FAMILY

Running in the FAMILY – Understanding and predicting the intergenerational transmission of mental illness

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COPSYCH – 10 year follow up

Open access Protocol

BMJ Open

Effects of prenatal nutrient supplementation and early life exposures on neurodevelopment at age 10: a randomised controlled trial - the COPSYCH study protocol

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BMJ

Mohammadzadeh P, *et al*. *BMJ Open* 2022;**12**:e047706. doi:10.1136/bmjopen-2020-047706

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The COPSYCH research alliance

COPSAC

COPENHAGEN PROSPECTIVE STUDIES ON ASTHMA IN CHILDHOOD

Prof **Klaus Bønnelykke**

CNSR

Centre for **N**europsychiatric **S**chizophrenia **R**esearch, **CNSR**

Prof **Bjørn H Ebdrup**

FUNCTIONAL IMAGING UNIT

https://copsac.com/home/research-clusters/copsych/

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Team COPSYCH

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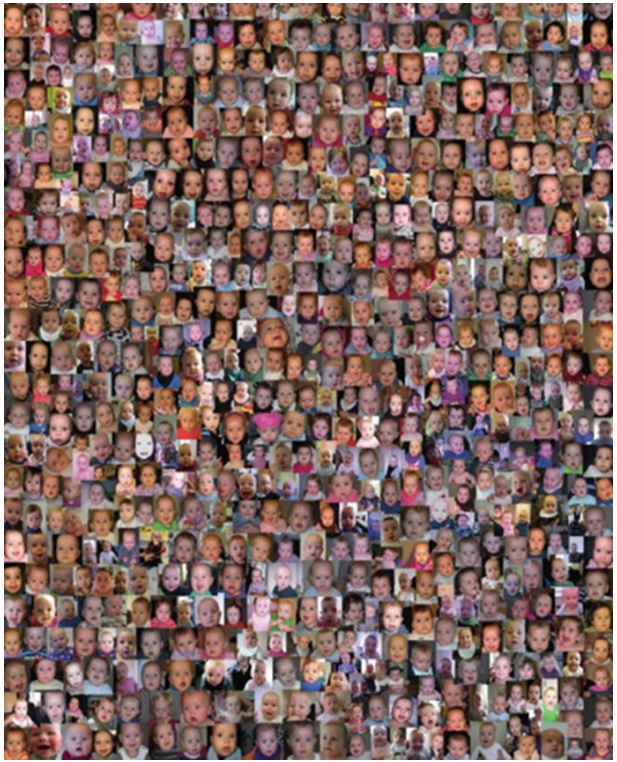
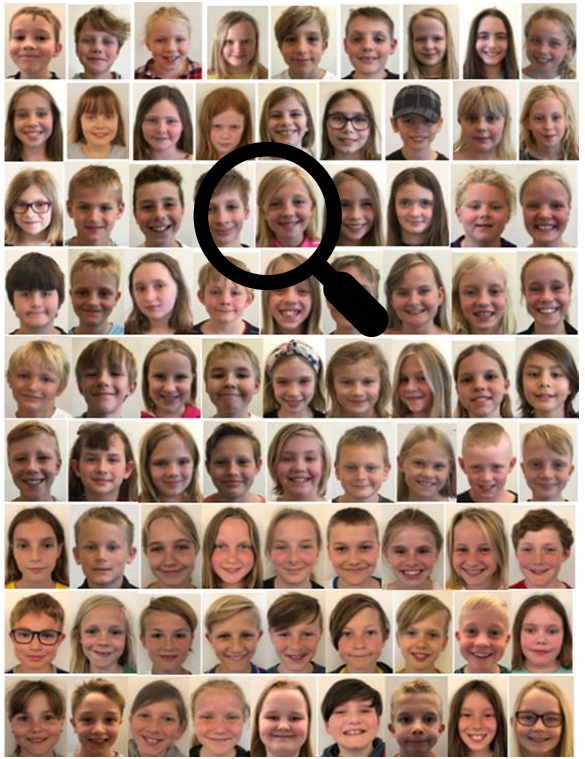
The COPSAC2010 cohort





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COPSAC$_{2010}$ - RCT

- Supplement during pregnancy from pregnancy week 24:
  - N-3 LCPUFA (fishoil), 2.4g/dag (55% EPA and 37% DHA) vs oliveoil
  - Vitamin D (2,400 IU/dag ~ 60 mikrogram/dag) vs placebo

