

Séminaire inaugural, Académie 3 "Espace, environnement, risques et résilience »

13 octobre 2023.



Exposition précoce à la pollution atmosphérique, co-expositions, et développement de l'enfant

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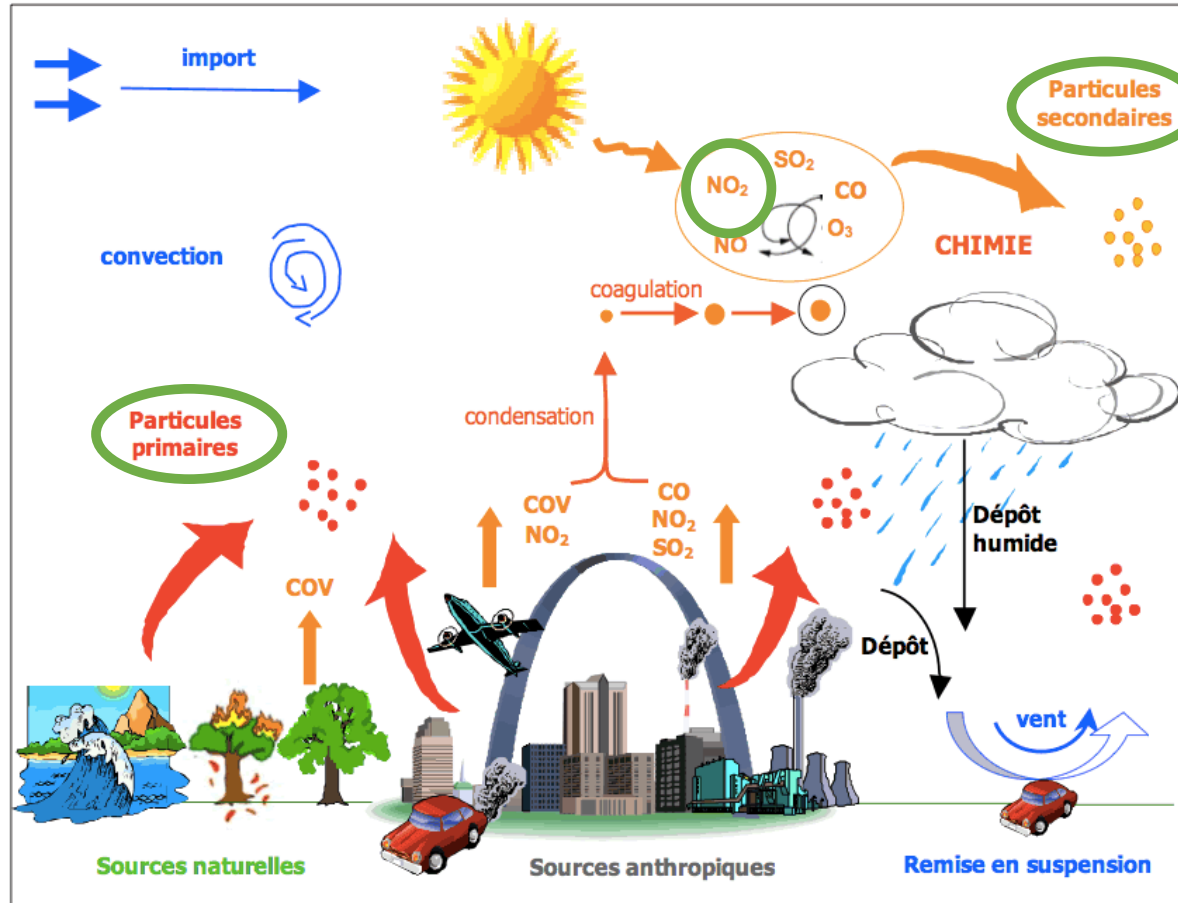


INSERM U1209, Team of Environmental epidemiology
applied to development and respiratory health



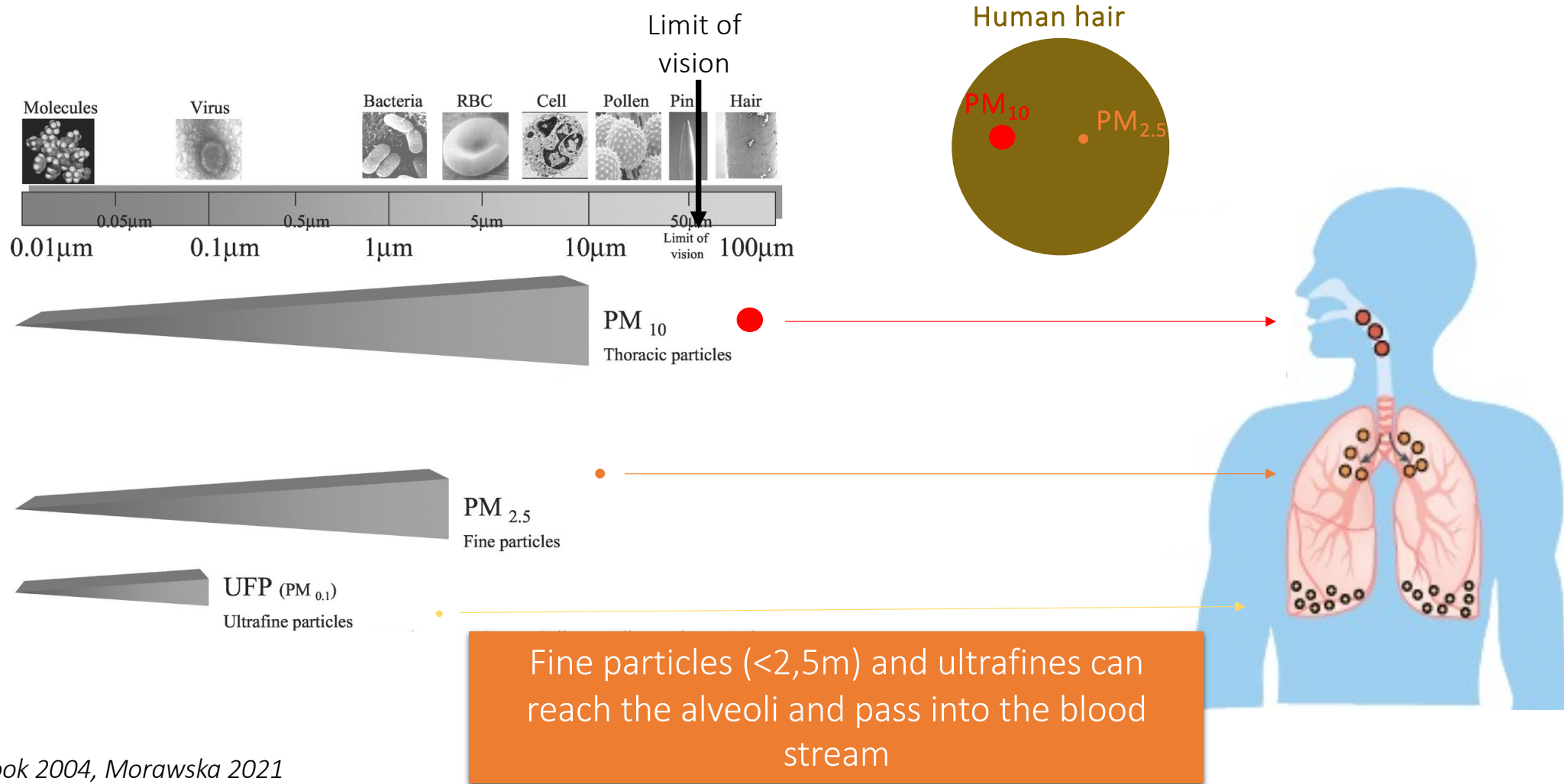
Air pollution

Gaseous, particulate matter



Source : Synthèse des connaissances sur les particules atmosphériques..., rapport disponible sur le site d'Airparif

Fine particulate matter



Air pollution and public health

High prevalence of exposure

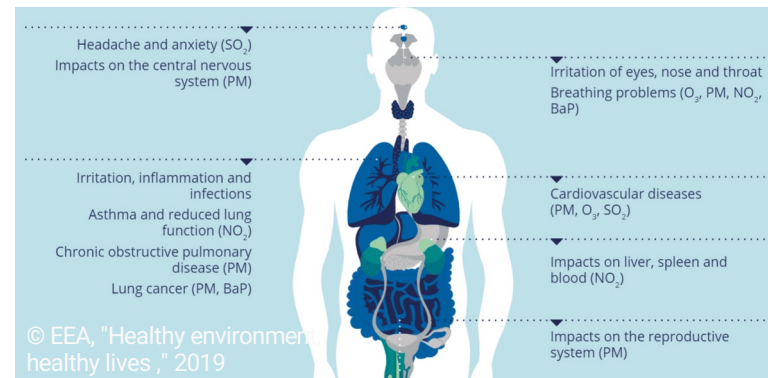
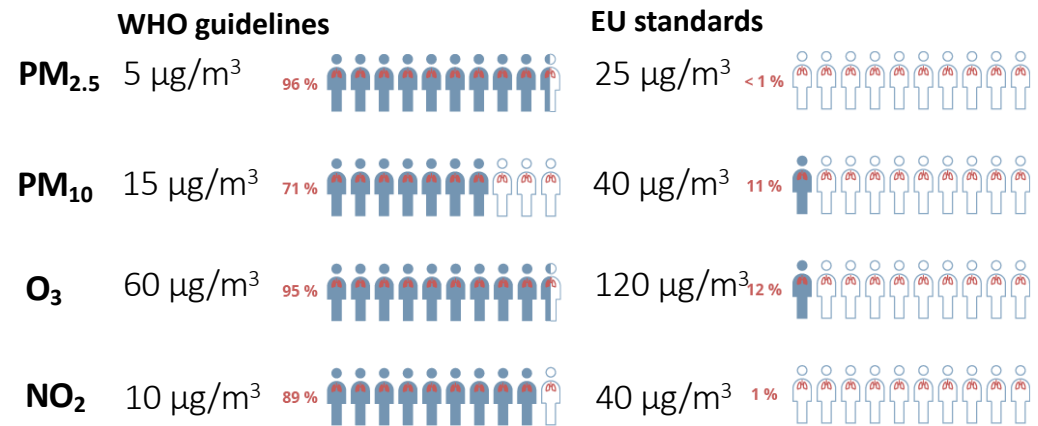
- 100%
- Controlable exposure
- Population exposure usually >recommended levels

Large list of health effects

Causal effect of PM_{2.5} on:

- mortality on the **short** and **long term**
- cardiovascular morbidity on the **short** and **long term**

