

Should we screen for thyroid disorders in pregnancy?

- Jim Thornton
 - Nottingham





Issues

- Maternal
 - ~~Hyperthyroidism~~
 - ~~Iodine deficiency~~
 - ~~Iodine supplementation~~
 - Hypothyroidism
 - ~~Clinically recognised~~
 - Subclinical
- Baby
 - ~~Congenital hypothyroidism~~



Hyperthyroidism

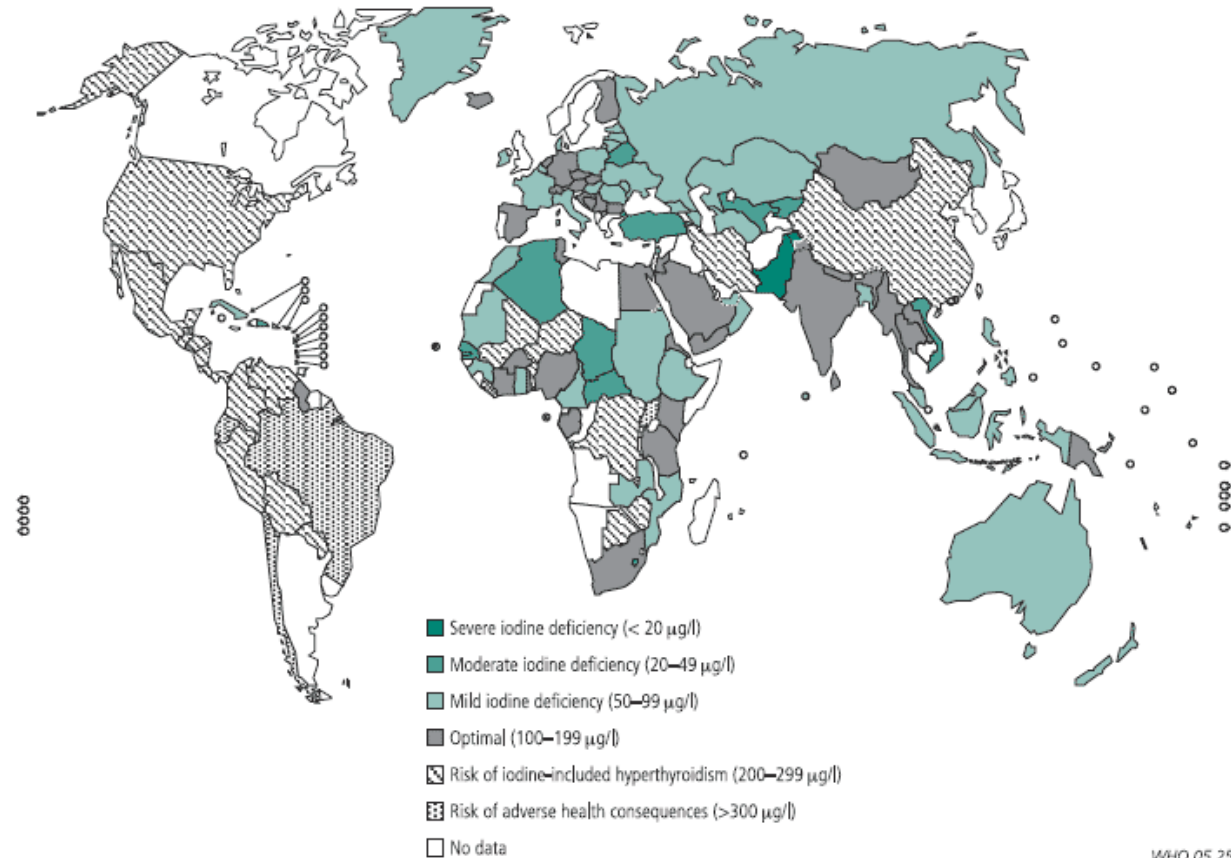
- Look out for clinically.

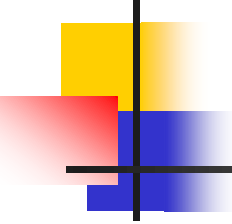
Iodine deficiency

Fig. 1. Degree of public health significance of iodine nutrition based on median urinary iodine

Pregnant women in Turkey need iodine. Iodised salt is adequate.