Group 1	Group 2	Group 3	Group 4
Vitamin D	Vitamin D	Placebo	Placebo
Fishoil~LPUFA	Placebo	Fishoil~LPUFA	Placebo

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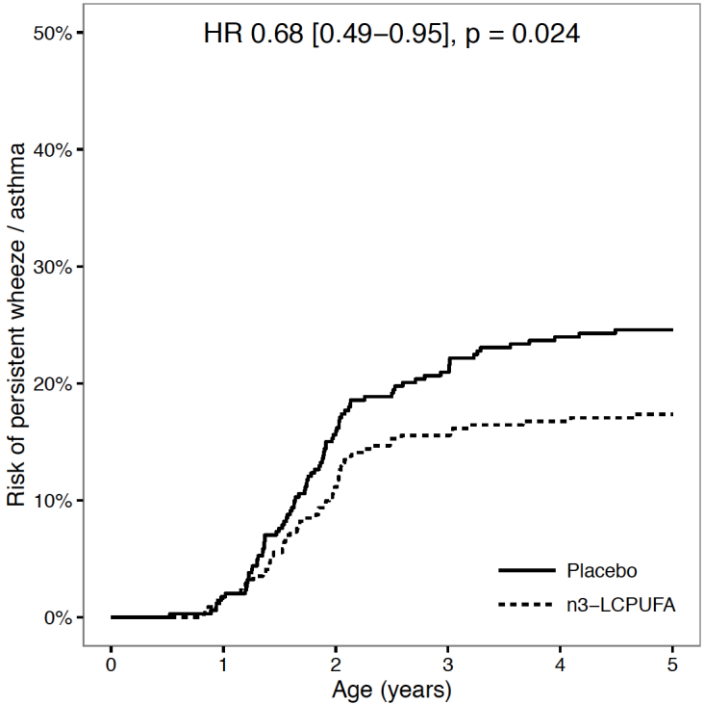
Primary endpoint:
Development of persistent wheeze/asthma



- Fish oil supplementation: 2,4 g/day
- Unchanged after adjustment for gender, vitamin-D supplementation and women's blood level of EPA+DHA

December 29, 2016
N Engl J Med 2016; 375:2530-2539
DOI: 10.1056/NEJMoa1503734

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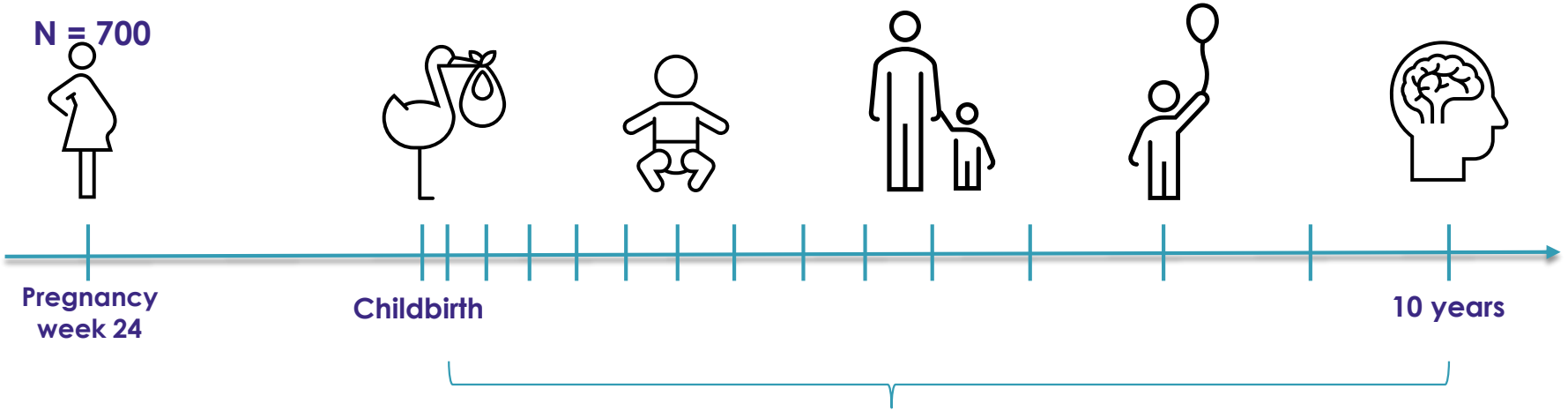

