Children's Health: Assessing the impact of the exposome

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CHE webinar
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La science pour la santé — From science to health

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ISGlobal Instituto de Salud Global Barcelona
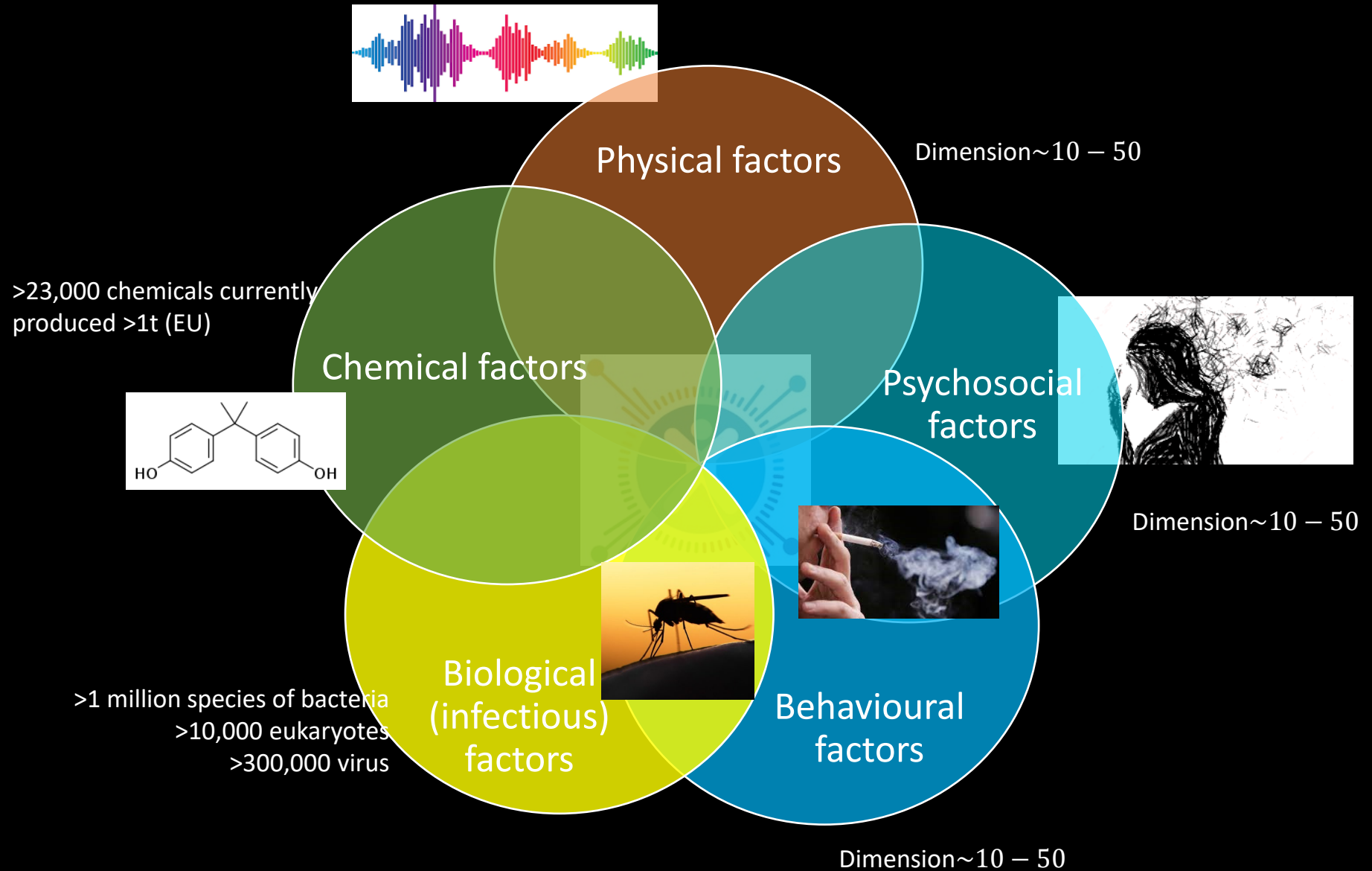
ATHLETE
The Exposome from Evidence to Translation

Ca. 100,000 chemicals currently marketed in the EU (EEA)

Including 23,000 with "high production" (REACH/ECHA, excludes drugs, pesticides, cosmetics)

Thousands of exogenous chemicals detected in the human body (NHANES, USA, and other biomonitoring studies)

The exposome

Physical factors

Chemical factors

Psychosocial factors

Biological (infectious) factors

Behavioural factors

$\text{Dimension} \sim 10 - 50$

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>23,000 chemicals currently produced >1t (EU)