EU urban population exposed to air pollutant levels above the WHO guidelines in 2020 <https://www.eea.europa.eu/>



Developmental Origins of Health and Diseases

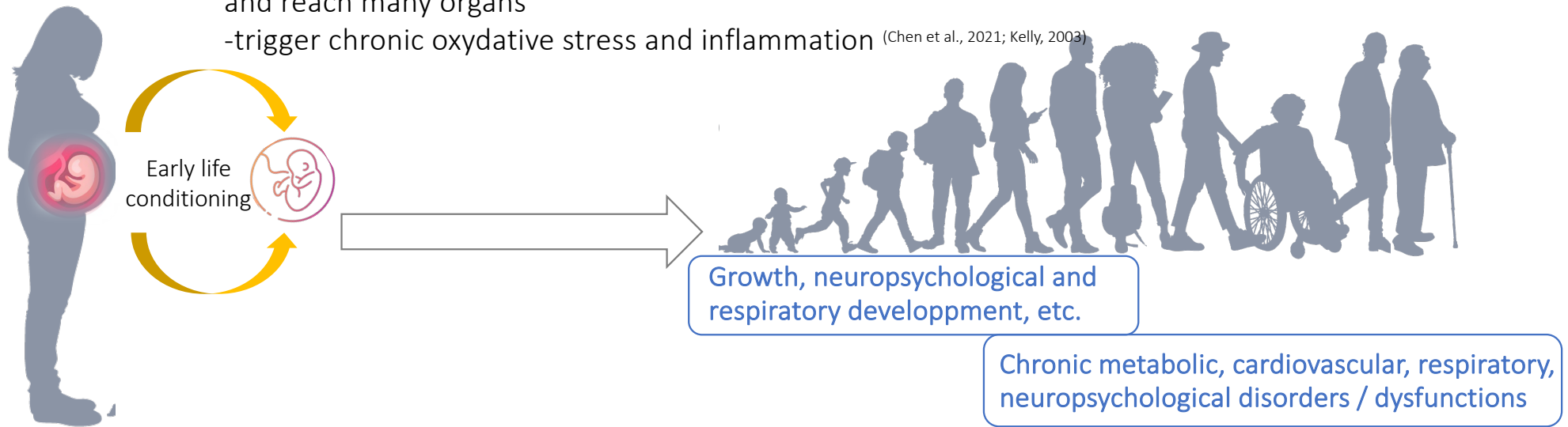
External exposures



David Barker, 1938-2013

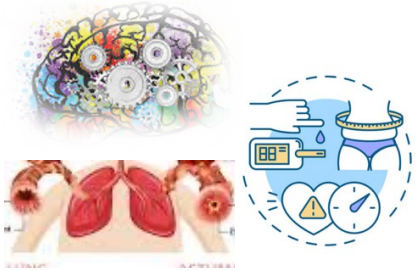
Air pollutants:

- can cross placental, blood-air, and blood-brain barriers (Bongaerts et al., 2020; Brockmeyer and D'Angiulli, 2016) and reach many organs
- trigger chronic oxydative stress and inflammation (Chen et al., 2021; Kelly, 2003)



Adapted from Agarwal et al 2018

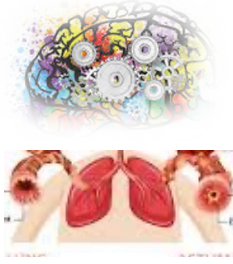
Neuro, respiratory and metabolic health disorders in childhood



- Prevalence of **neurodevelopmental disorders**: 10-15% in high income countries (Barican et al 2022, Francés et al 2022)
- **Asthma prevalence in childhood**: 10-15% in France (Delmas et al 2014)
- Rates of **childhood obesity** are increasing across the globe (NCD Risk Factor Collaboration (NCD-RisC) 2017)

- Start in childhood and adolescence, could **persist into adulthood**
- Significantly interfere with well-being and development: **high social and economic cost**
- Neurodevelopmental disorders are a leading cause of **childhood disability** globally (Erskine et al 2015)
- Robust services for mental health disorders are lacking, compared to child physical health issues

Air pollution exposure and children development



A Review of Epidemiological Research on Adverse Neurological Effects of Exposure to Ambient Air Pollution

Xiaohui Xu¹, Sandie Uyen Ha² and Rakshya Basnet¹



Particulate matter and early childhood body weight



Eunjeong Kim^a, Hyesook Park^b, Eun Ae Park^c, Yun-Chul Hong^d, Mina Ha^e, Hwan-Cheol Kim^f, Eun-Hee Ha^{g,*}

Exposure to air pollution and cognitive functioning across the life course – A systematic literature review

Angela Clifford^a, Linda Lang^{a,b}, Ruoling Chen^{a,b,*}, Kaarin J. Anstey^c, Anthony Seaton^d

Identifying critical windows of prenatal particulate matter (PM_{2.5}) exposure and early childhood blood pressure

Maria José Rosa^{a,*}, Gleicy Macedo Hair^a, Allan C. Just^a, Itai Kloog^b, Katherine Svensson^c, María Luisa Pizano-Zárate^d, Ivan Pantic^d, Lourdes Schnaas^d, Marcela Tamayo-Ortiz^{e,g}, Andrea A. Baccarelli^f, Martha M. Tellez-Rojo^g, Robert O. Wright^{a,h}, Alison P. Sanders^{a,h}

Prenatal Exposure to Air Pollution and Autism Spectrum Disorder: Sensitive Windows of Exposure and Sex Differences

Md Mostafijur Rahman,¹ Yu-Hsiang Shu,² Ting Chow,² Frederick W. Lurmann,³ Xin Yu,⁴ Mayra P. Martinez,²

Prenatal air pollution exposure and growth and cardio-metabolic risk in preschoolers

Serena Fossati^{a,b,c,*}, Damaskini Valvi^d, David Martinez^{a,b,c}, Marta Cirach^{a,b,c}, Marisa Estarlich^{c,e,f}, Ana Fernández-Somoano^{c,g,h}, Mònica Guxens^{a,b,c,i}, Carmen Iñiguez^{c,j}, Amaia Irizar^k, Aitana Lertxundi^{c,k,l}, Mark Nieuwenhuijsen^{a,b,c}, Ibon Tamayo^{a,b,c,m,n}, Jesus Vioque^{c,o}, Adonina Tardón^{c,g,h}, Jordi Sunyer^{a,b,c}, Martine Vrijheid^{a,b,c}

Prenatal particulate air pollution and neurodevelopment in urban children: Examining sensitive windows and sex-specific associations



Yueh-Hsiu Mathilda Chiu^{a,b}, Hsiao-Hsien Leon Hsu^b, Brent A. Coull^{c,d}, David C. Bellinger^{d,e}, Itai Kloog^f,

Prenatal Particulate Air Pollution and Asthma Onset in Urban Children

Identifying Sensitive Windows and Sex Differences

Hsiao-Hsien Leon Hsu¹, Yueh-Hsiu Mathilda Chiu², Brent A. Coull^{3,4}, Itai Kloog^{4,5}, Joel Schwartz^{4,6}, Alison Lee⁷, Robert O. Wright^{1,8}, and Rosalind J. Wright^{2,8}

HOW AIR POLLUTION ALTERS BRAIN DEVELOPMENT: THE ROLE OF NEUROINFLAMMATION

Sam Brockmeyer^{1,2}, Amedeo D'Angiulli^{1,2*}

Pre-natal exposure to NO₂ and PM_{2.5} and newborn lung function: An approach based on repeated personal exposure measurements

Johanna Lepeule^{a,*}, Isabelle Pin^{a,b}, Anne Boudier^{a,b}, Joane Quentin^{a,b}, Sarah Lyon-Caen^a, Karine Supernant^a, Emie Seyve^a, Ryan Chartier^c, Remy Slama^a, Valérie Siroux^a, the SEPAGES study group¹

Scientific weight of evidence

Causal > Likely to be causal > Suggestive of, but not sufficient > Inadequate > Not likely to be causal

Causality of long term exposure to NO₂

PM_{2.5}

On children health outcomes

Likely to be causal

Likely to be causal

Respiratory health

(asthma development, decreased lung function growth, etc)

Inadequate
(and few studies)

(likely to be causal)

Suggestive of, but not sufficient

Inconsistent

Inconsistent

Inconsistent
(and few studies)

Inconsistent
(and few studies)

- Littérature riche; plus récente sur les aspects cardiométaboliques
- Enjeux
 - Exposition : trajectoires, fenêtres de vulnérabilité, erreur de mesure
 - Co-expositions
 - Mécanismes physiologiques, effets différentiels filles/garçons

Inconsistent

Inconsistent
(and few studies)

Limited evidence

Congenital anomalies

Stillbirth

* Few epidemiological studies, disagreement regarding ASD between Europe/US

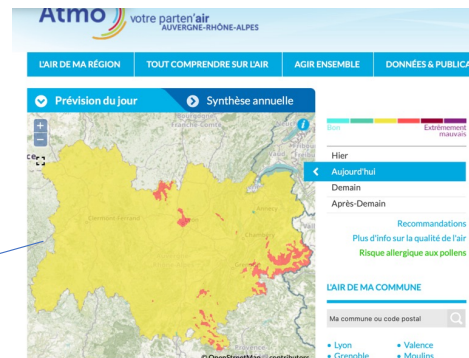
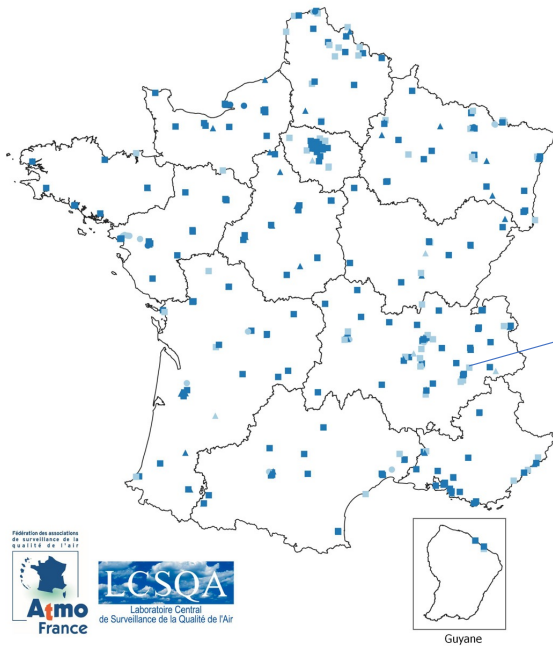
EPA, ISA, 2019 (PM_{2.5}), 2016 (NO₂)

Air quality monitoring network

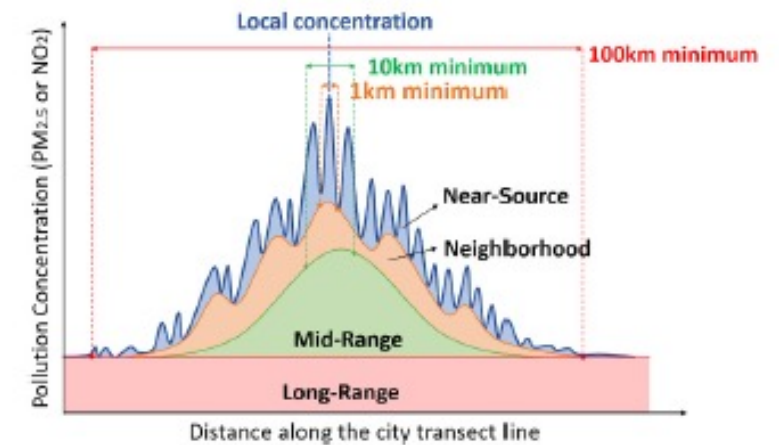


Associations Agréées de Surveillance de la Qualité de l'Air (AASQA)

Points de mesure réglementaires NO₂ 2020



! Hétérogénéité spatiale !



