

The Exposome and Health: Where Chemistry Meets Biology



Prof. Dr. Ir. Roel Vermeulen, PhD

- *Professor Environmental Epidemiology and Exposome Science, Utrecht University and UMCU*
- *Chair Institute for Risk Assessment Sciences, Utrecht University, the Netherlands*
- *Co-Chair Personalized medicine and Health Research Program, Utrecht Life Sciences*
- *Scientific director Data and Knowledge Hub Healthy Urban Living*
- *Steering group, Institute for Preventive Health. EWUU alliance*
- *Lead, EIRENE-NL, ESFRI Exposome research*



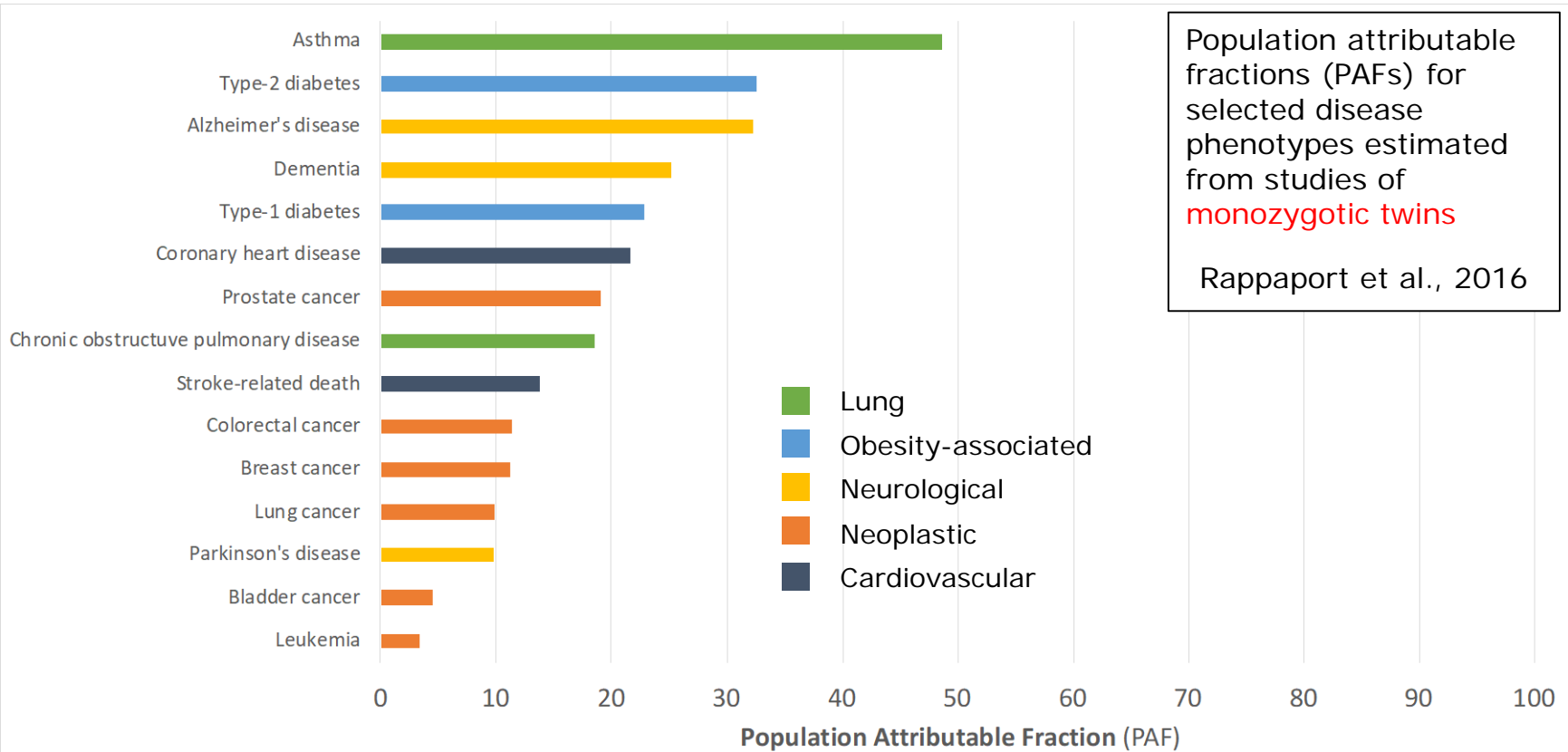
TOXICOLOGY
EPIDEMIOLOGY
ENVIRONMENTAL SCIENCE
PUBLIC HEALTH
MEDICINE
VETERINARY MEDICINE
DATA SCIENCE
MATHEMATICS
INFORMATICS
GEOSCIENCE
SOCIOLOGY
PHARMACOLOGY



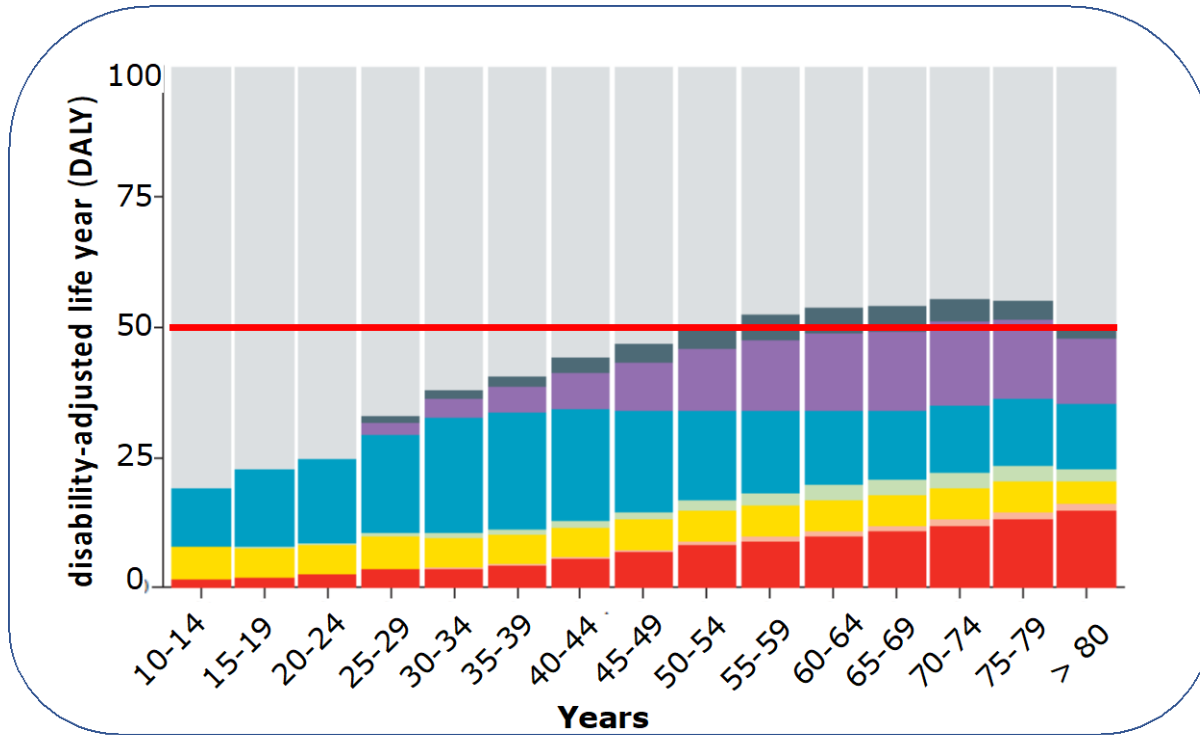
Outline

- Impact of environment on health
- Introduction to the 'Exposome' concept
- Some examples and current efforts
- Challenges future (policy) perspectives