>1 million species of bacteria
>10,000 eukaryotes
>300,000 virus

Exposome research ambitious road

Exposome

Quantification
Platforms
TD-TK modeling
Dosimeters
« Exposome-ready » cohorts

Link with socio-territorial characteristics
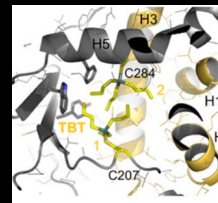**« Environmental justice »**

Mechanisms of action
Cross-omics studies
In vitro and in vivo toxicology, cohorts
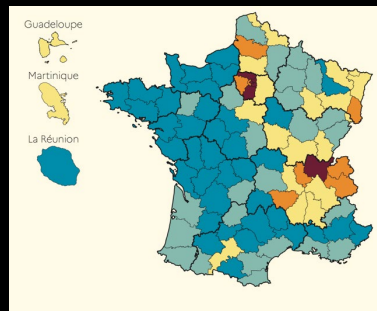
Health effects
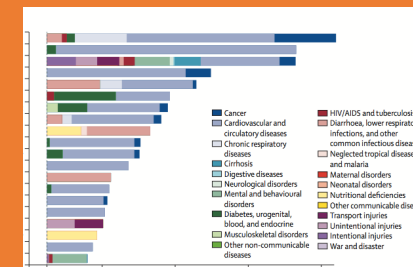**In vivo toxicology, Cohorts**

Modifying one's exposome
Individual interventions
Governance / regulatory framework

Health impact
Environmental disease burden

Burden of disease estimates (world, 2021)

Leading risks 2021	95% UI for Ranking	Percentage of total DALYs,
1 Particulate matter pollution	(1 to 2)	8·0 (6·7 to 9·4)
2 High systolic blood pressure	(1 to 2)	7·8 (6·4 to 9·2)
3 Smoking	(3 to 6)	5·7 (4·7 to 6·8)
4 Low birthweight and short gestation	(3 to 6)	5·6 (4·8 to 6·3)
5 High fasting plasma glucose	(3 to 6)	5·4 (4·8 to 6·0)
6 High body–mass index	(3 to 10)	4·5 (1·9 to 6·8)
7 High LDL cholesterol	(7 to 10)	3·0 (1·9 to 4·2)
8 Kidney dysfunction	(6 to 10)	3·0 (2·6 to 3·4)
9 Child growth failure	(6 to 14)	2·6 (1·4 to 3·5)
10 High alcohol use	(7 to 11)	2·5 (2·1 to 3·1)
11 Unsafe sex	(11 to 17)	1·5 (1·4 to 1·7)
12 Diet low in fruits	(11 to 22)	1·5 (0·6 to 2·3)
13 Unsafe water source	(11 to 24)	1·5 (0·8 to 2·0)
14 Diet high in sodium	(8 to 36)	1·4 (0·3 to 3·2)
15 Diet low in whole grains	(12 to 23)	1·4 (0·6 to 2·1)
16 Secondhand smoke	(11 to 26)	1·2 (0·6 to 1·8)
17 Iron deficiency	(12 to 23)	1·2 (0·9 to 1·6)
18 Lead exposure	(10 to 52)	1·2 (0·0 to 2·4)
19 Unsafe sanitation	(14 to 23)	1·1 (0·9 to 1·4)
20 Occupational injuries	(15 to 21)	1·1 (1·0 to 1·2)
21 Drug use	(17 to 24)	1·0 (0·8 to 1·1)
22 Low temperature	(19 to 26)	0·9 (0·8 to 1·0)
23 No access to handwashing facility	(11 to 53)	0·8 (−0·2 to 1·8)
24 Diet low in vegetables	(20 to 29)	0·7 (0·4 to 1·0)
25 Diet low in omega–6 polyunsaturated fatty acids	(11 to 53)	0·6 (−2·0 to 2·3)

Rather limited number of chemical and physical risk factors considered in most previous studies assessing the environmental burden of disease.

