Hypotyreos-Finns det en väg till en bättre behandling

23 oktober 2025 40 min

Helena Filipsson Nyström
Professor
Universitetssjukhusöverläkare
Endokrinolog
Göteborgs Universitet
Sahlgrenska Universitetssjukhuset
Göteborg, Sverige

Conflict of Interest

Föreläsararvode från: BMS; IBSA; Siemens, Equalis, MSD

Ingår i patientföreningens professionsråd

Ordförande Nationella arbetsgruppen för Hypertyreos, nu associerad till NPO endokrina

Regional processordförande hypertyreos

Kursledning CONSUL Tyreoidea-ben-Kalk Oslo Okt 2025

Kursledare för Tyreoideasjukdomar 7,5 hp för sjuksköterskor vid Göteborgs Universitet ht 2025

Sköldkörtelstatistik

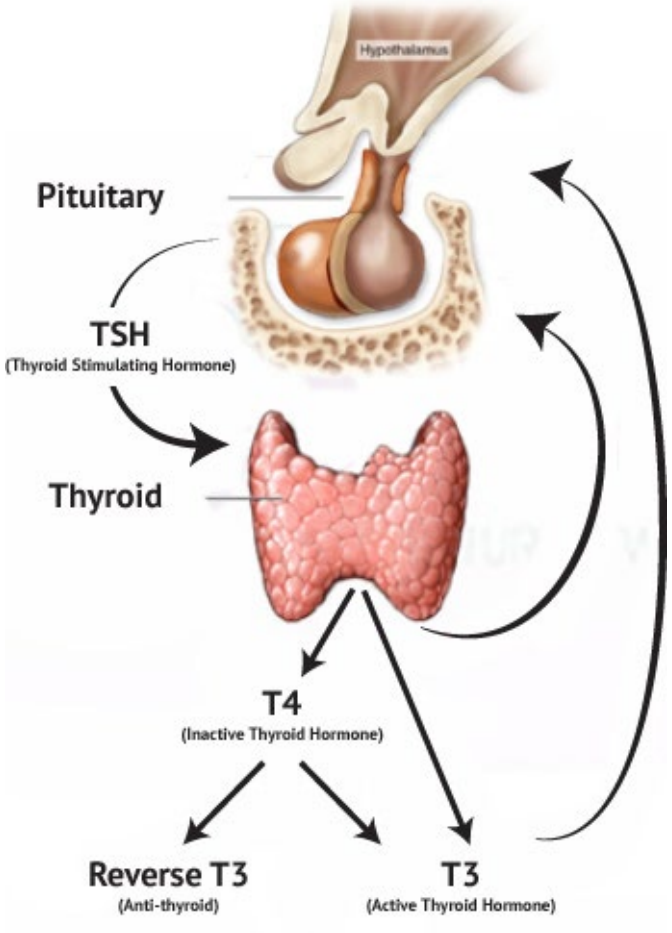
Här har vi sammanställt aktuell statistik om behandling av sköldkörtelsjukdom. I Socialstyrelsens statistikdatabas för läkemedel kan man fördjupa sig vidare. Koden för sköldkörtelbehandling är H03.

Till Socialstyrelsens läkemedelsdatabas

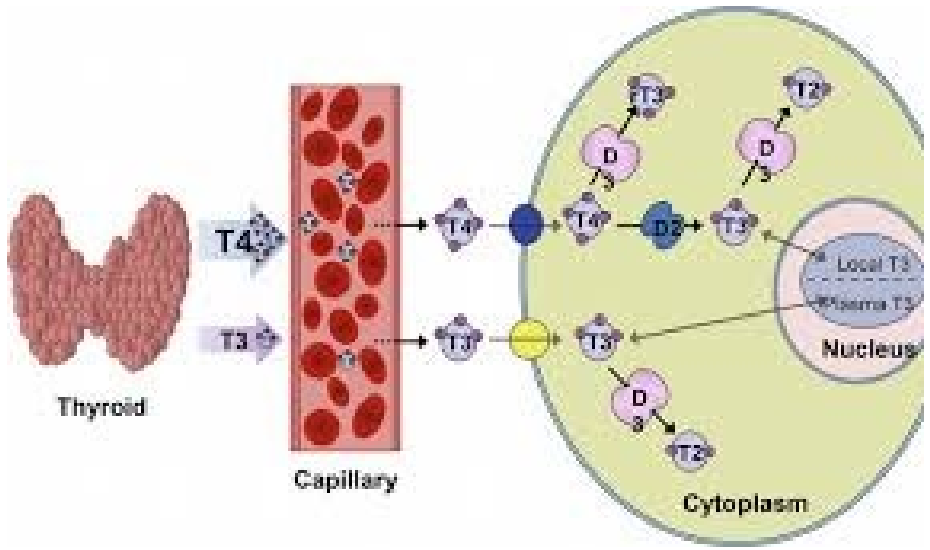
Du är inte ensam

493 000 personer i Sverige behandlas med levotyroxin (Levaxin, Euthyrox) för underfunktion i sköldkörteln, hypotyreos. Det motsvarar 4,7 % av befolkningen. Levotyroxin var Sveriges tredje mest förskrivna läkemedel till kvinnor och var tionde kvinna över 18 år behandlades med läkemedlet under 2024.

Läs mer om hypotyreos →


Hypothalamus
Pituitary
TSH
(Thyroid Stimulating Hormone)
Thyroid
T4
(Inactive Thyroid Hormone)
Reverse T3
(Anti-thyroid)
T3
(Active Thyroid Hormone)


Thyroid
Major
Minor
DIO1/DIO2
T4
T3


Thyroid
T4
T3
Capillary
D1
D2
D3
Local T3
Plasma T3
Nucleus
Cytoplasm

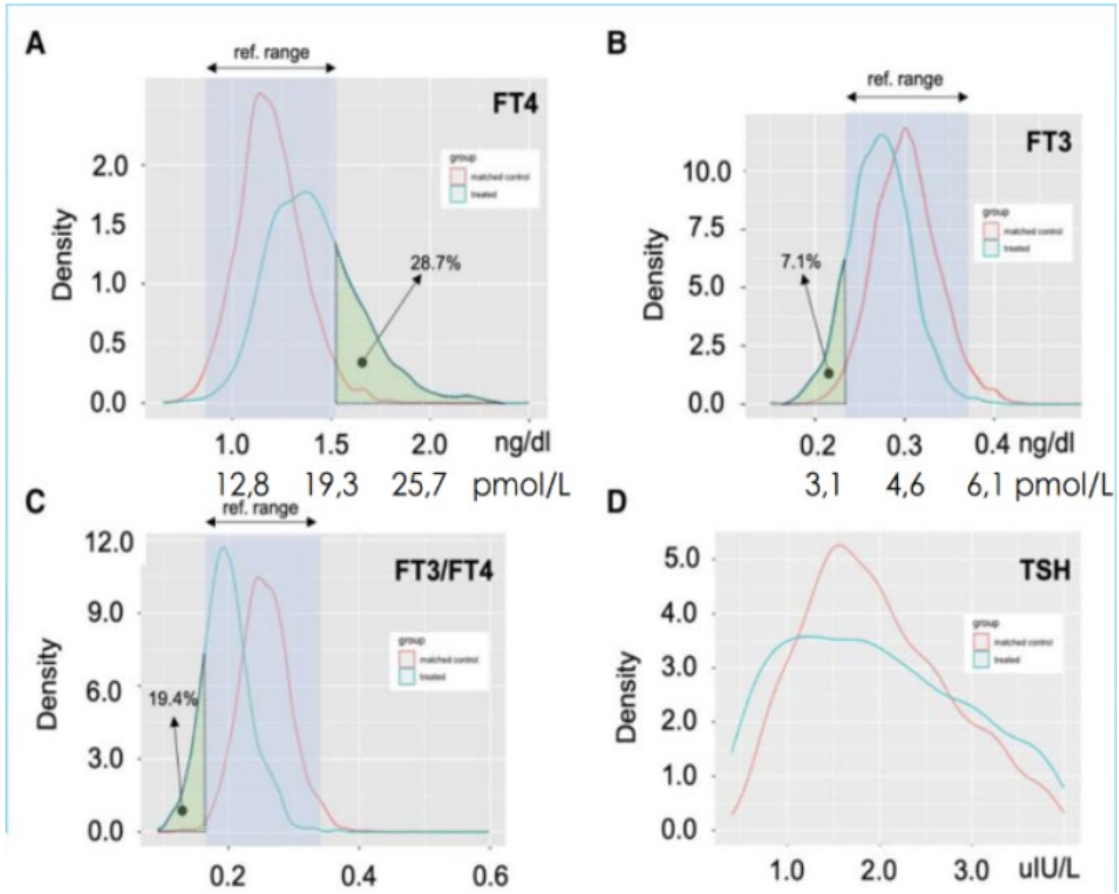
J Clin Endocrinol Metab. 2024 Sep 16;109(10):2504-2512. doi: 10.1210/clinem/dgae139.