Estimated Genetic related Population Attributable Fraction



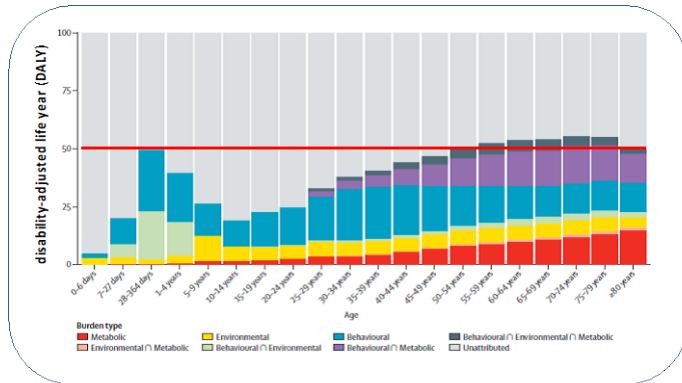
What do we know of environmental risks?



- Metabolic (M)
- Environmental (E)
- Behavioural (B)
- $E \cap M$
- $B \cap E$
- $B \cap M$
- $B \cap E \cap M$
- Unattributed

Proportion of global all-cause DALYs attributable to behavioral, environmental, and metabolic risk factors and their overlaps, by age (*Lancet* 2015;386:2287–323)

What do we know of environmental risks?

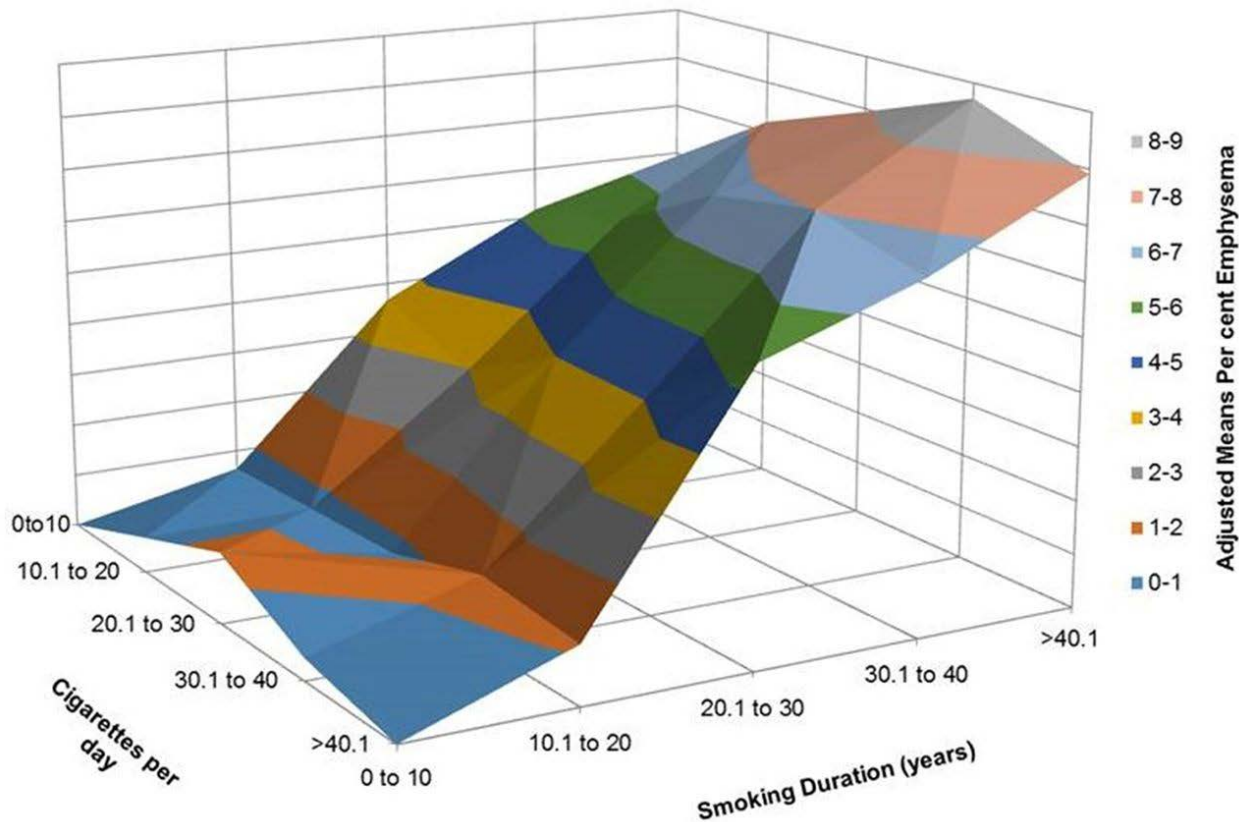


Proportion of global all-cause DALYs attributable to behavioral, environmental, and metabolic risk factors and their overlaps, by age (*Lancet* 2015;386:2287–323)

1. Current risks underestimated

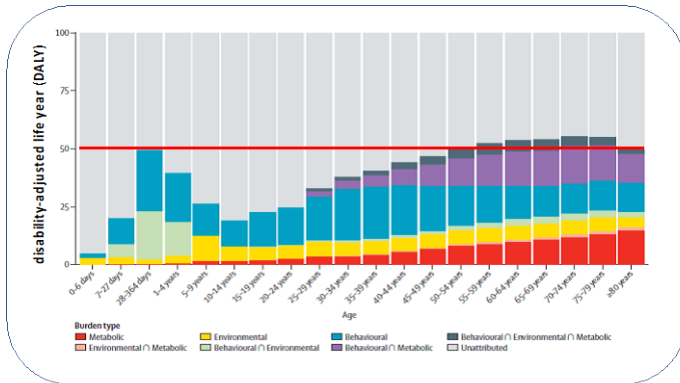
- Measurement error
- In appropriate risk models

Smoking duration alone provides stronger risk estimates of chronic obstructive pulmonary disease than pack-years



Bhatt SP, *et al.* Smoking duration alone provides stronger risk estimates of chronic obstructive pulmonary disease than pack-years
Thorax 2018;**73**:414-421

What do we know of environmental risks?



Proportion of global all-cause DALYs attributable to behavioral, environmental, and metabolic risk factors and their overlaps, by age (*Lancet* 2015;386:2287–323)

1. Current risks underestimated

- Measurement error
- In appropriate risk models

2. Unknown risks

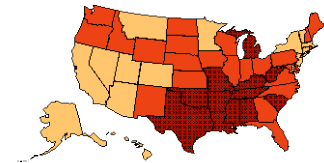
- Unknown chemical – health associations
- Unknown interactions between stressors

