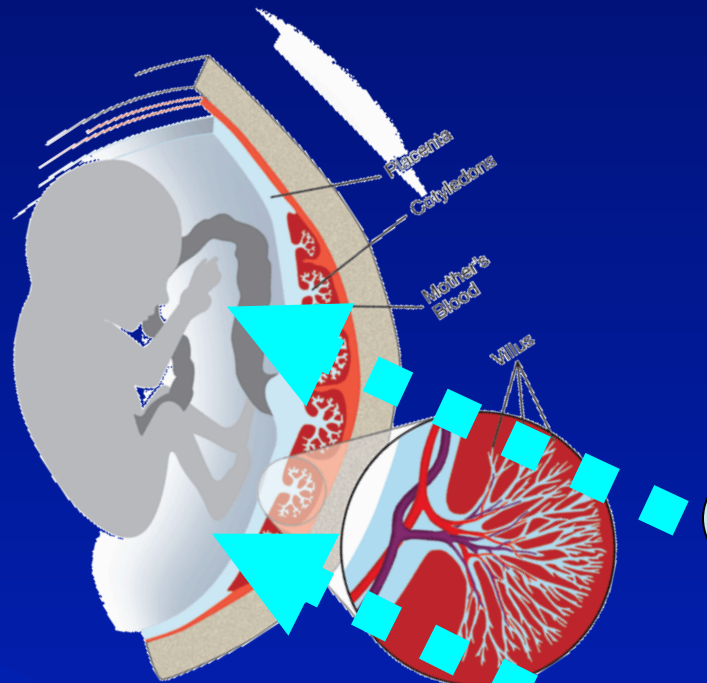


Iodio, Selenio & Levotiroxina in gravidanza

Roberto Negro

Iodine deficiency

- In 2011, 393 million Europeans (44.2%), including pregnant women and those of child-bearing age, were estimated to be iodine deficient



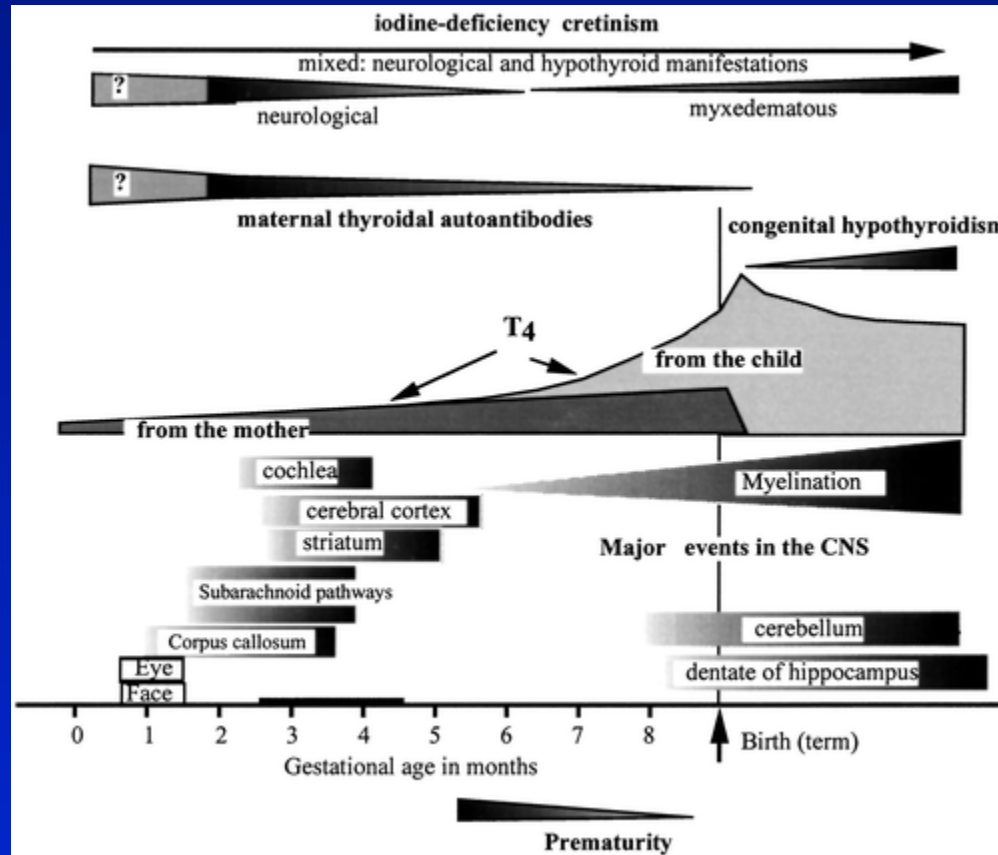
Placental Activity

Deiodinase

Iodine

Thyroxine

Is neuropsychological development related to maternal hypothyroidism or to maternal hypothyroxinemia?