Thyroid Hormone Homeostasis in Levothyroxine-treated Patients: Findings From ELSA-Brasil

Gustavo C Penna [1 2], Isabela M Bensenor [3], Antonio C Bianco [1], Matthew D Ettleson [1]

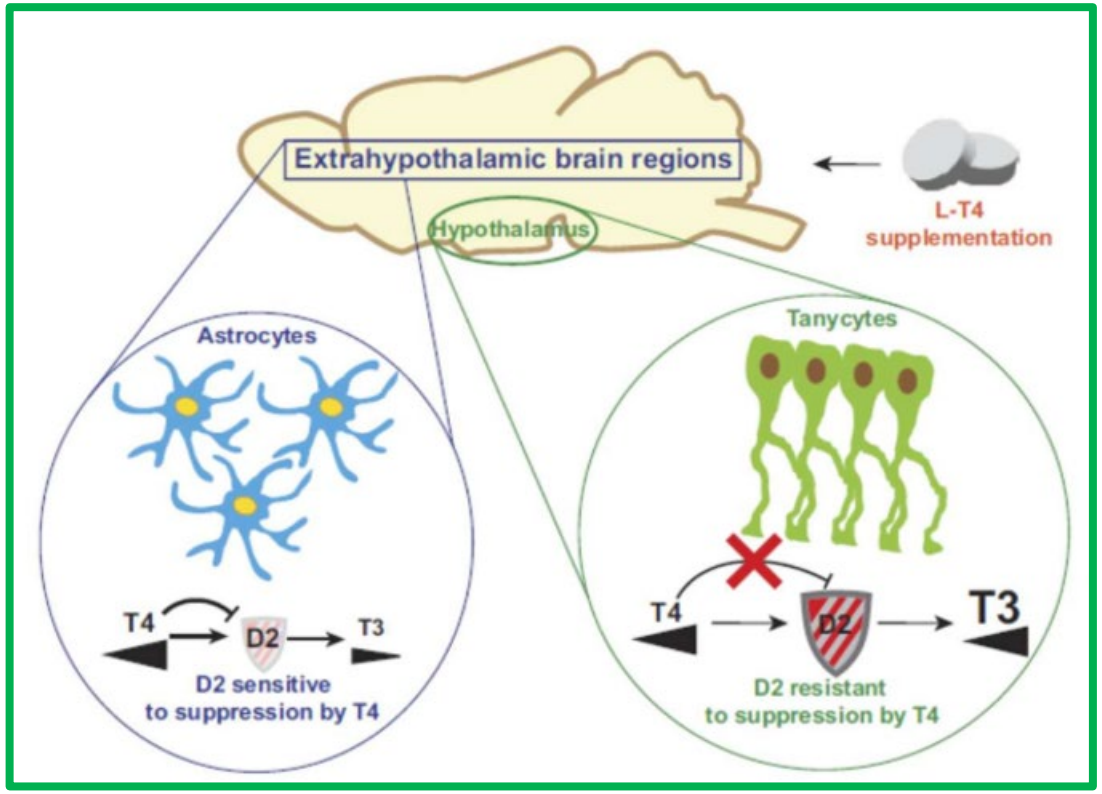
Affiliations + expand

PMID: 38506164 PMCID: PMC11403308 DOI: 10.1210/clinem/dgae139



Prospektiv kohort-studie i Brasilien
Prover taget x 3 under 8 år
LT4 behandlade (normalt TSH varje gång) n=243 och kontroller n=927

Kan det finnas en fysiologisk rational till varför det inte fungerar för vissa?



- 'Our study reveals that T4 therapy fails to restore T3-dependent actions across various brain structures. ..
- This phenomenon arises because the conversion of T4 to T3 can be self-limiting due to cell-type specific regulation of the D2 enzyme, particularly in cases of elevated T4 levels commonly observed in T4-treated patients
- Amid supraphysiological L-T4 exposure, the hypothalamic D2 efficiently produces T3 while extrahypothalamic brain regions face suboptimal TH signaling
- These findings offer valuable mechanistic insights into the limitations of T4 therapy and underscore the need for a more nuanced approach to managing hypothyroidism.'

Sinko R et al PNAS 2025: 122(6)

The Journal of Clinical Endocrinology & Metabolism, 2021, Vol. 106, No. 11, e4400–e4413
https://doi.org/10.1210/clinem/dgab478
Clinical Research Article

Clinical Research Article

Comparative Effectiveness of Levothyroxine, Desiccated Thyroid Extract, and Levothyroxine+Liothyronine in Hypothyroidism

Mohamed K.M. Shakir,[1,2] Daniel I. Brooks,[1] Elizabeth A. McAninch,[3] Tatiana L. Fonseca,[4] Vinh Q. Mai,[1,2] Antonio C. Bianco,[4] and Thanh D. Hoang[1,2]

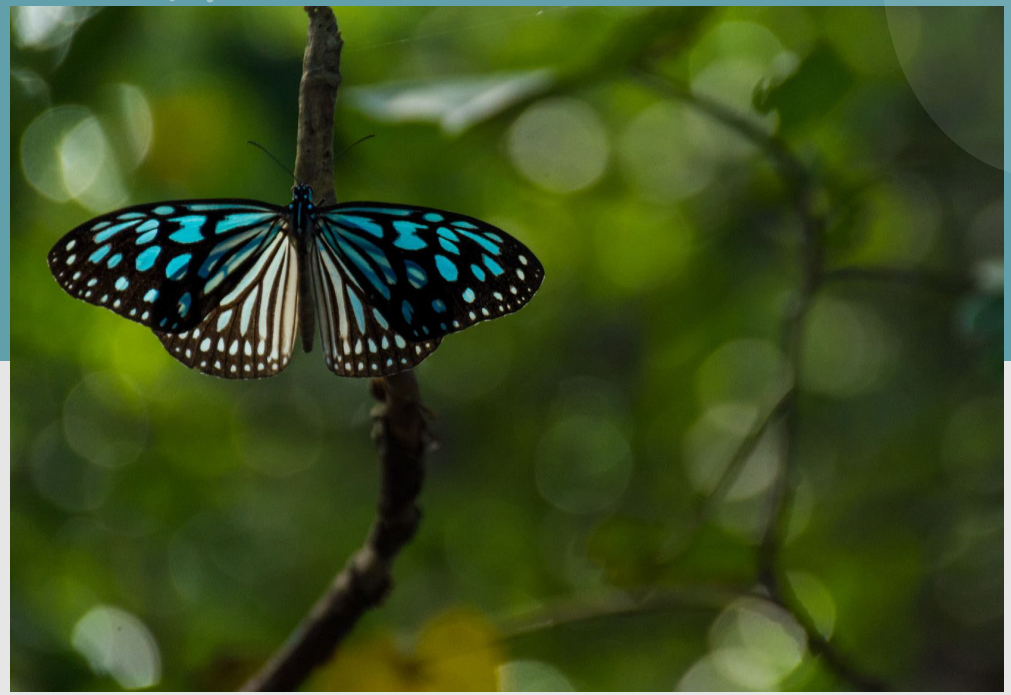
[1]Walter Reed National Military Medical Center, Bethesda, MD 20889-5600, USA; [2]Uniformed Services University of the Health Sciences, Bethesda, MD 20814, USA; [3]Division of Endocrinology and Metabolism, Rush University Medical Center, Chicago, IL 60612, USA; and [4]Section of Adult and Pediatric Endocrinology, University of Chicago, Chicago, IL 60637, USA

Oktober 2021

Outline
Behandling av hypotyreos

- Vad har hänt med synen på kvarvarande symptom vid hypotyreos?
- Var är vi forskningsmässigt nu?
- Vad för forskning pågår?
- Är det säkert att använda LT3?
- Finns det en väg till en bättre behandling?

Vad har hänt med synen på kvarvarande symptom vid hypotyreos?



Published in final edited form as:

Endocr Pract. 2022 March ; 28(3): 257–264. doi:10.1016/j.eprac.2021.12.003.

Brain Fog in Hypothyroidism: Understanding the Patient's Perspective

Matthew D. Ettleson, MD[1,*], Ava Raine[2], Alice Batistuzzo, PhD[3], Samuel P. Batista, MSc[3], Elizabeth McAninch, MD[4], Maria Cristina T.V. Teixeira, PhD[3], Jacqueline Jonklaas, MD[5], Neda Laiteerapong, MD, MS[6], Miriam O. Ribeiro, PhD[3], Antonio C. Bianco, MD, PhD[1]

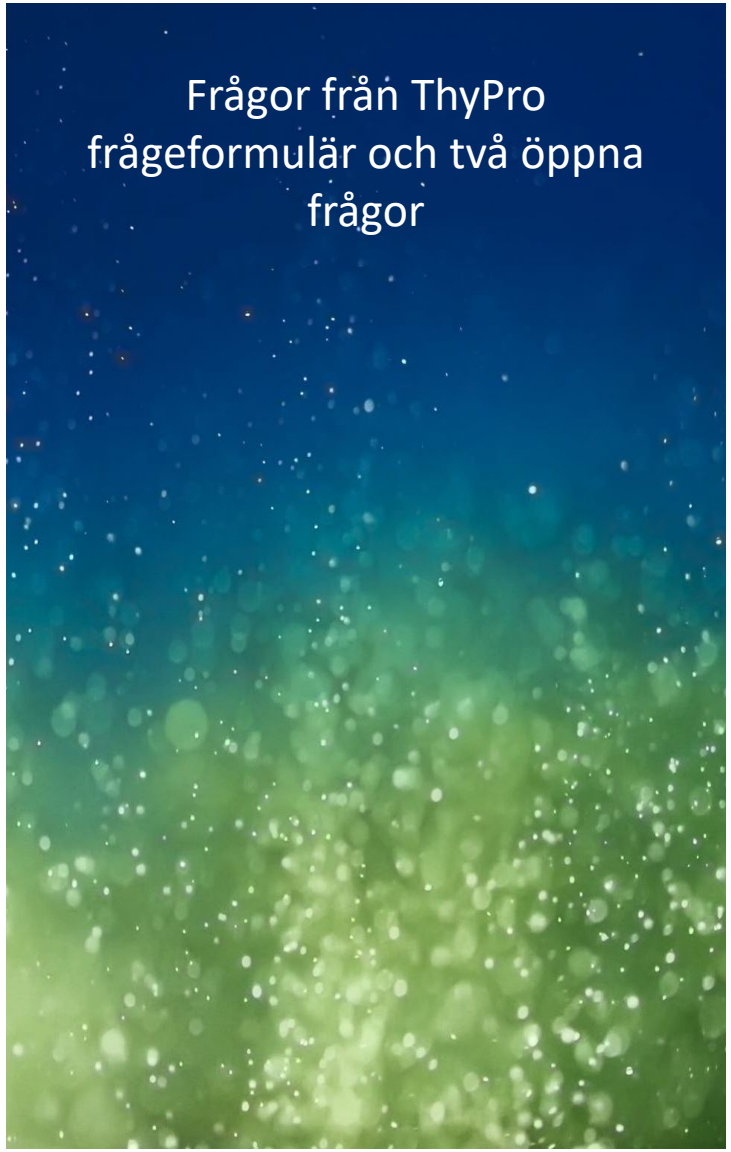
Online frågeformulär

Riktade sig till patienter med hypothyreos och “brain fog”

