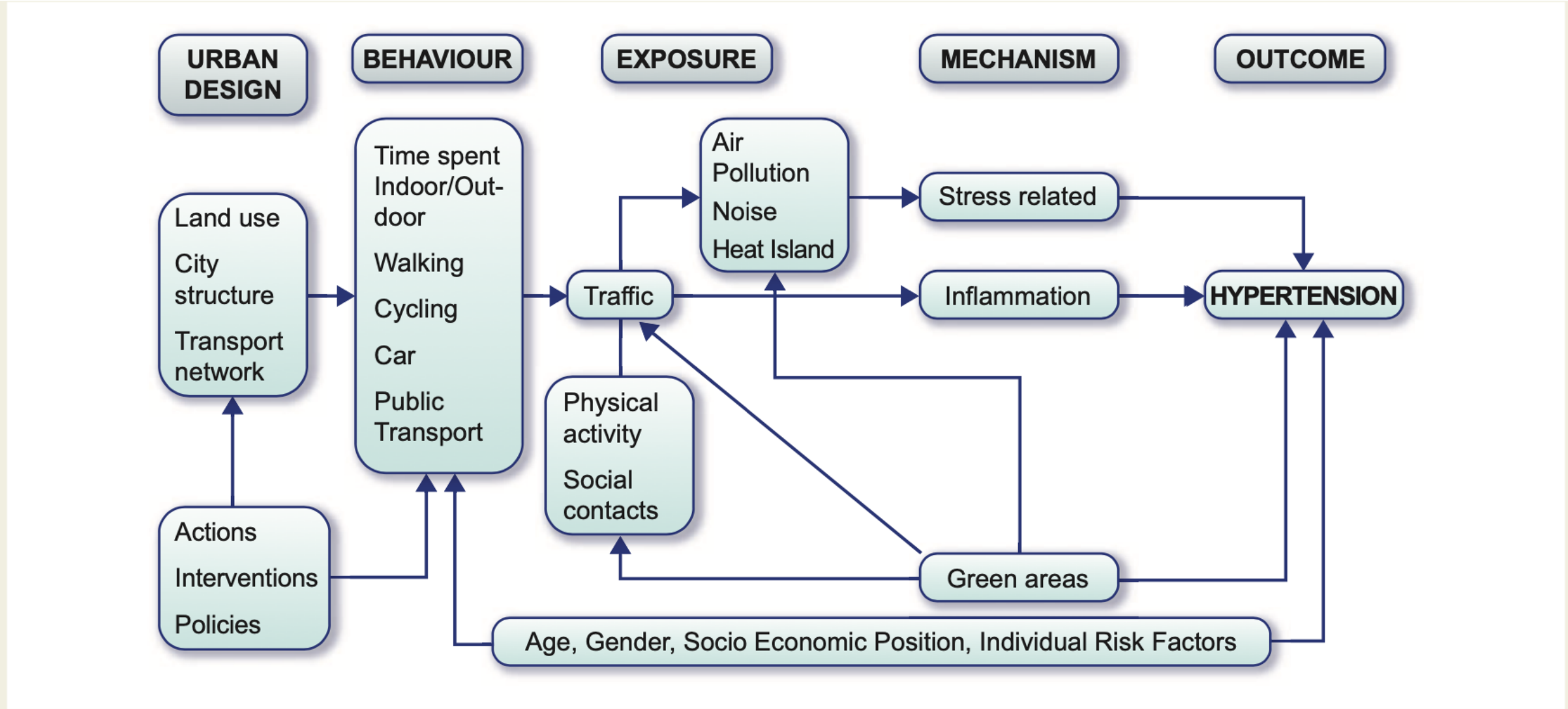


Initial pathways	Physiological changes	Sub clinical disease	Clinical events
Autonomic nervous imbalance	Endothelial dysfunction	Arrhythmias/atrial fibrillation	Cardiac arrest
Systemic inflammation	Thrombotic pathways	Blood pressure/hypertension	Heart failure
Oxidative stress	Epigenomic changes	Arterial stiffness	Stroke
Direct particles translocation	Atherosclerosis/arrhythmogenesis		Ischemic heart disease
	Activation of hypothalamic and pituitary adrenal axis (HPA)		Myocardial infarction

J Intern Med. 2022;**291**:779–800.

- ✓PM can also reduce daytime sodium excretion and decrease the normal nocturnal reduction in BP.

- ✓If this happens repeatedly, the impaired renal handling of excess sodium may partly contribute to elevated BP.



Graphical Abstract Conceptual framework of the relationship between hypertension and urban and transport planning, traffic noise, and air pollution.

- ✓A diverse group of conditions associate with increased noise level, including roadway traffic, airplanes, and occupational noises, has been implicated in increasing BP.

- ✓Nocturnal loud noise might be even more detrimental than daytime one.