Wang 2020

Exposure measurement error

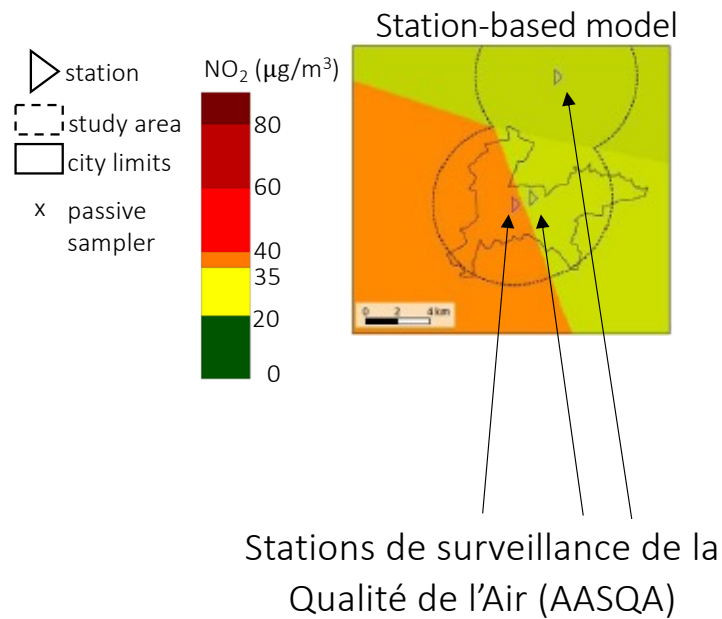
Bias toward the null (best case scenario)



Other types of exposure measurement errors can lead to bias away from the null (avoid)

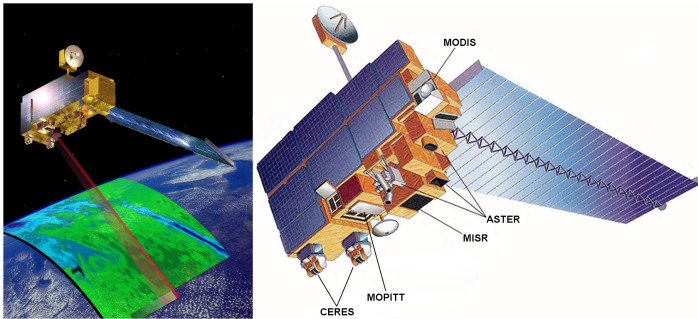
Ambient air pollution exposure models - locally

NO₂ and PM₁₀ exposure assessment in the metropolitan area of Poitiers



Lepeule et al 2010
Sellier et al 2014

Using satellite data to estimate ambient air pollution

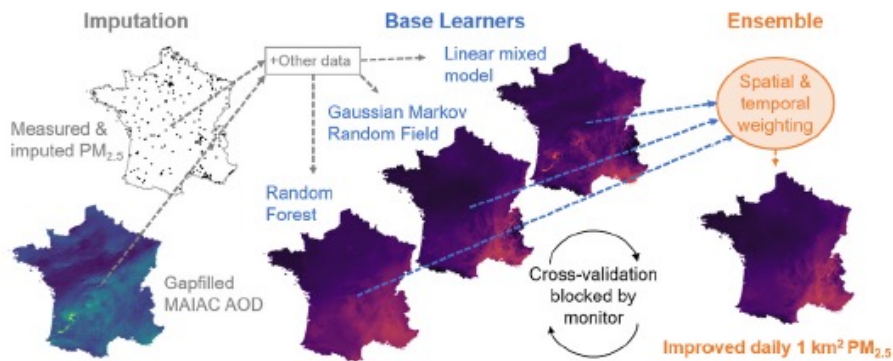


Advantages and limitations of using satellite data

👍	👎
Spatial Coverage	Data Availability (Cloud mask, glint, night time, etc.)
Surveying areas with limited ground access	No vertical profile (Integration of the whole atmospheric column)
Economic (one sensor for the whole globe !)	Different Scales

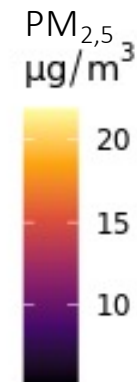
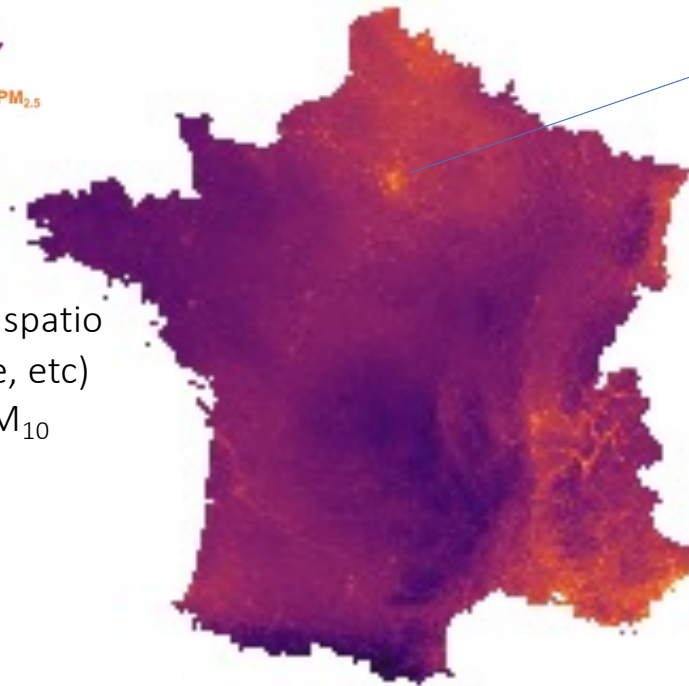
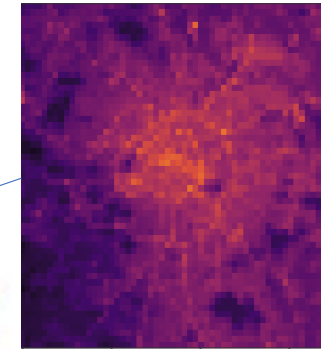
Figure courtesy of Itai Kloog

Hybrid PM₁₀ and PM_{2.5} exposure models based on satellite data



Prédictions journalières
2000-2019, 1x 1 km

Région Parisienne



Combine aerosol optical depth satellite data with spatio temporal predictors (vegetation, weather, altitude, etc) calibrated using ground measures of PM_{2.5} and PM₁₀

Hybrid exposure models based on satellite data



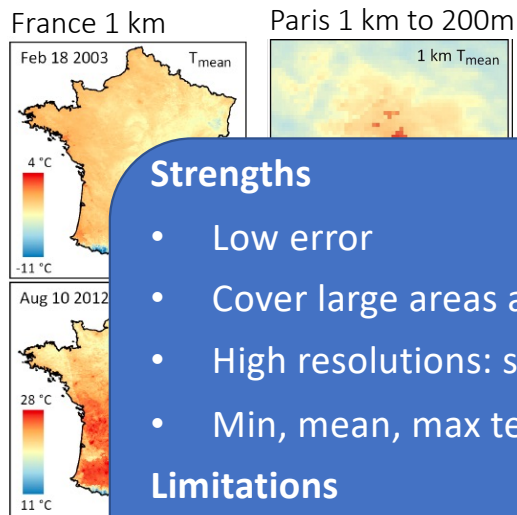
Air temperature

Input

- Surface temperature measurements
- Meteorological stations
- Spatio-temporal predictors (vegetation, population density, etc.)

Output

- Daily predictions
- 2000-2018
- 1km
- 200m, 103 large urban areas (>50k habitants)



Strengths

- Low error
- Cover large areas and time periods
- High resolutions: spatial and temporal, UHI
- Min, mean, max temperature

Limitations

- Technical issues: cloudy days, etc.

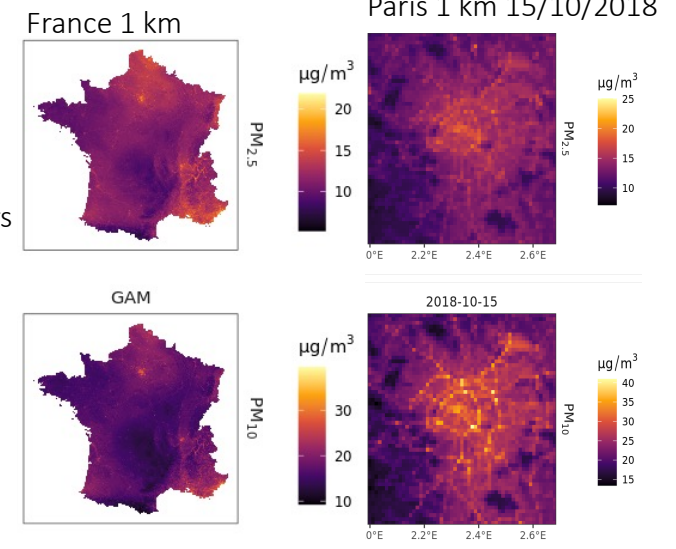
Average of all daily predictions 2000 - 2016

10-fold cross validation	R ²	Root mean square error	Mean absolute error
T _{mean}	0.97	1.29	0.94

PM_{2.5} & PM₁₀

Input

- Aerosol optical depth measurements
- Air quality stations



Average of all daily predictions 2000 - 2016

10-fold cross validation	R ²	Root mean square error	Mean absolute error
PM _{2.5}	0.76	4.02	2.72
PM ₁₀	0.71	4.26	6.28

