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Association of Maternal Iodine Status With Child IQ: A Meta-Analysis of Individual Participant Data

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Iodine is an essential trace element required for the production of thyroid hormones; optimal thyroid hormone availability is important for normal fetal brain development.

During pregnancy, there is a higher demand for maternal iodine intake due to

- the increased maternal thyroid hormone synthesis

- greater urinary iodine loss due to an increased glomerular filtration rate

- placental transfer of iodine to the fetus



Introduction (Cont.)



Although severe iodine deficiency is no longer common in Europe, mild to moderate iodine deficiency is still common, especially in pregnant women.

Severe iodine deficiency in pregnancy results in a higher risk of goiter, hypothyroidism, and mental retardation in the offspring.

However, the consequences of mild to moderate iodine deficiency in pregnancy on child neurodevelopment are less well established.



Introduction (Cont.)



Association of maternal iodine status with child IQ: a meta-analysis of individual-participant data

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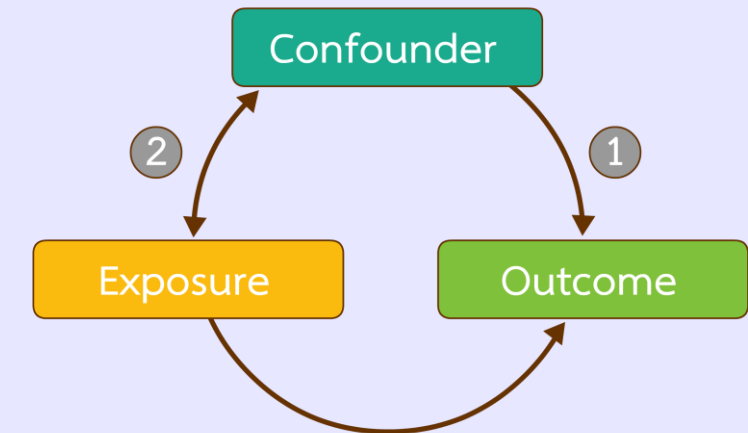
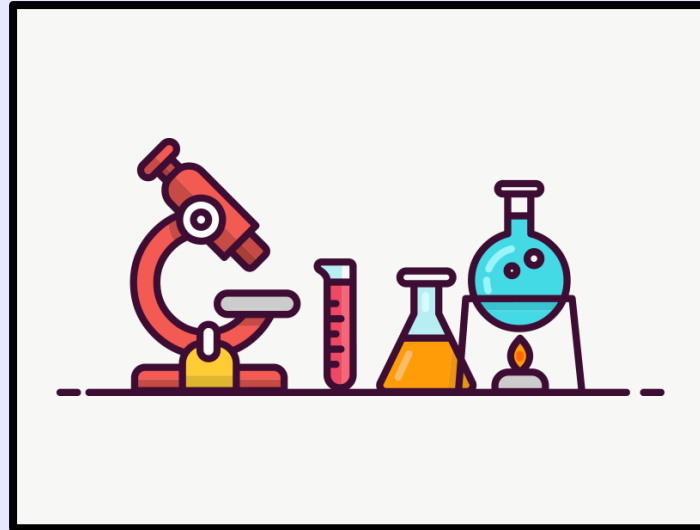
Mild to moderate iodine deficiency or low iodine intake during pregnancy has been associated with adverse child neurodevelopmental outcomes in some but not all studies.



Introduction (Cont.)



Differences in results between studies may be related to methodological differences the age at assessment of the neurodevelopmental outcome of interest, the timing of the iodine measurements, and the relative severity of iodine deficiency in the population.



↔ คือ มีความสัมพันธ์กัน (non-causal relationship หรือ association)
→ คือ เป็นสาเหตุกัน (causal relationship)

measurement of iodine status



Introduction (Cont.)



However, whether the effect of iodine on child cognition varies during different stages of pregnancy is unknown.