- ✓Nighttime noise causes sleep disturbances and activation of sympathetic nervous system that might prevent BP dipping.

SUBSETS VULNERABLE TO AIR POLLUTION EFFECTS

- ✓Elderly individuals
- ✓Coronary disease patients
- ✓Lower socioeconomic status,
- ✓Patients with diabetes
- ✓Smokers
- ✓Drinkers
- ✓Individuals with a high-fat diet,

Environmental Research 182 (2020) 109109

J Am Coll Cardiol. 2018;72(17):2054-70.

STRATEGIES TO MITIGATE EFFECTS OF AIR POLLUTION

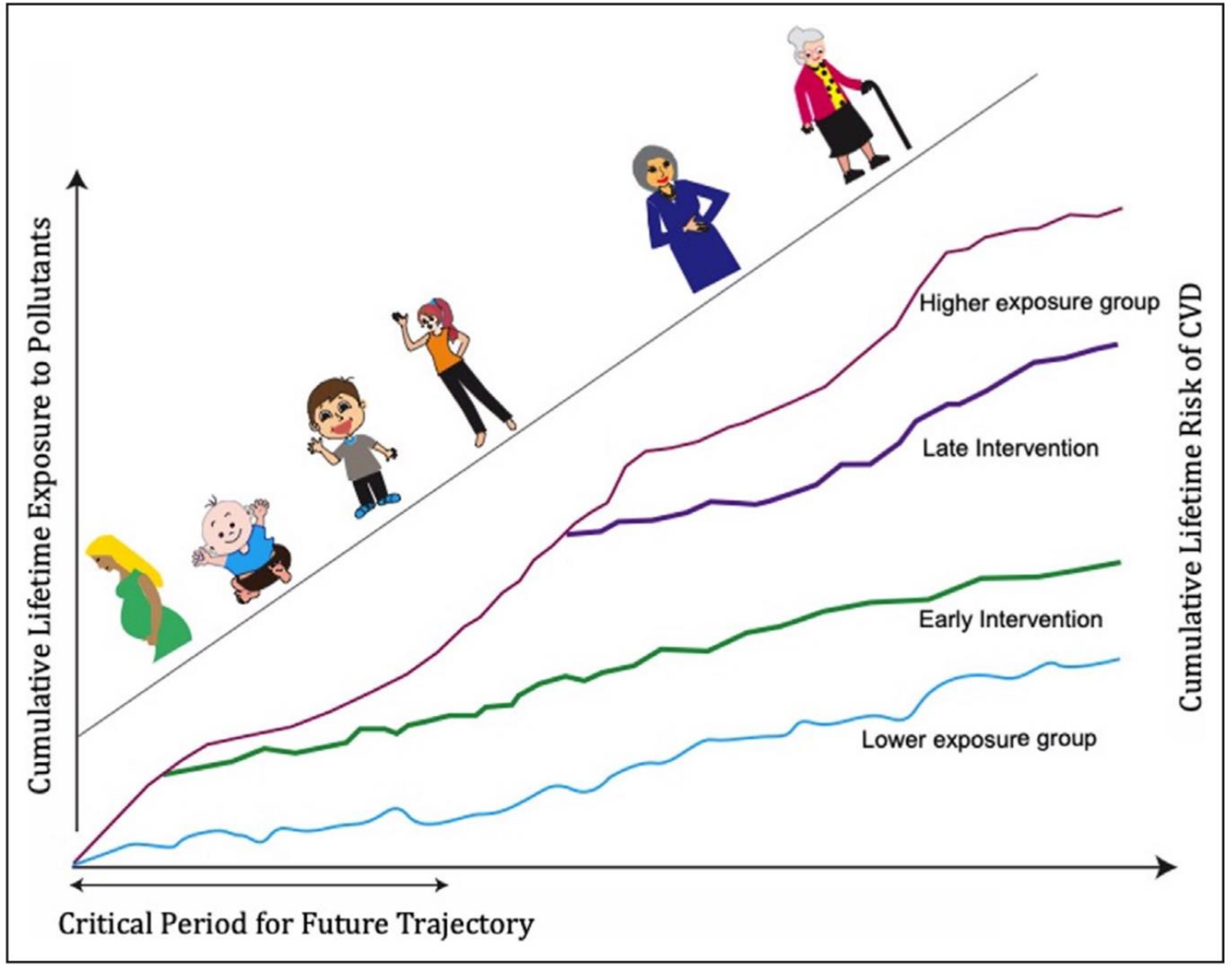


Figure 3. **Early intervention can improve cumulative lifetime risk of cardiovascular disease.**
CVD indicates cardiovascular disease.

