TSH

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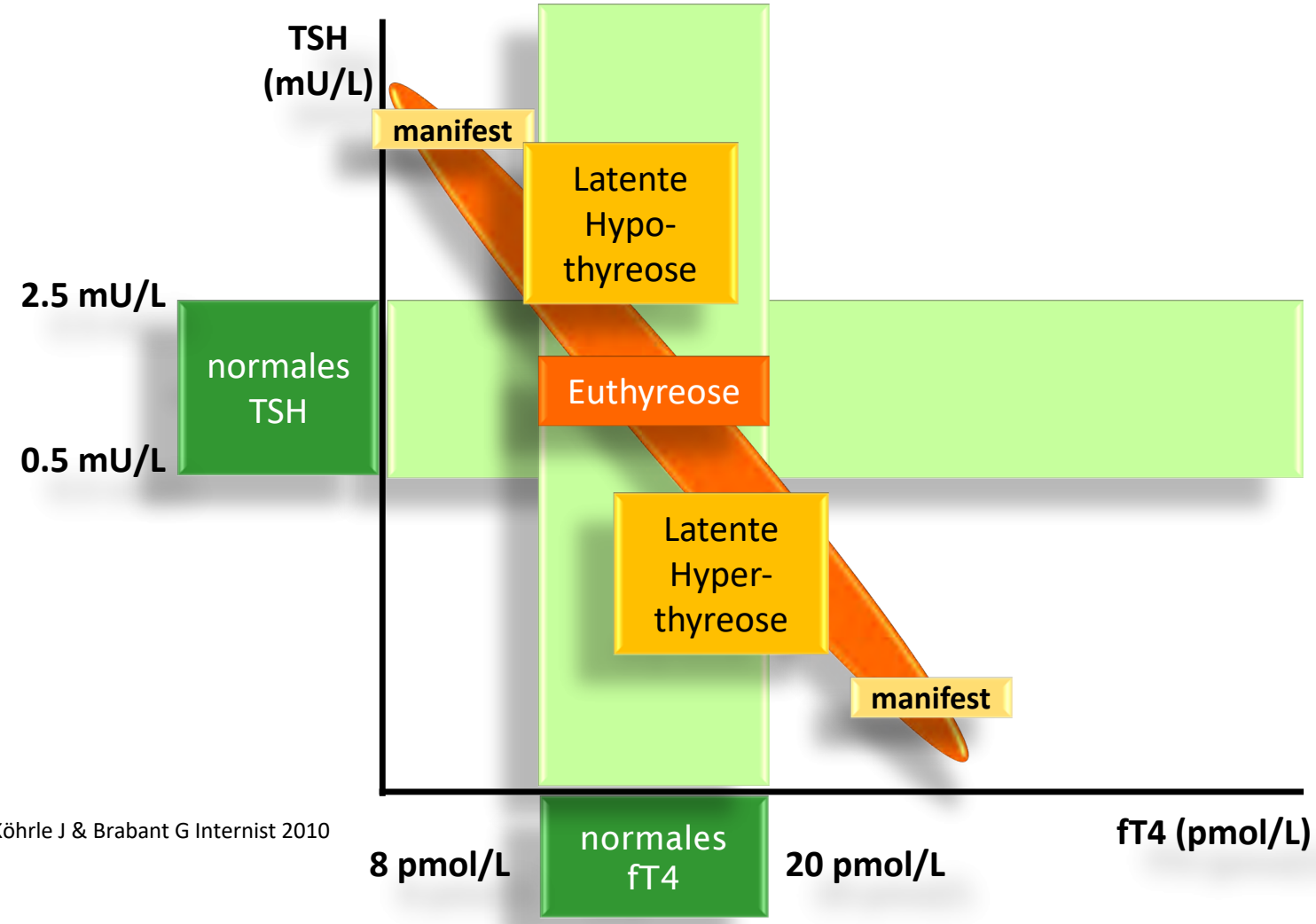
Med. Univ. Wien

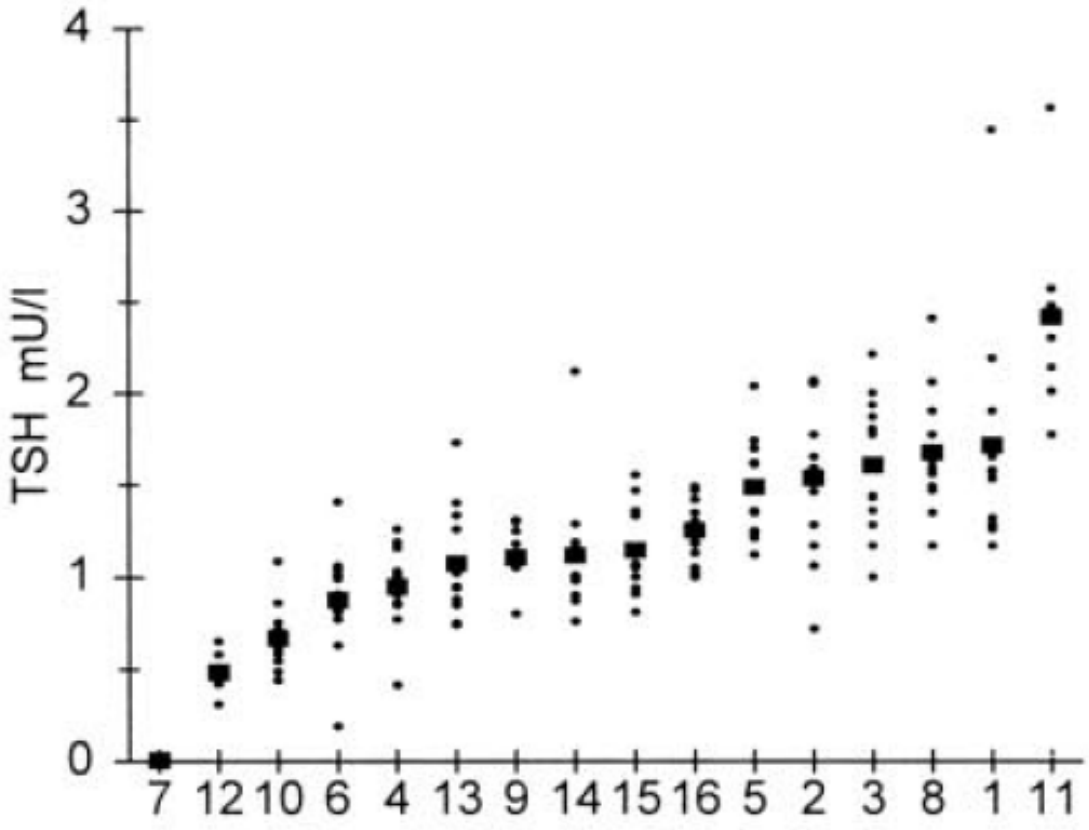
Definitionen



nach Köhrle J & Brabant G Internist 2010

TSH – Individuelle Variation

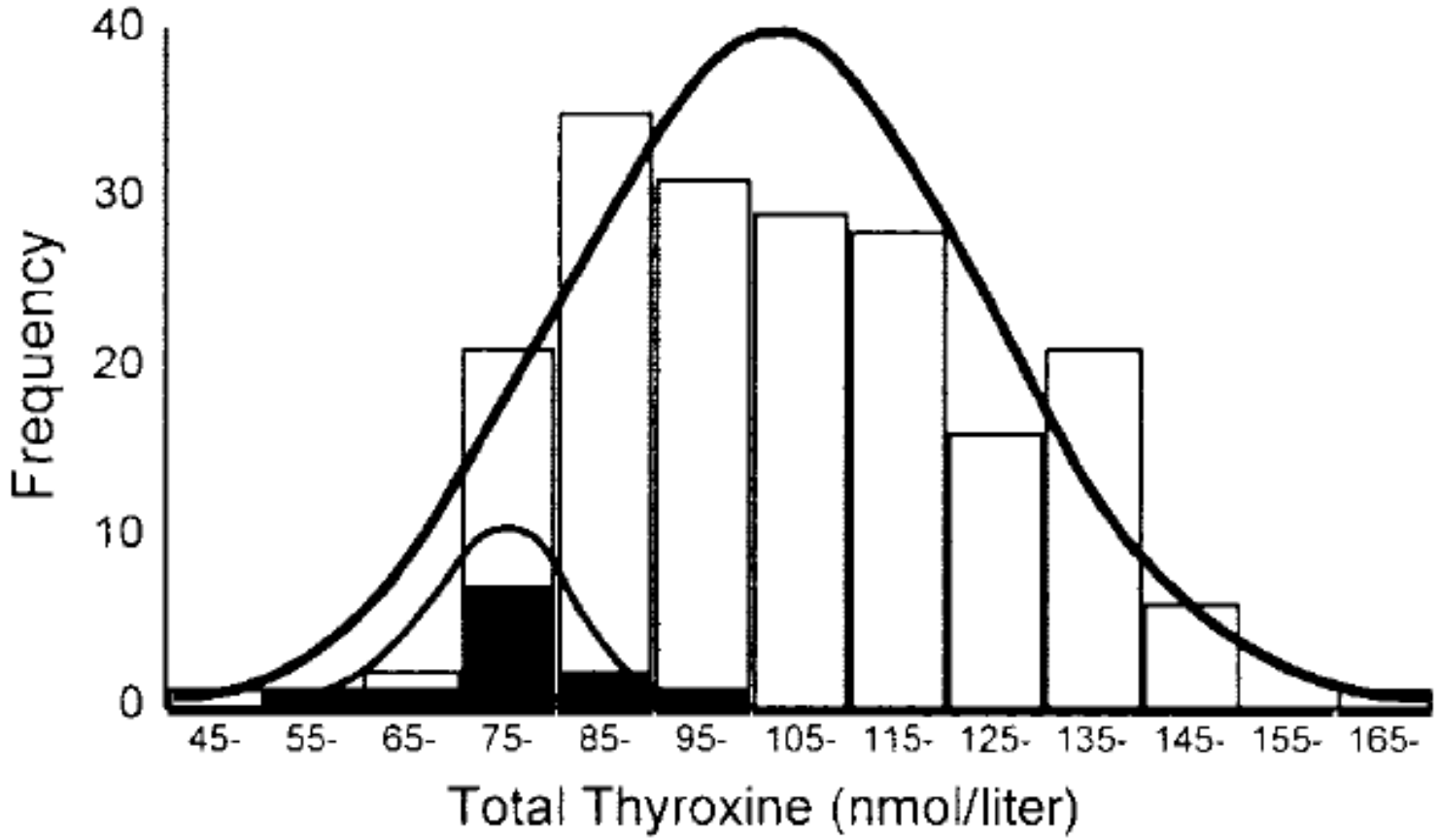
16 gesunde Männer – monatliche Blutabnahmen