Deep phenotyping through regular clinical visits

COPSYCH

Psychopathology

Clinical diagnoses and clinically evaluated traits of ASD and ADHD

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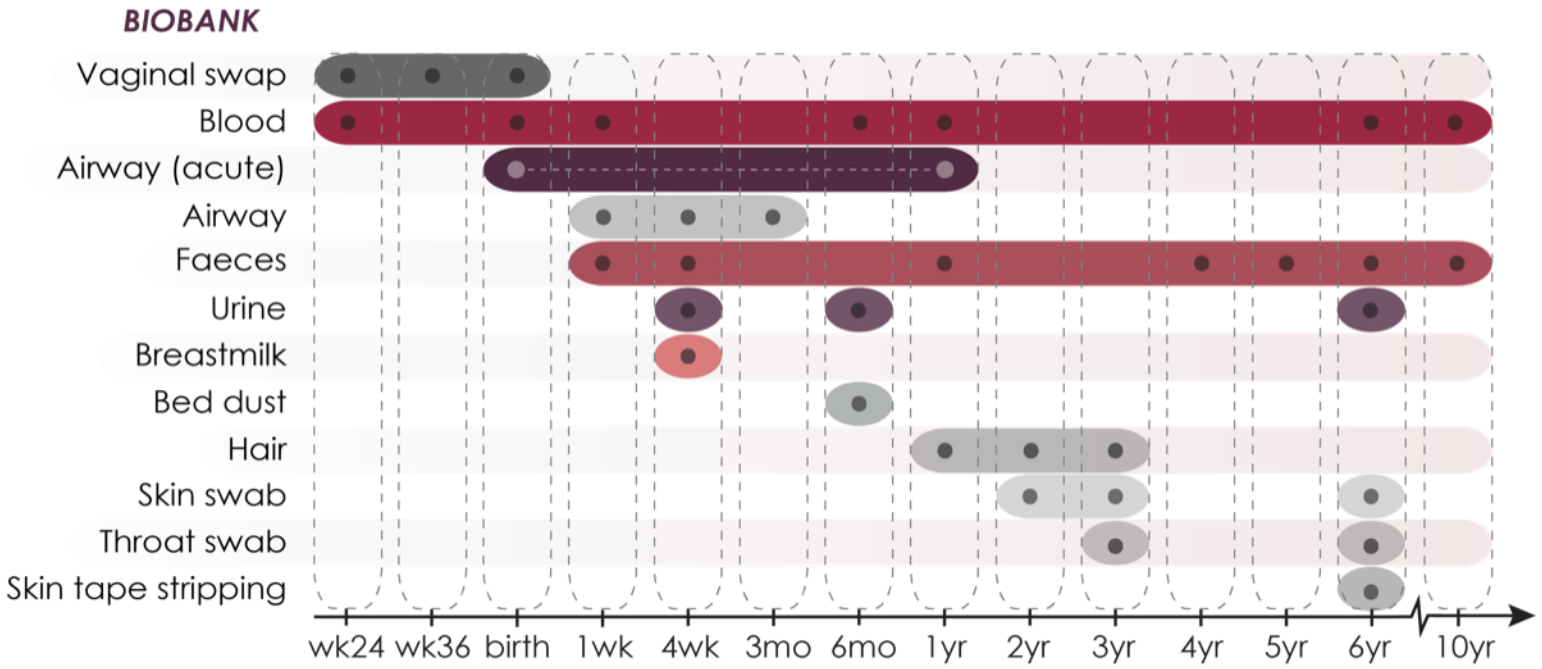
Biobank