J Am Heart Assoc. 2020;9:e014944. DOI: 10.1161/JAHA.119.014944

PERSONAL INTERVENTIONS	
Face masks and Air purifiers	• Wearing face masks and installing air purifiers in homes
Reduce in-traffic exposures	• Avoid commutes during rush hour
Reduce in-home penetration of outdoor air pollution	• Indoor air purifiers and closing windows; Air conditioners
Lifestyle changes and Preventive Medicine	• Exercise and healthy diet • Preventive medications and screening programs

J Am Coll Cardiol. 2018;72(17):2054-70.

SOCIETAL AND GOVERNMENTAL INTERVENTIONS

Shifting to Clean Fuels	• Switch coal-fired power plants to low-polluting renewable energy sources such as wind, tidal, geothermal, and solar.
Transportation Reform	• Promote use of low-emission and zero-emission vehicles, Reduce sulfur content of motor fuels, Restrict trucks from city centers, encourage active transport (walking and cycling)
Reduce Traffic Emission(s)	• Diesel particle traps, catalytic converters, alternative fuels (natural gas, electric cars)
Urban landscape reform	• Land use assessment, minimum distances between sources and people, relocation of traffic sources (including major trafficked roads), avoidance of mixed-use areas (industrial-residential)
Emission Trading Programs	• Revenues raised through taxes can be directed to pollution control. Emissions trading programs compensate companies who adhere to controls through credits that can be traded akin to carbon credits
Redirection of science and funding	• Modifying priorities of climate change mitigation investments to a focus on near-term health co-benefits. Focus on the imminent near term danger of health effects of air pollution.
Empowering civil society	• Publicity and awareness campaigns through local data on air pollution within cities, counties
Governmental and NGO-led publicity	• Hard-hitting media campaigns akin to smoking on media to mitigate lobbying by industries involved in power and automobiles

J Am Coll Cardiol. 2018;72(17):2054-70.

Diet and supplements

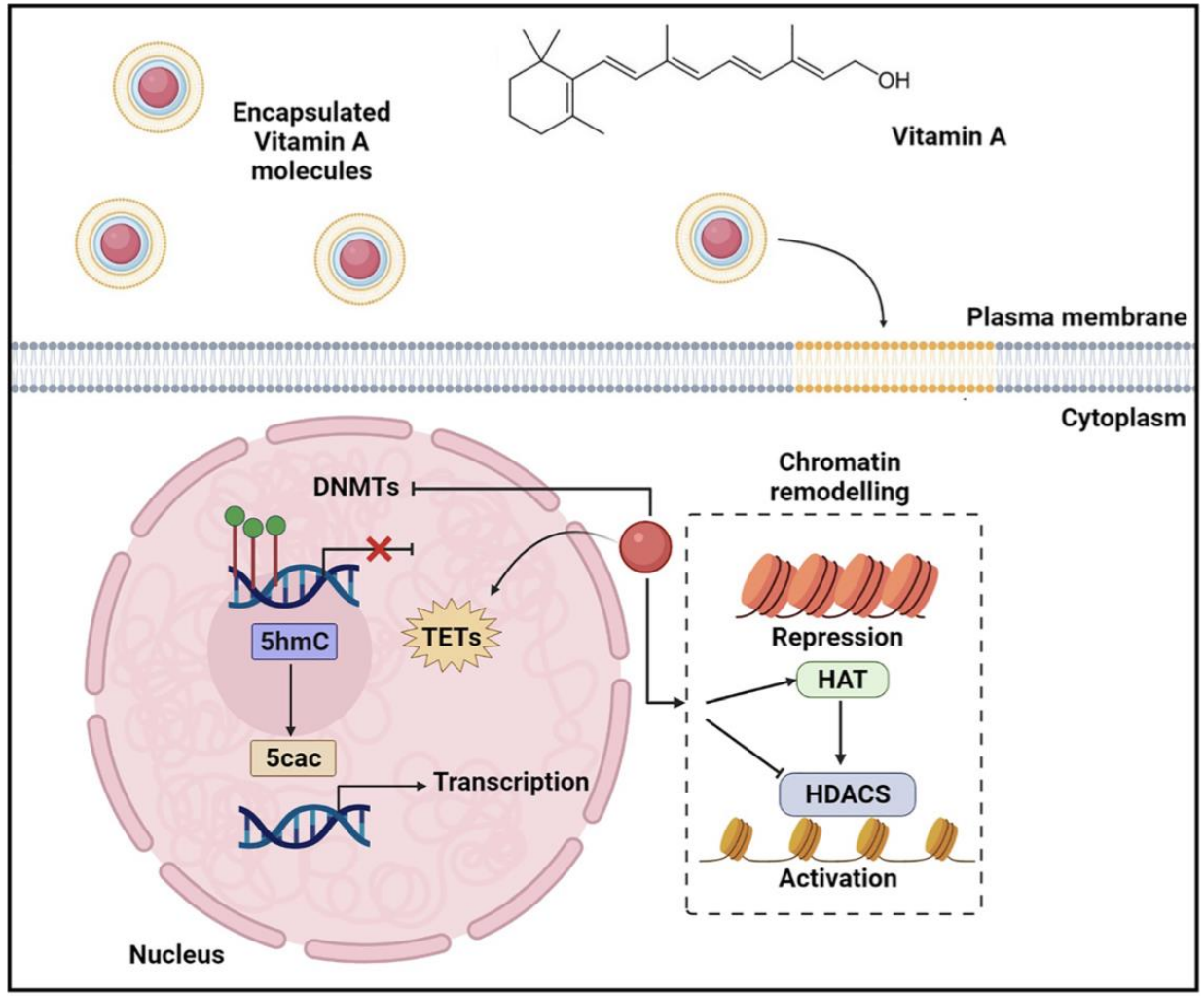
- ✓Consuming more fresh fruits, vegetables, dairy, and whole grains would reduce the risk of raised BP caused by PM.