Personal exposure assessment



Wearing backpack containing samplers and monitors

GPS



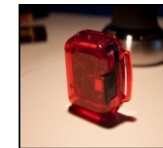
PM_{2.5}



NO₂, VOC
(incl.
benzene)



Accelerometer



Temperature



UV

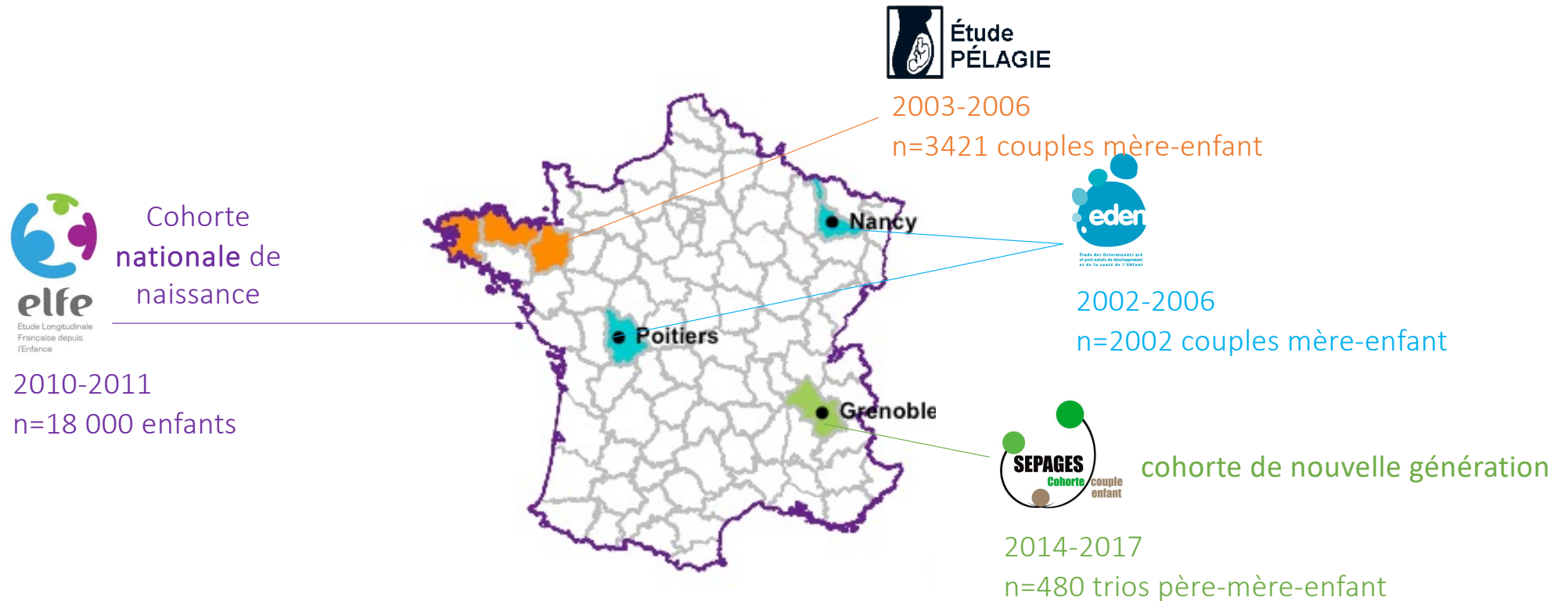


=> External dose

- Indoor air, travel
- Personal exposure monitoring expensive and complex
- Less exposure measurement error, **only for a limited time period**

Contributions de cohortes mère-enfant et de naissance

Objectifs: caractériser les facteurs associés au développement de l'enfant



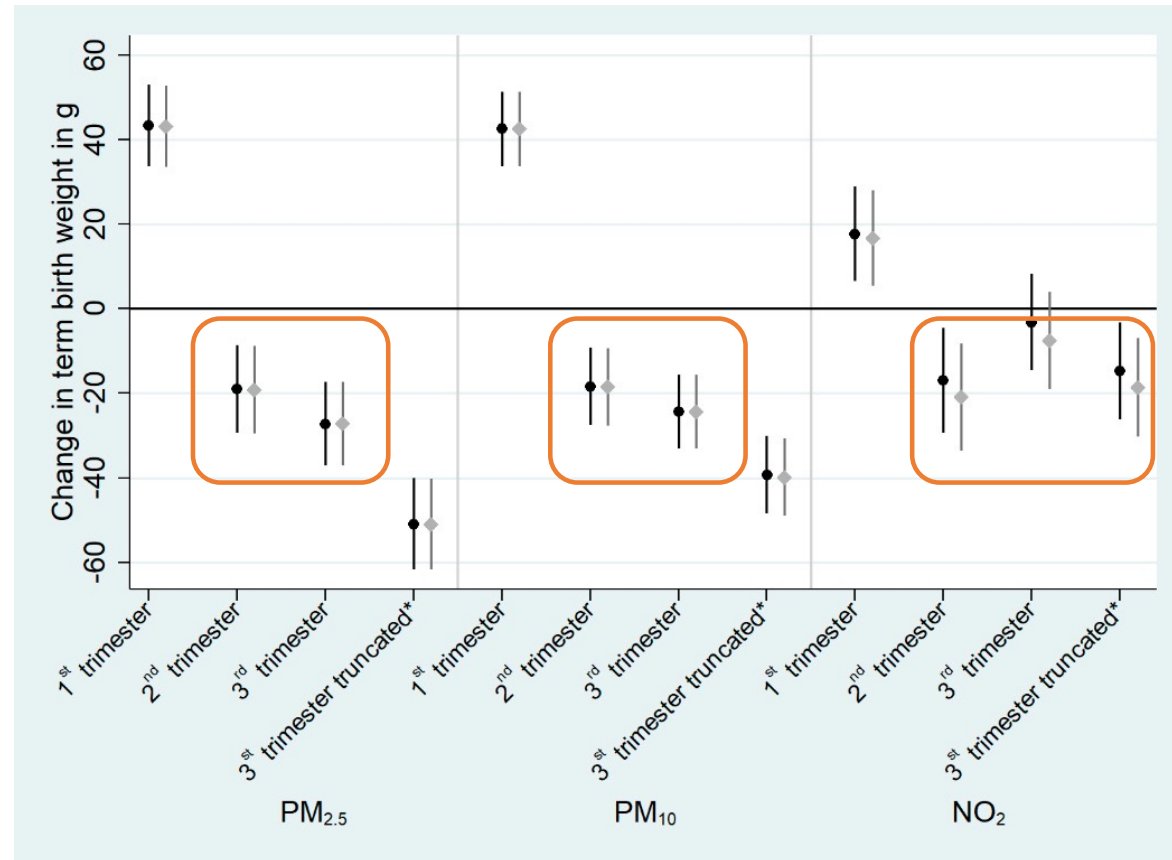
Maternal exposure to air pollution and newborn's birth weight



Ouidir et al 2021
IJERPH

13 334 mother-child dyads

No significant effect of whole pregnancy exposure on birth weight

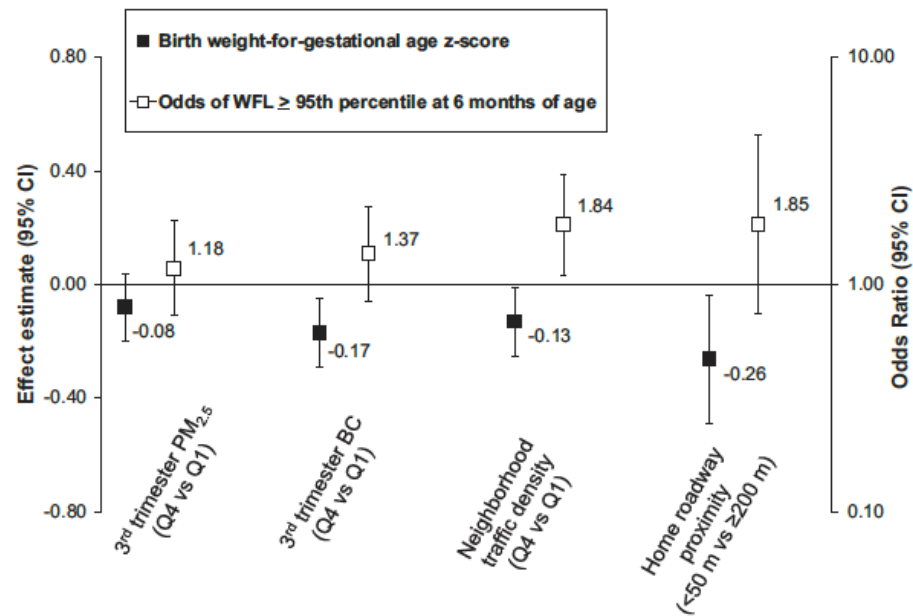


increase of 5 $\mu\text{g}/\text{m}^3$ for PM_{2.5} and PM₁₀ and 10 $\mu\text{g}/\text{m}^3$ for NO₂

Maternal exposure to air pollution and weight of the newborn and child

n=2115 mother child VIVA cohort

Associations of prenatal air pollution exposure with birth weight-for-gestational age z-score (fetal growth) and odds of weight-for-length ≥ 95 th percentile at 6 months of age.