1



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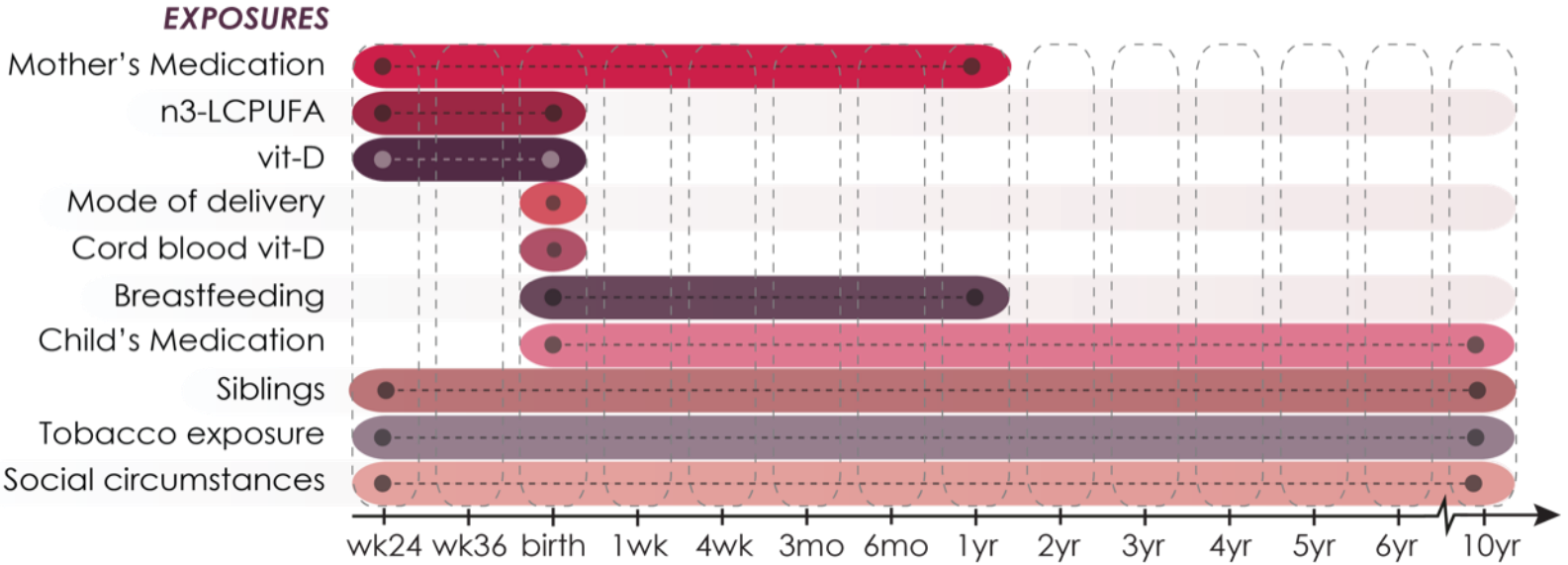
Environmental exposures

2



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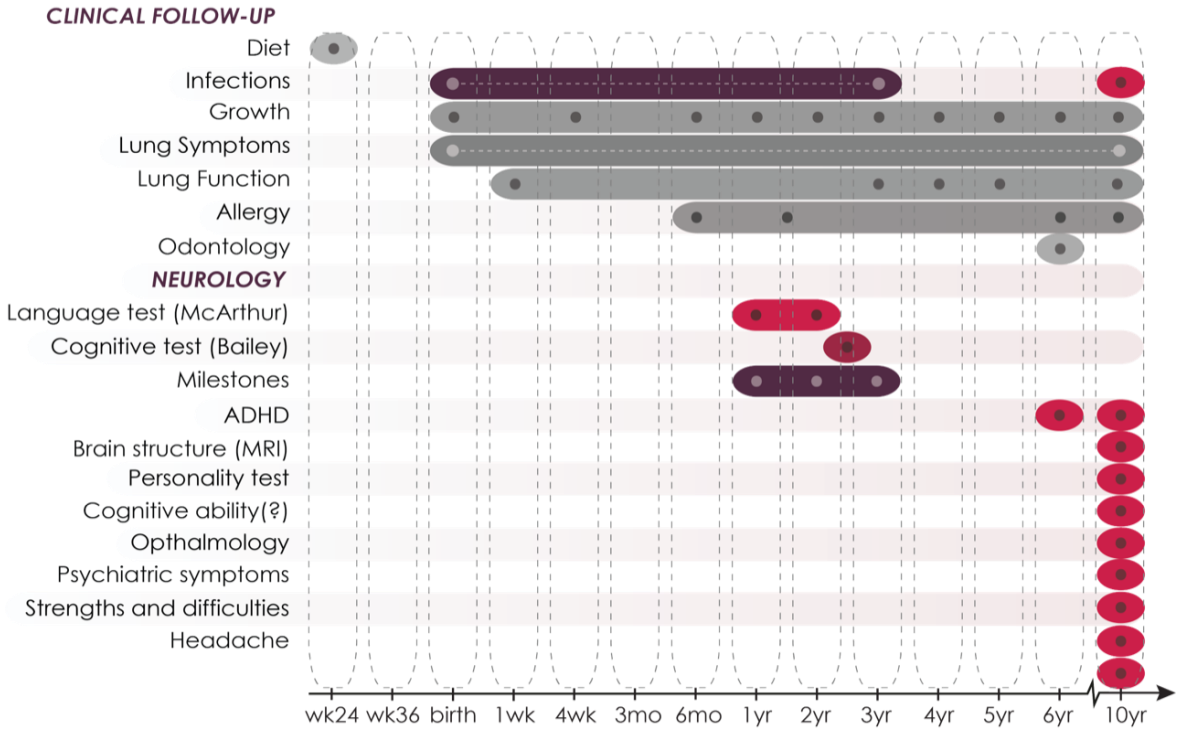
Clinical follow-up