3. Stochastic

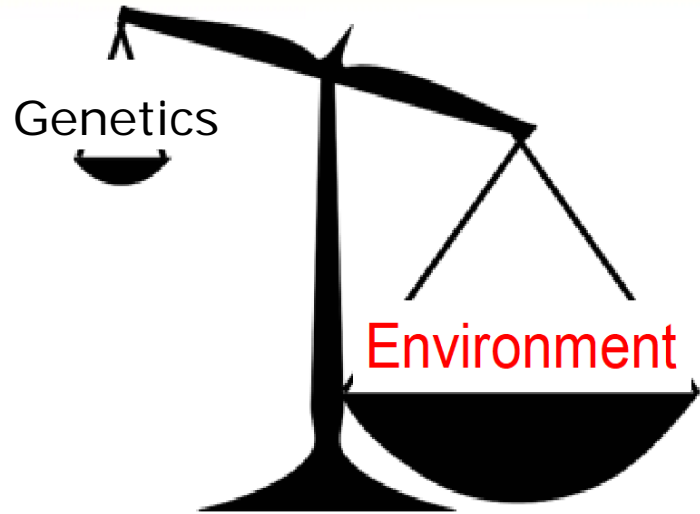
Obesity Trends* Among U.S. Adults

BRFSS, 2010

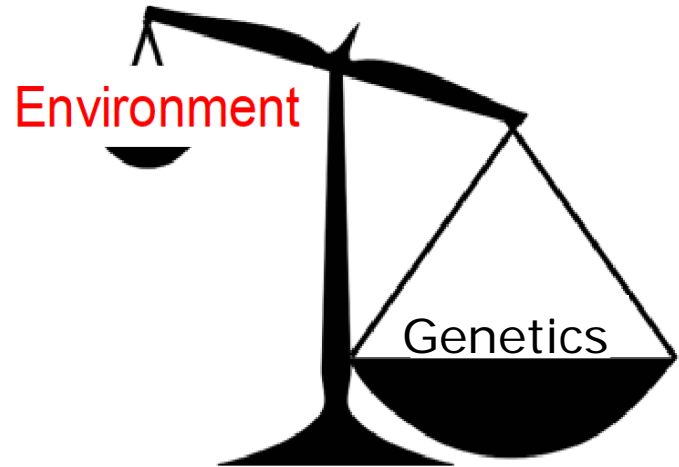
(*BMI ≥30, or ≥30 lbs. overweight for 5' 0" person)



Heritability provides an unbalanced view of human health and disease



Burden of disease



Analytical capacity

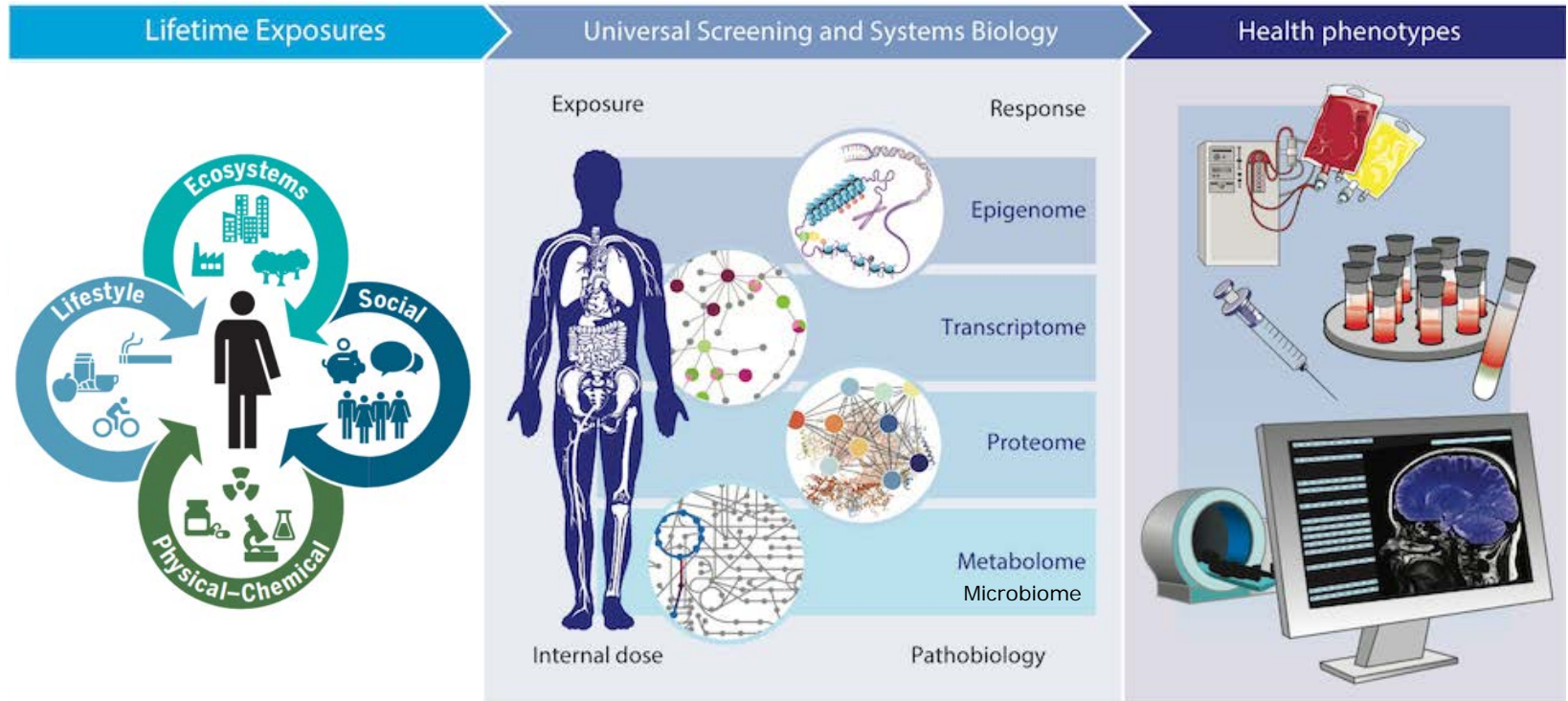
Exposome; A Wild idea

The **cumulative** measure of **environmental influences** and associated **biological responses** throughout the **lifespan**

Movement away from
The **One** exposure **One** disease paradigm

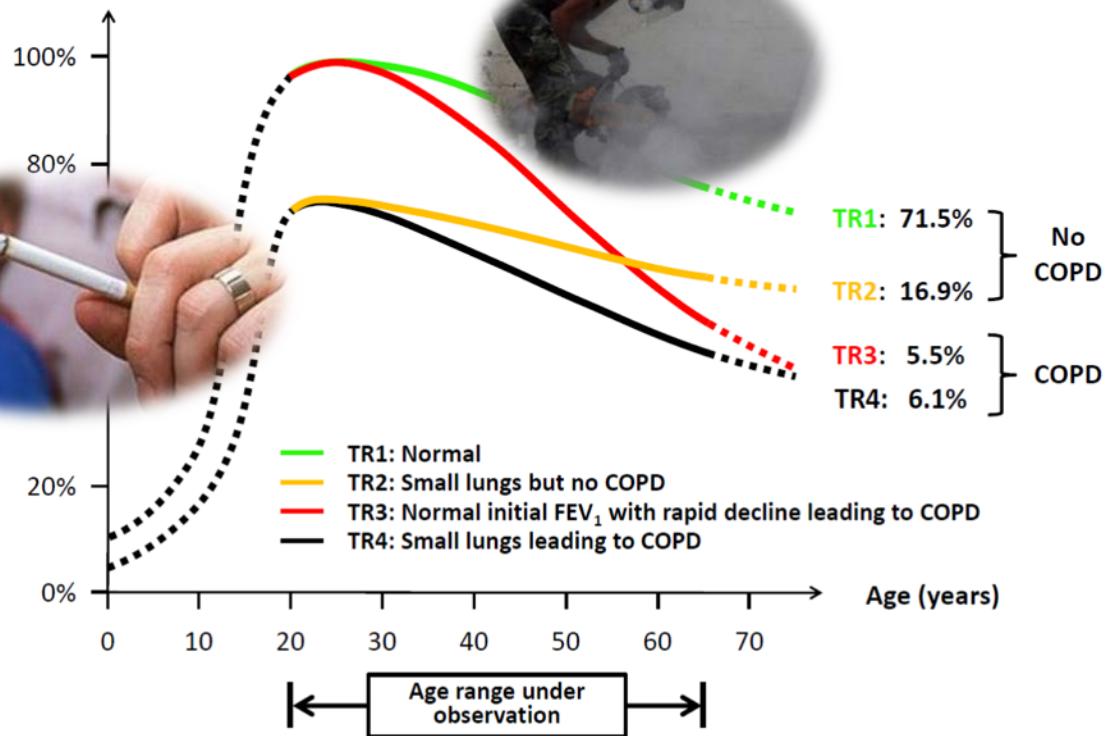
Overcome challenges in **multiplicity** and **fragmented** literature of associations that occur due to **nonsystematic testing**

