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Organization

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agence nationale de sécurité sanitaire
alimentation, environnement, travail



efsa
EUROPEAN FOOD SAFETY AUTHORITY



Inserm
Institut national
de la santé et de la recherche médicale

UNIVERSITÉ DU
LUXEMBOURG

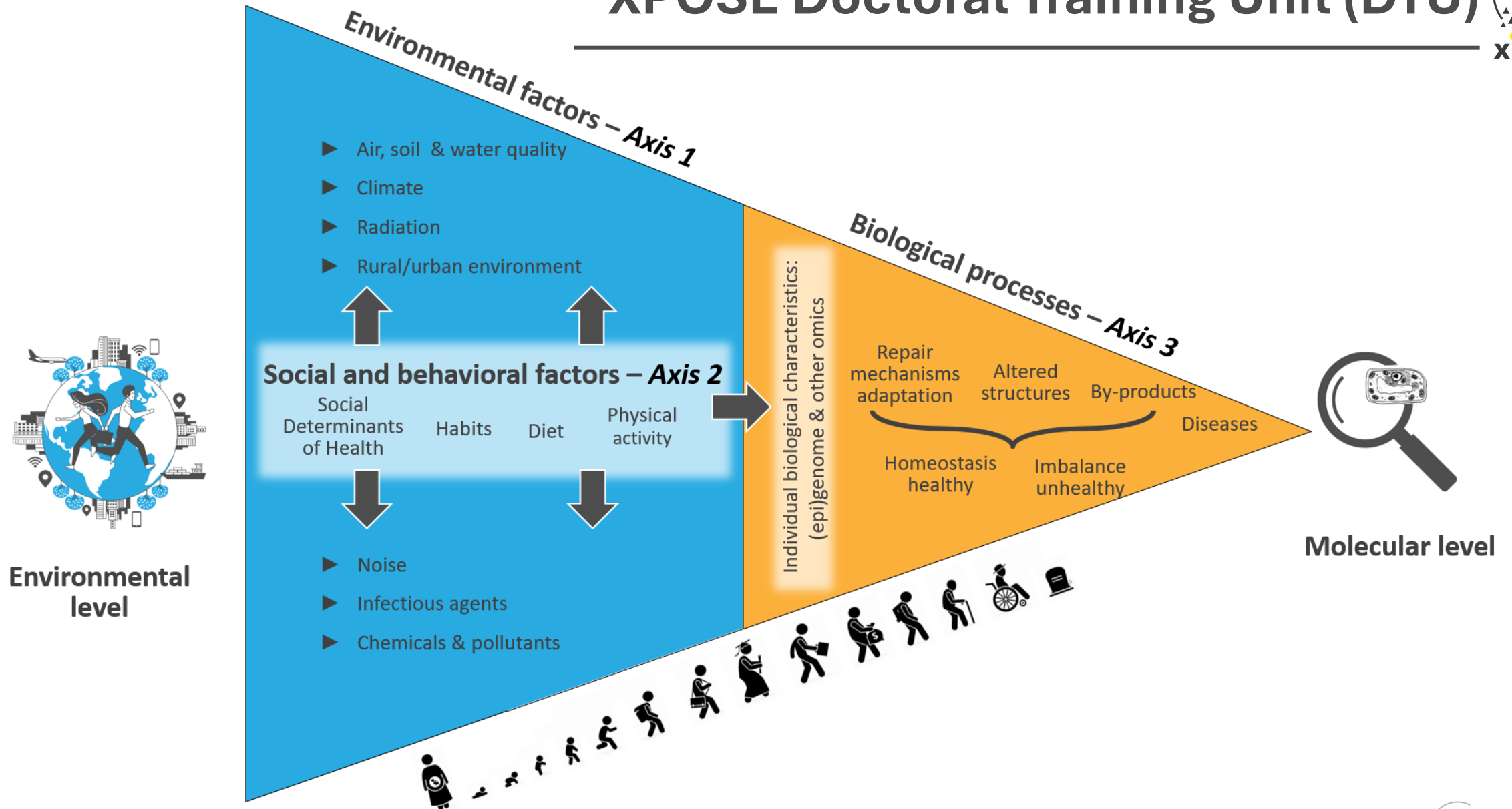


Polychlorinated Biphenyl Exposure and Type 2 Diabetes Risk: A Mediation Analysis of Obesity in the *European Prospective Investigation into Cancer and Nutrition Cohort*