Andersen et al., JCEM 87:1068, 2002

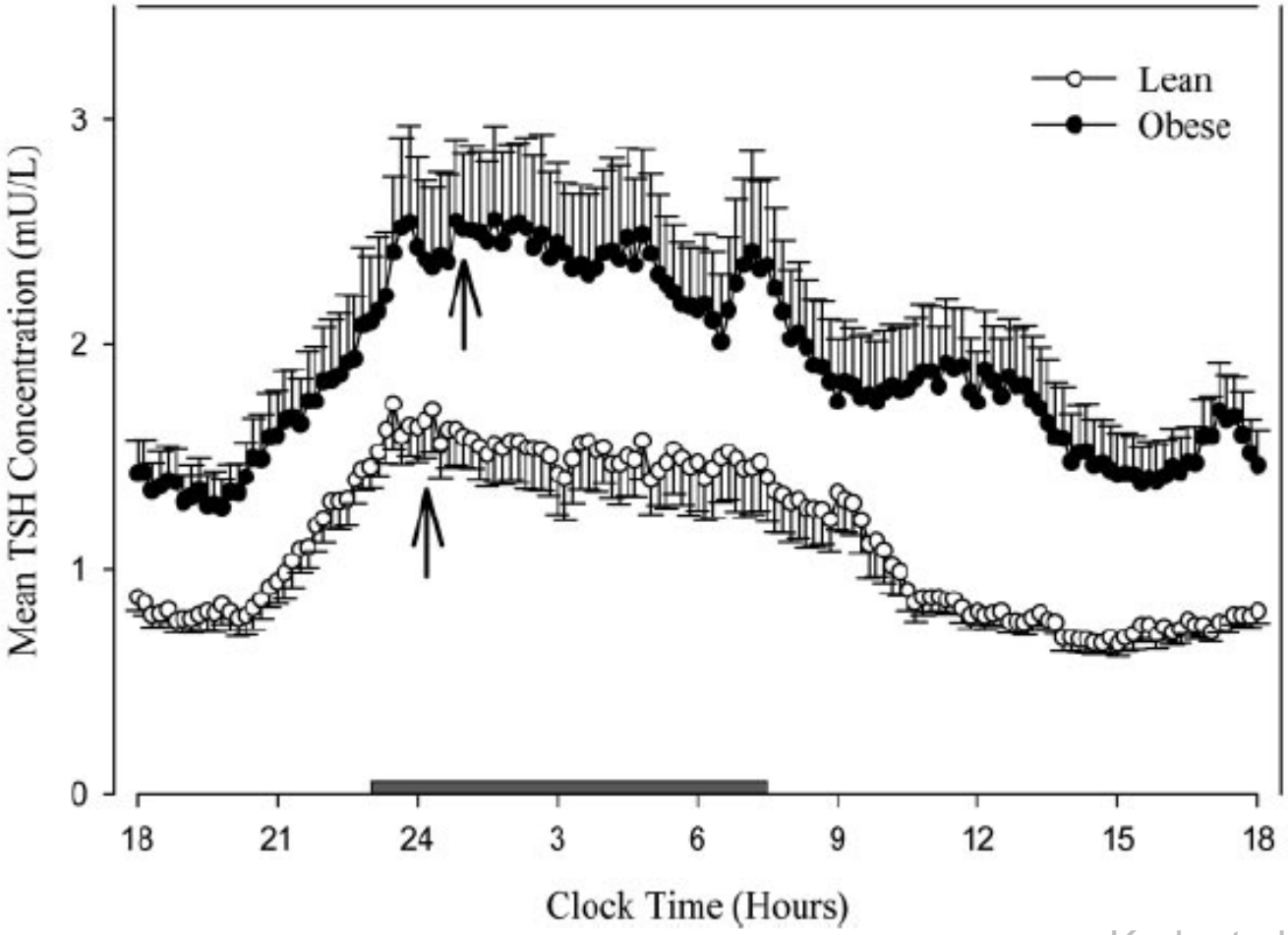
T4 – Individuelle Variation

16 gesunde Männer – monatliche Blutabnahmen



Andersen et al., JCEM 87:1068, 2002

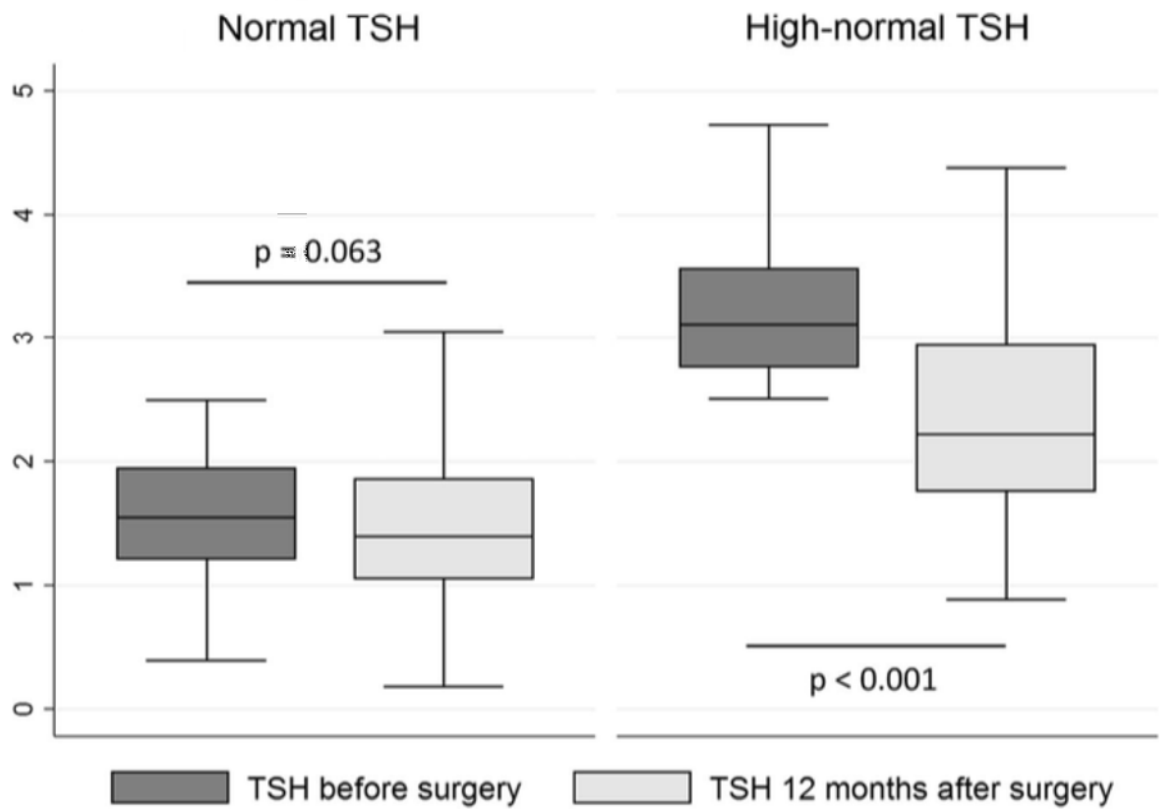
TSH und Adipositas



Kork et al, JCEM, 2005

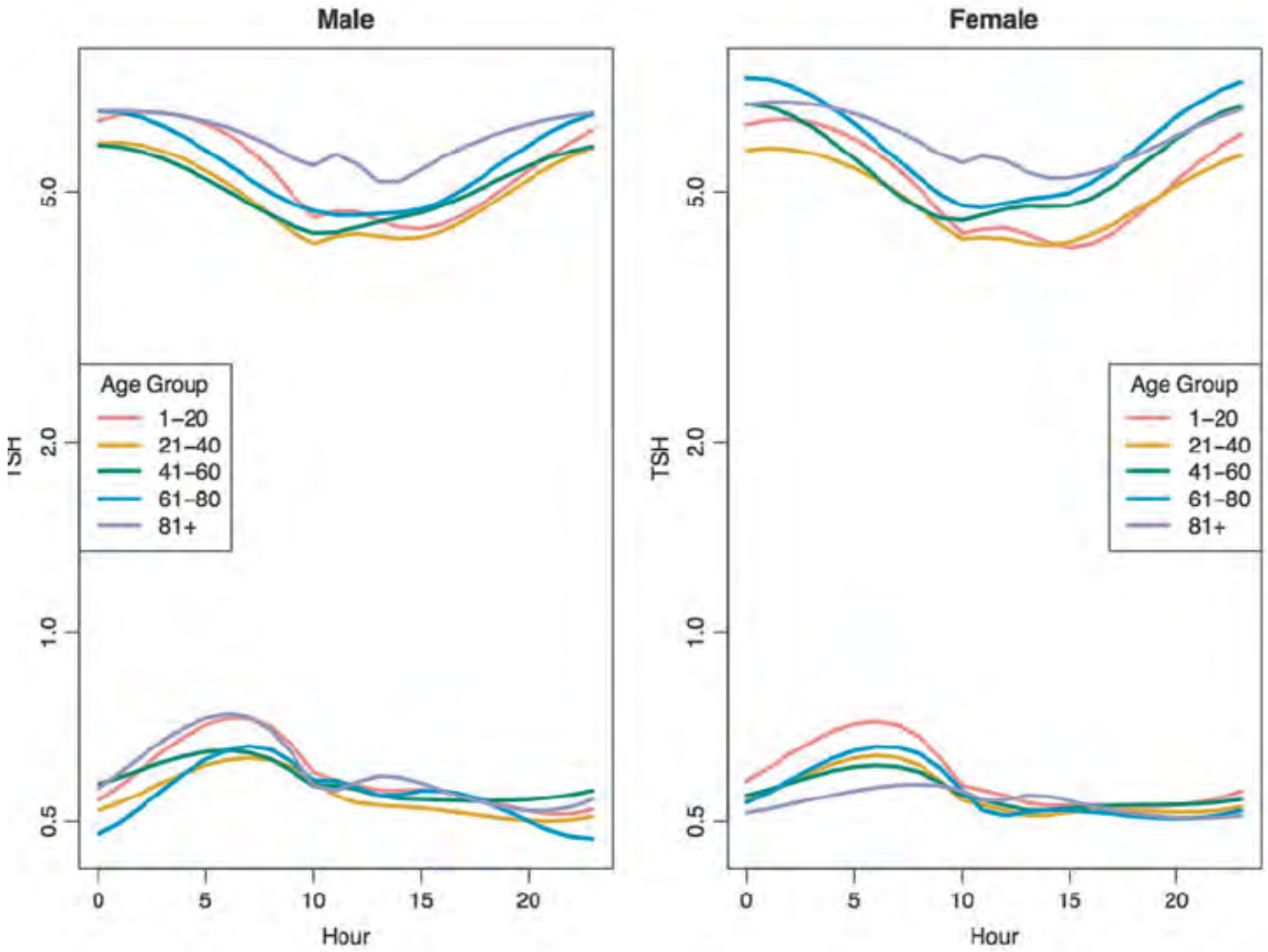
TSH und morbide Adipositas

bariatrische OP n=949



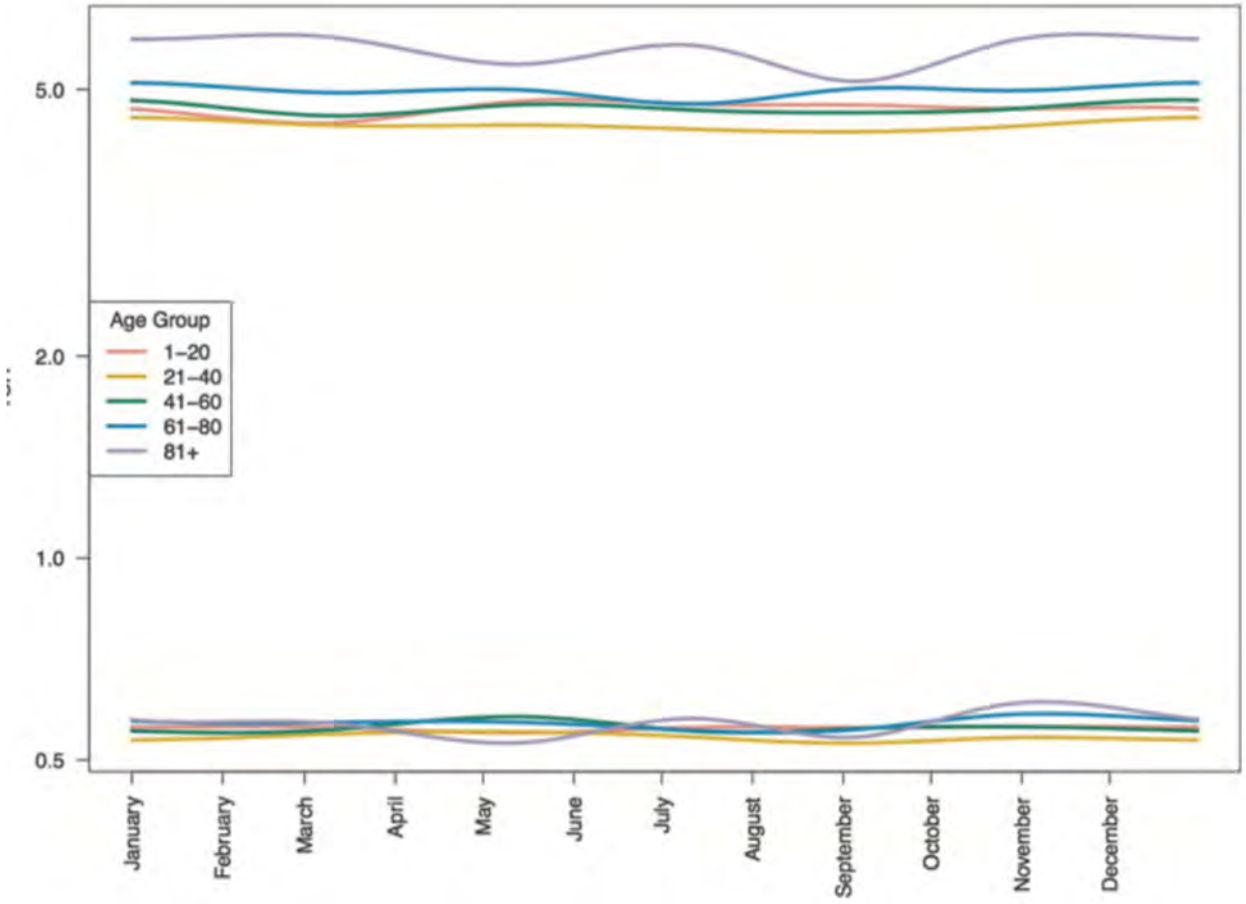
Neves et al, Obes Surg, 2017

TSH – Tageszeit



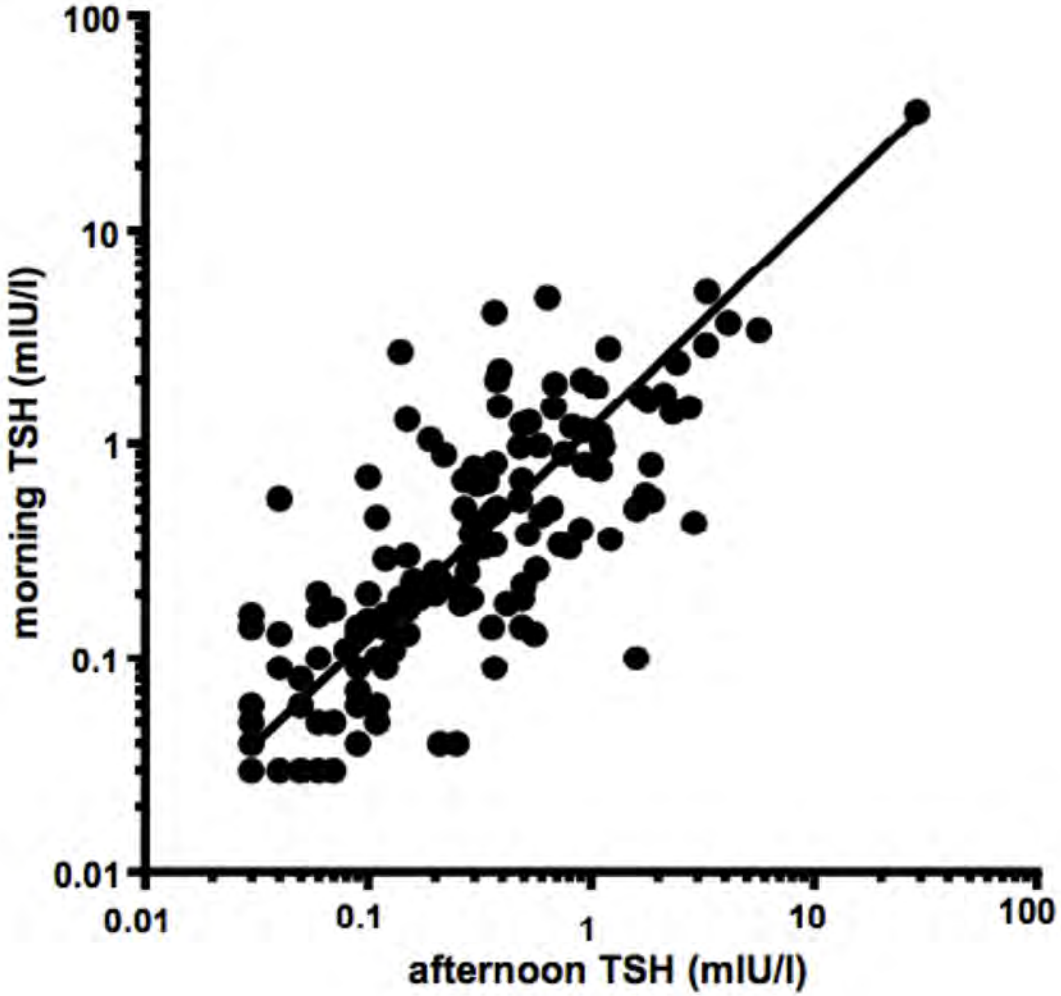
Ehrenkranz et al., Thyroid 2015

TSH– über das Jahr



Ehrenkranz et al., Thyroid 2015

TSH – Tageszeit

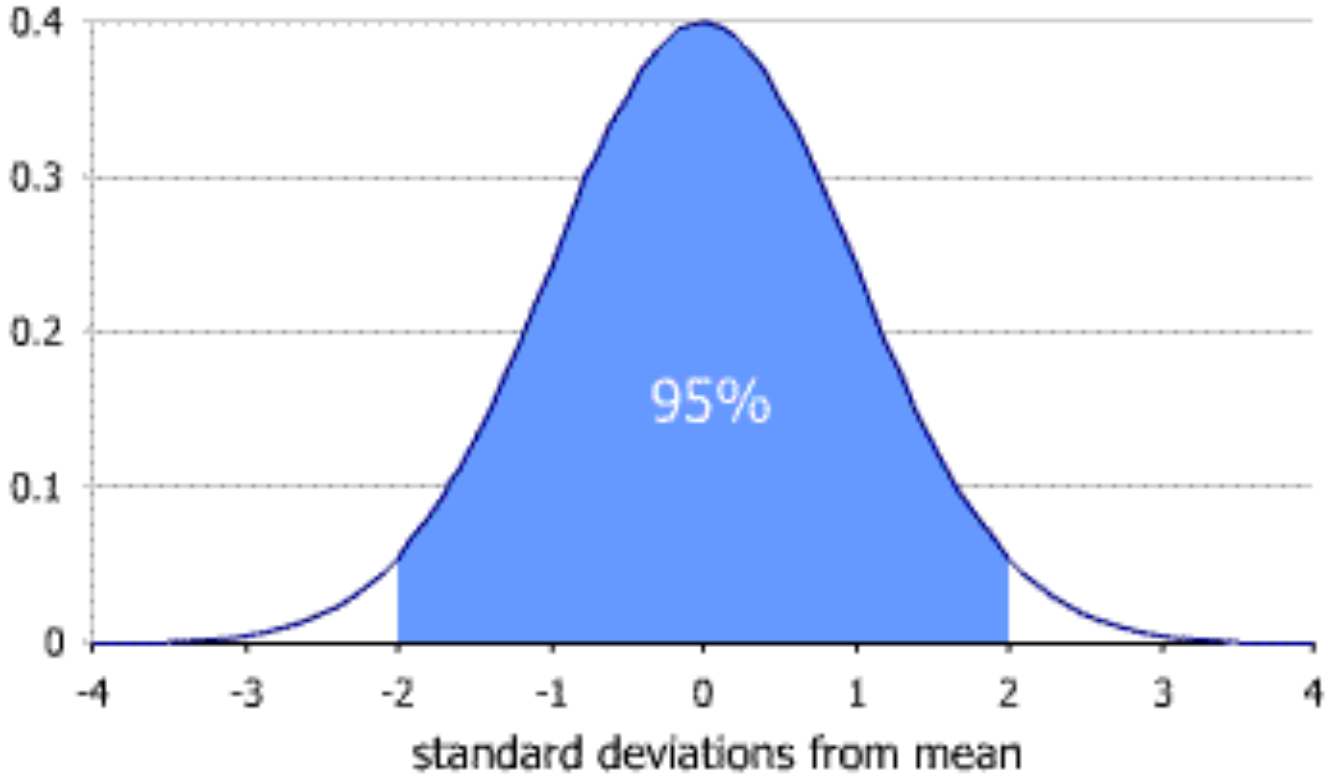


Conte et al., J Endocrinol Invest 2018

TSH

Was ist „normal“

Was ist normal ?
Statistik



TSH, fT4 – 25h Normalwerte

TABLE 8. COMPOSITE 24 HOUR THYROTROPIN AND FREE T4 REFERENCE INTERVALS (2.5–97.5%) BY AGE

Age (years)	*TSH (mIU/L)*	*Free T4 (ng/dL)*
1–20	0.53–6.45	0.78–1.45
21–40	0.52–6.25	0.76–1.44
41–60	0.53–6.55	0.74–1.46
61–80	0.54–6.80	0.75–1.50
80+	0.52–7.55	0.75–1.55