Environmental burden of disease studies in children considered up to 7 chemical and physical factors at a time (Rojas-Rueda, IJERPH, 2019)

Possible explanation: lack of synthesis of the evidence regarding the exposome health effects in children (possibly because only part of the evidence was considered, e.g., only human studies), lack of exposure response functions or exposure data

DALYs: Disability-adjusted life years (%)
GBD risk factors collaborators, *Lancet*, 2024)

Main aims

To summarize the overall level of evidence (LoE) regarding exposome effects on child health,

   Considering the human (epidemiological), toxicological and mechanistic streams of evidence

   Focusing on the chemical and physical (urban health) components of the exposome

To identify the corresponding dose-response functions in humans

Principle of Health Impact Assessment studies

Literature reviews
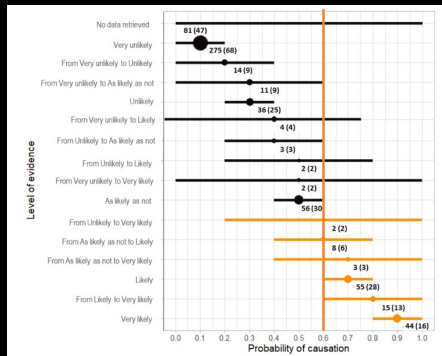
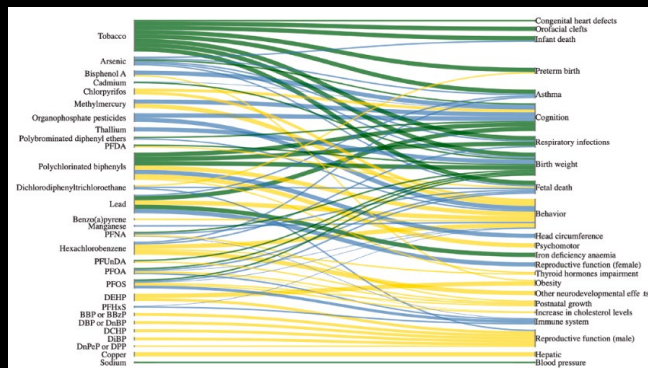| Level of evidence regarding association | x | Exposure-response functions | x | Distribution of exposures | x | Baseline number of cases or DALYs | → | Exposome-wide health impact |

(Colzin, *IJHEH*, 2024)
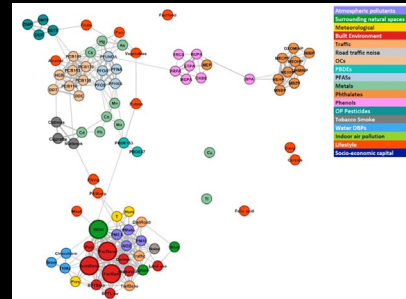
(Tamayo, *Env Int*, 2019)

Fig. 2. Overview of exposure-outcome pairs with dose-response relationships from meta-analysis (green), single epidemiological studies (blue), and without dose-response relationship (yellow); Width of the links reflects the probability of causation.

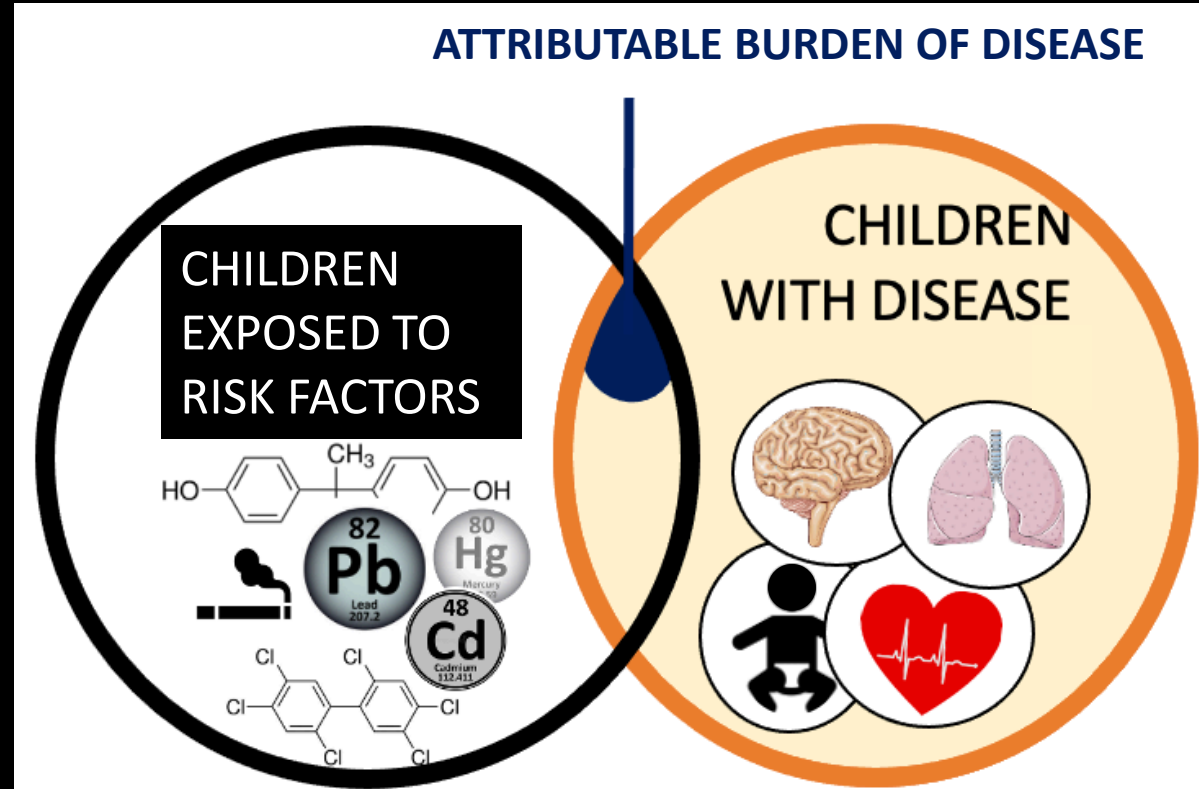(Rocabois, *Env Health*, 2024; Wies, *Env Res*, 2024)