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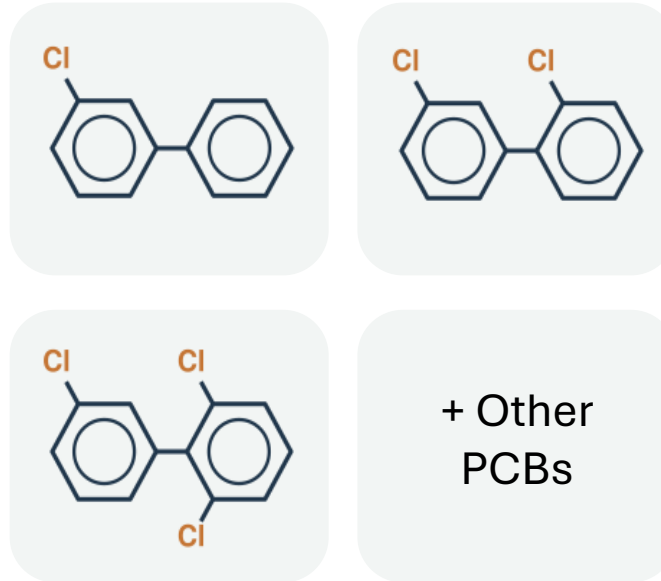
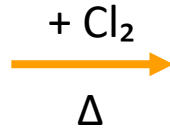


Chlorination creates many PCB congeners



Biphenyls naturally exist in:

- coal tar,
- crude oil,
- and natural gas



* The number and position of chlorine atoms create different congeners

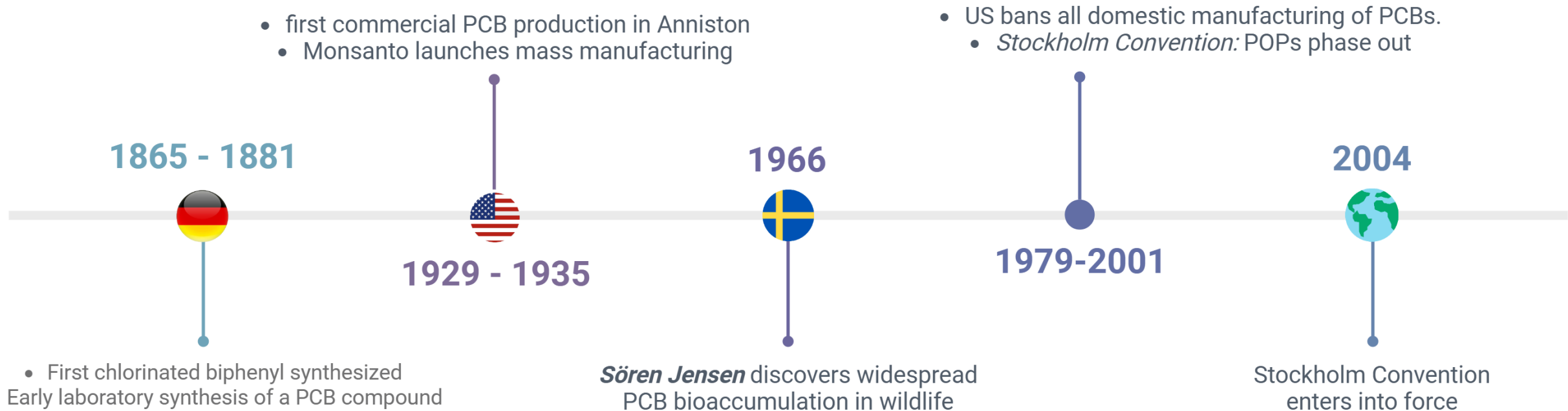
Dioxin-like PCBs

- **12** congeners
- **No ortho (2,2',6,6')** chlorines
- Structure is **coplanar (flat)**
- Acts like dioxins (binds AhR receptor)
- Alter CYP/drug metabolizing enzyme expression
- Associated with immunotoxicity