Pre and postnatal exposure to PM_{2.5} and cognitive function at 5-6 yrs old

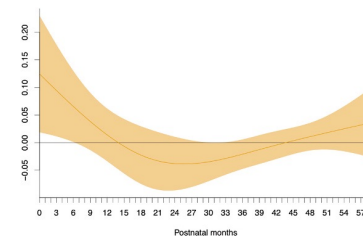
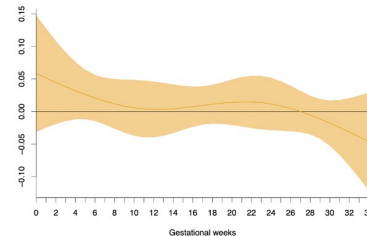
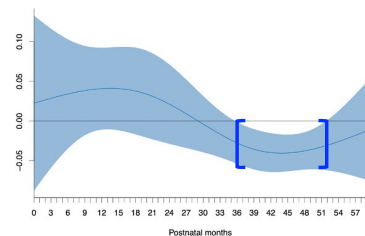
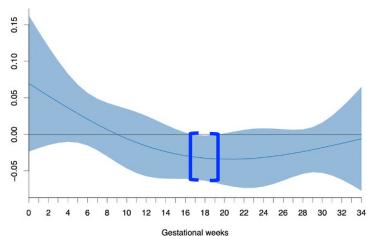


Ariane Guilbert
Env Res 2023

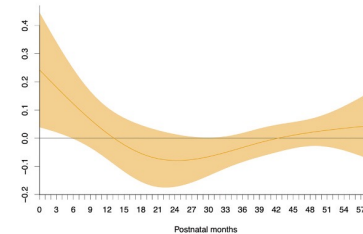
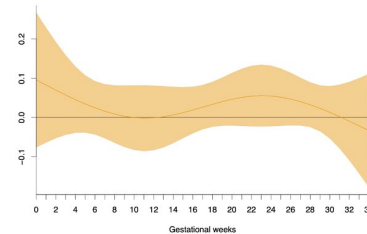
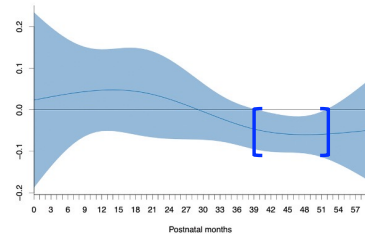
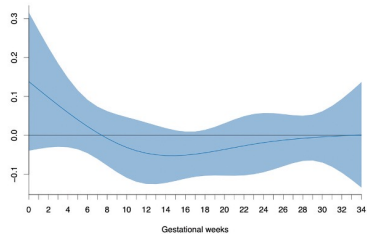
Males, n=650

Females, n=621

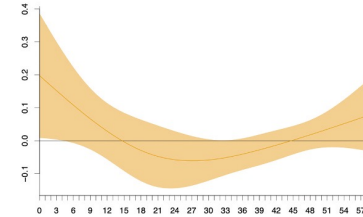
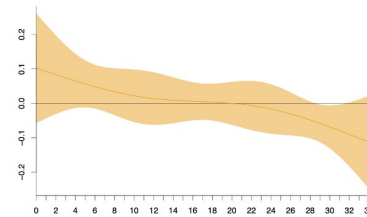
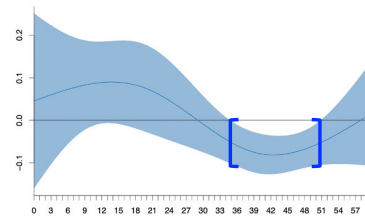
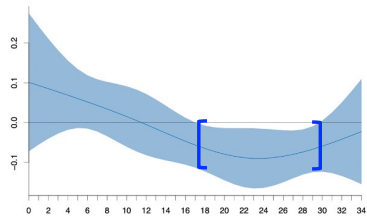
General abilities



Verbal abilities



Non verbal abilities



Gestational weeks

Postnatal months

Gestational weeks

Postnatal months

Maternal exposure to air pollution and newborn's lung function

391 mother-child dyads, 2 months old newborn

PM_{2.5} NO₂

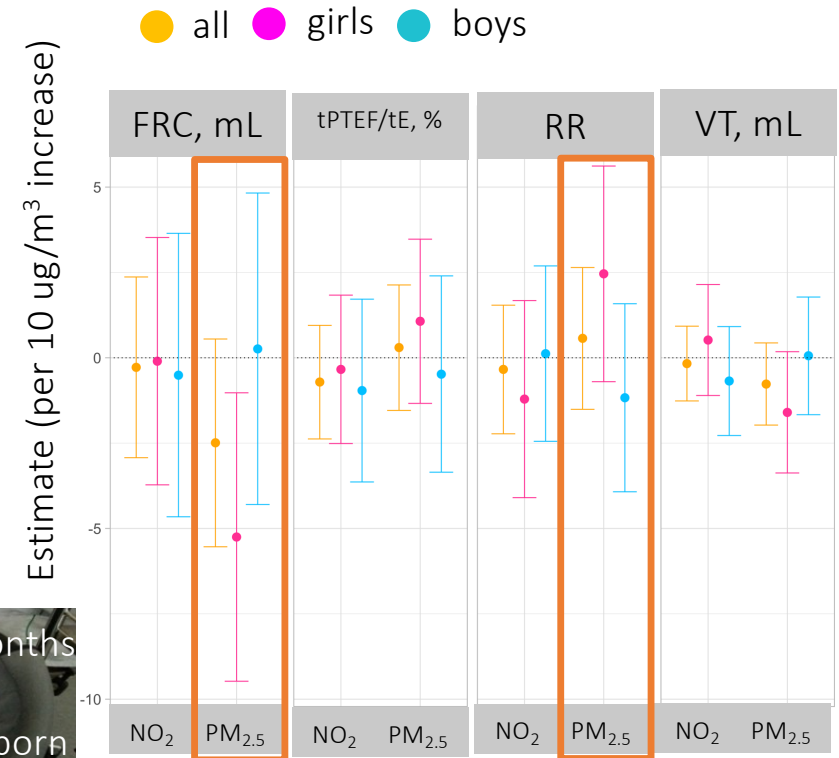


Nitrogen Multiple Breath Washout(N2MBW)

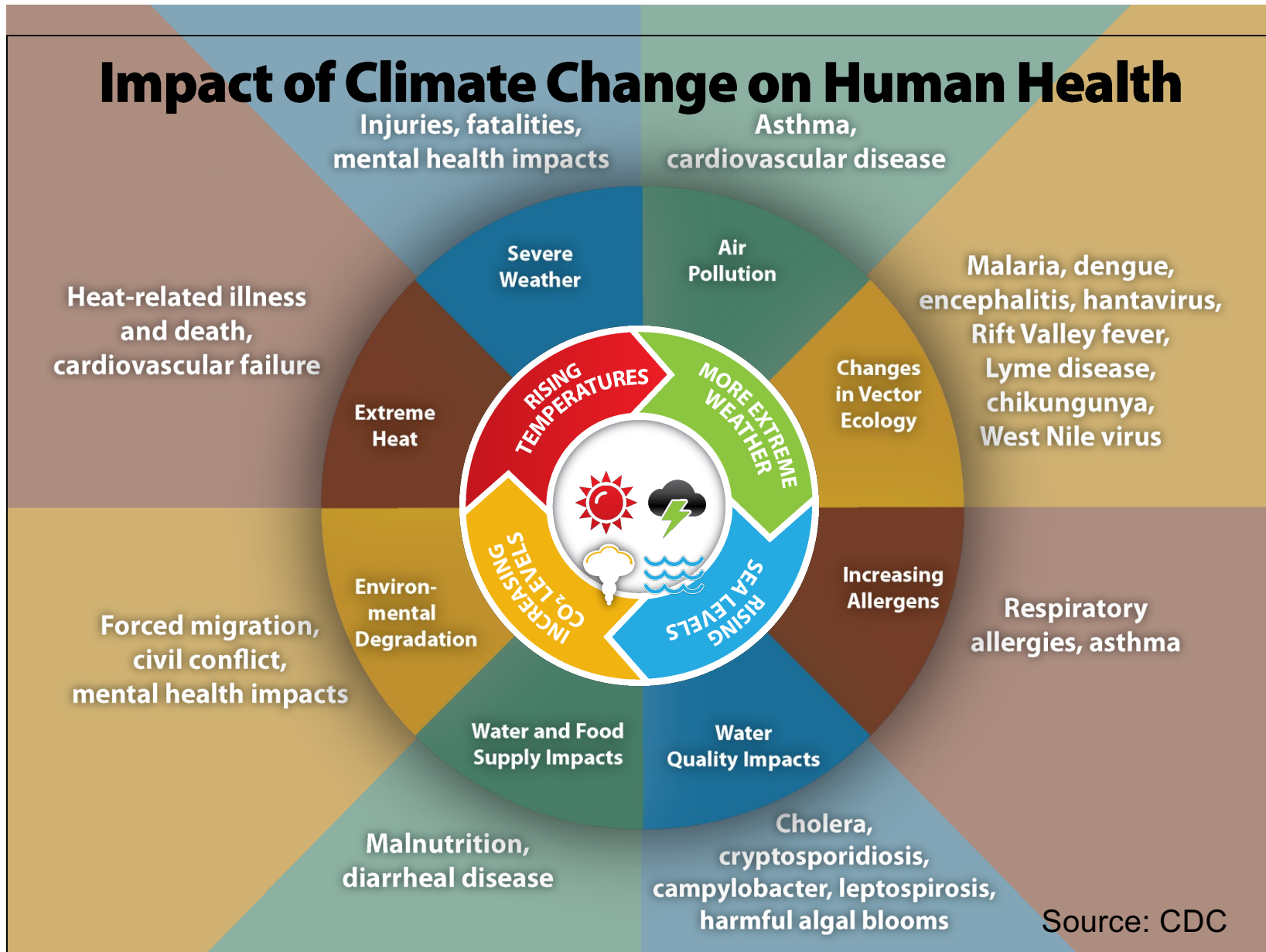
- Functional Residual Capacity(FRC, mL)
- Lung Clearance Index (LCI)

Tidal Breathing Flow-Volume Loops(TBFVL)

- Tidal Volume (VT, mL)
- Ratio of time to peak tidal expiratory flow to expiratory time (tPTEF/tE, %)