The Exposome Concept asks for a 4D-system understanding



Time-dimension: Lung-function trajectories from birth to death

FEV₁ in percent of predicted maximally attained value



Lange P, et al. Lung-Function Trajectories Leading to Chronic Obstructive Pulmonary Disease. N Engl J Med 2015 Jul 9; 373(2): 111-122.

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Recommended for children over 3 years old

STAR TREK[®] TRICORDER

30 MINUTE STAR TREK[®]
TRICORDER TAPE INCLUDED

One side of tape recorded with
actual Star Trek[®] sounds and voices.



* PATENT PENDING

© 1976 PARAMOUNT PICTURES CORPORATION

Manufactured Exclusively for Mego Corp., New York, N.Y.

The cumulative measure of environmental influences; external exposome

Lifetime Exposures

Ecosystems

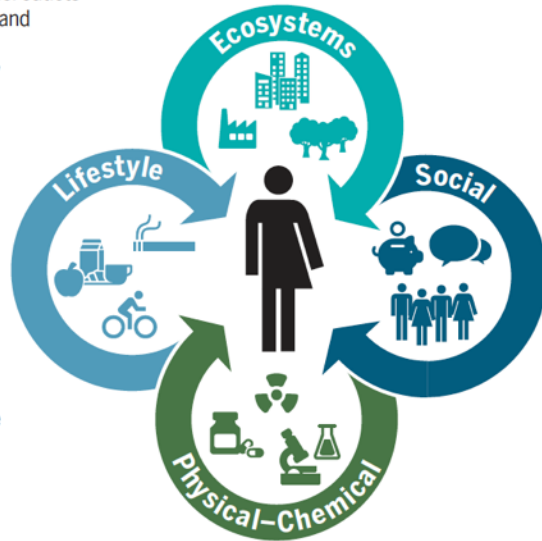
Food outlets, alcohol outlets
Built environment and
urban land uses
Population density
Walkability
Green/blue space

Lifestyle

Physical activity
Sleep behavior
Diet
Drug use
Smoking
Alcohol use

Social

Household income
Inequality
Social capital
Social networks
Cultural norms
Cultural capital
Psychological and mental stress



Physical-Chemical

Temperature/humidity
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Food contaminants
Soil contaminants
Drinking water contamination
Groundwater contamination
Surface water contamination
Occupational exposures

Tools for the assessment of the external exposome



Silicone Wristbands



ELSEVIER

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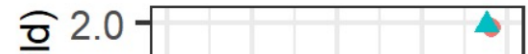
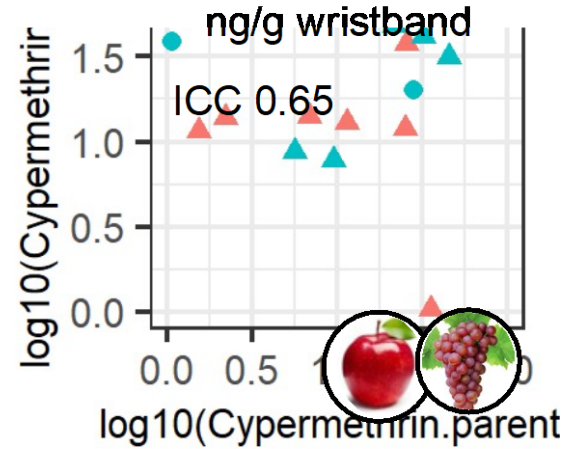
Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv



Quantitative assessment of multiple pesticides in silicone wristbands of children/guardian pairs living in agricultural areas in South Africa

Samuel Fuhrmann^{a,b,c,*}, Hans G.J. Mol^d, Jonatan Dias^d, Mohamed Aqiel Dalvie^e, Martin Rööslü^{b,c}, Céline Degrendele^{f,g}, Daniel M. Figueiredo^a, Anke Huss^a, Lutzen Portengen^a, Roel Vermeulen^a



The cumulative measure of environmental influences; external exposome

Lifetime Exposures

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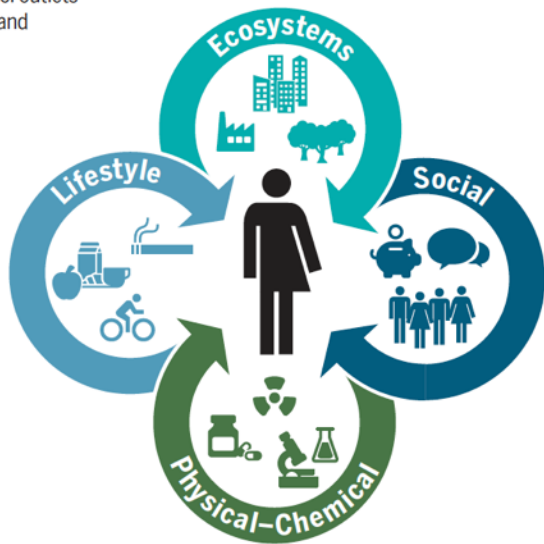
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Tools for the assessment of the external exposome





Google Air View

- Amsterdam
- Athens
- Barcelona
- Basel
- Copenhagen
- Munich
- Rome
- Rotterdam

Los Angeles

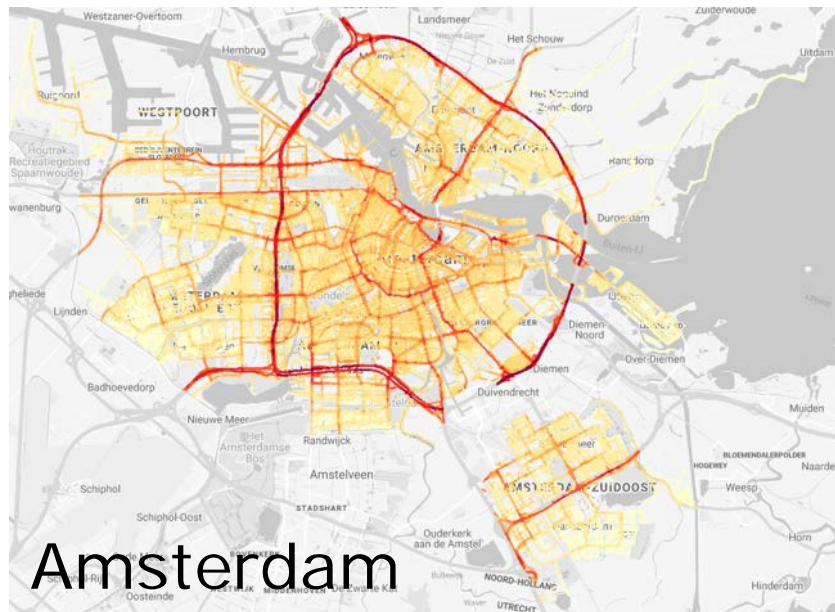
NO₂ concentration (ppb)