(Rigaud, *Env Health*, 2024)

Risk factors considered in ATHLETE project

88 risk factors:
- Air pollution
- Tobacco smoking
- Pesticides
- Bisphenols
- Phthalates
- Parabens
- Metals and elements
- Perfluoroalkyl substances
- Persistent organic pollutants
- Other urban factors (noise, temperature, green spaces)

Health domains:
- Neurodevelopment
- Cardiometabolism
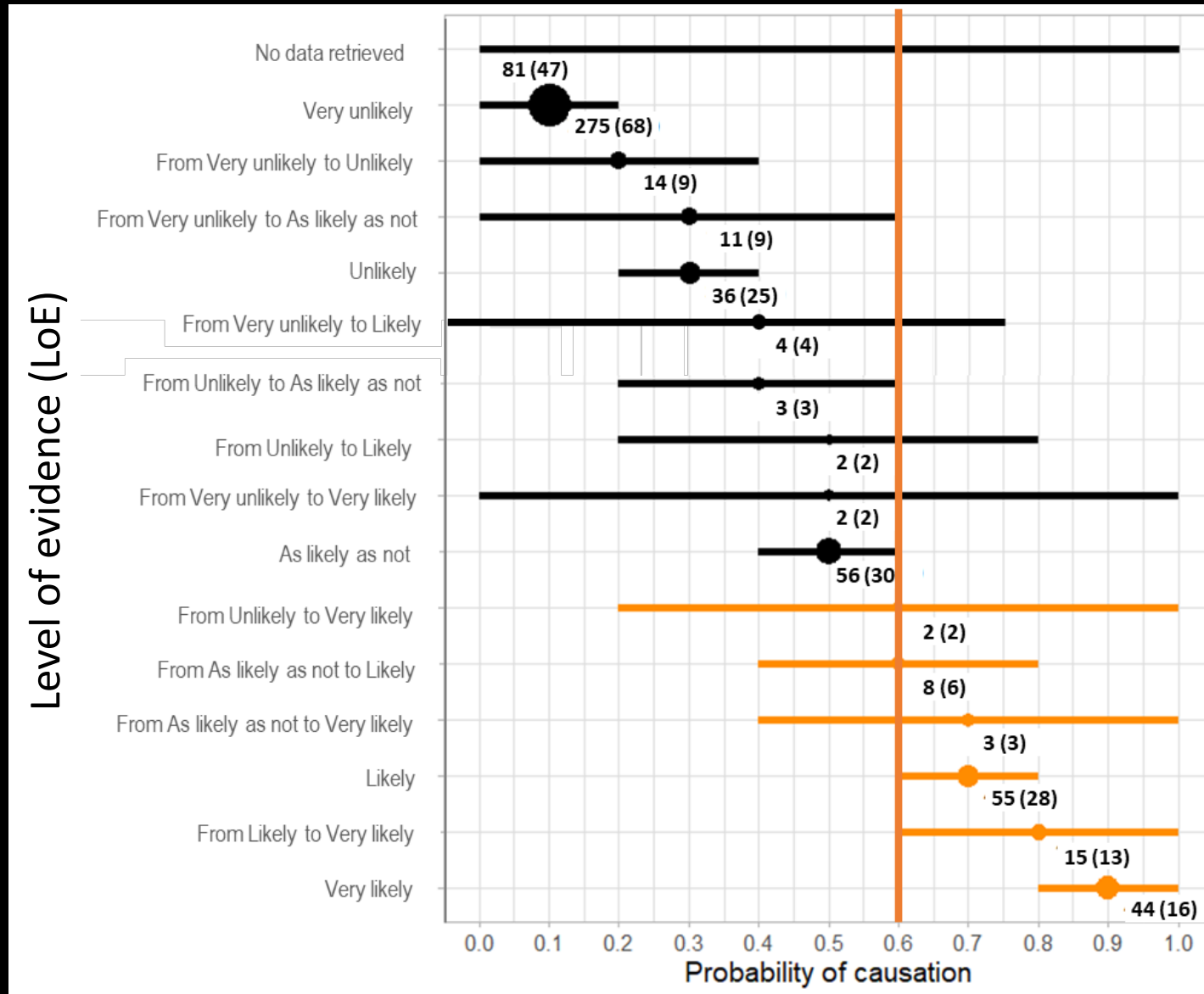- Respiratory health
- Others (mortality, reproductive health)

