

MERCURY EXPOSURE IN PRENATAL LIFE AND NEURODEVELOPMENT: FINDINGS FROM THE NORTHERN ADRIATIC BIRTH COHORT STUDY

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The Mediterranean study

Micro-nutrients



Exposure

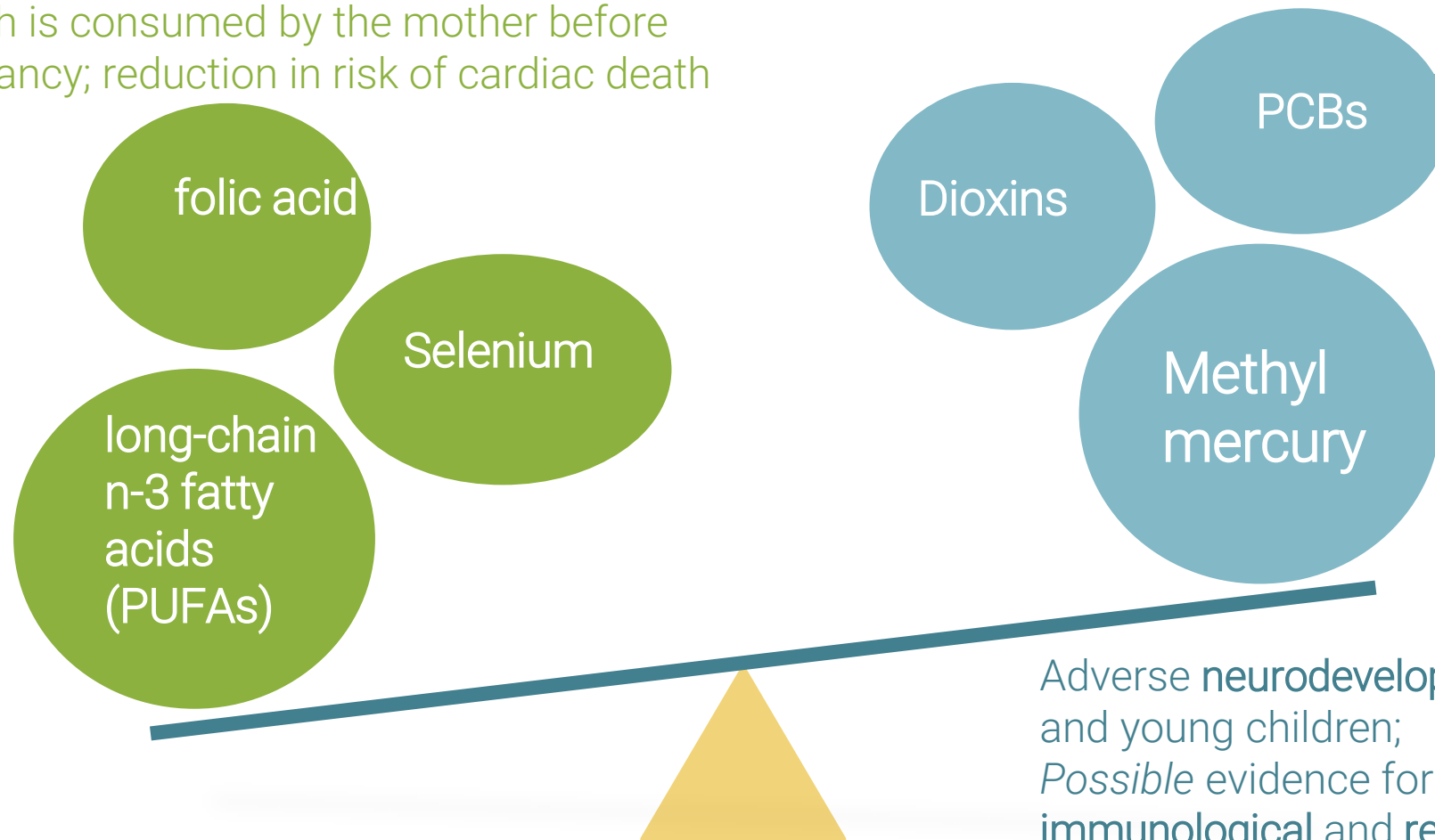
Health outcome

Goal: to assess whether there is a link between exposure to **low levels of mercury** (mainly through fish consumption) and neurodevelopment of prenatally exposed children



...fish also a healthy source of dietary proteins and nutrients

Improved neurodevelopment in infants and young children when fish is consumed by the mother before and during pregnancy; reduction in risk of cardiac death (PUFA!)