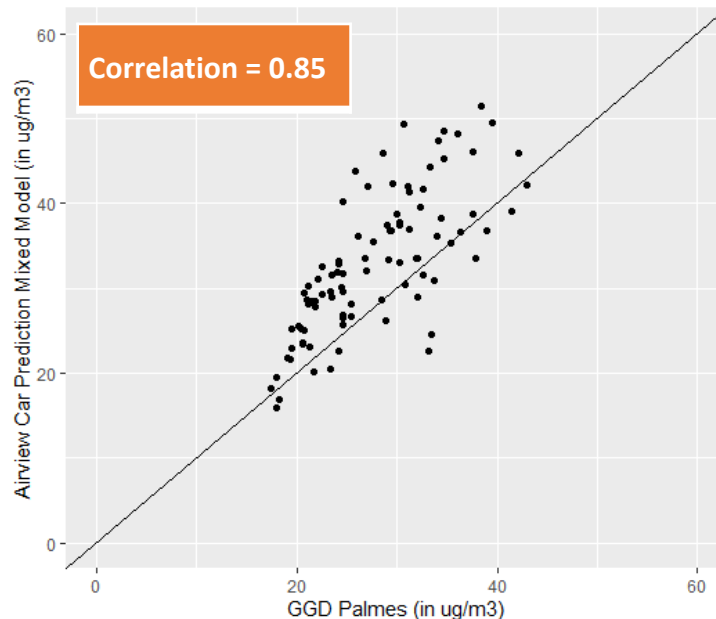
Air quality data from Google / Aclima

Google Earth

Hyper Local Air Quality Mapping



Correlation between GGD Palmes and Airview Car



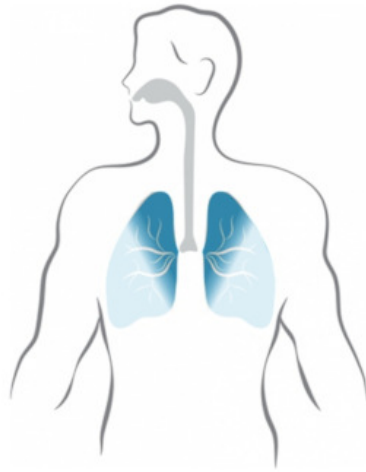
Unregulated components of air pollution

PM10



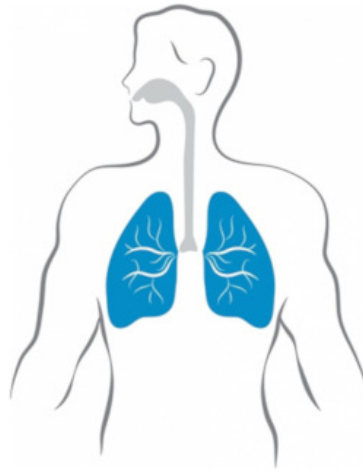
Coarse particles
Upper respiratory tract

PM2.5



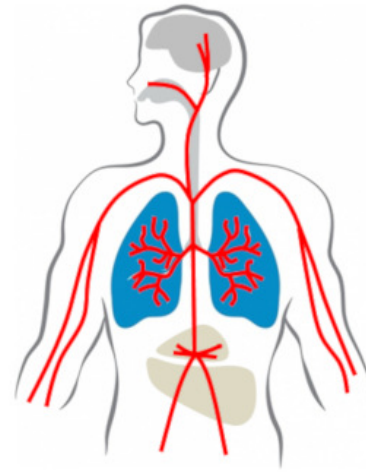
Fine particles
Lower respiratory tract

PM1



Very fine particles
Alveolus

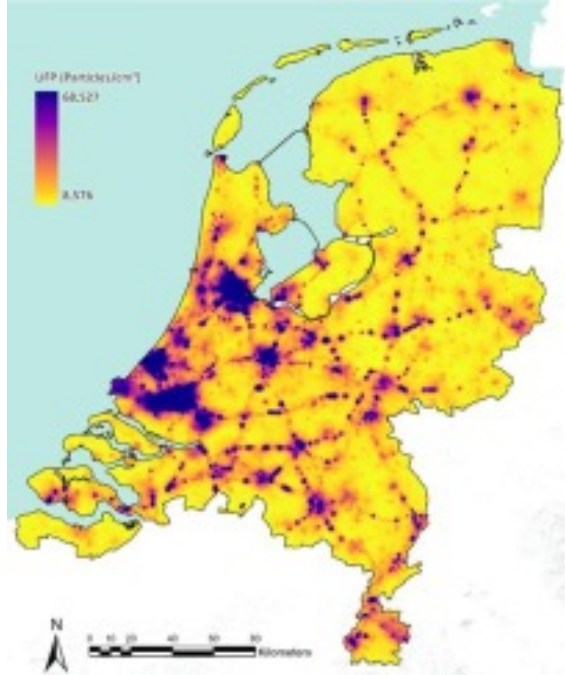
PM0.1



Ultrafine particles
Blood/Whole body

Mass based methods poor proxy for particle numbers

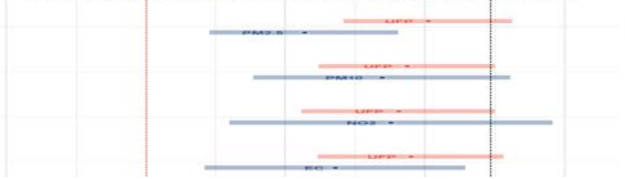
Ultrafine particulates and cause-specific mortality



Dutch administrative cohort of 10.8 million adults (30+ years)

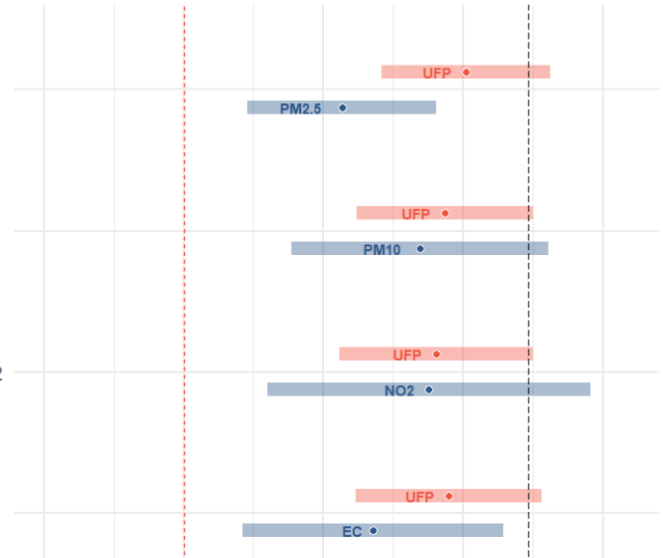
UFP + PM_{2.5}
UFP + PM₁₀
UFP + NO₂
UFP + EC