# Overall level of evidence (LoE) assessment
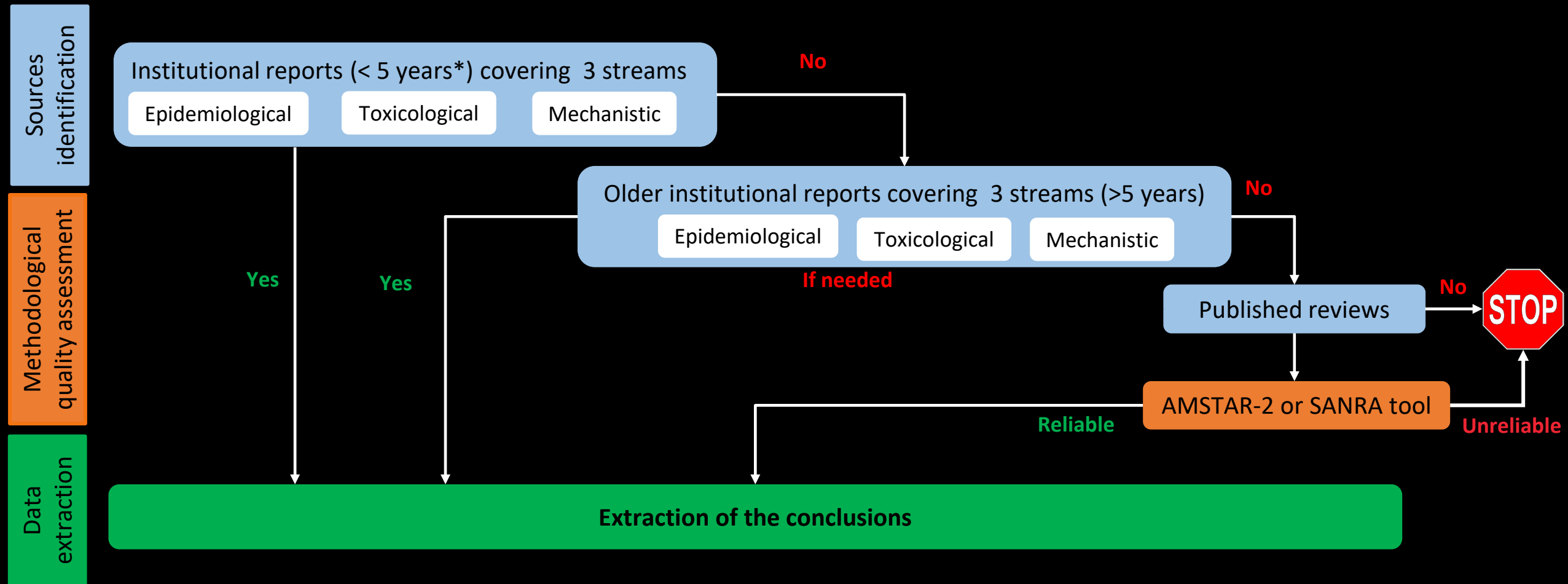
*2015-2021

Distribution of the level of evidence across the 611 considered factor-outcome pairs

81 exposure-outcome pairs (corresponding to 47 exposures) for which no relevant data was found

127*

prioritized factor-outcome pairs with probability of causation ≥ 60%
*Updated to 132

(Colzin et al., *IJHEH*, 2024)

