Subclinical Hypothyroidism

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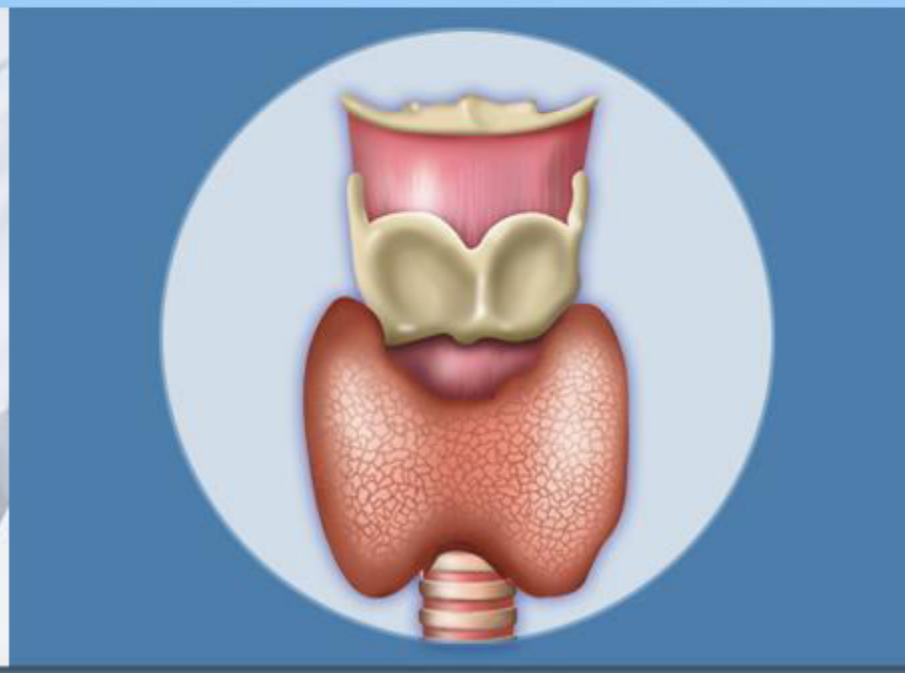
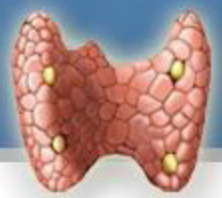
Dept of Endocrinology



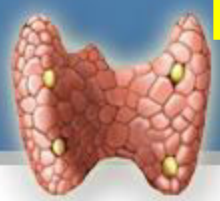


Subclinical Hypothyroidism

Defined as…

- Persistently (12 weeks/longer) elevated TSH level > 4.5 mIU/L
- Normal total or free serum T_4 and T_3 levels (after repeated measurements)
- Few or no signs/symptoms of hypothyroidism

RV Jayakumar et al , ITS Guidelines on Subclinical Hypothyroidism , 2016

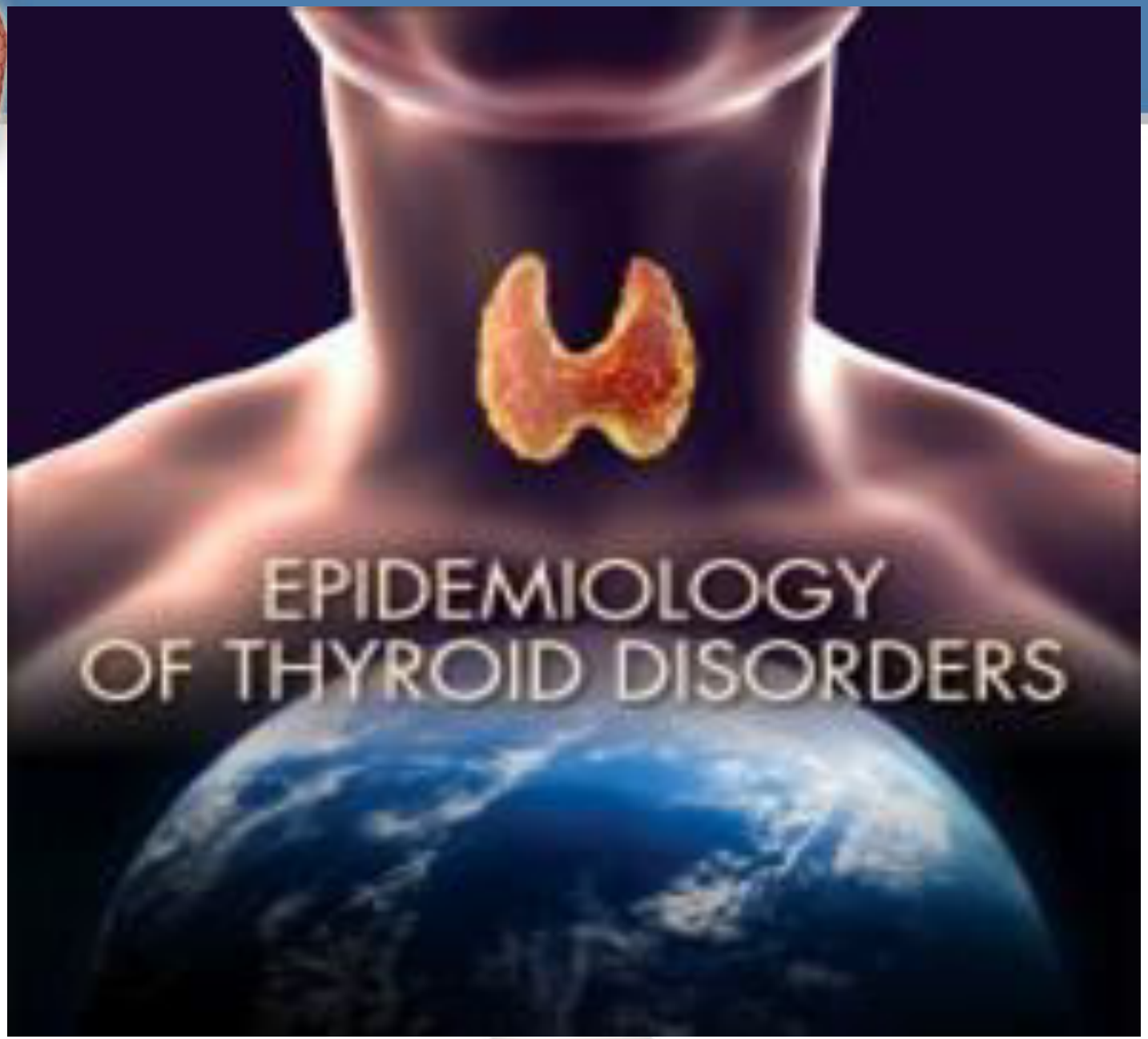


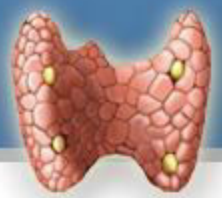
Patients with subclinical hypothyroidism can be categorized into those with..

Mildly elevated TSH at 4.5-10 mIU/L

Markedly Elevated >10 mIU/L

- Informed Health Online .**Underactive thyroid: Deciding whether or not to treat subclinical hypothyroidism** Last Update: August 10, 2017;