Two-pollutant models for natural mortality



Two-pollutant models for natural mortality

UFP + PM_{2.5}
UFP + PM₁₀
UFP + NO₂
UFP + EC



The cumulative measure of environmental influences; external exposome

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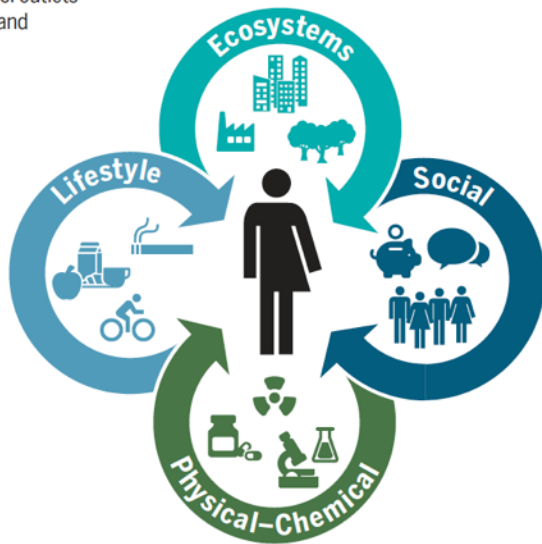
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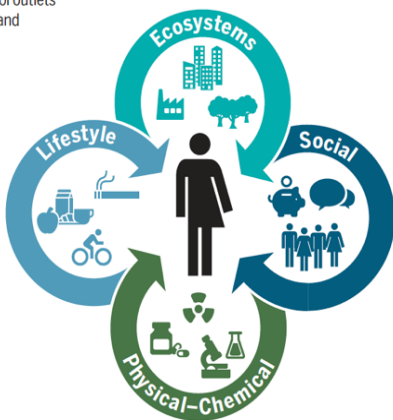
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Administrative cohorts

Number of individuals: >55M
Number of data elements: small
Age range: 0 -100
Biological data: no



Adult cohorts

Number of individuals: >2M
Number of data elements: medium
Age range: 15-100
Biological data: yes



Data sources



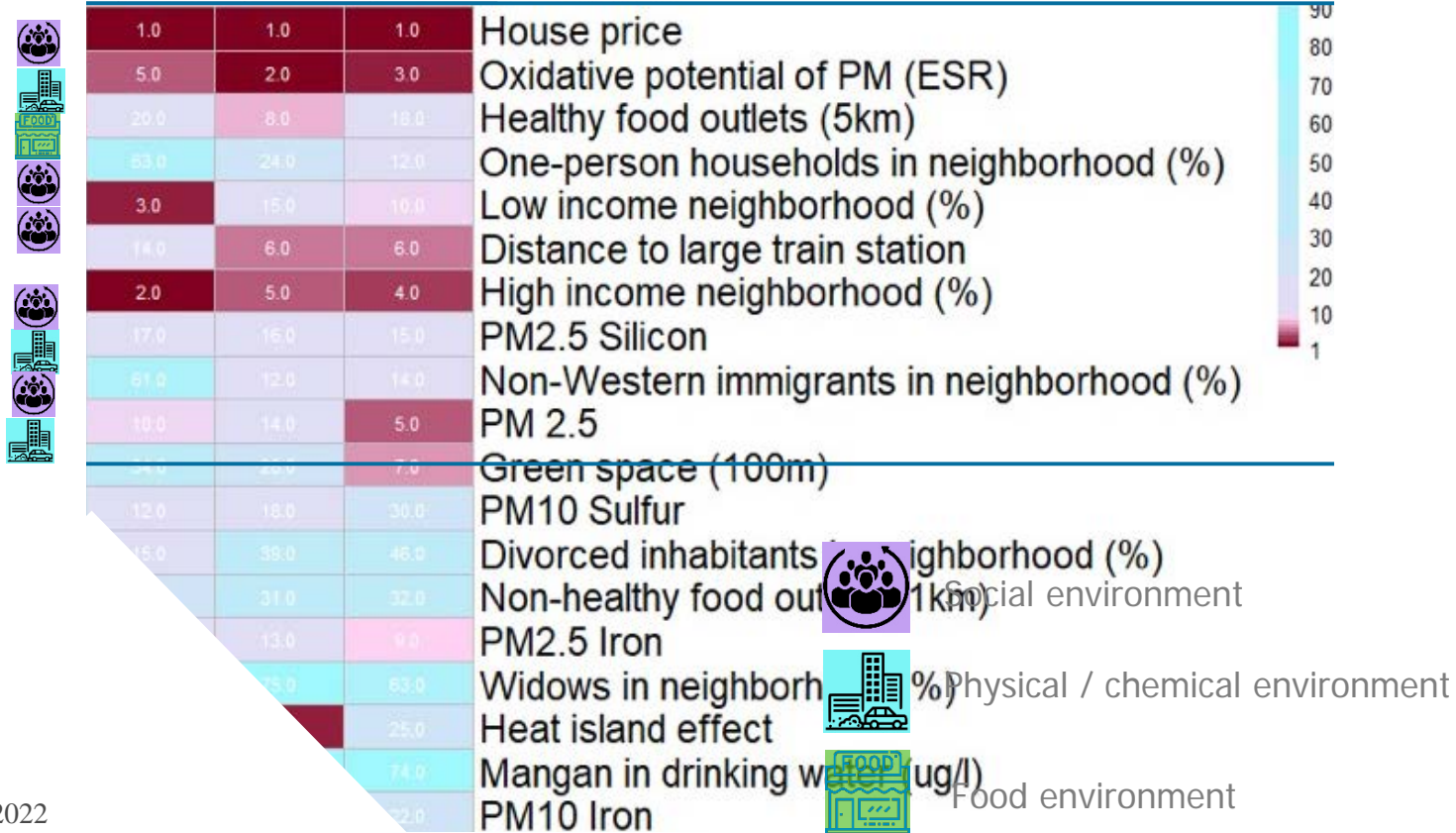
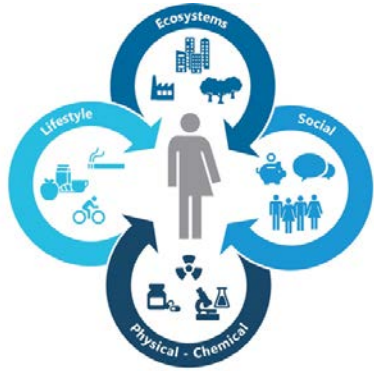
Matured birth cohorts

Number of individuals: >30,000
Number of data elements: medium
Age range: 0 - 30
Biological data: yes