Ehrenkranz et al., Thyroid 2015

Alter: TSH Normalwerte

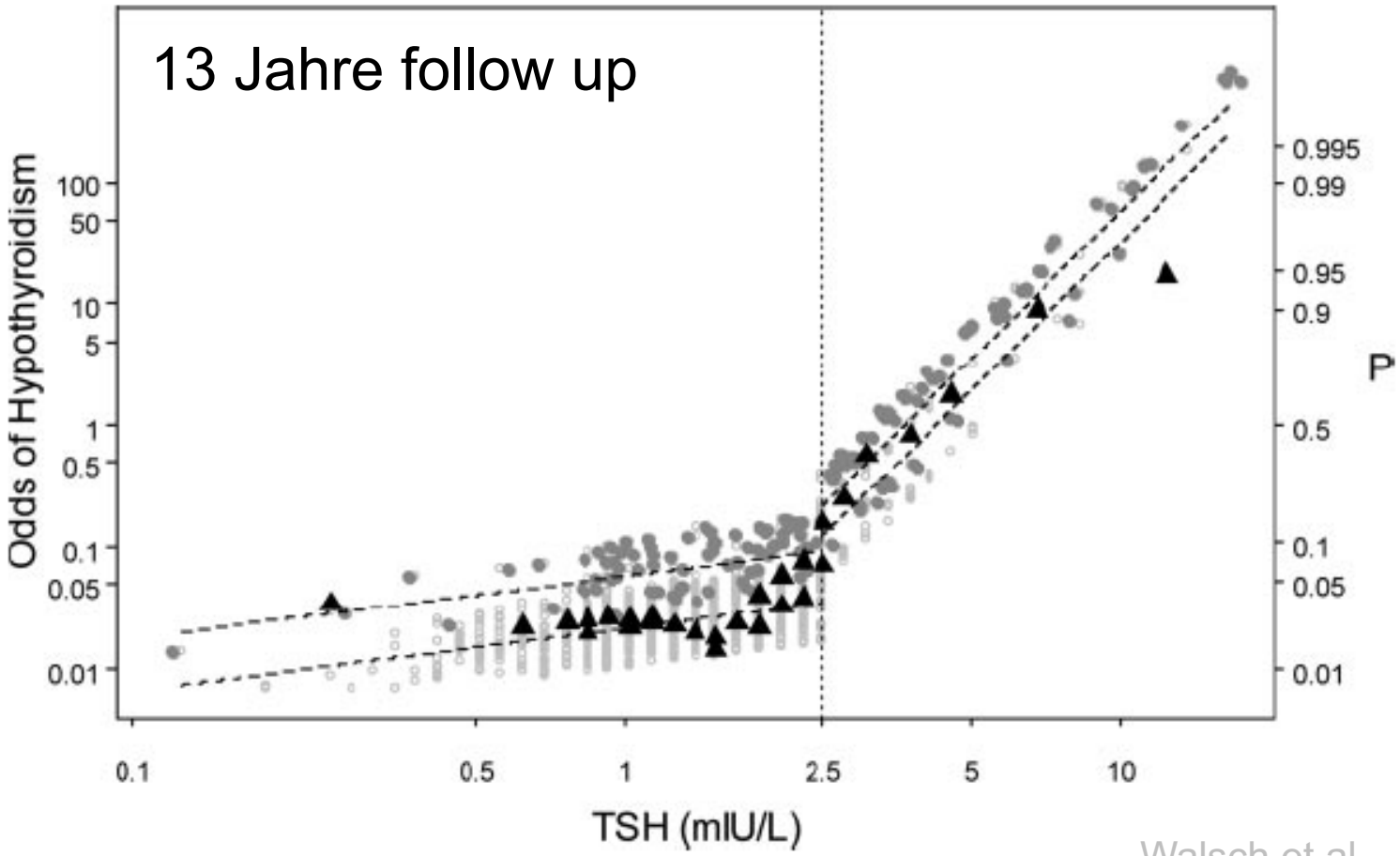
TABLE 2. Age-related reference ranges for TSH derived from the cross-sectional reference group (n = 1751)

Age (yr)	n	TSH reference range (mU/liter) Lower limit	Mean	Upper limit
<30	304	0.51	1.34	3.54
30–40	299	0.48	1.25	3.21
40–50	269	0.44	1.32	3.92
50–60	321	0.42	1.31	4.09
60–70	334	0.38	1.34	4.70
>70	224	0.52	1.66	5.28
All	1751	0.44	1.35	4.10

Reference ranges were calculated as mean ± 2 SD of log-transformed serum TSH concentrations for each age stratum.

Bremner et al., JCEM 97:1554, 2012

TSH und spätere Hypothyreose

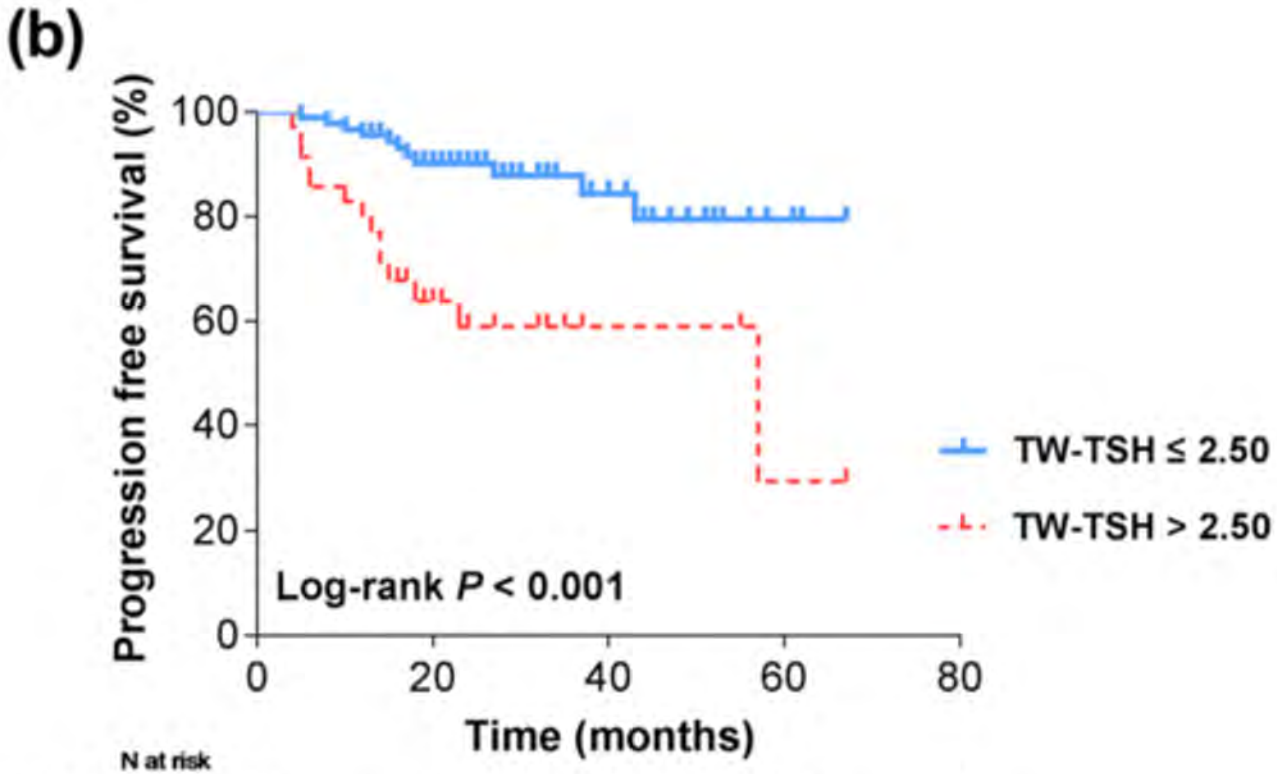


Walsch et al., JCEM, 2010

●, Antibody positive; ○ antibody negative; ▲ actual odds ratios

TSH: Progression mPTC

N = 127 mPTCs, active surveilance, TSH cutoff: 2.5 mU/l

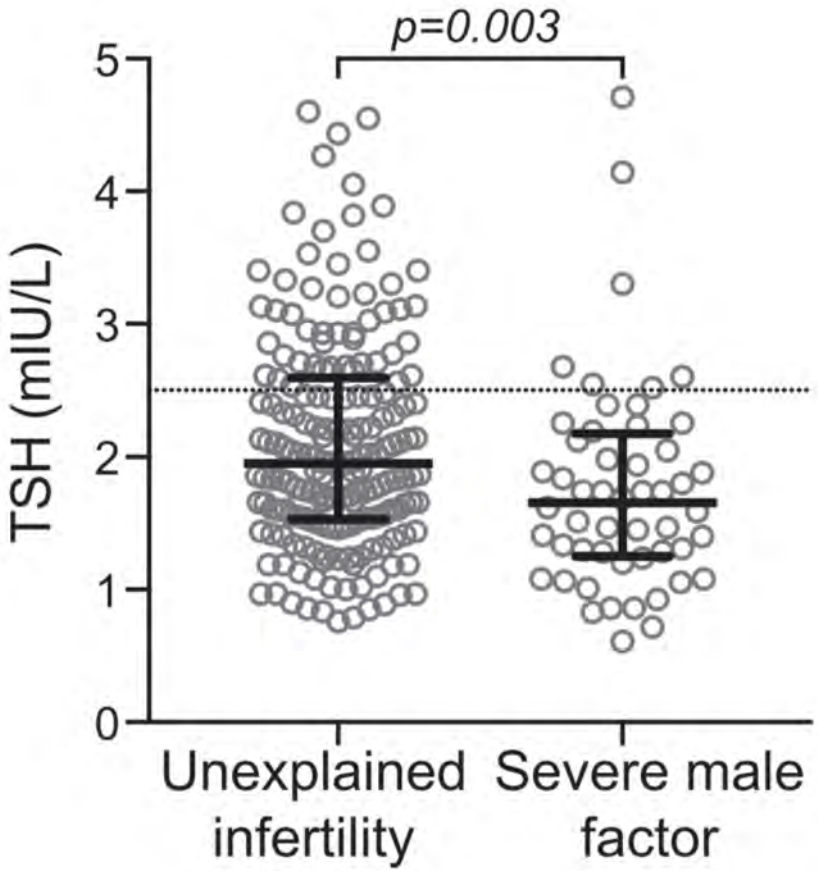


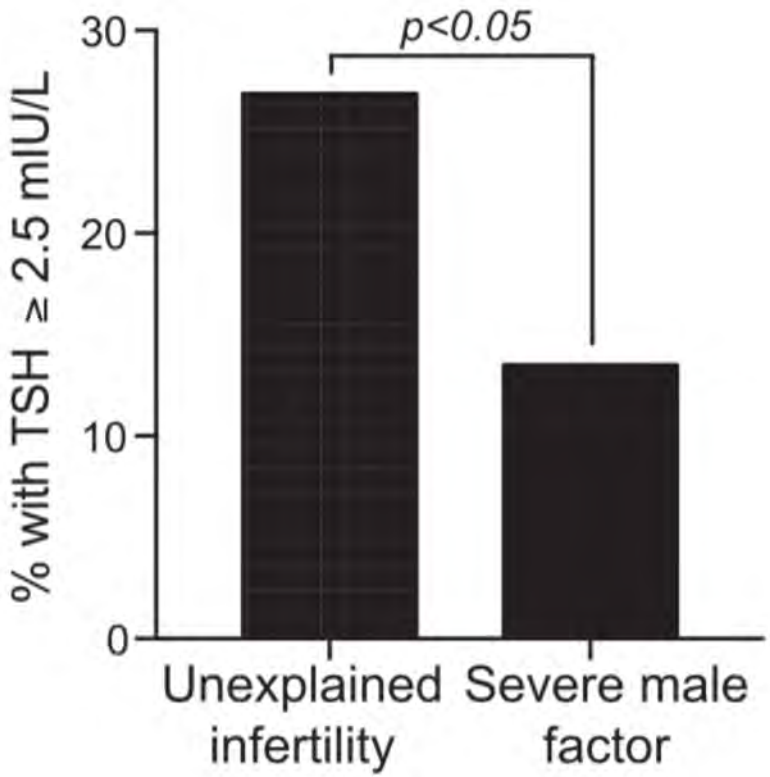
N at risk					
TW-TSH ≤ 2.50	92	72	52	32	12
TW-TSH > 2.50	35	15	0	0	0

Kim et al., JCEM 2018

TSH - Infertilität

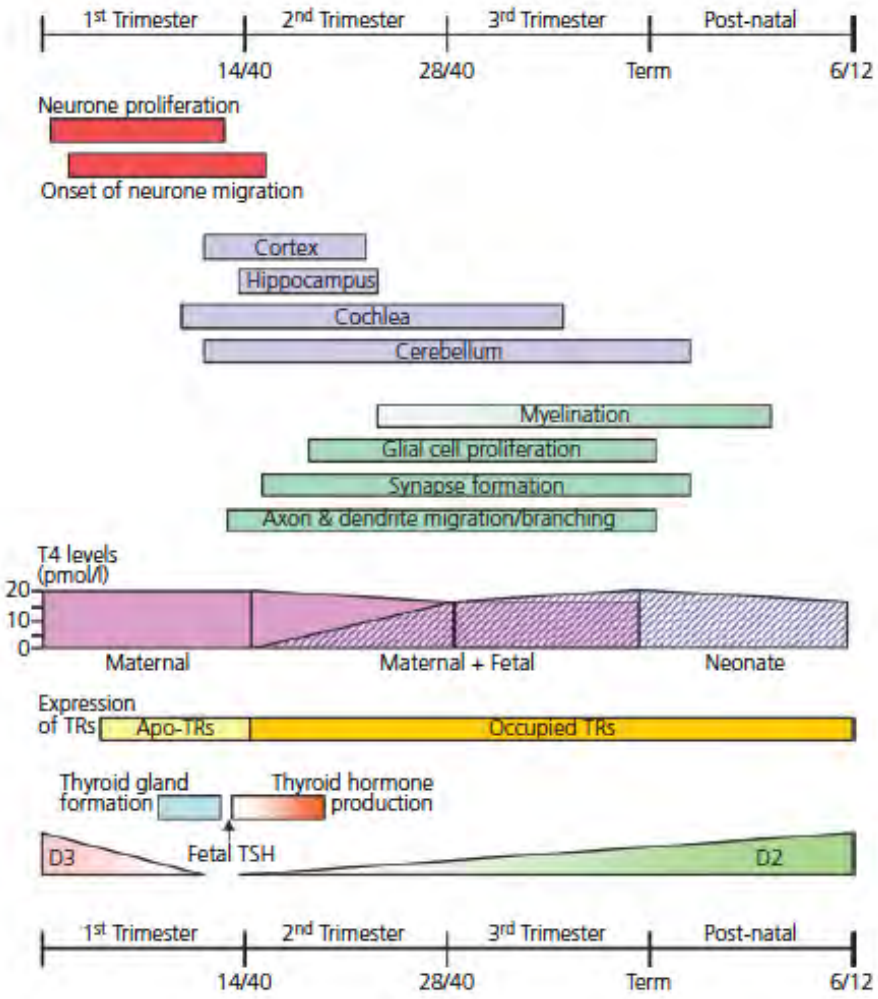
Frauen mit normalem TSH und unerklärter Infertiliät (N=187) und Frauen mit An-/Oligospermie des Partners