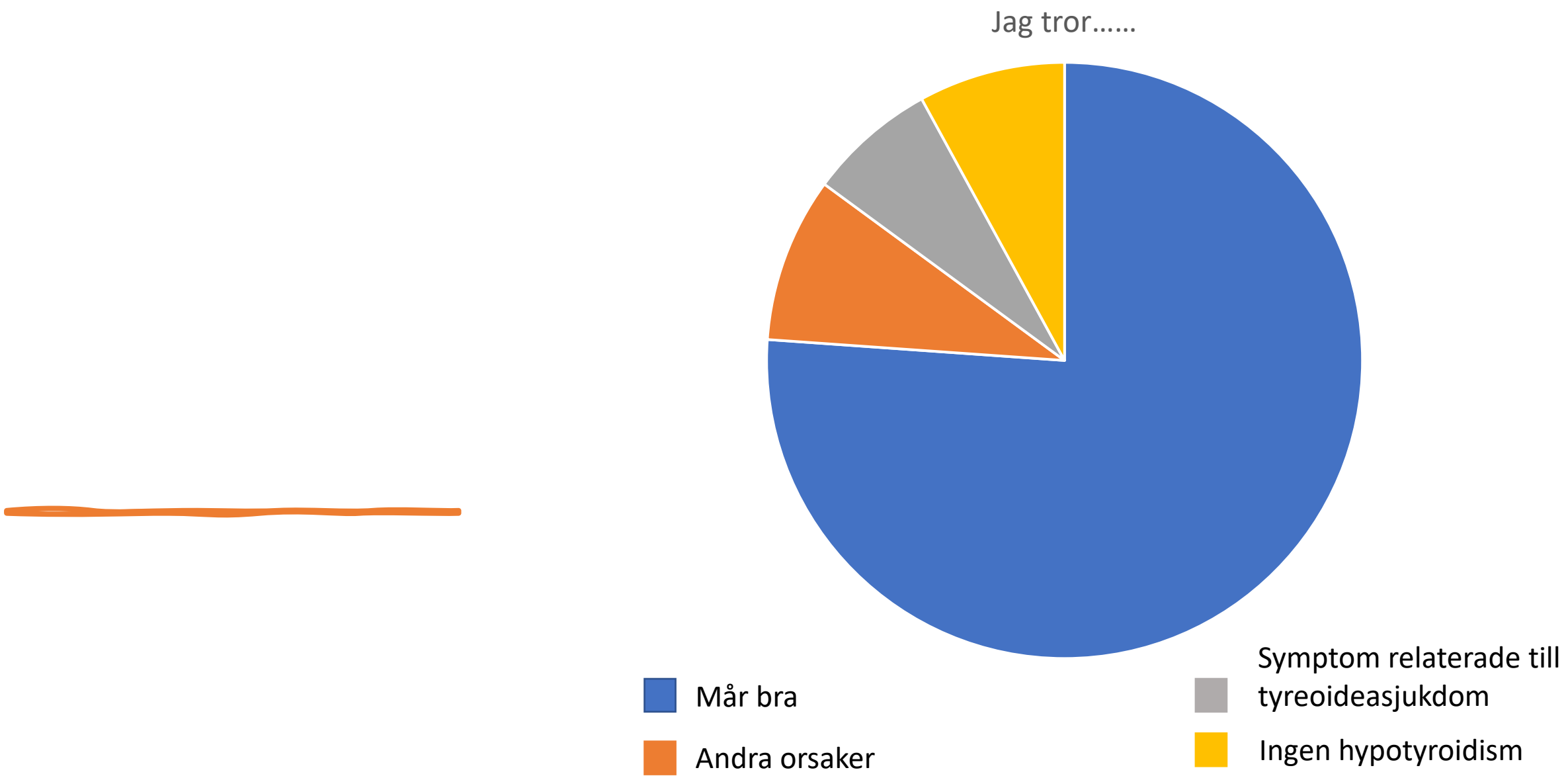
46.6% (av 5170) rapporterade start av symptom innan diagnosen av hypotyreoidism

79.2% hade symptom som påverkade livsföringen

Vila var den faktor som oftast förbättrade symptomen



Ettleson MD et al 2022 Endocr Pract


Jag tror……
Mår bra
Andra orsaker
Symptom relaterade till tyreoideasjukdom
Ingen hypotyroidism

Circle of Misery

Symptom
Trötthet, sliten, hjärntrötthet, depression, övervikt och smärta

Gå till läkaren
Tyreoideaprov FT4 TSH

Normala nivåer eller gränsvärde
Lätt ökade TSH, lågt normal FT4, Neg TPOak

Start av levotyroxin utan klar indikation
Ökande doser succesivt med låga TSH nivåer

Patienten blir inte bättre
Möjligen viss förbättring som försvinner efter några veckor (och som kan ha andra orsaker)

THYROID
Volume 32, Number 7, 2022

DOI: 10.1089/thy.2022.0139

REVIEW and SCHOLARLY DIALOG

Open camera or QR reader and scan code to access this article and other resources online.

Brain Fog in Hypothyroidism: What Is It, How Is It Measured, and What Can Be Done About It

Mary H. Samuels[1] and Lori J. Bernstein[2]

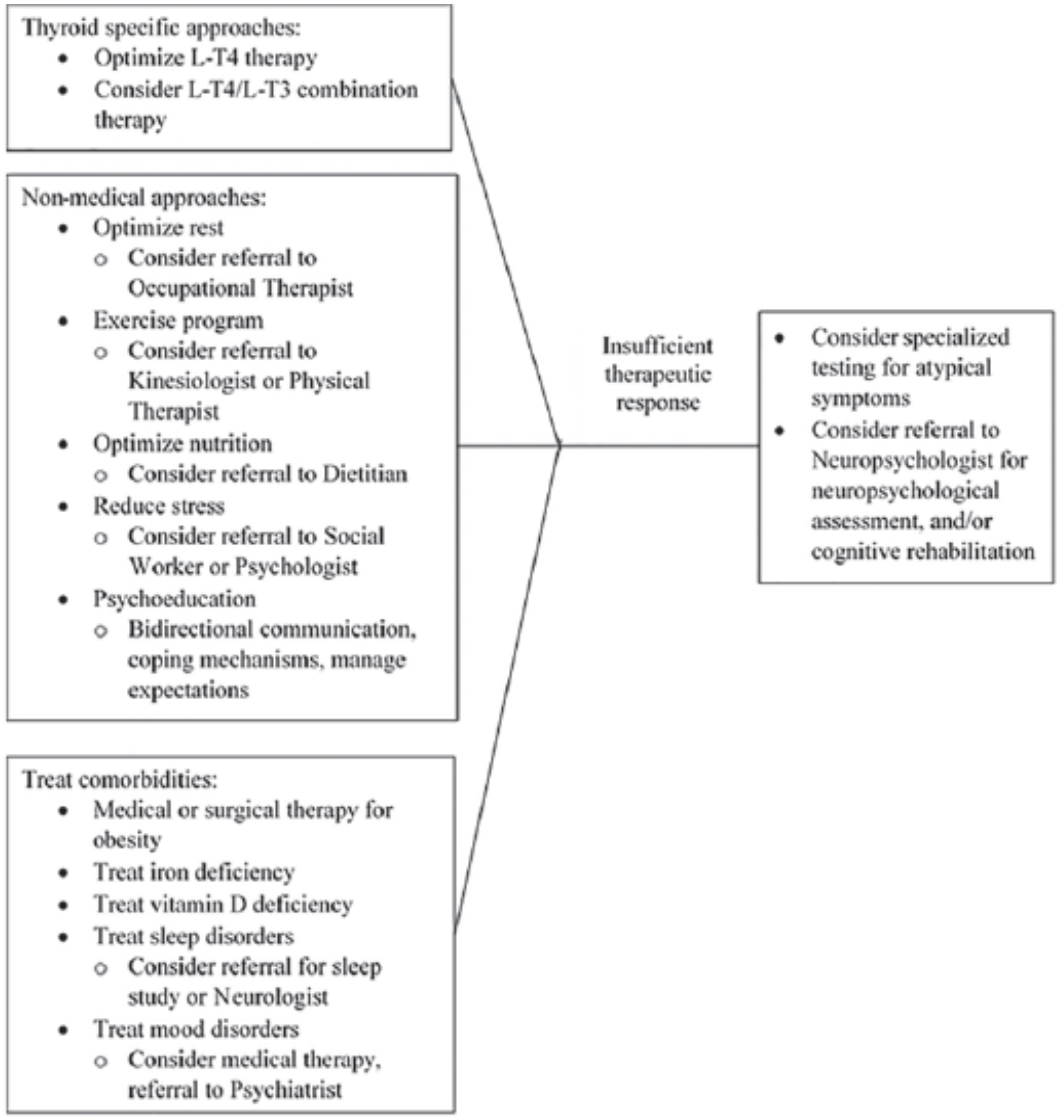
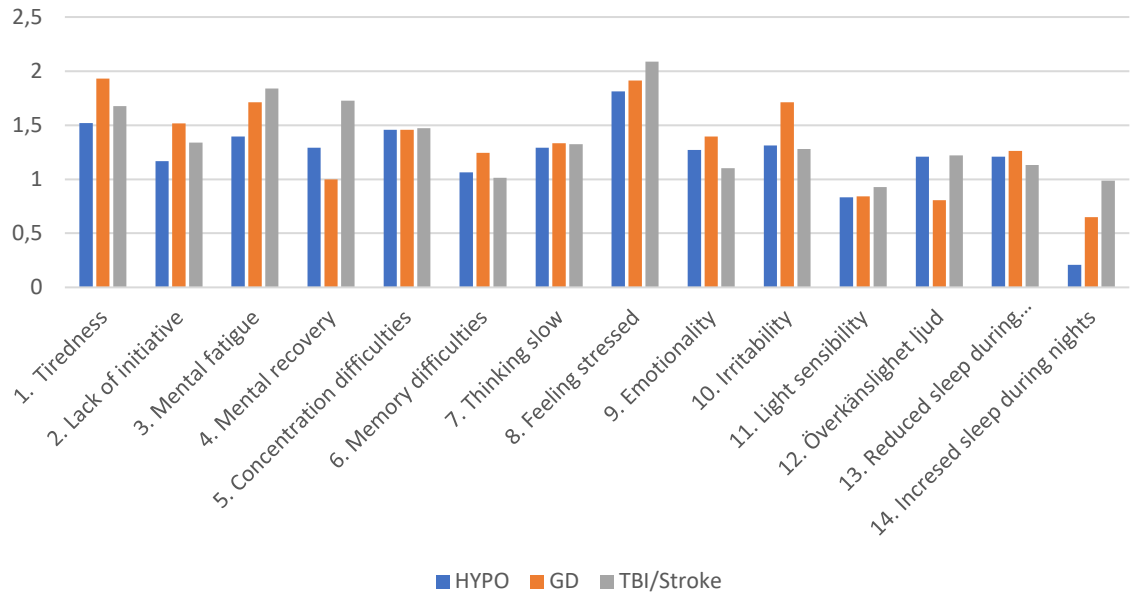