EPIDEMIOLOGY
OF THYROID DISORDERS

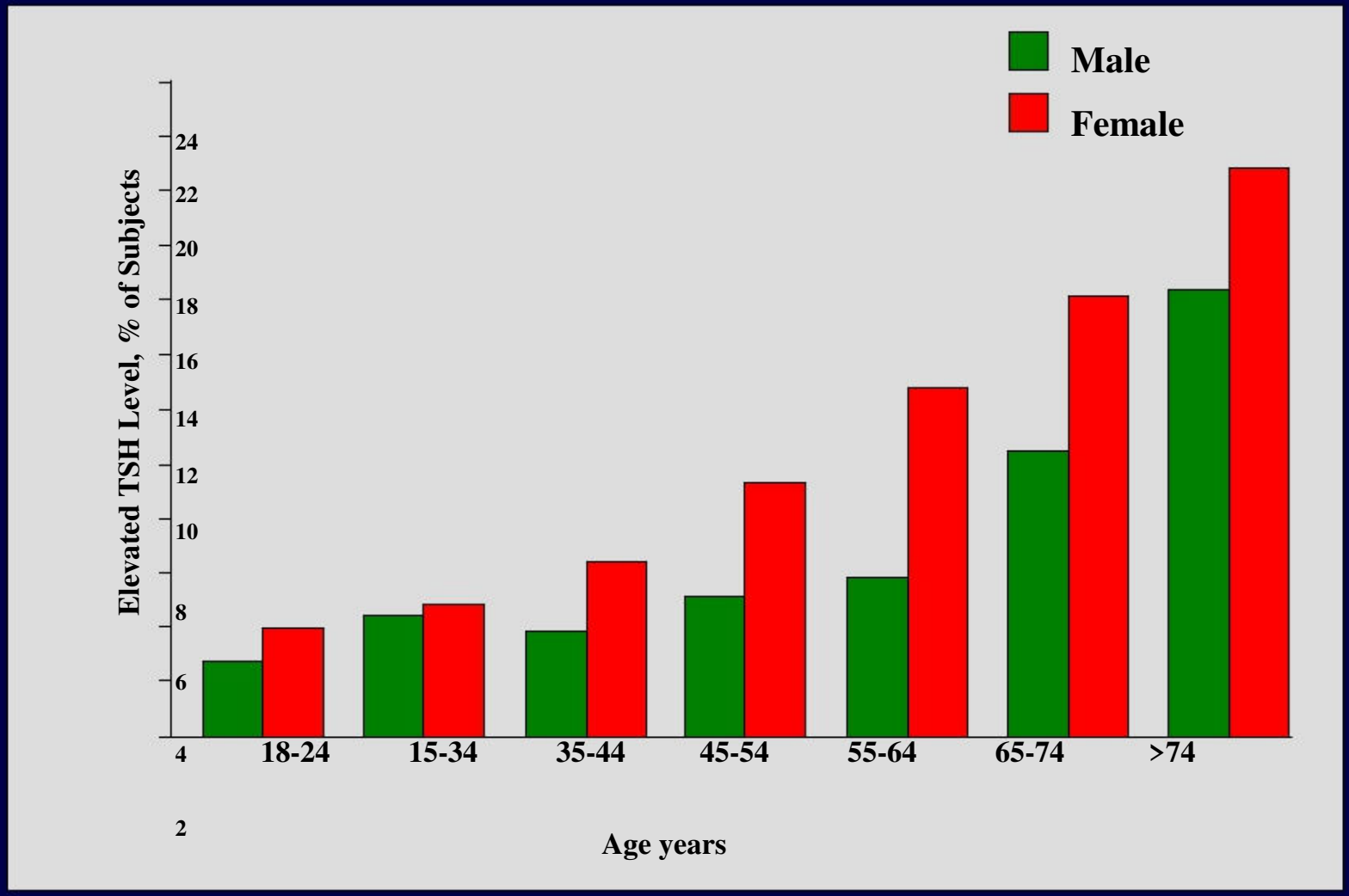


Incidence of subclinical hypothyroidism

The incidence of subclinical hypothyroidism varies among populations and ranges from **3 to 15** %.

Higher incidence associated with increasing **Age, Female Sex and a Suboptimal Iodine Status.**

Prevalence of Thyroid Dysfunction



Canaris GJ. Arch Intern Med 160: 526, 2000

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www.ijem.in

Prevalence of hypothyroidism in adults: An epidemiological study in eight cities of India

Ambika Gopalakrishnan Unnikrishnan, Sanjay Kalra[1], Rakesh Kumar Sahay[2], Ganapathi Bantwal[3], Mathew John[4], Neeraj Tewari[5]

- A total of 5376 adult male and non-pregnant female participants were evaluated.
- The overall prevalence of hypothyroidism was 10.95%.
- 8.02% (n=430) patients were diagnosed to have subclinical hypothyroidism (normal serum free T4 and TSH>5.50 mIU/ml).

Prevalence, clinical and biochemical profile of subclinical hypothyroidism in normal population in Mumbai

Vaishali Deshmukh, Anish Behl, Vagesh Iyer, Harish Joshi, Jayashree P. Dholye, Prema K. Varthakavi

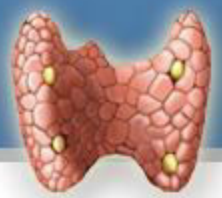
Department of Endocrinology, B.Y.L. Nair Hospital, Mumbai, India

11.3% of patients from the city of Mumbai are diagnosed with subclinical Hypothyroidism

Place of study	Reference	Age (in years)	Sex (%)		Number	Prevalence %			TSH Cut off (μIU/mL)
			M	F		Total	M	F	
Rotterdam	A.E. Hak *et al.*[12] (2000)	55+	0	100	1149	10.8	-	10.8	>4.0
U.S.A.	Canaris *et al.*[14]	70-79	49	51	2799	3.9	-	11.1	>5.5
Colorado	Kanaya *et al.*[18] (2002)	18+	44	56	2336	9.5	-	-	>5.1
Mumbai	Present study (2003)	20-60	13	87	237	11.3	3.3	12.5	>5

Epidemiology of SCH in India

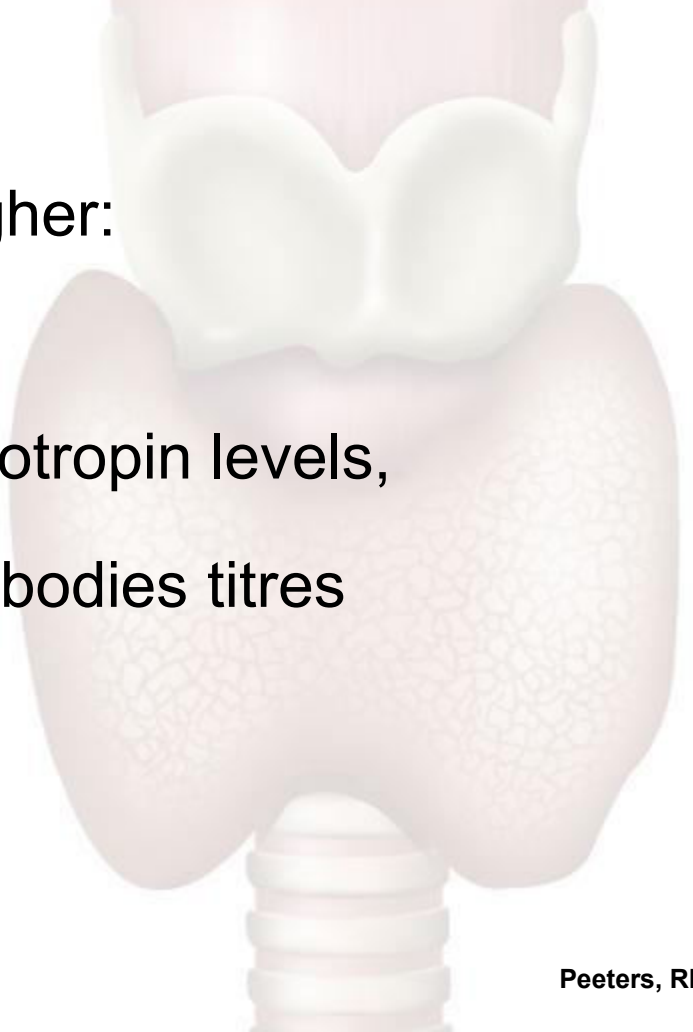
Reference	N	SCH %
Unnikrishnan et al; 2013	5370	8
Marwaha et al; 2012	4409	19.3
Unnikrishnan et al;2011	971	9.4
Rohil et al; 2010	1714	26
Abraham et al; 2009	505	9.5
Sahu et al; 2009	633	6.4



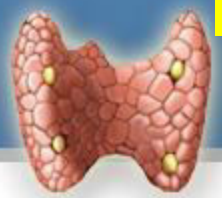
The Risk

- The risk of progression of subclinical hypothyroidism to overt hypothyroidism is approximately 2 to 6% per year.

- The risk is higher:
  - women
  - Higher thyrotropin levels,
  - Higher Antibodies titres



Peeters, RP et al. Engl J Med 2017;376:2556-65.



Indications Of Screening For Subclinical Hypothyroidism

- Presence of other autoimmune disease
  - type 1 diabetes,
  - pernicious anemia
  - alopecia
- H/o of first degree relative with autoimmune thyroid disease
- H/o of neck radiation for treatment of hyperthyroidism and neck malignancies
- H/o of hemithyroidectomy
- Presence of goitre
- Psychiatric disorders
- Drugs- amiodarone , lithium

Rule out transient increase in the TSH before a diagnosis of SCH is made

Table 1. Causes of Elevated Thyrotropin Levels, Unrelated to Chronic Mild Thyroid Failure.*

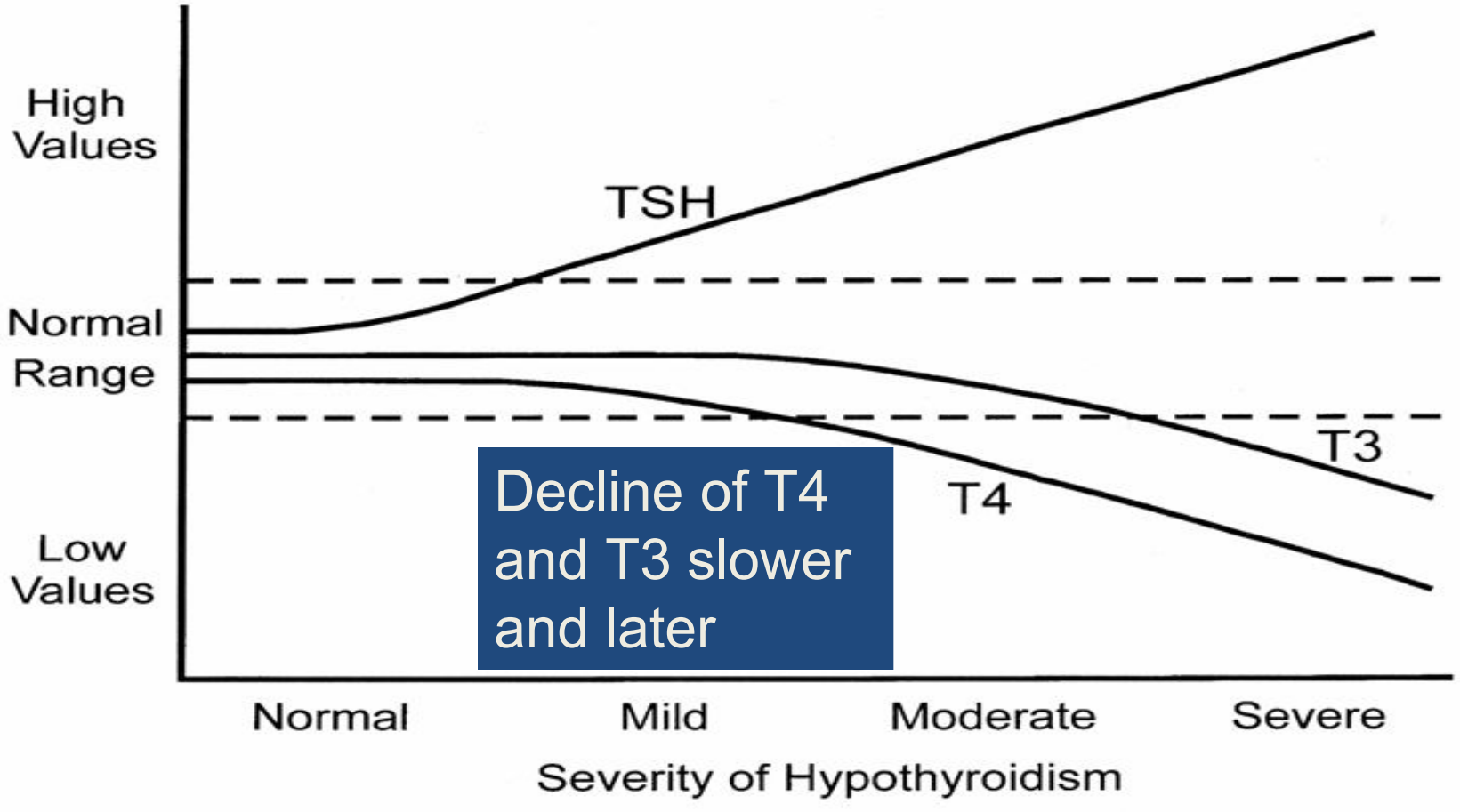
Causes of a transient increase in the thyrotropin level combined with a normal free T_4 level
Recovery from nonthyroidal illness
Recovery phase of various types of thyroiditis
Medication, such as amiodarone and lithium
Lack of adherence to treatment with levothyroxine or problems with resorption of levothyroxine in persons with hypothyroidism who are already receiving levothyroxine
Causes of a persistent increase in the thyrotropin level combined with a normal free T_4 level
Physiologic adaptation to aging (a widening of the reference range in elderly persons who have lived in regions with historical iodine sufficiency has been described)
Assay interference (e.g., caused by heterophilic antibodies)
Obesity
Adrenal insufficiency (very rare)
Thyrotropin-releasing hormone resistance or thyrotropin resistance (extremely rare)