Jokar et al., JCEM 2018

Schilddrüse und fetale Entwicklung



Williams, J Neuroendocrinology 2008

Leitline SD-Schwangerschaft 2017

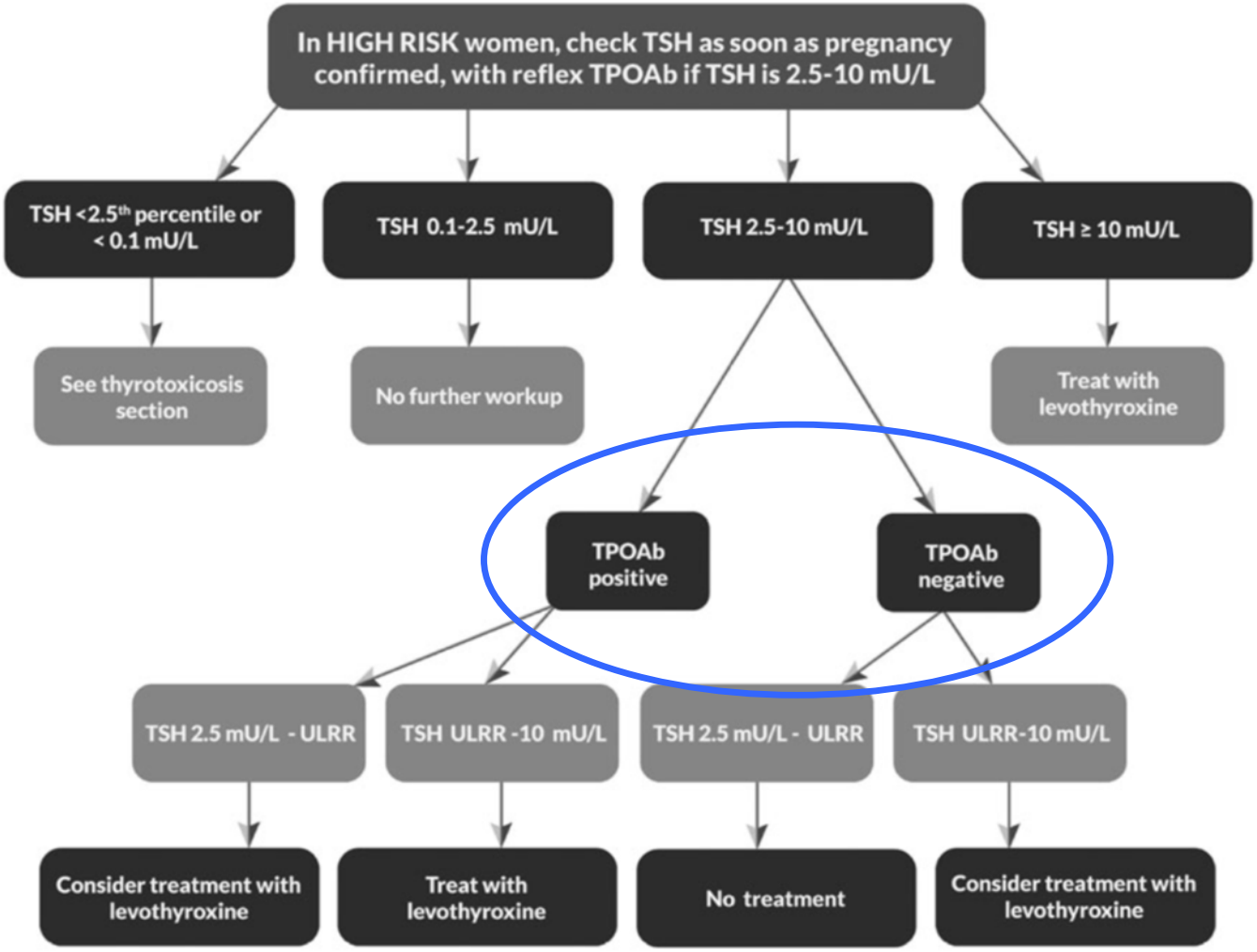


FIG. 1. Testing for thyroid dysfunction in pregnancy. ULRR, upper limit of the reference range.

Alexander et al., Thyroid 2017

TSH

Normalwert als Therapieziel ?

„Normalität“ in Abhängigkeit von „nachgewiesener“ Begleiterkrankung ?

Was ist Normal in der Schwangerschaft ?

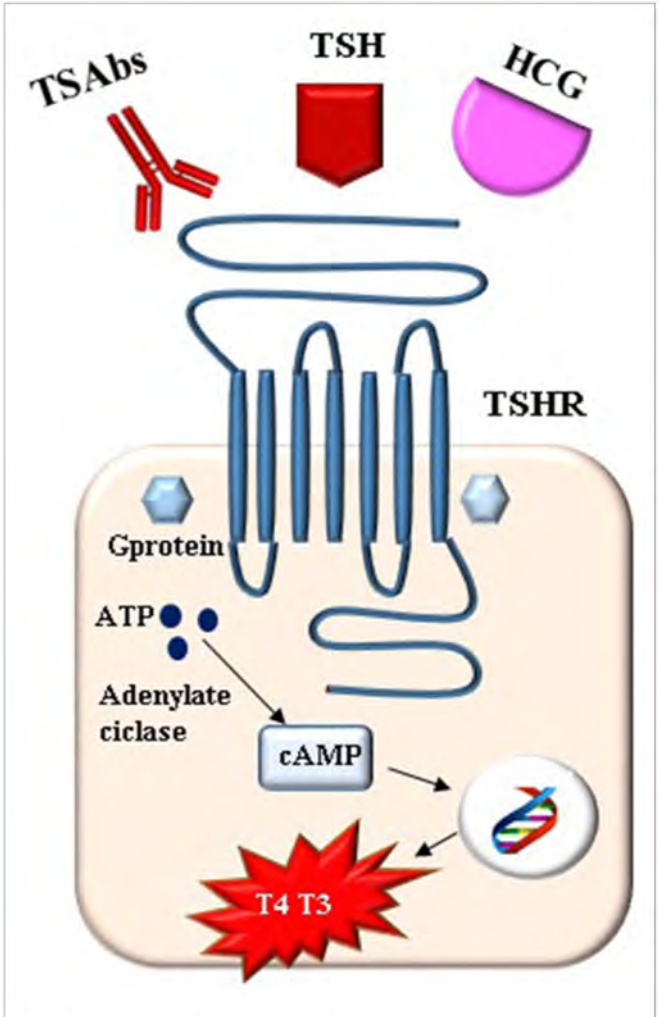
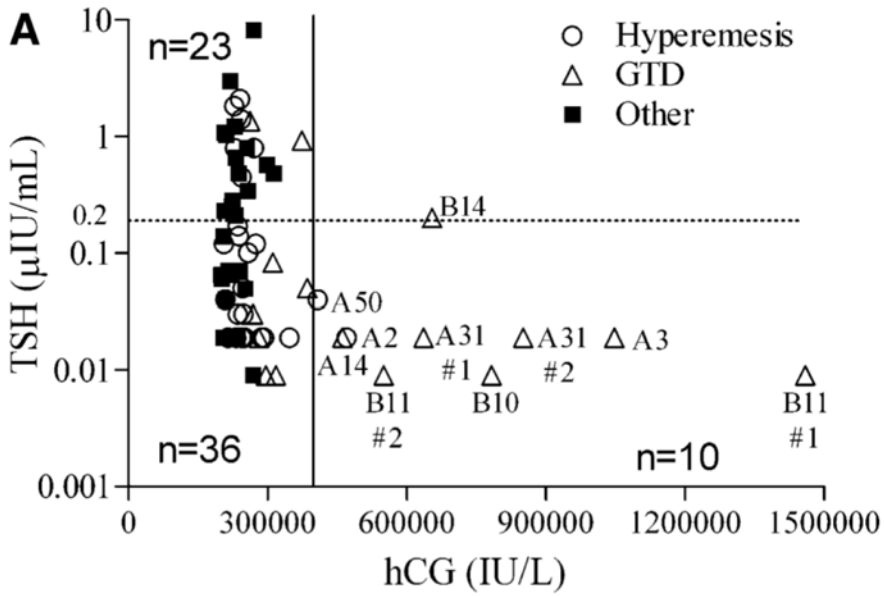


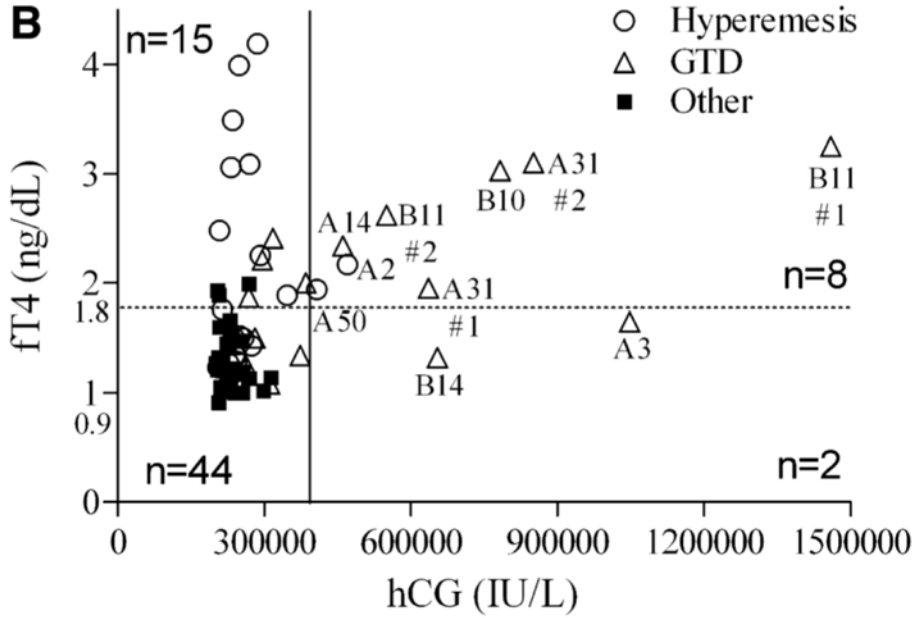
FIGURE 1 | The stimulation of TSH receptor (TSHR) in pregnancy.

Bucci et al., Frontiers in Endocrinology 2017

TSH - HCG

GTD: gestational trophobast disease



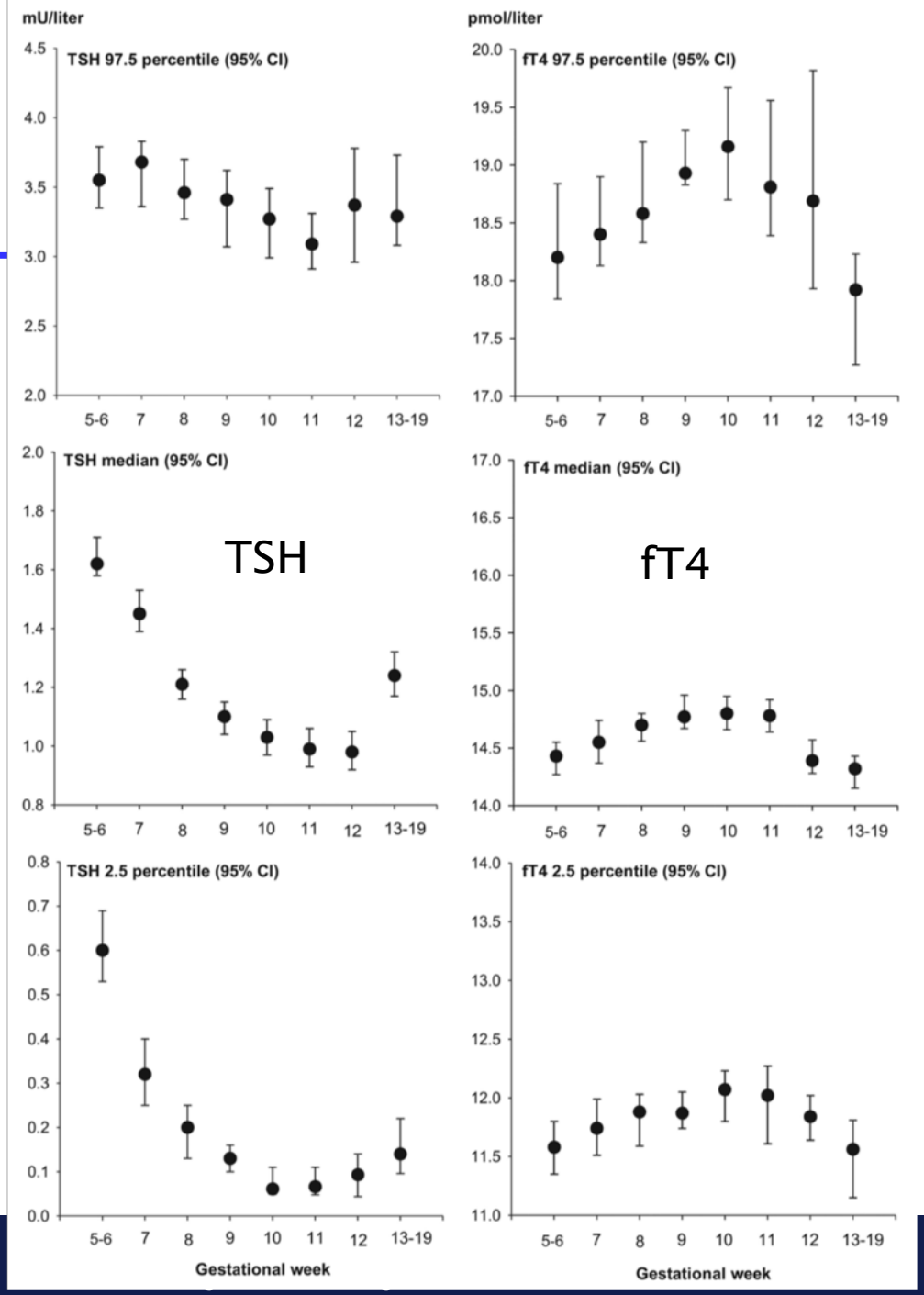


TSH Suppression (<0.2 mU/l): 67 % bei hCG > 200,000 IU/l und 100% bei hCG > 400,00 IU/l

Lockwood et al., Thyroid 2009

Normalwerte in der Schwangerschaft

6671 schwangere Frauen in Dänemark



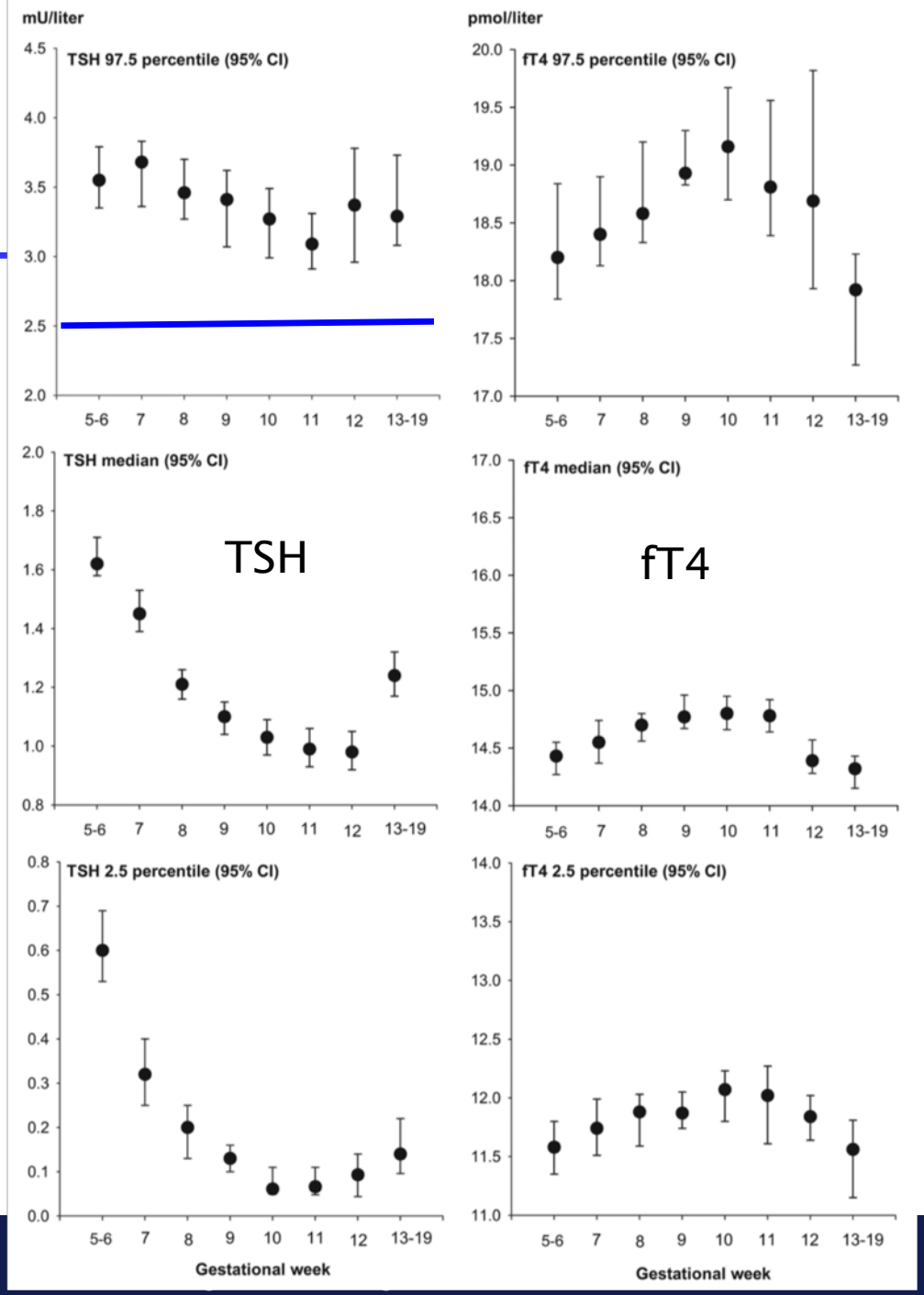
Lauerberg et al. JCEM 2016

Normalwerte in der Schwangerschaft

6671 schwangere Frauen in Dänemark

Bei TSH Grenzwert > 2.5 mU/l:

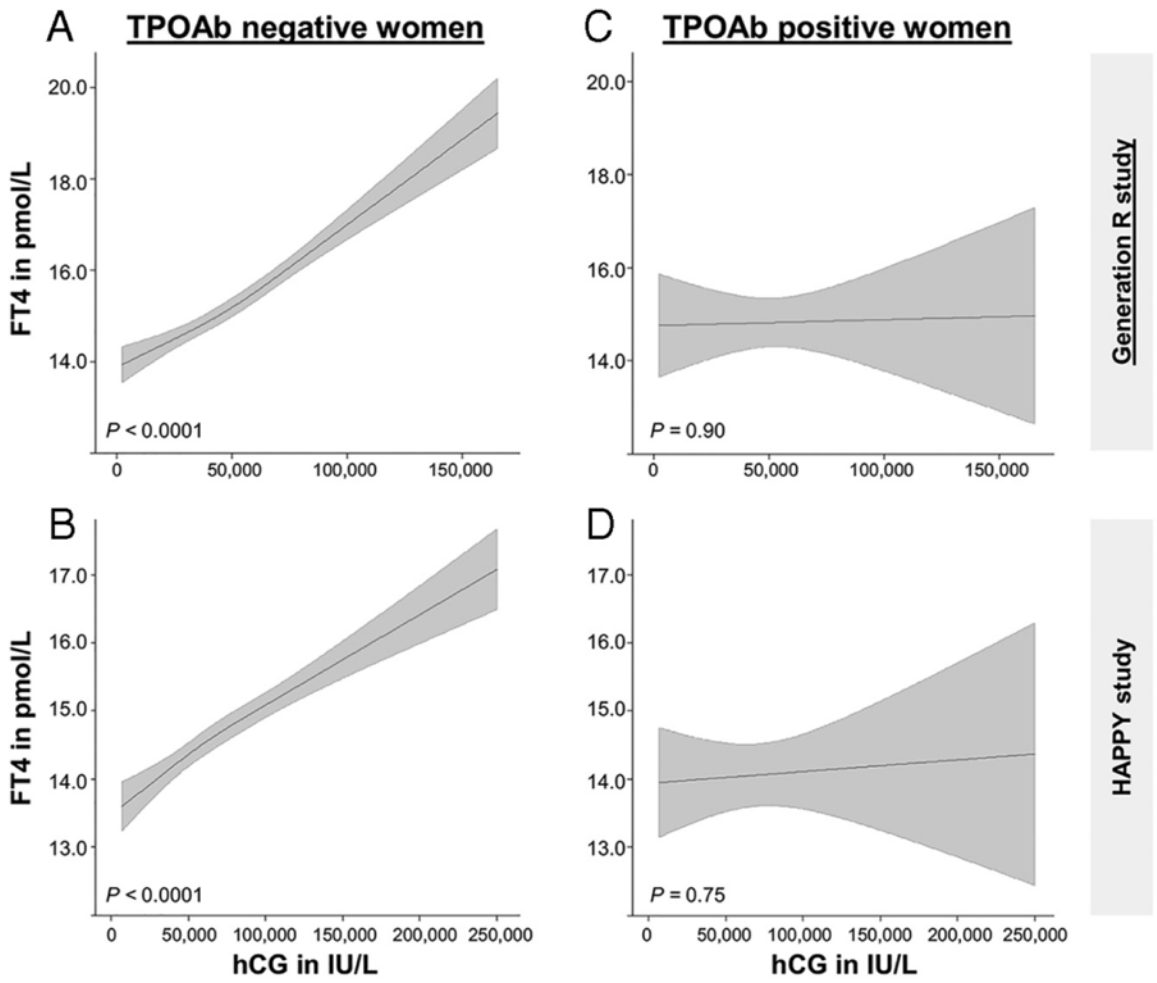
10 % der „gesunden“ Frauen hypothyroid



Lauerberg et al. JCEM 2016

SD-Antikörper in der Schwangerschaft

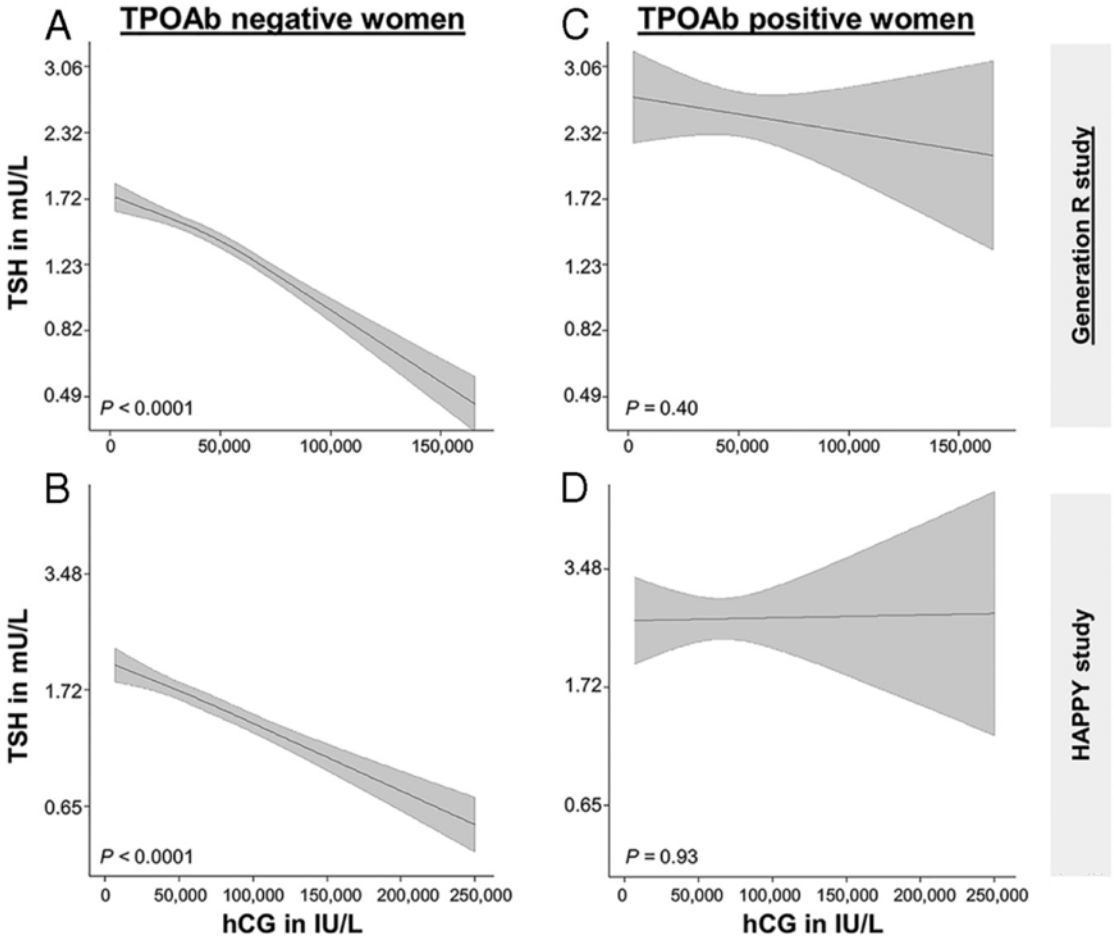
fT4



Korevaar et al., JCEM 2016

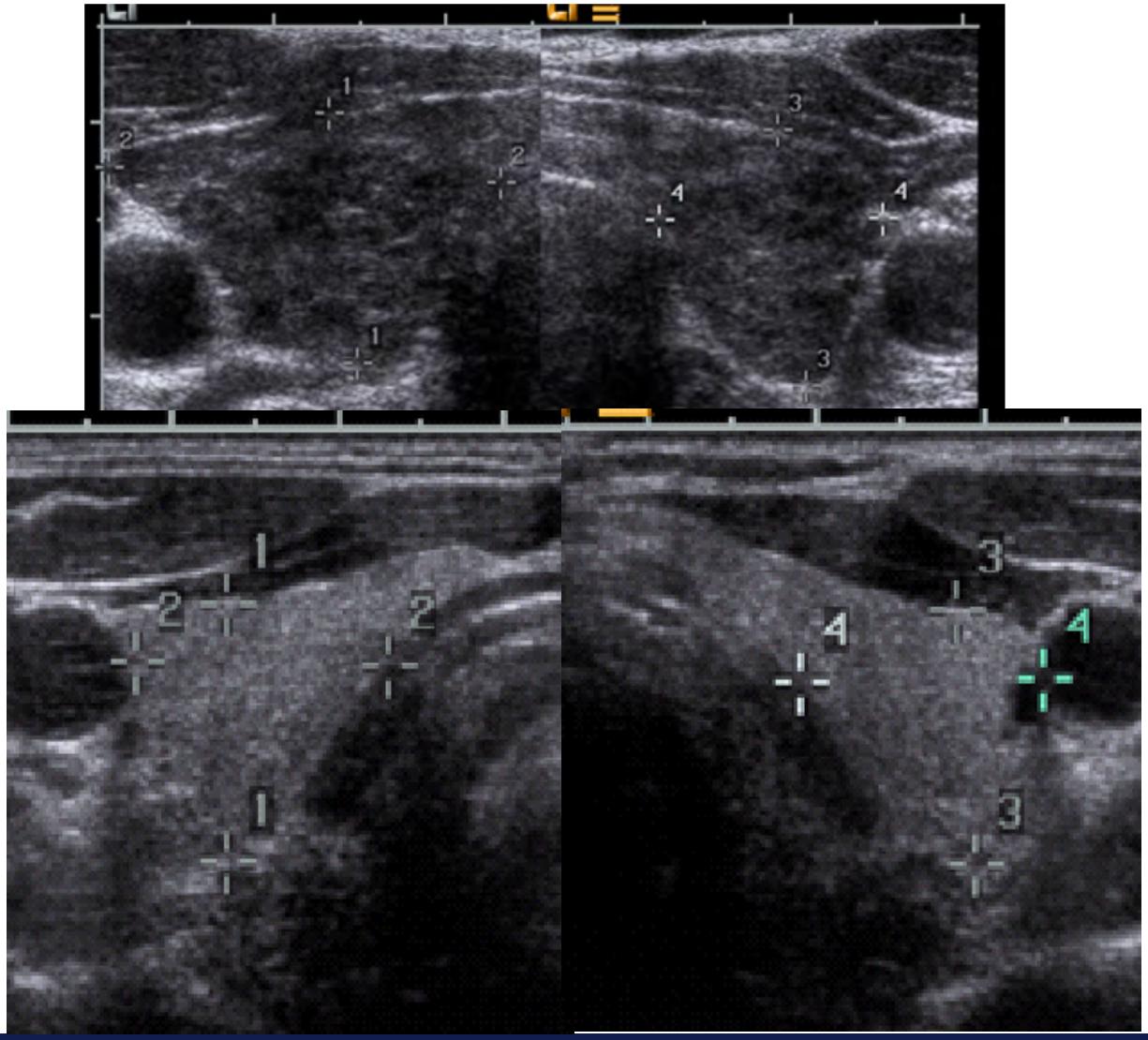
SD-Antikörper in der Schwangerschaft

TSH

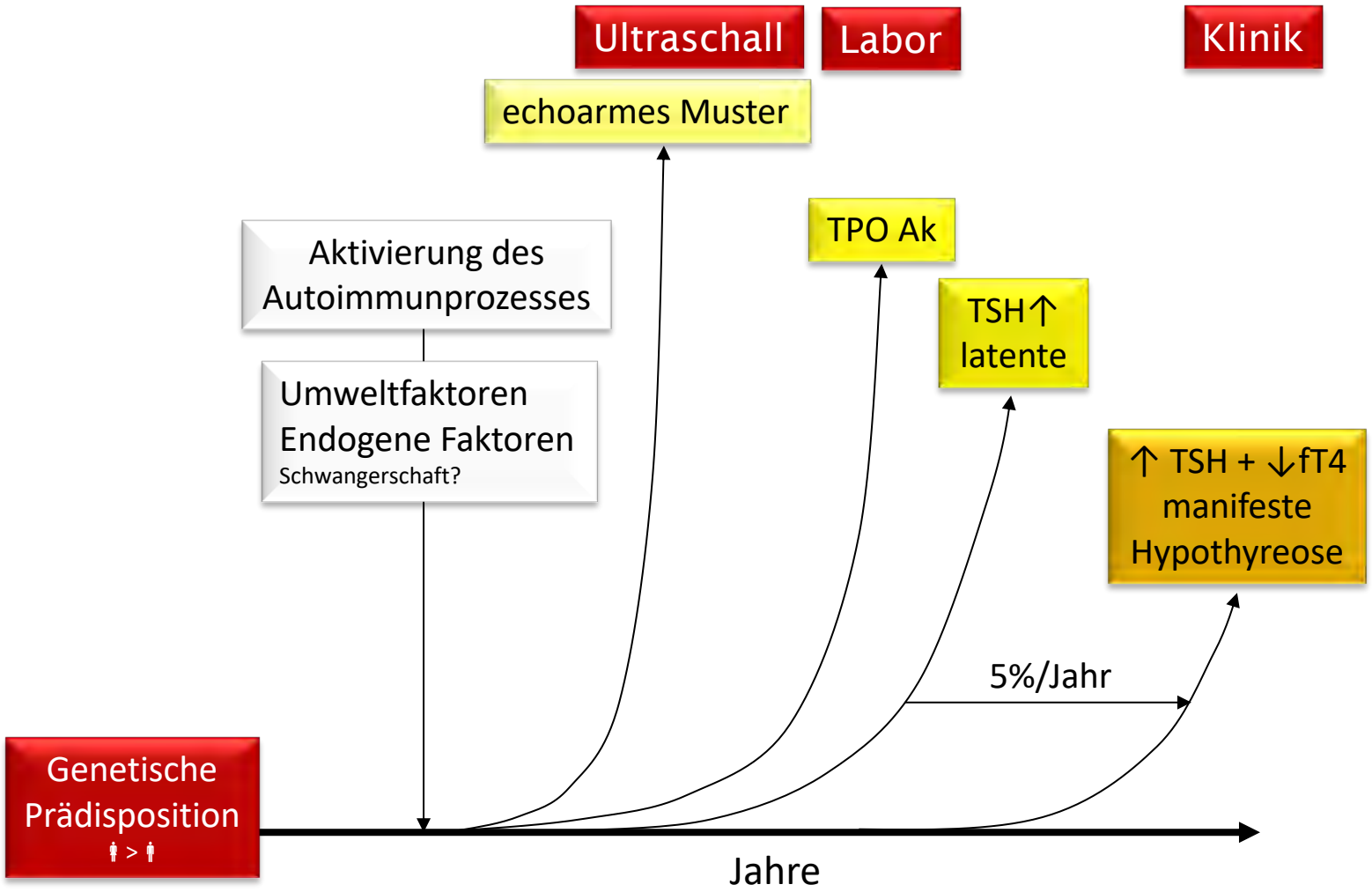


Korevaar et al., JCEM 2016

Hashimoto-Thyreoiditis Sonographie



Autoimmunthyreoiditis (AIT)
eine dynamische Entwicklung



Nach Spencer C et al. 2004; Vanderpump MP et al. 1995

Normalwerte : TSH

Erwachsene: 0.44 - 3.77 uU/ml
Graubereich: bis 0.1 bzw. 4.0 uU/ml

1.Trimenon: 0.1 - 2.5 uU/ml
2 Trimenon: 0.2 - 3.0 uU/ml
3 Trimenon: 0.3 – 3.5 uU/ml

Lazarus et al., Europ Thyroid Journal 2014

Normalwerte in der Schwangerschaft

4800 schwangere Frauen in China

		TSH, mIU/L			
		Percentile			
Population	**n**	**2.5th**	**50th**	**97.5th**	***P* Value**
Nonpregnant	640	0.69	2.07	5.64	
Pregnant					
4–6 wk	384	0.56	2.15	5.31	0.784
7–12 wk	640	0.10	1.47	4.34	0.000[b]
4–12 wk	1024	0.14	1.66	4.87	0.000[b]