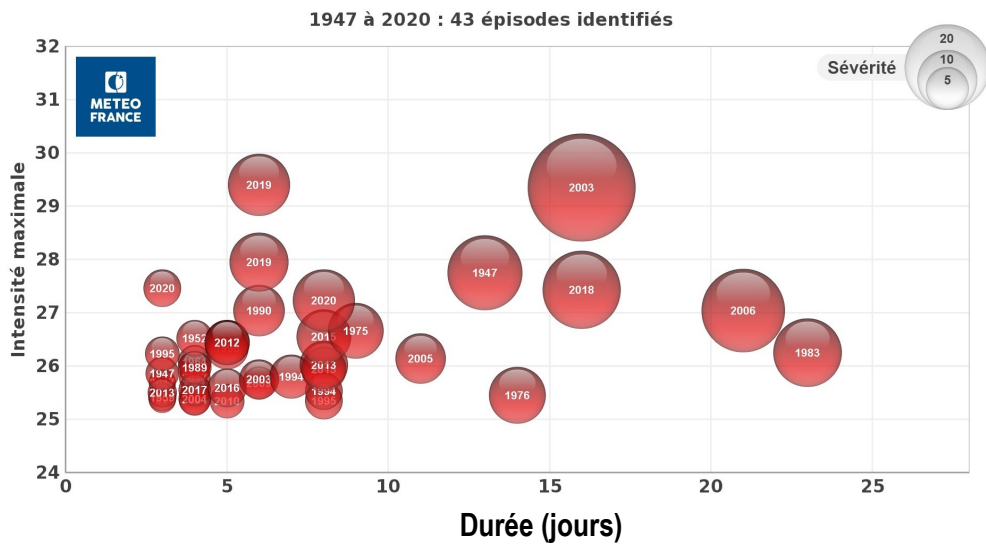


Impact of Climate Change on Human Health



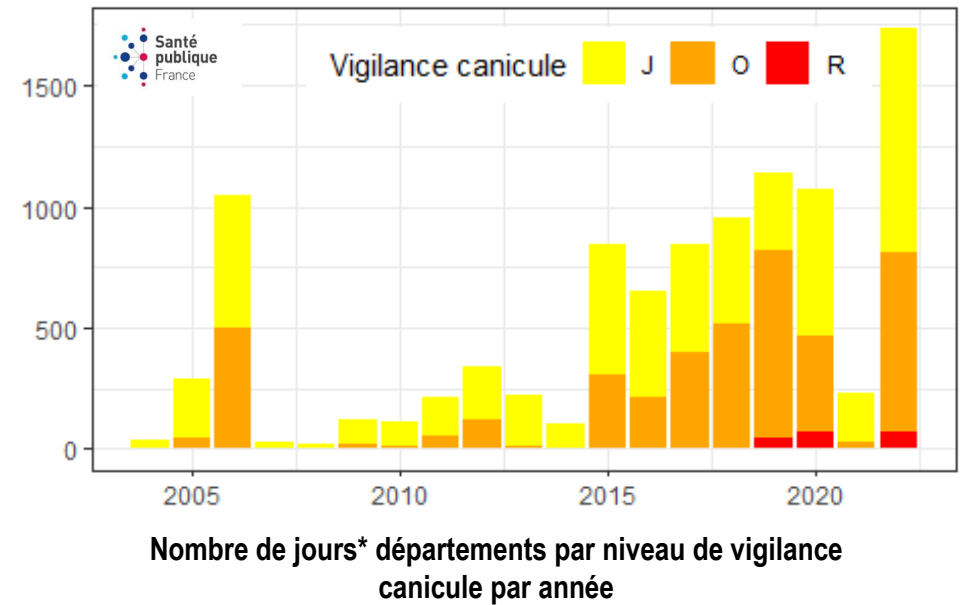
Source: CDC

Heat waves frequency and length in France



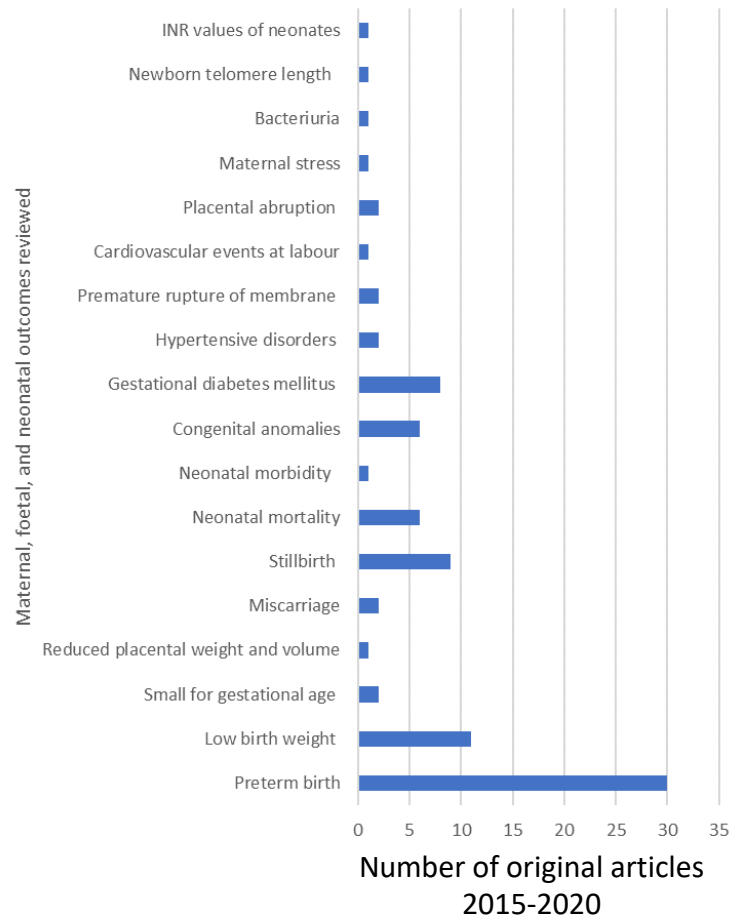
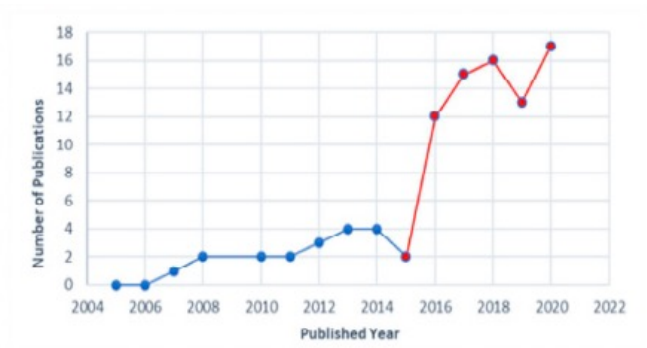
10 épisodes recensés dans la période 1947-1983 (37 années)

33 épisodes recensés dans la période 1984-2020 (37 années)



Augmentation de la fréquence, de la durée, de l'intensité, de l'étendue géographique et de la période de survenue des vagues de chaleur

Temperature and pregnancy outcomes



Recent reviews and meta-analyses
 Dalugoda et al 2022,
 Sexton et al 2021,
 Chersich et al 2020,
 Zhang et al 2017,
 Poursafa et al 2015,
 Beltran et al 2013,
 Strand et al 2011

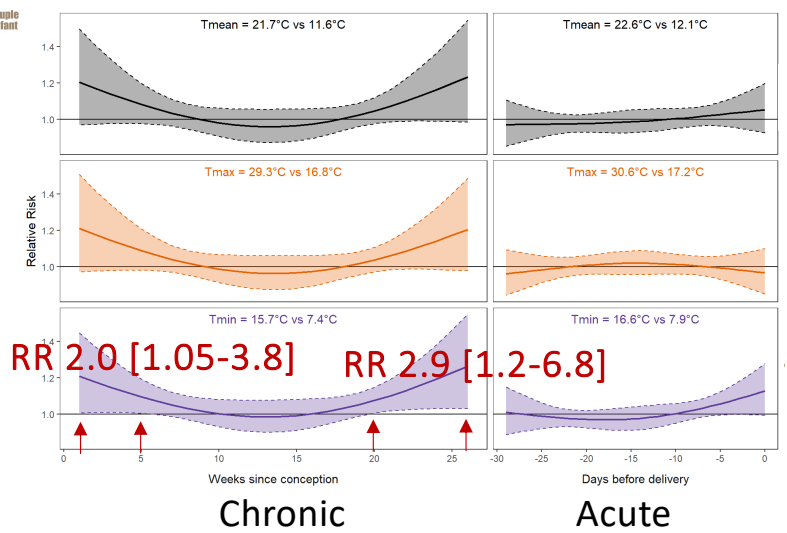
Dalugoda et al 2022, IJERPH

Temperature and preterm birth in France

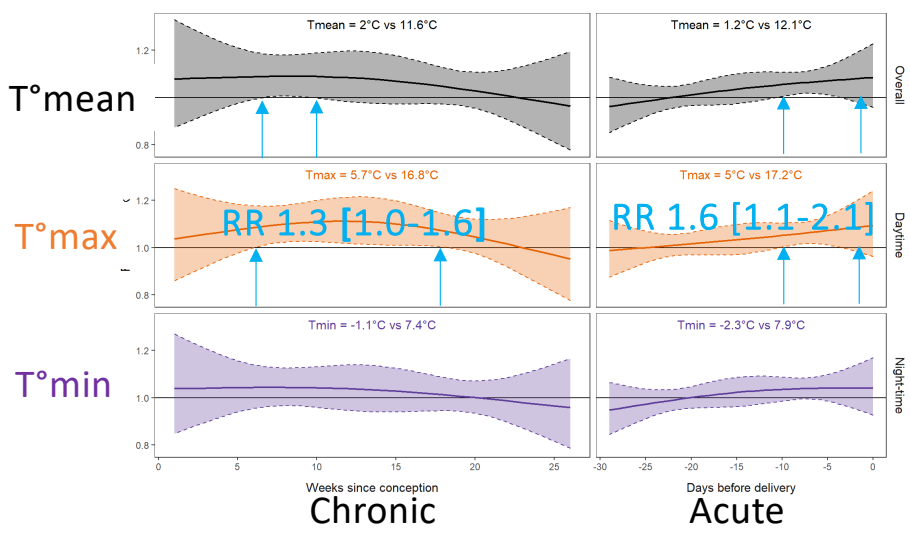


Hough et al 2022, IJE

Heat and preterm birth



Cold and preterm birth



- Chronic and acute windows of vulnerability, for cold and heat
- Clearest association for night time heat
 - Echoes results from mortality studies (*Murage et al 2017, Laaidi et al 2033*)
 - Consistent with studies in California and Belgium (*Avalaas et al 2017; Cox et al 2016*)
- No association with temperature variability and heat waves

Temperature effects - beyond birth



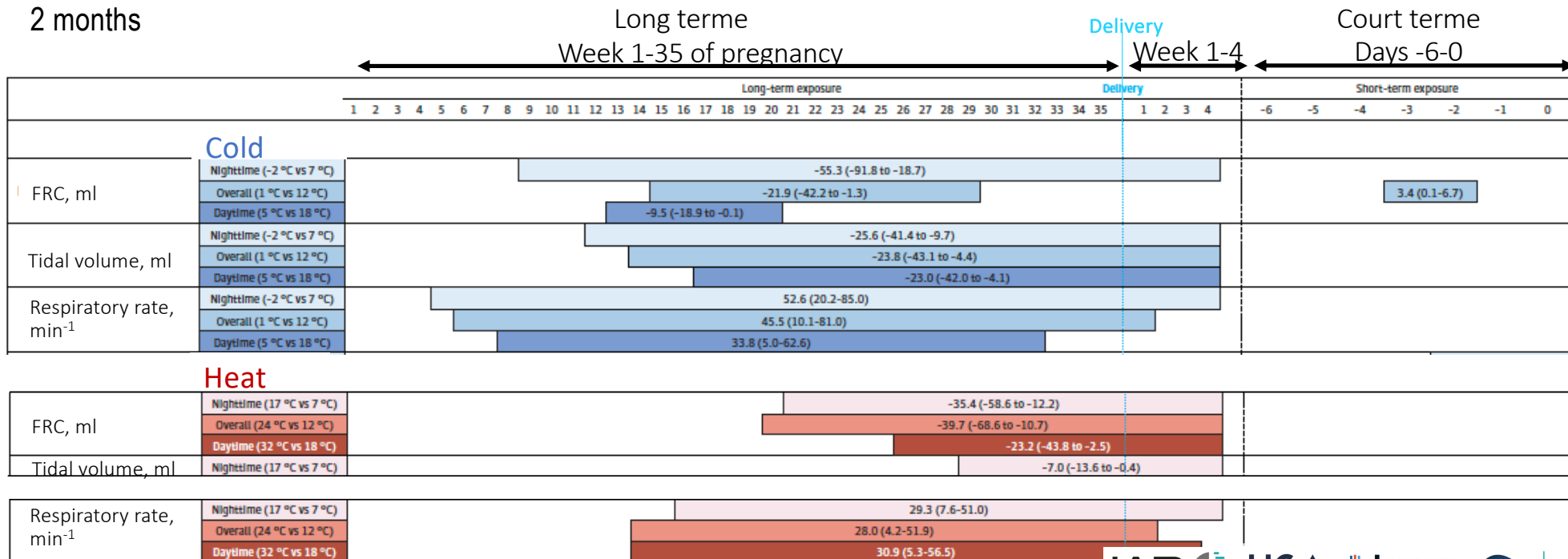
Guilbert et al 2023
JAMA Net

Burgeoning literature:

- Few studies on long term effects and impact of chronic exposures
- Heat in 1st year of life and rapid infant weight gain (*Dionicio et al 2021*)



Lung function
2 months



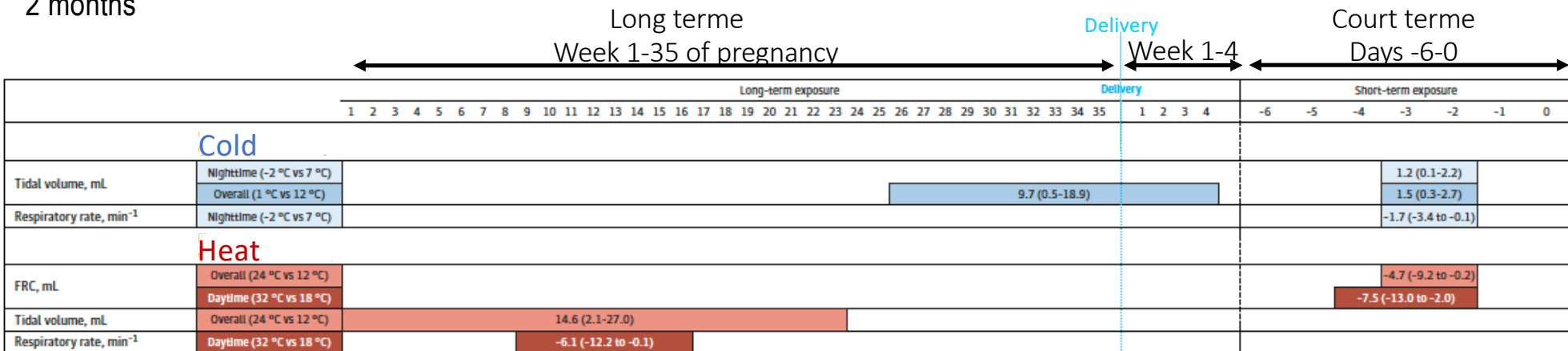
Temperature effects - beyond birth



Guilbert et al 2023
JAMA Net



Lung function
2 months



Environmental co-exposures

Closely linked to air pollution...

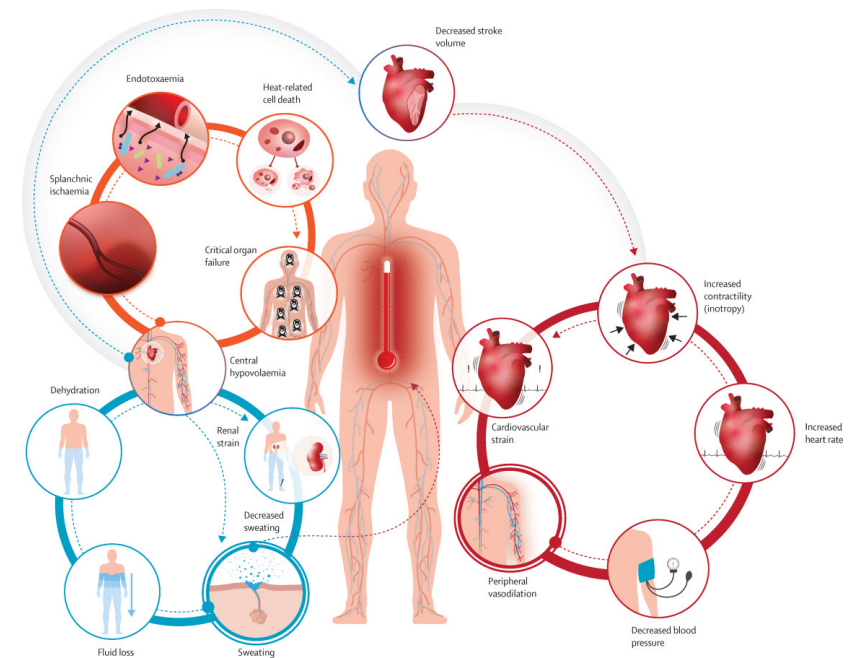


...and impact on children health

Biological mechanisms

- Body temperature above 39°C could be teratogen for the fetus (CVD defects, neural tube defects)
- **Cardiovascular changes:** increase in cardiac output, blood pressure, viscosity
 - Effects of temperature on pre eclampsia and blood pressure
- **Placenta:** reduced blood flow (increased IUGR LBW), epigenetic changes (*Abraham et al 2018, Env int*)
- Lower thermoregulatory abilities
- Acute effect on trigger birth
 - Release of prostaglandins and oxytocin : directly or by dehydration
 - **Oxidative stress, inflammation, heat shock protein**
 - Uterine contractions

Physiological pathways of human heat strain



Ebi et al., 2021, the Lancet

Samuels et al 2022, Int J Biomet

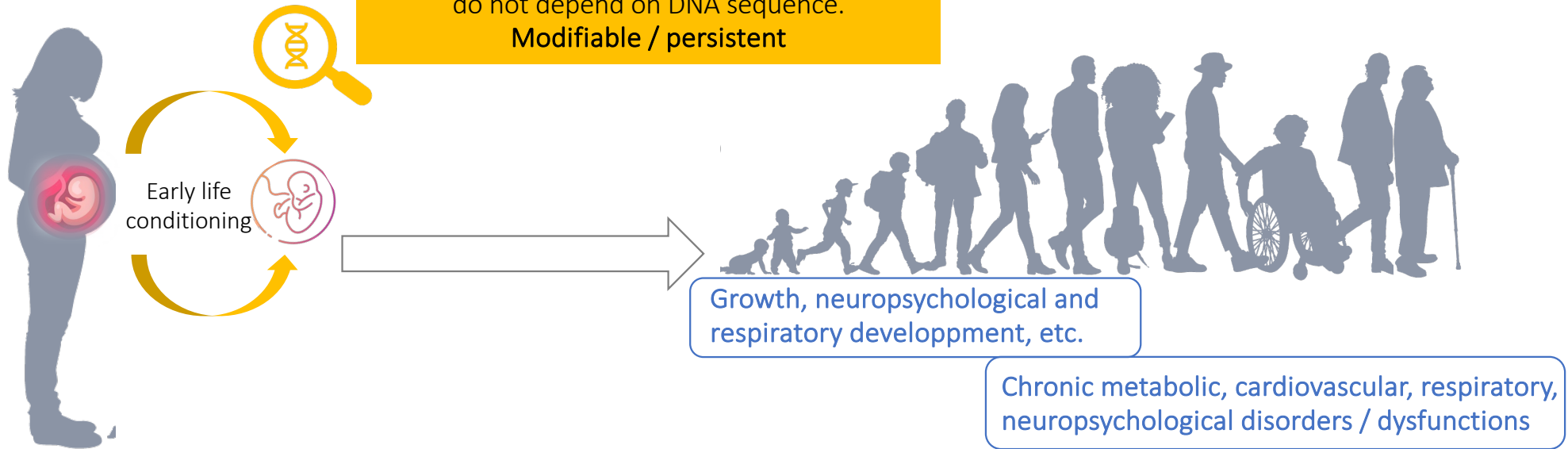
Developmental Origins of Health and Diseases

External exposures



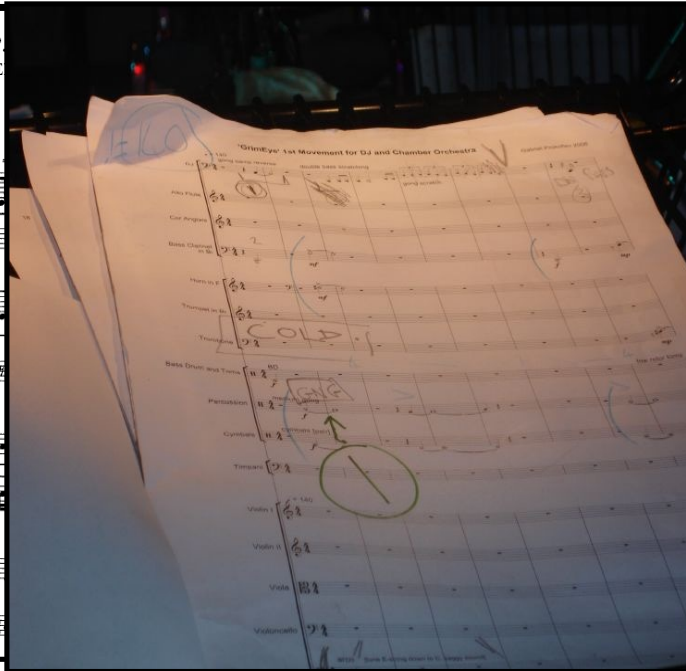
David Barker, 1938-2013

Epigenomics:
 mechanisms of gene expression regulation that do not depend on DNA sequence.
Modifiable / persistent