FIG. 1. Recommended treatment algorithm for hypothyroid-associated brain fog.

Samuels et al Thyroid 2022

Varje fråga i MFS presenterat för de som ligger över cut-off för hypotyreoidism, Graves' sjukdom eller TBI/ stroke

Liknande presentation oavsett bakomliggande orsak



Preliminary data borrowed from Birgitta Johansson in our group

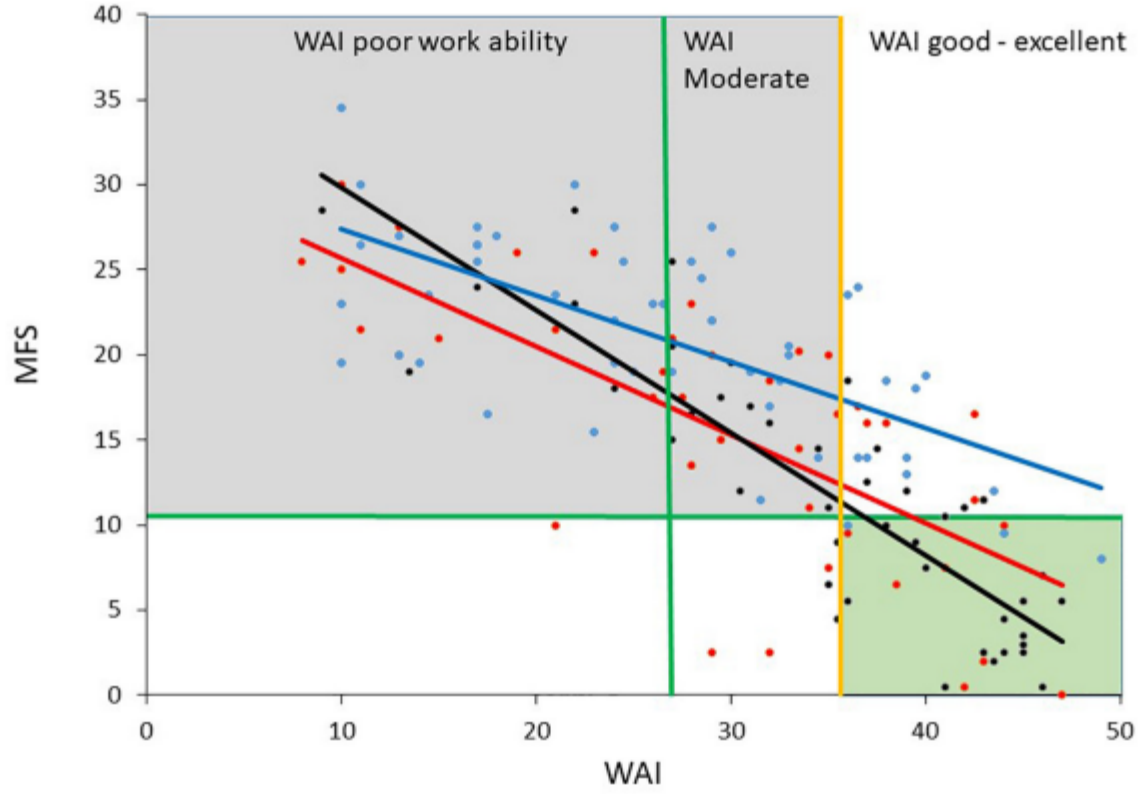
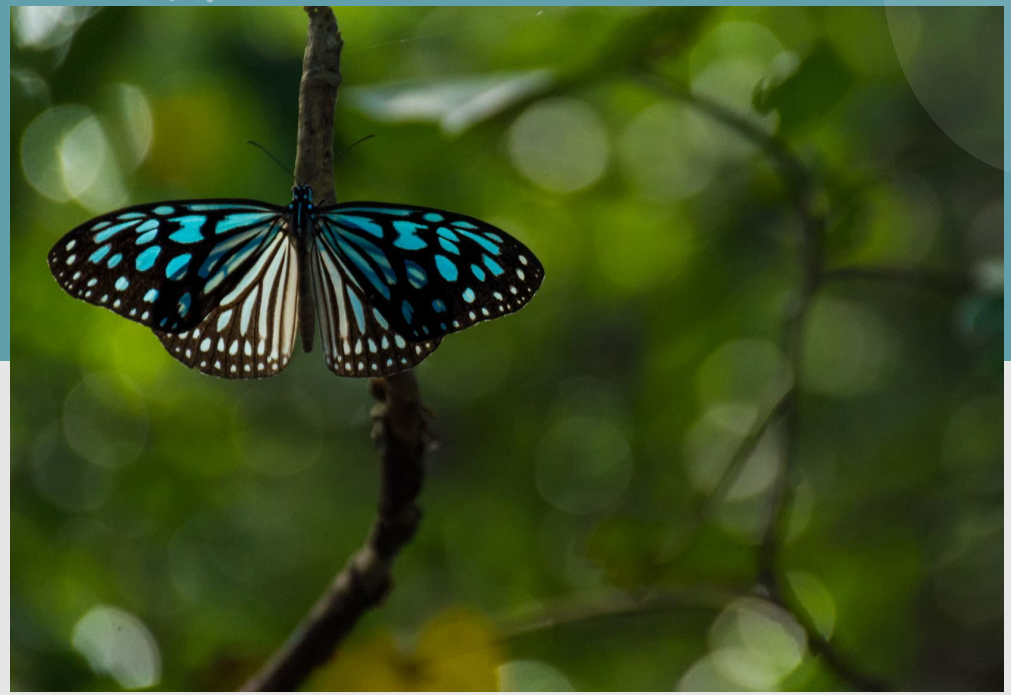
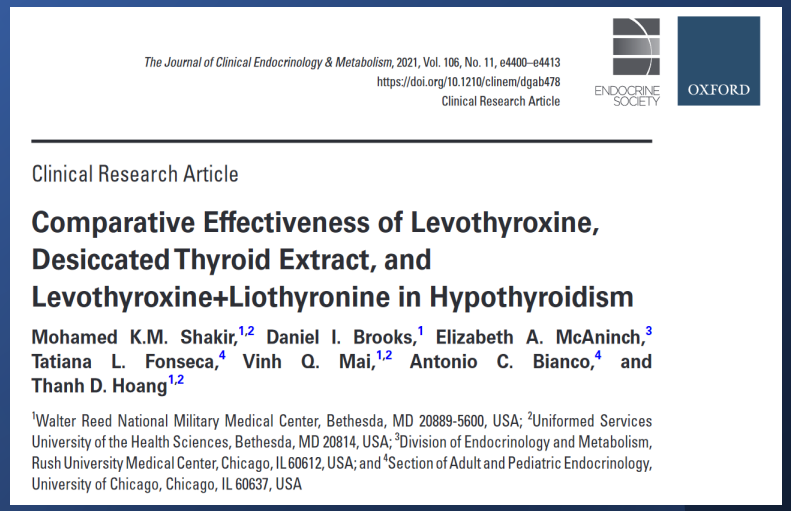


FIGURE 1 | The figure shows the diagnostic groups ABI (acquired brain injury, red), HYT (hypothyroidism black) and BO (burn-out syndrome, blue), and the relationship between WAI (Work Ability Index) and MFS (Mental Fatigue Scale). The gray square indicates poor and moderate work ability according to WAI, together with mental fatigue above cutoff. The green square indicates good work ability and no significant mental fatigue.

Johansson B 2022 Frontiers in Behavioural Neuroscience

Var är vi forskningsmässigt nu?