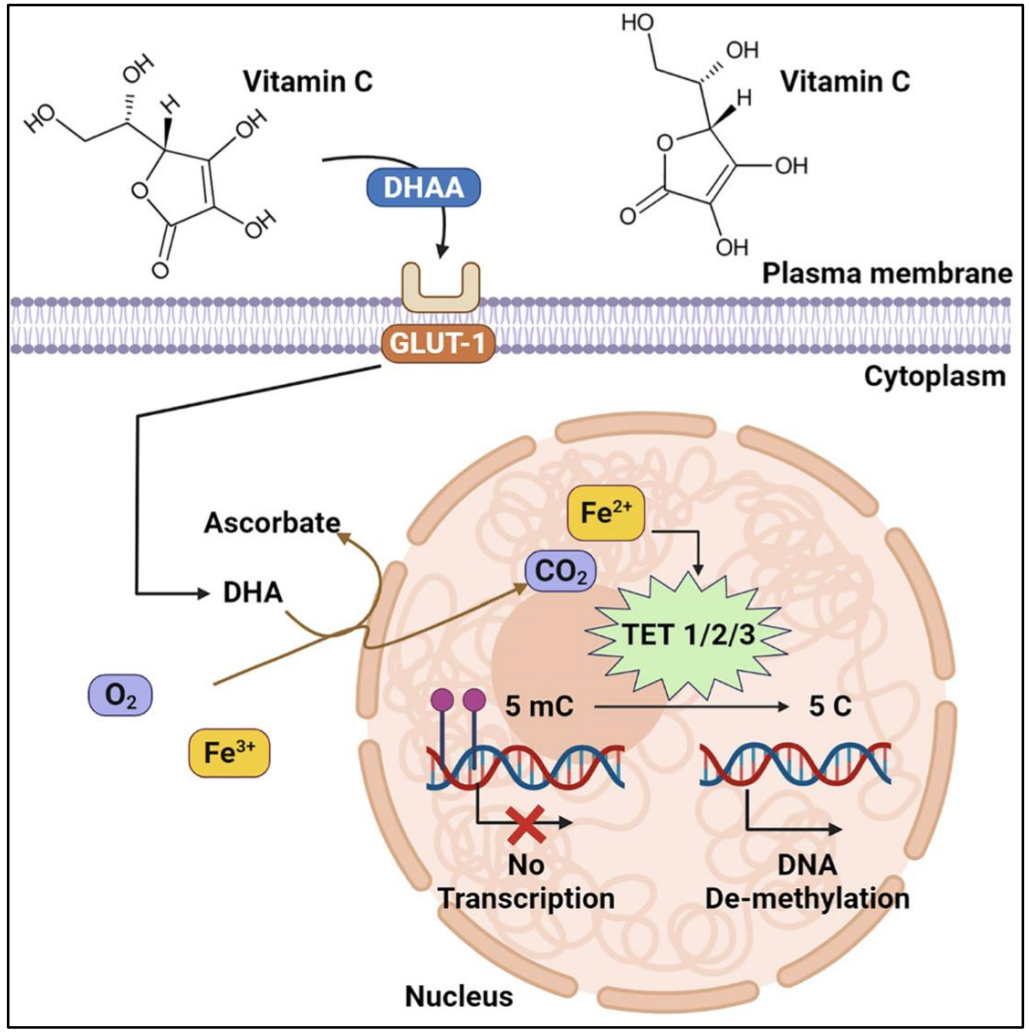
- ✓DASH diet rich in antioxidant compounds may be a wide-reaching intervention to reduce the deleterious impact of PM.

(*Hypertension*. 2021;78:184–194. DOI: 10.1161/HYPERTENSIONAHA.121.17205

- ✓L-arginine is precursor for the synthesis of nitric oxide
- ✓Oral L-arginine supplementation was safe and well-tolerated, and could improve BP levels in adults with elevated BP during outside walk under TRAP. Environment International 156 (2021) 106631

- ✓L-arginine: seafood, water- melon juice, nuts, algae, animal products and soy protein isolate.