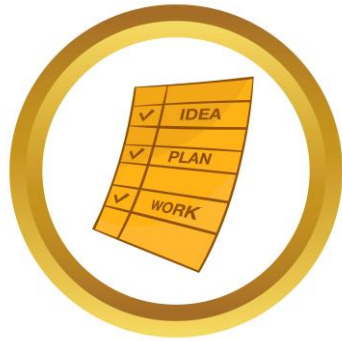
We therefore assessed the association between maternal iodine status in pregnancy and child IQ across three cohorts of differing iodine status and investigated potential effect modification by gestational age.



subject matter



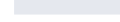
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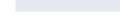
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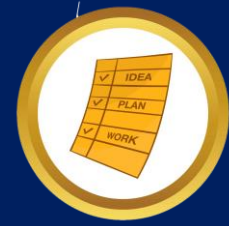


Study design and populations

This study was embedded in three cohort studies: Generation R (Netherlands), the Infancies y Medio Ambiente Project (INMA; Spain, three regions), and the Avon Longitudinal Study of Parents and Children (ALSPAC; United Kingdom).



Material and Methods (Cont.)



Exclusion criteria were multiple pregnancies, fertility treatment, medication affecting the thyroid, and preexisting thyroid disease.



Ethical approval was obtained from the Medical Ethical Committee of the Erasmus Medical Center

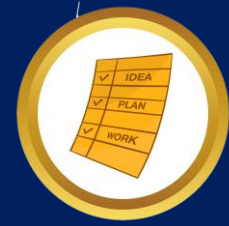
Material and Methods (Cont.)



Urinary iodine concentration (UIC) and creatinine concentration

were measured in spot urine samples stored at -20°C after collection. As part of this study, additional urine samples were analyzed for iodine and creatinine concentrations, and existing measurements from each cohort were also included.

Material and Methods (Cont.)



In a subset of women, repeated measures of urinary iodine and creatinine were available; we used the earliest available sample as an indicator of iodine status.

Material and Methods (Cont.)

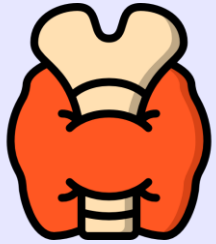


The urinary iodine/creatinine ratio (UI/Creat) was used as a measure of iodine status. Because of possible contamination of UIC by the use of iodine-containing test strips in ALSPAC, UIC $>500 \mu\text{g/L}$ and/or UI/Creat $>700 \mu\text{g/g}$ was excluded from the analyses in this cohort (N = 363)

Material and Methods (Cont.)



Maternal thyroid function



TSH and free thyroxine (FT4) were measured according to different methodologies between cohorts, which are described in detail elsewhere.

Nonverbal and verbal IQ scores

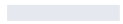


Children with IQ scores <50 or >150 ($n = 3$) were considered outliers and were excluded from the analyses. Suboptimal IQ was defined as an IQ score <85 .