The Journal of Clinical Endocrinology & Metabolism, 2021, Vol. 106, No. 11, e4400–e4413
https://doi.org/10.1210/clinem/dgab478
Clinical Research Article

Clinical Research Article

Comparative Effectiveness of Levothyroxine, Desiccated Thyroid Extract, and Levothyroxine+Liothyronine in Hypothyroidism

Mohamed K.M. Shakir,[1,2] Daniel I. Brooks,[1] Elizabeth A. McAninch,[3] Tatiana L. Fonseca,[4] Vinh Q. Mai,[1,2] Antonio C. Bianco,[4] and Thanh D. Hoang[1,2]

[1]Walter Reed National Military Medical Center, Bethesda, MD 20889-5600, USA; [2]Uniformed Services University of the Health Sciences, Bethesda, MD 20814, USA; [3]Division of Endocrinology and Metabolism, Rush University Medical Center, Chicago, IL 60612, USA; and [4]Section of Adult and Pediatric Endocrinology, University of Chicago, Chicago, IL 60637, USA

- Ingen skillnad mellan monoterapi eller kombinationsterapi
- Behandlingspreferenser skilde sig inte
- Ingen skillnad vad gäller etiologin till hypotyreosen
- Ingen skillnad avseende Thr92Ala-DIO2 gen polymorfismen

- En sub-analys visade att 1/3 av de mest symptomatiska patienterna på LT4 förbättrades genom att använda en kombination med T3, antingen LT4 + LT3 eller DTE.

Shakir M et al JCEM 2021

Meta-Analysis > J Clin Endocrinol Metab. 2025 Feb 18;110(3):887-900.
doi: 10.1210/clinem/dgae651.

Treatment Preferences in Patients With Hypothyroidism

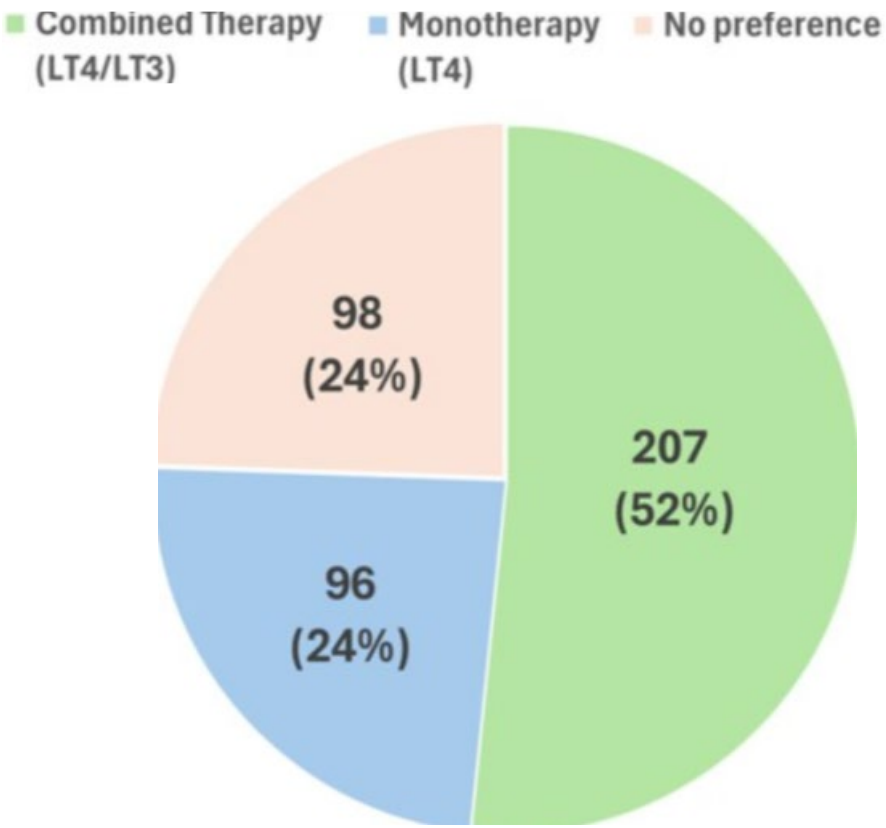
Fabyan Esberard de Lima Beltrão [1 2], Giulia Carvalhal [3], Daniele Carvalhal de Almeida Beltrão [2 4], Fabricia Elizabeth de Lima Beltrão [1 2], Miriam O Ribeiro [5], Matthew D Ettleson [6], Helton Estrela Ramos [7 8 9], Antonio C Bianco [6]

Affiliations + expand

PMID: 39290156 PMCID: PMC11834714 DOI: 10.1210/clinem/dgae651

Preference for LT4+LT3 vs LT4
Metaanalysis of 8 cross-over RCTs, n=1135

Conclusion: Patients with hypothyroidism prefer combination therapy (L-T3 + L-T4 or DTE) over L-T4 monotherapy. The strength of these findings justifies considering patient preferences in the setting of shared decision-making in the treatment of hypothyroidism.



Pie chart depicting patients' preferences at the end of the crossover study periods

Svagheter med kliniska studier hittills

- 18 RCT sista dryga 25 år, flera meta-analyser
  - Ingen säker skillnad mellan LT4 och LT4+LT3 behandling av hypotyreos patienter generellt
  - Preferens för LT4/LT3 kombination i flera studier
- Synpunkter på målgrupp – ej specifikt på de med fortsatta symptom på LT4
- Andra metodologiska synpunkter:
  - QoL mätmetoder
  - Fel LT4 till LT4/LT3, DTE konvertering
  - Oftsiologisk/ variabel LT4/LT3 dosratio
  - Oselekterade hypotyreos patienter
  - Ej exkluderat patienter med osäker hypotyreos diagnos
  - För små studier, med för låg power
  - För kort duration av intervention
- Vi behöver mer träffsäkra RCT med adekvat metodik och storlek för subgruppsanalyser


THYROID
Volume 00, Number 00, 2021
© Mary Ann Liebert, Inc.
DOI: 10.1089/thy.2021.0270

Benefits and Harms of Levothyroxine/L-Triiodothyronine Versus Levothyroxine Monotherapy for Adult Patients with Hypothyroidism: Systematic Review and Meta-Analysis


European Thyroid Journal

Clinical Thyroidology / Review Article

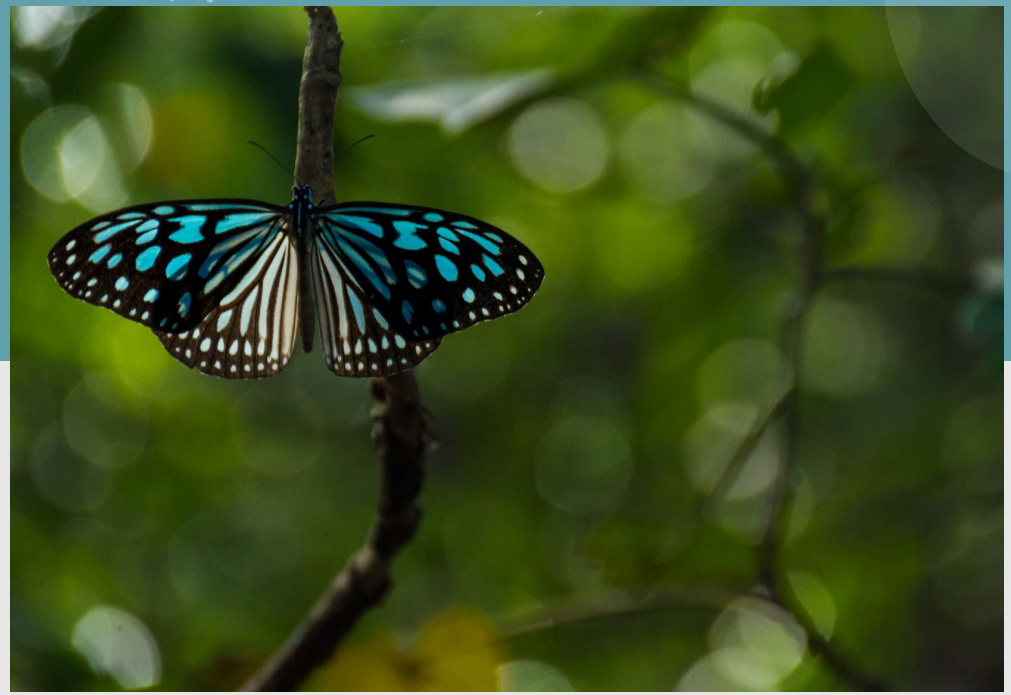
Evidence-Based Use of Levothyroxine/ Liothyronine Combinations in Treating Hypothyroidism: A Consensus Document


frontiers in Endocrinology

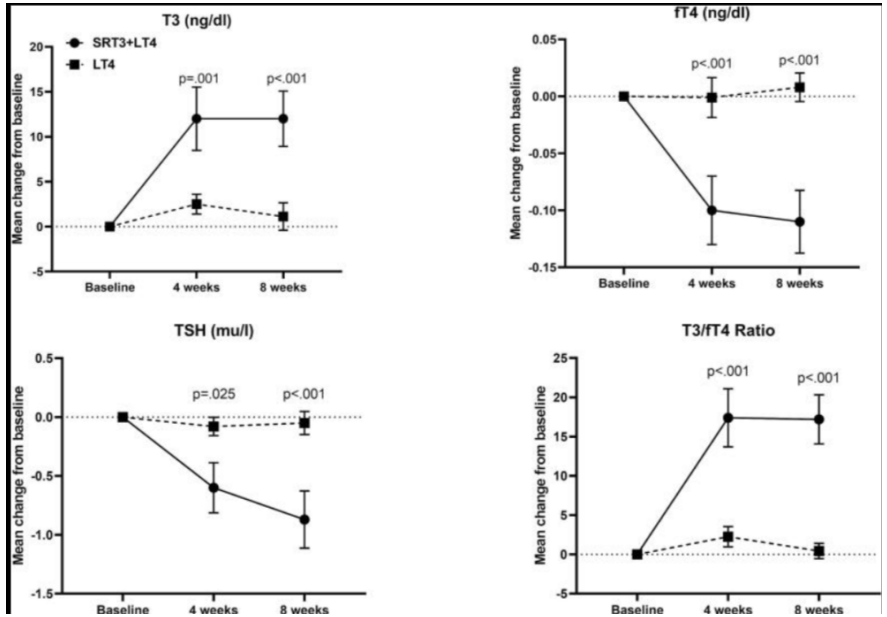
PERSPECTIVE

Design of the Optimal Trial of Combination Therapy

Vad för forskning pågår?