If not available, oral supplement 250 micrograms/day





Neonatal screening for congenital hypothyroidism

- 1 in 4,000 babies
- Blood spot test at birth
- Same sample as Guthrie test for PKU
- Treatment thyroxine



Maternal hypothyroidism

- Severe is associated with infertility
- Subclinical (raised TSH) may be associated with developmental delay

Stored samples from 25,000 pregnant women

- 62 raised TSH &/or low thyroxine
- 124 controls

TEST	CHILDREN OF WOMEN WITH HYPOTHYROIDISM (N=62)	CONTROL CHILDREN (N=124)	MEAN DIFFERENCE†	P VALUE
Intelligence				
WISC-III full-scale IQ score	103 ± 15	107 ± 12	-4.1 ± 2.1	0.06
WISC-III full-scale IQ score ≤ 85 (%)	15	5	3 (1-8)	0.08

TEST	CHILDREN OF TREATED WOMEN WITH HYPOTHYROIDISM (N=14)	P VALUE†	CHILDREN OF UNTREATED WOMEN WITH HYPOTHYROIDISM‡ (N=48)	P VALUE§	CONTROL CHILDREN (N=124)
Intelligence					
WISC-III full-scale IQ score	111	0.20	100	0.005	107
WISC-III full-scale IQ score ≤ 85 (%)	0	0.90	19	0.007	5

Haddow
NEJM 1999

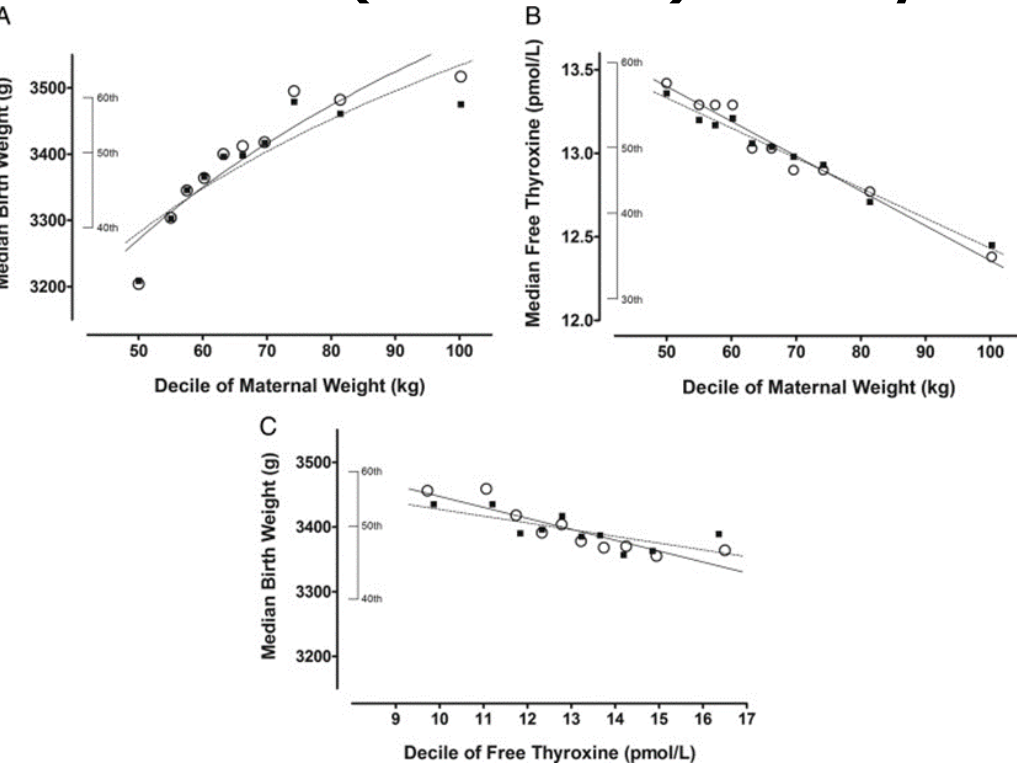


Subclinical hypothyroidism

- Possible associations with
 - Preterm birth
 - Miscarriage
 - Low IQ
- Not all confirmed