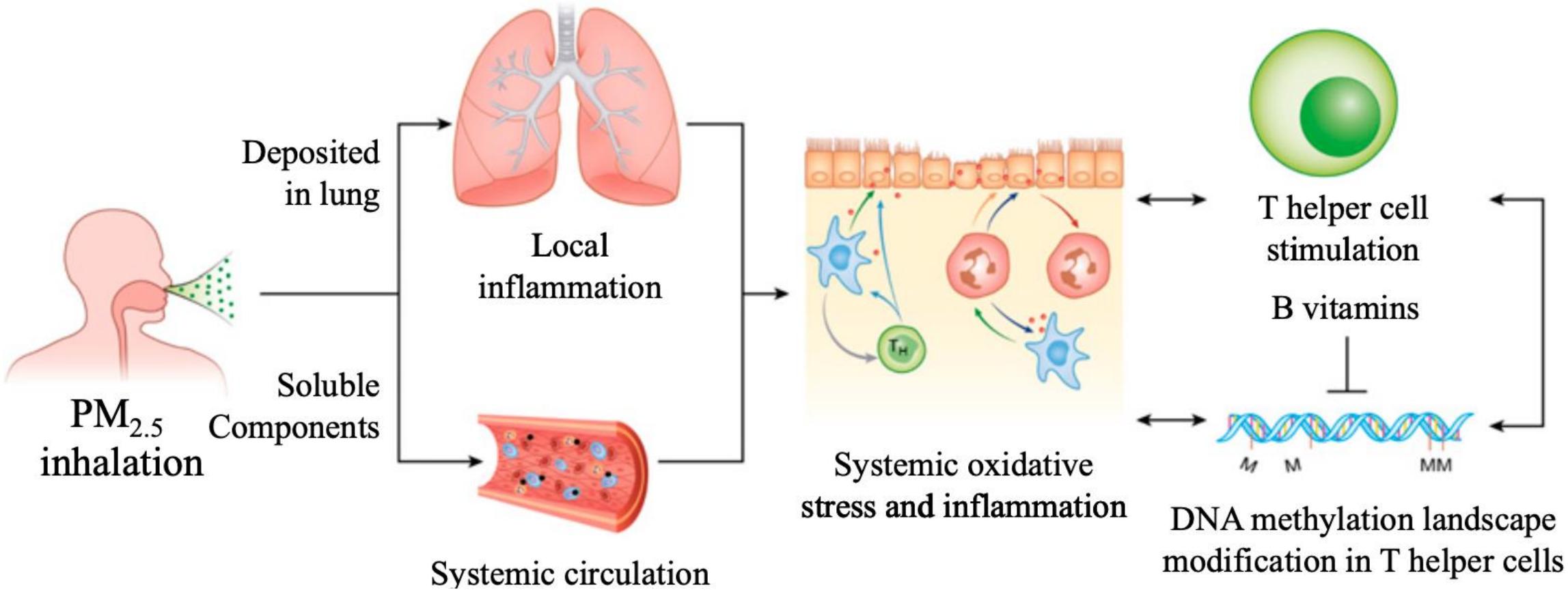




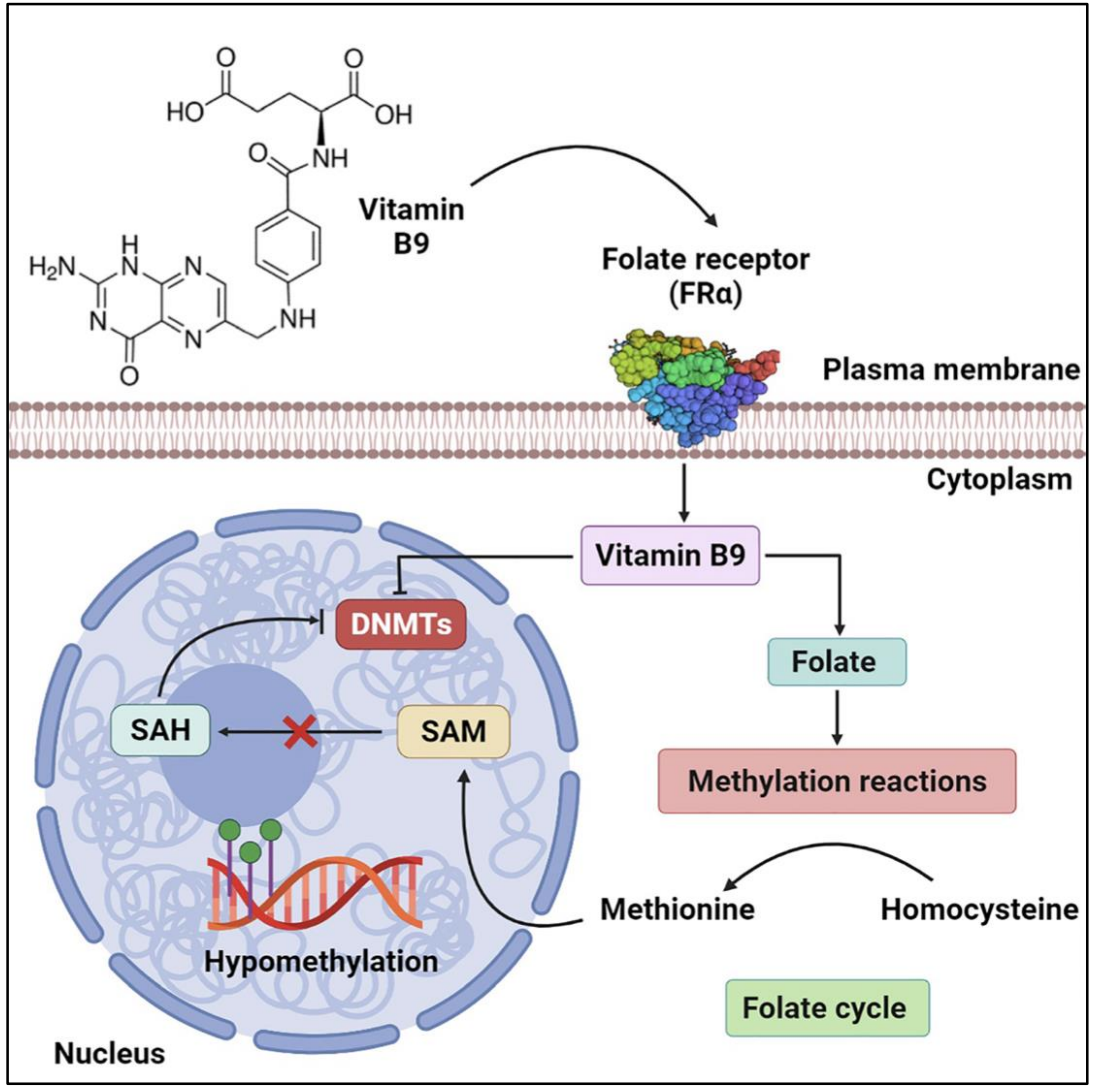
https://doi.org/10.1515/reveh-2022-0027