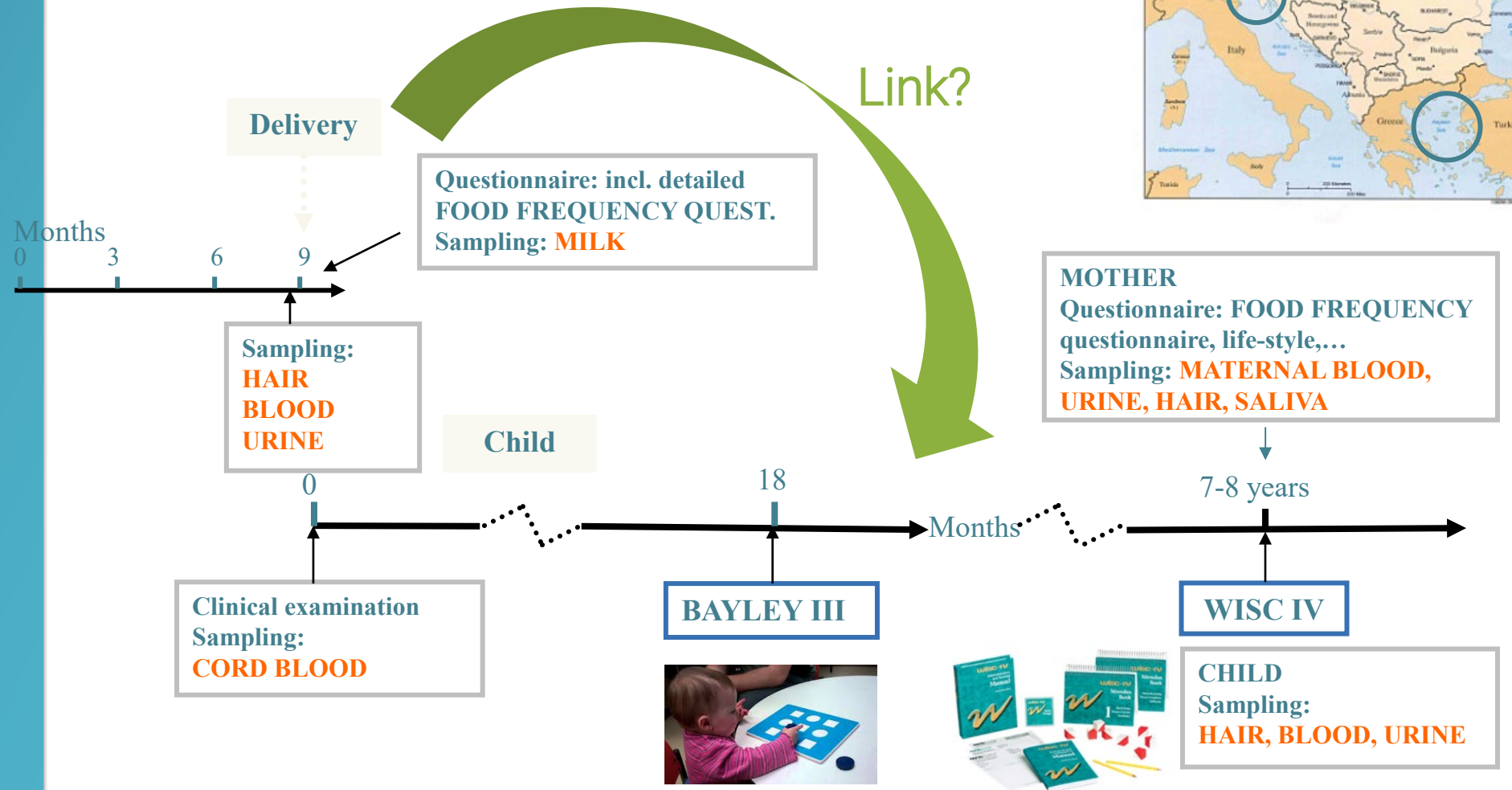


Adverse neurodevelopmental outcomes in infants and young children;
Possible evidence for cardiovascular, immunological and reproductive effects