3



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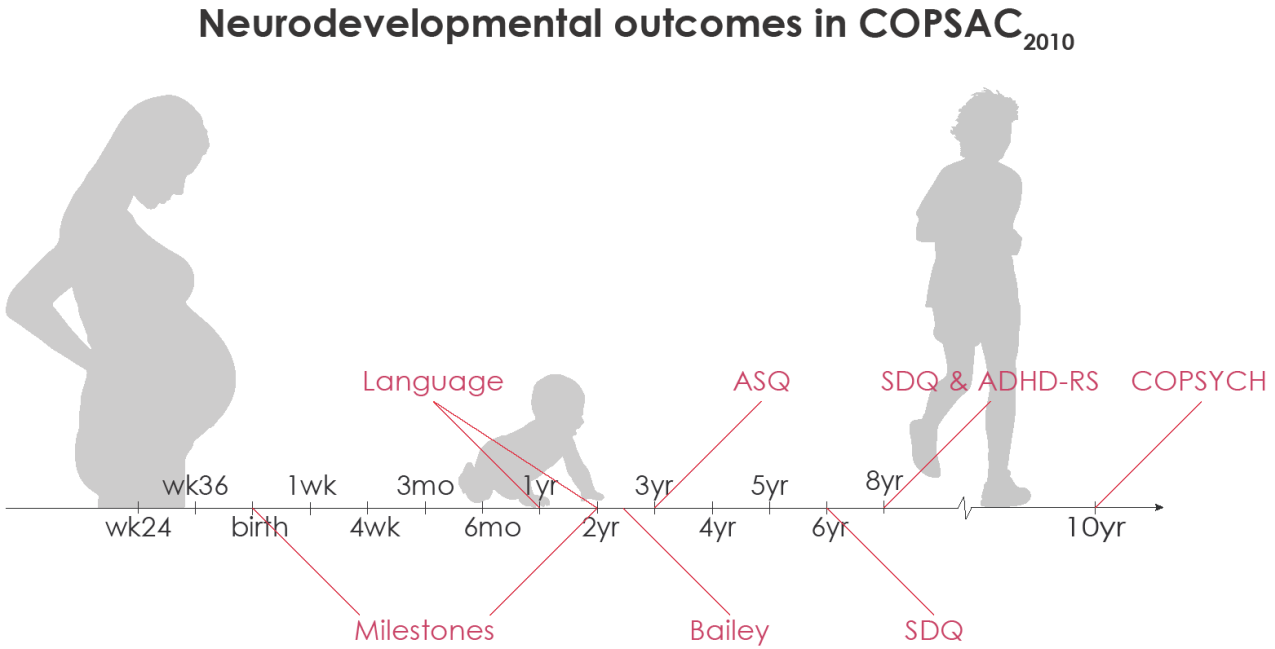
Neurodevelopmental outcomes



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Previous neurodevelopmental findings