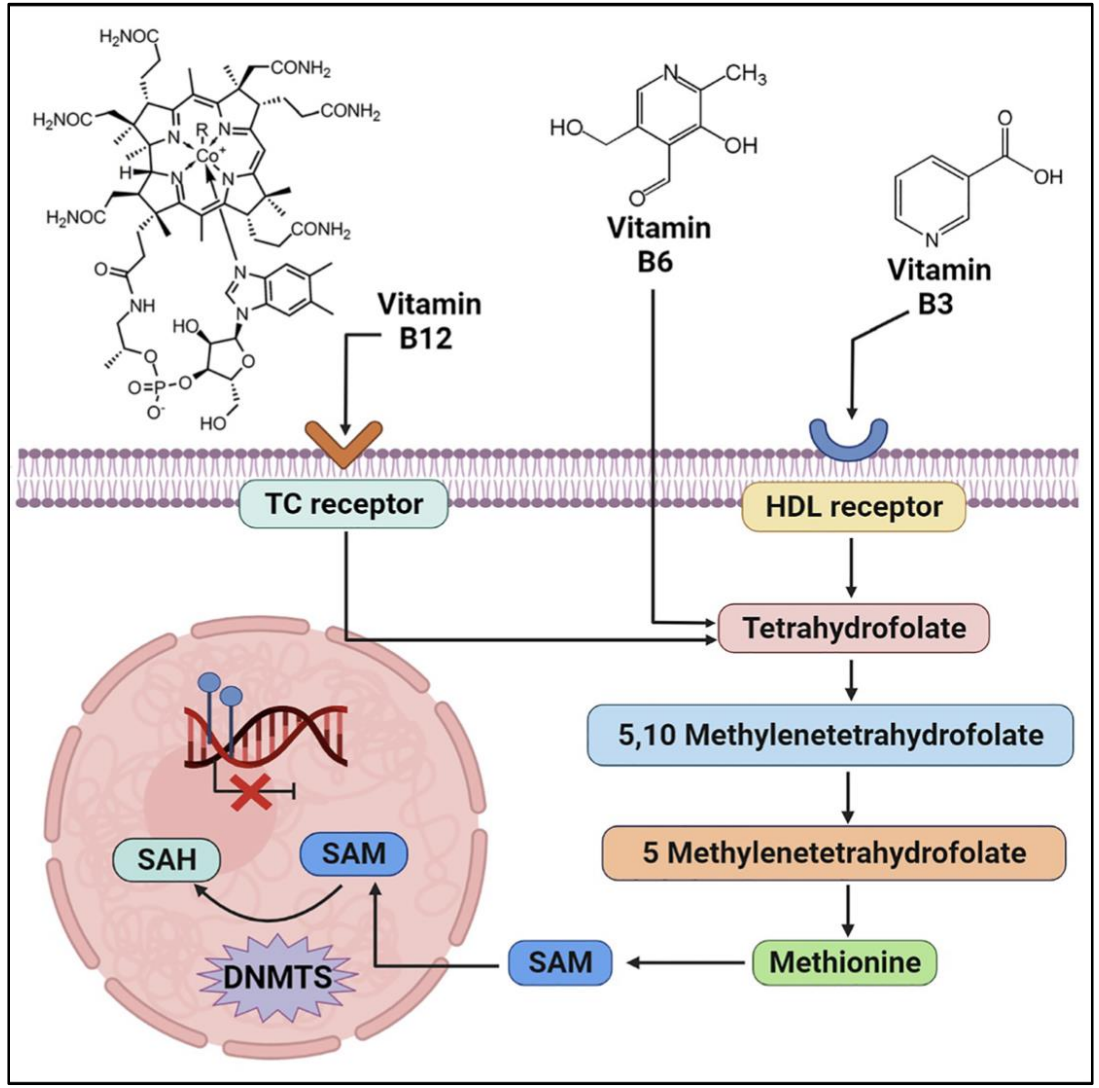
B vitamins attenuate the epigenetic effects of ambient fine particles in a pilot human intervention trial

