Air Pollution and COVID-19 mortality

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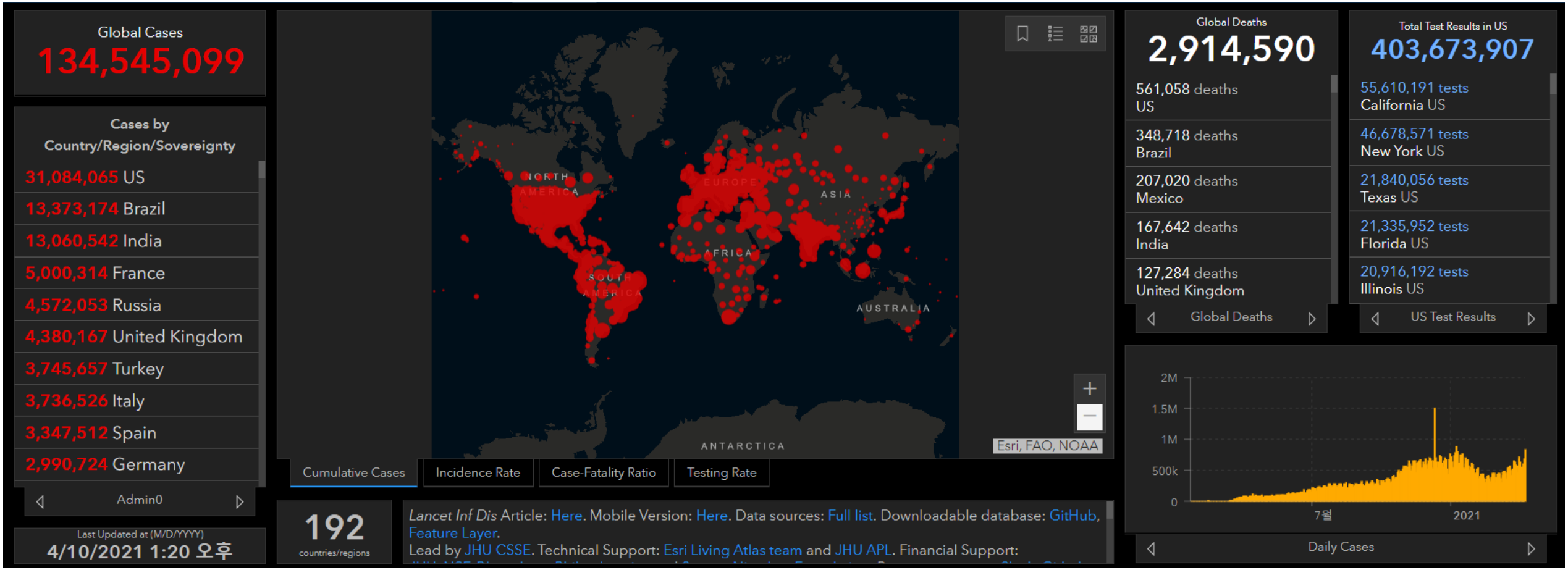
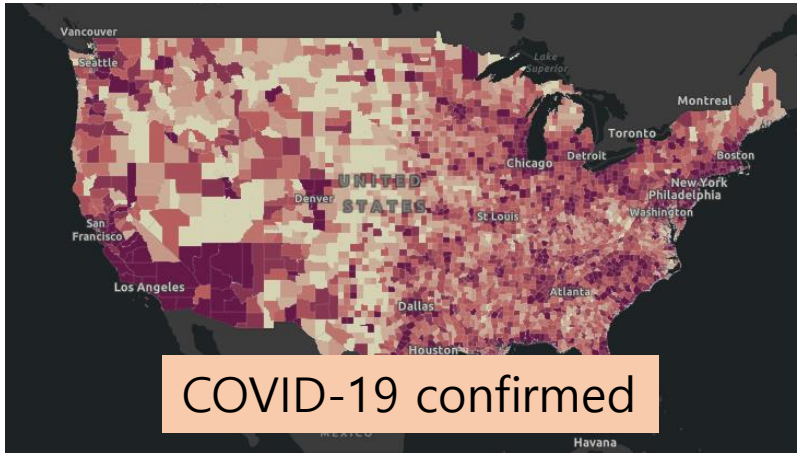
COVID-19 in worldwide



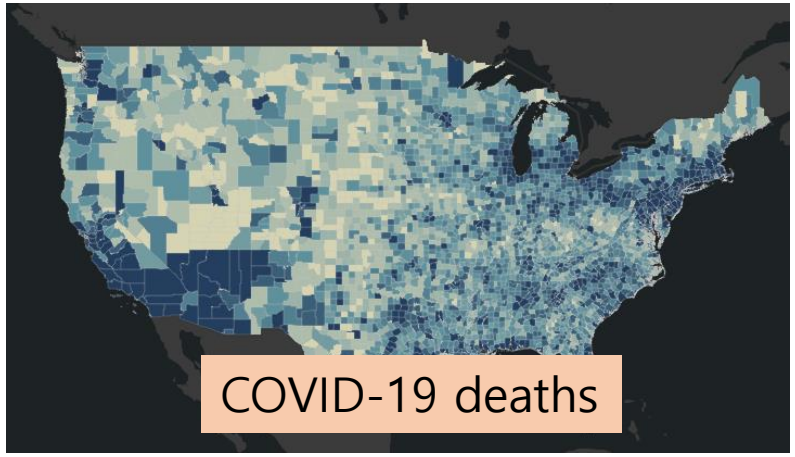
Geographic difference in COVID-19 incidence and mortality

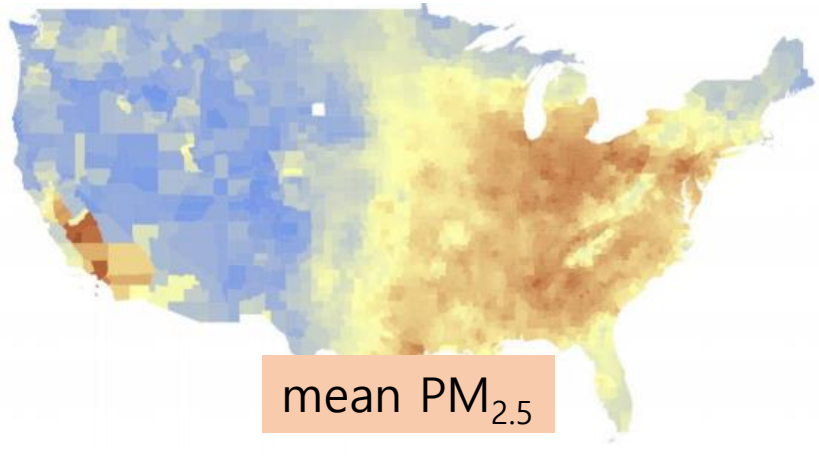
COVID-19 Dashboard by the Centers for Systems Science and Engineering at Johns Hopkins University

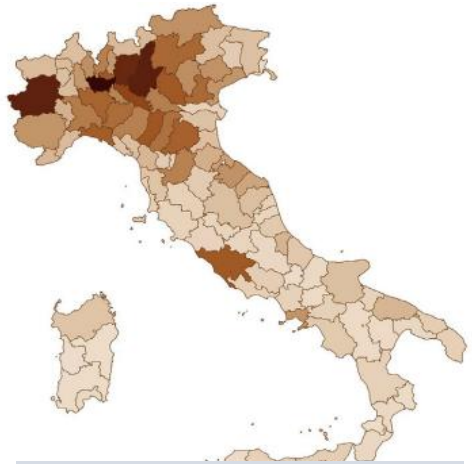
Let`s see few maps



COVID-19 confirmed


COVID-19 deaths


mean $PM_{2.5}$


COVID-19 confirmed


mean NO_2


mean $PM_{2.5}$


mean PM_{10}

Wu et al. MedRxiv 2020
D.Fattorini, F.Regoli. Environmental Pollution 264 (2020) 114732

Geographic difference of COVID-19

- Different incidence and mortality between countries and within countries

- Why ? → Multiple factors..

- One of them,

Atmospheric condition (Temperature, Humidity etc.) + Outdoor air pollution + Indoor air pollution

Definition of Air Pollution

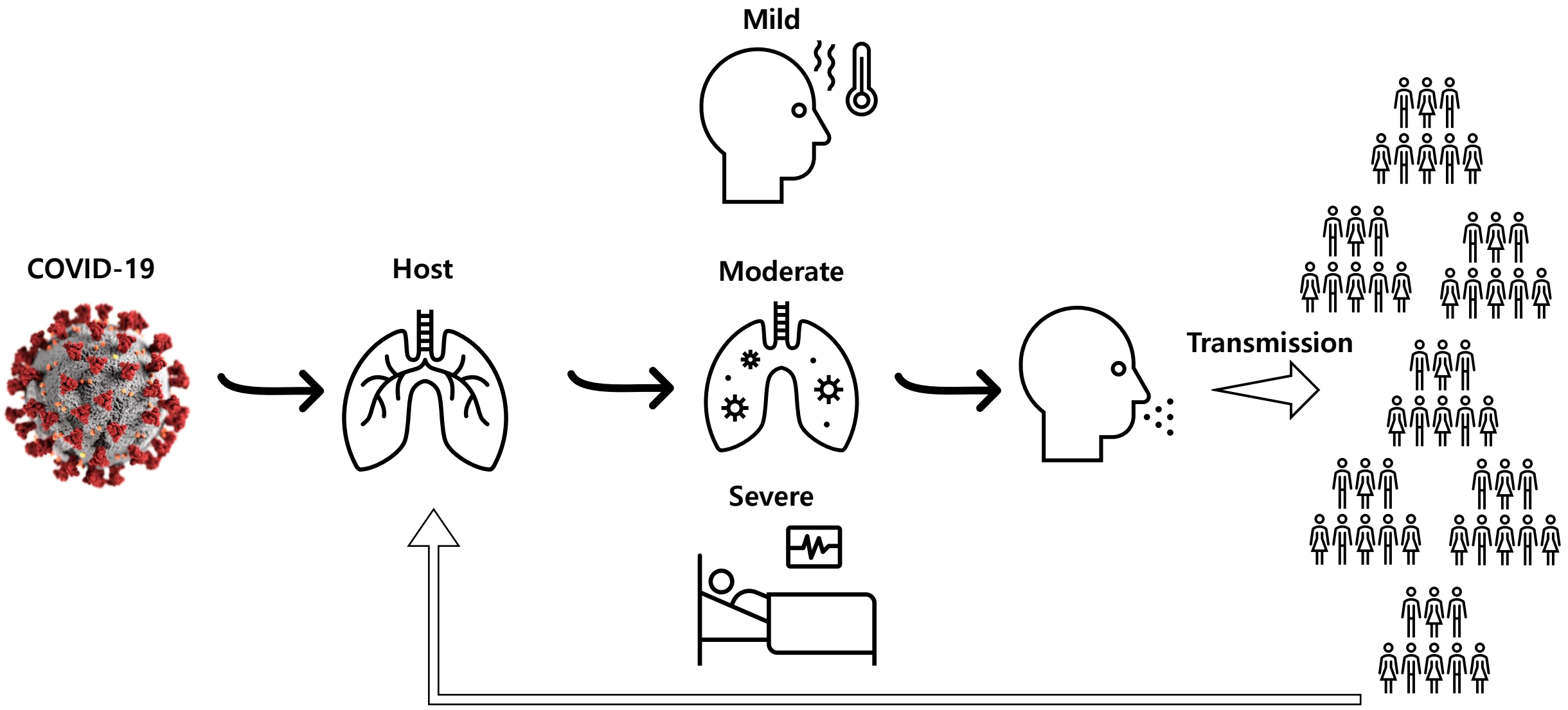
- Definition

: the presence of substances in the atmosphere that are *harmful to the health of humans* and other living beings

- Risk factors of *respiratory infection*, heart disease, COPD, stroke and lung cancer

- Category
  - Outdoor air pollution → $PM_{2.5}$, PM_{10}, NO_x, and O_3
  - Indoor air pollution → CO, Radon, indoor PM, Smoking, Volatile Organic Compounds (VOCs)

Clinical course of COVID-19



Contents

- Air pollution and infection and transmission in COVID-19
- Air pollution and disease severity of COVID-19
- Air pollution and prognosis of COVID-19
- Indoor air pollution and COVID-19

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COVID-19: Transmission

- Transmission of COVID-19
  - Airborne
  - Droplet
  - Direct
- In airborne and droplet transmission, R_0 is affected by few factors
  - Vector
  - Viability

Potential role of air pollution as Vectors of COVID-19

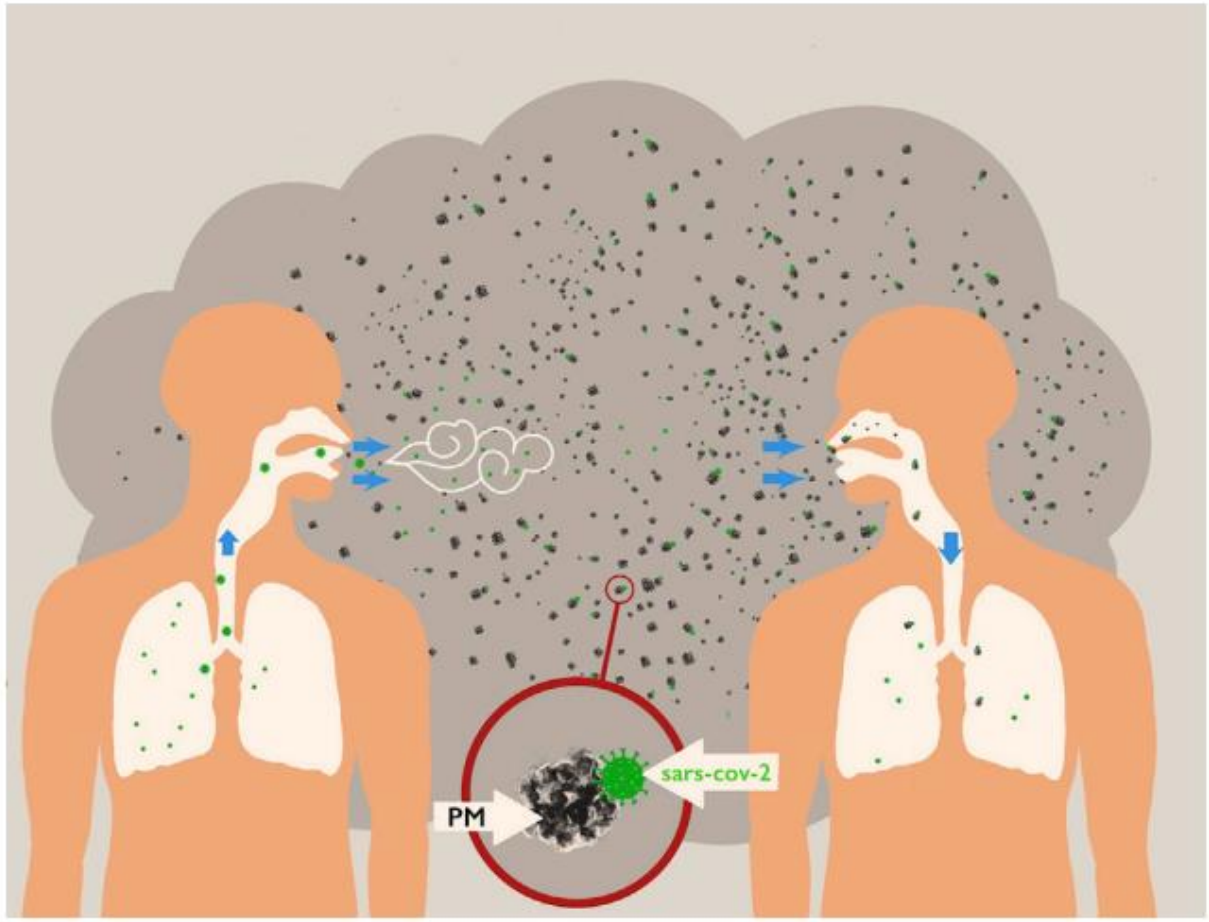


Figure 1. Schematic Representation of the Potential Role of PM as Vectors of SARS-CoV-2