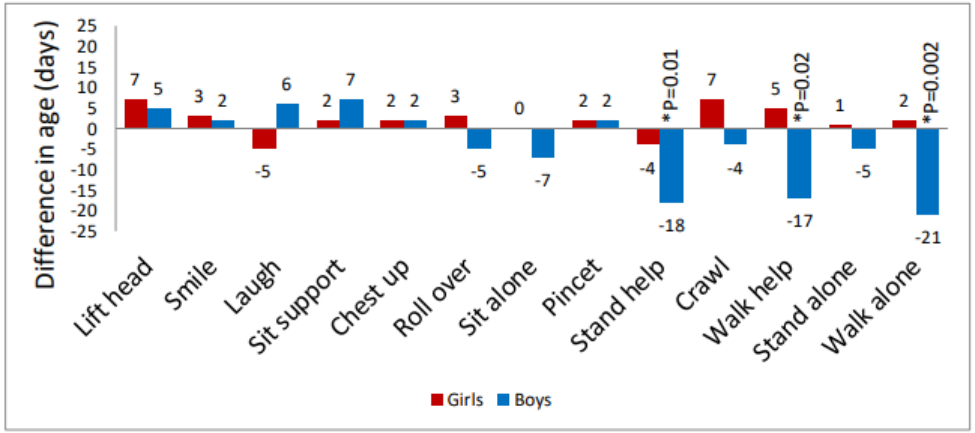

Figure 2. Effect of the n-3 LCPUFA pregnancy supplementation on age of milestone achievement for boys and girls. The effect is illustrated as the difference (in days) in milestone achievement, using the control group as the reference.
Significant difference is indicated with asterisk (*) and p-value.

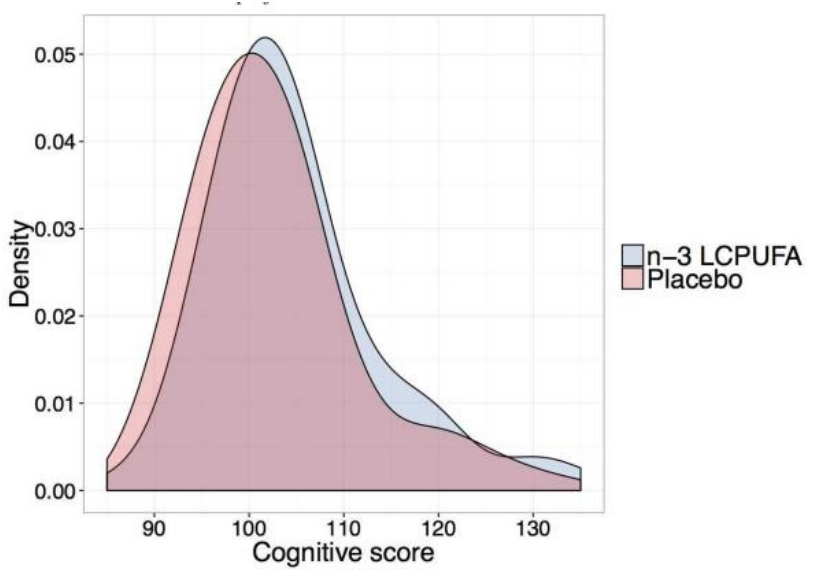

Figure3:
The effect of n-3 LCPUFA intervention in pregnancy on composite score of the Bayley cognitive test at age 2 ½ years among boys.

Sass et al., Child Dev 2021

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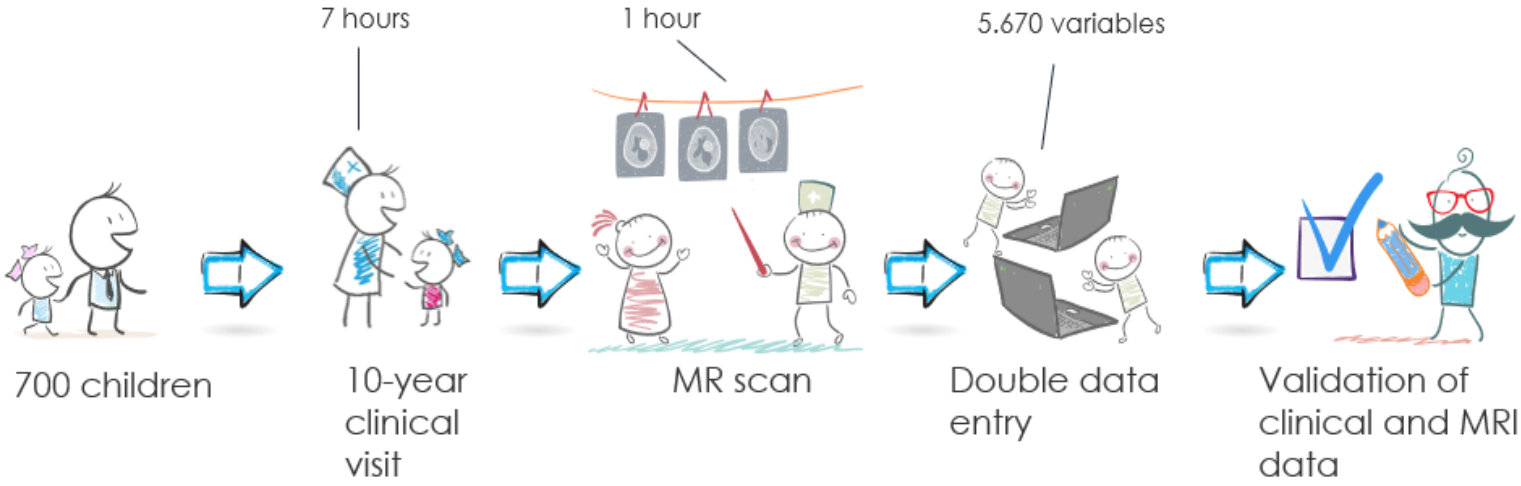
COPSYCH 10-year visit