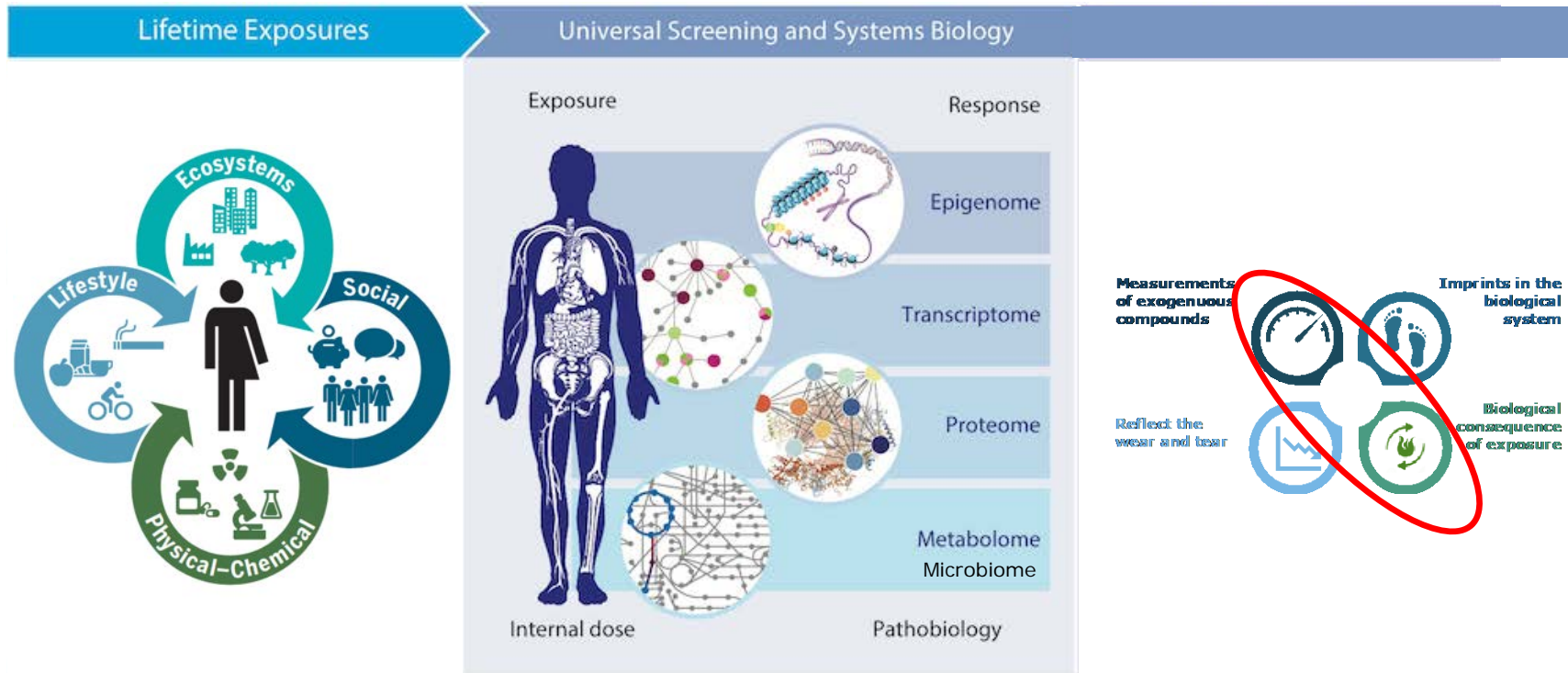
Urban labs

Number of individuals: 5,000
Number of data elements: large
Age range: 18-100
Biological data: yes

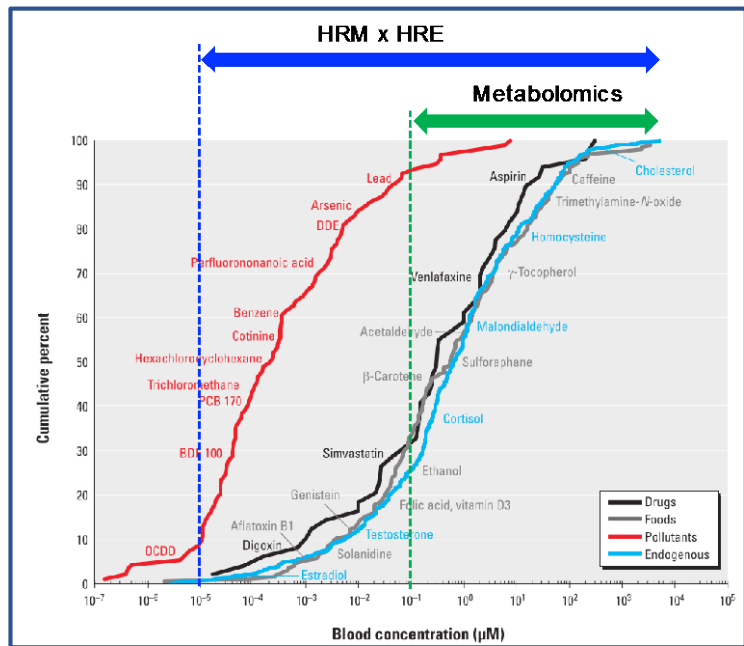
URBAN EXPOSOME AND OBESITY



Environmental influences and associated biological responses; internal exposome



The combination of HRE and HRM provides the functional measures and sensitivity needed for EWAS of human health and disease



Thomas Hankemeier



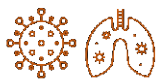
Doug Walker



Gary Miller



Jeroen Meier



Bacteria / Virus



Food

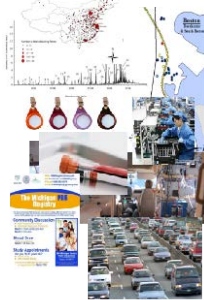


Chemical pollutants

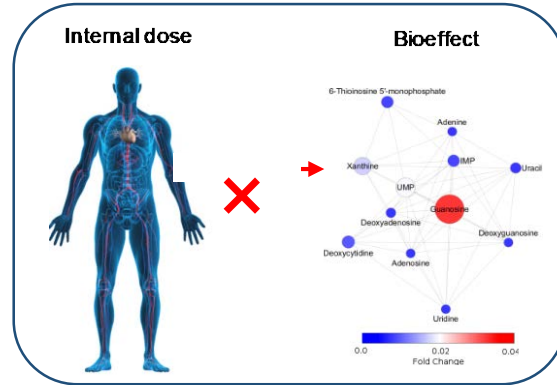
High-resolution metabolomics of occupational exposure to trichloroethylene



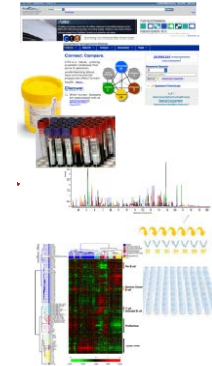
Exposure



High-resolution metabolomics



Additional biomarkers

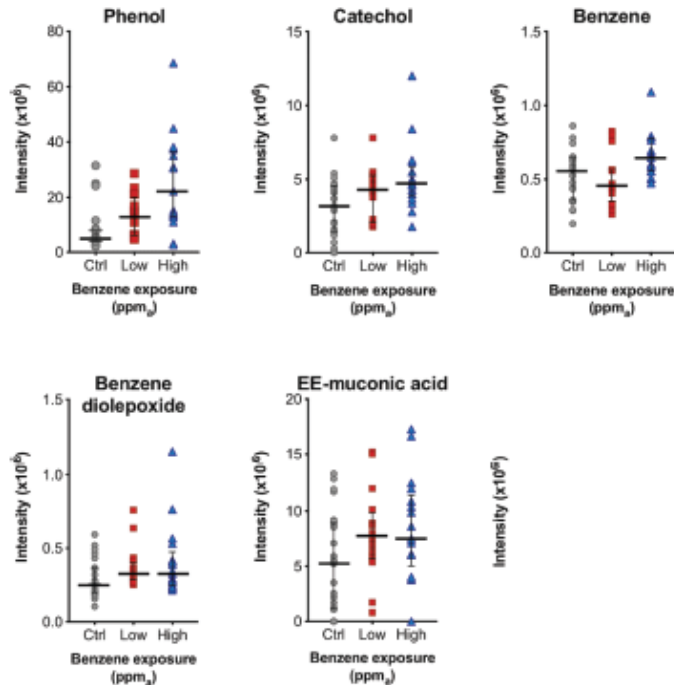


- 25 unexposed workers
- 33 exposed workers
- Post-shift plasma collected
- MWAS using linear regression; FDR 20%