* T_4 denotes thyroxine.

Severity of Primary Hypothyroidism

TSH rises first and abruptly

McDermott and Ridgway

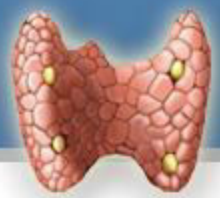


'Subclinical Hypothyroidism'

Natural Course of the Syndrome During a Prolonged Follow-up Study

- Prospective study of 30 subjects with "subclinical hypothyroidism" were followed up for 4 to 15 years.
- 50% subjects developed definitive primary hypothyroidism within 3 months to 2 years.

Arch Intern Med. 1993;153(8):957-961.



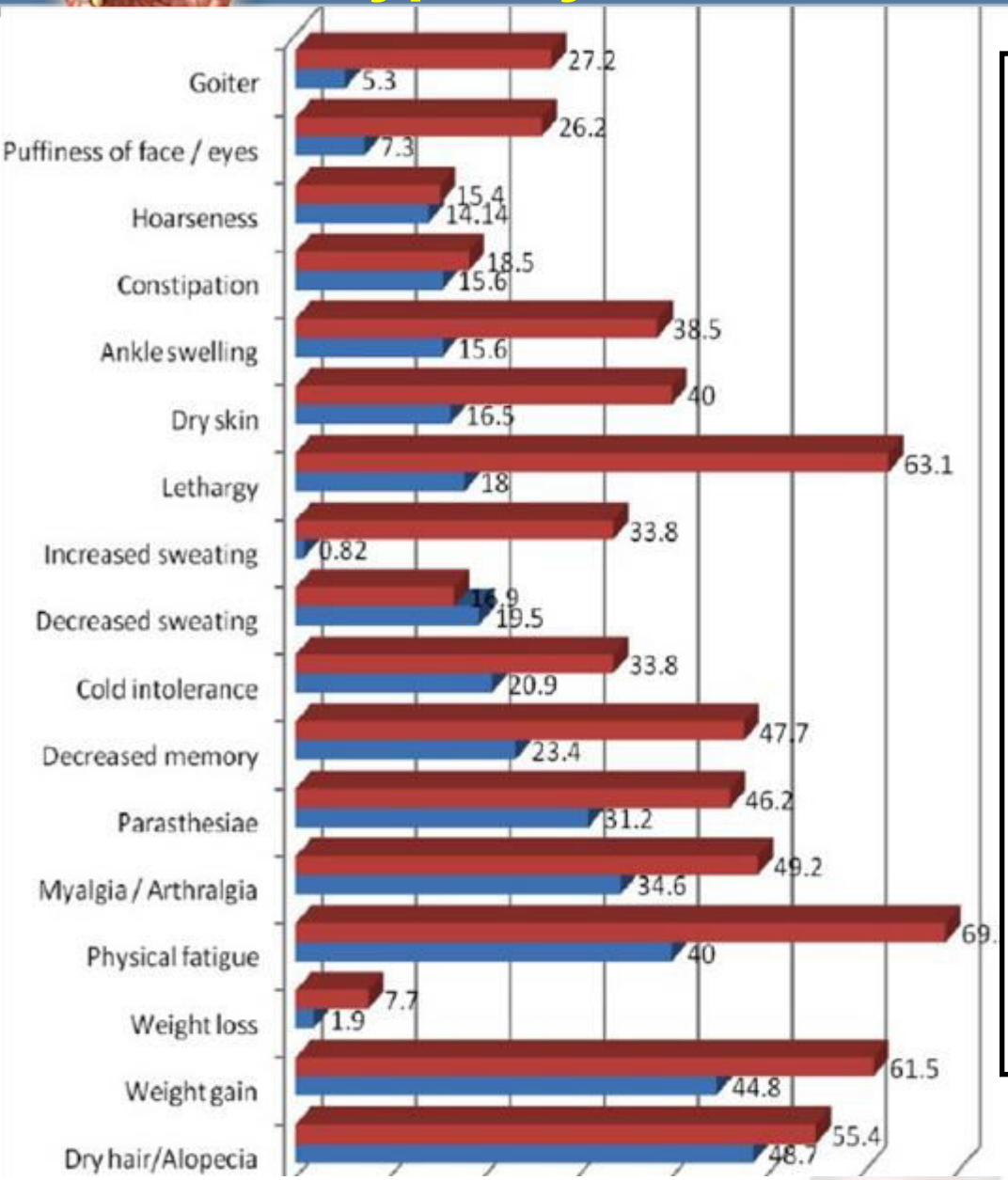
Spontaneous TSH normalization

- In contrast, TSH levels normalize in 15% to 65% of those with a single elevated TSH without treatment, over follow-up periods going from 1 to 6 years.

- The likelihood of spontaneous recovery is higher with TSH levels <10 mIU/l.

Somwaru LL et al. The natural history of subclinical hypothyroidism in the elderly: the cardiovascular health study. Journal Clin Endocrinol Metabol 97: 1962-1969, 2012.

Clinical presentation of Subclinical Hypothyroidism



Results of a study on Subclinical Thyroid Dysfunction in 237 Patients suggest that a higher % of these patients complained of symptoms of Hypothyroidism.

Most common symptoms include:

Weight gain (61.5%),

Fatigue (69.2%),

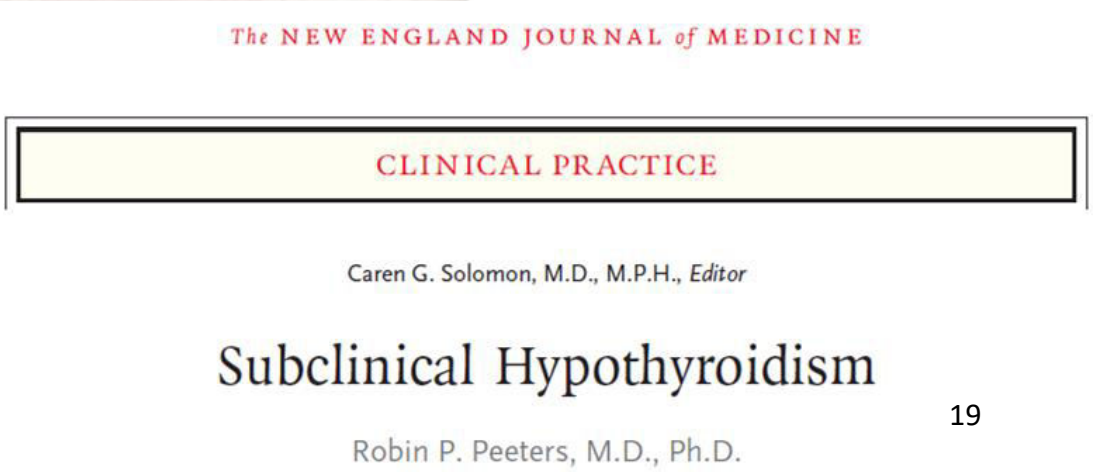
Lethargy (63.1%),

Dry Hair/Alopecia (55.4%)

Indian J Endocrinol Metab. 2013 May-Jun; 17(3): 454–459.