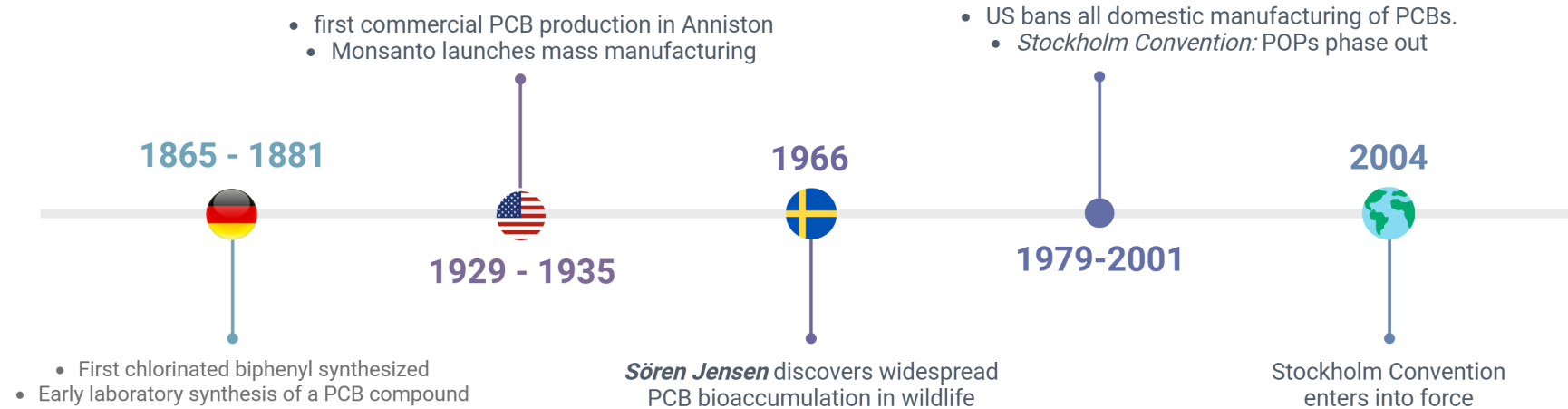
Non-dioxin-like PCBs

- **Contains ortho chlorines (2,2')**
- Structure is **non-coplanar (twisted)**
- Does **not** act like dioxins
- Common in food chain with varying toxicity
- Indicator congeners: 28, 52, 101, 138, 153, 180

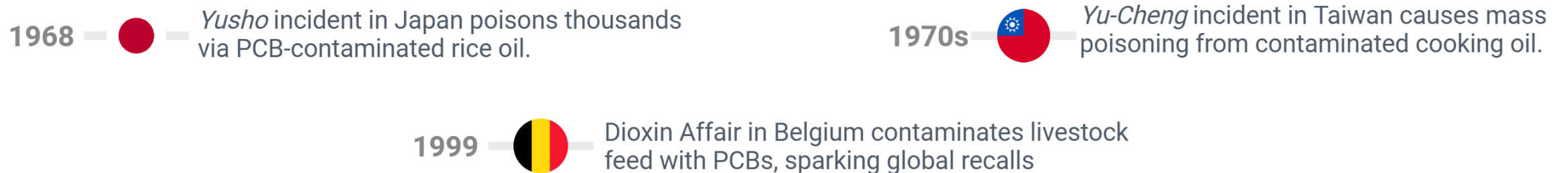
PCB history: production regulation, and exposure



PCB history: production regulation, and exposure



Food contamination revealed the human cost

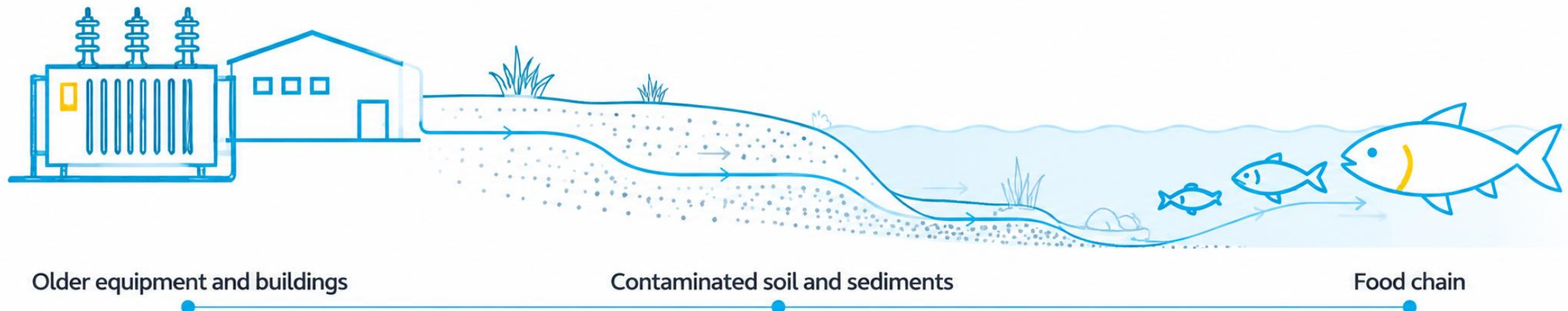


Why were PCBs used in so many products?

PROPERTY		HISTORICAL APPLICATION
Electrical insulation	>	Transformers and capacitors
High boiling point	>	Heat transfer fluids
Low flammability	>	Hydraulic fluids
Plasticizing ability	>	Paints and sealants

*Some of the properties that made PCBs useful also contribute to their persistence after release.

Where can PCBs still be found?



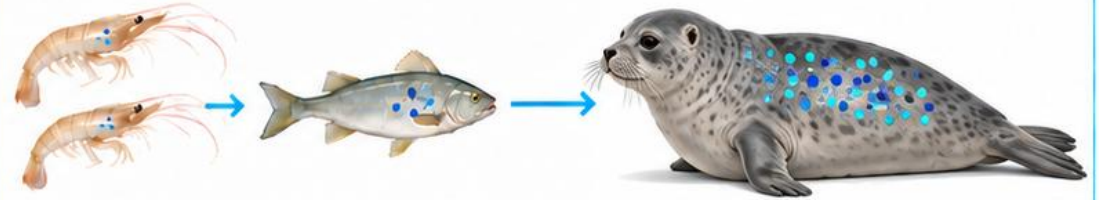
PCBs environmental fate

BIOACCUMULATION



Build-up within one organism over time

BIOMAGNIFICATION



Higher concentrations at successive feeding levels

PCBs environmental degradation half-lives:

- Weeks in the air
- Decades to over 100 years in soil, water, and sediment depending on degree of chlorination