Exposure-outcome pairs with the highest level of evidence regarding an adverse effect on children's health
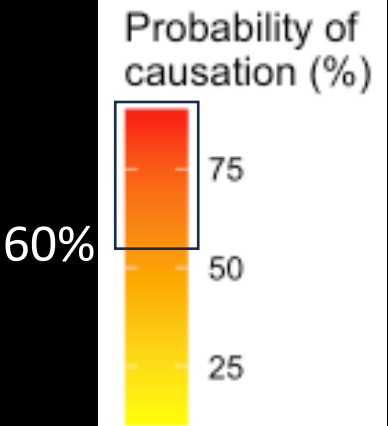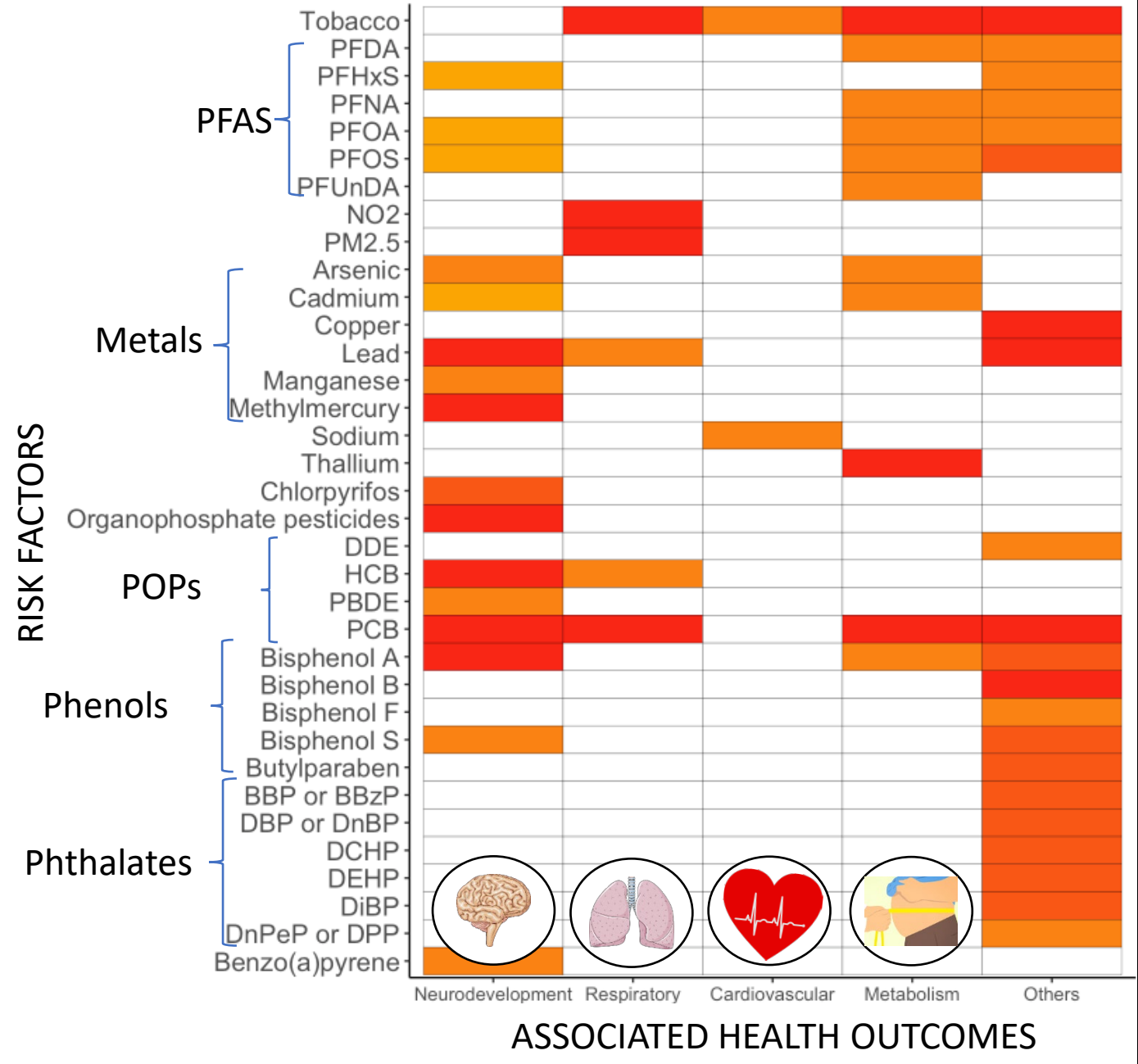