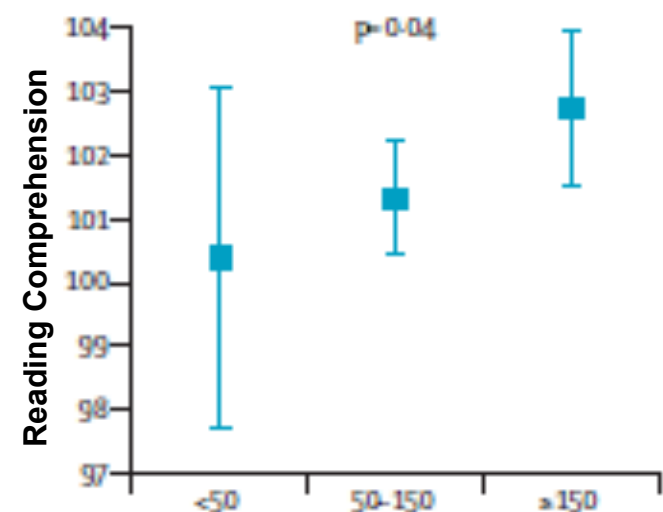
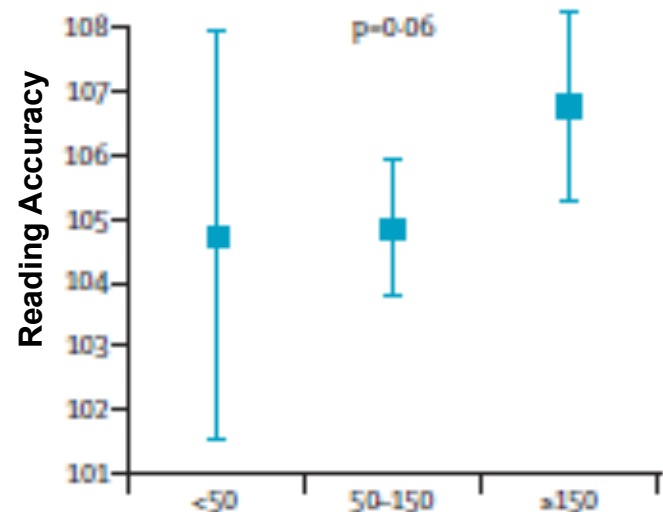
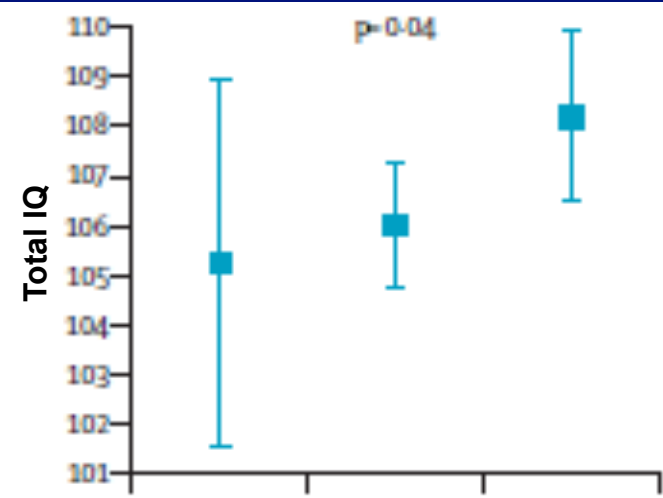
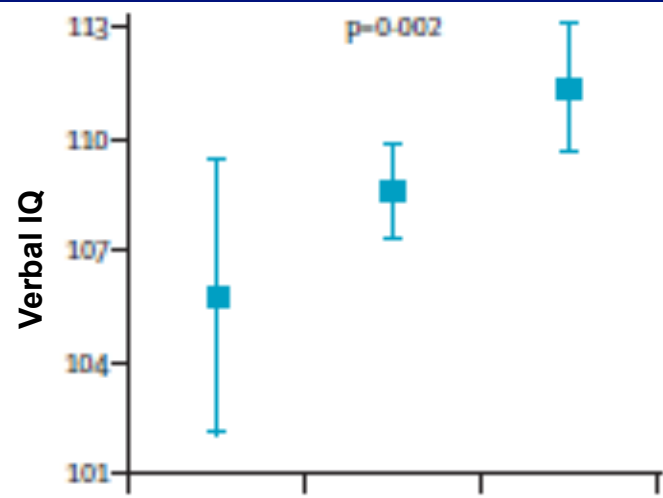


Effect of inadequate iodine status in UK pregnant women on cognitive outcomes in their children: results from the Avon Longitudinal Study of Parents and Children (ALSPAC)

Sarah C Bath, Colin D Steer, Jean Golding, Pauline Emmett, Margaret P Rayman

Methods We analysed mother–child pairs from the Avon Longitudinal Study of Parents and Children (ALSPAC) cohort by measuring urinary iodine concentration from 1040 first-trimester (median 10 weeks) pregnant women, and a measure of intelligence quotient (IQ) in the off spring at age 8 years.

Women's results for iodine-to-creatinine ratio were dichotomised to less than 150 $\mu\text{g/g}$ or 150 $\mu\text{g/g}$ or more on the basis of WHO criteria for iodine deficiency or sufficiency in pregnancy.



Maternal iodine-to-creatinine ratio (mcg/g) in the first trimester

Maternal iodine-to-creatinine ratio (mcg/g) in the first trimester

Iodine supplementation

- 133 women supplemented with 300mcg of potassium iodine (<10w)
- 61 women not supplemented
- Children 3-18 months tested