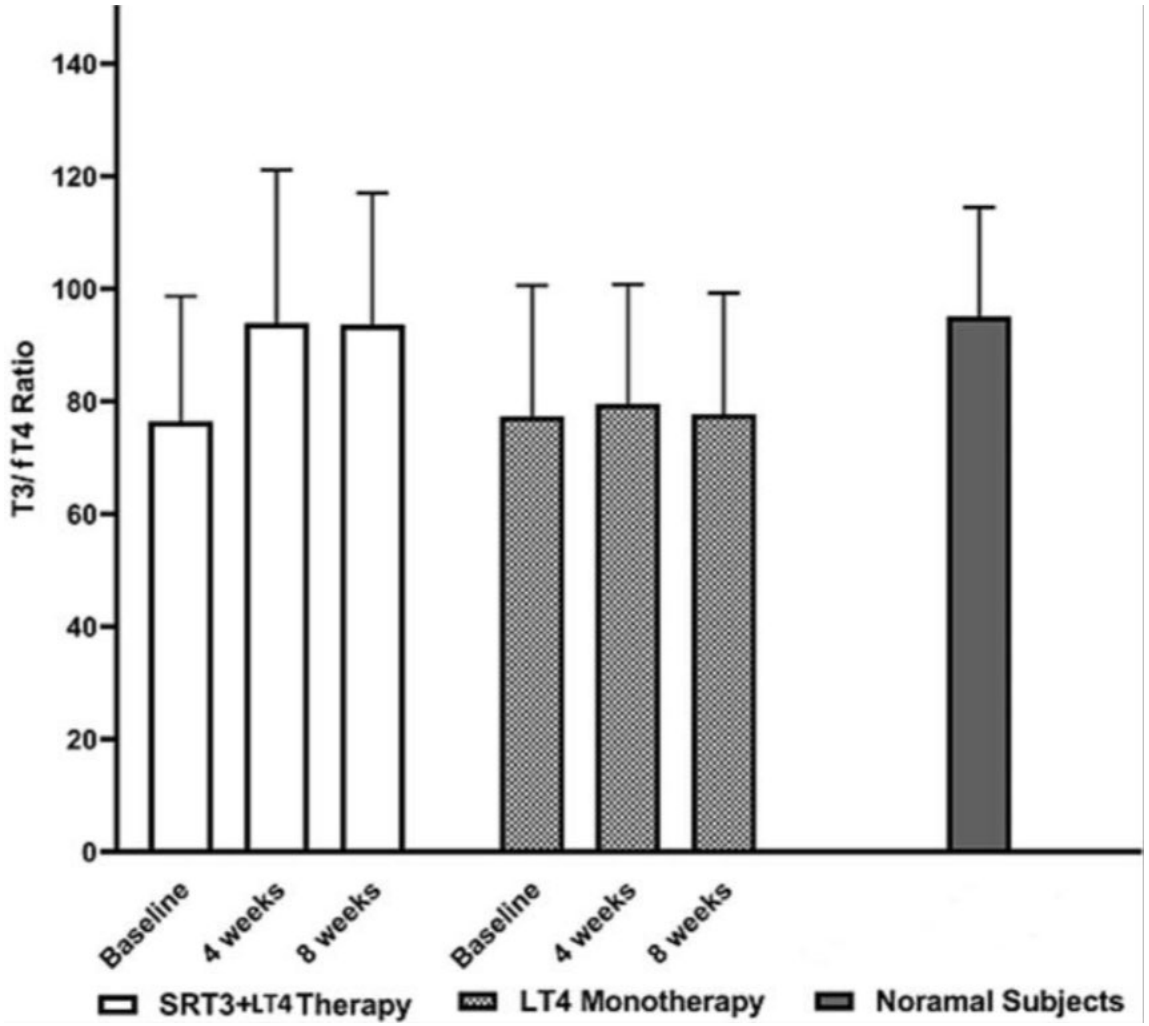
- Pågående rekrytering multicenter RCT från Nederländerna
  - Mål n=600 med hypotyreos
  - Inkl: Behandling med LT4 dos 1,2 µg/kg med normalt TSH och svår trötthet varande minst 6 månader
  - Exkl: Icke autoimmun etiologi, hjärta/ kärl sjd, graviditet (el planer, andra uppenbara förklarningar till trötthet
  - LT4 mono vs LT4/LT3 dosratio 16:1
  - 12 mån behandlingstid
  - Primär outcome: ThyPRO trötthetsscore (förändring), effect size i genetiska subgrupper (D2, MCT10)
  - Sekundära outcomes ThyPro-39 composite och subscale scores
  - Förvänt färdig 2028
- Synpunkter förbättringar jmf med tidigare RCT men vissa hävdar för låg LT3 dos, LT4/LT3 dosratio



J Clin Transl Endocrinol. 2025 Apr 23:40:100395. doi: 10.1016/j.jcte.2025.100395. eCollection 2025 Jun.

Treatment of hypothyroidism with the combination of levothyroxine and slow-release triiodothyronine: a randomized clinical trial

F Azizi [1], A S Moeini [1], L Mehran [1], S Masoumi [1], H Abdi [1], S M Foroutan [2], A E Saghafinia [3], A Amouzegar [1]



Sleep and Mental Wellbeing Targeted Cognitive Behavioural Therapy for Patients with Autoimmune Hashimoto's Thyroiditis

PhD student Elizabeth Mackenzie, University of Strathclyde,

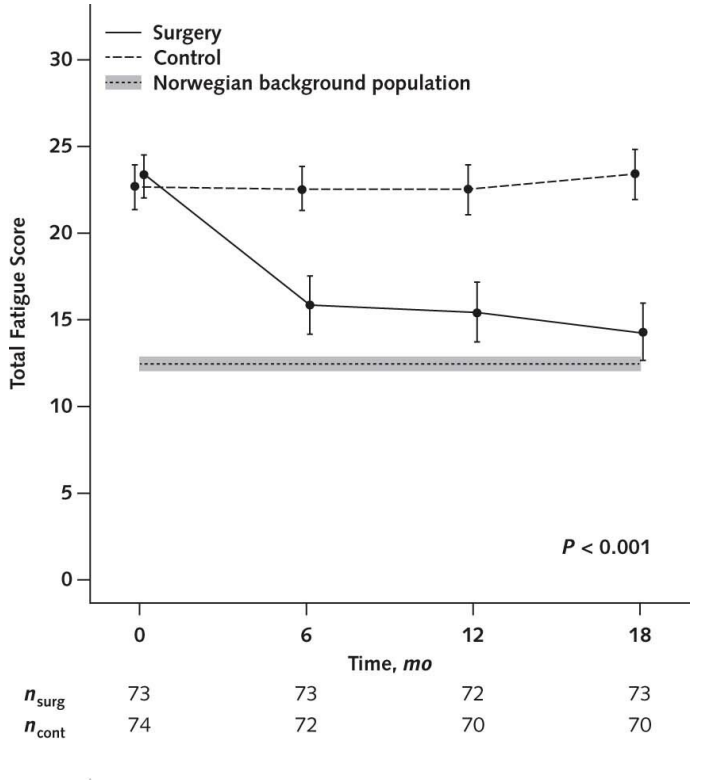
under the supervision of Dr Megan Crawford (University of Strathclyde), Professor Leanne Fleming (University of Strathclyde), and Professor Kristien Boelaert (University of Birmingham).

The aim is to develop a non-pharmacological intervention to support patients who experience low mood and excessive daytime sleepiness despite adequate treatment through LT4 (both overt and subclinical Hashimoto’s hypothyroidism)

Original Research 2 April 2019
Annals of Internal Medicine

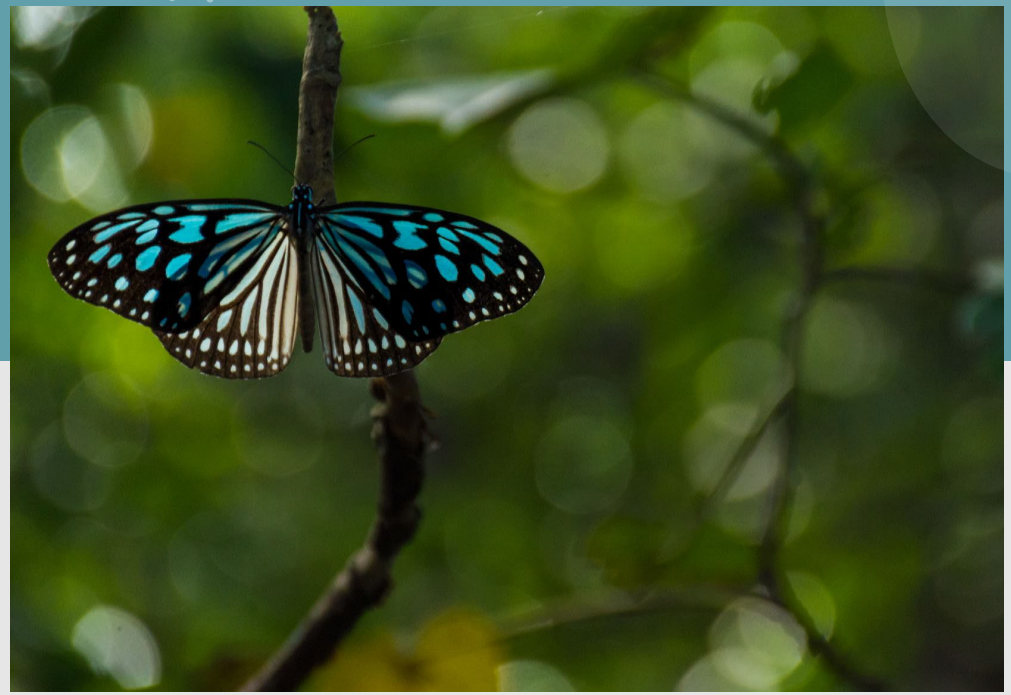
Thyroidectomy Versus Medical Management for Euthyroid Patients With Hashimoto Disease and Persisting Symptoms

A Randomised Trial
Guldvog I et al



TPOak nivår blev lägre med tyroidea kirurgi och symptomen förbättrades.