Lee et al. JCEM 2014

Normalwerte in der Schwangerschaft

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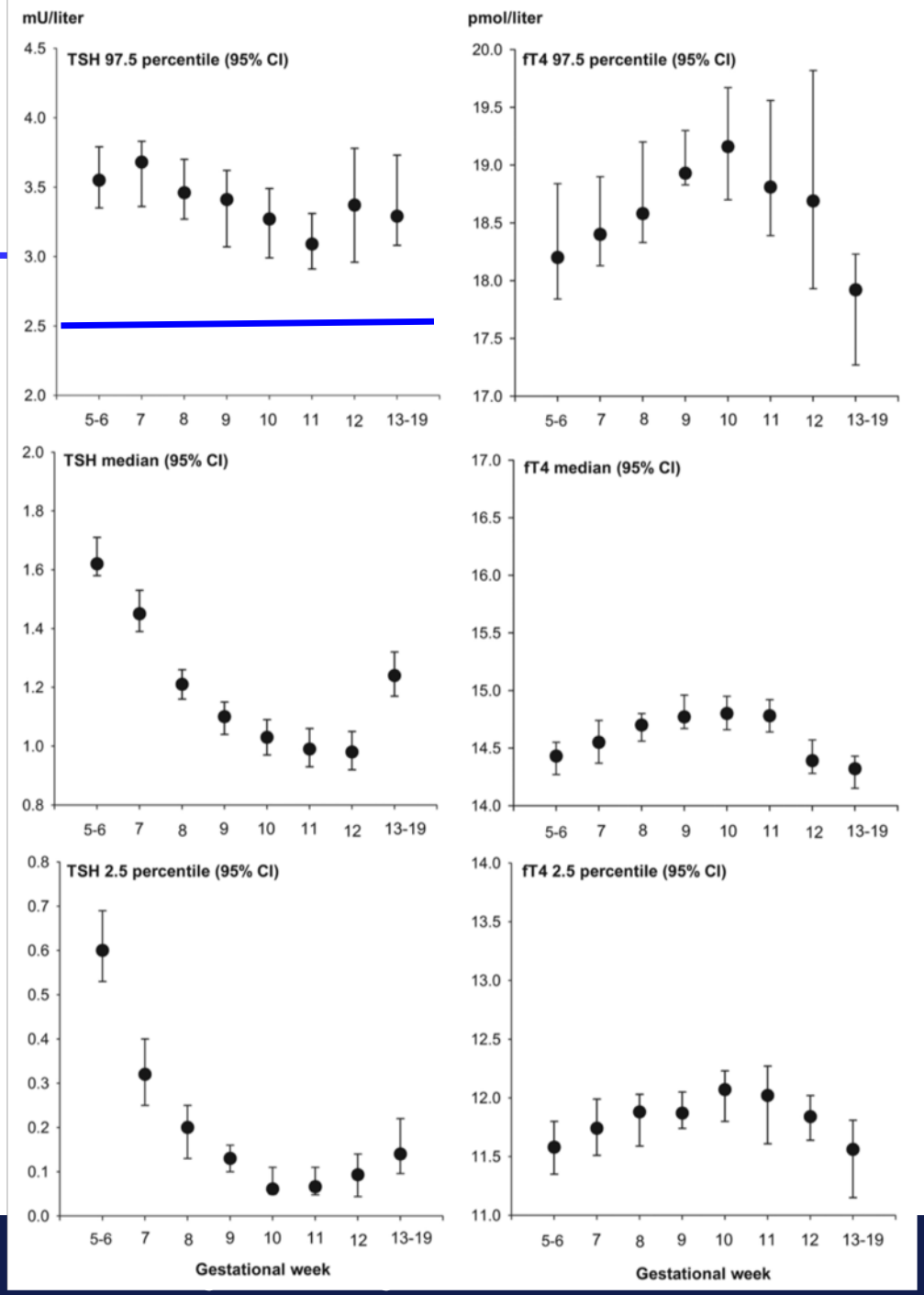


Lauerberg et al. JCEM 2016

Leitlinen SD-Schwangerschaft

ATA 2017

Reccomendation 1: When possible, **population-based trimester-specific reference ranges for serum TSH should be defined through assessment of local population data representative of a health care provider's practice**. Reference range determinations should only include pregnant women with no known thyroid disease, optimal iodine intake, and negative TPOAb status.

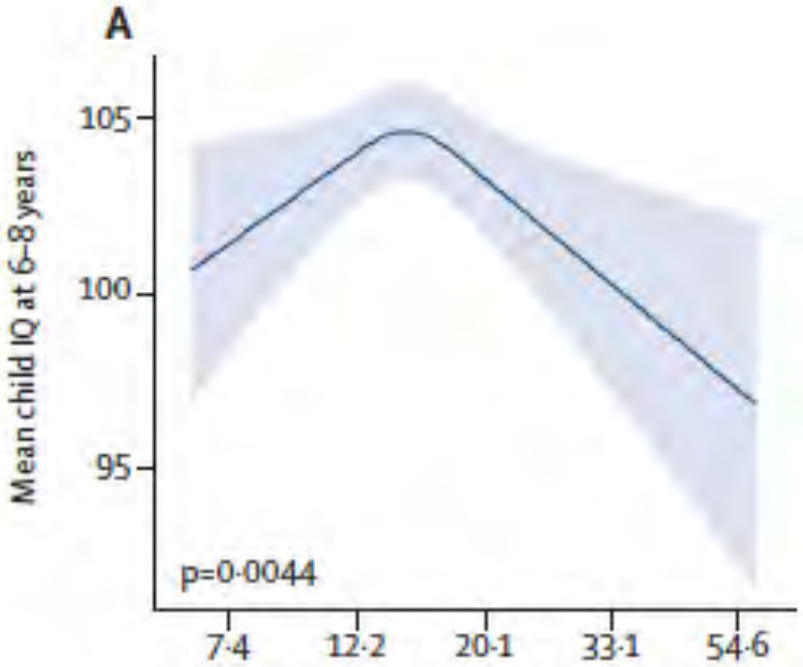
Falls nicht verfügber:

TSH Normalwert:	oberer Normalwert	- 0.5 mU/L (**4.0 mU/l**)
Erstes Trimester	unterer Normalwert	- 0.4 mU/L

Alexander et al., Thyroid 2017

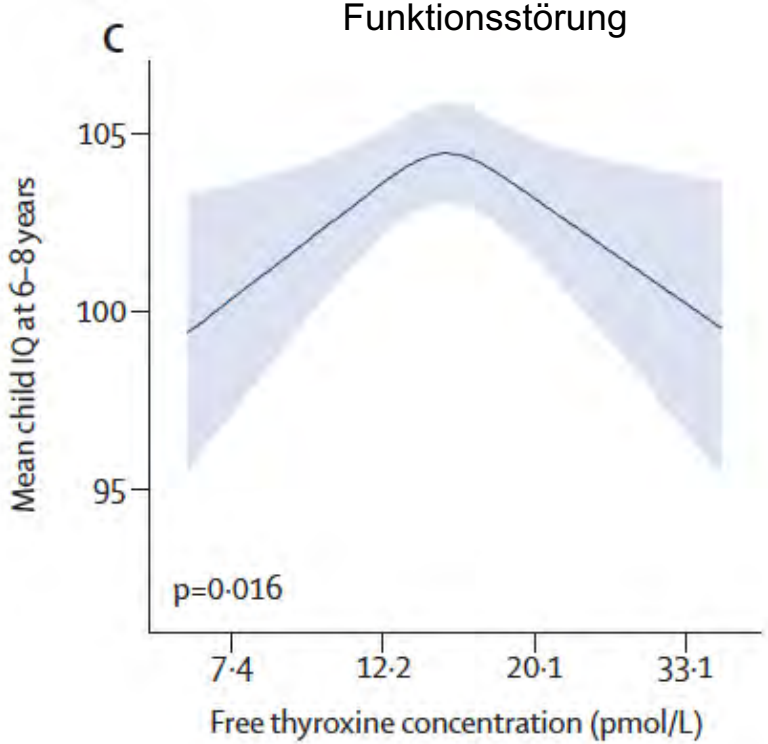
Zu viel ist auch nicht gut

Generation R Study (Rotterdam)
Blutabnahme in der Schwangerschaft (< 18 SSW)
Nicht verbaler Intelligenztest der Kinder 6 LJ (n = 3839)



ftT4 (pmol/L)

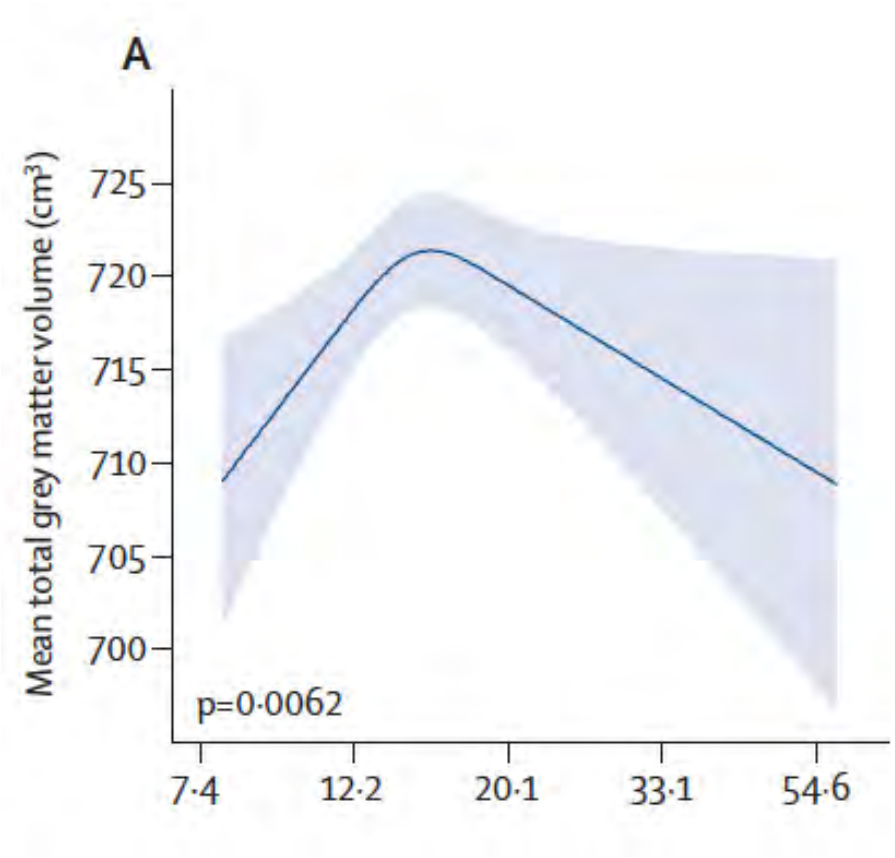
Ohne Mütter mit manifester SD Funktionsstörung



Korevaar et al., Lancet Diabetes Endocri

Zu viel ist auch nicht gut !

MRI Scan 8 LJ (n=646)



Korevaar et al., Lancet Diabetes Endocrinol 2015

Normalwerte: fT4

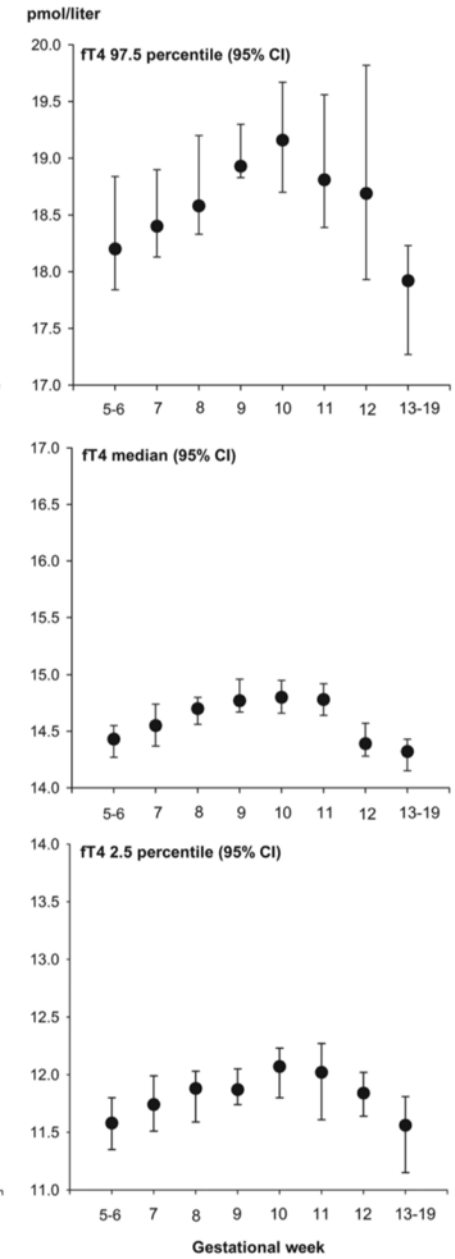
fT4 Assay Med. Univ. Wien

Erwachsene: 0.76 - 1.66 ng/dl

Schwangerschaft:

1. Trimenon: 0,94 - 1,52 ng/dl
2. Trimenon: 0,75 - 1,32 ng/dl
3. Trimenon: 0,65 - 1,21 ng/dl

Änderungen in TBG, Albumin: fT4 Test in der Schwangerschaft verlässlich ?



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Lauerberg et al. JCEM 2016

Therapieziel ?

> 19 Jahre 0.76 - 1.66 ng/dl

Schwangerschaft:
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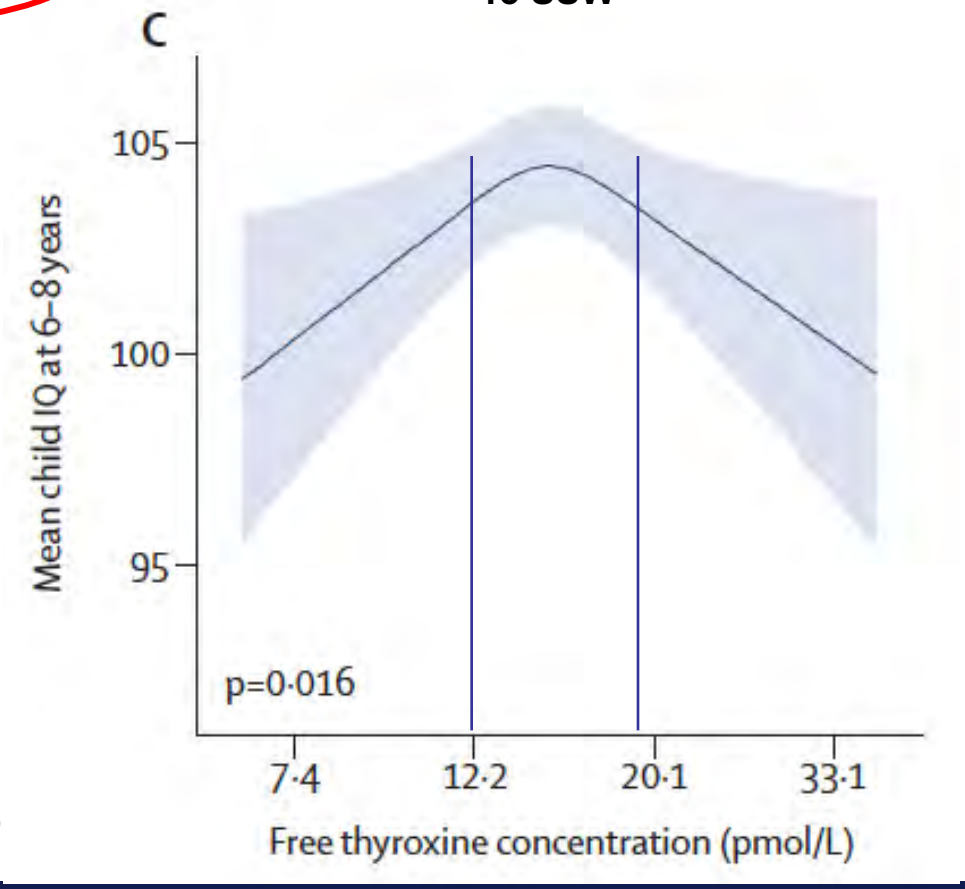
Nur schwache Assoziation TSH mit IQ !