T. Barakat et al. Cell Press 3, 977-980, October 7, 2020

More viable virus in polluted area

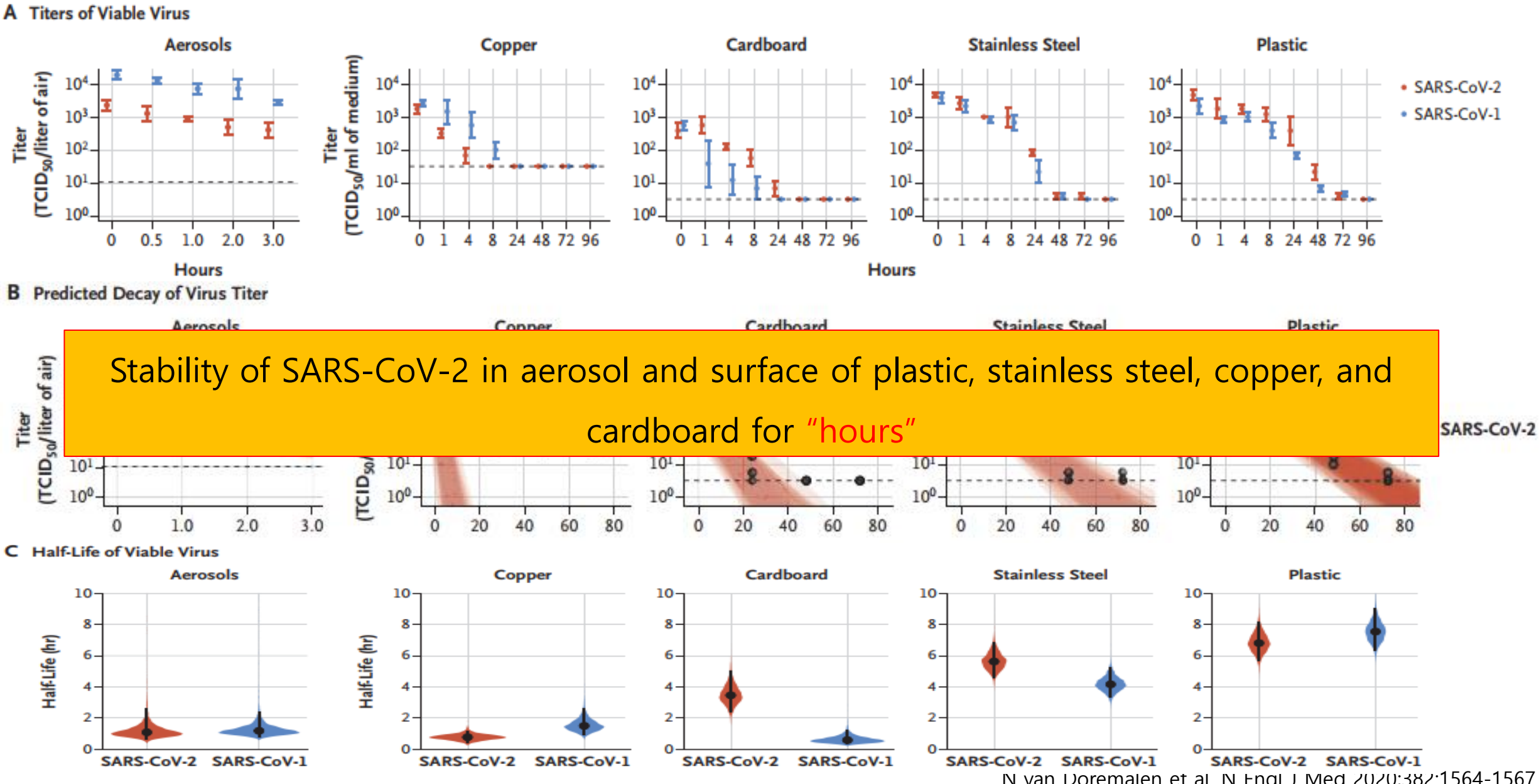
The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1

N van Doremalen et al. N Engl J Med 2020;382:1564-1567

More viable virus in polluted area



Stability of SARS-CoV-2 in aerosol and surface of plastic, stainless steel, copper, and cardboard for "hours"

N van Doremalen et al. N Engl J Med 2020;382:1564-1567

Air pollution and COVID-19 transmission?

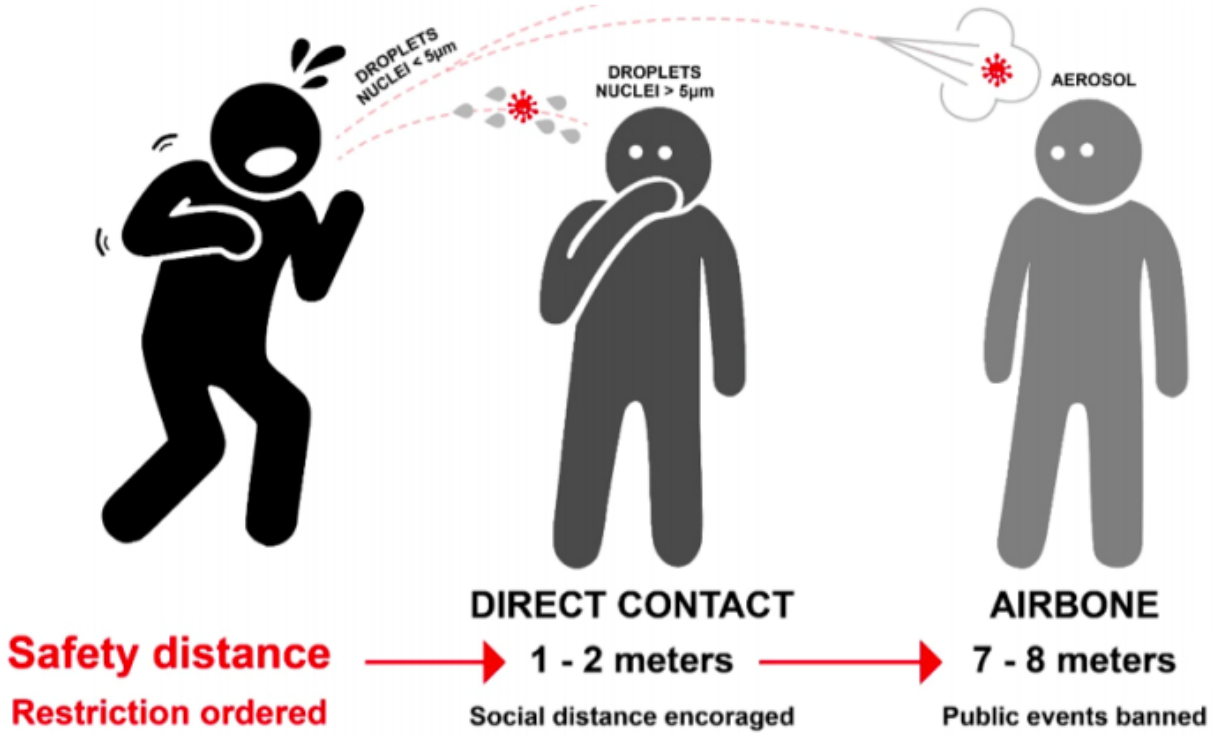
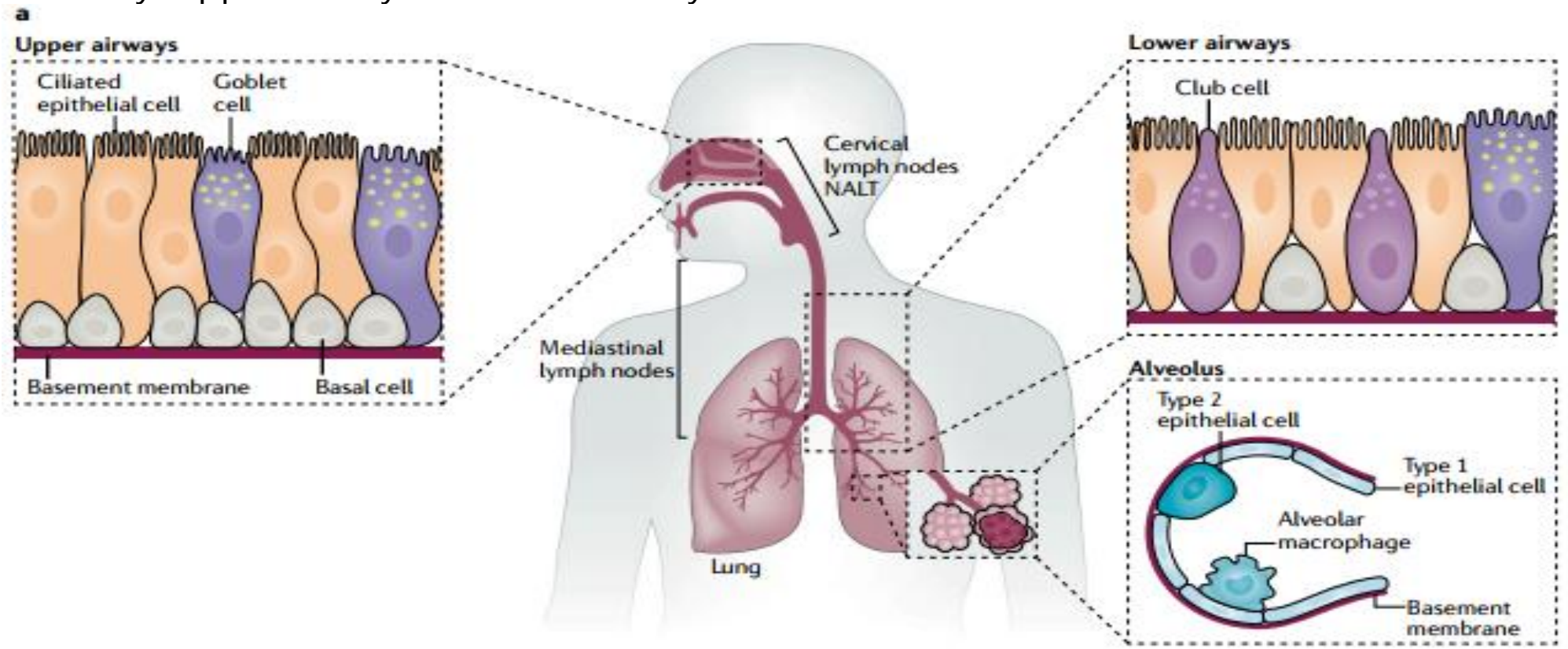


Figure 5 Scheme of possible enhancement of viral transmission through stabilised human exhalation on particulate matter (PM).

COVID-19: Infection

- Infection: Viral entry to host (human)
- COVID-19: Usually mediated by ACE2 and TMPRSS2
- Main entry: upper airway and lower airway



Virus entry via nose – increased ACE2 and TMPRSS2

nature medicine

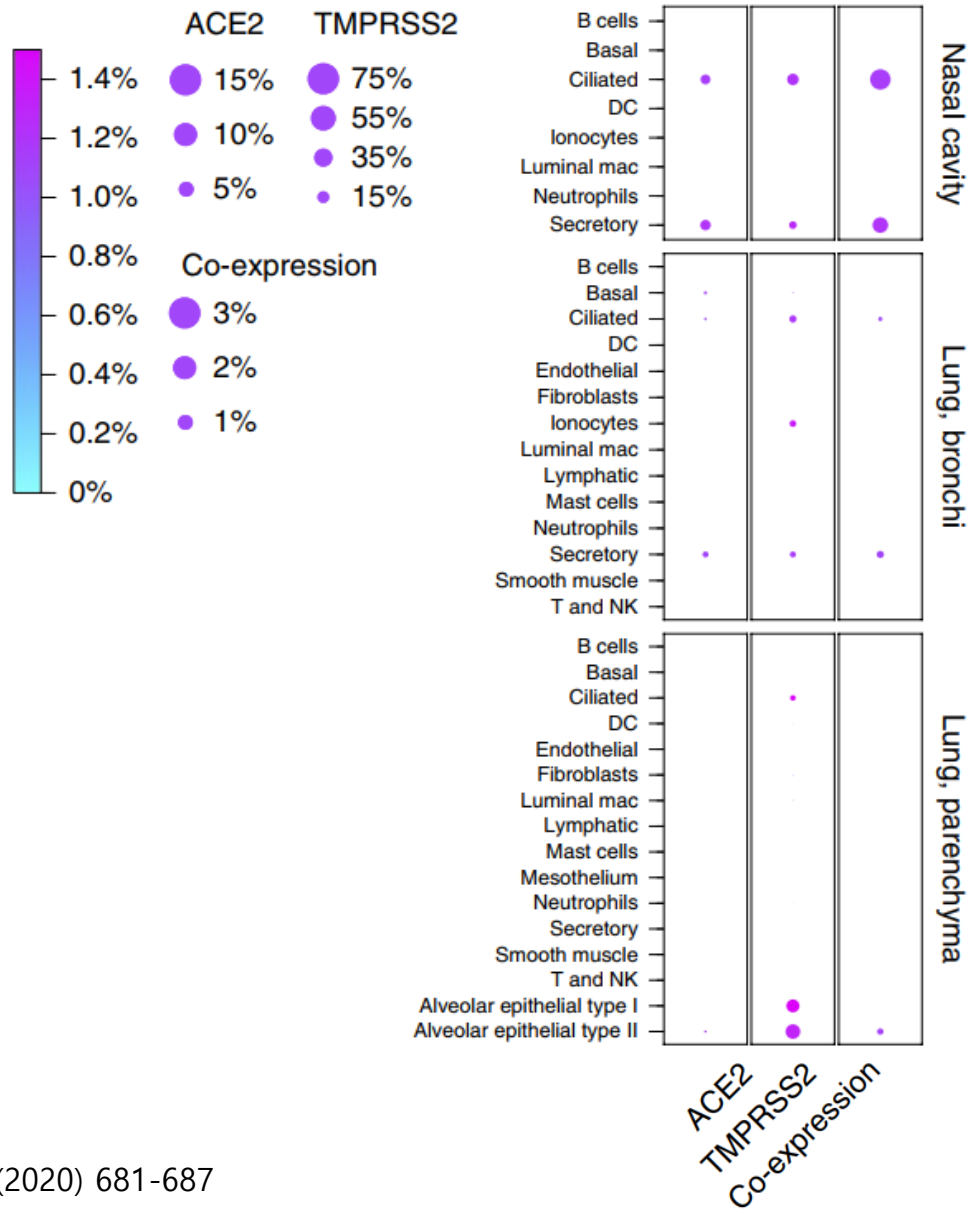
BRIEF COMMUNICATION

https://doi.org/10.1038/s41591-020-0868-6

Check for updates

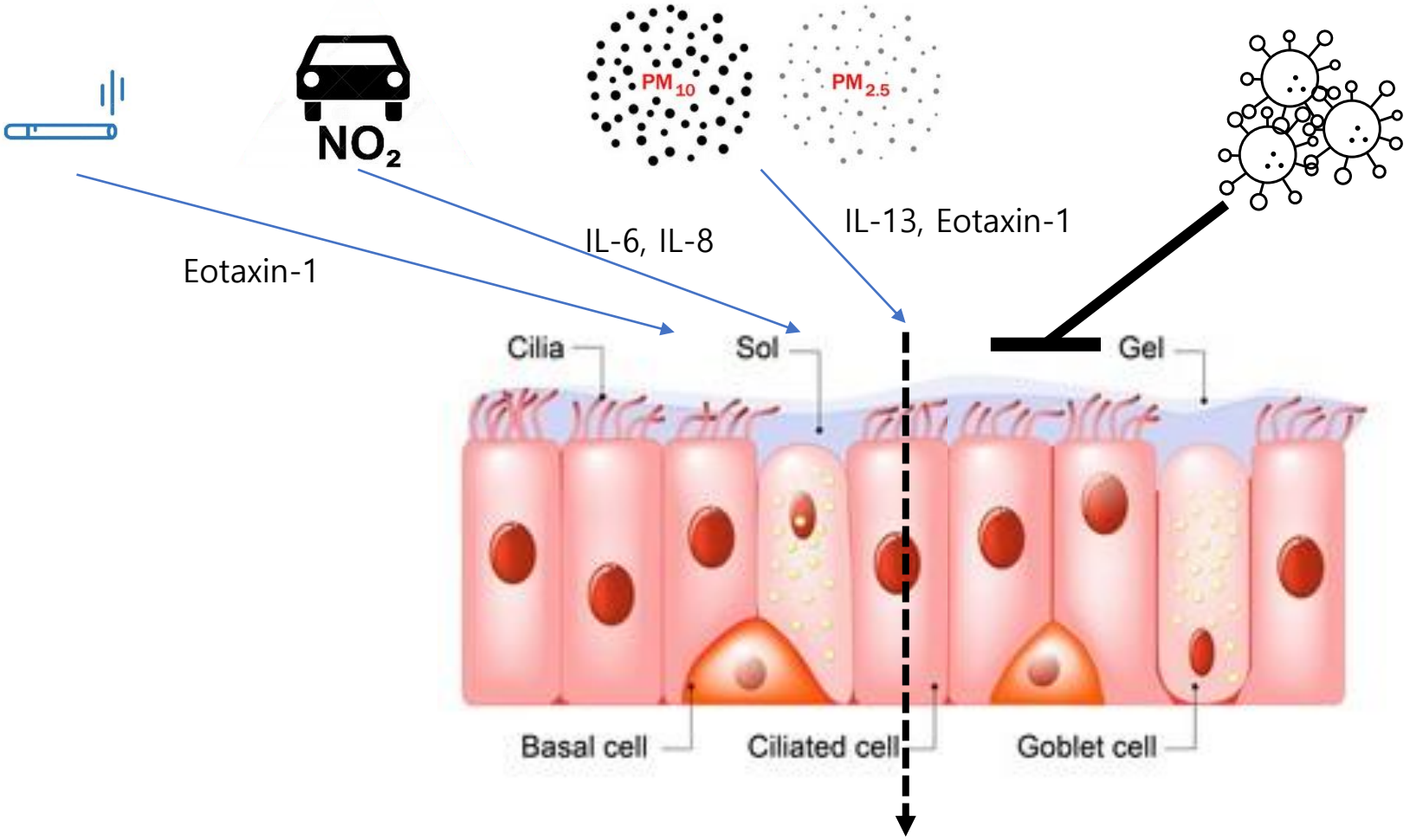
SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes

Waradon Sungnak[1]✉, Ni Huang[1], Christophe Bécavin[2], Marijn Berg[3,4], Rachel Queen[5], Monika Litvinukova[1,6], Carlos Talavera-López[1], Henrike Maatz[6], Daniel Reichart[7], Fotios Sampaziotis[8,9,10], Kaylee B. Worlock[11], Masahiro Yoshida[11], Josephine L. Barnes[11] and HCA Lung Biological Network*✉



