

## Supplementary Appendix

Supplement to Lazarus JH, Bestwick JP, Channon S, et al. Antenatal hypothyroid screening and childhood cognitive function.

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**Web Appendix Table 1:** Number of women randomised to screen or control group, and number of women in each group who were positive and whose children completed testing

Centre	Recruited		Positive <sup>3</sup>		Psychological tests completed	
	Screen <sup>1</sup>	Control <sup>2</sup>	Screen <sup>1</sup>	Control <sup>2</sup>	Screen <sup>1</sup>	Control <sup>2</sup>
Britain						
Bristol	297	297	12	14	10	9
Glan Clwyd	263	261	11	12	7	12
Llandough	1,087	1,086	51	54	40	40
Neville Hall	495	492	22	14	18	13
Princess of Wales	279	281	24	28	19	20
Royal Glamorgan	876	874	47	42	39	37
Royal Gwent	1,710	1,705	79	69	62	52
Singleton and Morriston University Hospital	921	922	45	34	37	26
Wales	2,000	1,998	83	91	66	73
Wrexham	250	252	8	13	6	7
Turin	2746	2754	117	180	86	115
<i>Total</i>	<i>10924</i>	<i>10922</i>	<i>499</i>	<i>551</i>	<i>390</i>	<i>404</i>

<sup>1</sup>Immediate assay of TSH and FT4

<sup>2</sup>Assay of TSH and FT4 post delivery

<sup>3</sup>High TSH and/or low FT4

**Web Appendix Table 2:** Observed IQ scores according to randomisation group and psychologist

Randomisation group	Britain 1			Britain 2			Turin		
	N	Mean	SD	N	Mean	SD	N	Mean	SD
Screen	207	107.3	11.7	97	110.3	13.2	86	109.2	16.2
Control	208	106.5	12.7	81	110.9	13.1	115	114.1	14.5

**Web Appendix Table 3:** Full scale child IQ Z-scores according to group\*

	Screen group (Mothers treated with T4, N=390)	Control group (N=404)	Difference (95% CI) ( <i>control-screen</i> )	p-value
Mean IQ z-score (SD)	-0.05 (1.00)	0 (1)	0.05 (-0.09 to 0.19)	0.47
IQ z-score < -1	13.1%	16.6%	3.5% (-1.4 to 8.4%)	0.16

\*Z-scores calculated within psychologist as (IQ score-Control group mean)/Control group standard deviation

**Web Appendix Table 4:** Relative risk and risk difference (with 95% confidence intervals) of full scale IQ and verbal and performance IQ components being below specified cut-offs in the screen group compared with the control group.

IQ cut-off	Relative risk (95% CI)	Risk difference (95% CI) ( <i>control-screened</i> )	p-value
Full scale IQ			
75	1.43 (0.71 to 2.89)	-1.40 (-4.10 to 1.30)	0.31
80	0.87 (0.55 to 1.37)	1.21 (-2.68 to 5.10)	0.54
85	0.85 (0.60 to 1.22)	2.06 (-2.63 to 6.74)	0.39
90	1.01 (0.78 to 1.31)	-0.29 (-6.09 to 5.52)	0.92
95	1.02 (0.85 to 1.23)	-0.74 (-7.39 to 5.91)	0.83
100	1.08 (0.94 to 1.24)	-3.74 (-10.69 to 3.21)	0.29
Verbal IQ			
75	1.61 (0.71 to 3.68)	-1.36 (-3.70 to 0.98)	0.25
80	1.00 (0.61 to 1.65)	0.00 (-3.59 to 3.59)	0.99
85	0.93 (0.63 to 1.37)	0.86 (-3.57 to 5.28)	0.71
90	0.97 (0.71 to 1.34)	0.44 (-4.68 to 5.55)	0.87
95	0.97 (0.78 to 1.20)	0.99 (-5.32 to 7.30)	0.76
100	0.93 (0.79 to 1.09)	3.25 (-3.65 to 10.14)	0.36
Performance IQ			
75	0.90 (0.54 to 1.49)	0.76 (-2.80 to 4.32)	0.68
80	0.97 (0.67 to 1.41)	0.33 (-4.23 to 4.88)	0.89
85	1.06 (0.79 to 1.43)	-1.15 (-6.54 to 4.24)	0.68
90	1.06 (0.83 to 1.34)	-1.41 (-7.49 to 4.67)	0.65
95	1.09 (0.90 to 1.31)	-3.03 (-9.70 to 3.64)	0.37
100	1.13 (0.97 to 1.30)	-5.73 (-12.67 to 1.21)	0.11

**Web Appendix Table 5:** TSH and FT4 levels at initial visit (median 12,3 weeks gestation), 6 weeks after starting thyroxine therapy (median 20,0 weeks gestation) and at about 30 weeks (median 30,1 weeks gestation).