Ohne Mütter mit manifester SD Funktionsstörung
13 SSW



Korevaar et al., Lancet Diabetes

Schilddrüse und Lebenserwartung

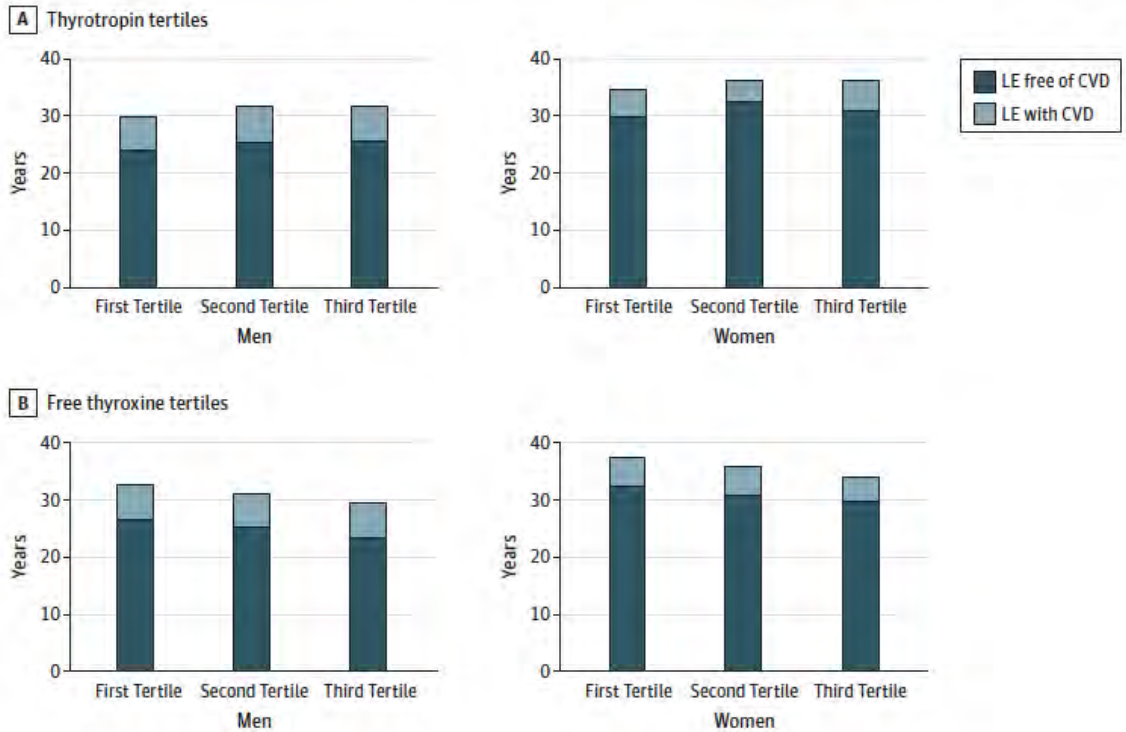
N=7785, 65 Jahre, 53 % Frauen, FU: 8 Jahre

Menschen mit niedrig normale Schilddrüsenfunktion (fT4) leben 3.5 Jahre länger

Figure. Life Expectancy (LE) With and Without Cardiovascular Disease (CVD) at Age 50 Years Among Thyrotropin and Free Thyroxine Tertiles, in Men and Women

TSH

fT4



Rotterdam Study; Bano et al, JAMA 2017

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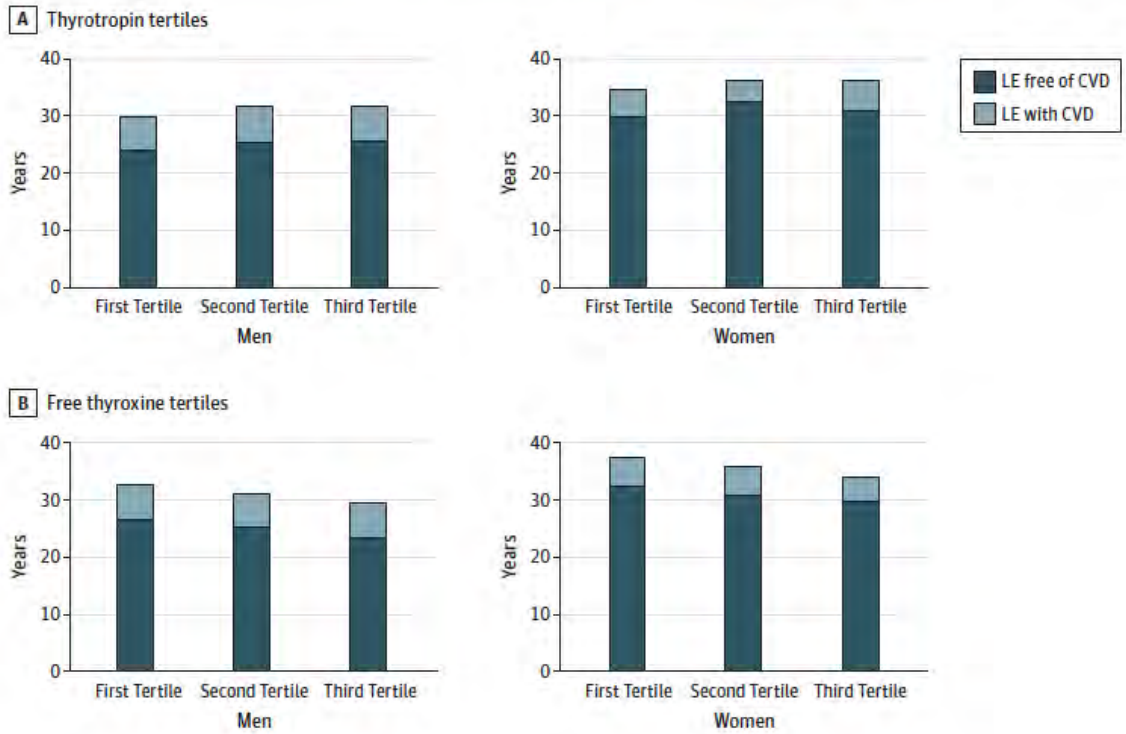
TSH

fT4



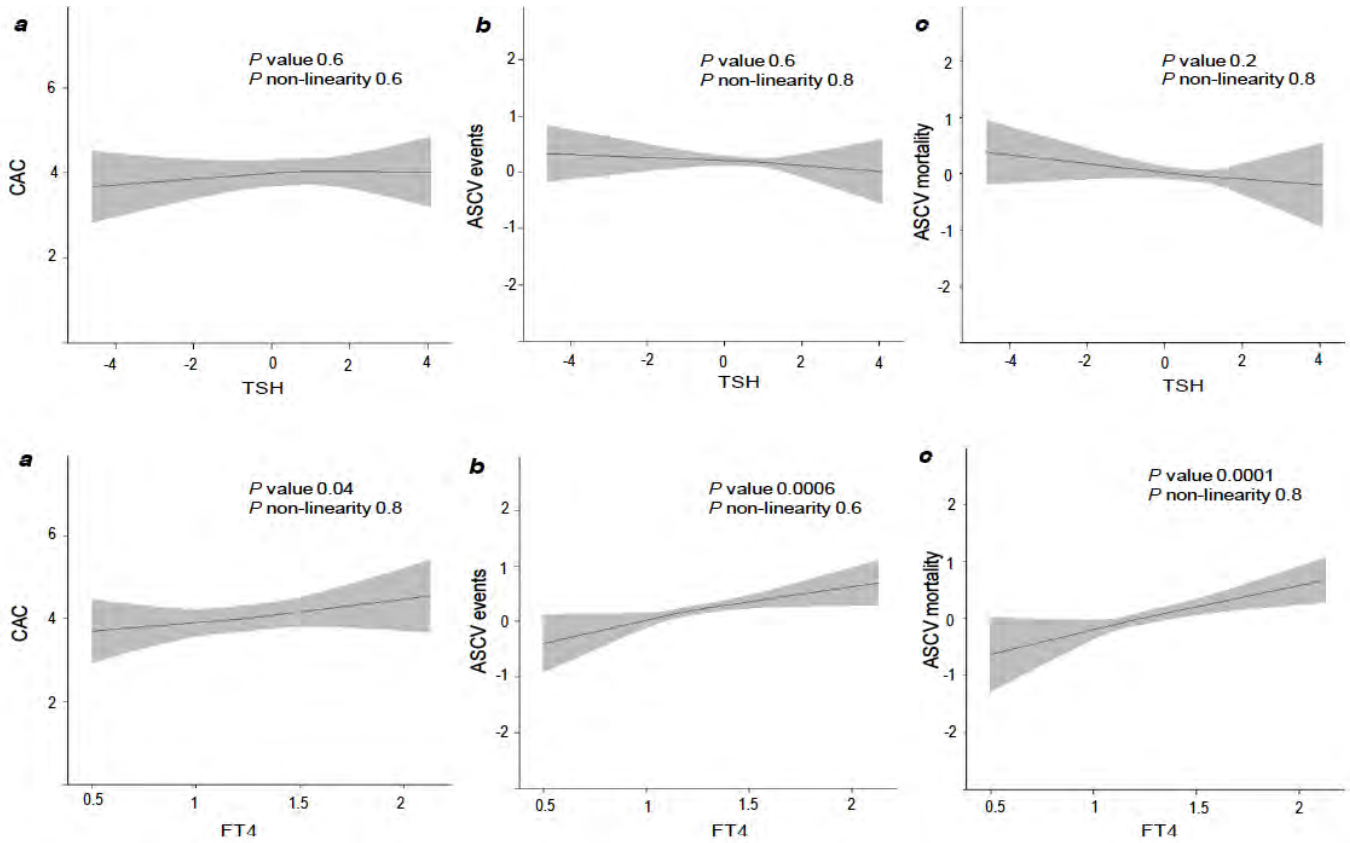
Rotterdam Study; Bano et al, JAMA 2017

Schilddrüse und Atherosklerose

N=9420, 65 Jahre, 57 % Frauen, FU: 8,8 Jahre
fT4 ist mit einem erhöhten Atherosklerose-Risiko assoziiert.

TSH

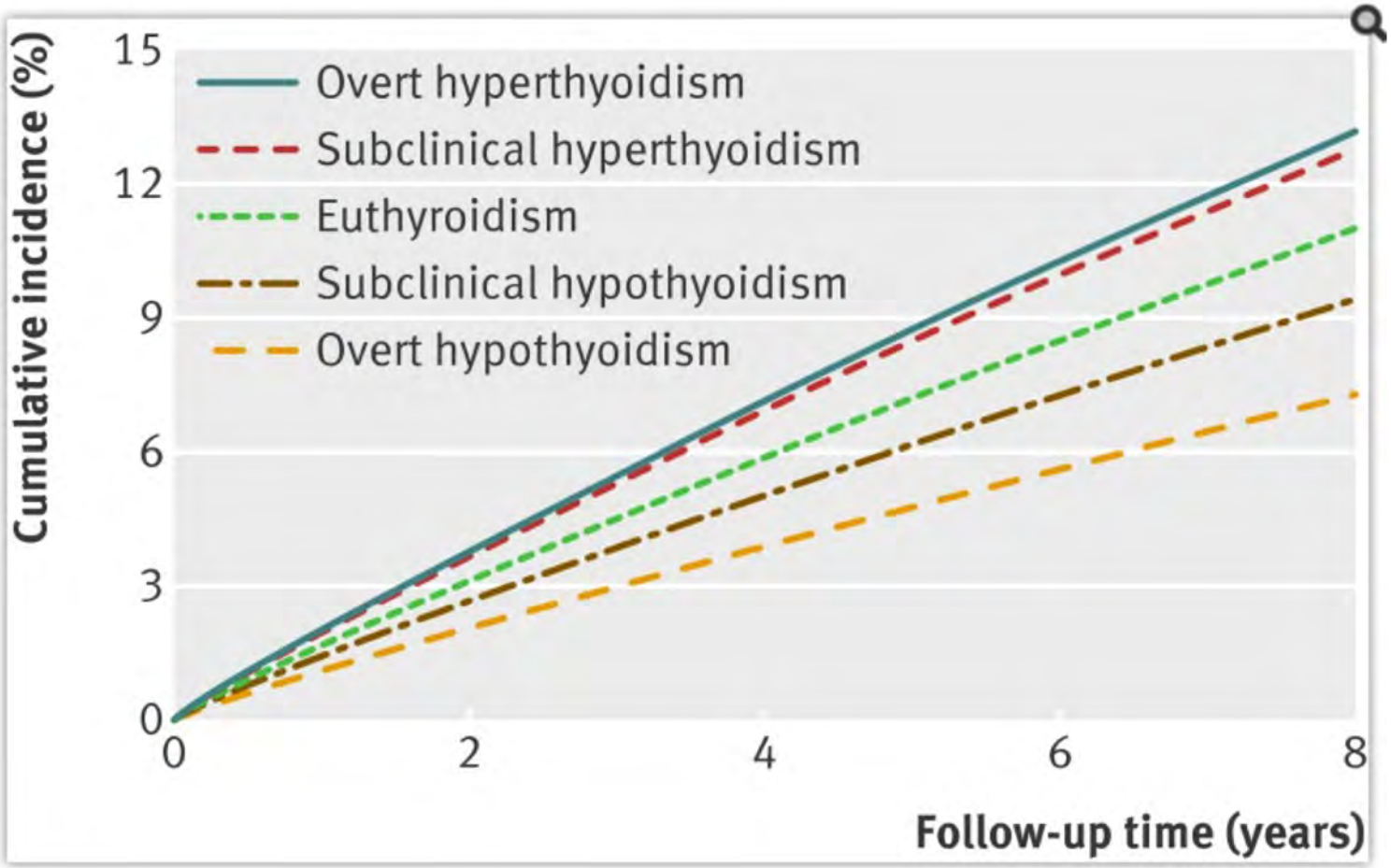
fT4



Rotterdam Study; Bano et al, Circ Res 2017

Schilddrüse und Vorhofflimmern

Register N=586 460, 65 Jahre, 57 % Frauen

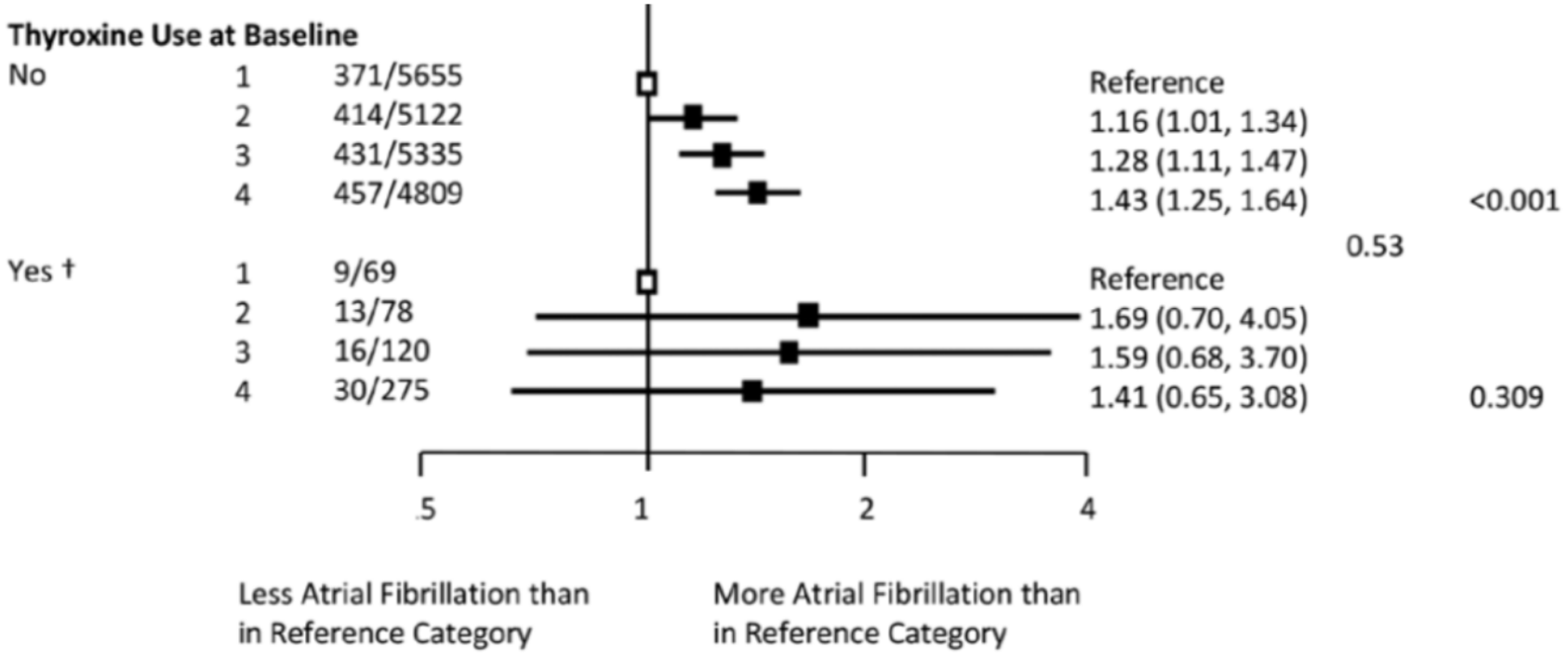


Selmer et al, BMJ 2017

fT4 und Vorhofflimmern

Metaanalyse N=30 085, 65 Jahre, 57 % Frauen

fT4 ist bei euthyreoten (TSH und fT4 im Normalbereich) Personen mit einem erhöhten Risiko für FH-Flimmern assoziiert.