Number of health outcomes associated with each exposure, restricted to *likely* or *very likely* effects
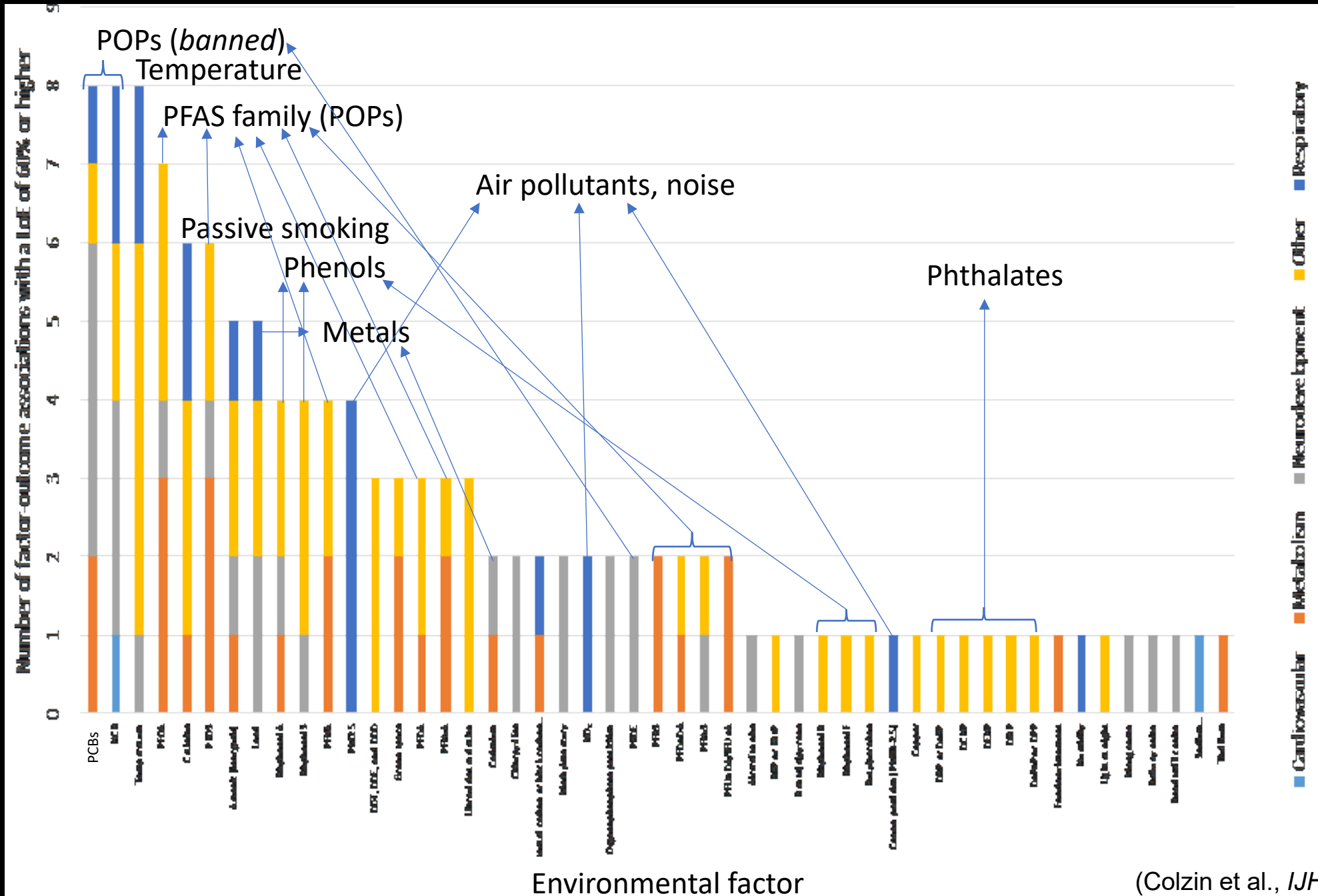
(Colzin et al., *IJHEH*, 2024)