Median gestation at sampling	Britain			Turin		
	N	TSH (mIU/L)	FT4 (pmol/L)	N	TSH (mIU/L)	FT4 (pg/ml)
12.3 weeks	304	3.78 (1.49-4.68)	11.1 (10.5-13.3)	86	3.05 (1.29-3.99)	7.4 (7.1-8.6)
20.0 weeks	285	0.31 (0.06-0.87)	15.9 (14.4-17.7)	84	0.10 (0.02-0.64)	10.4 (9.1-12.1)
30,1 weeks	268	0.21 (0.02-0.83)	15.3 (13.8-17.2)	82	0.17 (0.03-0.73)	9.2 (8.2-10.2)

**Web Appendix Table 6:** On treatment analysis in 308 (79%) women judged to have complied with treatment (a fall of at least 10% in TSH and a rise of at least 10% in FT4 measurements: Relative risk and risk difference of standardised full scale IQ and verbal and performance IQ components being below specified cut-offs in screen group compared with control group

IQ cut-off	Relative risk (95% CI)	Risk difference (95% CI) ( <i>control-screened</i> )	p-value
<b>Full scale IQ</b>			
75	1.31 (0.62 to 2.79)	-1.00 (-3.83 to 1.83)	0.48
80	0.78 (0.47 to 1.29)	2.02 (-2.01 to 6.04)	0.33
85	0.71 (0.47 to 1.08)	4.04 (-0.73 to 8.82)	0.10
90	0.92 (0.69 to 1.22)	1.82 (-4.24 to 7.89)	0.56
95	0.98 (0.80 to 1.20)	0.81 (-6.23 to 7.85)	0.82
100	1.06 (0.91 to 1.23)	-2.65 (-10.05 to 4.76)	0.48
<b>Verbal IQ</b>			
75	1.60 (0.67 to 3.82)	-1.34 (-3.87 to 1.18)	0.28
80	0.90 (0.52 to 1.57)	0.68 (-3.04 to 4.41)	0.72
85	0.79 (0.51 to 1.23)	2.47 (-2.07 to 7.00)	0.29
90	0.78 (0.54 to 1.12)	3.67 (-1.50 to 8.85)	0.17
95	0.88 (0.69 to 1.12)	3.48 (-3.13 to 10.09)	0.31
100	0.90 (0.76 to 1.07)	4.39 (-2.94 to 11.72)	0.24
<b>Performance IQ</b>			
75	0.96 (0.57 to 1.63)	0.28 (-3.57 to 4.13)	0.89
80	0.89 (0.59 to 1.34)	1.34 (-3.41 to 6.09)	0.58
85	1.06 (0.77 to 1.44)	-1.01 (-6.75 to 4.73)	0.73
90	1.05 (0.82 to 1.35)	-1.30 (-7.78 to 5.18)	0.69
95	1.06 (0.87 to 1.29)	-1.96 (-9.05 to 5.14)	0.59
100	1.09 (0.93 to 1.27)	-4.05 (-11.45 to 3.34)	0.28