Jia Zhong[a,1], Oskar Karlsson[b,c], Guan Wang[d], Jun Li[e,f], Yichen Guo[g], Xinyi Lin[h], Michele Zemplenyi[g],



www.pnas.org/cgi/doi/10.1073/pnas.1618545114





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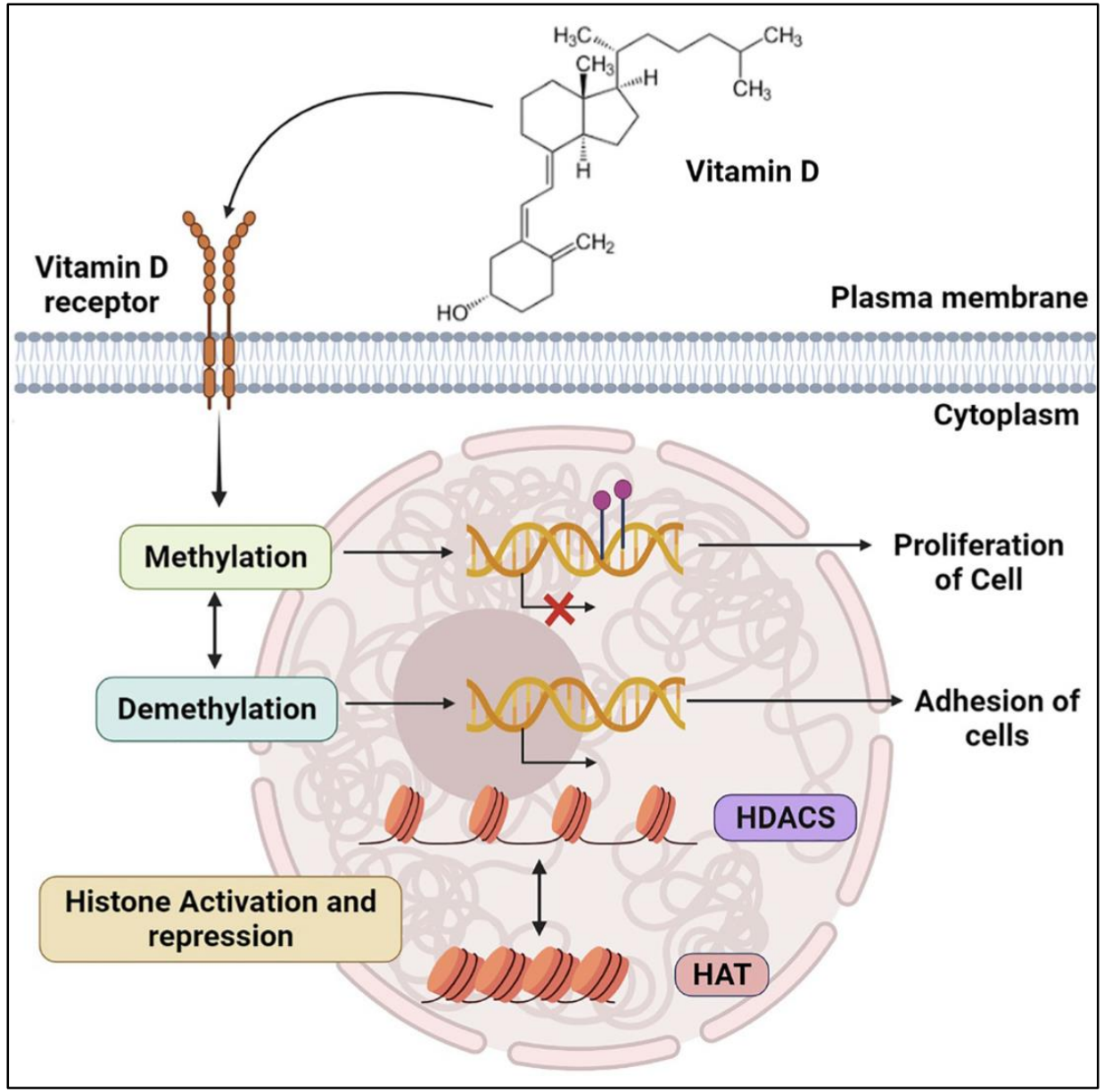