Possible confounders

■ (FASTER) study United States





If it works it's cost effective

Cost-Effectiveness of Universal and Risk-Based Screening for Autoimmune Thyroid Disease in Pregnant Women

Chrysoula Dosiou, James Barnes, Alan Schwartz, Roberto Negro, Lawrence Crapo, and Alex Stagnaro-Green

Results: Risk-based screening and universal screening were both cost-effective relative to no screening, with incremental cost-effectiveness ratios (ICERs) of \$6,753/QALY and \$7,138/QALY, respectively. Universal screening was cost-effective compared with risk-based screening, with an ICER of \$7,258/QALY. Screening remained cost-effective in various clinical scenarios, including when only overt hypothyroidism was assumed to have adverse obstetrical outcomes. Universal screening was cost-saving in the scenario of untreated maternal hypothyroidism resulting in decreased child intelligence, with levothyroxine therapy being preventive.

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Antenatal Thyroid Screening and Childhood Cognitive Function

John H. Lazarus, M.D., Jonathan P. Bestwick, M.Sc., Sue Channon, D.Clin.Psych., Ruth Paradice, Ph.D.,
Aldo Maina, M.D., Rhian Rees, M.Sc., Elisabetta Chiusano, M.Psy., Rhys John, Ph.D.,
Varvara Guaraldo, M.S.Chem., Lynne M. George, H.N.C., Marco Perona, M.S.Chem., Daniela Dall'Amico, M.D.,
Arthur B. Parkes, Ph.D., Mohammed Joomun, M.Sc., and Nicholas J. Wald, F.R.S.



Lazarus et al 2012

- UK and Italy
 - 21,000 women screened at 12 weeks
 - Half tested immediately and half tested at end of pregnancy
 - If TSH raised or free T4 low Rx thyroxine
 - 390 treated and followed up till 3 years
 - 404 not treated and followed up till 3 years.



Lazarus 2012

	Screened	Control	
GA at birth	40.1 wks	40.2 wks,	P=0.1
<37 weeks	5.6%	7.9%	P=0.2
Birth weight	3.5 kg	3.3 kg	P=0.15

Lazarus results - 1

Table 2. Standardized Full-Scale Child IQ and Scores on the Child Behavior Checklist (CBCL) and the Behavior Rating Inventory of Executive Function, Preschool Version (Brief-P), According to Study Group.*

Test	Screening Group (N = 390)	Control Group (N = 404)	Difference (95% CI) (Control Group – Screening Group)†	P Value
IQ				
Mean	99.2±13.3	100.0±13.3	0.8 (–1.1 to 2.6)	0.40
<85 (% of children)	12.1	14.1	2.1 (–2.6 to 6.7)	0.39
CBCL T score‡				
Mean	44.4±12.4	45.1±13.6	0.7 (–1.2 to 2.5)	0.49
Brief-P T score§				
Median	40	40	0	0.59
Interquartile range	47–55	47–55		