The Mediterranean study

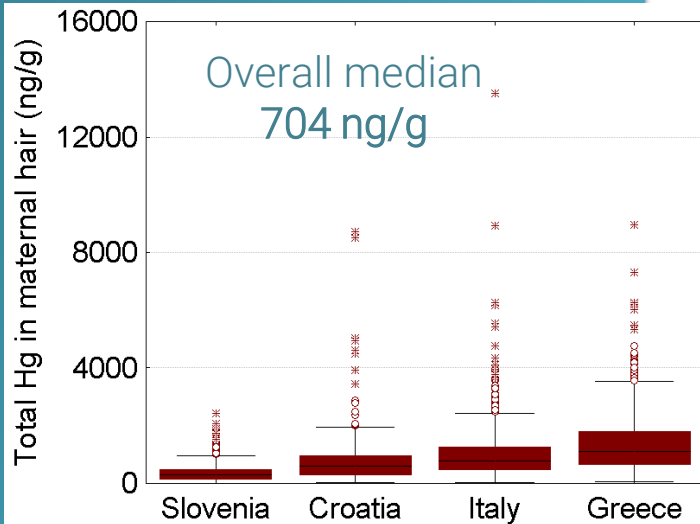
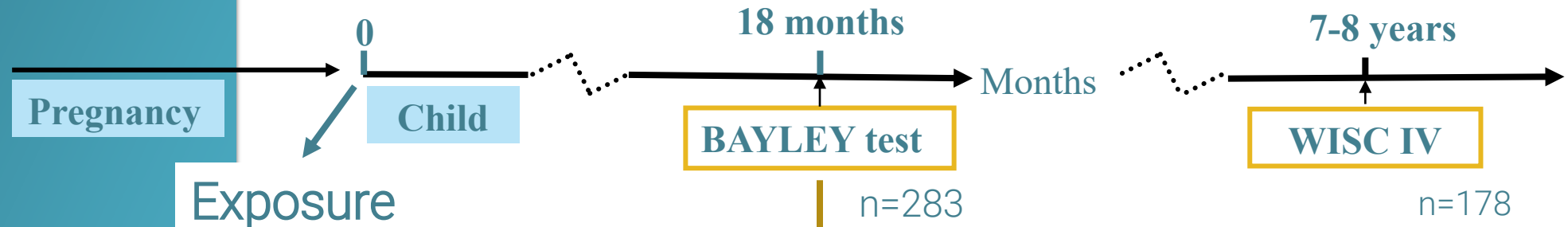
Study was designed in order to find out whether exposure to Hg in prenatal life can affect cognitive, language and motor abilities later in childhood...

...and whether the effects can be compensated by beneficial elements (selenium) or other factors.



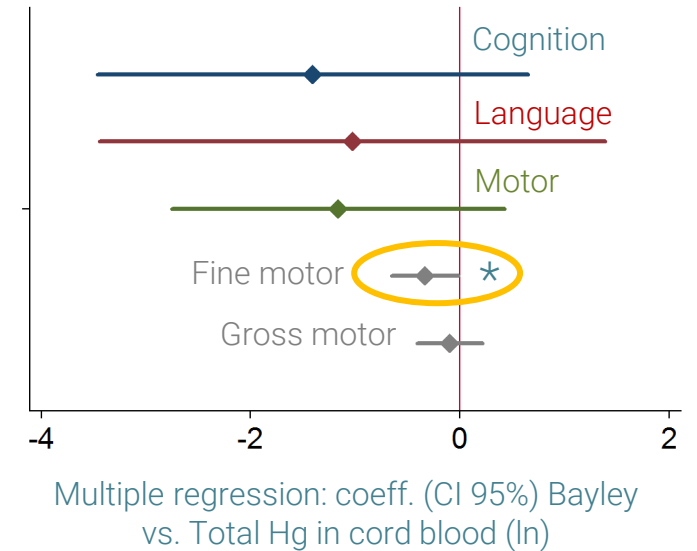
Previous findings

The overall results at 18 months



No evidence of detrimental effects of total Hg was found for cognitive and language outcomes at these concentrations and age

Slovenian and Croatian cohorts: lower **fine motor score** with increasing total Hg concentrations in cord blood

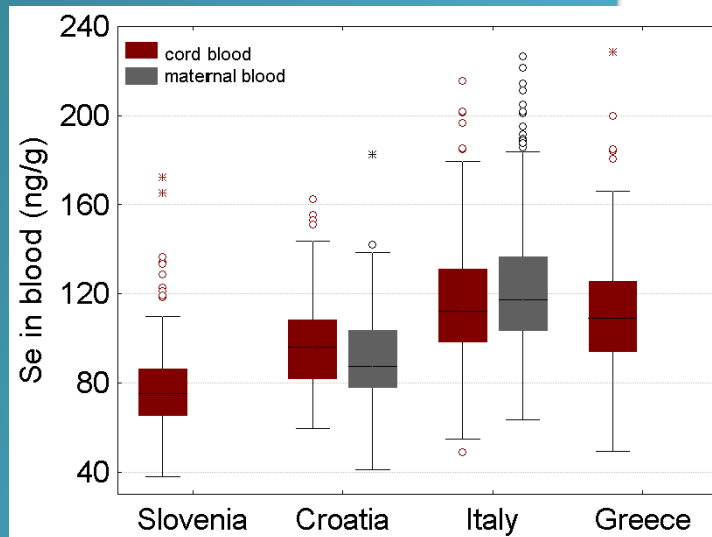
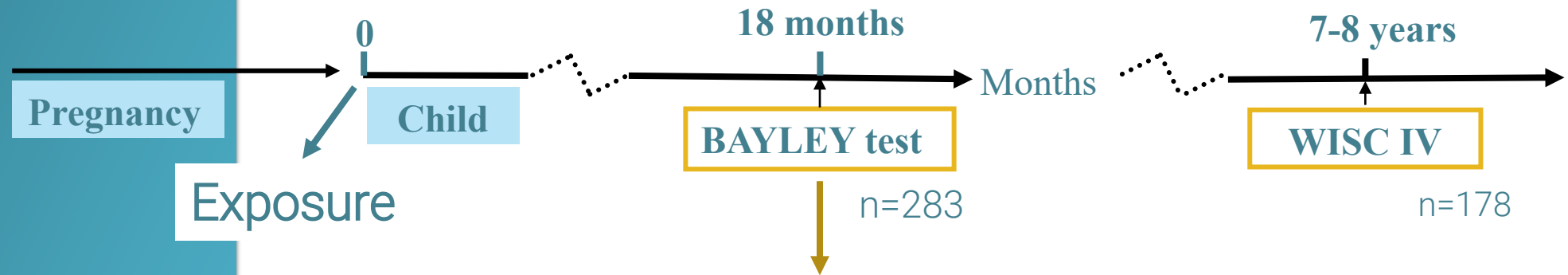