W. Sungnak et al. Nature Medicine Vol 26 (2020) 681-687

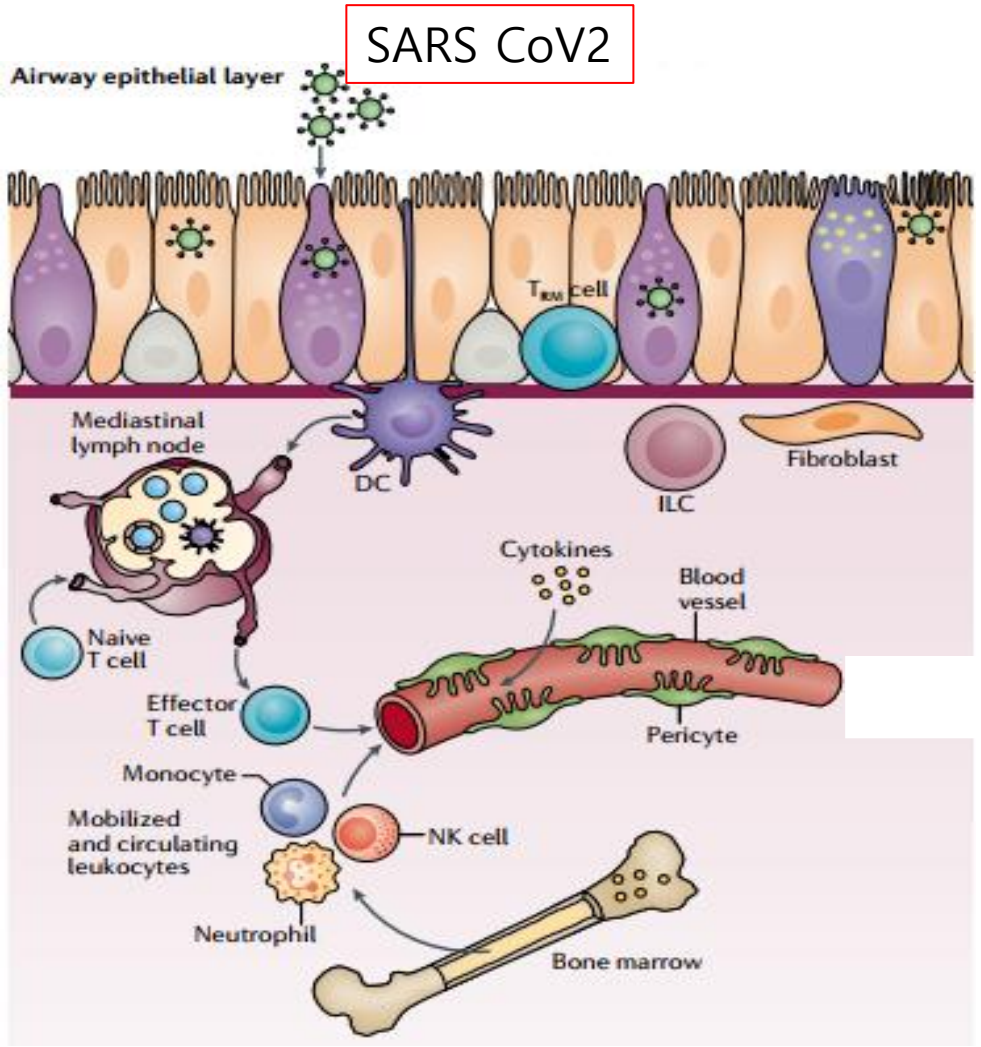
SARS-CoV-2 penetrated nasal mucosa easier due to air pollution



ROS scavenger → Oxidative stress → Exacerbated rhinosinusitis, weakening mucosal barrier

N. London et al. World J Otorhinolaryngol Head Neck Surg. 2018 Sep;4(3):209-215

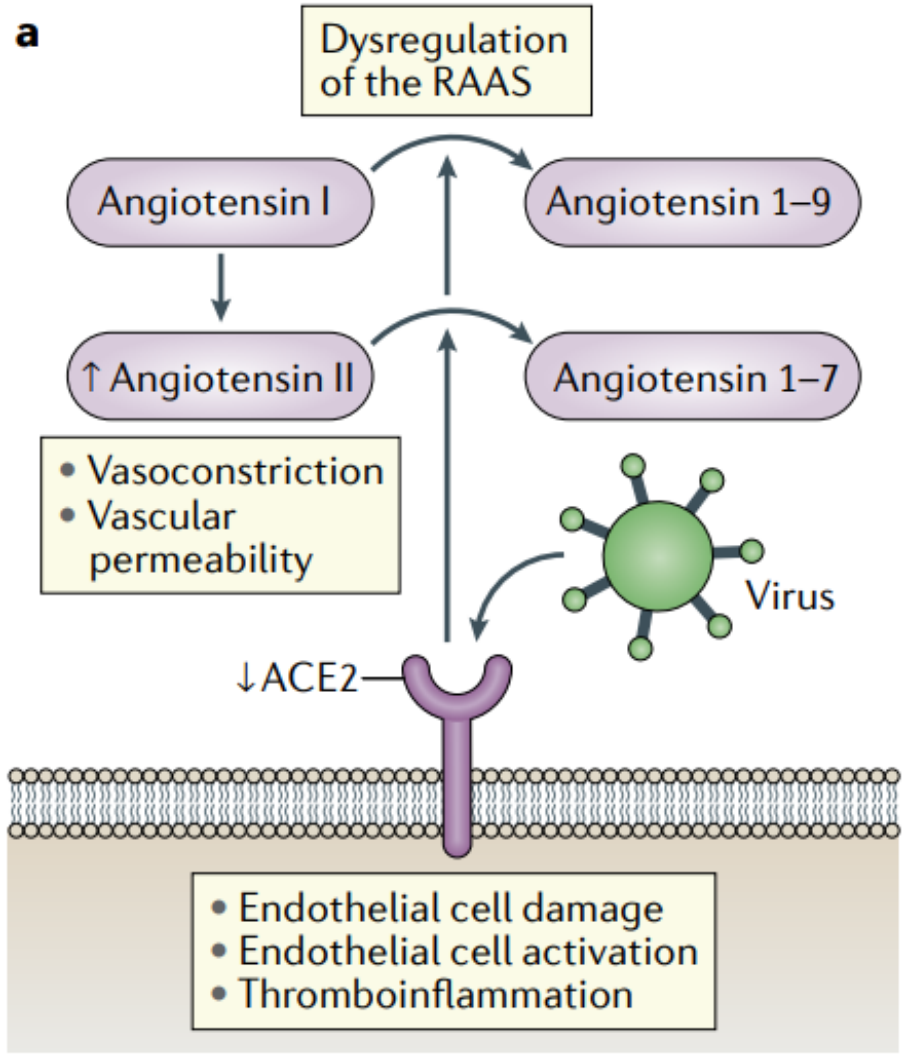
Virus entry via airway - alveolar epithelial barrier



R. Alon et al. Nature reviews

Alveolar epithelial barrier affected by air pollution

- RAS
  - Pro-inflammatory axis (ACE/AngII/AT1R)
  - Anti-inflammatory axis (ACE-2/Ang1-7/Mas)



A. Frontera et al. Journal of Infection 81 (2020) 255-259

Alveolar epithelial barrier affected by air pollution

- $PM_{2.5}$
  - Invasion into deep space of lung by it`s size → response with RAS → infectivity of virus
    - Alveolar edema → More virus penetration

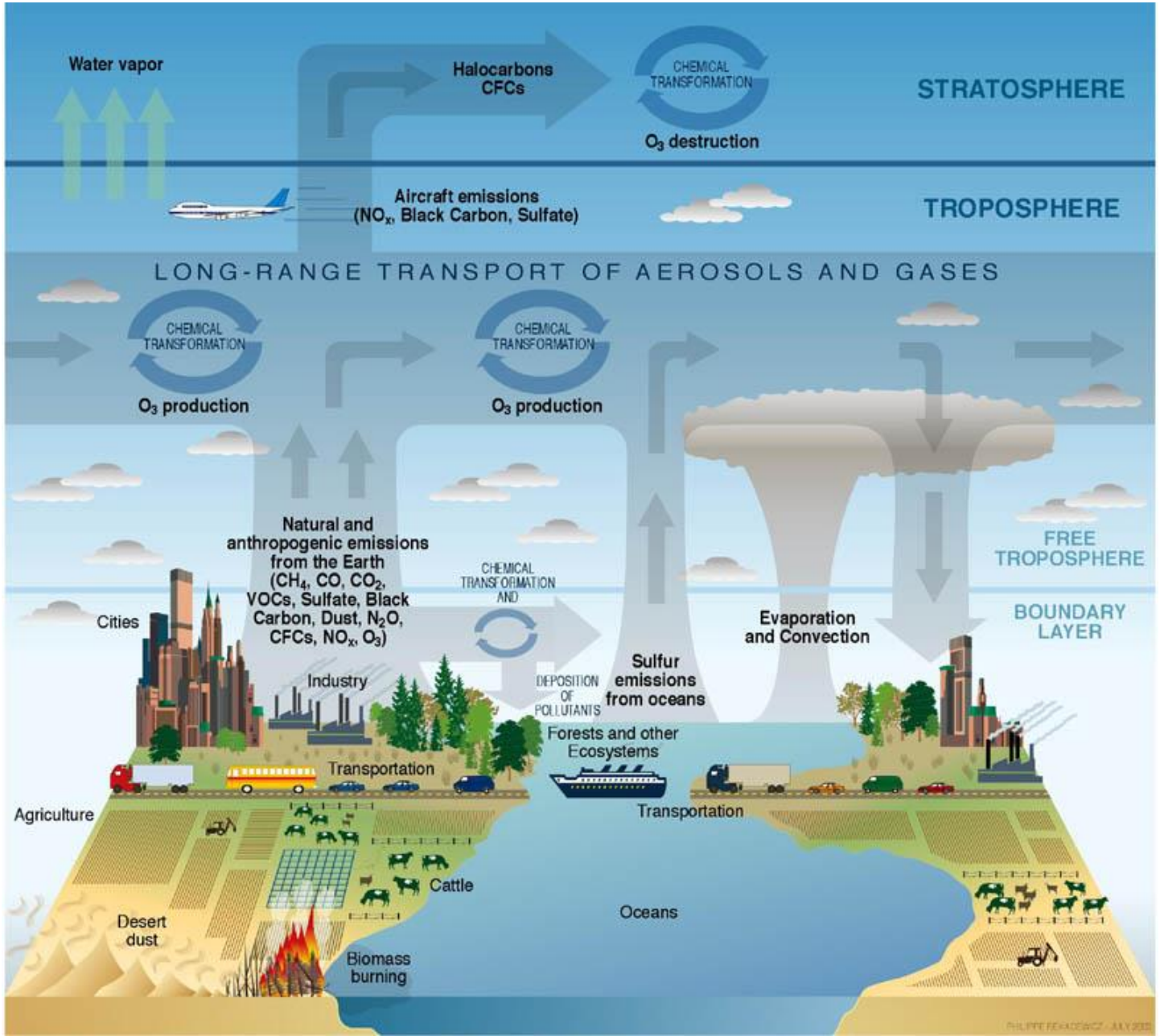
Air pollution → host defense ↓, Host immunity ↓, Disease susceptibility ↑

- Reactive nitrogen species, reactive oxygen species

→ High expression of ACE2 in human epithelial cell surface

→ Alveolar edema by NO_X

A. Frontera et al. Journal of Infection 81 (2020) 255-259
M. Griffiths et al. N Engl J Med 2005;353:2683-95



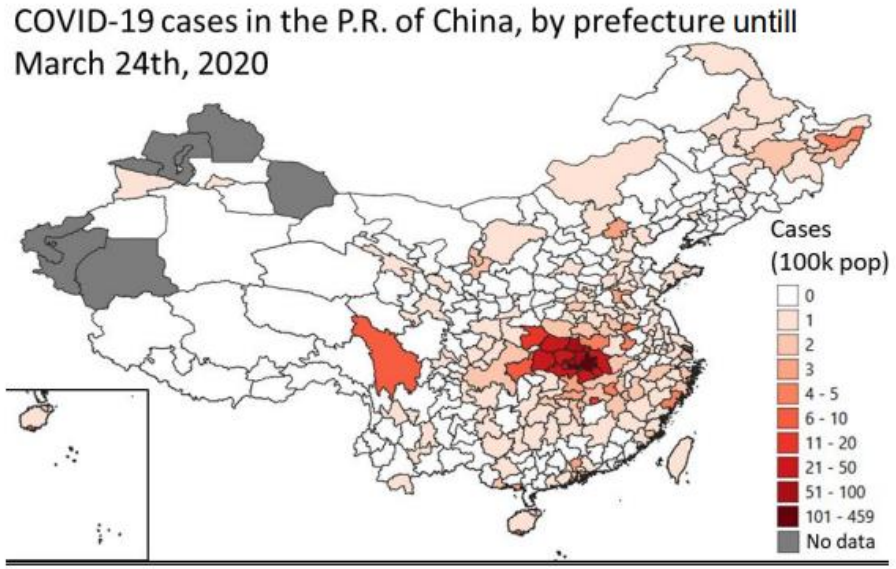
Satellite

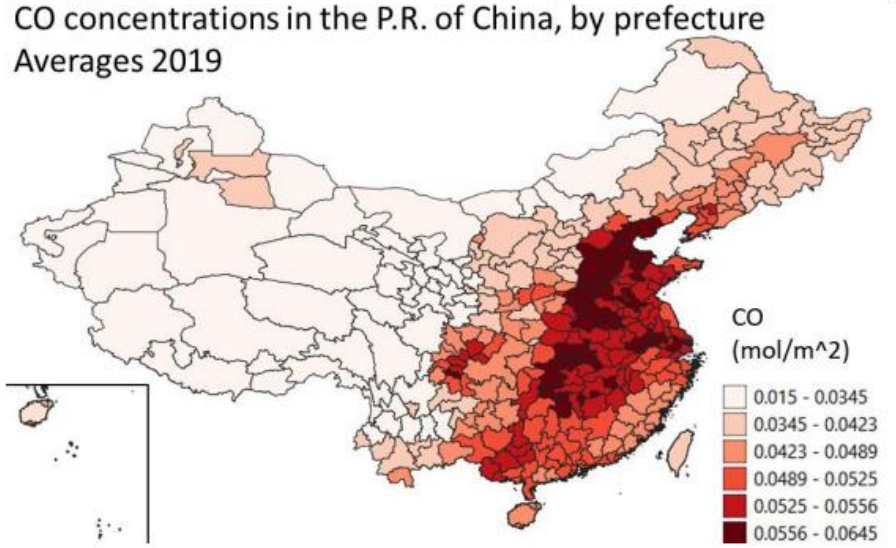
Ground level

Individual level

COVID-19 and air pollution of atmosphere level

- Air quality by Satellite (Sentinel-5)
  - Orbiting around China, Italy, and USA
  - CO, NO2, PM2.5

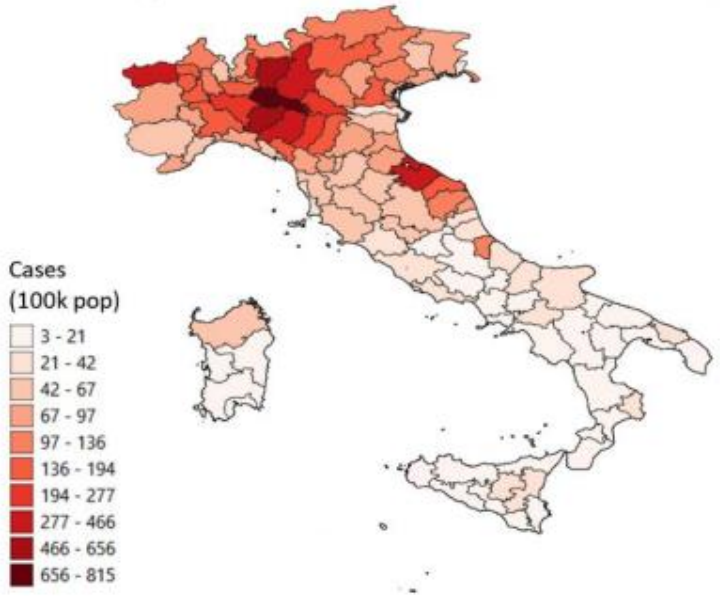




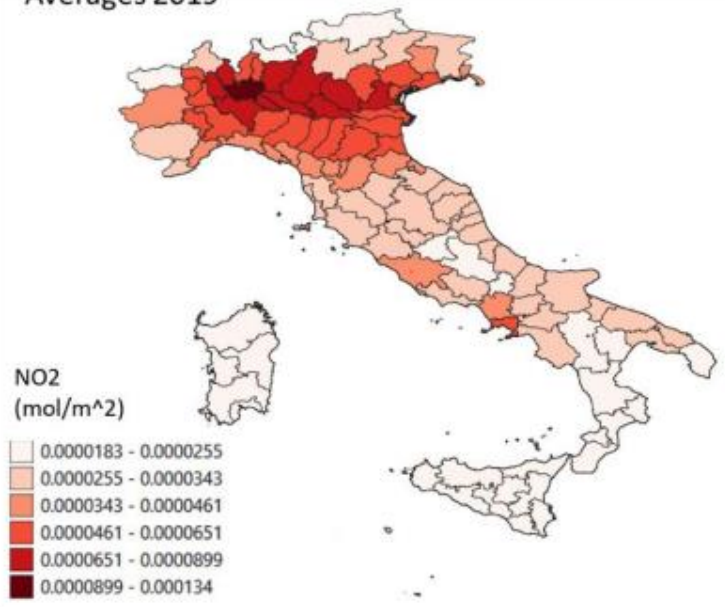
R.Pansini and D.Fornacca preprint on medRxiv