**Web Appendix Table 7: Sub-group analyses of standardised full scale child IQ according to group\***

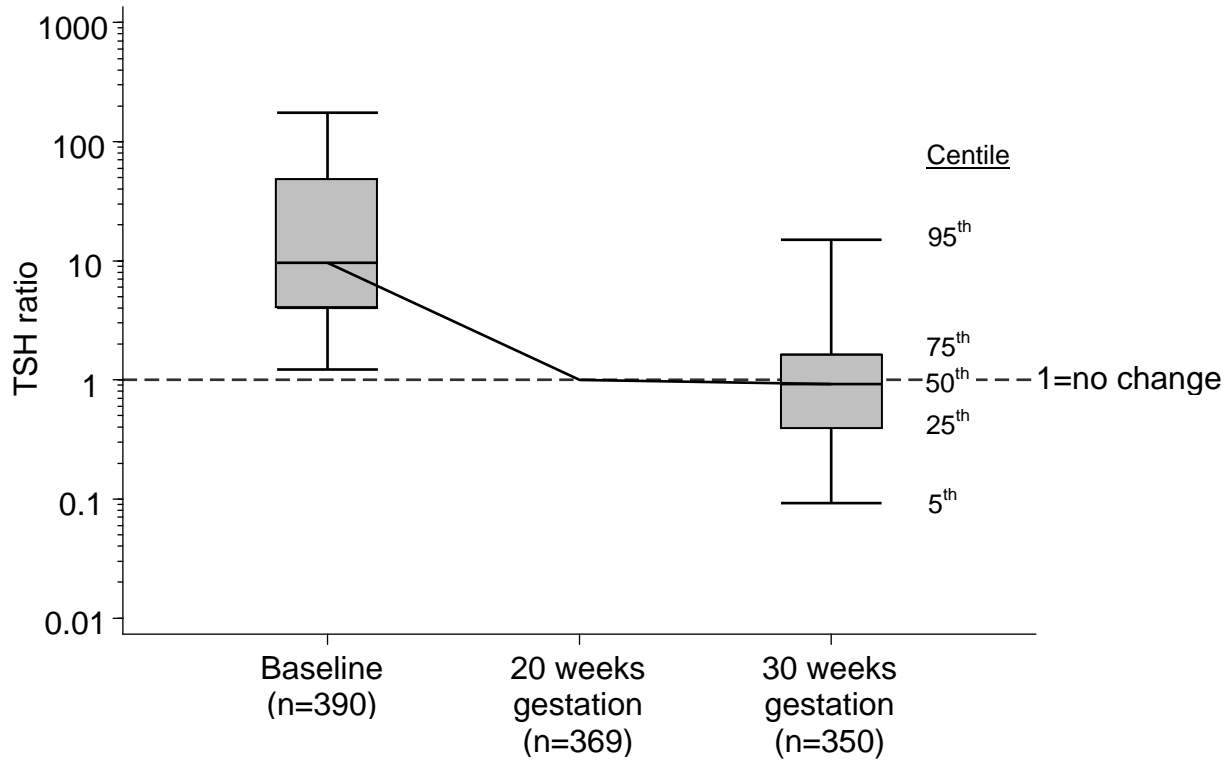
Sub-group	Screen group (Mothers treated with T4)	Control group	Difference (95% CI) ( <i>control-screen</i> )	p-value
<b>Overall</b>				
N	390	404		
Mean IQ (SD)	99.2 (13.3)	100.0 (13.3)	0.8 (-1.1 to 2.6)	0.40
IQ<85	12.1%	14.1%	2.1% (-2.6 to 6.7%)	0.39
<b>Positive on TSH<sup>1</sup></b>				
N	209	219		
Mean IQ (SD)	100.4 (13.7)	100.7 (13.0)	0.3 (-2.2 to 2.8)	0.82
IQ<85	11.0%	13.7%	2.7 (-3.5 to 8.9%)	0.40
<b>Positive on FT4<sup>2</sup></b>				
N	204	207		
Mean IQ (SD)	97.8 (12.7)	99.2 (13.3)	1.3 (-1.3 to 3.8)	0.28
IQ<85	13.2%	14.5%	1.3% (-5.4 to 7.9%)	0.71
<b>Positive on TSH and FT4<sup>3</sup></b>				
N	23	22		
Mean IQ (SD)	97.7 (11.6)	99.4 (11.4)	1.7 (-5.2 to 8.6)	0.61
IQ<85	13.0%	13.6%	0.6% (-19.3 to 20.5%)	0.95
<b>Thyroxine started &lt; 14 weeks gestation<sup>4</sup></b>				
N	190 (62%)	404		
Mean IQ (SD)	98.7 (14.1)	100.0 (13.3)	1.3 (-1.1 to 3.6)	0.28
IQ<85	14.2%	14.1%	-0.1% (-6.1 to 5.9%)	0.97
<b>Thyroxine started ≥ 14 weeks gestation<sup>4</sup></b>				
N	116 (38%)	404		
Mean IQ (SD)	99.4 (13.2)	100.0 (13.3)	0.6 (-2.1 to 3.4)	0.65
IQ<85	11.2%	14.1%	2.9% (-3.8 to 9.6%)	0.42
<b>Target TSH reached at 6 week appointment<sup>5</sup></b>				
N	292 (79%)	404		
Mean IQ (SD)	99.3 (12.9)	100.0 (13.3)	0.7 (-1.3 to 2.7)	0.49
IQ<85	10.3%	14.1%	3.8% (-1.0 to 8.7%)	0.13
<b>Target TSH reached at 30 week appointment<sup>5</sup></b>				
N	277 (79%)	404		
Mean IQ (SD)	100.0 (13.0)	100.0 (13.3)	-0.0 (-2.0 to 2.0)	0.99
IQ<85	11.2%	14.1%	2.9% (-2.1 to 7.9%)	0.26