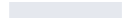
subject matter



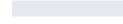
Introduction



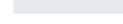
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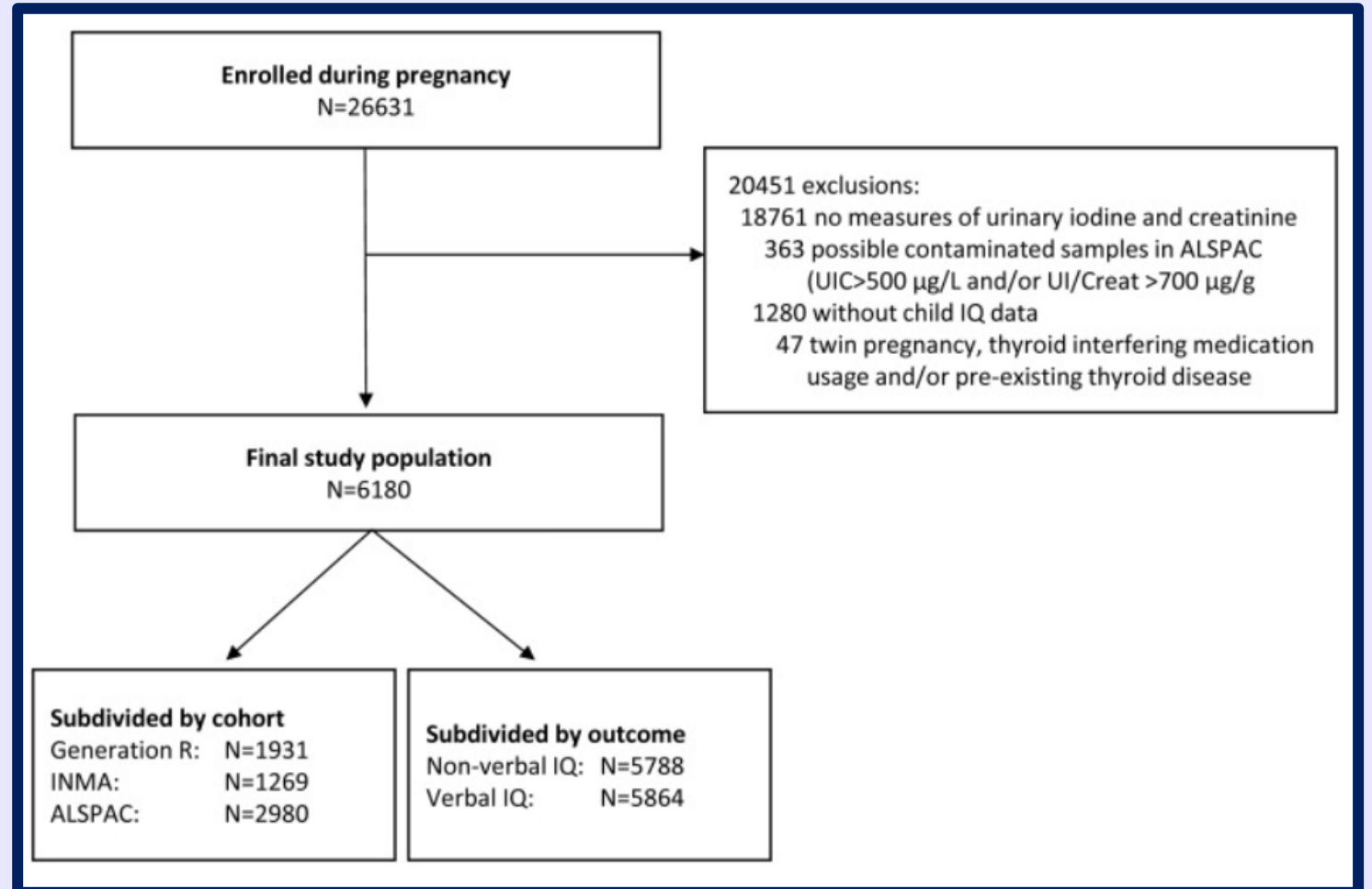
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Statistical analyses

- The decision to use linear regression models instead of multilevel models
- The final study population consisted of 6180 mother–child pairs.



Result (Cont.)



	Generation R (n = 1931)		INMA (n = 1269)		ALSPAC (n = 2980)	
	n	Values	n	Values	n	Values
Offspring neurodevelopment, no. (%)						
Suboptimal nonverbal IQ ^a	1540	175 (11.4)	1269	216 (17.0)	2979	479 (16.1)
Suboptimal verbal IQ ^a	1618	279 (17.2)	1269	211 (16.6)	2977	480 (16.1)
Female sex, no. (%)	1931	963 (49.9)	1268	632 (49.8)	2980	1514 (50.8)
Iodine status	1931		1269		2980	
UI/Creat, µg/g, median (IQR)		214 (143–308)		152 (96–258)		124 (82–199)
UI/Creat <150 µg/g, no. (%)		531 (27.5)		623 (49.1)		1831 (61.4)
UI/Creat >500 µg/g, no. (%)		97 (5.0)		52 (4.1)		81 (2.7)
UIC, µg/L, median (IQR)		159 (90–275)		128 (75–213)		96 (57–153)
Gestational age at urine sampling, wk	1931		1267		2980	
Median (IQR)		13.1 (12.1–14.8)		13.0 (12.4–14.1)		12.0 (8.0–16.0)
Range (min–max)		6.1–30.5		8.6–39.4		1.0–42.0
>20th week of gestation, no. (%)		66 (3.4)		130 (10.2)		211 (7.1)
Maternal thyroid function						
TSH, mIU/L, median (IQR)	1719	1.29 (0.79–1.95)	1227	1.25 (0.85–1.80)	1102	0.97 (0.64–1.38)
FT4, pmol/L, median (IQR)	1728	14.6 (12.9–16.5)	1229	10.6 (9.7–11.6)	1108	16.2 (14.9–17.7)
TPOAb positivity, no. (%)	1737	98 (5.6)	NA	NA	1111	146 (13.1)
Gestational age, wk, mean (SD)	1733	13.3 (1.9)	1228	13.2 (1.4)	1118	10.3 (2.7)