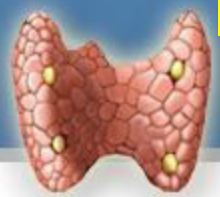
Associations Between Subclinical Hypothyroidism and Clinical Outcome

- Progression to overt hypothyroidism- Symptoms of hypothyroidism (e.g. tiredness, decreased cognition)
- Surrogate markers of cardiovascular risk (e.g., elevation in total cholesterol and LDL cholesterol levels, increased carotid wall intima–media thickness, and decreased cardiac function)
- Risk of coronary heart disease and congestive heart failure



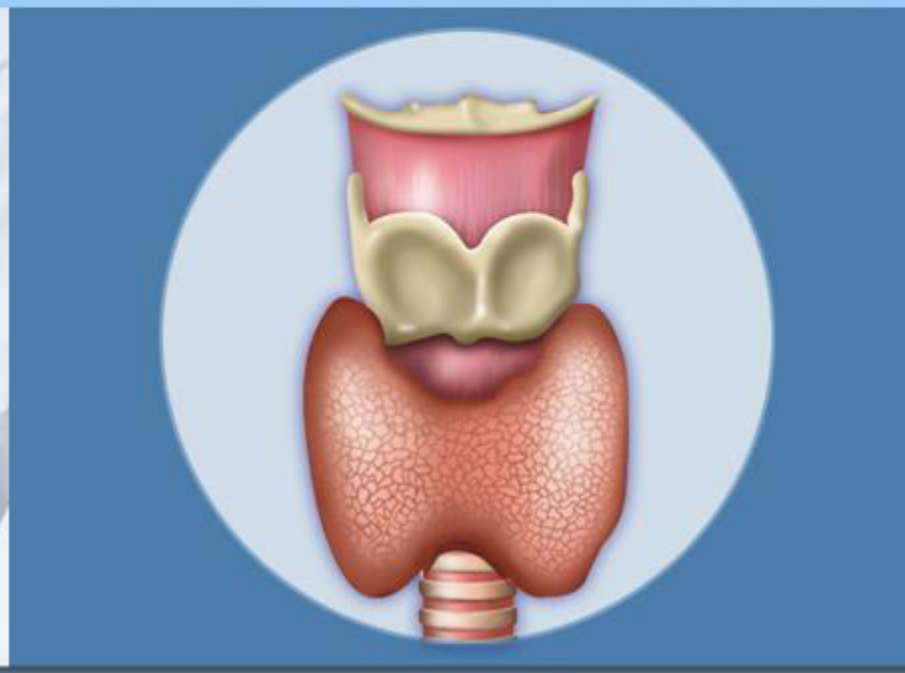
N Engl J Med 2017;376:2556-65.

Indications for screening of high-risk group

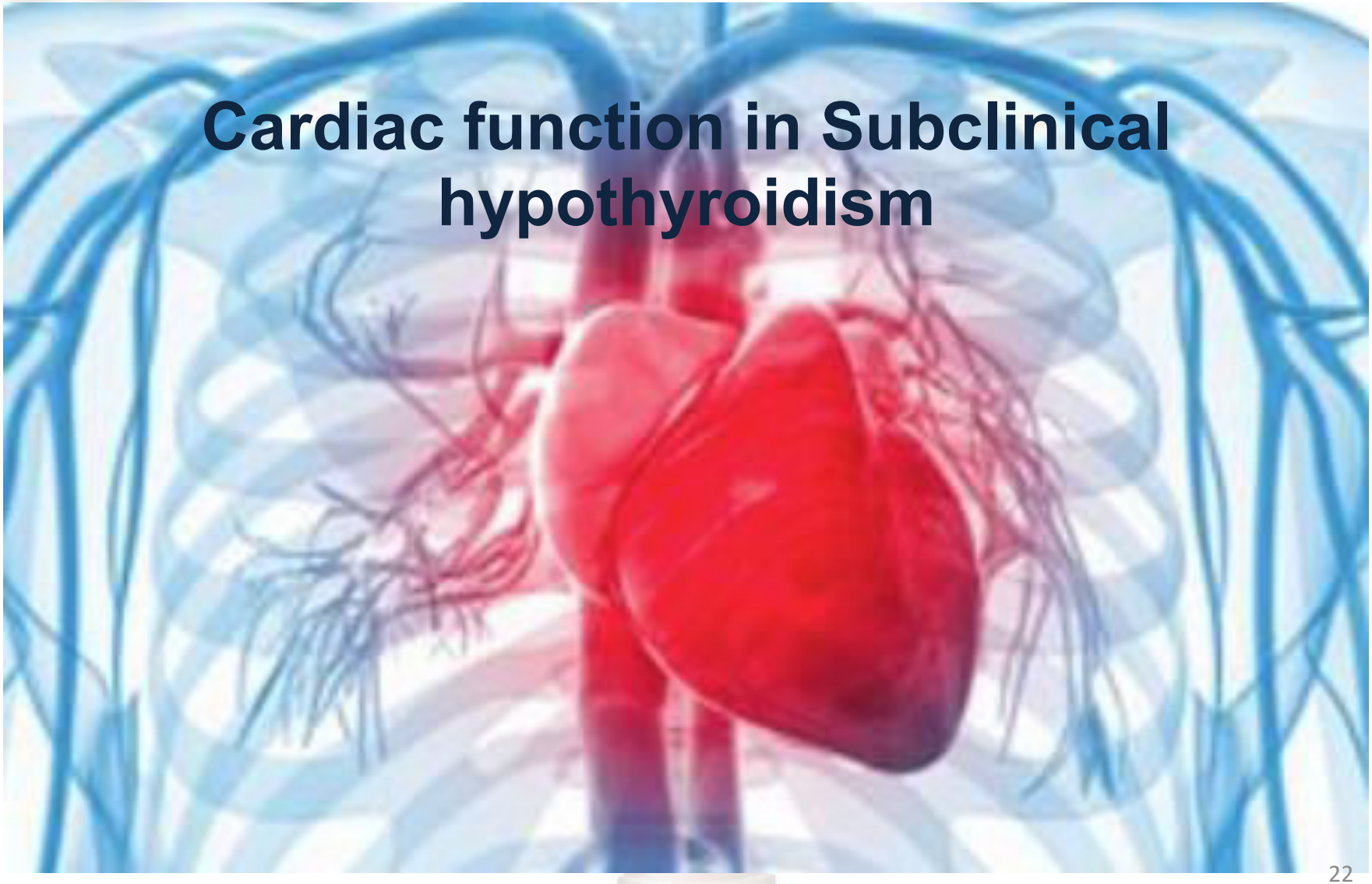


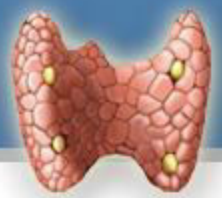
American Thyroid Association	Women and men >35 years of age should be screened every 5 years
American Association of Clinical Endocrinologists	Older patients, especially women, should be screened
American Academy of Family Physicians	Patients ≥60 years of age should be screened
American College of Physicians	Women ≥50 years of age with an incidental finding suggestive of symptomatic thyroid disease should be evaluated
U.S. Preventive Services Task Force	Insufficient evidence for or against screening
Royal College of Physicians of London	Screening of the healthy adult population unjustified

SYSTEMIC EFFECTS OF SUB CLINICAL HYPOTHYROIDISM



Cardiac function in Subclinical hypothyroidism



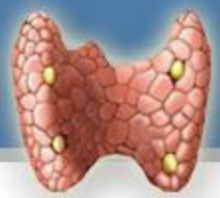


Cardiac function in Subclinical hypothyroidism

- The most consistent cardiac abnormality reported in patients with SCH is Impaired Left Ventricular Diastolic Function, characterized by slowed myocardial relaxation and impaired ventricular filling.

- Results concerning systolic function at rest are not consistent, by new more sensitive techniques -Doppler echocardiography and CMR

Biondi B et al. The Clinical Significance of Subclinical Thyroid Dysfunction. Endocrine Reviews. 2008;29(1):76–131



Subclinical hypothyroidism: Cardiac effects

Rotterdam Study

- Population based study studying chronic disease in the aging population (>55 years at entry)
- 3105 men, 4878 women
- TSH > 4.0 with normal free thyroxine levels

Hak, A. E. et. al. Ann Intern Med 2000;132:270-278

Rotterdam Study

1.7 1.9

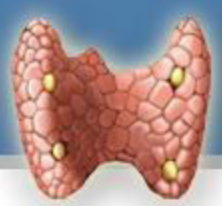
Table 3. Odds Ratios for Aortic Atherosclerosis and Myocardial Infarction*

Variable	Condition Present	Condition Absent	Odds Ratio (95% CI)†	Odds Ratio (95% CI)‡
	n			
Aortic atherosclerosis				
Women with subclinical hypothyroidism	77	37	1.7 (1.1–2.6)	1.9 (1.2–3.1)
Euthyroid women	474	376	1§	1§
Women with subclinical hypothyroidism and antibodies to thyroid peroxidase	39	16	1.9 (1.1–3.6)	2.2 (1.1–4.3)
Euthyroid women without antibodies to thyroid peroxidase	398	301	1§	1§
Myocardial infarction				
Women with subclinical hypothyroidism	17	99	2.3 (1.3–4.0)	2.3 (1.3–4.2)
Euthyroid women	61	806	1§	1§
Women with subclinical hypothyroidism and antibodies to thyroid peroxidase	11	46	3.1 (1.5–6.3)	3.5 (1.7–7.4)
Euthyroid women without antibodies to thyroid peroxidase	52	660	1§	1§

* The number of women may not be exactly the same as in Table 2 because data on some covariates were missing.
† Adjusted for present age.
‡ Adjusted for present age, body mass index, cholesterol level, high-density lipoprotein cholesterol level, systolic and diastolic blood pressure, and smoking status (current, past, or never).
§ Reference risk.