COVID-19 and air pollution of atmosphere level

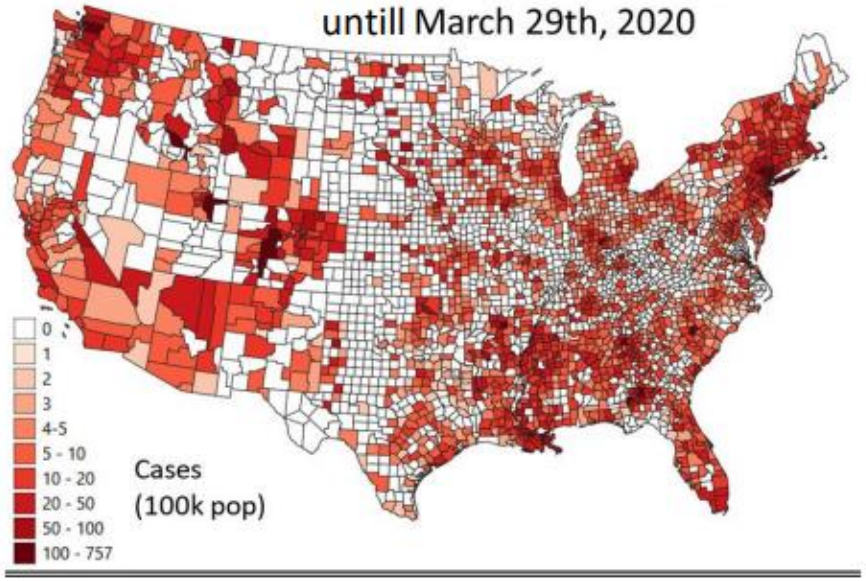
COVID-19 cases in Italy, by province untill March 23rd, 2020



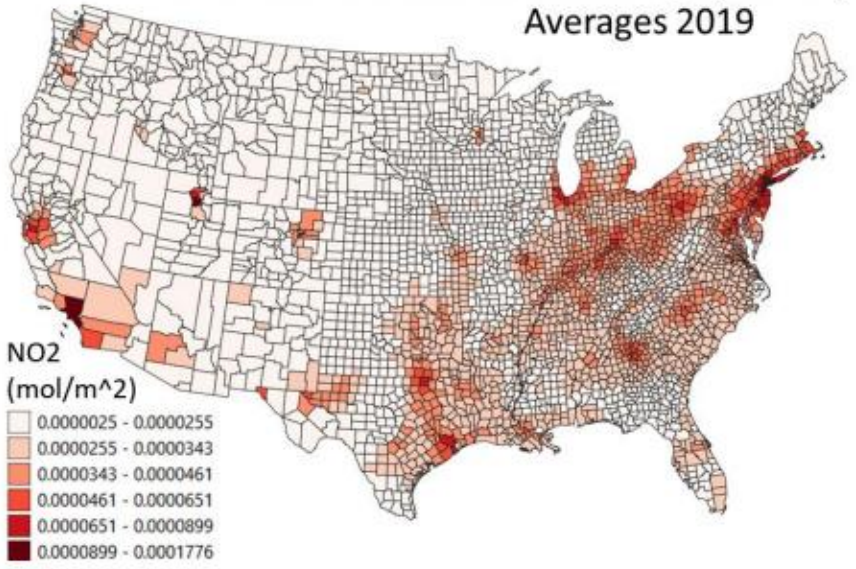
NO2 concentrations in Italy, by province Averages 2019



COVID-19 cases in the U.S.A, by county untill March 29th, 2020



NO2 concentrations in the U.S.A, by county Averages 2019



R.Pansini and D.Fornacca preprint

COVID-19 and air pollution of atmosphere level

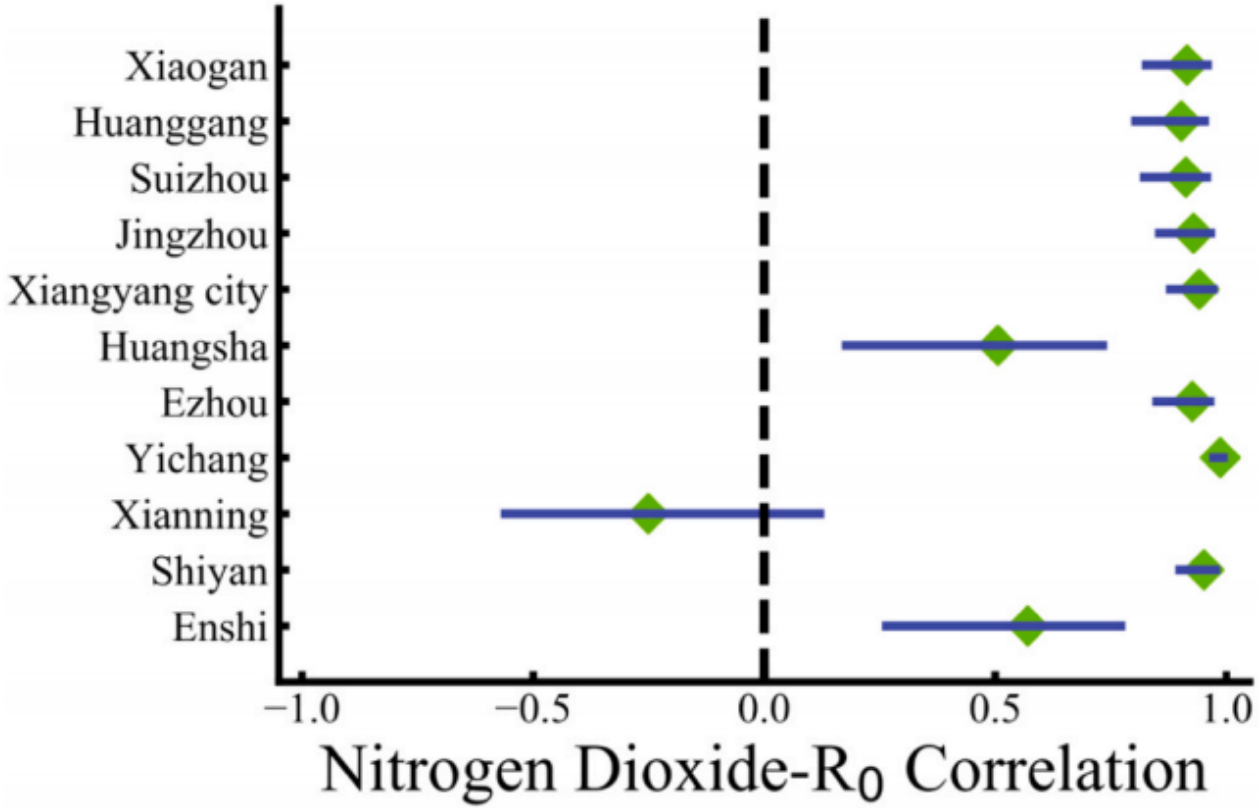
cases_100k	China			Italy			USA		
	df (N-2)	tau	*p*-value	df (N-2)	tau	*p*-value	df (N-2)	tau	*p*-value
Aerosol_sat	345	.01	.797	105	-0.1	.000	3106	-.12	.000
CO_sat	345	.34	**.000**	105	0.15	**.024**	3106	.14	**.000**
HCHO_sat	345	.13	**.001**	105	0.18	**.007**	3106	.04	**.006**
NO_2_sat	345	.12	**.004**	105	0.52	**.000**	3106	.20	**.000**
O_3_sat	345	-.16	.000	105	0.35	**.000**	3106	-.06	.000
SO_2_sat	345	-.14	.001	105	-0.1	.323	3106	.00	.863

R.Pansini and D.Fornacca preprint

COVID-19 and air pollution of ground level

- R_0 is correlated with NO_2 level

- R_0 value and NO level
- At Hubei
- Adjusted temperature and humidity

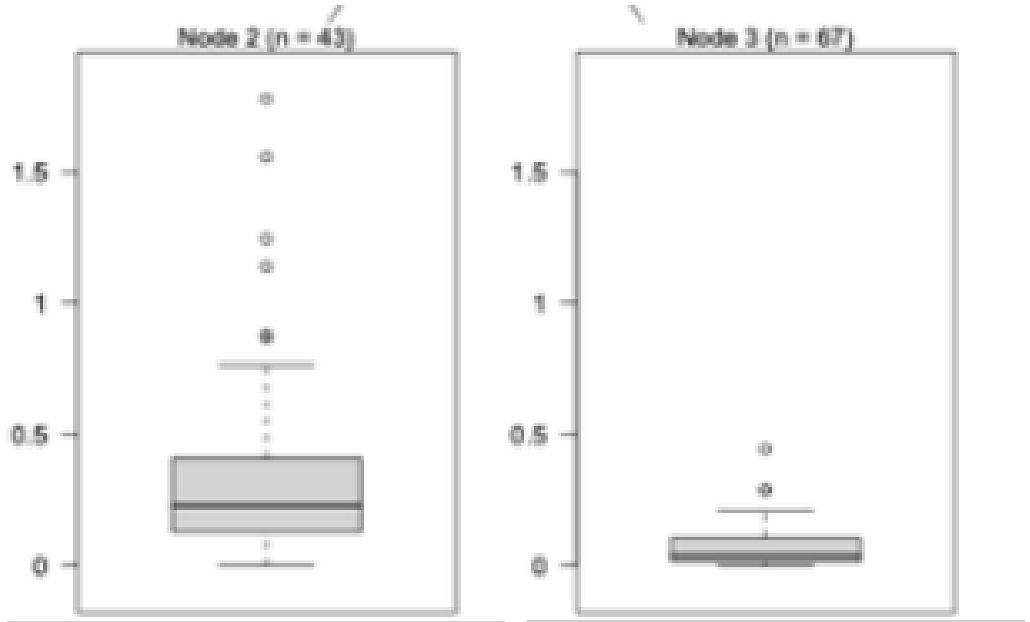


Y. Yao et al. Ecotoxicology and Environmental Safety 208 (2021) 111421

COVID-19 and air pollution of ground level

- Short-term exposure of PM_{10}

- European daily limit of PM_{10} = 50 μg/m^3

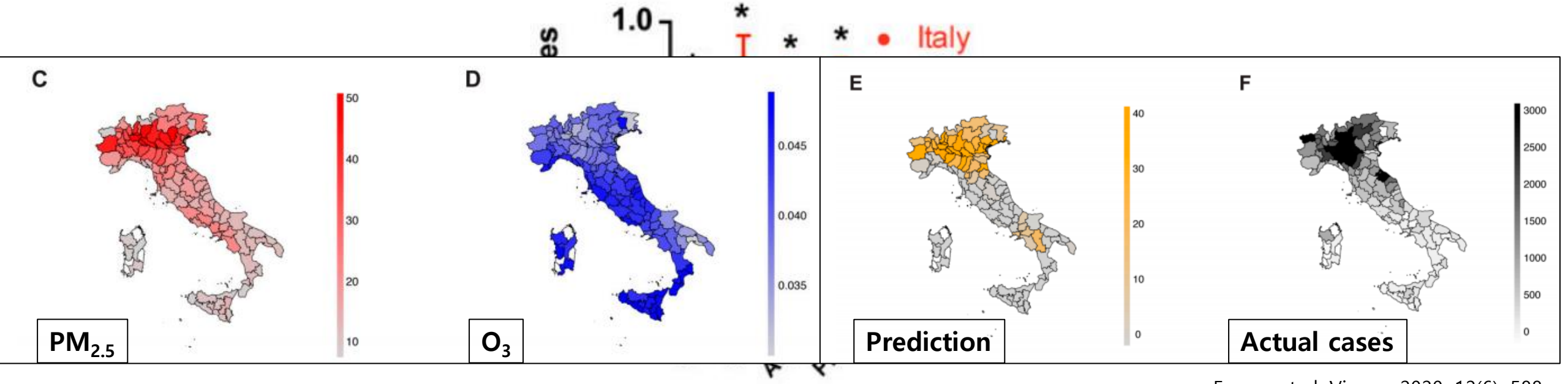


L. Setti et al. BMJ open 2020;10:e039338

COVID-19 and air pollution of ground level

- Hourly air pollution concentration

- Hourly concentration (μg/m^3): $PM_{2.5}$, PM_{10}, O_3, NH_3 in 47 regional capitals of Europe and 107 major Italian cities + Hourly temperature, speed of wind, surface pressure
- Prediction model by ANN (validation by Monte Carlo cross-validation strategy)
- Performance of model



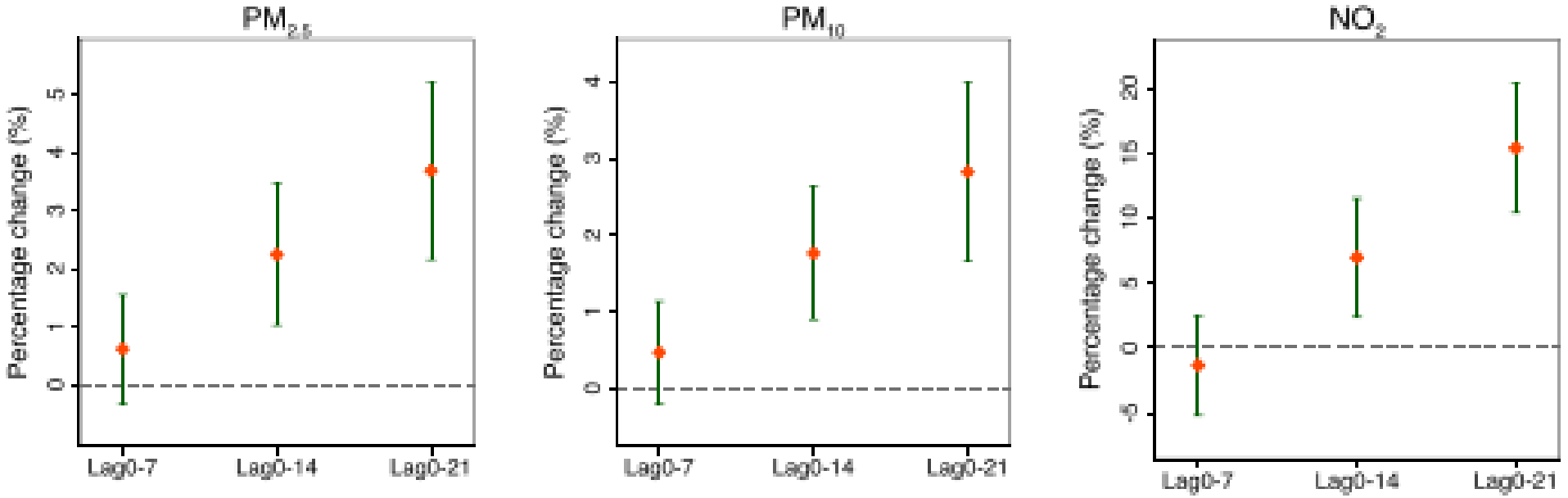
Fronza et al. Viruses 2020, 12(6), 588

COVID-19 and air pollution of ground level

- Lagged effect of short-term exposure in COVID-19

Association between short-term exposure to air pollution and COVID-19 infection: Evidence from China

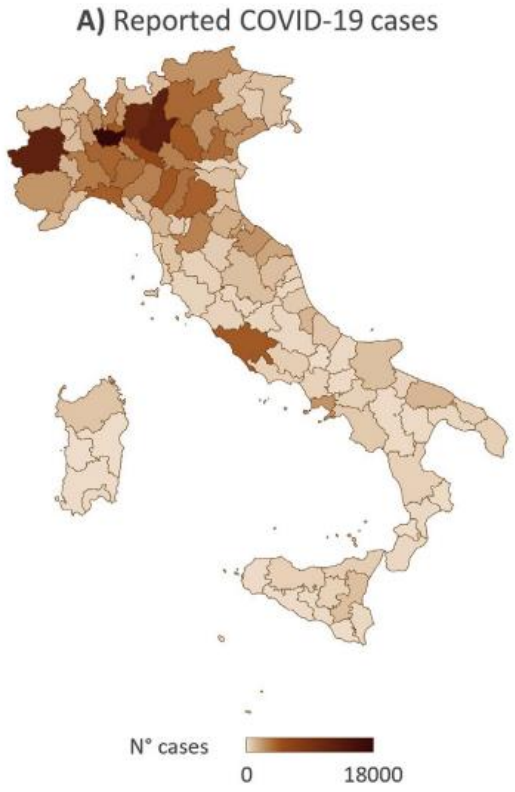
Yongjian Zhu [a], Jingui Xie [b,c,*], Fengming Huang [b], Liqing Cao [b]