<sup>1</sup>p, interaction =0.74<sup>2</sup>p, interaction =0.73<sup>3</sup>p, interaction=0.88<sup>4</sup>Date thyroxine first given not recorded in all women<sup>5</sup>Target TSH 1.0 mIU/L, not all women attended appointment

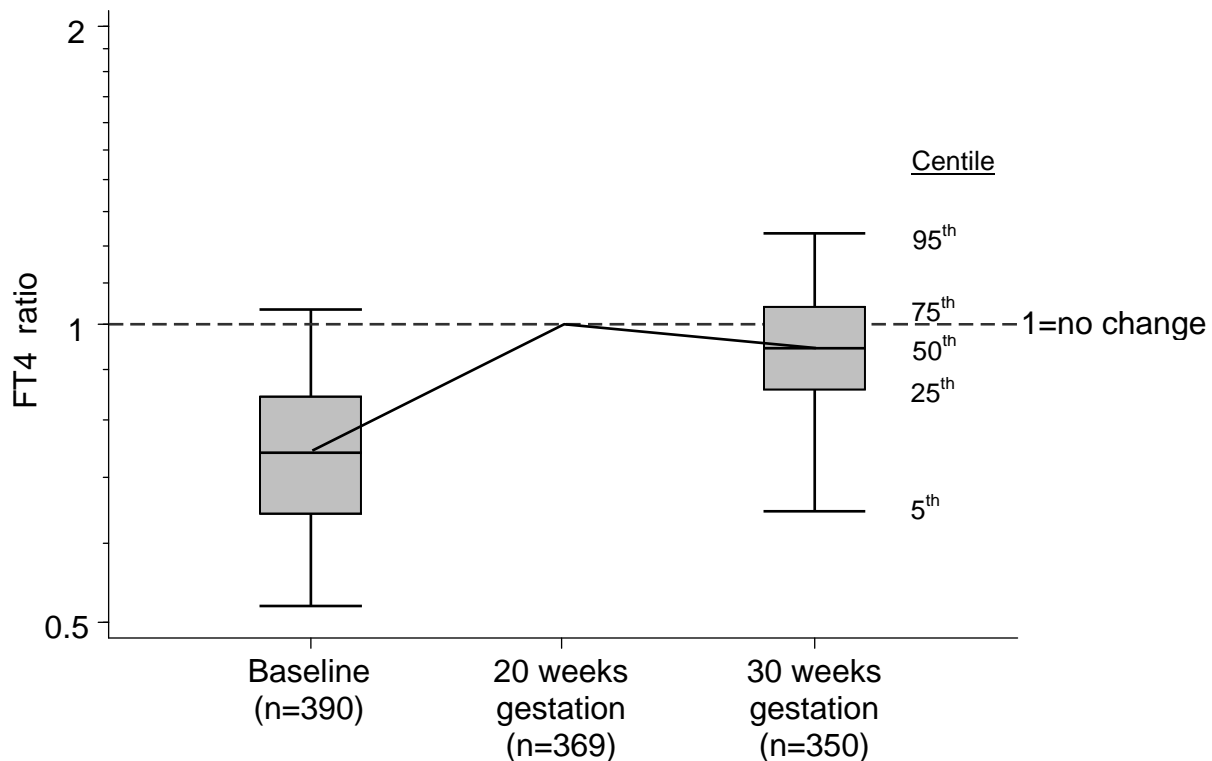


**Web Appendix Figure 1:** Ratio of TSH (a) and FT4 (b) at sampling (baseline, median 12.3 weeks gestation) to about 6 weeks after starting thyroxine therapy (median 20.0 weeks gestation) and ratio at about 30 weeks (median 30.1 weeks gestation) to about 6 weeks after starting thyroxine therapy in screen group women (treated with T4).

**(a) TSH**



**(b) FT4**



Participating Obstetric Hospitals and clinicians  
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