	No Iodine	Iodine 300	P value
MDI	108.9	109.2	ns
PDI	102.6	108.6	0.02

Hypothyroxinemia

Case-Control Studies

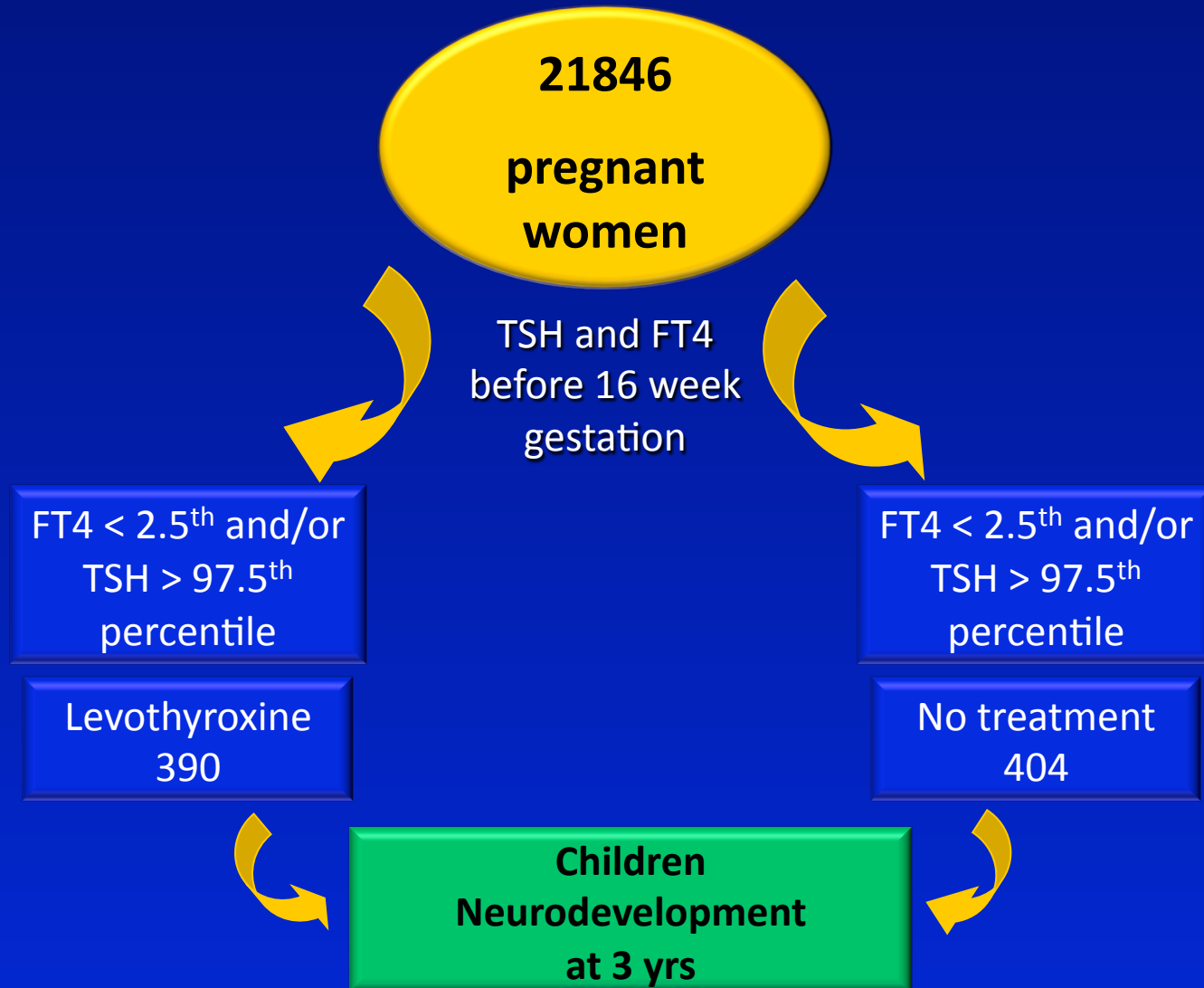
(Henrichs J. JCEM 2010)

- **Mild Hypothyroxinemia <5% (FT4=0.85ng/dl)**
Expressive language delay at 18 and 30 months
- **Severe Hypothyroxinemia <10% (FT4=0.91ng/dl)**
Expressive language delay at 18 and 30 months
Nonverbal cognitive delay at 30 months

(Ghassabian A. JCEM 2014)

- **Hypothyroxinemia <5% (FT4=0.85ng/dl)**
4.3 points IQ lower at 6 yr

Antenatal Thyroid Screening and Childhood Cognitive Function



Antenatal Thyroid Screening and Childhood Cognitive Function

Cognitive function of children from women with TSH above the 97.5th percentile, FT4 below the 2.5th percentile, or both show similar IQ whether treated or untreated with LT4.

Recommendations

- ATA, ES, AACE
 - Daily iodine intake should be at least 250 μg
 - Recommend that all pregnant and breast-feeding women take a prenatal vitamin that contains 150 μg of potassium iodide

