

Controlled Antenatal Thyroid Screening (CATS) II: long-term cardiometabolic effects of treating maternal sub-optimal thyroid function

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Introduction

- Alterations of the thyroid function, even if minor, have been found to affect body composition and cardiometabolic risk in adults (1,2). Similar effects of maternal thyroid function on offspring have not been investigated so far.
- The Controlled Antenatal Thyroid Screening (CATS) study I was a randomized trial investigating the effects of levothyroxine (LT4) treatment for suboptimal gestational thyroid function (SGTF) on offspring's cognitive function. SGTF was defined as FT4 <2.5th percentile and/or TSH >97.5th percentile at 12 weeks median gestation (3). The CATS II is a follow-up study evaluating cognitive outcomes in the offspring at a later mean age of 9.5 years (4).

Objectives

Evaluate in CATS II cohort whether SGTF and LT4 correction impact on long-term anthropometric - cardiometabolic outcomes of mothers and children.

Methods

332 mothers (and 326 paired children) evaluated 5-11 years after pregnancy:

- 197 with normal gestational thyroid function (NGTF)
- 56 with untreated SGTF (SGTF-U)
- 79 with treated SGTF (SGTF-T): 150 µg LT4 daily

Data collection:

- Medical & lifestyle history
- Body mass index (BMI). For children BMI standard deviation scores (SDS) were also considered, based on UK 1990 reference population (5,6). For mothers CATS II BMI was also compared with baseline BMI at CATS I.
- Current thyroid function (TSH, FT4, FT3, TPOAb)
- Blood (fasting) metabolic indicators: insulin, glucose, adiponectin, full lipid profile (triglycerides, total and HDL cholesterol)
- Vicorder[®] analysis of vascular function: heart rate, systolic pressure, diastolic pressure, augmentation index, total peripheral (vascular) resistance, aortic pulse wave velocity.
- Dual-energy x-ray absorptiometry (DXA) scan of lean/fat mass

Comparison of NGTF, SGTF-U, SGTF-T groups using Linear Regression adjusted for age, social class, ethnicity, smoke during pregnancy, gender (children).

Results - Children

- Age at evaluation (mean ± SD): 9.3 ± 1.0 years.
- Gender: 168 males (M): 51.5%, 158 females (F): 48.5%.
- No significant differences were observed across the 3 groups in terms of:
 - BMI SDS, but tot children were +0.49 SDS compared with 1990 (Tab 1)
 - Vicorder[®] and DXA scan analyses
 - Blood metabolic indicators and thyroid function

	TOT	NGTF	SGTF-U	SGTF-T	p ¹	p ²	p ³
BMI, Kg/m ²	17.2	17.3	17.0	16.8	0.587	0.822	0.464
Median [IQR]	[15.8 - 19.2]	[15.9 - 19.5]	[15.8 - 19.3]	[15.5 - 18.7]			
SDS UK90 mean ± SD	0.49 ± 1.15	0.48 ± 1.15	0.57 ± 1.15	0.46 ± 1.15	0.646	0.763	0.481