Barbone et al., *International Journal of Hygiene and Environmental Health* 222 (2019), 9-21

Snoj Tratnik et al., *Environmental Research* 152 (2017) 375-385

Previous findings

The overall results at 18 months



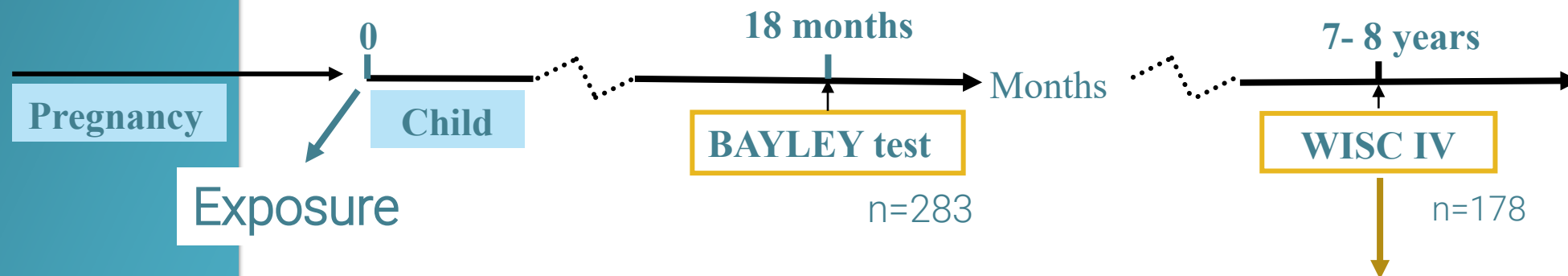
Regression models revealed a positive association between serum selenium levels and language composite score

Coeff. = 7.6 (p = 0.094)

Barbone et al., *International Journal of Hygiene and Environmental Health* 222 (2019), 9-21

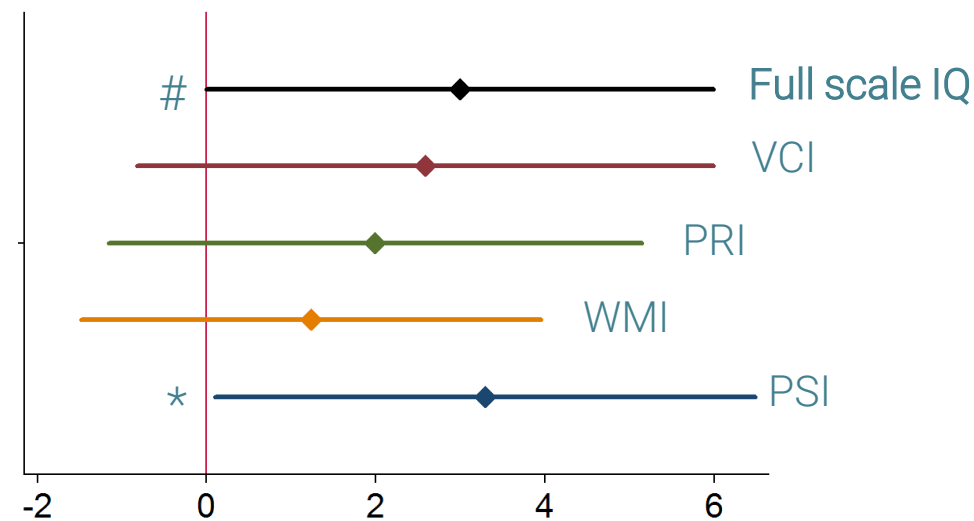
Snoj Tratnik et al., *Environmental Research* 152 (2017) 375–385