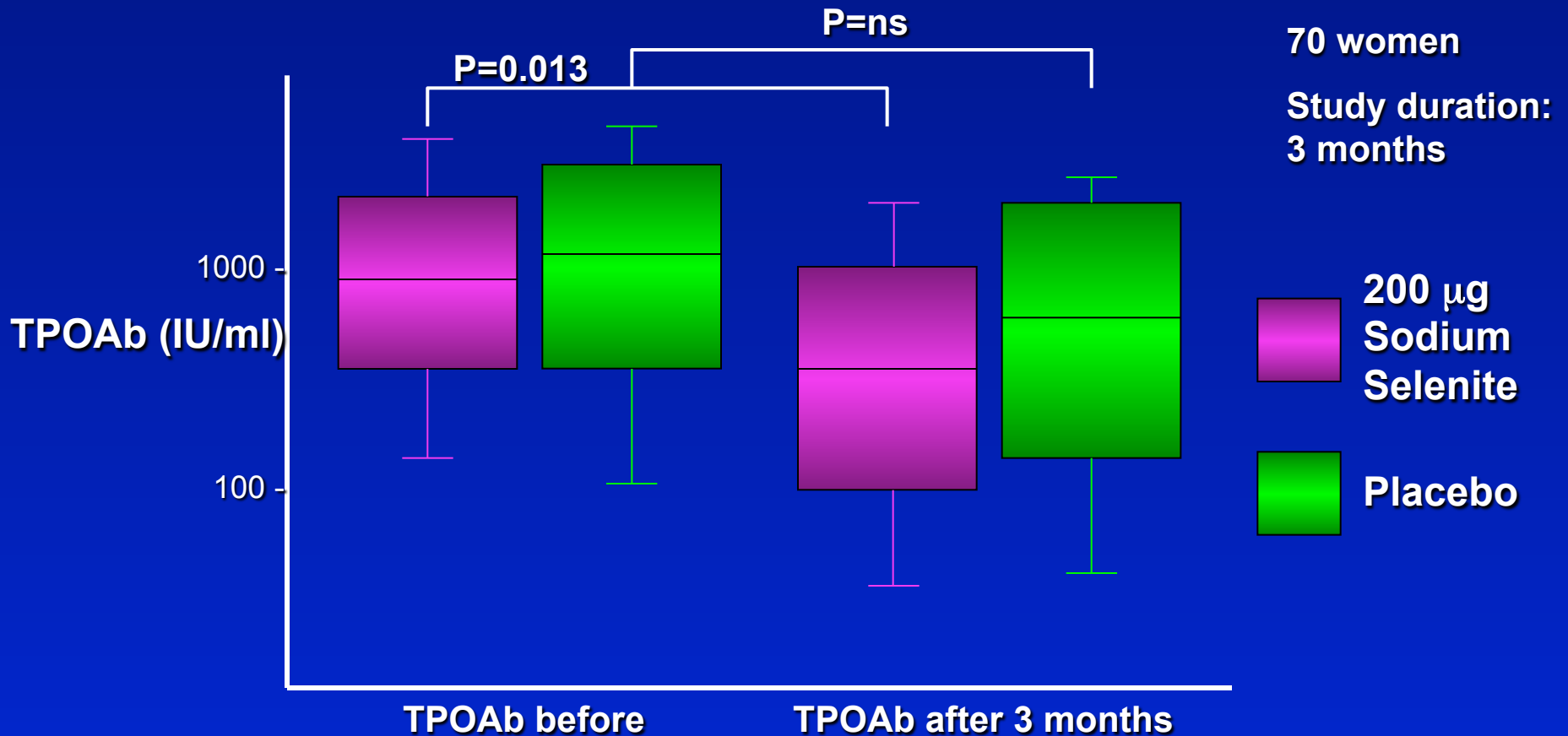
Something about Selenium

- Selenium (Se) is an essential mineral which is incorporated into polypeptide chain as part of the amino acid **selenocysteine** (Sec)
- The group of proteins that contain Sec as an integral part of their polypeptide chain are defined as **selenoproteins**
- Selenoproteins exert multiple effects, mostly associated with **oxidoreductase** functions