https://doi.org/10.1515/reveh-2022-0027

Design	Population	Sample Size	Air Pollutant	Nutrient Intervention	Objectives	Main Outcome Measures	Interpretation
Randomized, controlled	Subjects exposed to emissions from a coal electric-power plant	$N = 80$	Particulate matter (PM)	Vitamin C (500 mg/day), Vitamin E (800 mg/day)	To better understand the relations between PM exposure derived from a coal electric-power plant and the oxidative damage in subjects directly or indirectly exposed to airborne contamination	Biomarkers of oxidative stress	Antioxidant intervention was able to confer a protective effect of vitamins C and E against the oxidative insult associated with airborne contamination derived from coal burning of an electric-power plant
Randomized, double-blinded, controlled	Healthy middle-aged adults	$N = 29$	Particulate matter (PM)	Omega-3 fatty, acid (3 g fish oil/day), Olive oil (3 g/day)	To evaluate the efficacy of fish oil supplements in attenuating adverse cardiac effects of exposure to concentrated ambient fine and ultrafine particulate matter (CAP)	Heart rate variability (HRV) and electrocardiographic (ECG) repolarization changes. Plasma lipids changes	Omega-3 fatty acid supplements offer protection against the adverse cardiac and lipid effects associated with air pollution exposure

Nutrients **2015**, *7*, 10398–10416; doi:10.3390/nu7125539

✓The role of vitamins as potential epigenetic modifiers.

https://doi.org/10.1515/reveh-2022-0027

✓B vitamins, vitamin C, vitamin E, vitamin D and omega-3 PUFA (fish oil and olive oil) have protective effects against the damage induced by PM.

Nutrients **2015**, *7*, 10398–10416; doi:10.3390/nu7125539

doi: 10.1016/j.bbagen.2016.05.014

- ✓Medications with antioxidant or anti-inflammatory properties protect the cardiopulmonary system against air pollution exposure.

doi: 10.1016/j.bbagen.2016.05.014

- ✓ARBs might attenuate the adverse effects of PM2.5 on BP.

Hypertension. 2021;77:174–183. DOI: 10.1161/HYPERTENSIONAHA.120.16611

Overview of the number of studies providing evidence for an effect of a pharmacological agent on cardiovascular parameters linked to air pollution exposure.

		Cardiovascular mortality	Cardiac parameters		Vascular parameters*		Thrombotic parameters	
			human	animal/cell	human	animal/cell	human	animal/cell
Antioxidants	Diet (Mediterranean diet or fish/olive oil supplements	✓ / ? / X	✓✓		✓ / ? / X		✓✓	
Antioxidants	Antioxidant agents (may also have anti-inflammatory properties)			✓✓	X	✓✓		✓✓
Beta-blockers			✓✓	✓✓				✓
Statins			✓		✓/X		?	
Angiotensin pathway inhibitors			?			✓	?	
Endothelin inhibitors					✓✓	✓		
Others	vanilloid inhibitors			✓✓				
Others	Rho kinase inhibition			✓				
Others	NOS co-factors					✓		
Others	TNFα inhibitor					✓		
Others	Anti-platelet agent						✓	
Others	Histamine antagonists							✓

Take Home Massage

- ✓PM2.5 air pollution is contributing to global cardiovascular mortality and disability.
- ✓ Primary initiating pathways: Oxidative stress, Direct translocation, Biological intermediates.
- ✓Secondary effector pathways: Autonomic imbalance, Endothelial dysfunction, Thrombotic pathways, Epigenetic changes, Systemic inflammation.
- ✓ Along with reducing PM2.5, diet, supplements, vitamins and drugs like β-blockers, ARBs, and statins might help.


برای توجه شما
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