Är det säkert att använda LT3?



Mortality & Cancer: Data from Sweden

Triiodothyronine use in hypothyroidism and its effects on cancer and mortality

[1,2]Tereza Planck, MD, PhD, [3,4]Fredric Hedberg, MD, [3,4]Jan Calissendorff, MD, PhD, and [5]Anton Nilsson, PhD

Planck T et al; Thyroid 2021; 31(5)

- Full adult population of individuals living in Sweden with at least 3 purchases of TH therapy between July 2005 and Dec 2017
- 575,461 individuals with at least 3 purchases
- 11,147 had made at least 3 purchases of LT3, including combinations of LT4 and LT3.
- Individuals were followed for a median follow-up time of 8.1 years
- Cox regression with a time-varying exposure variable

- Comparing LT3 users with LT4-only users (the rest)
  - HR 0.93 [0.75–1.15] – Breast cancer (females)
  - HR 0.97 (0.87–1.08) - Any cancer incidence
  - HR 0.69 (0.61–0.77) - All-cause mortality
  - HR 0.78 (0.62–0.98) - Any cancer mortality
  - HR 0.91 (0.50–1.66) - Breast cancer mortality

- 'The use of LT3 did not lead to increased breast cancer incidence, any cancer incidence, all-cause mortality, any cancer mortality, or breast cancer mortality compared with LT4 use.
- Somewhat surprisingly, there was evidence of lower mortality in LT3 users in models adjusting for dose, potentially an artifact'

J Clin Endocrinol Metab. 2024 Feb 20;109(3):e1143-e1150. doi: 10.1210/clinem/dgad629.

A Cross-Sectional Analysis of Cardiovascular and Bone Health Care Utilization During Treatment With Thyroid Hormone

Gustavo C Penna [1], Antonio C Bianco [1], Matthew D Ettleson [1]

Affiliations + expand

PMID: 37878964 PMCID: PMC10876406 DOI: 10.1210/clinem/dgad629

- 5106 participants were treated with LT4 monotherapy, 252 with DTE, and 79 with LT4 + LT3.

- **Conclusion:** No significant differences in CVD- and BH-related health care utilization were identified between LT4 and DTE/LT4+LT3 users after covariate balancing. Non-MD providers were more likely to prescribe DTE.

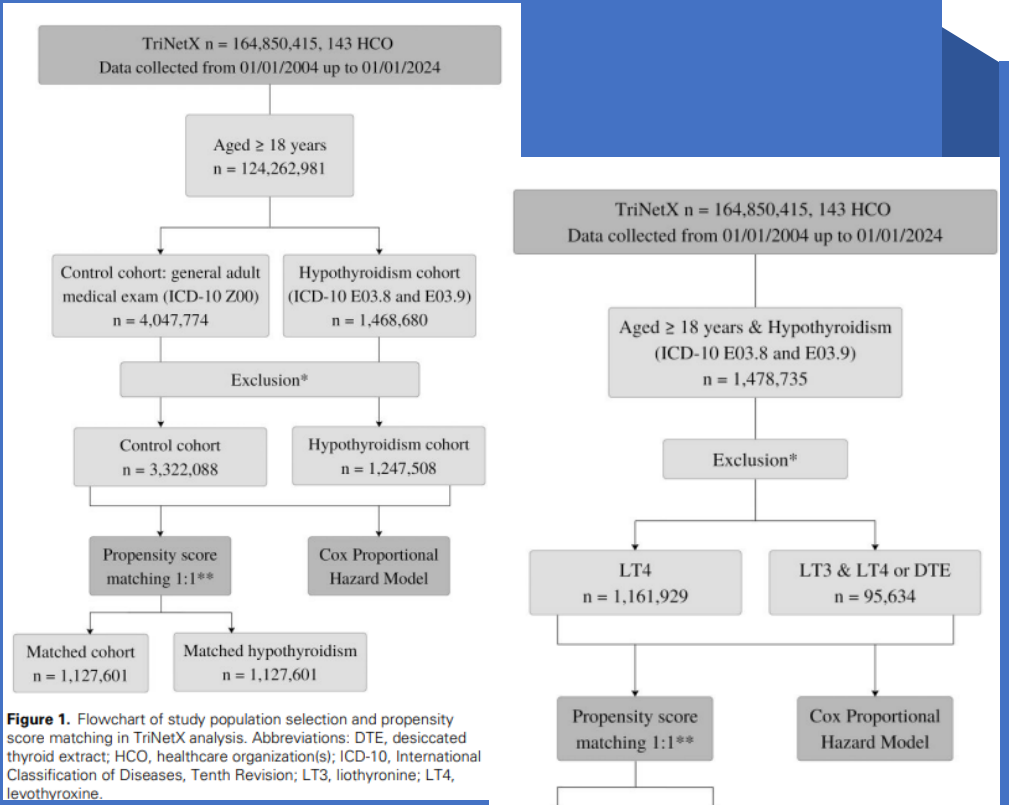


Figure 1. Flowchart of study population selection and propensity score matching in TriNetX analysis. Abbreviations: DTE, desiccated thyroid extract; HCO, healthcare organization(s); ICD-10, International Classification of Diseases, Tenth Revision; LT3, liothyronine; LT4, levothyroxine.

Figure 3. Flowchart of study population selection and propensity score matching in TriNetX analysis for LT4 vs LT3 and LT4 or DTE treatment comparison. Abbreviations: DTE, desiccated thyroid extract; HCO, healthcare organization(s); ICD-10, International Classification of Diseases, Tenth Revision; LT3, liothyronine; LT4, levothyroxine.

JOURNAL ARTICLE CORRECTED PROOF

Treatment of Hypothyroidism That Contains Liothyronine is Associated With Reduced Risk of Dementia and Mortality

Fabyan Esberard de Lima Beltrão, Giulia Carvalhal, Vandrize Meneghini, Danielle Albino Rafael Matos, Daniele Carvalhal de Almeida Beltrão, Bruna Albino Rafael Matos Andrade, Fabyo Napoleão de Lima Beltrão, Helton Estrela Ramos, Miriam O Ribeiro, George Golovko ... Show more

The Journal of Clinical Endocrinology & Metabolism, dgaf367,
https://doi.org/10.1210/clinem/dgaf367
Published: 20 June 2025 **Article history ▾**

Compared with controls, patients with hypothyroidism were older, more frequently White females, and had a higher prevalence of smoking. They also had a higher burden of comorbidities, body mass index, and TSH and HbA1c levels.

Table 5. Multivariable regression analyses comparing levothyroxine (LT4) therapy with LT4 + LT3 or DTE (follow-up to 20 years)