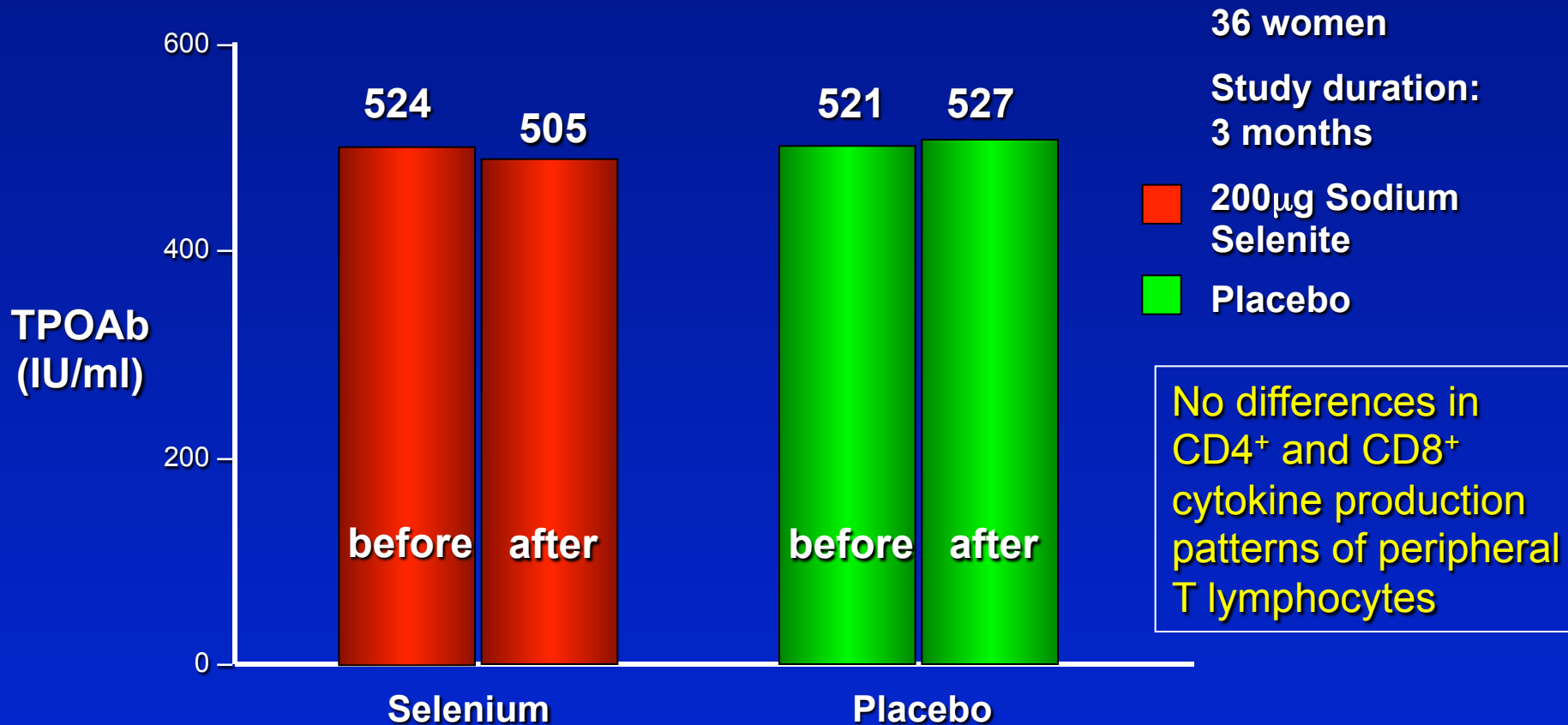
Human Selenoproteins

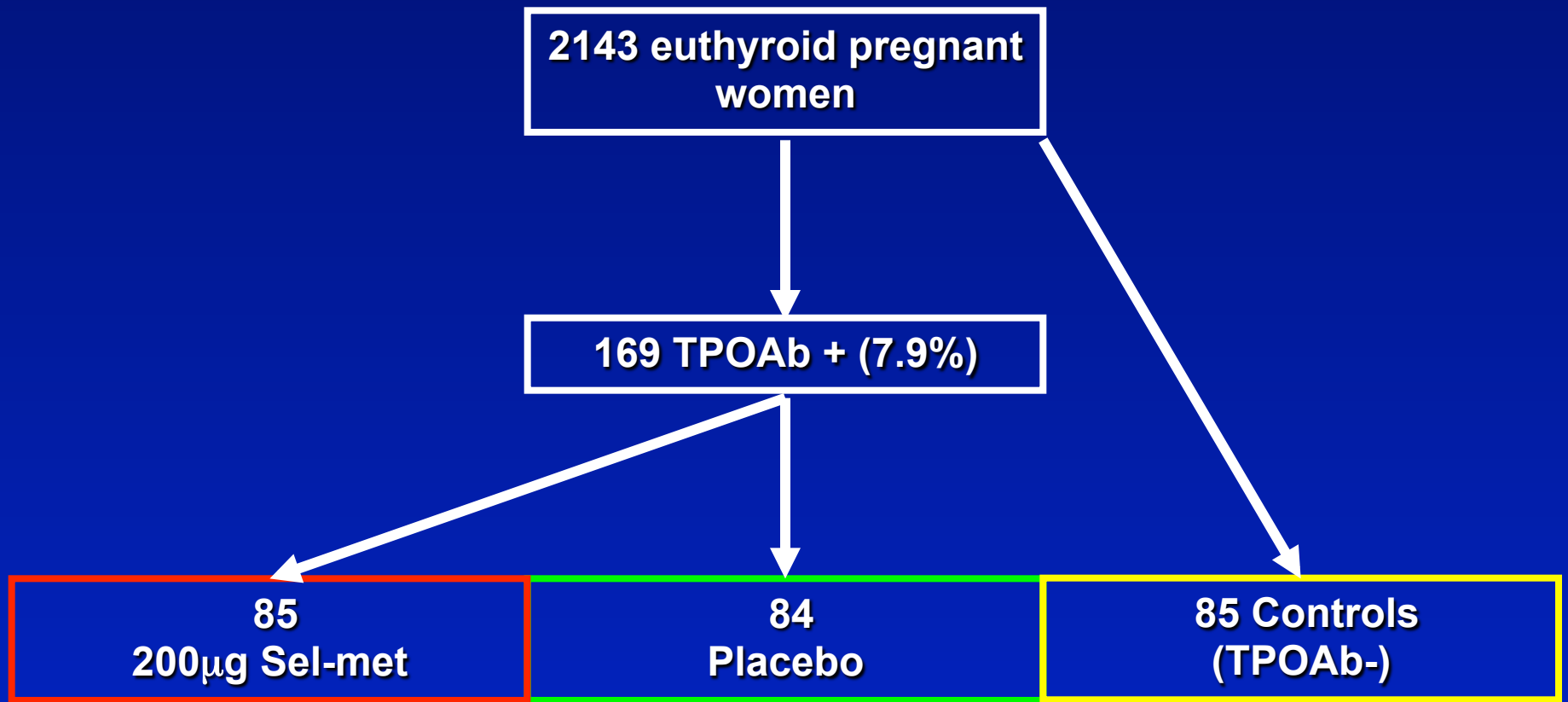
Antioxidant enzymes	Redox signalling	Thyroid hormones metabolism	Sec synthesis	Transport and storage of Se	Protein folding	Unknown function
GPx1	Trx R1	DIO 1	SPS 2	Sel P	SelP15	Sel H
GPx2	Trx R2	DIO 2			Sel N	Sel I
GPx3	Trx R3	DIO 3			Sel M	Sel O
GPx4					Sel S	Sel T
GPx6						Sel V
Sel K						
Sel R						
Sel W						