Results: Follow-up at 7-8 years of age



Re-evaluation later in the childhood showed **positive association** between Hg in cord blood and **cognitive development!**

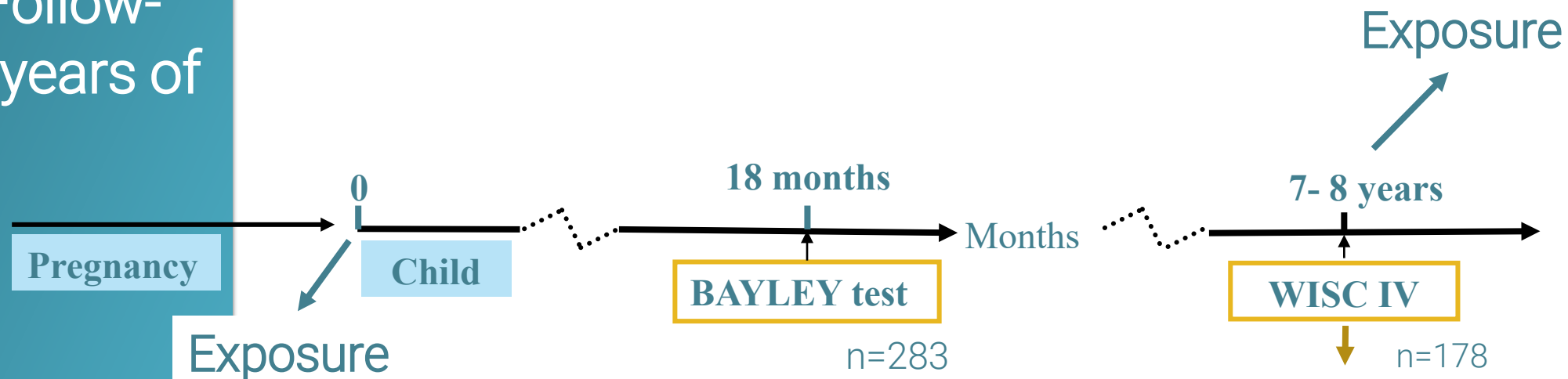
→ Confirmation of **beneficial effect** of fish consumption in pregnancy



Multiple regression: Coeff. (CI 95%) WISC vs. total Hg in cord blood (ln)

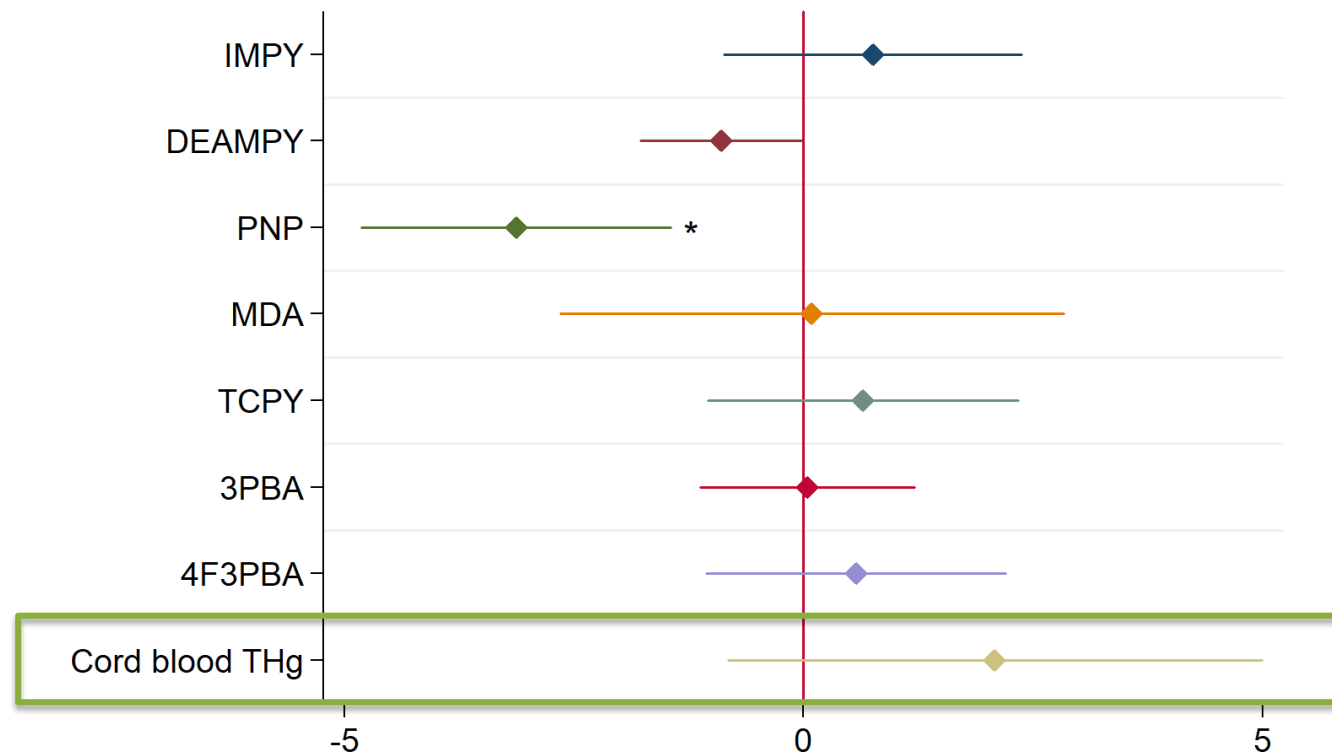
VCI=Verbal Comprehension Index
 PRI=Perceptual Reasoning Index
 WMI=Working Memory Index
 PSI=Processing Speed Index
 FSIQ=Full Scale Intelligence Quotient