PCBs environmental fate

BIOACCUMULATION



Build-up within one organism over time

BIOMAGNIFICATION



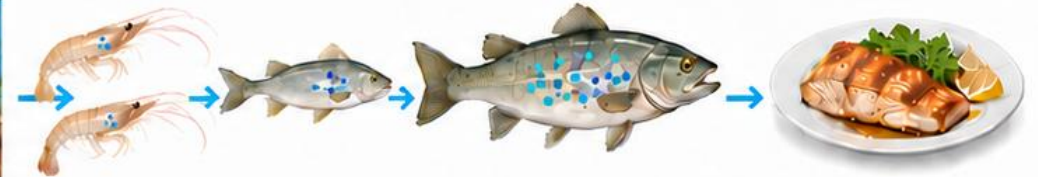
Higher concentrations at successive feeding levels



Legacy sources



Soil and water



Food chain

Main dietary sources of PCBs



Fish and seafood



Meat



Milk and dairy

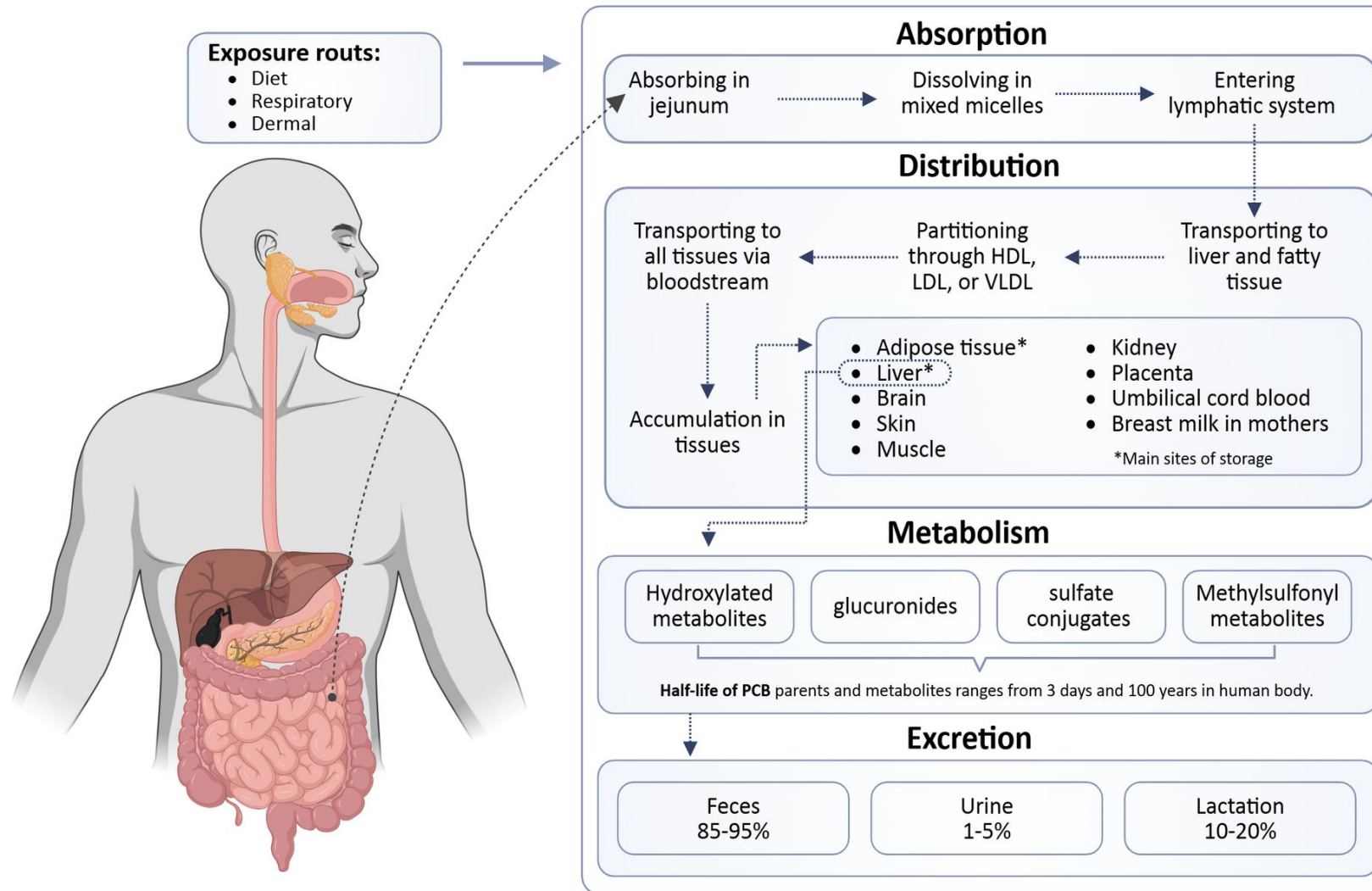


Eggs

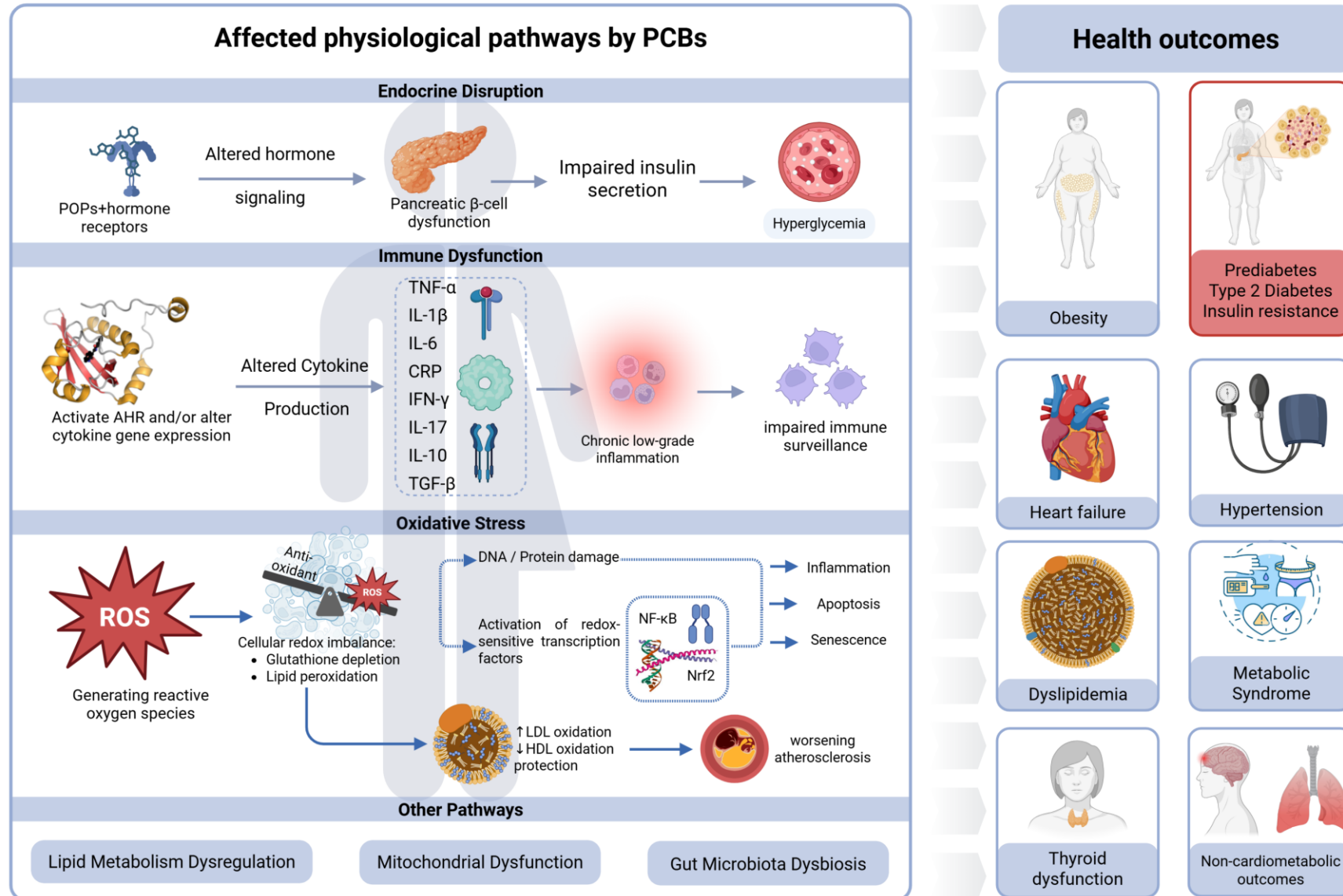
Dietary contribution depends on **PCB levels in food** and **the amount of consumption**

European monitoring programs measure PCB levels in food. EFSA brings these results together with food-consumption data to estimate dietary exposure.

Absorption, distribution, metabolism, excretion of PCBs in human body



Affected physiological pathways related to dietary PCB exposure



Project 5-XPOSE DTU work-packages

WP00 | Review of the topic

What do we know about the role of diet in PCBs and T2D relationship?

Literature synthesis

WP01 | Obesity as a mediator

Does obesity partly explain the PCB-T2D association?

EPIC cohort (using EFSA contamination data)

WP02 | Diet as an effect modifier

Does diet change the strength of this association?

EPIC cohort (using EFSA contamination data)

WP03 | Effect of pollutant mixtures

How is exposure to mixture of pollutants associated with T2D risk?