Selenium Reduces TPOAb Titers in Patients with Hashimoto's Thyroiditis



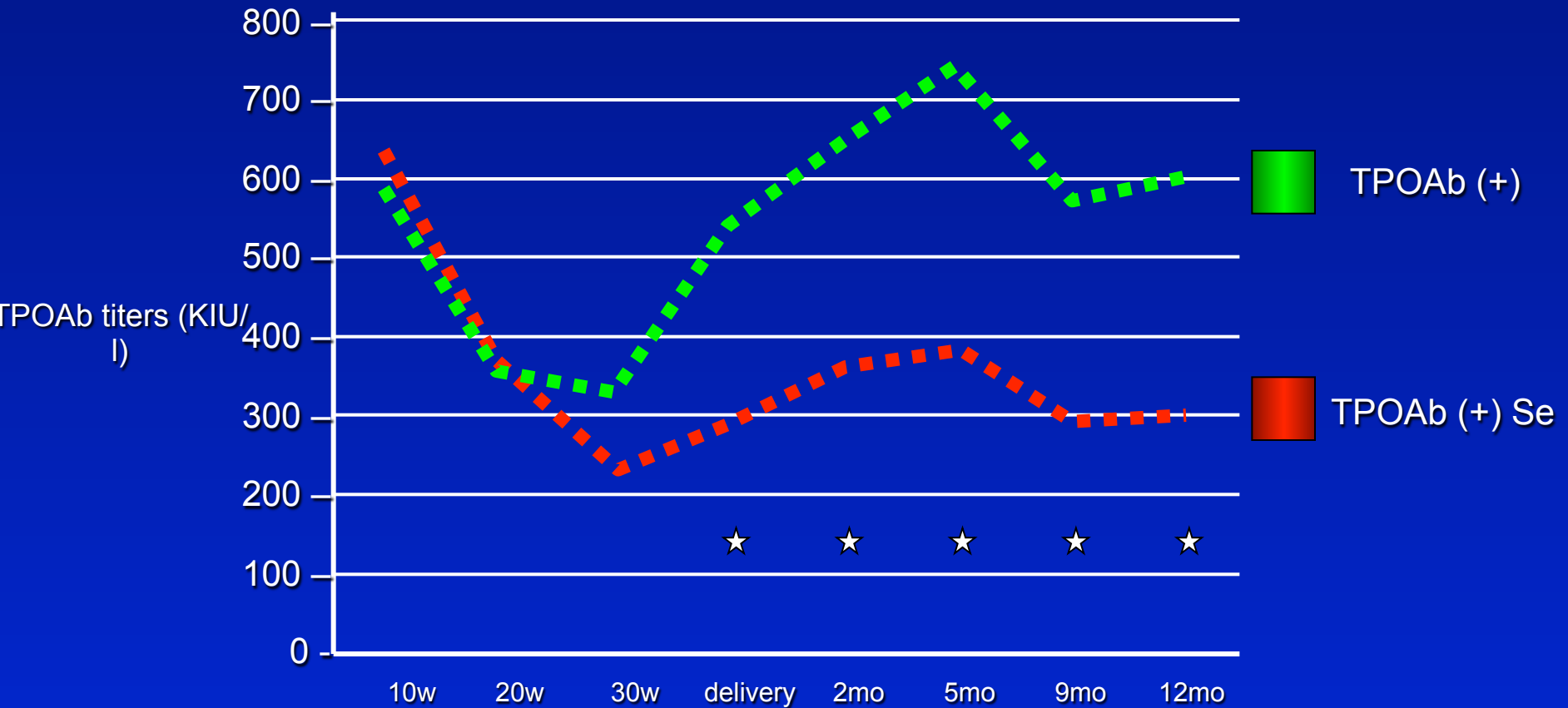
No Benefits From Selenium in Autoimmune Thyroiditis