p¹: NGTF vs SGTF-U. p²: NGTF vs SGTF-T. p³: SGTF-U vs SGTF-T

References

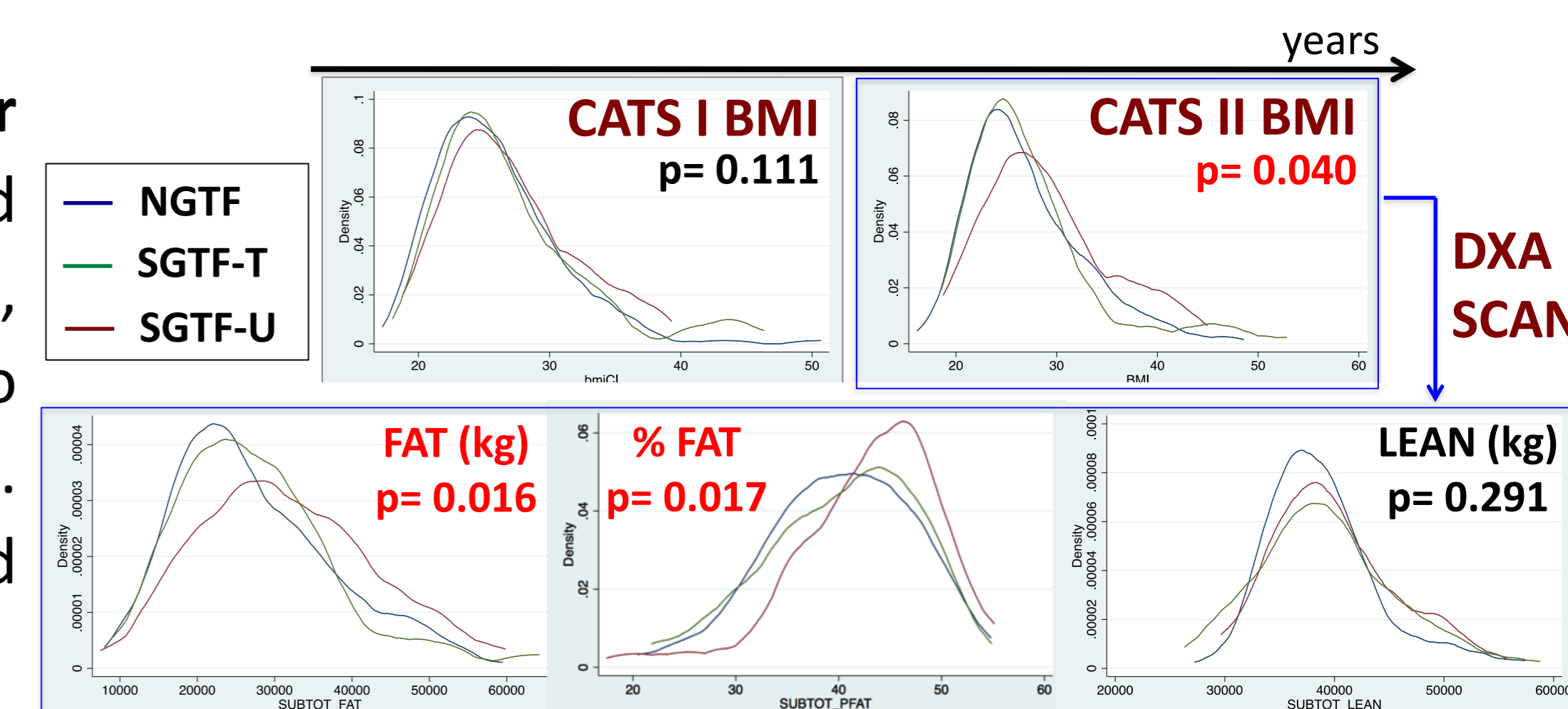
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Results - Mothers

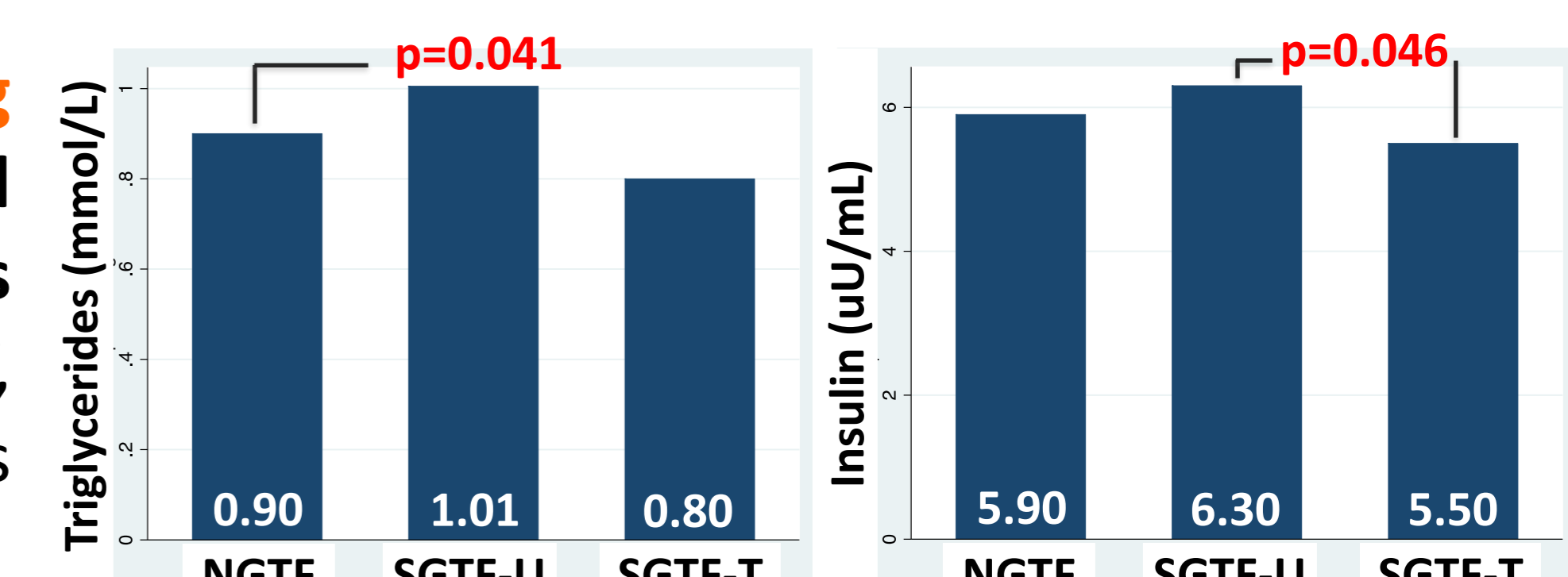
Age at evaluation (mean ± SD): 41.2 ± 5.3 years