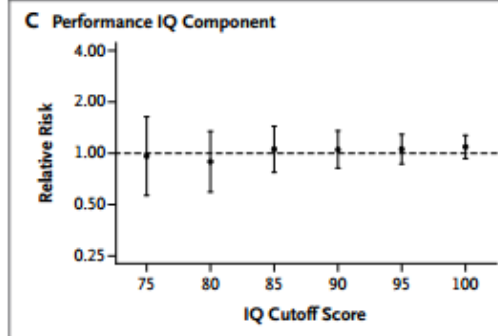
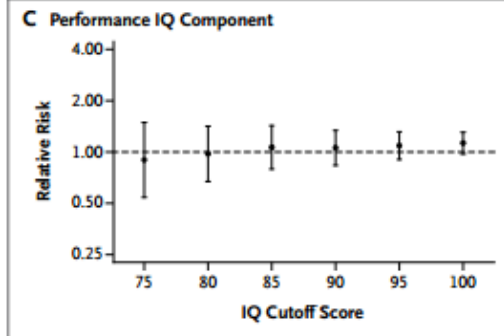
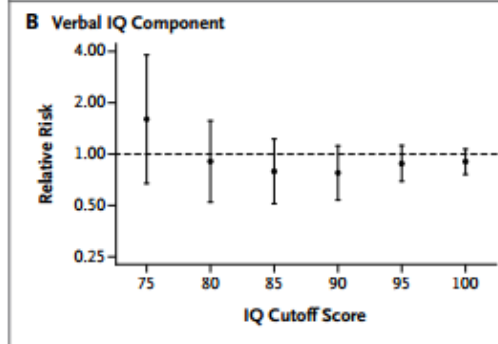
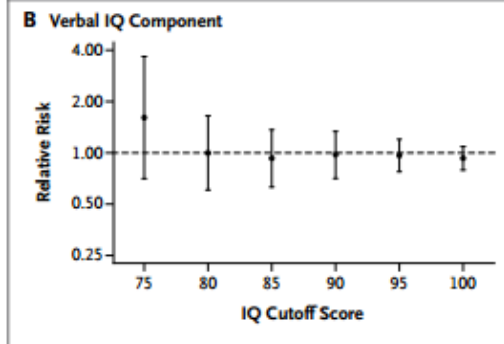
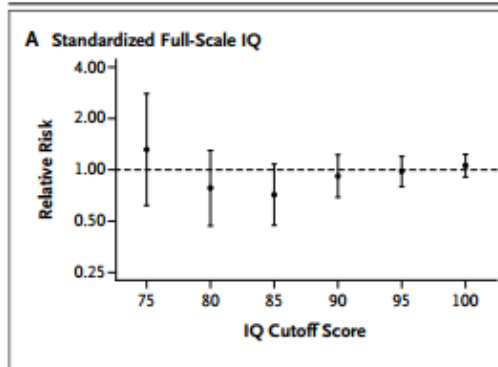
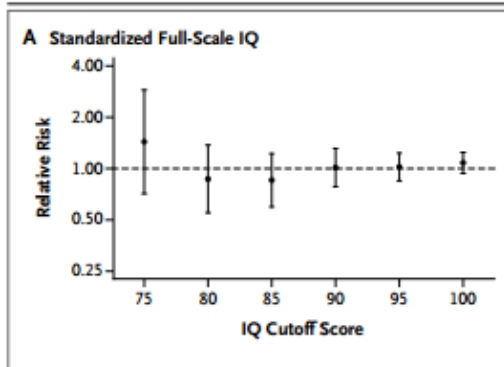
* Plus–minus values are means ±SD. The full-scale child IQ test was standardized so that for each psychologist, the mean score among the children in the control group whom they tested was 100. In the screening group, the women were assigned to treatment with levothyroxine.

† For percentages of children with an IQ below 85, the absolute (percentage-point) differences are shown.

‡ For the CBCL, a T score above the 98th percentile is indicative of a clinically significant problem.

§ For the Brief-P, a T score above 65 is indicative of a clinically significant problem.

Lazarus results - 2



RR of IQ score below cutoff in screened group. i.e. $RR > 1$ favours no screening

All participants left

Compliant right



National Institute for Health & Clinical Excellence (NICE)

- Does not recommend thyroid function screening in pregnancy



NIH trial – Brian Casey



120,000 women screened

- P – 1,203 women with TSH (≥ 3.00 mU/L) & normal T4, or normal TSH & low T4 (<0.86 ng/dL)
- I – Thyroxine
- C – Placebo
- O - Wechsler IQ (WPPSI-III) at 5 years



Caution

- Neither Lazarus nor Casey trial treated before 12 weeks. At risk period.
- Established maternal disease needs treatment.



Summary

- Don't screen for hyperthyroidism
- Do iodise salt
- Do screen for newborn congenital hypothyroidism
- Don't screen for subclinical hypothyroidism in pregnancy
- yet
- Casey trial





First and Second Trimester Assessment of Aneuploidy Risk (FASTER) study