2.3 2.3

Hak, A. E. et. al. Ann Intern Med 2000;132:270-278



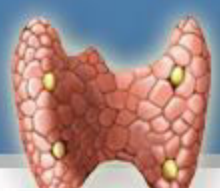
LV diastolic function in patients with SCH in comparison with Euthyroid control individuals

First author, year (Ref.)	No. of patients	Age (yr)	TSH (mIU/liter)	Cardiac findings	Cardiac methods
Biondi, 1999 (129)	26	36 ± 12	8.6 ± 4.8	↑ A, ↓ E/A, ↑ IRT	Doppler echo
Di Bello, 2000 (131)	16	32 ± 12	5.3 ± 1.9	↑ A, ↔ E/A, ↑ IRT	Doppler echo
Monzani, 2001 (133)	20	33 ± 12	5.4 ± 2.4	↔ E/A, ↑ A, ↑ IRT	Doppler echo
Vitale, 2002 (132)	20	38 ± 12	10.6 ± 4.05	↔ E/A, ↑ IRT	Doppler echo
Brenta, 2003 (130)	10	50 ± 8.7	11.0 ± 4.2	↑ TPFR	Radionuclide ventriculography
Yazici, 2004 (134)	45	40 ± 7.9	8.41 ± 2.1	↑ A, ↑ IRT, ↓ E/A	Doppler echo
Aghini-Lombardi, 2006 (135)	24	35 ± 6.2	5.3 ± 1.1	↑ A, ↑ IRT, ↓ E/A	Doppler echo

Values represent mean ± SD. IRT, Isovolumic relaxation time; TPFR, time-to-peak filling rate; E/A, early-to-late transmitral peak flow velocity ratio.

P values for SHypo *vs.* control subjects: IRT, Biondi and Yazici, $P < 0.001$; Di Bello, $P < 0.04$; Monzani, $P < 0.03$; Vitale, $P < 0.005$; Aghini-Lombardi, $P < 0.01$. E/A, Biondi and Yazici, $P < 0.001$; Monzani, $P < 0.01$; Vitale, $P < 0.005$; Aghini-Lombardi, $P < 0.02$. A, Biondi, $P < 0.05$; Yazici, $P < 0.01$; Di Bello, $P < 0.01$; Monzani, $P < 0.01$; Aghini-Lombardi, $P < 0.01$. TPFR, $P < 0.001$.

Biondi B et al. The Clinical Significance of Subclinical Thyroid Dysfunction. Endocrine Reviews. 2008;29(1):76–131

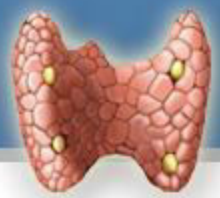


LV systolic function in patients with SCH in comparison with Euthyroid control individuals

First author, year (Ref.)	No. of patients	TSH (mIU/liter)	Cardiac findings	Cardiac methods
Bough, 1978 (142)	10	8.1 ≥ 50	↔ PEP, ↔ PEP/ET	Weissler's method
Foldes, 1987 (143)	17	10.3 ± 6.34	↔ PEP, ↔ PEP/ET	Weissler's method
Tseng, 1987 (144)	22	10.7 ± 10.3	↔ PEP, ↔ PEP/ET	Concurrent aortic and mitral valve echo
Staub, 1992 (145)	35	<6		
	14	6–12	↔ PEP, ↔ PEP/ET	Weissler's method
	20	>12		
Di Bello, 2000 (131)	16	5.3 ± 1.9	↑ PEP, ↑ PEP/ET	Doppler echo
Vitale, 2002 (132)	20	10.5 ± 4.05	↑ PEP, ↑ PEP/ET	Doppler echo
Monzani, 2001 (133)	20	5.4 ± 2.4	↑ PEP, ↑ PEP/ET	Doppler echo
Yazici, 2004 (134)	45	8.4 ± 2.1	↔ PEP, ↑ PEP/ET	Doppler echo
Aghini-Lombardi, 2006 (135)	24	5.3 ± 1.1	↑ PEP, ↑ PEP/ET	Doppler echo

Values represent mean ± SD. ET, Ejection time; PEP, preejection period.

P values for SHypo *vs.* control subjects: PEP, Di Bello, $P < 0.03$; Vitale, $P < 0.05$; Monzani, $P < 0.02$; Aghini-Lombardi, $P < 0.05$. PEP/ET, Di Bello, $P < 0.01$; Vitale, $P < 0.05$; Monzani, $P < 0.03$; Yazici, $P < 0.05$; Aghini-Lombardi, $P < 0.02$.

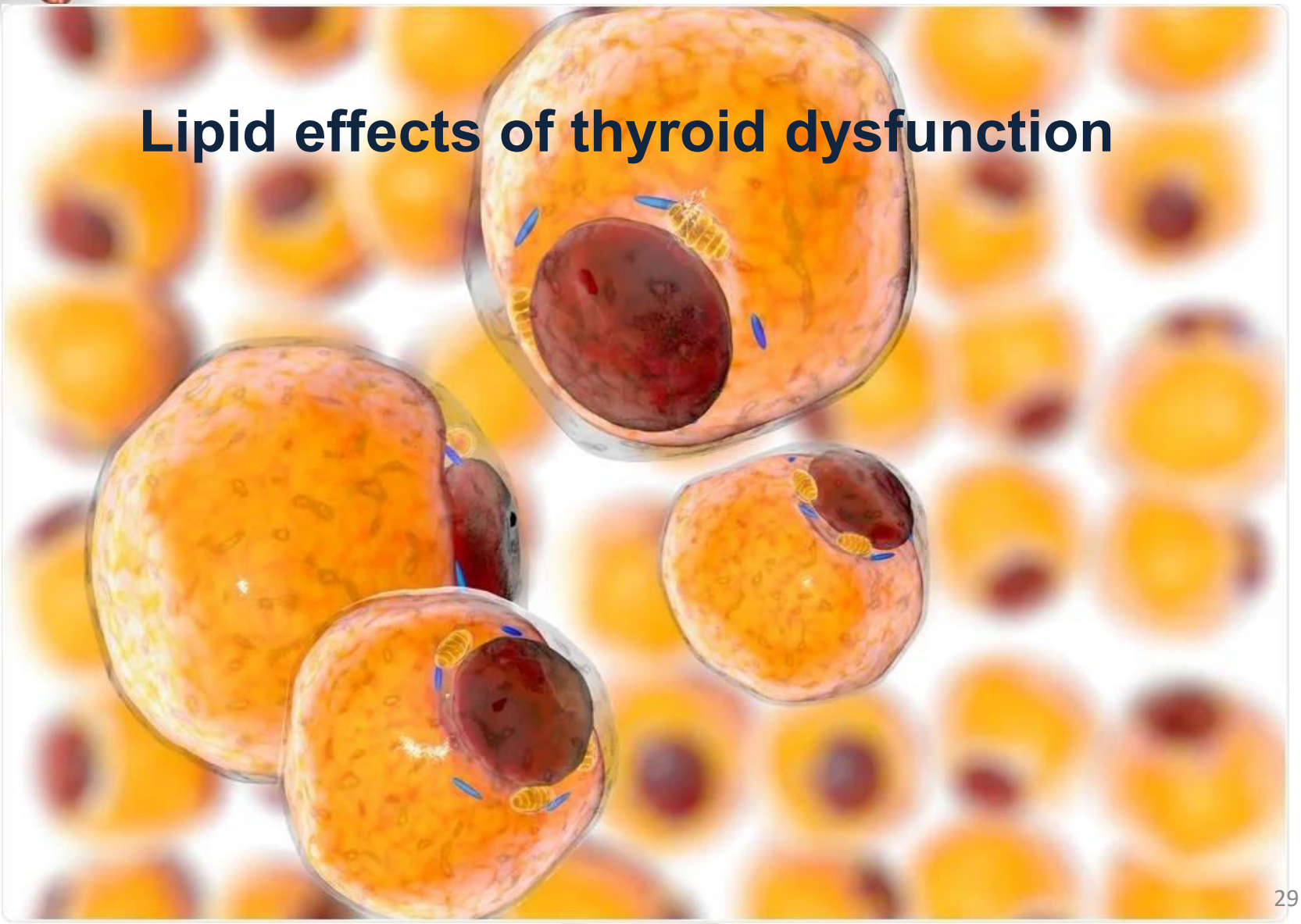


Summary of meta-analyses

Author	Number	Cardiovascular events	Cardiovascular mortality	All cause mortality
Singh 2008	13,267	**1.53 (1.31–1.79)**	**1.28 (1.02–1.60)**	1.12 (0.99-1.26)
Ochs 2008	14,449	1.20 (0.97-1.49)	1.18 (0.98-1.42)	1.12 (0.99-1.26)
Haentjens 2008	14,619	NI	NI	1.22 (0.95-1.57)
Razvi 2008	29,022	**1.23 (1.02– 1.48)**	1.09 (0.84 –1.41)	NI
Rodondi 2010	55,287	1.18 (0.99- 1.42)	1.14 (0.99- 1.32)	1.09 (0.96-1.24)
Thvilum 2012	35,740	NI	NI	**1.17 (1.00-1.37)**

Relative risks (5-95% confidence intervals)