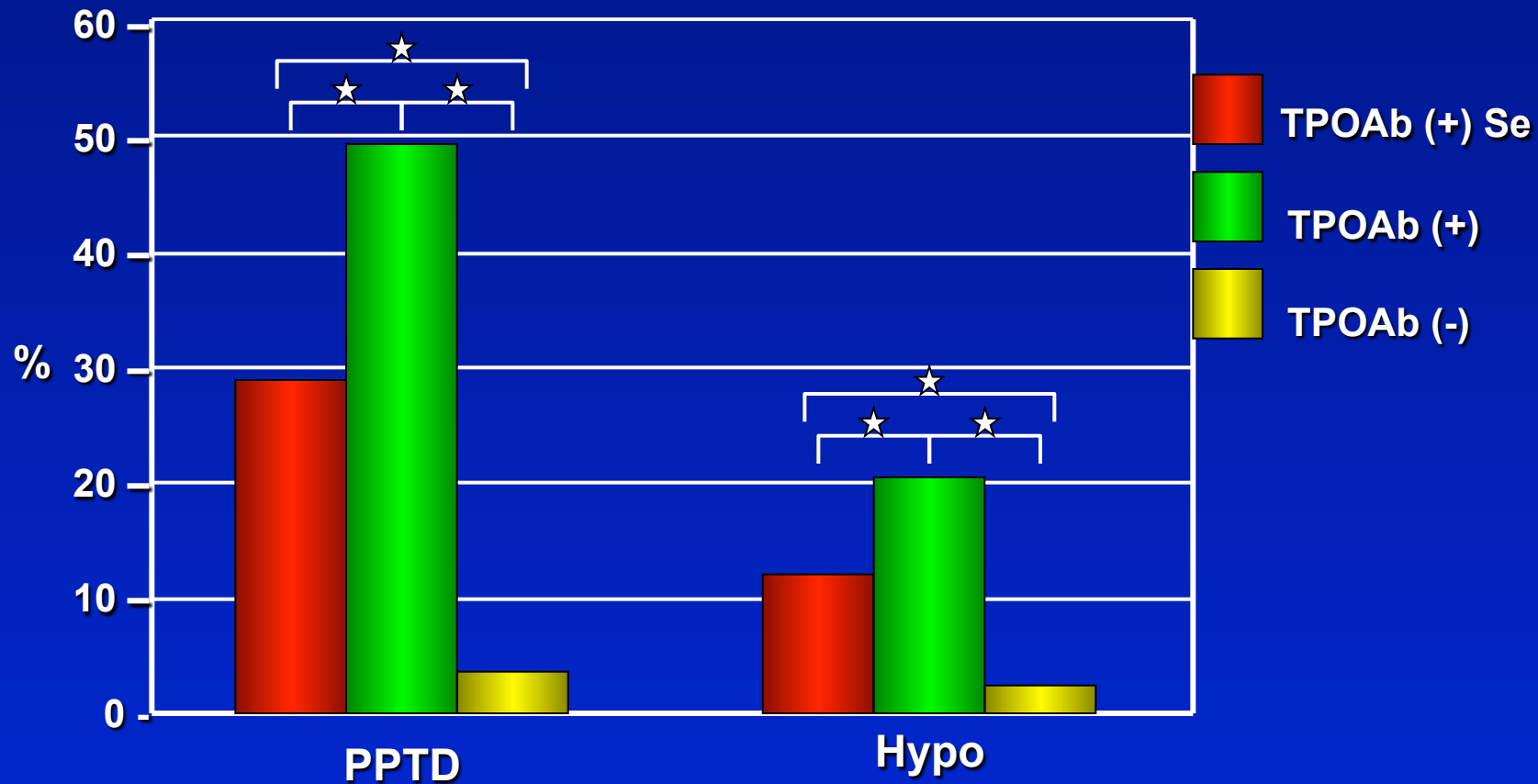


PPTD

Postpartum Thyroiditis: Selenium Effects on TPOAb Titers



Postpartum Thyroiditis: Selenium Effects on PPTD and Permanent Hypo



Guidelines of the American Thyroid Association for the Diagnosis and Management of Thyroid Disease During Pregnancy and Postpartum

The American Thyroid Association Taskforce on Thyroid Disease During Pregnancy and Postpartum

■ **RECOMMENDATION 21**

A single RCT has demonstrated a reduction in postpartum thyroiditis from selenium therapy. No subsequent trials have confirmed or refuted these findings. At present, selenium supplementation is not recommended for TPOAb+ women during pregnancy. **Level C-USPSTF**

Condition	ATA 2011	ES 2012	ETA 2014
Overt hypothyroidism	LT4 Recommended	LT4 Recommended	LT4 Recommended
Subclinical hypothyroidism (TPOAb+)			
Subclinical hypothyroidism (TPOAb-)			
HypoT4			

TSH reference range

TSH	First trimester	Second trimester	Third trimester
Haddow	0.08-2.73	0.39-2.70	
Stricker	0.09-2.83	0.20-2.79	0.31-2.90
Panesar	0.3-2.30	0.03-3.10	0.13-3.50
Soldin	0.24-2.99	0.46-2.95	0.43-2.78
Vermiglio	0.03–2.3	0.29–2.8	0.34–3.0

TSH reference range

TSH (first trimester)	2.5 Percentile	97.5 Percentile
Asian	0.02	2.81
Black	0.01	2.40
Hispanic	0.02	2.69
White	0.11	2.69