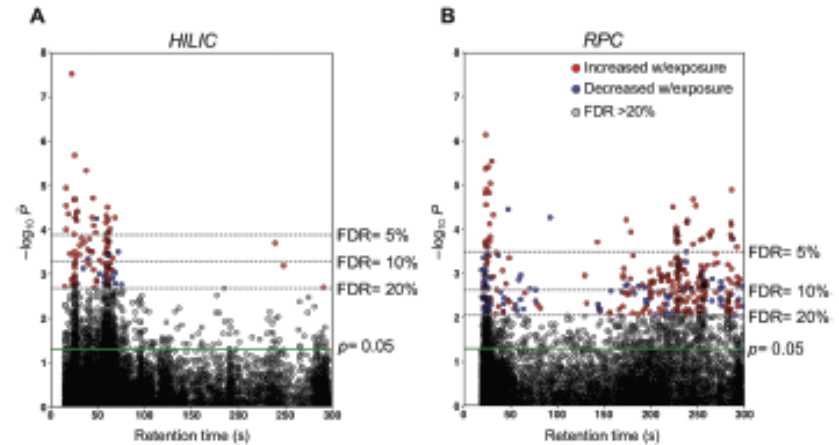
Urinary benzene biomarkers
Hematologic cell counts
Chromosomal aberrations
Telomere length

Metabolome-wide association study of occupational exposure to benzene

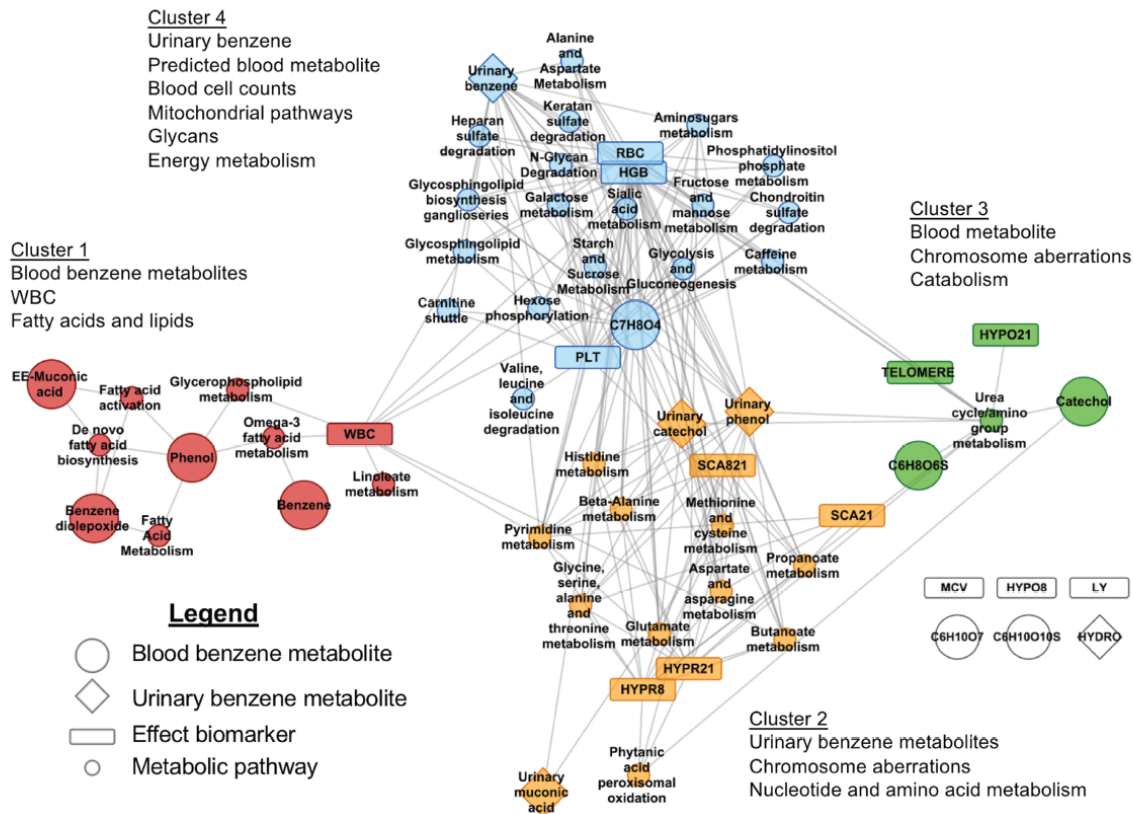
Exposure signal



Response signal



Metabolome-wide association study of occupational exposure to benzene



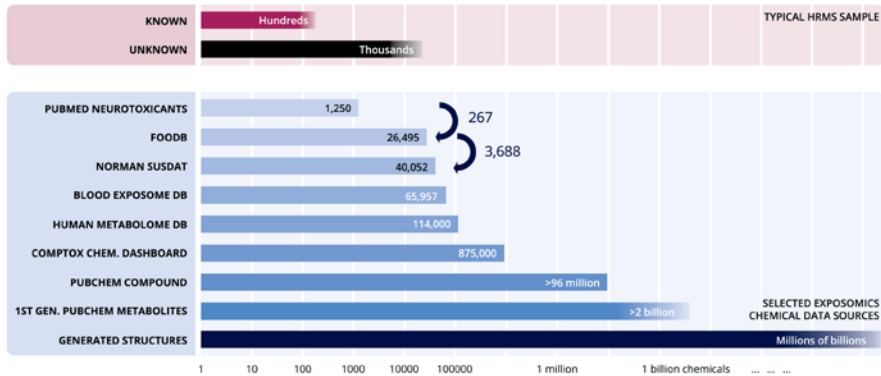
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The world is complex

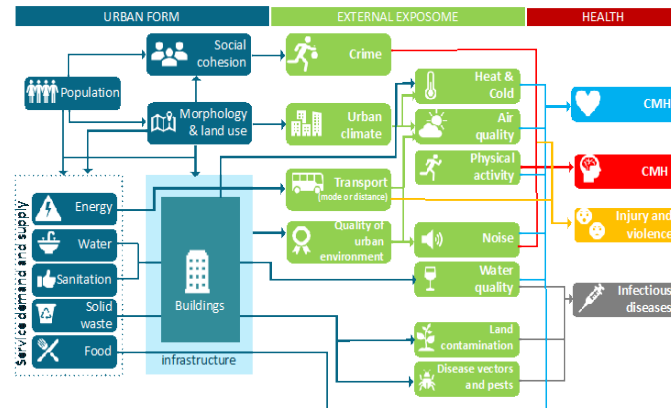


Chemical Complexity



Vermeulen et al., Science, 2020

Societal Complexity



Adapted from Rydin et al., 2012

Systematic (untargeted) discovery of non-genetic drivers of health

"Discovery-based"



The exposome approach provides opportunities to develop preventive strategies that are potentially more effective than traditional approaches, because it sheds **light on the accumulation of, and interactions between, various environmental factors**. As a result, the exposome approach could better explain health differences between population groups.

Exposome research also has the potential to detect the emergence of new risks, for example resulting from the introduction of certain innovations.



- **Connection to policy**
 - *integrated living environment and health policy*
- **Adopt precautionary policy**
 - *adopt proportional precautionary policy in good time in the event of uncertainty regarding the exact nature and scale of warning signs from exposome research*
- **Develop additional criteria for weighting research results**
 - current guidelines were developed for the assessment of a single environmental factor, whereas exposome research concerns combinations of substances and other factors, as well as their interactions.
- **Encourage interdisciplinarity in research and policy application**



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EMORY
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Dean Jones



Douglas Walker



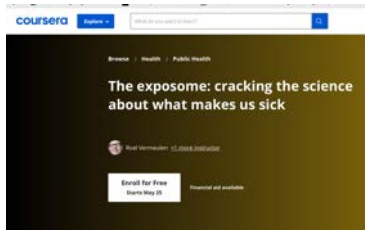
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