No differences in Vicorder[®] analysis data observed across the 3 groups.

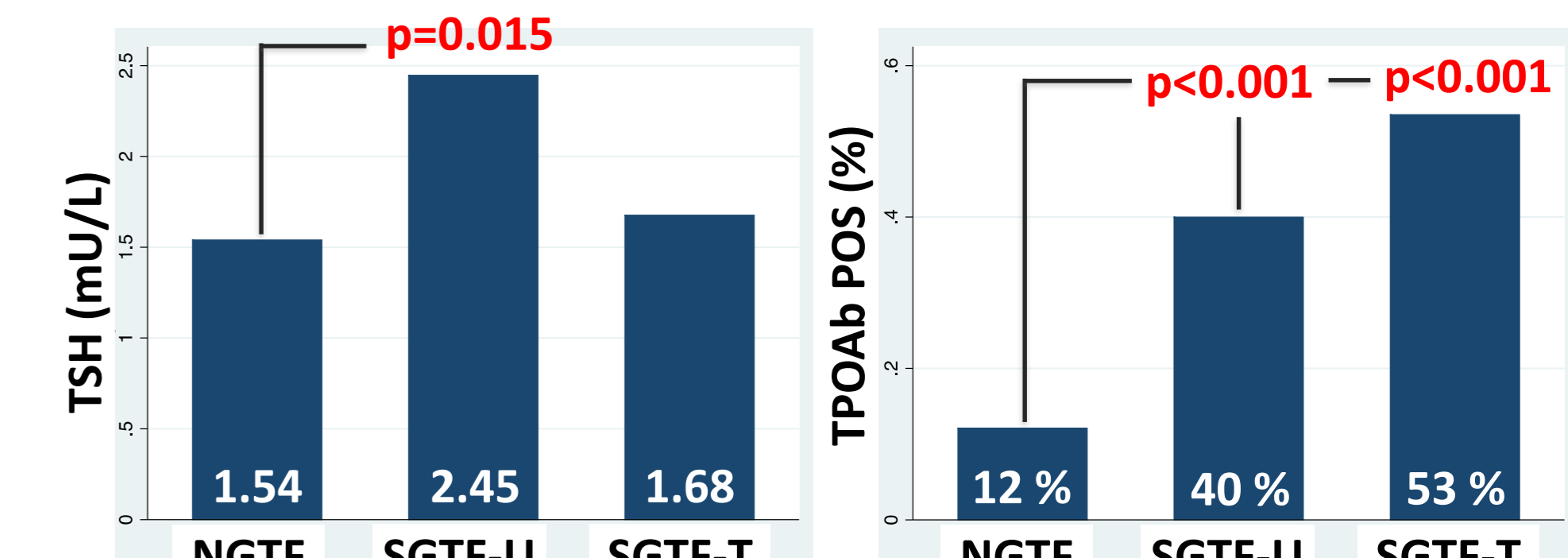
SGTF-U mothers had higher BMI (28.3 Kg/m²) compared with NGTF (25.8 Kg/m²), SGTF-T (25.8 Kg/m²); no difference in CATS I BMI. SGTF-U also had increased fat mass (DXA): Fig 1.