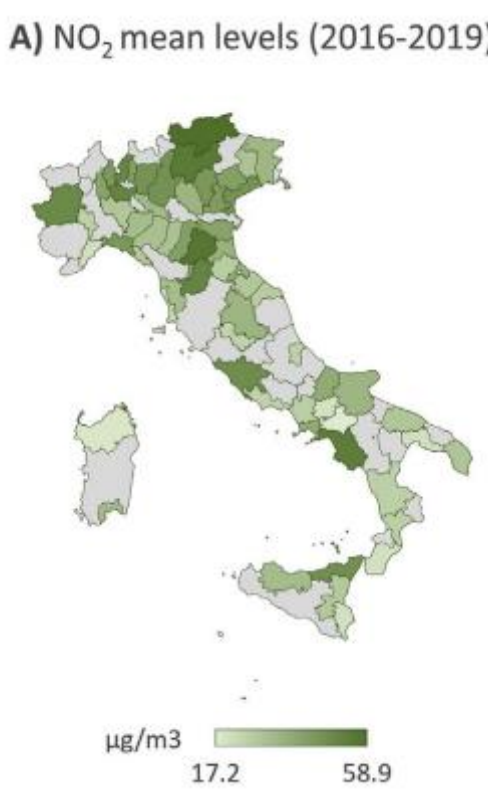


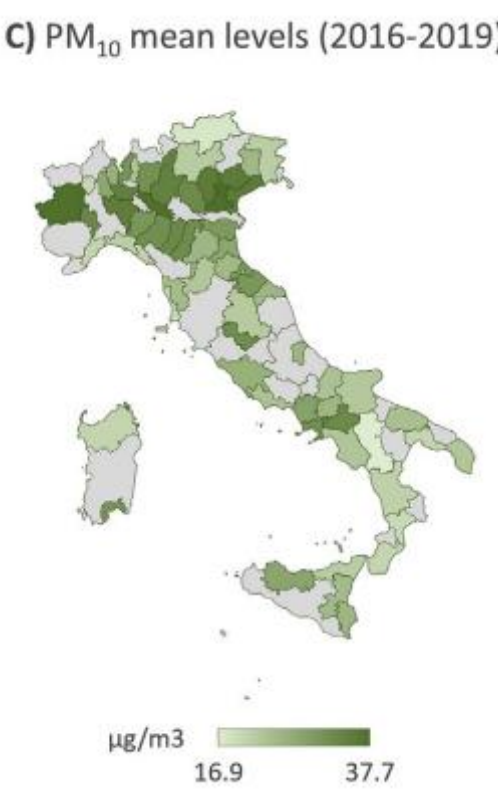
Y. Zhu et al. Science of the Total Environment 727 (2020)

COVID-19 and air pollution of ground level

- Long-term exposure



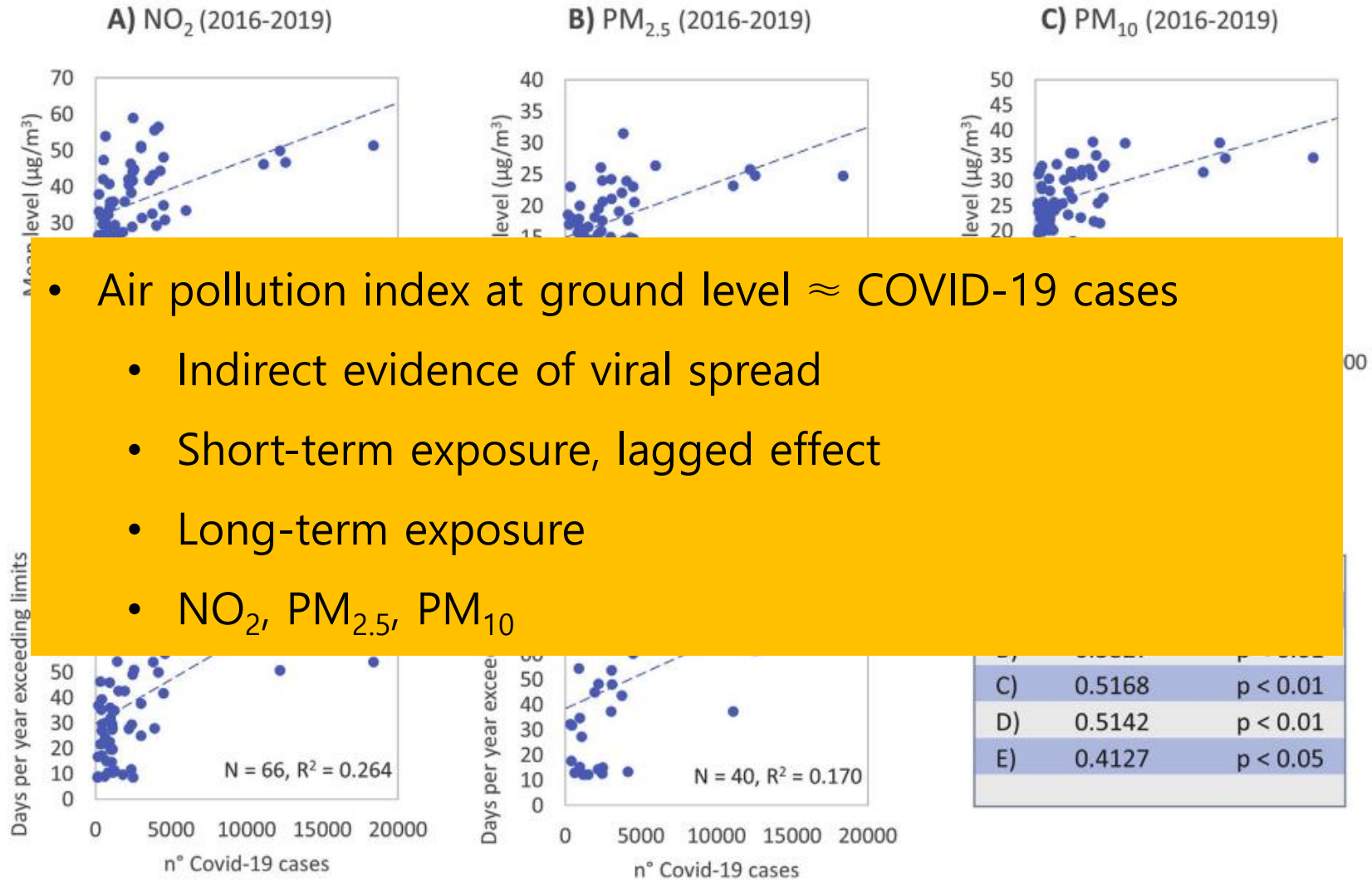




D.Fattorini, F.Regoli. Environmental Pollution 264 (2020) 114732

COVID-19 and air pollution of ground level

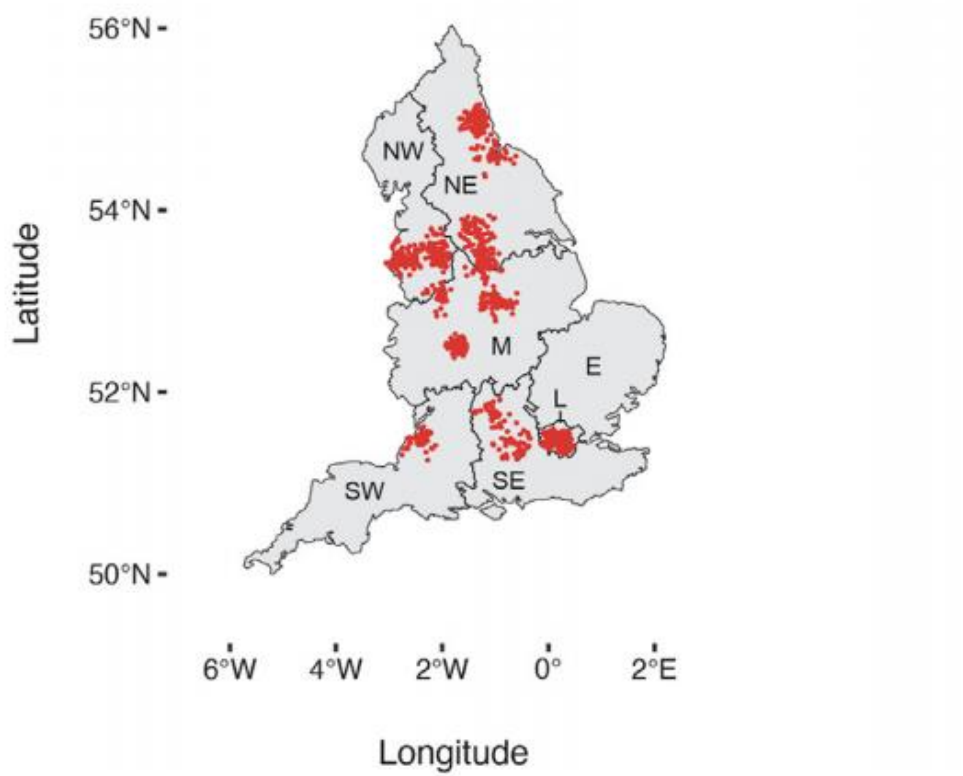
- Long-term exposure

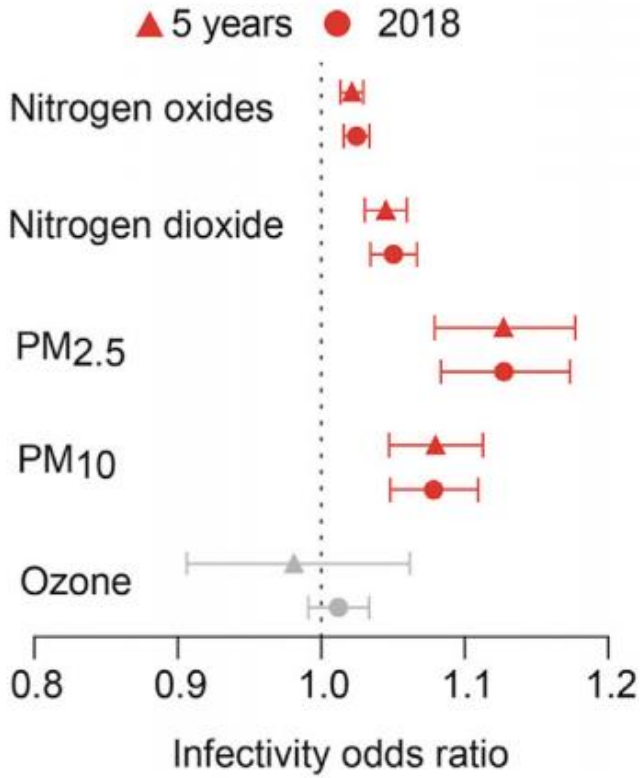


- Air pollution index at ground level ≈ COVID-19 cases
  - Indirect evidence of viral spread
  - Short-term exposure, lagged effect
  - Long-term exposure
  - NO_2, $PM_{2.5}$, PM_{10}

D.Fattorini, F.Regoli. Environmental Pollution 264 (2020) 114732

COVID-19 and air pollution of individual level





- Use individual exposure level data (UK biobank)

  → COVID-19 infectivity : ↑ 1μg/m^3 $PM_{2.5}$ (↑ 12%), ↑ 1μg/m^3 PM_{10} (↑ 8%)

M. Travaglio et al. Environmental pollution 268 (2021)

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Severity of disease

- Factors of disease severity
  - Viral entry
  - Viral replication
  - Key: Anti-inflammatory and pro-inflammatory effect of ACE2

Weakened host immunity

- Wood smoke particle (WSP)
- IP-10 (CXCL10) : recruit cytotoxic lymphocyte to live attenuated influenza virus (LAIV)
- WSP exposure → weak response to LAIV → more viral loads

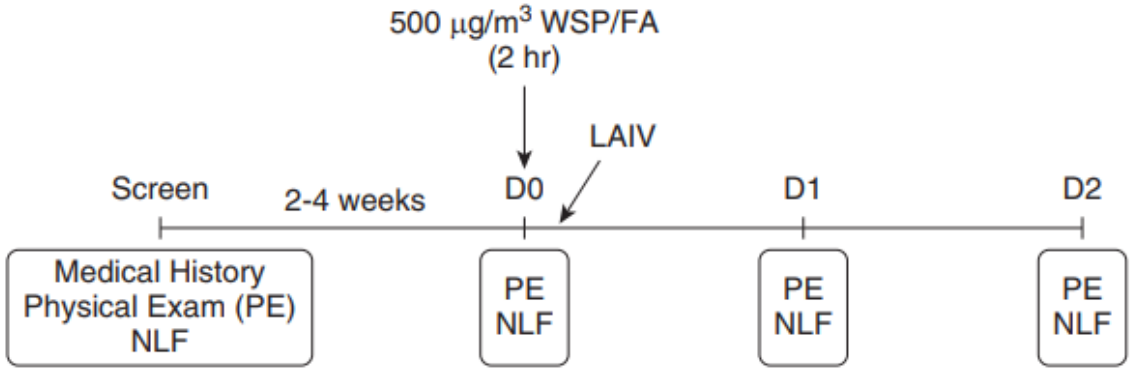
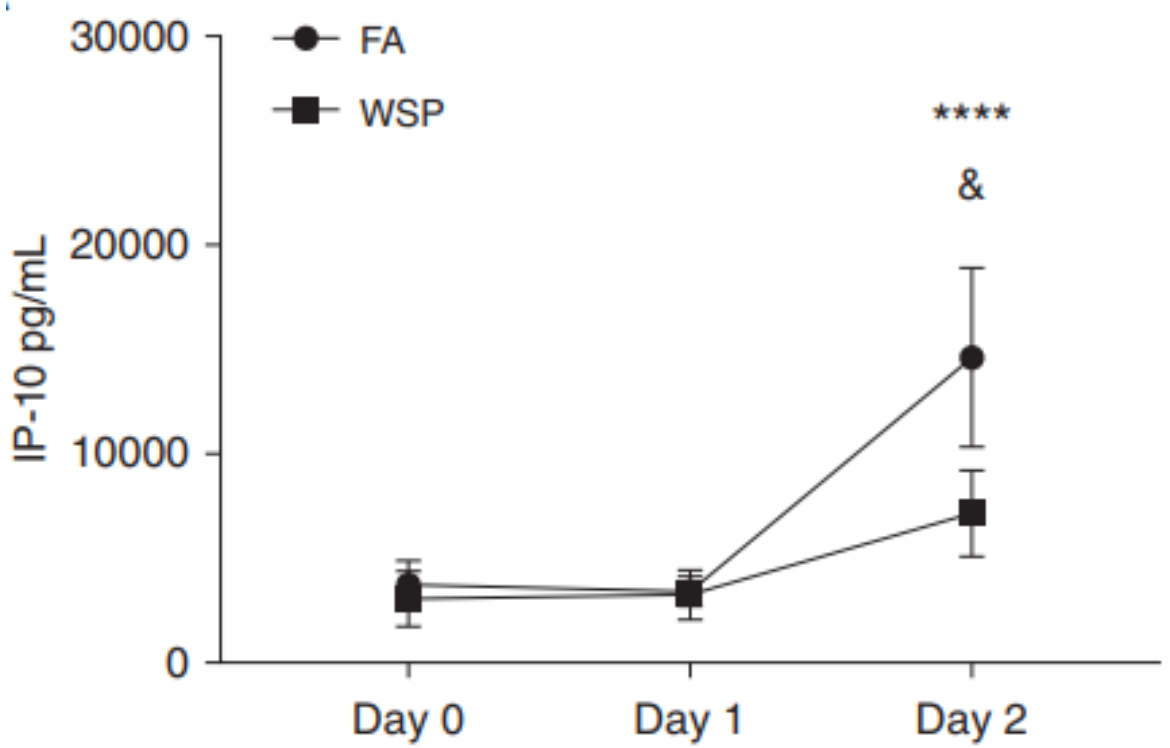
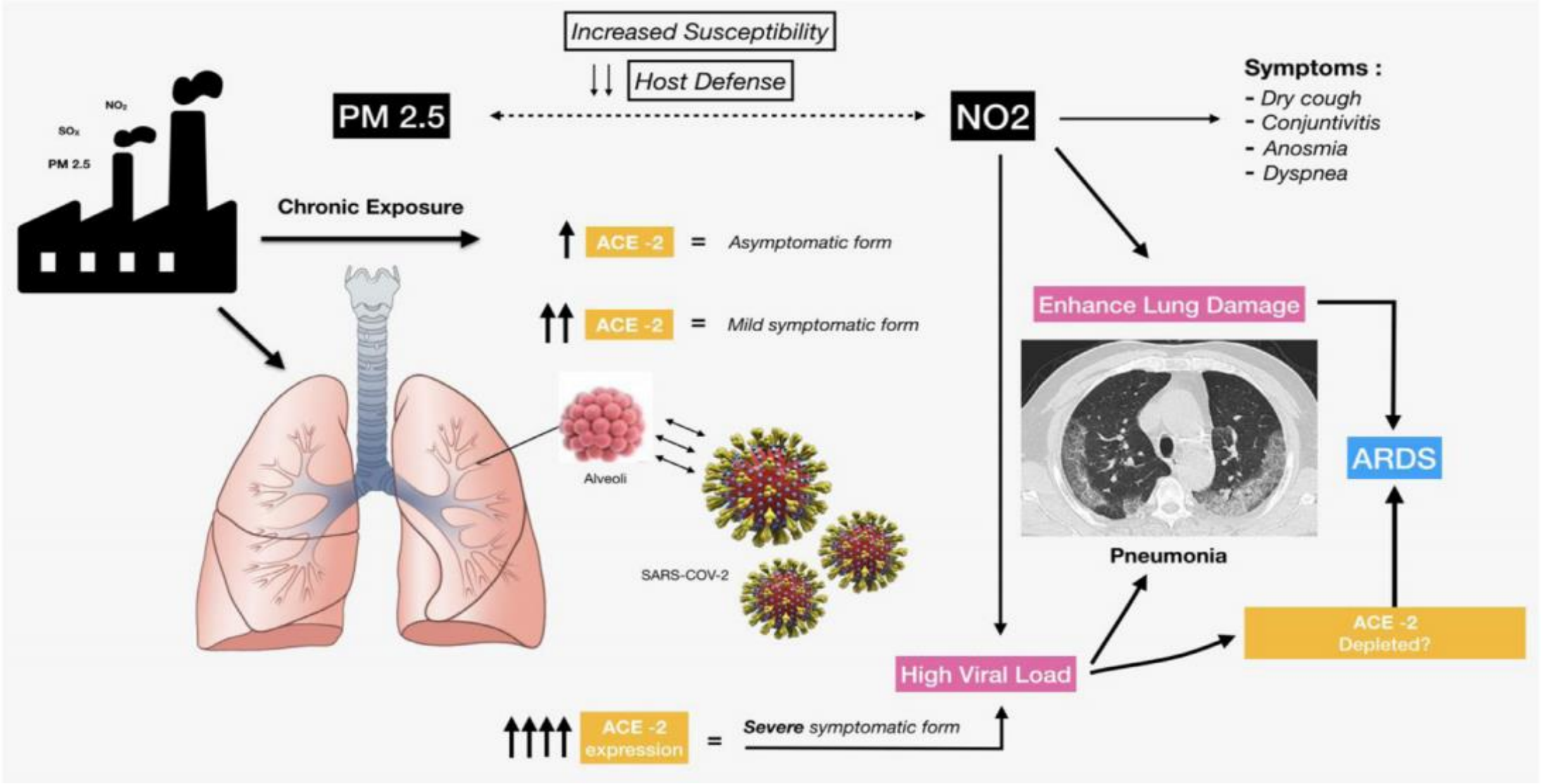


Figure 2. Study design and sample collection timeline. FA = filtered air; LAIV = live attenuated influenza virus; NLF = nasal lavage fluid; PE = physical exam; WSP = wood smoke particles.