L'épigénétique: un exemple musical

ADN – genes

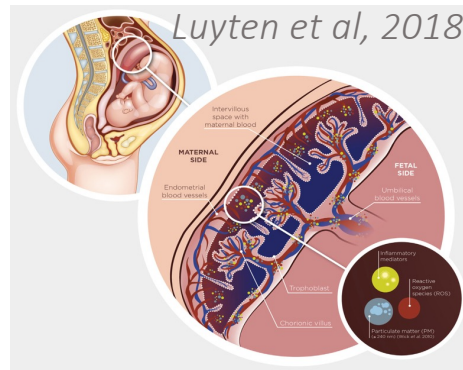


Phénotype

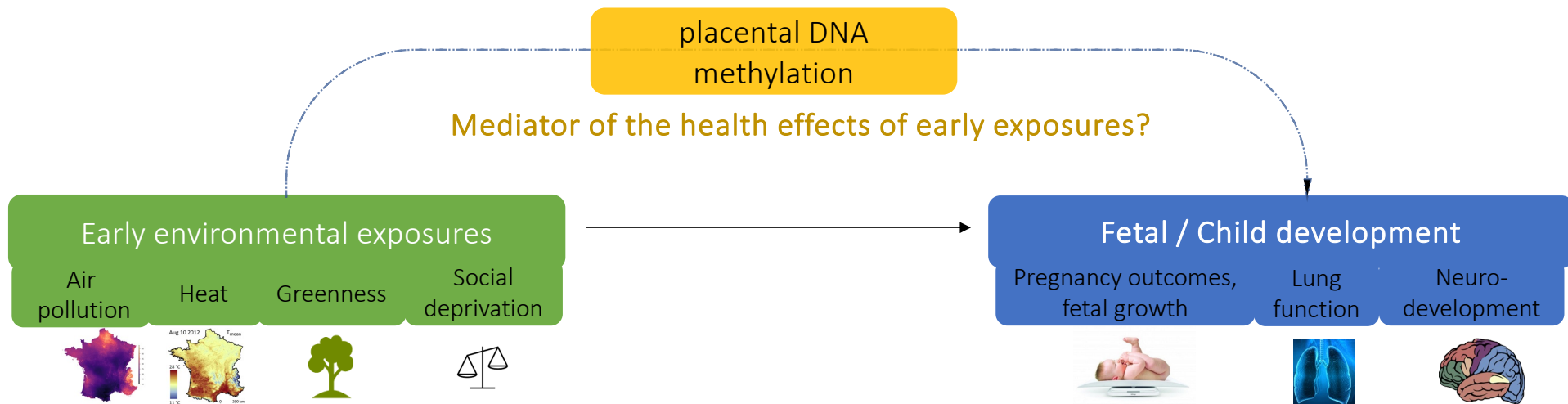
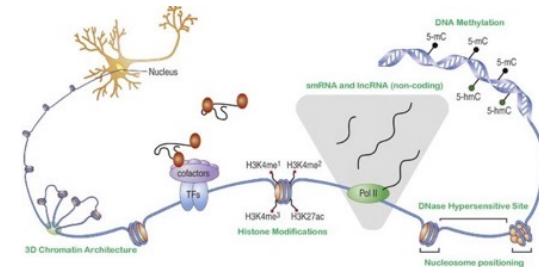


Epigenetique

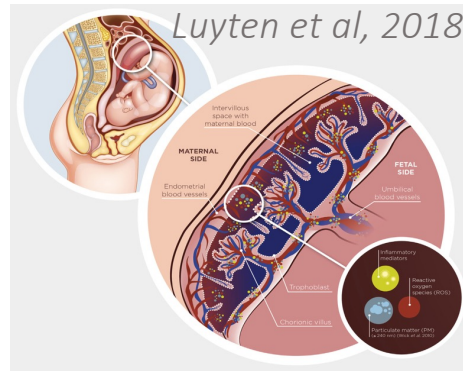
Mechanistic approach: role of placental DNA methylation



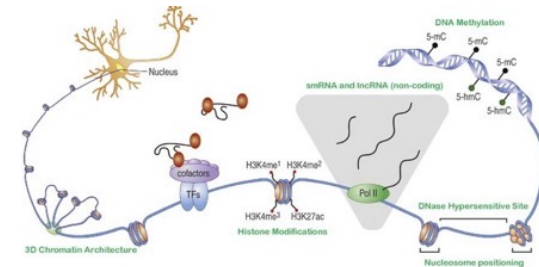
DNA methylation
Methyl marks added to certain DNA bases (CpG) that repress gene transcription



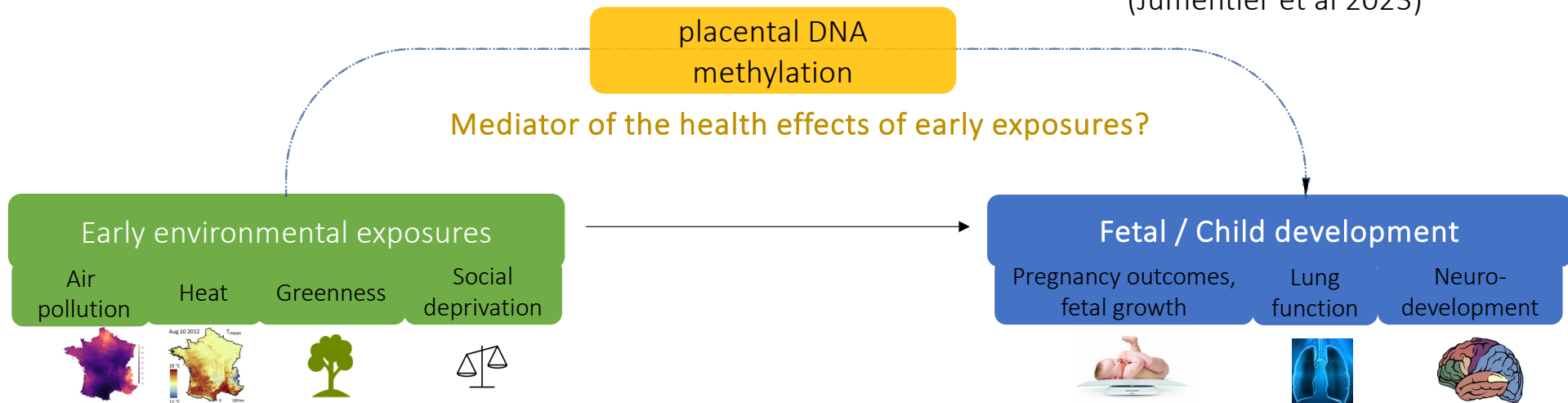
Mechanistic approach: role of placental DNA methylation



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Mediation en haute dimension
(Jumentier et al 2023)

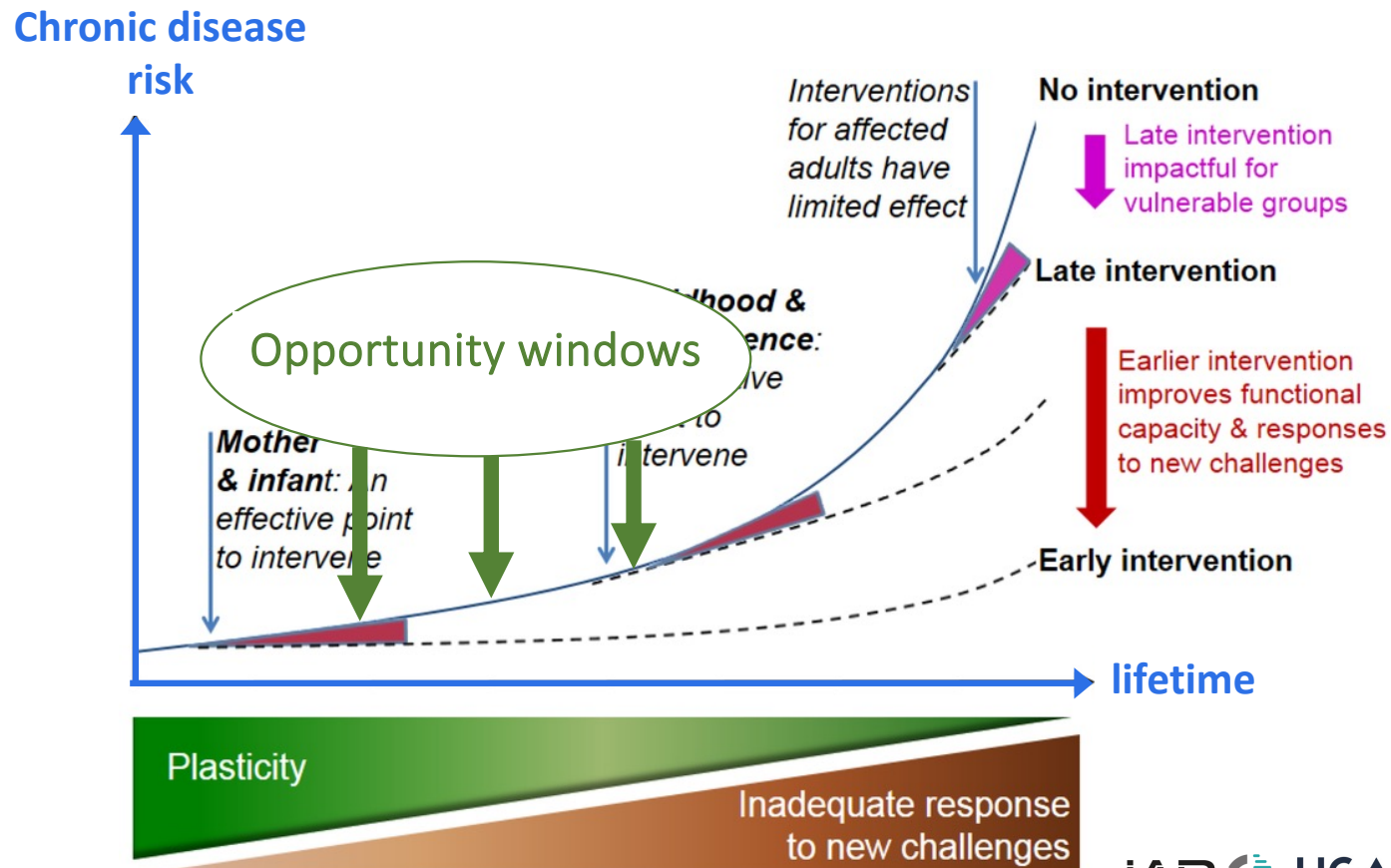


Conclusions

- High and **growing** level of evidence regarding the effects of developmental exposure to air pollution (PM_{2.5}) on
 - Birth weight, fetal growth
 - Respiratory health (asthma development and exacerbations, lung function development)
 - Neurodevelopment disorders
- Higher level of evidence for PM_{2.5} than NO₂
- Improve understanding: including sex-specific effects, vulnerability windows, biological mechanisms.
- Epigenetic is a promising field of research, but still in its infancy
- Role of co-exposures, exposome approaches



DOHaD – a perspective for improving public health



Hanson and Gluckman 2014