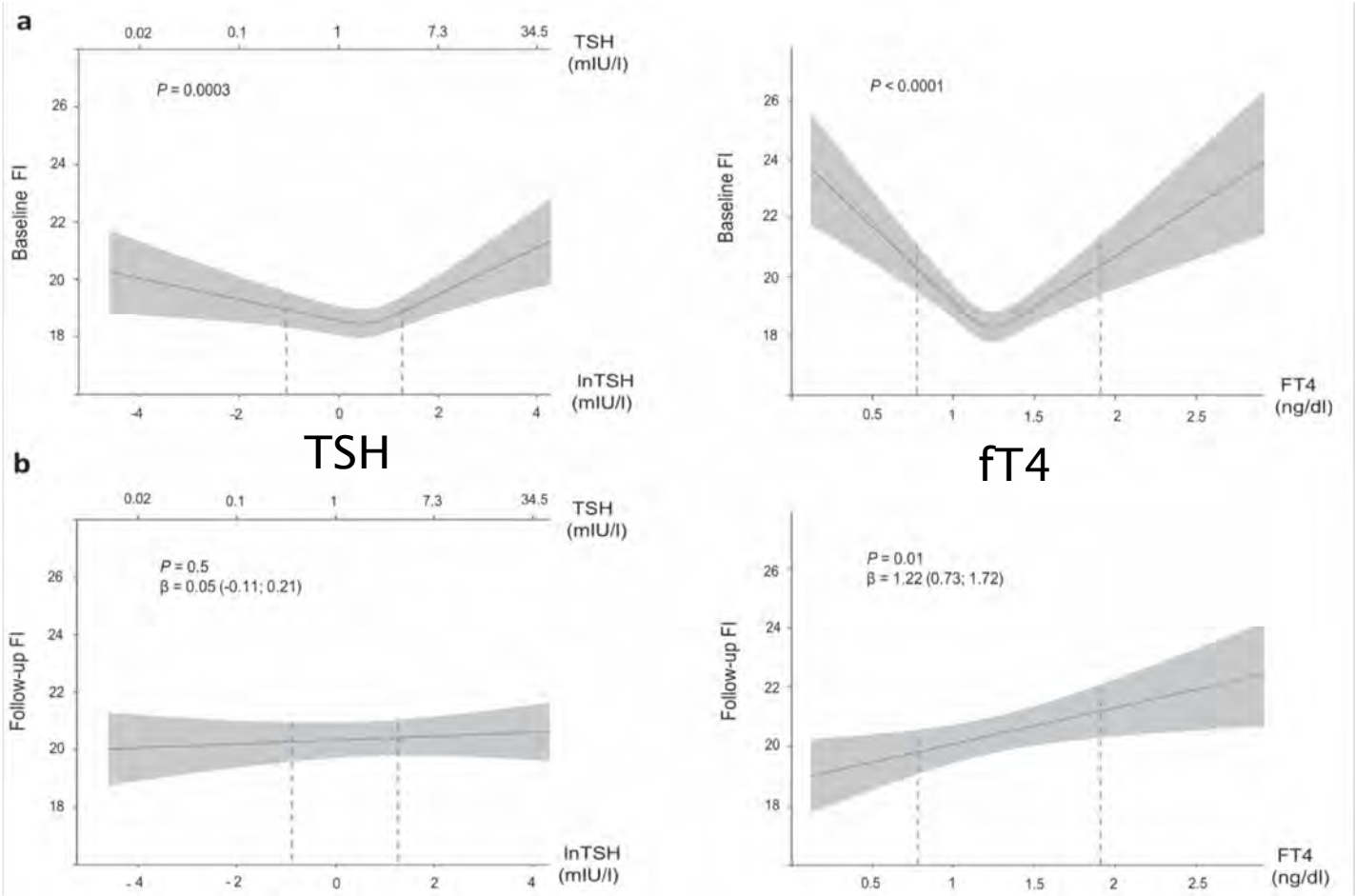
Baumgartner et al, Circulation 2017

TSH, fT4 und Frailty

N = 9640, 65 Jahre, frailty index basal und nach 10 Jahren

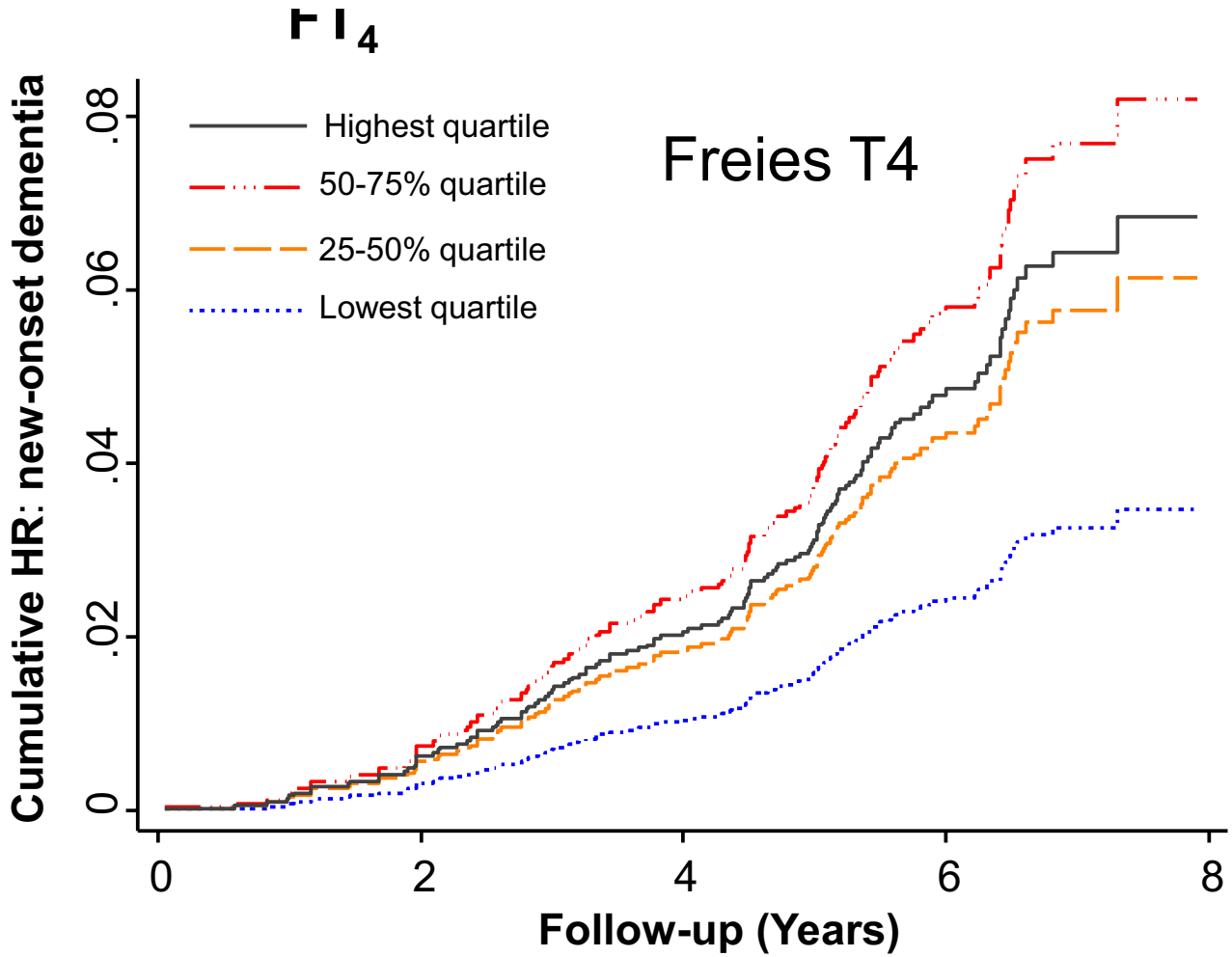
basal

FU



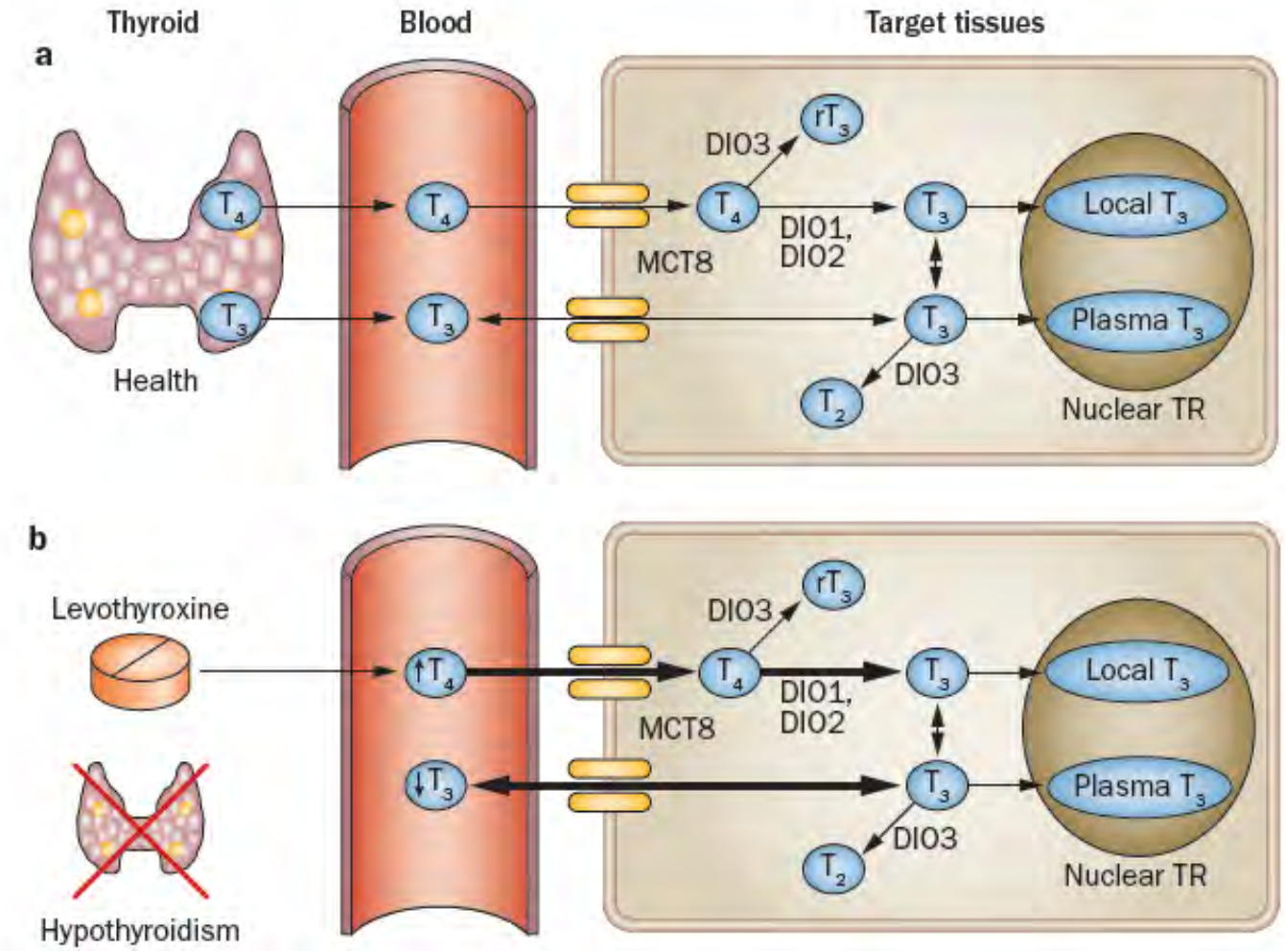
Bano et al., JCEM 2018, Rotterdam Study

Latente Hyperthyreose – Demenz



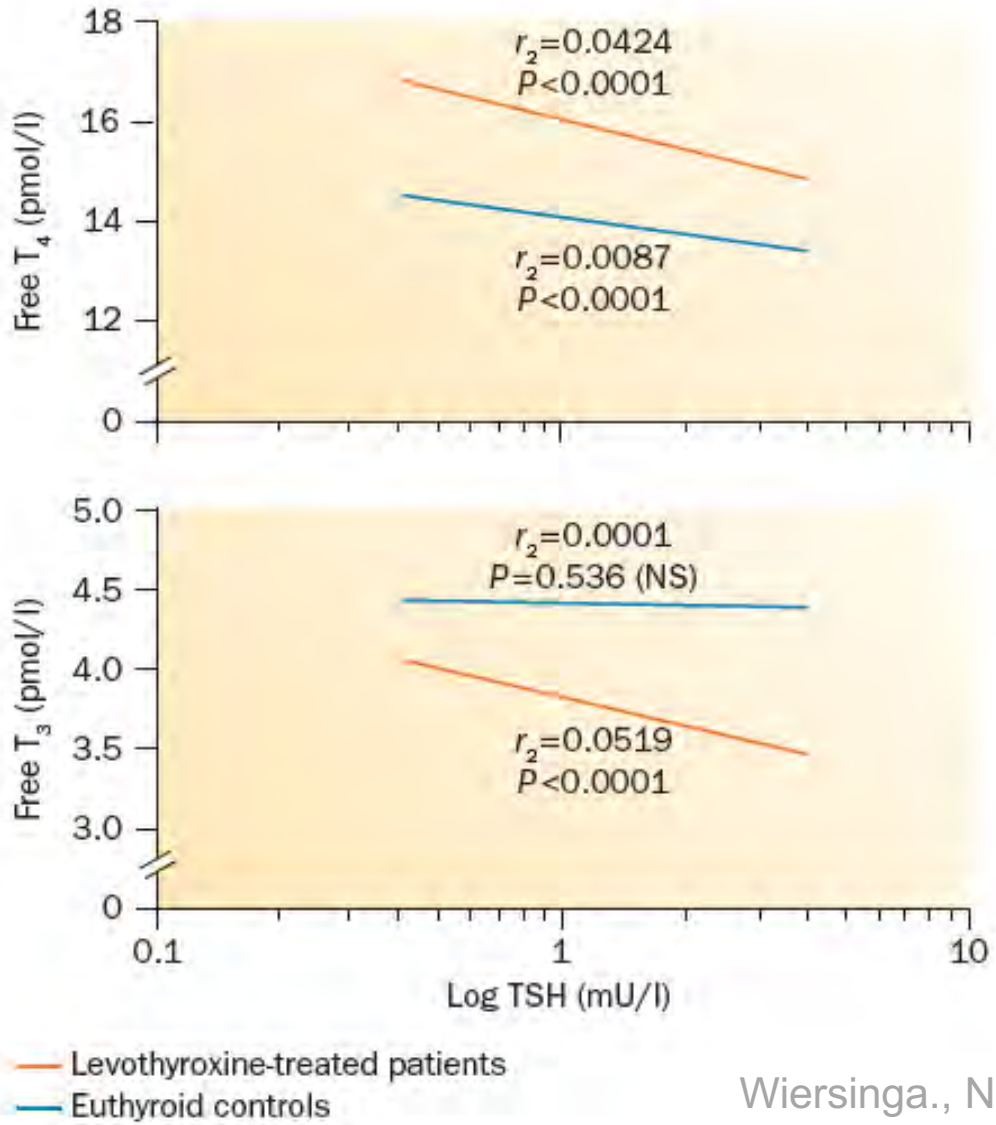
Yeap et al., JCEM 2012

T4 Therapie



Wiersinga., Nat Rev Endocrinol 2014

T4 Therapie



Wiersinga., Nat Rev Endocrinol 2014

Zusammenfassung

Spannende neue Entwicklungen:

- Normalwerte
- Therapieindikationen
- fT4 scheint immer wichtiger zu werden
- Hohe T4 und niedrige T3 Konzentration bei Thyroxintherapie