Results: Follow-up at 7-8 years of age



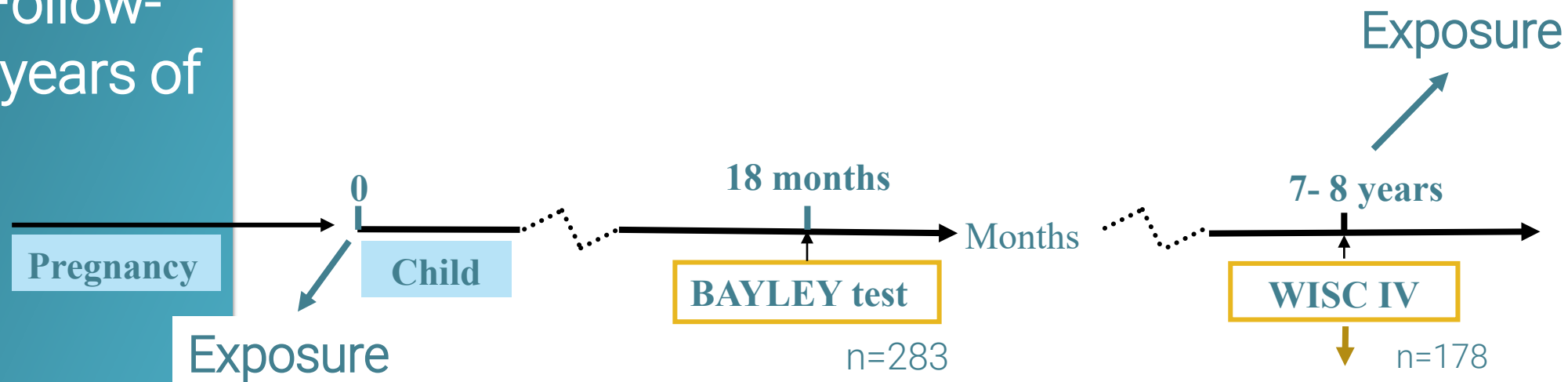
Metabolite	pesticide
PNP	Parathion
TCPY	Chlorpyriphos
DEAMPY	Pirimiphos
IMPY	Diazinon
MDA	Malathion
3-PBA	Common pyrethroids
4-F-3-PBA	cyfluthrin

*CMHC (representing coumaphos) below LOD in all subjects.



Multiple regression: Coeff. (CI 95%) FSIQ vs. urine pesticide/CB Hg levels (ln)

Results: Follow-up at 7-8 years of age



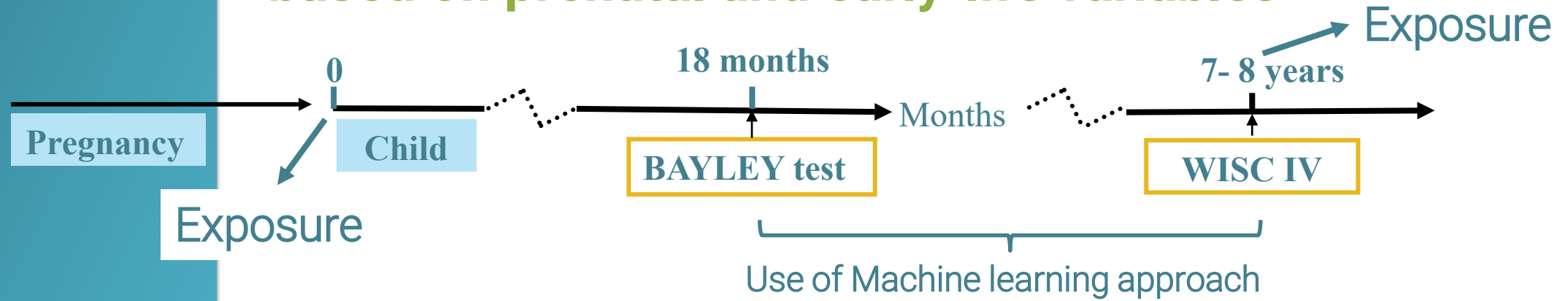
WISC score (FSIQ) $R^2 = 0.14, p < 0.001$	Coef. (95% CI)	P>t
PNP in urine (ln)	-1.85 (-3.81; 0.10)	0.063
Pb in blood (ln)	4.98 (-1.49; 11.5)	0.130
Cu in blood (ln)	-26.7 (-45.0; -8.39)	0.005
Se in blood (ln)	14.6 (-1.69; 30.9)	0.079
THg in cord blood (ln)	3.24 (0.39; 6.09)	0.026