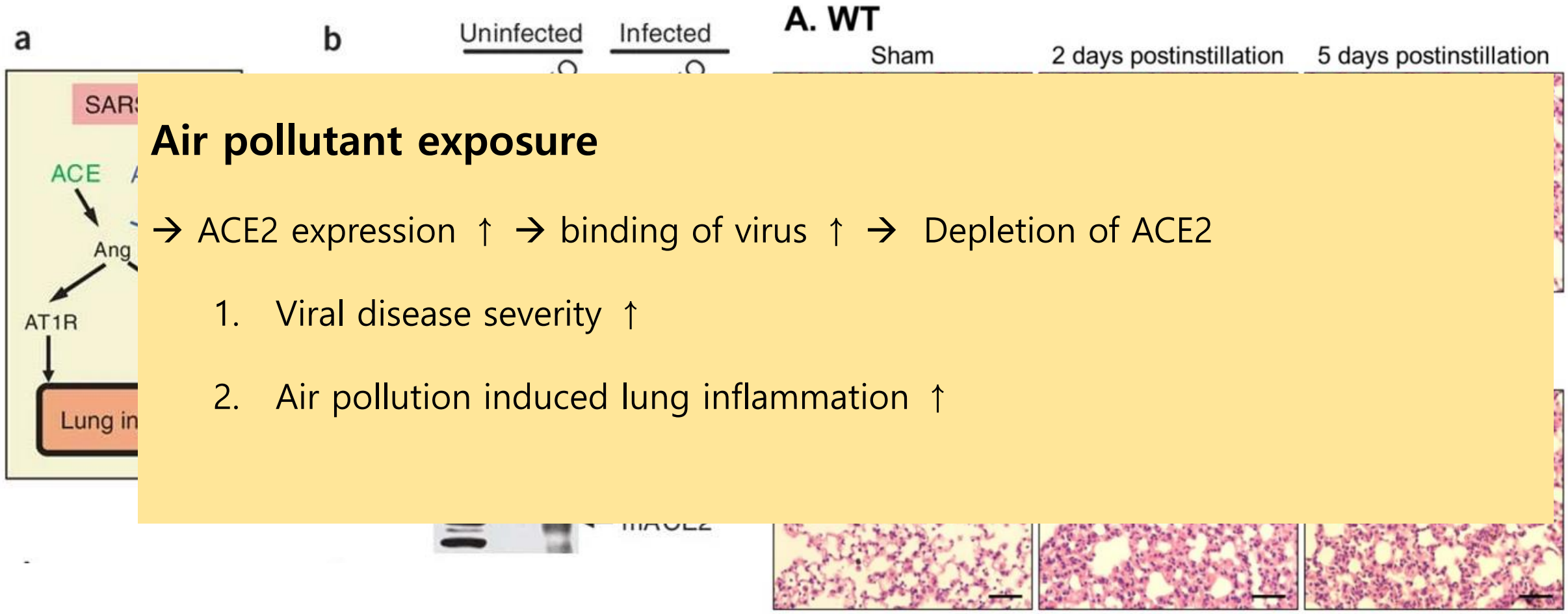
ACE2 expression and ACE2 depletion



A. Frontera et al. Journal of Infection 81 (2020) 255-259

COVID-19: Air pollution and severity

PM induced inflammation was severe in ACE2 KO mouse



Air pollutant exposure

→ ACE2 expression ↑ → binding of virus ↑ → Depletion of ACE2

1. Viral disease severity ↑
2. Air pollution induced lung inflammation ↑

K. Kuba et al. Nature Medicine 11, 875-879 (2005)
C. Lin et al. Int. J. Biol. Sci. 2018;14(3):253-265

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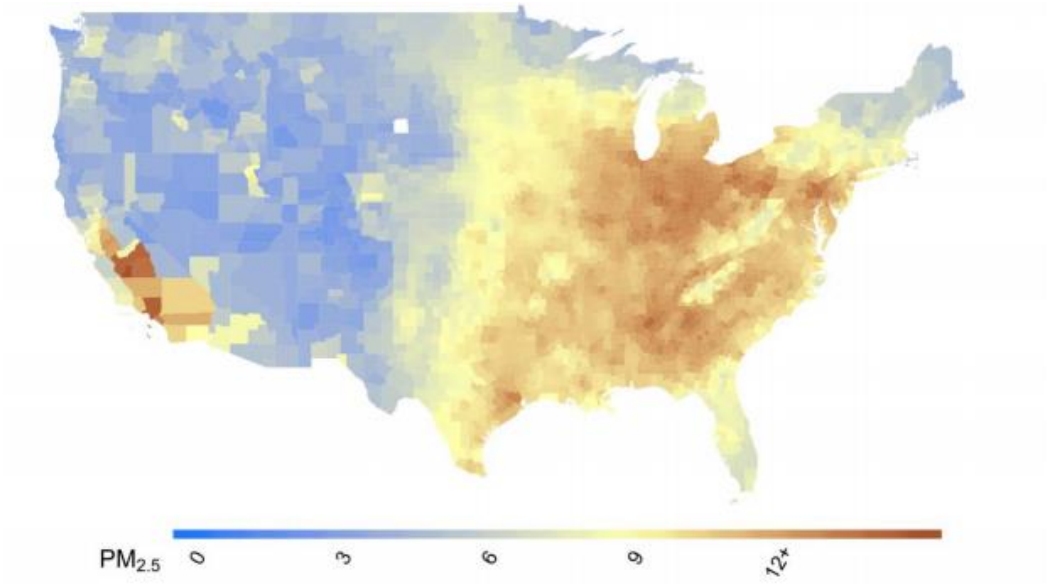
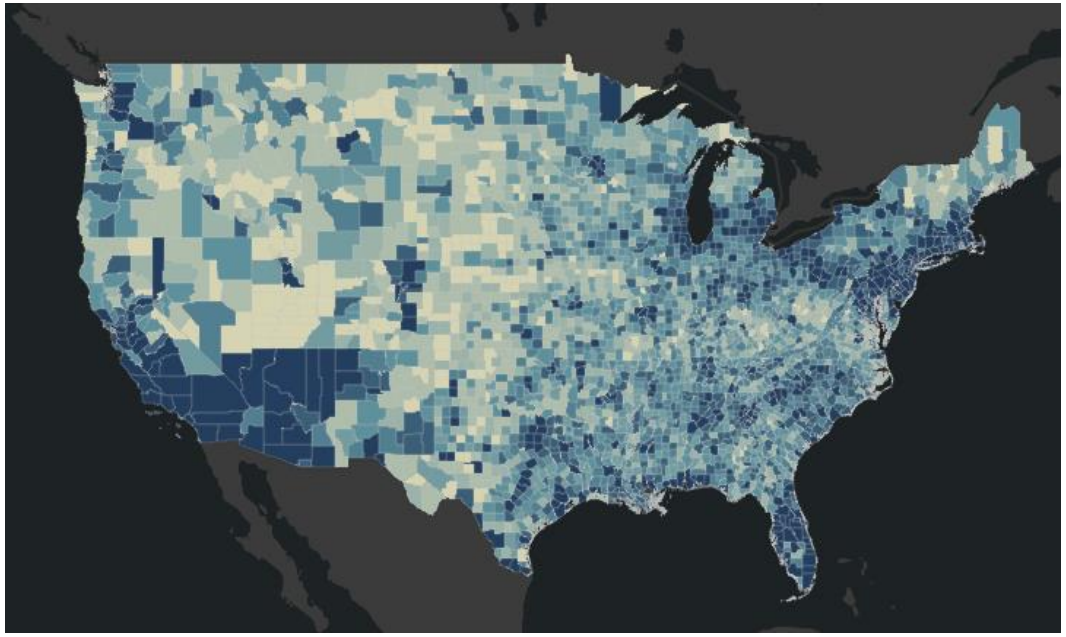
Factors affecting the prognosis of COVID-19

- Incidence (infection and transmission)
- Severity (direct and indirect)
- Mortality (direct and indirect) - Comorbidities



COVID-19 Deaths



Wu et al. MedRxiv 2020

Air pollution and COVID-19: same target

COVID-19

Air pollution

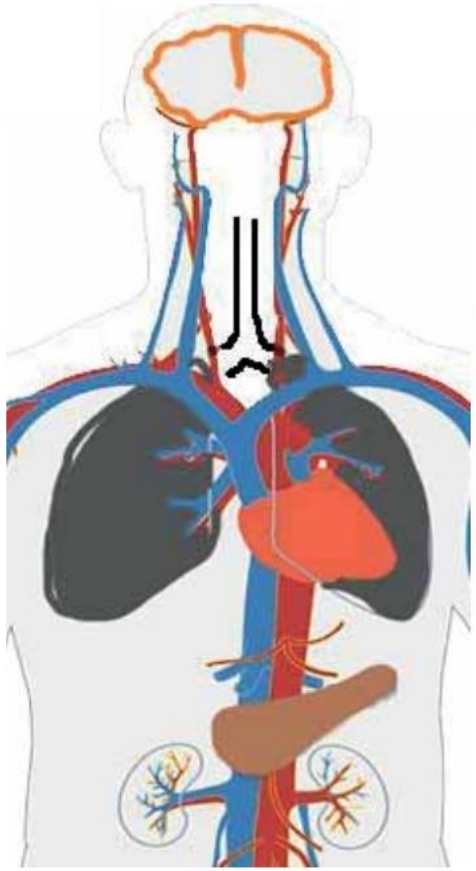


FIGURE 1 Target organs and the main diseases that coronavirus disease 2019 (blue) and air pollution (green) share. ARDS: acute respiratory distress syndrome.

T. Bourdrel et al. Eur Respir Rev 2021;30:200242

Respiratory system affected by air pollution

- COVID-19
  - Main entry of SARS CoV-2
  - From URI to ARDS
- Air pollution → lung inflammation and oxidative stress
  - Weakening respiratory system → poor outcome of chronic respiratory disease

Cardiovascular system affected by air pollution

- Air pollution → small particle → cardiovascular mortality ($PM_{2.5}$ 10μg/m^3 ↑ → 11%↑)
  - Stroke, IHD by oxidative stress & systemic inflammatory reaction

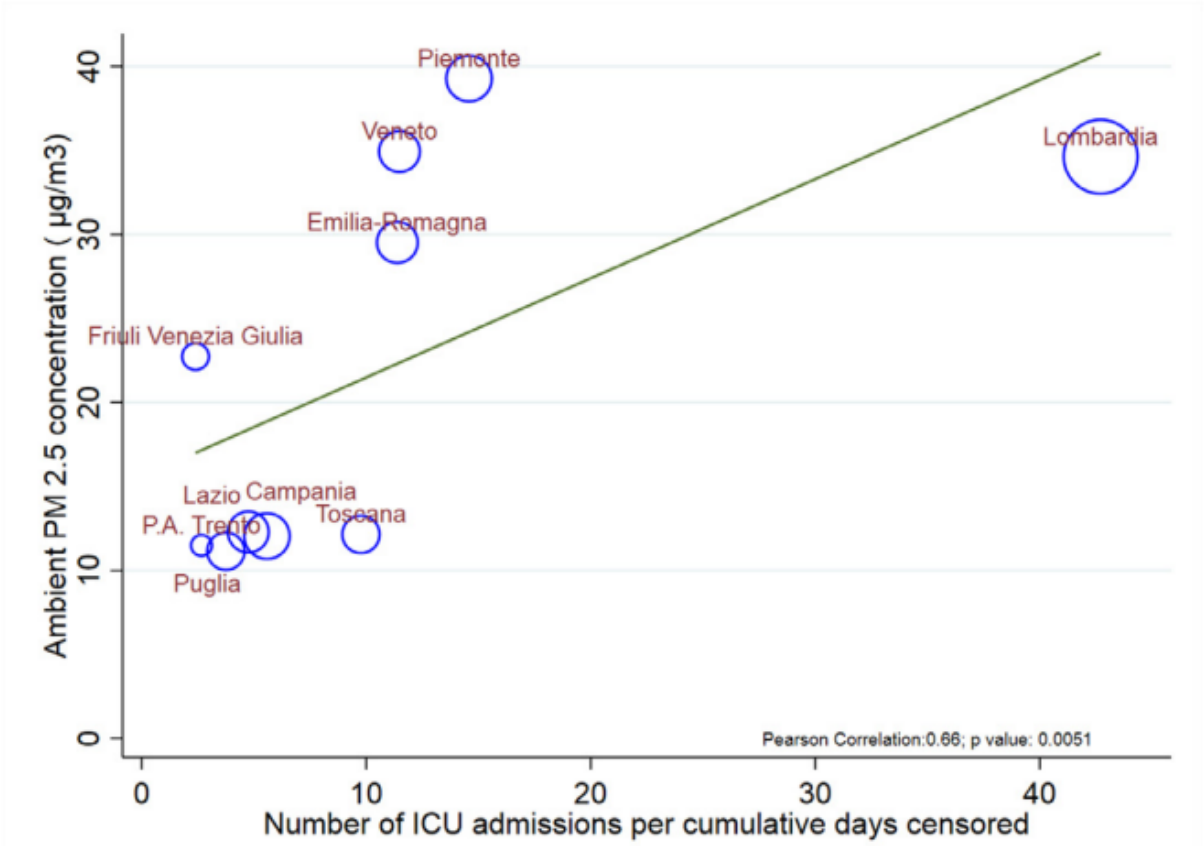
- COVID-19

  : vascular endothelial inflammation and dysfunction

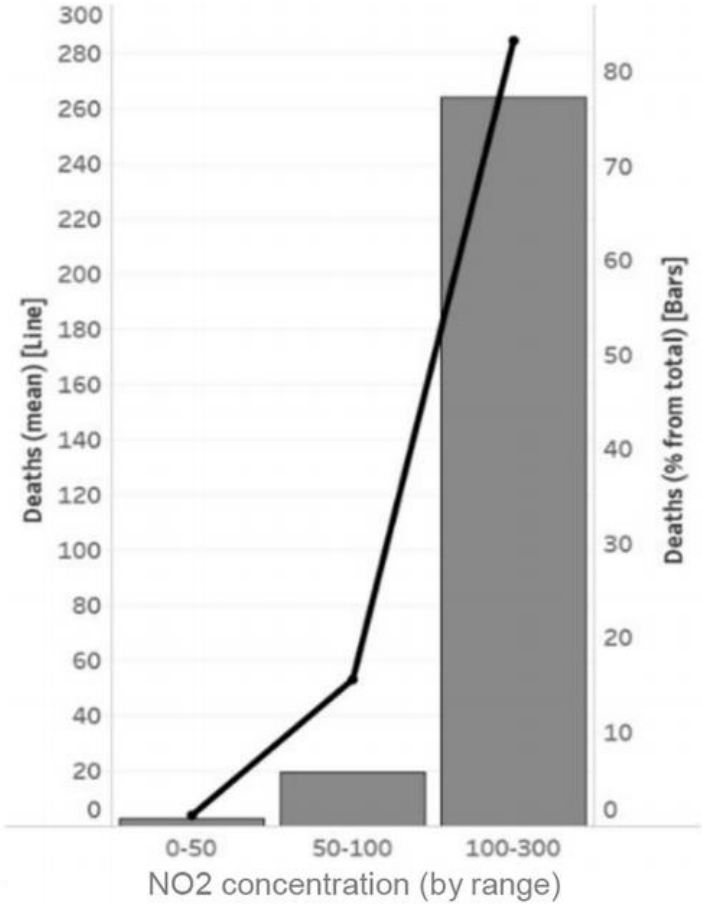
  → myopericarditis, ACS (developing coronary plaque), HF, thrombosis (pro-thrombotic factor), vasculitis, DIC