E3N cohort (ANSES contamination data)

WP04 | Management, Training, and Dissemination

Obesity as a mediator in PCB-T2D relationship - Materials

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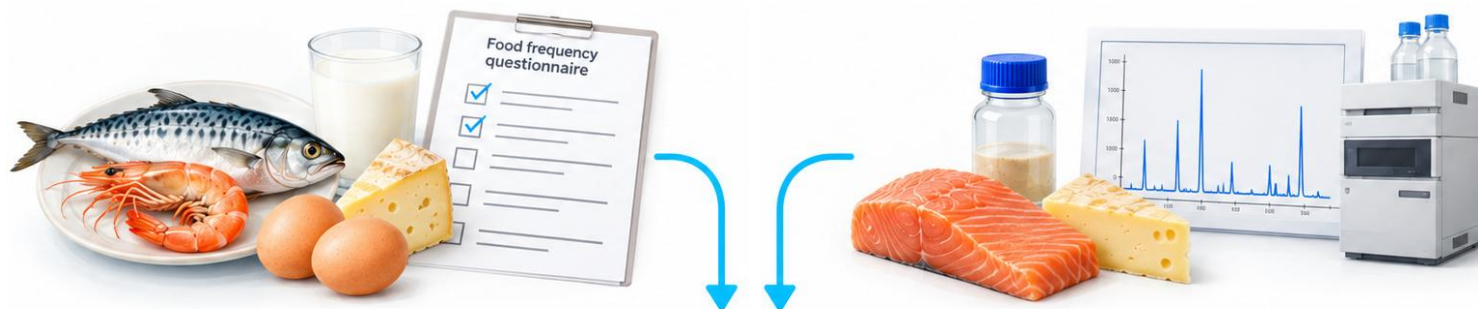
EPIC cohort:

Dietary data from 500.000 participants from 10 European countries



EFSA food contamination data:

Measured contaminants including PCBs in food items



Exposure variables

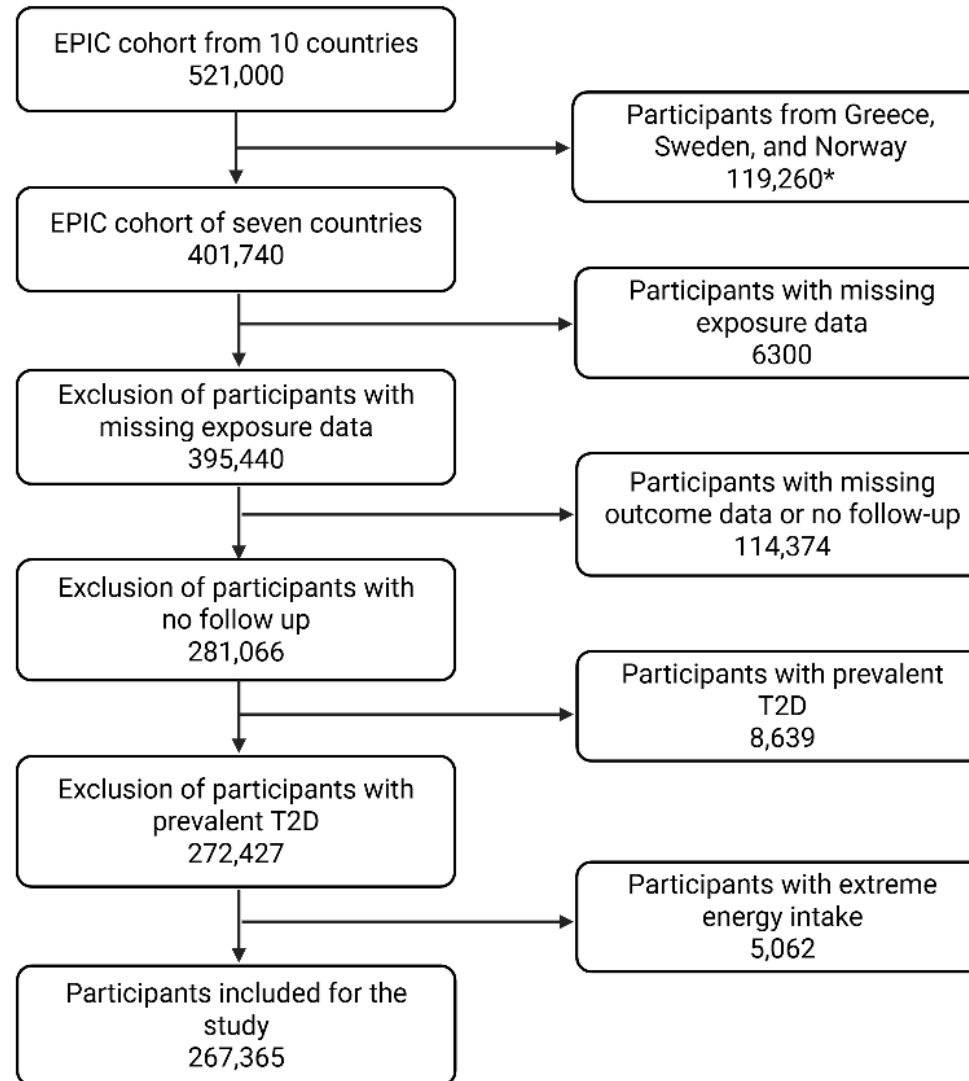
Estimated daily PCB intake (pg/day)

$$= \sum_{\text{foods}} \left[\left(\text{Daily food consumption} \left(\frac{g}{day} \right) \right) \times \left(\text{Median PCB concentration in food} \left(\frac{pg}{day} \right) \right) \right]$$