- **2-day visit**
  - Clinical visit, COPSAC
  - MRI brain scanning, Glostrup



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Cognition ~ 2.5 hours incl. small breaks

- Executive Functions
- Verbal memory
- Attention and reaction time
- Processing speed
- Fine motor skills
- Intelligence

- TOF

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Psychopathology ~ 2 hours

Parent – 45 min

- Clinical interviews:
  - K-SADS-PL
- ADHD-RS
- Strengths and difficulties
- Social Responsiveness Scale-2
- Child Behavior Checklist
- BRIEF-2 on Executive Functions

Child – 1 hour

- Clinical interviews:
  - K-SADS-PL
  - Psychosis Supplement
- Magical thinking questionnaire

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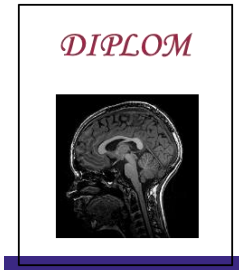
MRI, Functional Imaging Unit

- Survey scan + Head coil ref. scan 1:15 min
- T1W 3D high resolution 10:01 min
- DTI (30 dir) 8:42 min
- MTR 2:55 min
- Q-flow (total CBF) 3:00 min
- T1 4:00 min
- MR Spectroscopy 10:00 min

Total scanning time **39:13 min ~ 1 hour**



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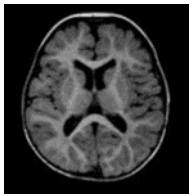
Status

- COPSAC visits: **604** participated in the COPSYCH-visit
  86 % of the original cohort

- MR scans: **489** completed visits
  70 % of entire cohort
  (61 MRI scans excluded →
  428 MRI scans after QC)



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Neurocognitive test battery

Table 1 Neurocognitive test battery

Neurocognitive domain	Test	Outcome variable
Speed of processing	Coding (WISC-IV)*	Total number correct.
	Symbol search (WISC-IV)	Sum of total number correct, errors subtracted.
	Trail making test 2—number sequencing (D-KEFS)†	Time to complete in seconds.
Attention/vigilance	Rapid visual information processing (CANTAB)‡	A' (A prime).**
	Reaction time (CANTAB)	Simple and five-choice reaction time.
Motor functioning	Reaction time (CANTAB)	Simple and five-choice movement time.
Fine motor dexterity	Grooved pegboard	Time to complete for the dominant and non-dominant hand.
Verbal memory	Word selective reminding—immediate recall (TOMAL-2)§	Total number of words recalled over six learning trials.
	Object recall (TOMAL-2)	Total number of objects recalled over five learning trials.
Verbal working memory	Digit span (WISC-IV)	Total number of correcr forward and backward digit sequencing.
	Letter-number sequencing (WISC-IV)	Total number of correct sequences.
Visual memory	Paired associates learning (CANTAB)	First trial memory score, total errors (adjusted).
Executive functions		
Flexibility/set shift	Intra–extra dimensional set shift (CANTAB)	Extra-dimensional stage errors.††
	Trail making test 4—number–letter switching (D-KEFS)	Time to complete in seconds.
Spatial working memory	Spatial span task (CANTAB)	Span length.‡‡
	Spatial working memory (CANTAB)	Total errors§§ and strategy formation.
Planning	Stockings of cambridge (CANTAB)	Problems solved in minimum moves.
Behaviour rating of executive functions	BRIEF-2¶	Impulse control, self-monitoring, flexibility, emotional control, initiating, planning/organisation, working memory and task monitoring.
Intelligence	Vocabulary (WISC-IV)	Total number correct.
	Matrices (WISC-IV)	Total number correct.

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