COVID-19 prognosis related with air pollution

ICU admission ∝ ambient $PM_{2.5}$

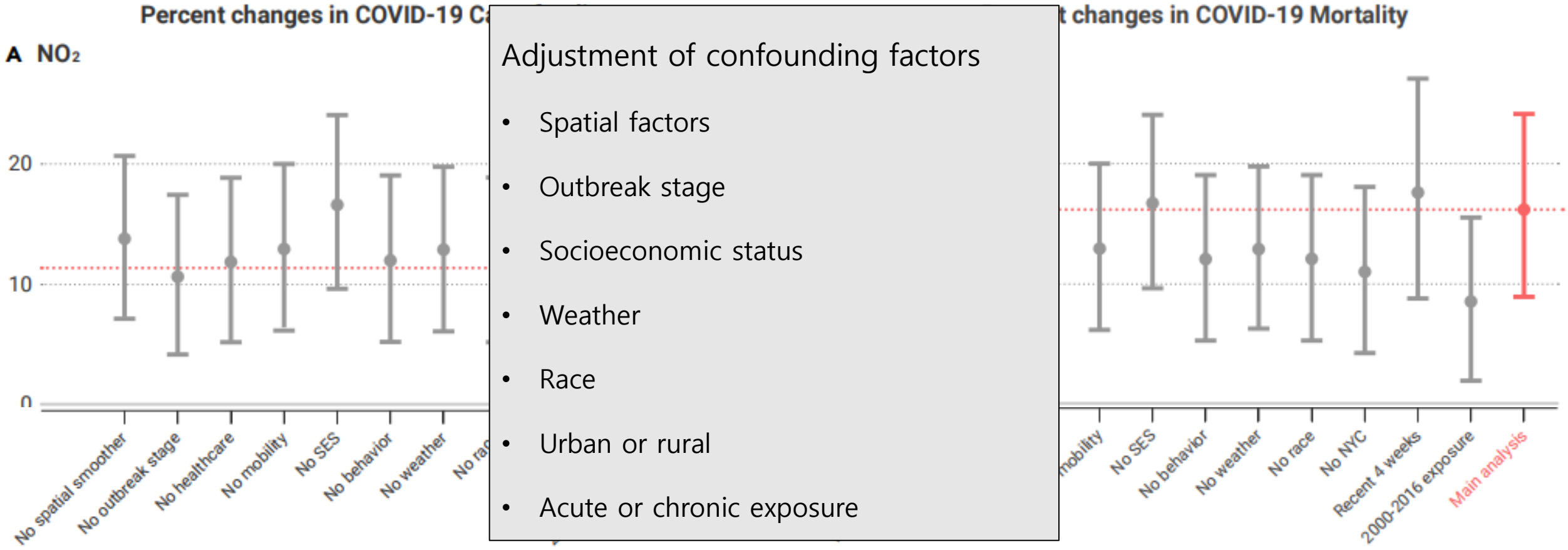


COVID-19 deaths ∝ NO_2 concentration



A. Frontera et al. Journal of Infection 81 (2020) 255-259
Y. Ogen Science of the Total Environment 726 (2020)

COVID-19 prognosis related with air pollution

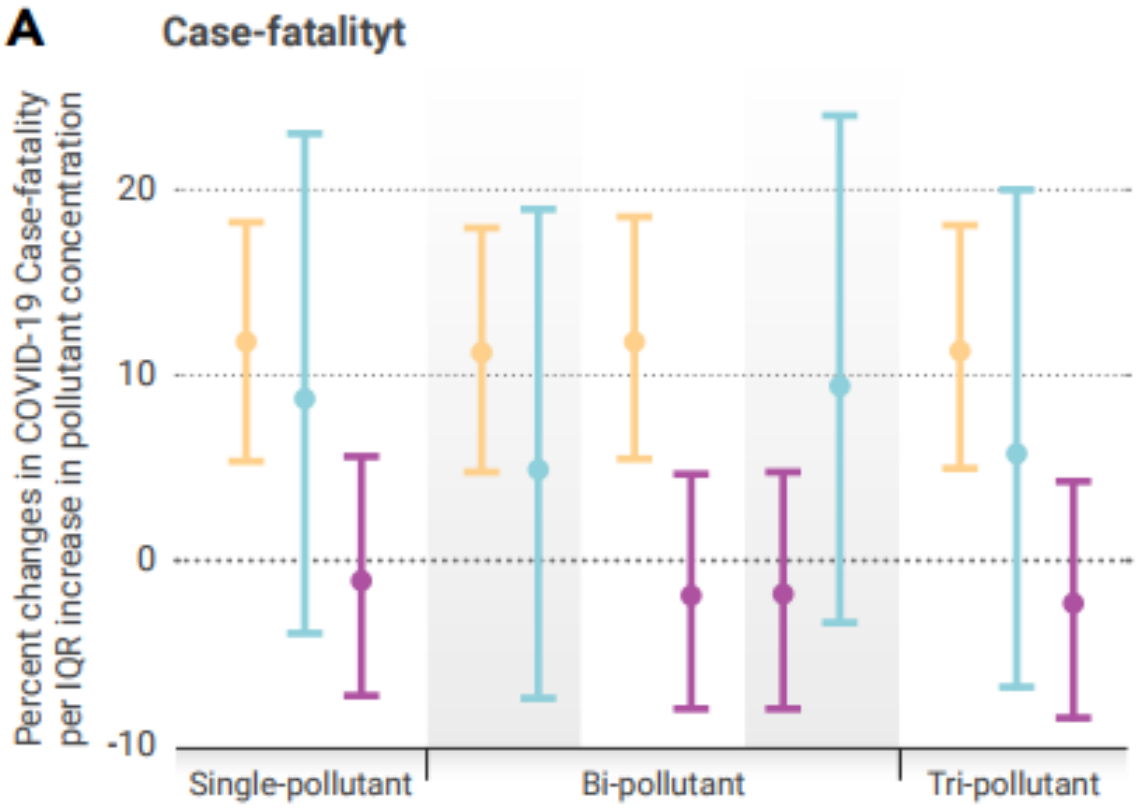


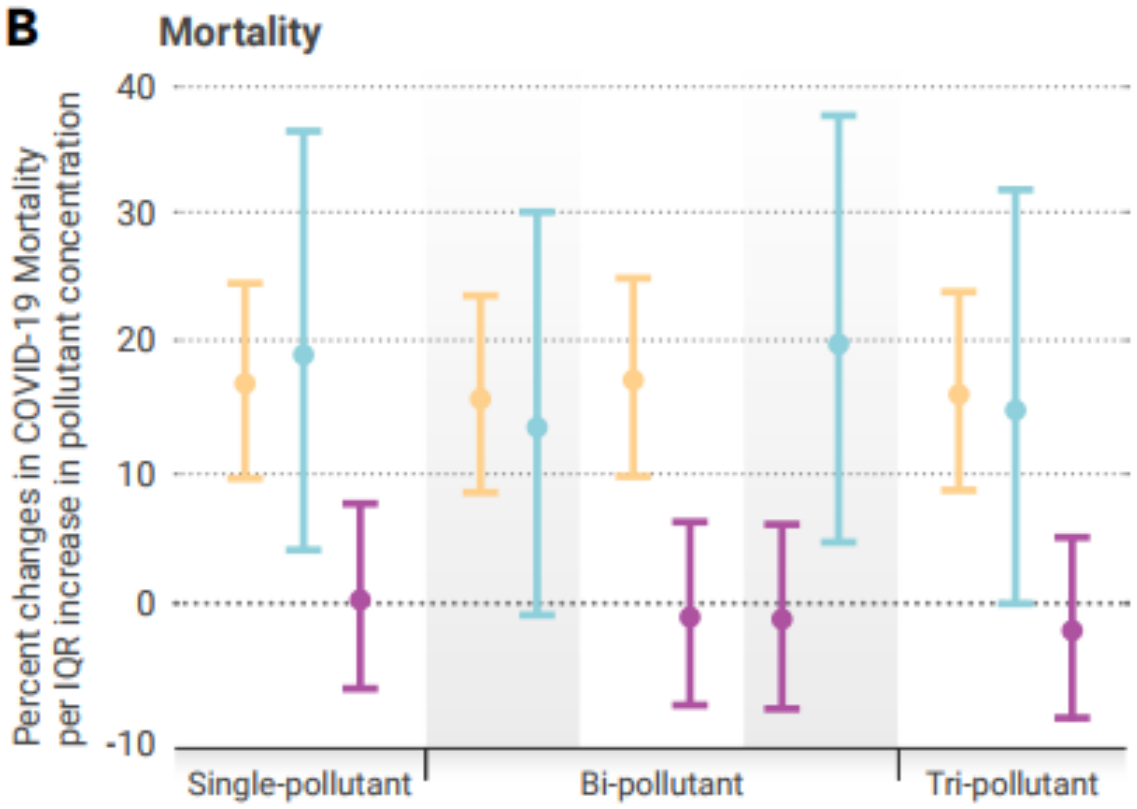
Adjustment of confounding factors

- Spatial factors
- Outbreak stage
- Socioeconomic status
- Weather
- Race
- Urban or rural
- Acute or chronic exposure

NO_2 level related with COVID-19 case-fatality and mortality

COVID-19 prognosis related with air pollution





NO_X, $PM_{2.5}$ ↔ O_3

COVID-19 prognosis related with air pollution

- Lagged effect of short-term exposure

Temporal Association Between Particulate Matter Pollution and Case Fatality Rate of COVID-19 in Wuhan, China

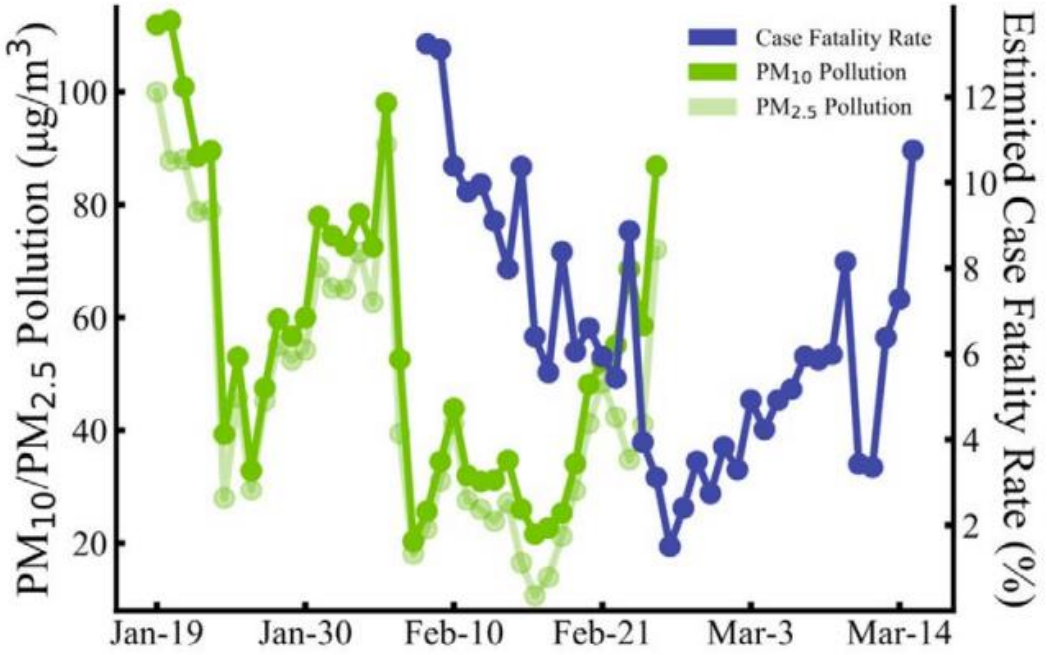


Figure 1 Daily Case Fatality Rate (blue points), $PM_{2.5}$ (light green points) and PM_{10} (green points) Level from February 19 to March 15.

Y. Wu et al. MedRxiv Preprint (2020)

COVID-19 prognosis related with air pollution

- Long-term exposure

Long-term exposure to air-pollution and COVID-19 mortality in England: A hierarchical spatial analysis

Garyfallos Konstantinoudis *, Tullia Padellini, James Bennett, Bethan Davies, Majid Ezzati, Marta Blangiardo

MRC Centre for Environment and Health, Department of Epidemiology and Biostatistics, School of Public Health, Imperial College London, London, UK

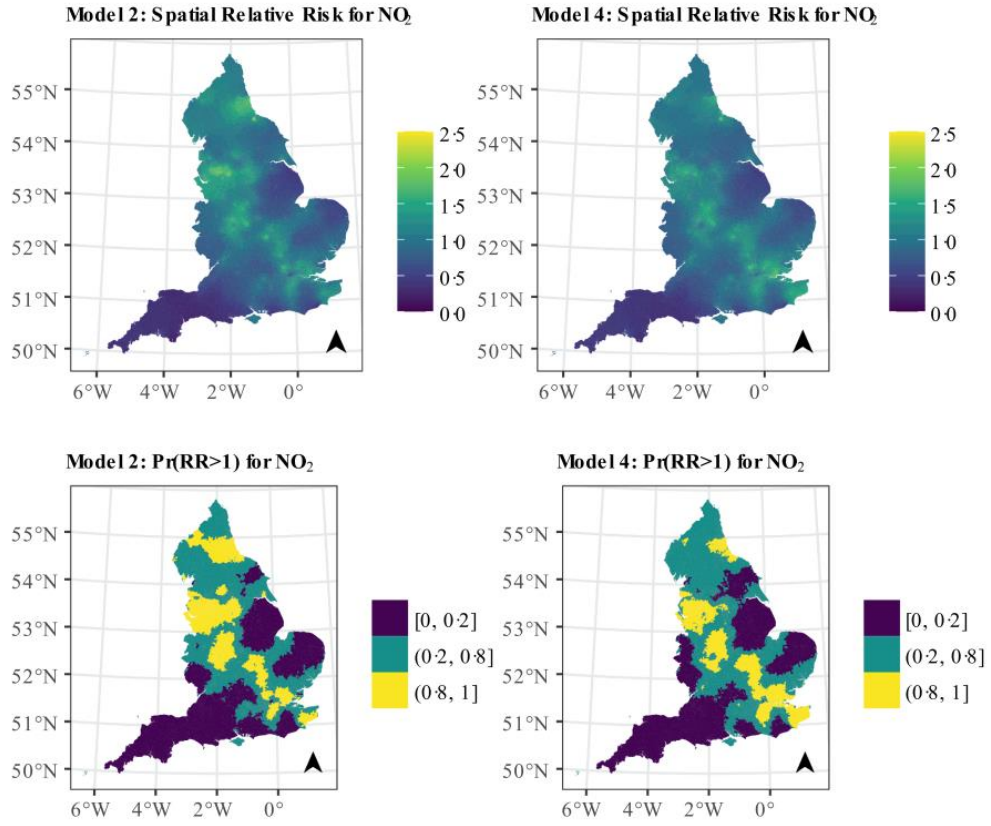


Fig. 4. Median posterior spatial relative risk (exponential of the spatial autocorrelation term) and posterior probability that the spatial relative risk is larger than 1 for the models with NO_2 and a spatial autocorrelation term and the fully adjusted NO_2 model.

- Use Bayesian hierarchical model for adjust "spatial autocorrelation"
- Mortality risk
  - ↑ 1μg/m^3 NO_2 (↑ 0.5%)
  - ↑ 1μg/m^3 $PM_{2.5}$ (↑ 1.4%)

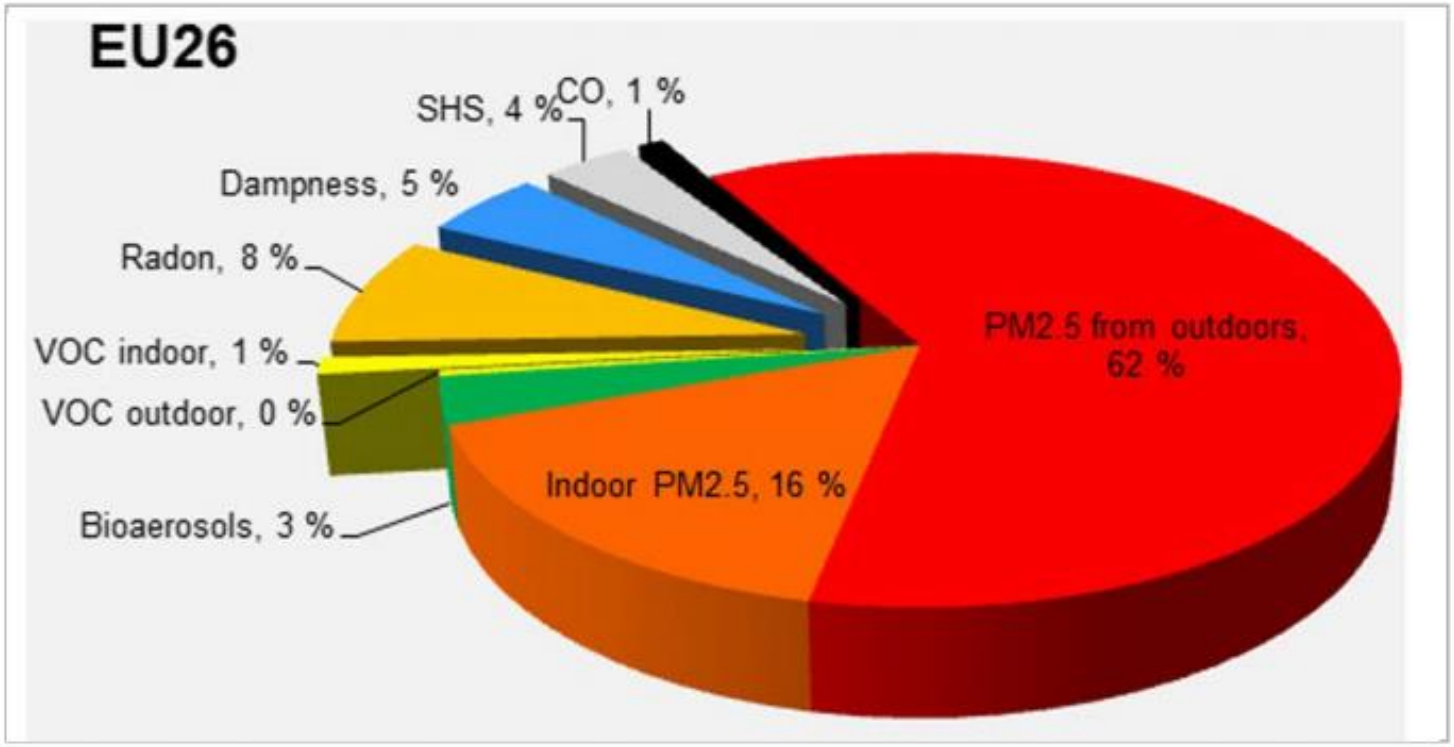
G. Konstantinoudis et al. Environmental International 146 (2021)