Blood metabolic indicators (Fig 2): SGTF-U had increased triglycerides and insulin levels compared with NGTF and SGTF-T, respectively. No differences among the other parameters.



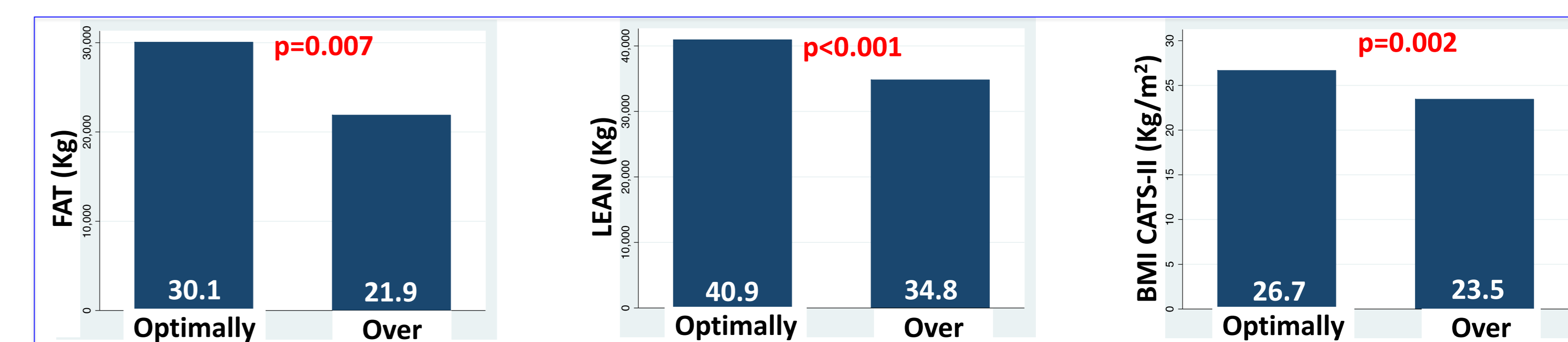
Thyroid function (Fig 3): SGTF-U had higher TSH levels compared with NGTF (no differences in FT4, FT3). As expected TPOAb positive % was higher in both SGTF-U and SGTF-T compared with NGTF.



Only a minority of SGTF-U mothers had been treated with LT4, compared with SGTF-T: data obtained from interviews during CATS II (Tab 2). This likely explains the persistently higher TSH levels in the SGTF-U group.

	TOT (n=294)	NGTF (n=173)	SGTF-U (n=50)	SGTF-T (n=71)	p
NEVER	191 (65.0%)	154 (89.0%)	32 (64.0%)	5 (7.0%)	<0.001
YES stopped	26 (8.8%)	2 (1.2%)	0 (0.0%)	24 (33.8%)	<0.001
YES current	55 (18.7%)	7 (4.0%)	12 (24.0%)	36 (50.7%)	0.004
Unknown	22 (7.5%)	10 (5.8%)	6 (12.0%)	6 (8.5%)	0.549

In CATS I 30% of SGTF-T were overtreated (Over): FT4>97.5th perc (4). Sub analysis showed that Over have been thinner than Optimally treated from baseline (mean height ± SD= 161.8 ± 7.7 cm vs 164.9 ± 7.4 cm respectively, p=0.087; BMI, DXA Fig 4), but received the same dose of LT4 (150 µg daily), causing overtreatment.



Conclusions

- LT4 supplementation of SGTF women during pregnancy did not affect children's anthropometric and cardiometabolic parameters.
- However, screening for SGTF during pregnancy identified women that would benefit from LT4 replacement: absence of such treatment resulted in sustained long-term BMI increase.
- LT4 dose always needs adjustment for body weight and size.
- Today children have higher BMI than 30 years ago, likely resulting from more sedentary lifestyle and unhealthy diet.