Lipid effects of thyroid dysfunction

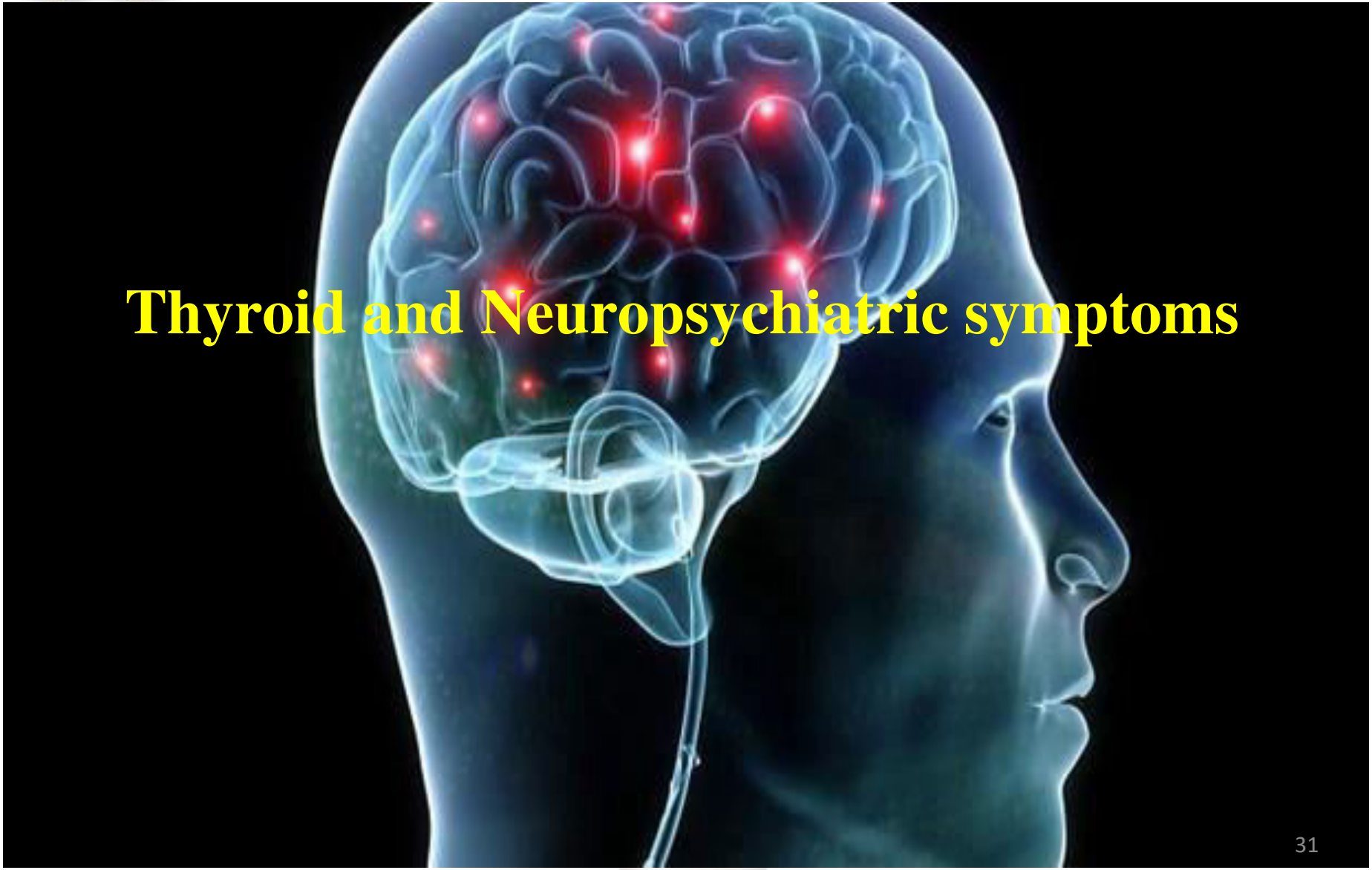


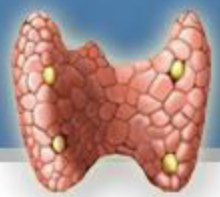
Lipid effects of thyroid dysfunction

	Hyperthyroidism	Overt hypothyroidism	Subclinical hypothyroidism
Total cholesterol	Decreased	Increased 30%	Increased
LDL cholesterol	Decreased	Increased 30%	Increased
HDL cholesterol	Decreased	Normal to slightly increased	No change
Triglycerides	No change	Normal to increased	Normal to increased
Lp(a)	Decreased	Increased	No change
ApoB	Decreased	Increased	Increased

- Thyroid hormones significantly affect lipoprotein metabolism causing varied effects on cholesterol levels *(IIa/B).*
- Thyroid dysfunction also predisposes an individual to other cardiovascular risk factors such as the metabolism and production of adipokines, oxidative stress and metabolic syndrome *(IIa/B).*
- In many cases hypothyroidism and hypercholesterolemia co-exist.

ITS Clinical Guideline 2012; Guidelines for Management of Dyslipidemia and Thyroid Dysfunction


Thyroid and Neuropsychiatric symptoms



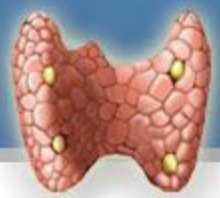
Neuropsychiatric symptoms

- Evidence of the association between cognitive dysfunction and SCH is conflicting.
- An association between subclinical hypothyroidism and mood disorders including depression and increased anxiety, as well as a reduced quality of life have been suggested in some studies, but other studies did not confirm these findings.

Baumgartner C et al. Subclinical hypothyroidism: summary of evidence in 2014. Swiss Med Weekly 144: 1 - 9, 2014.

Gussekloo J et al. Thyroid status, disability and cognitive function, and survival in old age. JAMA 292: 2591-2599, 2004.

Ceresini G et al. Thyroid function abnormalities and cognitive impairment in elderly people: results of the Invecchiare in Chianti study. J Am Geriatr Soc 57: 89-93, 2009.

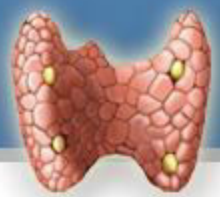


Neuropsychiatric symptoms

- A population-based cross-sectional study examining 2,050 participants including 141 – SCH; did not show an association with mild cognitive impairment, which represents the earliest detectable clinical stage of cognitive impairment.
- In a RCT evaluating the impact of thyroxine replacement on cognitive function with inclusion of 94 elderly participants with subclinical hypothyroidism, treatment did not lead to an improvement of cognitive function after a follow-up of 12 months.

Parsaik AK et al. Hypothyroidism and risk of mild cognitive impairment in elderly persons: a population-based study. JAMA Neurol 71: 201-207, 2014.
Parle J et al. A randomized controlled trial of the effect of thyroxine replacement on cognitive function in community-living elderly subjects with subclinical hypothyroidism: the Birmingham Elderly Thyroid study. J Clin Endocrinol Metab 95: 3623-3632, 2010.


Thyroid on Gastrointestinal system



Thyroid on Gastrointestinal system

- The influence of overt hypothyroidism on gastrointestinal mobility with symptoms such as constipation are well known.
- One study demonstrated impaired gastric motility and consecutive symptoms in premenopausal women with subclinical hypothyroidism.
- A cross-sectional study and found a dose-dependent relation between TSH levels and non-alcoholic fatty liver disease in individuals with subclinical and overt hypothyroidism.

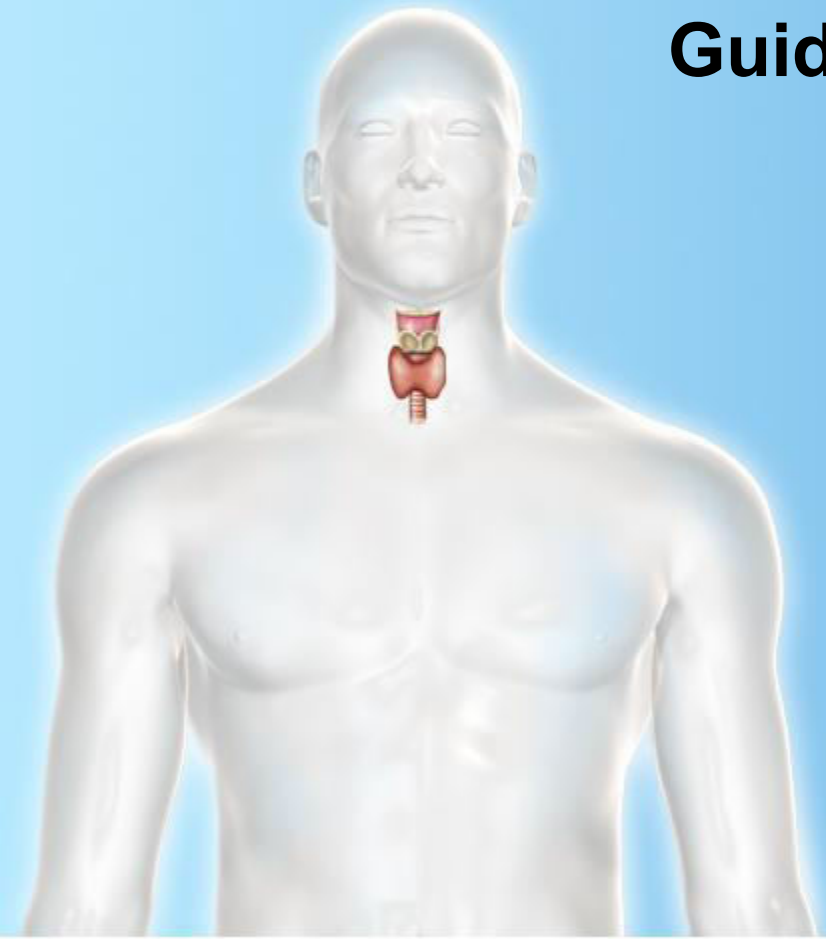
Canpolat AG et al. Effects of L-thyroxine on gastric motility and ghrelin in subclinical hypothyroidism: a prospective study. J Clin Endocrinol Metab 98: E1775-E1779, 2013.

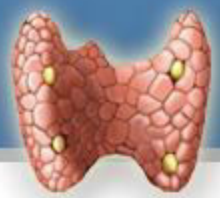
Chung GE et al. Non-alcoholic fatty liver disease across the spectrum of hypothyroidism. J Hepatol 57: 15-156, 2012.

Recommendations for treatment

Management of Subclinical Hypothyroidism

Guidelines…???





Whether or Not to Treat

- People who have no symptoms and only mildly elevated TSH levels usually don't need treatment.
- Many doctors donot recommend treatment unless the TSH levels are very high (over 10 mU/L).
- Treatment is sometimes recommended already starting at TSH levels of over 6 mU/L in people with high levels of thyroid antibodies (Hashimoto's thyroiditis), to prevent subclinical hypothyroidism from progressing to overt hypothyroidism.
- Deciding treatment comes down to personal preference since so many questions are still unanswered.