Other variables in EPIC:

- Age
- Dietary pattern
- Anthropometry measures
- Physical activity
- Smoking
- Blood samples
- Medical history
- Socioeconomic status

Study population

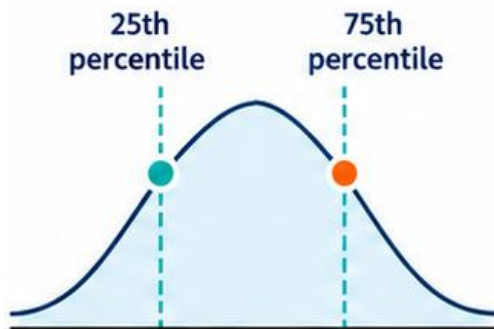


*participants from these countries were excluded from the cohort due to GDPR regulations of the countries

Obesity as a mediator in PCB-T2D relationship – Method

1

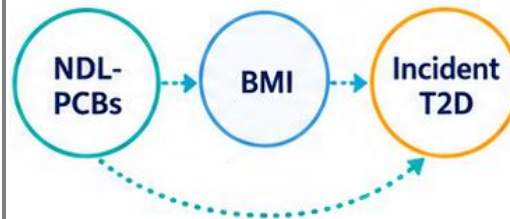
Exposure contrast



NDL-PCBs
(11.45 – 12.7 pg/day)

2

Pathway



Evaluating BMI, WC, WHR, and BSA (markers of obesity) as mediators in PCB-T2D relationship.