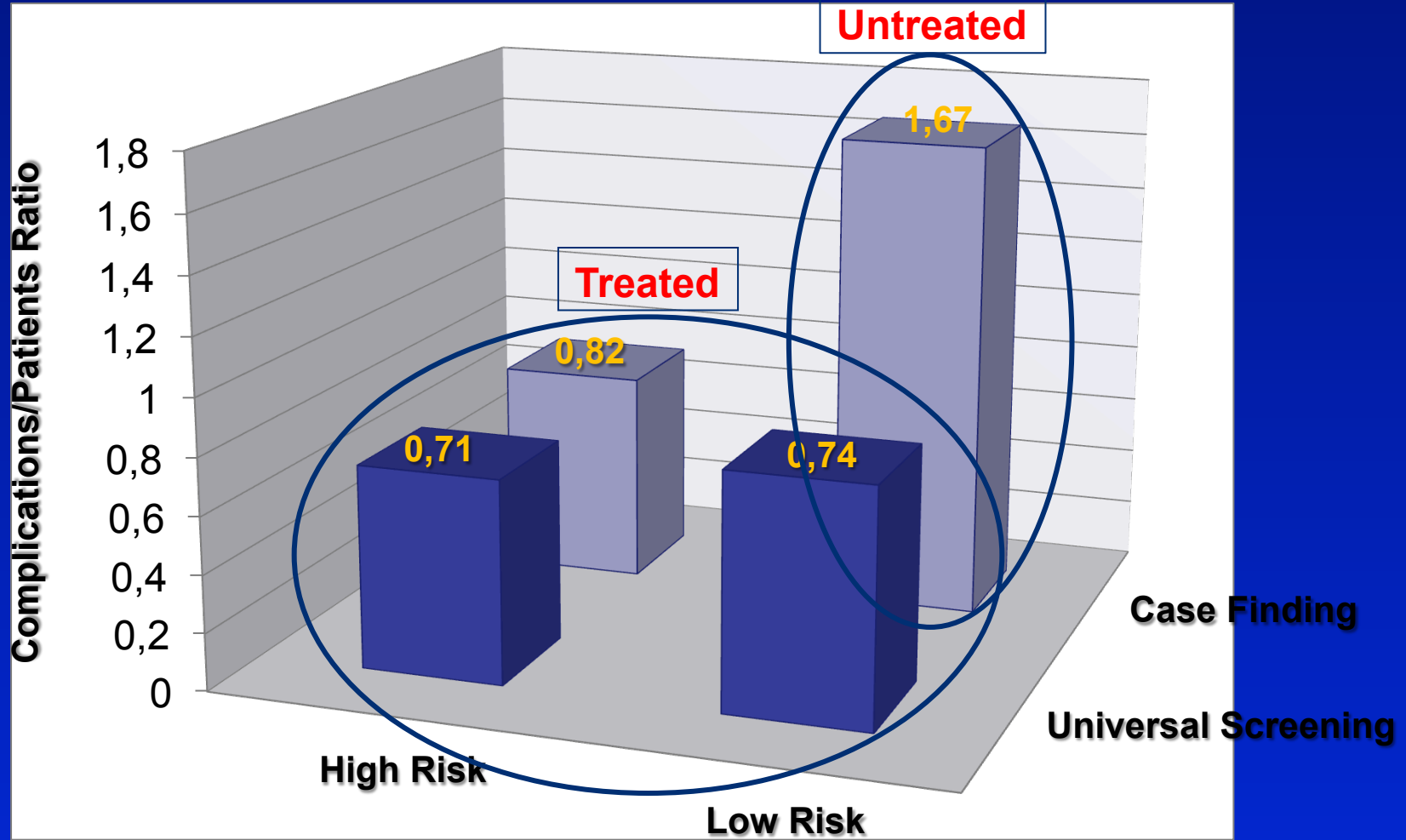
TSH reference range

First trimester	Second trimester	Third trimester
0.1-2.5	0.2-3.0	0.3-3.5

TSH and Miscarriage

Author	Results
Benhadi (2009)	<p>Fetal loss vs No fetal loss TSH 1.48 vs 1.11 mIU/L</p> <p>Incidence of child loss increased by 60% for every doubling of TSH</p>
Negro (2010)	<p>TSH < 2.5 vs 2.5-5.0 Preg. loss 3.6% vs 6.1%</p>
Ashoor (2010)	<p>Fetal loss vs No fetal loss TSH 1.1 vs 1.0 mIU/L</p>

Universal Screening vs Case-Finding for Detection and Treatment of Thyroid Hormonal Dysfunction During Pregnancy



Condition	ATA 2011	ES 2012	ETA 2014
Overt hypothyroidism	LT4 Recommended	LT4 Recommended	LT4 Recommended
Subclinical hypothyroidism (TPOAb+)	LT4 Recommended	LT4 Recommended	LT4 Recommended
Subclinical hypothyroidism (TPOAb-)			
HypoT4			

Condition	ATA 2011	ES 2012	ETA 2014
Overt hypothyroidism	LT4 Recommended	LT4 Recommended	LT4 Recommended
Subclinical hypothyroidism (TPOAb+)	LT4 Recommended	LT4 Recommended	LT4 Recommended
Subclinical hypothyroidism (TPOAb-)	Insufficient evidence to recommend for or against LT4	LT4 Recommended	LT4 Recommended
HypoT4			

SCH

Studies of Association

Author	Year	Country	n° of SCH	Type of study	Trimester	Definition of SCH	Miscarriage	Fetal Death	Pre term Delivery	Gestation Diabetes	Hyper tension	Eclampsia	Placental Abruption	Low Birth Weight
Leung	1993	USA	45	Retrospecti		> 5.0					+			
Allan	2000	USA	209	Retrospecti	2	> 6.0		+						
Casey	2005	USA	404	Prospective	2	2.74-5.09			+				+	
Cleary-G.	2008	USA	240	Prospective	1 & 2	4.0 & 4.3	-		-	-	-	-	-	
Mannisto	2009	Finland	224	Prospective	1	> 3.6	-	-	-					-
Sahu	2010	India	41	Prospective	2	> 5.5			-		-			-
Kuppens	2010	Netherlan	108	Prospective	1	> 2.5								
Mannisto	2010	Finland	224	Prospective	1	> 3.6				-	-		-	
Negro	2010	Italy	642	Prospective	1	2.5-5.0	+		-					
Goel	2011	India	34	Prospective	1, 2, 3	> 5.0			-		-	-	-	
Su	2011	China	41	Prospective	1 & 2	> 4.3	-	-	+					
Wilson	2012	USA	528	Prospective	1 & 2	> 4.1					+	+		
Tudela	2012	USA	528	Prospective	1 & 2	> 4.1				+				
Schneuer	2012	Australia	152	Retrospecti	1st	> 2.9	+	-	+			-		
Karakosta	2012	Greece	79	Prospective	1 & 2	2.5 & 2.7			-	+				+
Korevaar	2013	Netherlan	188	Prospective	1 & 2	4,04			+					

Antenatal Thyroid Screening and Childhood Cognitive Function

Cognitive function of children from women with TSH above the 97.5th percentile, FT4 below the 2.5th percentile, or both show similar IQ whether treated or untreated with LT4.

TSH reference range

TSH	First trimester	Second trimester	Third trimester
YQ Yan (China)	0.03-4.51	0.05-4.50	0.47-4.54
Marwaha (India)	0.6-5.0	0.44-5.78	0.74-5.7
Li C (China)	0.12-5.08		



The prevalence of subclinical hypothyroidism in the 4,800 pregnant women was 27.8% on the diagnostic criteria of TSH > 2.5 mIU/L utilizing the reference interval derived by our laboratory. Of those with first trimester TSH > 2.5 mIU/L, 20% in the second, and 30% in the third trimester had TSH > 3.0 mIU/L.

Condition	ATA 2011	ES 2012	ETA 2014
Overt hypothyroidism	LT4 Recommended	LT4 Recommended	LT4 Recommended
Subclinical hypothyroidism (TPOAb+)	LT4 Recommended	LT4 Recommended	LT4 Recommended
Subclinical hypothyroidism (TPOAb-)	Insufficient evidence to recommend for or against LT4	LT4 Recommended	LT4 Recommended
HypoT4	Should not be treated	At the discretion of the caregiver	May be considered in the first trimester

1. La supplementazione iodica in gravidanza è raccomandata, ma non esistono RCT a supporto
2. La supplementazione con Se ha dimostrato di ridurre PPTD, ma non è raccomandata
3. La terapia con LT4 in caso di ipotiroidismo subclinico è raccomandata, ma le evidenze a supporto sono scarse