Informed Health Online [Internet].**Underactive thyroid: Deciding whether or not to treat subclinical hypothyroidism** Last Update: August 10, 2017;

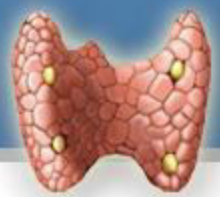
SCH with TSH > 10 mIU/L

2013 ETA Guideline: Management of Subclinical Hypothyroidism

Even in the absence of symptoms, replacement therapy with L -thyroxine is recommended for younger patients (<65 years) with serum TSH >10 mIU/L.

ITS guidelines on the Management of Subclinical Hypothyroidism

Evidence exists to recommend treatment in all patients with a TSH > 10 mIU/L.

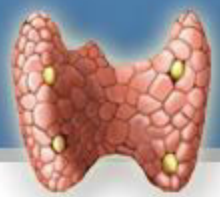


SCH with TSH < 10 mIU/L

2013 ETA Guideline: Management of Subclinical Hypothyroidism

In younger SCH patients (<65 years; serum TSH <10 mIU/L) with symptoms suggestive of hypothyroidism, a trial of L-thyroxine replacement therapy should be considered.

Patients with persistent SCH and diffuse or nodular goiter should be treated with L-thyroxine replacement with the aim of normalizing serum TSH levels.

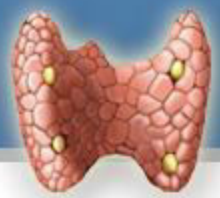


SCH with TSH < 10 mIU/L

ITS guidelines on the Management of Subclinical Hypothyroidism

Patients with symptoms of hypothyroidism especially fatigue may be treated.

Patients with high titers of antibodies or goiter or patients with cardiovascular risk factors under the age of 70 may be candidates for therapy



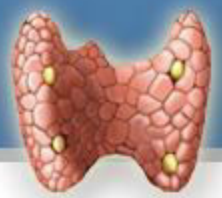
Factors favouring levothyroxine treatment in patients having mild-SCH (4.5–10 mIU/L)

Therapeutic trial for clinical symptoms	Goitre
Degree of TSH raised (TSH levels >8 mIU/L)	Antithyroid antibodies
Progressive TSH increase	Patient preference
Young age of the patient	Cardiovascular risk factors or prevalent CHD
Smoking	Dyslipidaemia
Pregnancy or intention of pregnancy	Infertility, ovulatory dysfunction

Baumgartner et al. Swiss Med Wkly. 2014 Dec 23;144:w14058.; Pearce et al. Eur Thyroid J 2: 215–228.
Fatourechi Mayo Clin Proc. 2009;84(1):65-71. Lazarus et al. Eur Thyroid J. 2014 Jun;3(2):76-94.

2013 ETA Guideline: Management of Subclinical Hypothyroidism

- If the decision is to treat SCH, then oral L -thyroxine, administered daily, is the treatment of choice.
- There is no evidence to support use of lio-thyronine (T 3) or combined L -thyroxine/lio-thyronine in the treatment of SCH.



Treatment for age >70 yrs or with thyrotropin levels <10 mIU

- Treatment decisions should be guided by individual patient factors, such as:

  - The extent of thyrotropin elevation
  - Whether the patient has symptoms of hypothyroidism
  - Antibodies to thyroid peroxidase
  - Goiter
  - Evidence of atherosclerotic cardiovascular disease, heart failure, or associated risk factors.

Peeters, RP et al. **Engl J Med 2017;376:2556-65.**

2013 ETA Guideline: Management of Subclinical Hypothyroidism

Dose of L-thyroxine

- For patients without cardiac disease, a weight-related dose of L -thyroxine should be used, approximating upto 1.5 µg/kg/day (e.g. 75 or 100 µg/day for woman, 100 or 125 µg for a man).
- For patients with cardiac disease and in the elderly, a small dose of L -thyroxine should be started, 25 or 50 µg daily.
- The dose of L -thyroxine should be increased by 25 µg/day every 14–21 days until a full replacement dose is reached.

2013 ETA Guideline: Management of Subclinical Hypothyroidism

Follow up

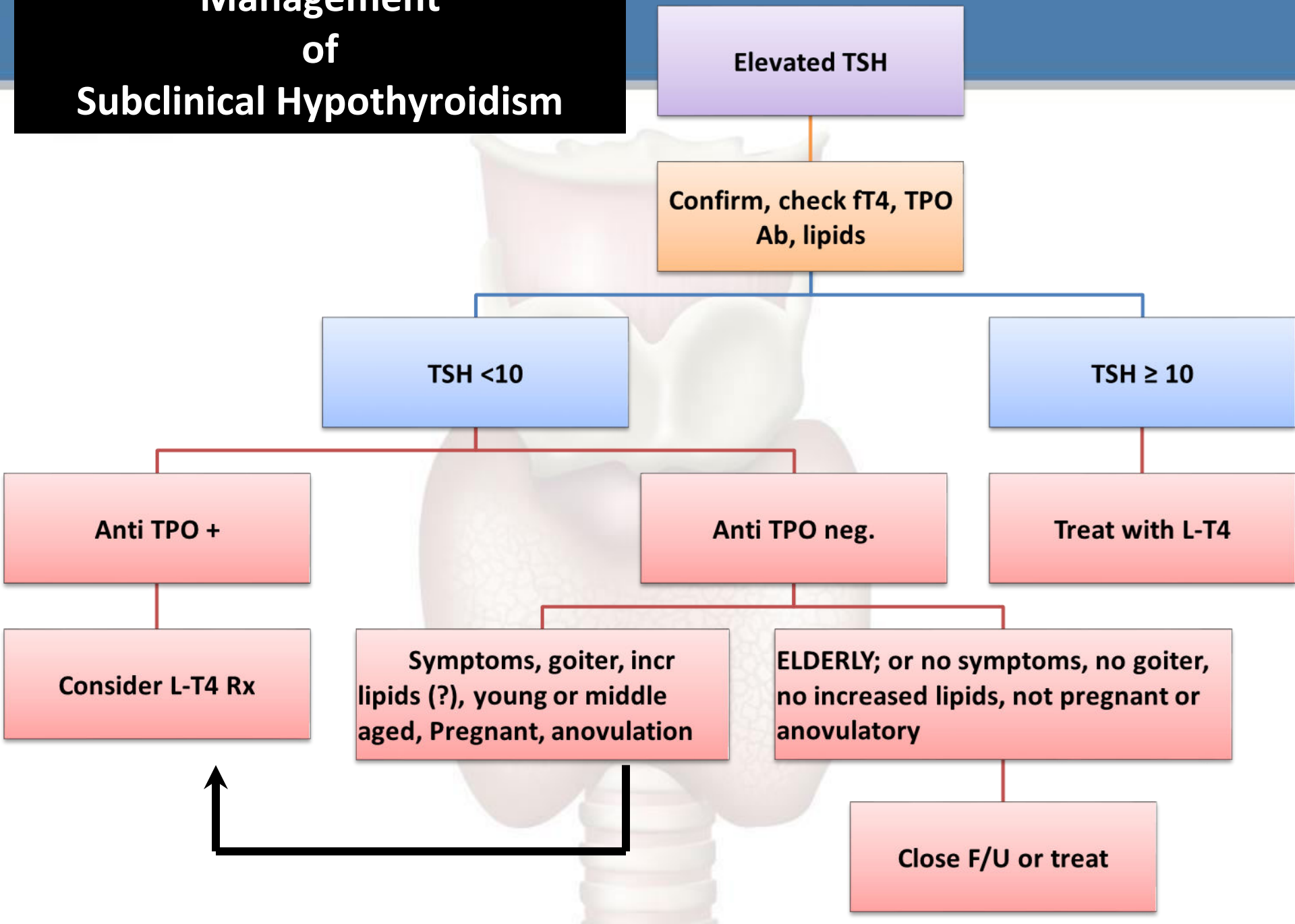
- The serum TSH should be re-checked 2 months after starting L -thyroxine therapy, and dosage adjustments made accordingly.
- The aim for most adults should be to reach a stable serum TSH in the lower half of the reference range (0.4–2.5 mIU/L).

Clinical Practice Guidelines for Hypothyroidism in Adults: Cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association.
Thyroid 2012; 12:1200