3

Adjustments



Age, sex, center, and other relevant confounders

4

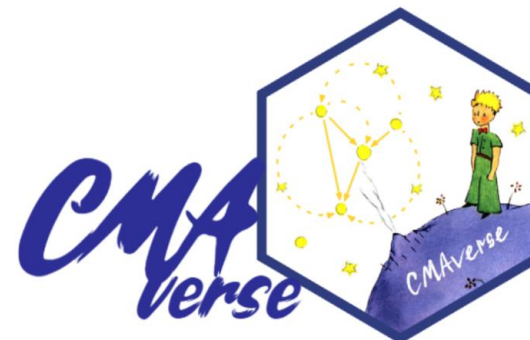
Estimations

Total effect

Direct effect

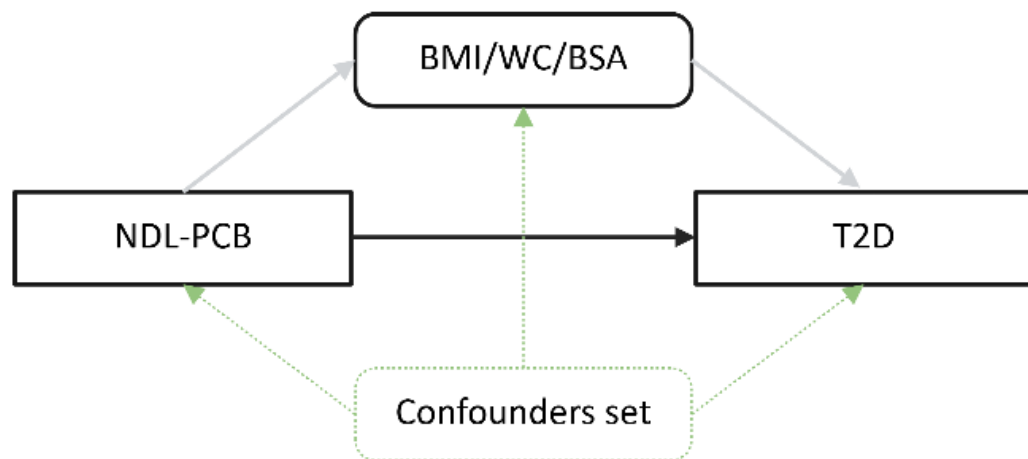
Indirect effect

With 95% confidence intervals and 1000 bootstraps

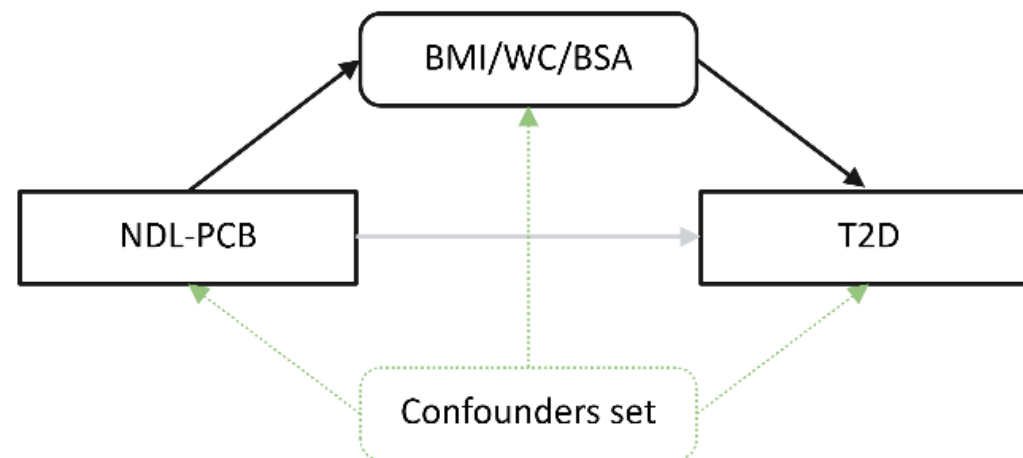


Mediation literature

Natural direct effect (NDE)

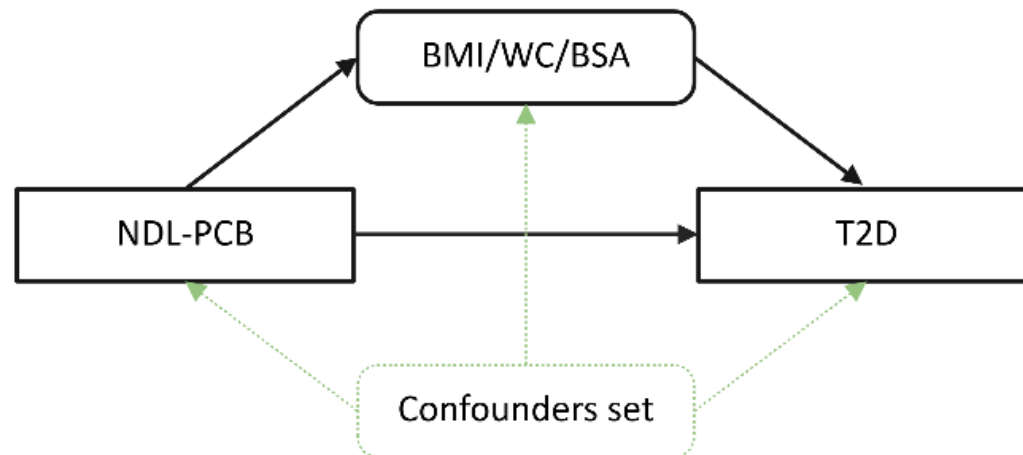


Natural indirect effect (NIDE)



Total effect (TE)

* No adjustment for mediator



Take home message

01 |

PCBs; banned from use. Still in the food chain. Still a health question.

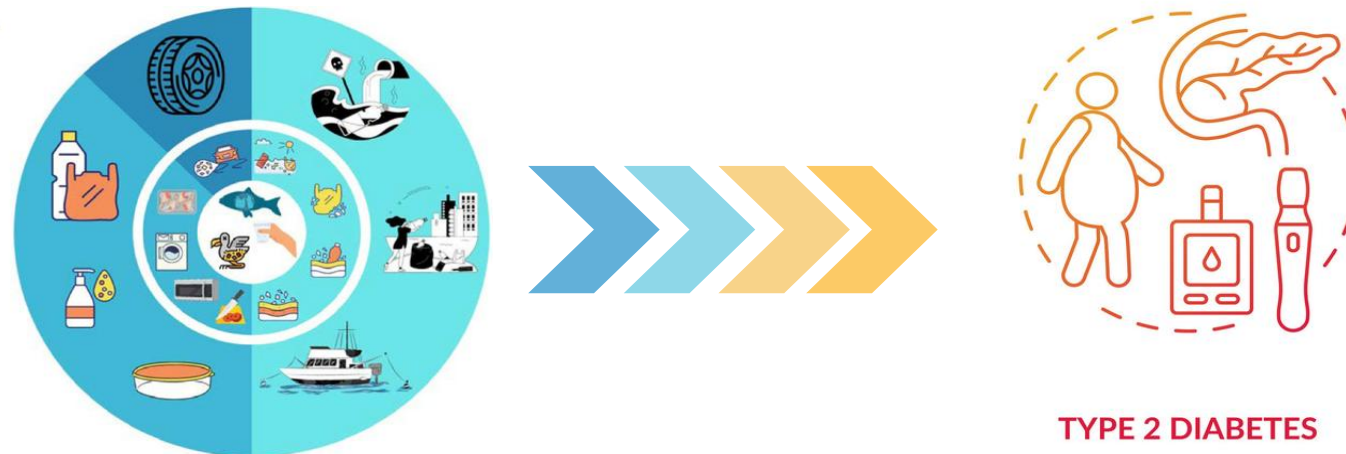
02 |

Higher estimated dietary PCBs exposure was associated with higher BMI and greater T2D risk.

03 |

Obesity markers account for part of the observed PCB–T2D association. Other pathways may also be involved.

* The observed associations warrant further study; they do not establish that PCBs cause T2D.





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THANK YOU

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