Contents

- Air pollution and infection and transmission in COVID-19
- Air pollution and disease severity of COVID-19
- Air pollution and prognosis of COVID-19
- Indoor air pollution and COVID-19

Burden of Indoor air pollution

Figure 7: Burden of disease due to indoor pollution



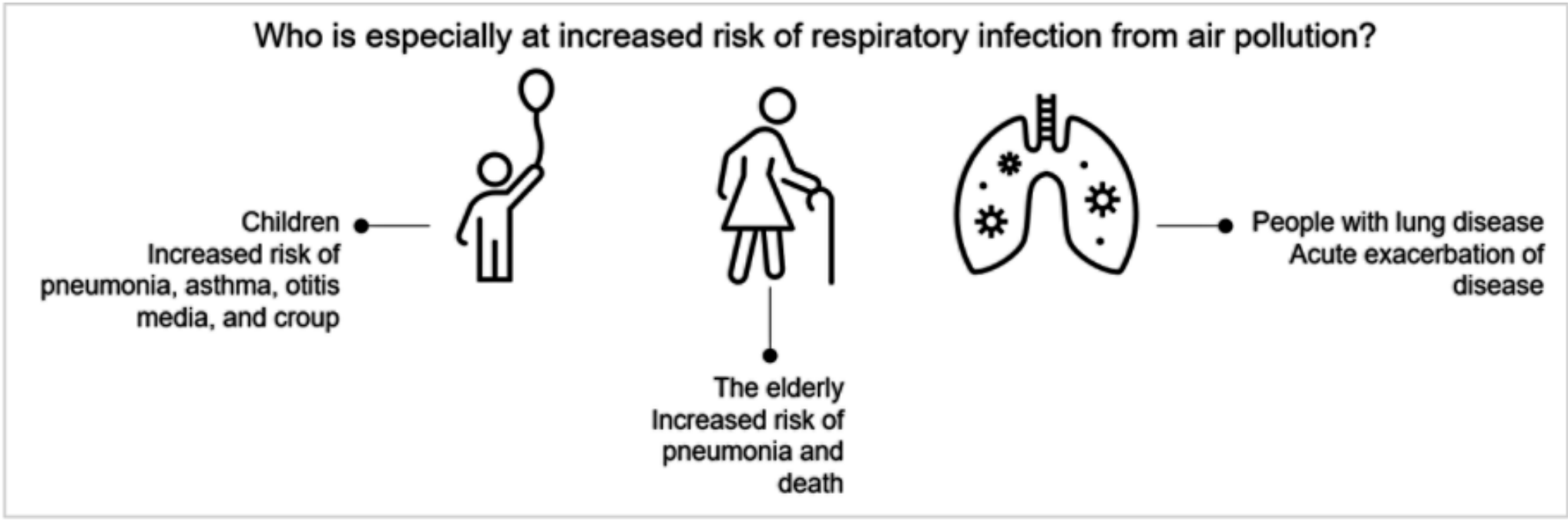
Spend most of time in “indoor”, not outdoor

Asikainen et al. 2016

Indoor air pollution and COVID-19

- Indoor air quality
  - Immediate effect: by irritation, like colds or other viral diseases
  - Long-term effect: actually, very long time of exposure than outdoor air pollution
    - e.g.) home, workplace etc.
    - Respiratory, circulatory, and cancer
    - 2^{nd}-hand smoke, cooking, CO_2, O_3, PM
  - However, the role of indoor air pollution in COVID-19 continues to be undervalued

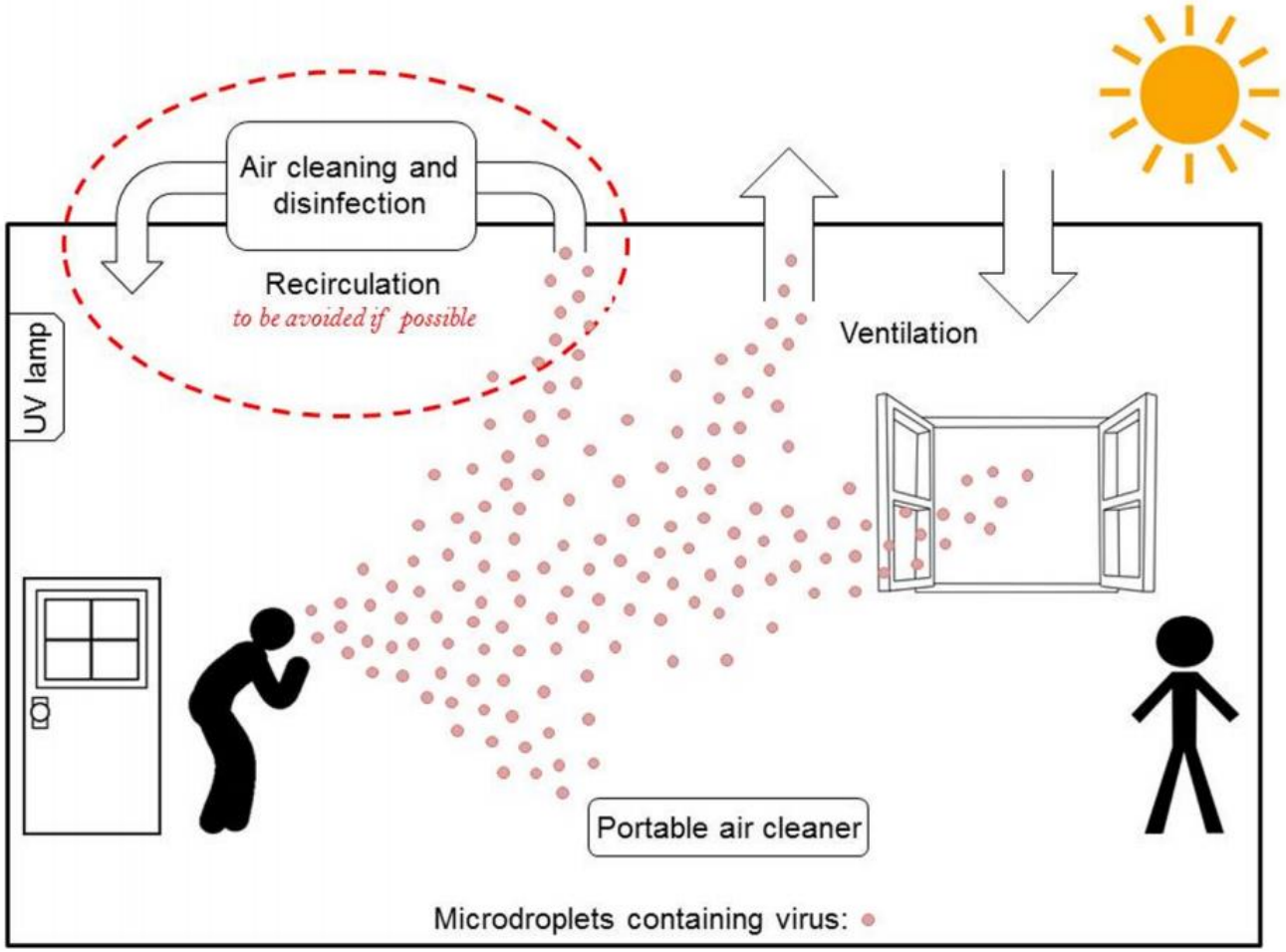
High risk group of respiratory infection from indoor air pollution



EU Policy Department for Economic, Scientific and Quality of Life Policies 2020

Transmission of COVID-19 in indoor air pollution

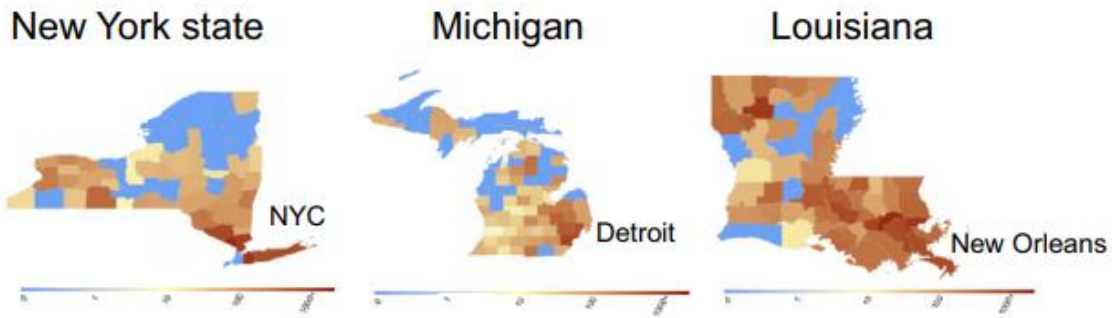
- COVID-19 transmission through aerosols in indoor environment



A. Covaci Environmental International 142 (2020) 105832

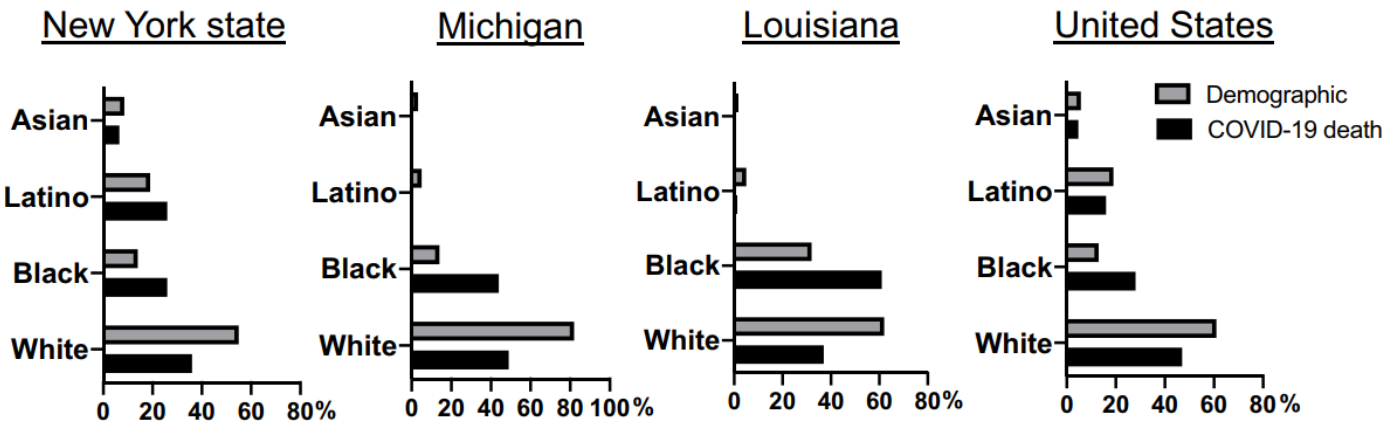
Indirect evidence of importance of indoor air pollution

Yearly average $PM_{2.5}$ (g/m^3) levels



# of COVID-19 deaths per 1 million

COVID-19 fatality rates



- Crowded living condition
- Multi-generational homes
- Limited access to health care
- Working in low paying "essential" jobs
- Chronic exposure to air pollution

A. Frontera et al. Journal of Infection 81 (2020) 255-259
Y. Ogen Science of the Total Environment 726 (2020)

Controversial

Journal of Exposure Science & Environmental Epidemiology
https://doi.org/10.1038/s41370-020-0247-x

COMMENT

Another invisible enemy indoors: COVID-19, human health, the home, and United States indoor air policy

Jamaji C. Nwanaji-Enwerem[1] · Joseph G. Allen[2] · Paloma I. Beamer[3]

- Stay-at-home order + remote working

  → Avoiding outdoor virus vs. ↑ indoor air pollution exposure

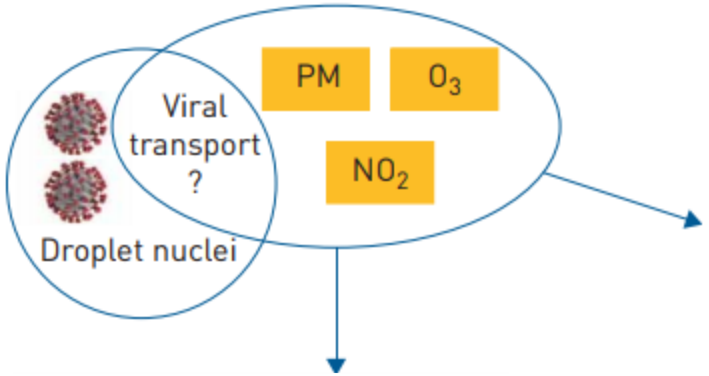
J. Nwanaji-enwerem et al. Journal of Exposure Science & Environmental Epidemiology (2020)

Methods to improve indoor air pollution

- Remove the individual emission source
  - Reduce outdoor air pollution (flow-on effect)
  - Appropriate ventilation, not always closing the windows
  - Developing ventilation standards for removing SARS CoV-2
  - Air purifiers: removing particulate matter from the indoor space
    - HEPA (High-Efficiency Particulate Air) filter
      - ~0.3 μm (SARS Co-V2 : ~0.1μm)

A. Covaci Environmental International 142 (2020) 105832
B. J. Nwanaji-enwerem et al. Journal of Exposure Science & Environmental Epidemiology (2020)

Summary: Interaction of virus and air pollutant

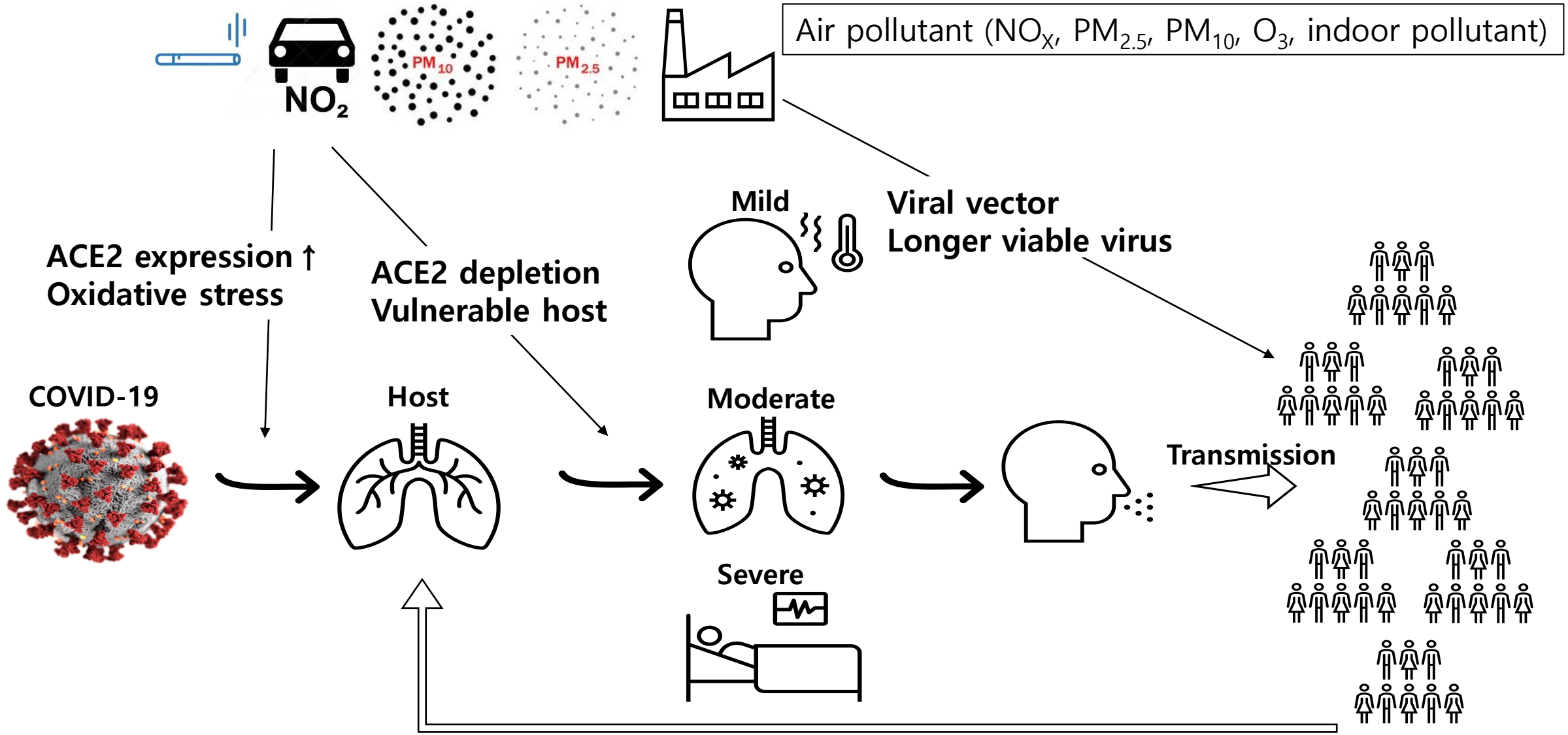


↓ Immune respiratory defense ↑ Viral entry in host cell

↑ Respiratory virus morbidity and mortality

T. Bourdrel et al. Eur Respir Rev 2021;30:200242

Summary: Interaction of virus and air pollutant



Thank you for your attention.