Nonverbal IQ

Using pooled data in the one-step approach

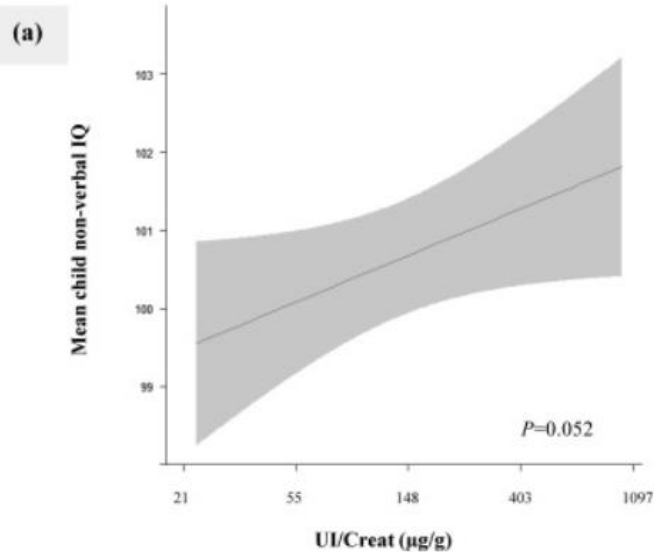
we observed a positive linear association between the UI/Creat and mean nonverbal IQ score ,although this association was not statistically significant.

Result (Cont.)

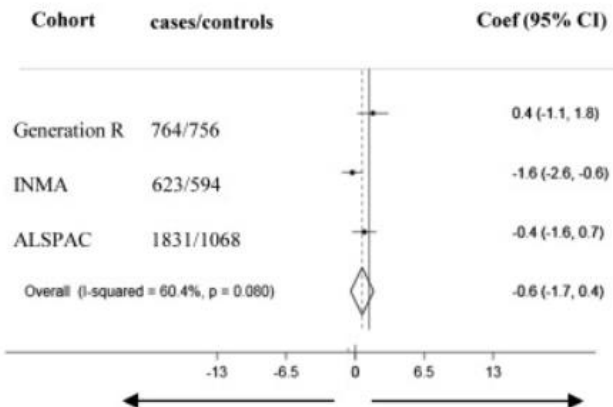


Nonverbal IQ

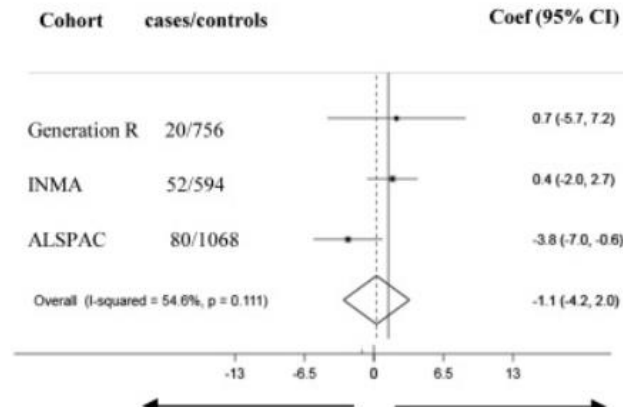
UI/Creat was not associated with suboptimal nonverbal IQ.