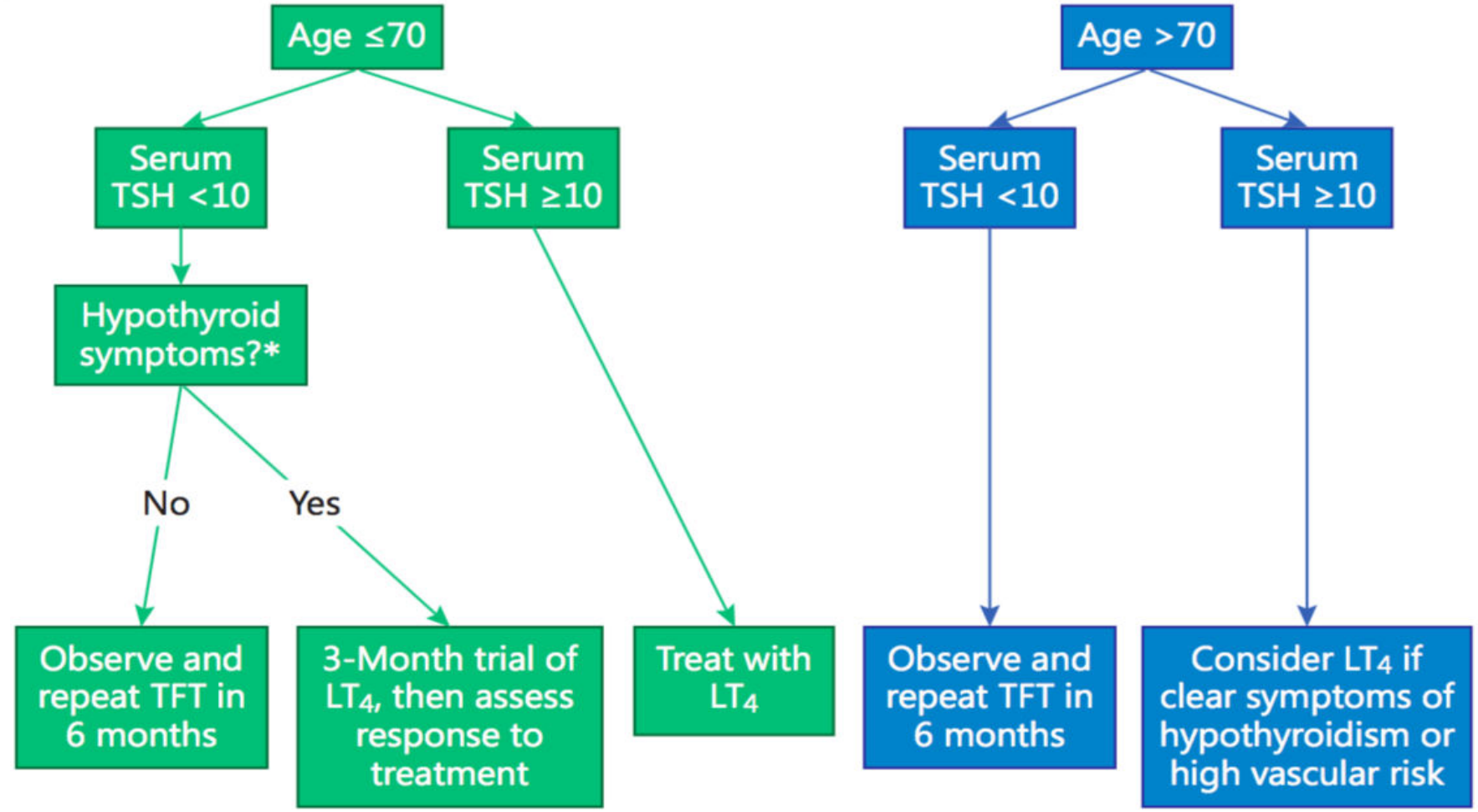
2013 ETA Guideline: Management of Subclinical Hypothyroidism
Eur Thyroid J 2013;2:215–228

Combining the two….

Management of Subclinical Hypothyroidism



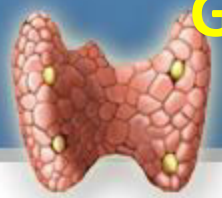
2013 ETA Guideline: Management of Subclinical Hypothyroidism



Pearce SHS. Et al Eur Thyroid J 2013;2:215–228

Subclinical hypothyroidism in pregnancy

Global - How common is subclinical hypothyroidism in pregnant women



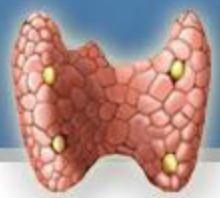
Prevalence among women of childbearing age	Autoimmune thyroiditis – 5-15%
	Overt hypothyroidism – 0.3-0.5%
	Subclinical hypothyroidism - 2-3%

Prevalence rates are similar during pregnancy

In a prospective population study of 9471 pregnant women, autoimmune thyroiditis was present in 55% of the women with subclinical hypothyroidism and in more than 80% of women with overt hypothyroidism

BMJ 2007;335:300-2 BMJ 2014;349:g492

In prospective studies, the prevalence of undiagnosed subclinical hypothyroidism in pregnant women ranges from 3% to 15%.

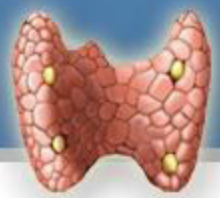


Indian scenario

- Prevalence of hypothyroidism in pregnancy = 4.8-12%.
- Another Indian study = 12% was hypothyroid, of which 3% was Overt and 9% was SCH.
- Incidence of hypothyroidism & SCH in women with recurrent pregnancy loss up to 12 weeks is 4.1-16.6%.
- TPO antibodies are positive in around 50% pregnant women in SCH, as compared to 7% in euthyroid pregnant women

	Miscarriage rate	Still birth rate	Preeclampsia	Abruptio placentae	IUGR	Preterm delivery
SCH (%)	12-21	0 - 16.6	22	5	8	11
OVERT (%)	21	4.2	16	16	25	33

National Guidelines for Screening of Hypothyroidism during Pregnancy. Maternal Health Division Ministry of Health & Family Welfare. Government of India December 2014



Subclinical hypothyroidism and pregnancy

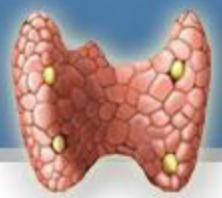
The classic definition of SCH is a thyrotropin (TSH) level greater than the upper limit of normal range (4.5–5.0 mIU/L) with normal free thyroxine (FT4) levels. With this definition, the incidence of SCH in the reproductive-age population is approximately 4%–8%.

.

Hypothyroidism potentially can have a significant impact on reproductive outcomes.

Inadequate treatment of overt hypothyroidism or subclinical hypothyroidism (SCH) can lead to infertility, miscarriage, & adverse obstetrical and neurodevelopmental outcomes

SARKAR D. Recurrent pregnancy loss in patients with thyroid dysfunction. Indian J Endocrinol Metab 2012; 16(Suppl 2): S350-S351.



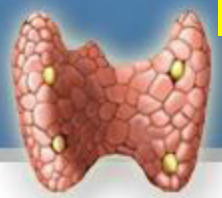
Impact of SCH on pregnancy outcome and intellectual development of the fetus

- Studies provided clear evidence of a link between overt hypothyroidism and adverse events.

- Subclinical hypothyroidism has been associated with multiple negative outcomes

- Spontaneous abortion
- Pre-eclampsia
- Gestational hypertension
- Preterm Delivery
- Gestational Diabetes
- impaired neurologic development in the offspring

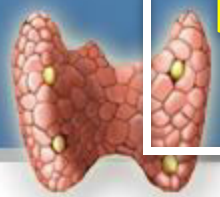
BMJ 2014;349:g4929



Indications for screening of high-risk reproductive age group

- History of thyroid dysfunction or prior thyroid surgery
- Age >30 years
- Symptoms of thyroid dysfunction or the presence of Goitre
- Thyroid peroxidase antibody (TPO-Ab) positivity
- Type 1 diabetes or other autoimmune disorders
- History of miscarriage or preterm delivery (RPL)
- History of head or neck radiation
- Family history of thyroid dysfunction
- Morbid obesity (body mass index [BMI] ≥40 kg/m2)
- Use of amiodarone or lithium, or recent administration of iodinated
- History of infertility and residing in an area of known moderate-to-severe iodine sufficiency.

Indian Journal of Clinical Practice 2014;25(5):449-54



Treatment of subclinical hypothyroidism in pregnancy

Pregnant women with TSH concentrations >2.5 mU/L should be evaluated for TPO antibody status.

A: Levothyroxine therapy is recommended for:

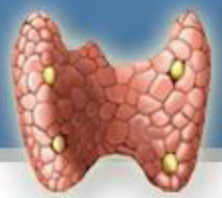
- TPO Ab +ve women with a TSH > pregnancy specific reference range
- TPO Ab –ve women with a TSH > 10.0 mU/L

B: Levothyroxine therapy may be considered for:

- TPO Ab +ve women with TSH concentrations > 2.5 mU/L and below the upper limit of the pregnancy specific reference range
- TPO Ab –ve women with TSH concentrations > pregnancy specific reference range and below 10.0 mU/L

C: Levothyroxine therapy is not recommended for:

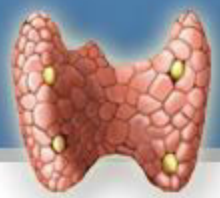
- TPO Ab –ve women with a normal TSH (TSH within the pregnancy specific reference range, or < 4.0 mU/L if unavailable)



Maintenance and monitoring of levothyroxine therapy- ATA

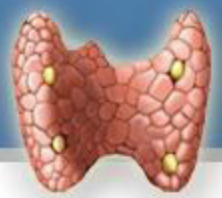
- Whether LT-4 therapy should be continued postpartum, is an important question
- All pregnant women with TSH > 2.5 mIU/L and normal free thyroxine who are TPO-Ab positive; all women with TSH > 10.0 mIU/L, irrespective of the free thyroxine value, be continued.
- However insufficient data were available for TPO-Ab negative pregnant women with a thyrotropin greater than 2.5 mIU/L.
- Testing indicated every four weeks until 16-20 weeks, and at least once between 26 and 32 weeks' gestation.

BMJ 2014;349:g4929



Summary

- Most common symptoms of subclinical hypothyroidism include weight gain (61.5%), fatigue (69.2%), lethargy (63.1%), dry hair/alopecia (55.4%)
- Studies have demonstrated an increased risk of complications with mildly elevated TSH .
- Despite the limitations of available interventional trials of levothyroxine therapy in this subclinically hypothyroid group, the data taken in aggregate appear to suggest a benefit of treatment.



Summary

- It is recommended to treat all patients of SCH with a TSH > 10 mIU/L.
- SCH patients with serum TSH 4.5-10 mIU/L with symptoms suggestive of hypothyroidism a trial of L-thyroxine replacement therapy should be considered.

Subclinical thyroid disease

Minor biochemical Abnormality

?

Potential hidden impact on quality of life and survival

?