WISC score (FSIQ) $R^2 = 0.30, p < 0.001$	Coef. (95% CI)	P>t
PNP in urine (ln)	-3.13 (-4.83; -1.43)	<0.001
Pb in blood (ln)	4.05 (-1.70; 9.79)	0.166
Cu in blood (ln)	-26.7 (-41.9; -11.5)	0.001
Se in blood (ln)	20.7 (6.30; 35.1)	0.005
Father's years of schooling	1.05 (0.35; 1.75)	0.004
Language classes (no vs. yes)	4.61 (1.14; 8.10)	0.010
Watching TV during weekdays (h)	-3.02 (-5.63; 0.42)	0.023
Child's sex	-4.03 (-8.17; 0.10)	0.056
Frequency of seafood consumption	2.19 (0.37; 4.01)	0.019

PNP – metabolite of pesticide parathion

Machine learning approach

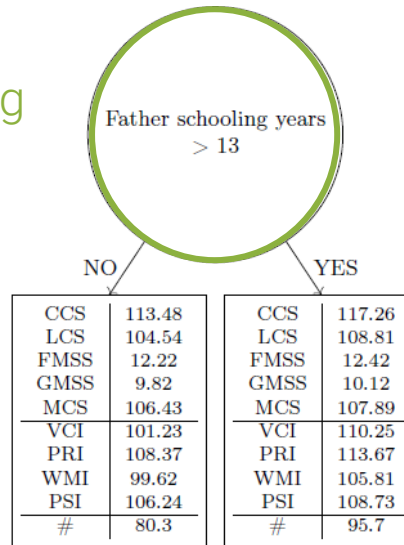
Prediction of Bayley III and WISC IV scores based on prenatal and early-life variables



Socio-economic and nutritional attributes seem to be among the main factors driving neurodevelopmental response at low levels of environmental exposure.

Multi-target Predictive Clustering Tree:

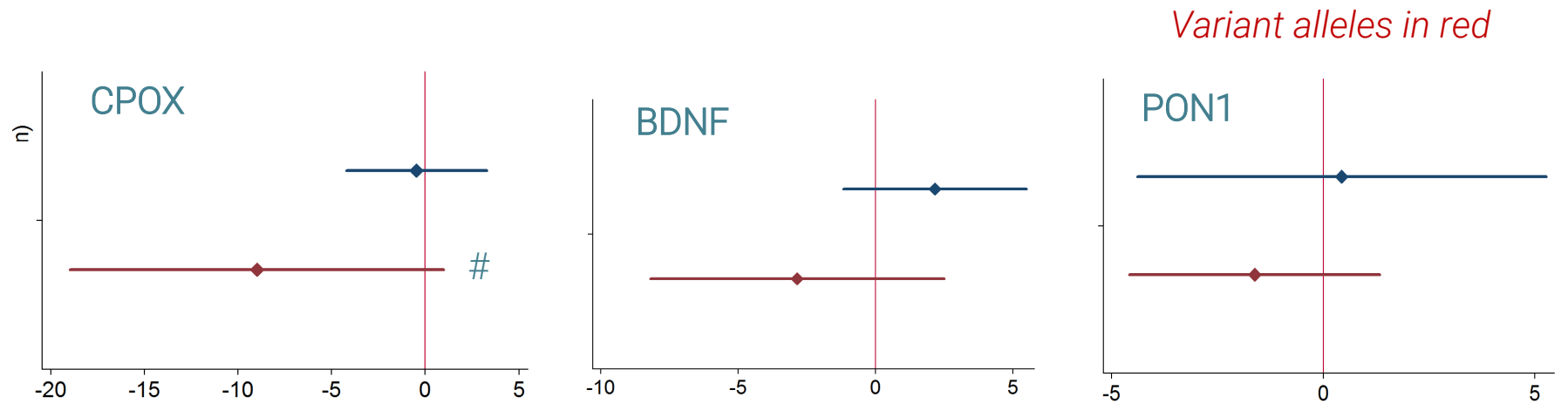
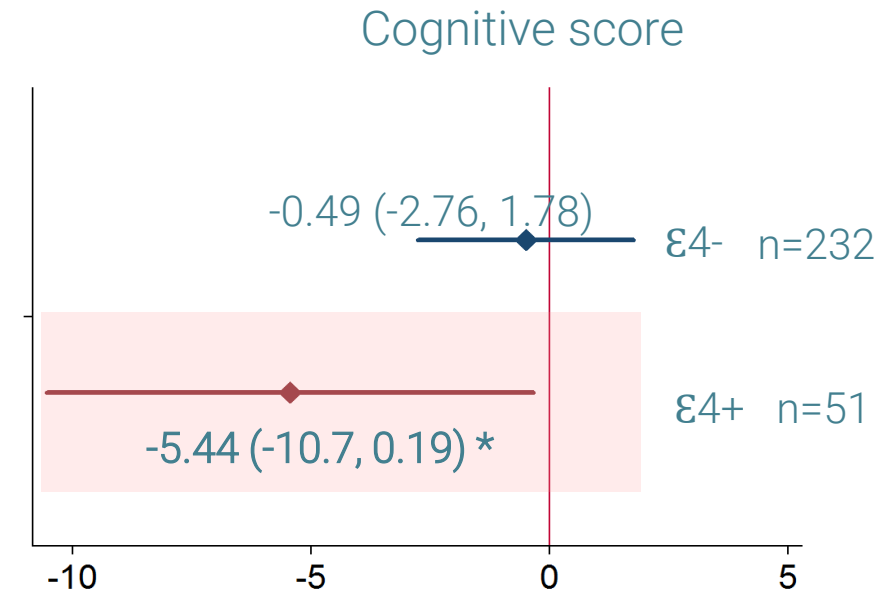
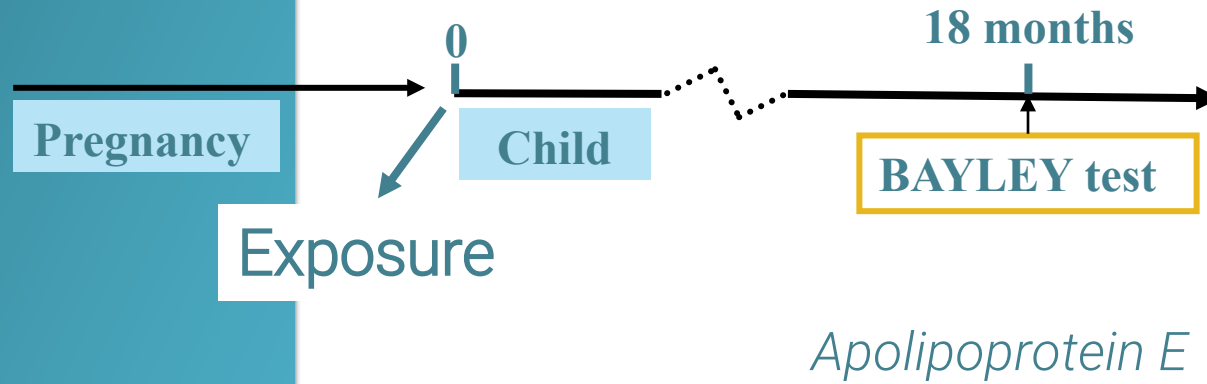
CCL=Cognitive Composite Score
 LCS=Language Composite Score
 FMSS=Fine Motor Scaled Score
 GMSS=Gross Motor Scaled Score
 MCS=Motor Composite Score
 VCI=Verbal Comprehension Index
 PRI=Perceptual Reasoning Index
 WMI=Working Memory Index
 PSI=Processing Speed Index



Feature ranking:

Rank	Attribute	Importance score
1	mother_bmi_gaindelivery	208.07
2	yearsschooling_father	193.81
3	milk_skim_pregn	186.88
4	M_Se	172.90
5	mother_bmi_before	171.70
6	mother_bmi_delivery	152.47
7	CB_Pb	150.64
8	H_THg	150.49
9	father_bmi_birth	150.13
10	birthlength	144.93
...
519	anemia_pregnancy	0
520	apricote_noskin_pregn	0
521	breastfeeding1	0

Genetic susceptibility



Multiple regression: Coeff. (CI 95%) Cognitive performance vs. Hg in cord blood (ln)

What did we learn from one of the largest epidemiological studies in Europe



- No evidence of adverse neurodevelopmental effects due to prenatal exposure to low-to-moderate levels of **mercury** for the majority of the study cohort
- Beneficial effect of **selenium**
- Confounding for relevant factors important at such levels of exposure (co-exposure to **other neurotoxic substances, nutrients, socio-economic factors,...**)
- Stratification of statistical models based on **genotypes** enables identification of more susceptible or more resilient individuals

Thank you!

Acknowledgements



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