(b) UI/Creat < 150 $\mu\text{g/g}$



(c) UI/Creat ≥ 500 $\mu\text{g/g}$



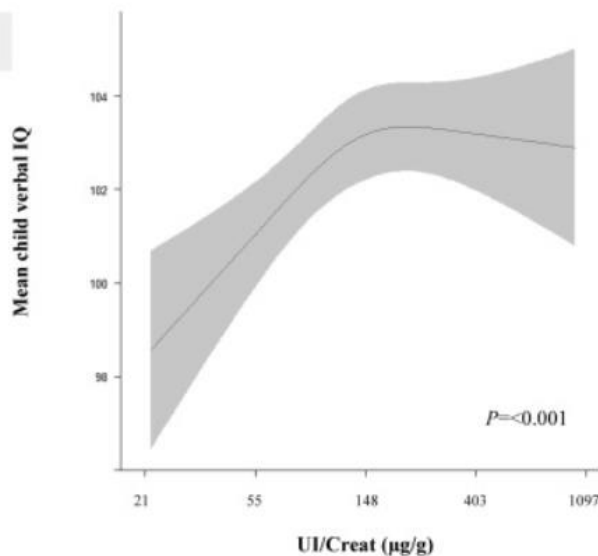
Result (Cont.)



Verbal IQ

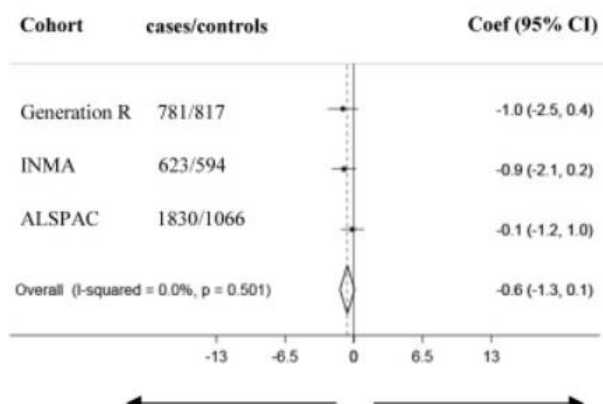
Using the one-step approach, we observed a positive curvilinear association between UI/Creat and verbal IQ score.

(a)



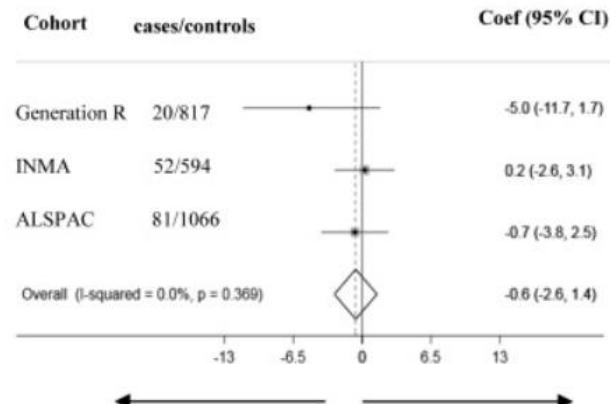
(b)

UI/Creat $< 150 \mu\text{g/g}$



(c)

UI/Creat $\geq 500 \mu\text{g/g}$



The continuous association of UI/Creat with nonverbal IQ score did not differ according to gestational age at measurement (P for interaction term = 0.306).

Result (Cont.)



By contrast, we identified possible effect modification by gestational age in the association with verbal IQ (*P for interaction term* = **0.078**)

Iodine status and thyroid function

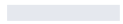
UI/Creat was not associated with TSH (0.007, 95 CI%: -0.044 to 0.058 ; $P = 0.789$) or with FT4 (-0.044 , 95 CI%: -0.092 to 0.005 ; $P = 0.079$).



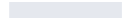
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This meta-analysis of individual participant data showed that a lower UI/Create during pregnancy was associated with lower verbal IQ score.

The importance of iodine status in the preconceptionally stage for child IQ

In early pregnancy, the fetus is fully dependent on the placental transfer of thyroid hormone to support the crucial processes of brain development.

Effects on verbal IQ could possibly be explained by the impact of mild iodine deficiency, via thyroid hormone, on the auditory system.



Discussion (Cont.)



showed that maternal iodine status is particularly important in the first trimester.

it suggests that the trial might have missed a critical period of vulnerability in women with iodine deficiency.

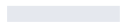
additional randomized controlled trials should start with iodine supplementation early in the first trimester or preferably even before pregnancy.



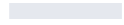
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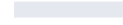
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Discussion (Cont.)



In conclusion, this study confirms that iodine status in pregnancy is associated with child IQ scores, and results indicate that the development of verbal IQ of the fetus is particularly vulnerable to suboptimal iodine

However, further studies should replicate these data and investigate the effects of iodine supplementation.



thank
you