Available exposure-response functions for 50 exposure-outcome pairs

Chemical exposome only

21 exposure-outcome pairs with exposure-response functions from a meta-analysis

29 exposure-outcome pairs with exposure-response function from a single study

28 exposure-outcome pairs with no exposure-response function
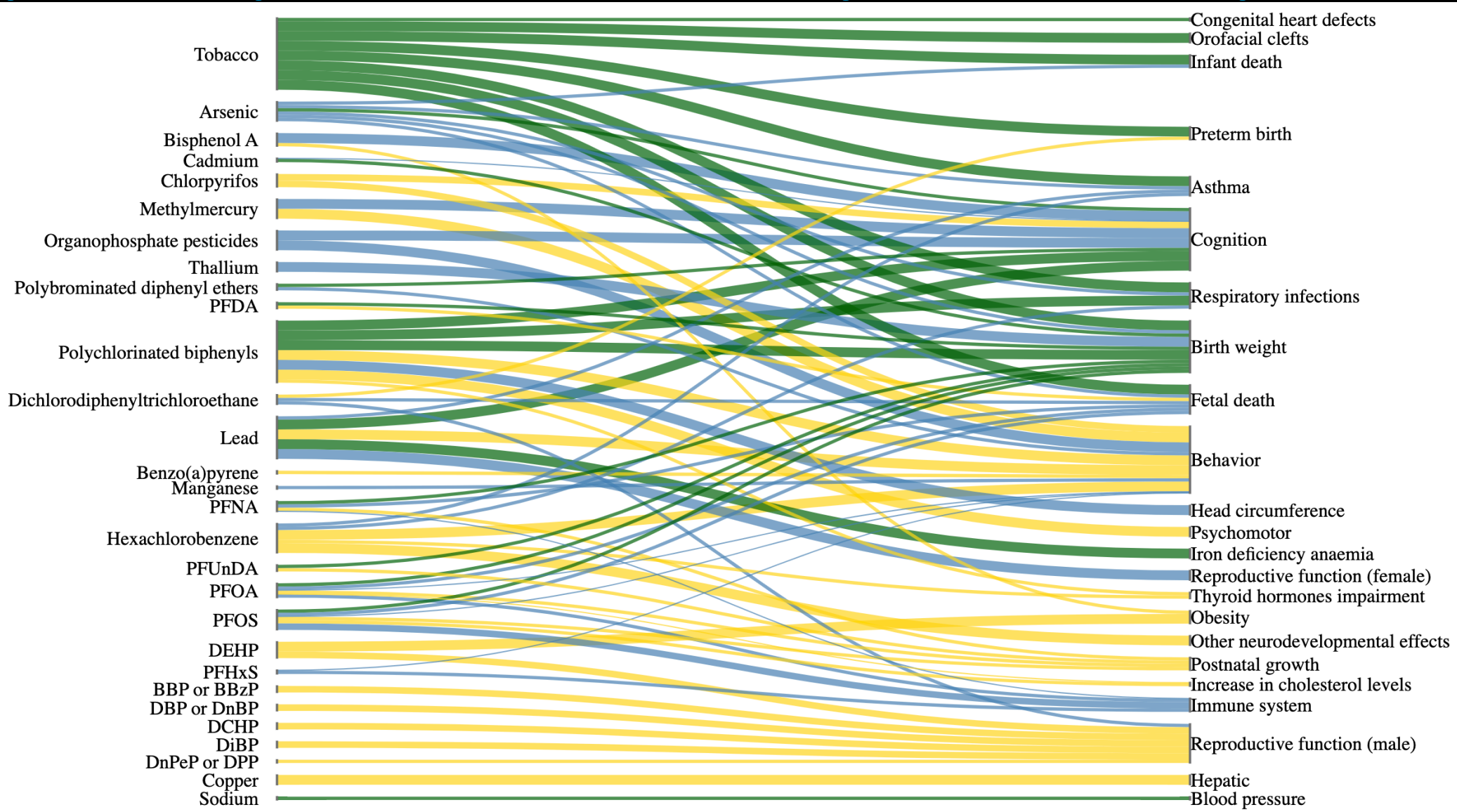
Width of the links reflects the probability of causation.

Overview of exposure-outcome pairs with exposure-response function from meta-analysis, single epidemiological studies, or without dose-response relationship

Rocabois et al. (2024), Environmental Research

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Overview – From science to health protection

- Starting from 88 risk factors, we synthesized the scientific knowledge published worldwide regarding their possible effects on children health, considering human, animal (toxicological) and *in-vitro* evidence

  Other methodologies had been previously proposed to review a large number of environmental health studies - e.g., *Navigation guide methodology* (Woodruff & Sutton, *EHP*, 2014)

- Strong concerns regarding specific risk factors, which can influence several types of children health outcome (neurodevelopment, respiratory and metabolic health…)

  PCBs, HCB, temperature *(8 outcomes)*, PFOA *(7 outcomes)*, PFOS, cotinine *(6 outcomes)*, arsenic, lead *(5 outcomes)*, bisphenols A and S, PFNA and PM$_{2.5}$ *(4 outcomes)*

- Some of these risk factors are strongly regulated (PCBs, PFOA, PFOS via the Stockholm international convention)

- For other factors, regulations and efforts are more limited

  e.g., other PFAS than PFOA and PFOS, temperature, phenols (including parabens)
  although interesting initiatives exist in some areas (e.g., PFAS ban in toys in EU, sectorial PFAS ban in France; new tolerable intake for bisphenol A in the EU…)

- The project also identified risk factors with limited level of evidence, which could be areas for future research

Thank you for your attention

ANSES — agence nationale de sécurité sanitaire alimentation, environnement, travail — Connaître, évaluer, protéger

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