		Any Dementia		Vascular Dementia		Alzheimer's disease		Mortality	
		HR	CI 95%	HR	CI 95%	HR	CI 95%	HR	CI 95%
	Unadjusted	1.94	1.85-2.04	1.94	1.76-2.22	1.82	1.68-1.96	1.94	1.87-2.01
Model 1	Age	1.29	1.23-1.35	1.32	1.17-1.49	1.21	1.11-1.32	1.52	1.47-1.58
Model 1	Gender (male)	1.27	1.21-1.34	1.29	1.15-1.46	1.22	1.12-1.34	1.43	1.38-1.49
Model 1	Nicotine dependence	1.28	1.21-1.34	1.30	1.15-1.47	1.21	1.11-1.32	1.49	1.43-1.54
Model 1	Alcohol use disorder	1.28	1.22-1.35	1.31	1.17-1.48	1.21	1.10-1.32	1.52	1.46 -1.58
Model 1	Ever Hospitalized	1.29	1.23-1.36	1.32	1.17-1.49	1.21	1.11-1.32	1.53	1.47-1.58
Model 1	**Model 1**	**1.28**	**1.22-1.34**	**1.36**	**1.21-1.53**	**1.22**	**1.12-1.33**	**1.42**	**1.36-1.47**
Model 2	Diabetes	1.26	1.19-1.32	1.27	1.12-1.43	1.20	1.10-1.31	1.44	1.39-1.50
Model 2	Dyslipidemia	1.28	1.22-1.35	1.31	1.16-1.47	1.21	1.11-1.32	1.52	1.47-1.58
Model 2	Hypertension	1.27	1.21-1.34	1.27	1.13-1.44	1.21	1.11-1.32	1.48	1.42-1.53
Model 2	Obesity	1.28	1.22-1.35	1.32	1.17-1.49	1.21	1.10-1.32	1.53	1.47-1.58
Model 2	Atrial fibrillation	1.29	1.22-1.35	1.32	1.17-1.48	1.21	1.10-1.32	1.51	1.46 -1.57
Model 2	Depression	1.33	1.26-1.39	1.37	1.22-1.54	1.25	1.14-1.36	1.55	1.49-1.61
Model 2	**Model 2**	**1.30**	**1.24-1.37**	**1.36**	**1.20-1.53**	**1.22**	**1.12-1.33**	**1.41**	**1.35-1.46**
Model 3	TSH	1.29	1.23-1.36	1.34	1.18-1.50	1.22	1.12-1.33	1.52	1.46 -1.57
Model 3	TSH < 0.45	1.35	1.28-1.43	1.32	1.17-1.49	1.23	1.12-1.34	1.51	1.45 -1.57
Model 3	TSH > 7	1.28	1.22-1.35	1.32	1.17-1.49	1.21	1.10-1.32	1.52	1.47 -1.59
Model 3	CRP	1.35	1.29-1.43	1.34	1.18-1.51	1.21	1.11-1.32	1.56	1.50 -1.62
Model 3	Hemoglobin	1.35	1.29-1.43	1.33	1.18-1.50	1.23	1.12-1.35	1.54	1.48-1.60
Model 3	Vitamin B12	1.37	1.30-1.45	1.39	1.23-1.57	1.28	1.17-1.39	1.56	1.50-1.62
Model 3	HbA1c	1.29	1.22-1.35	1.39	1.18-1.50	1.21	1.11-1.32	1.53	1.47-1.59
Model 3	**Model 3**	**1.35**	**1.28-1.41**	**1.41**	**1.26-1.58**	**1.24**	**1.15-1.35**	**1.57**	**1.51-1.63**
Model 4	**Model 4**	**1.30**	**1.24-1.36**	**1.30**	**1.16-1.46**	**1.23**	**1.13-1.33**	**1.39**	**1.34-1.44**
Model 5	**Model 5**	**1.34**	**1.27-1.40**	**1.36**	**1.21-1.52**	**1.28**	**1.18-1.39**	**1.41**	**1.36-1.46**

Cox proportional hazards model: All individual variables and models were adjusted for age. Model 1: additionally adjusted for gender (male), nicotine dependence, alcohol use disorder, and hospitalization history. Model 2: additionally adjusted for diabetes, dyslipidemia, obesity, atrial fibrillation, and depression. Model 3: additionally adjusted for TSH, CRP, hemoglobin, vitamin B12, and HbA1c. Model 4: adjusted for all variables in models 1 and 2. Model 5: fully adjusted for all the above variables. All evaluated variables showed a P value < .0001.
Abbreviations: CRP, C-reactive protein; HbA1c, glycated hemoglobin; HR, hazard ratio.

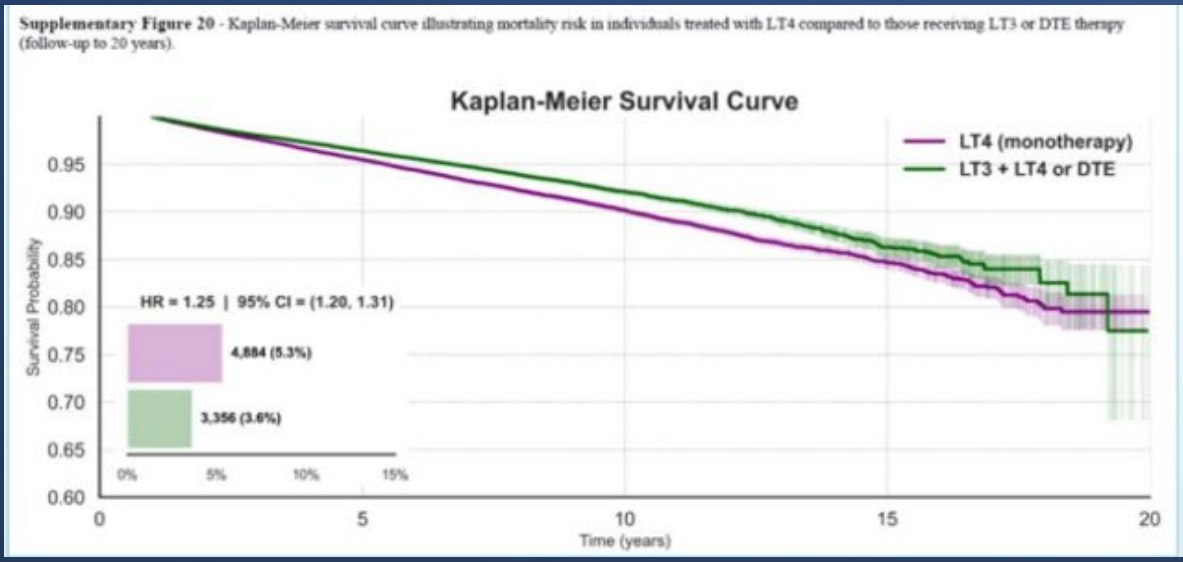
Table 6. Comparison of dementia, and mortality outcomes between LT4 monotherapy and LT3 + LT4 or DTE (follow-up to 20 years)

	LT4 monotherapy No. with event/total No.	LT3 + LT4 or DTE No. with event/total No.	RR (95% CI)	HR (95% CI)[a]
Dementia	1722/ 93 583	1261/ 93 922	**1.371 (1.275- 1.473)**	**1.16 (1.079-1.248)**[a]
Vascular dementia	355/ 95 208	264/ 95 213	**1.345 (1.147-1.577)**	1.135 (0.968-1.332)
Alzheimer	623/ 94 914	483/ 95 034	**1.291 (1.147-1.454)**	1.095 (0.972-1.234)
Atrial fibrillation	3260/ 89 325	2609/ 89 221	**1.248 (1.186-1.313)**	**1.069 (1.015-1.125)**
Mortality	4884/ 93 215	3356/ 93 439	**1.459 (1.397-1.523)**	**1.253 (1.199-1.309)**

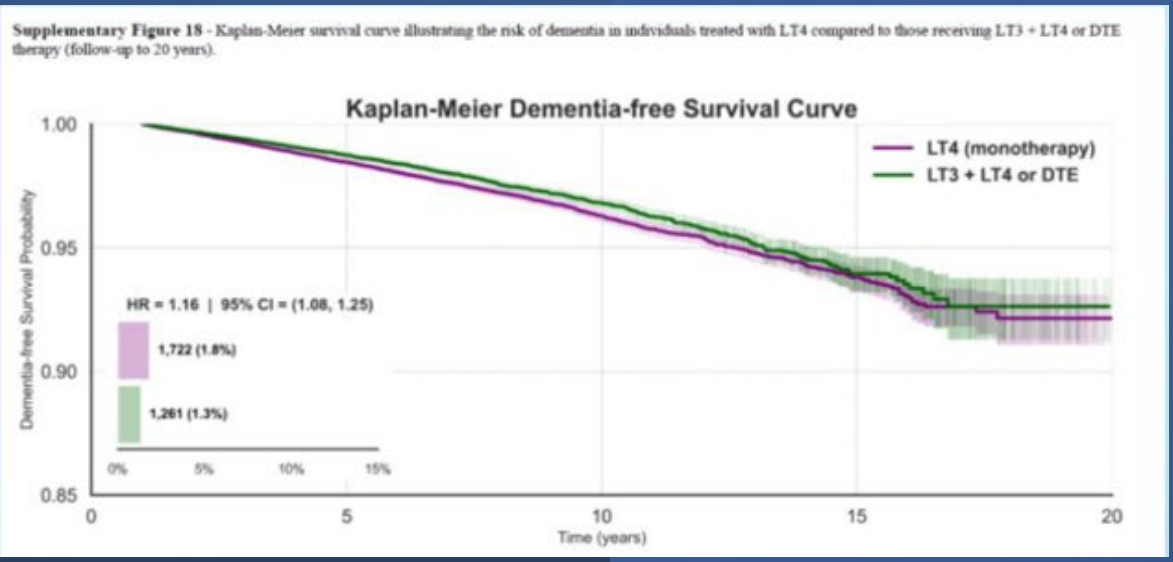
Bold values indicate statistical significance with $P < 0.05$.
Abbreviations: DTE, desiccated thyroid extract; HR, hazard ratio; LT3, liothyronine; LT4, levothyroxine; RR, relative risk.
[a]Proportionality ($P <$ .01)

Conclusion: Despite standard LT4 therapy, hypothyroidism remains associated with heightened risks of dementia and mortality. Adding T3 may more effectively mitigate these risks than LT4 alone, but further studies are needed to confirm the cognitive and survival benefits of T3-containing regimens.

Supplementary Figure 20 - Kaplan-Meier survival curve illustrating mortality risk in individuals treated with LT4 compared to those receiving LT3 or DTE therapy (follow-up to 20 years).



Supplementary Figure 18 - Kaplan-Meier survival curve illustrating the risk of dementia in individuals treated with LT4 compared to those receiving LT3 + LT4 or DTE therapy (follow-up to 20 years).



Volume 110, Issue 11
November 2025

Article Contents

JOURNAL ARTICLE

Risk of Death and Adverse Effects in Patients on Liothyronine: A Multisource Systematic Review and Meta-analysis

Suhani Bahl ✉, Peter N Taylor, Lakdasa D Premawardhana, Mike Stedman, Adrian Heald, Colin M Dayan, Onyebuchi E Okosieme

The Journal of Clinical Endocrinology & Metabolism, Volume 110, Issue 11, November 2025, Pages 3278–3288, https://doi.org/10.1210/clinem/dgaf449

Published: 08 August 2025 **Article history** ▾

Abstract

Context: Although some patients with hypothyroidism prefer combination therapy with liothyronine (LT3) and levothyroxine (LT4), the safety of LT3 remains unresolved.

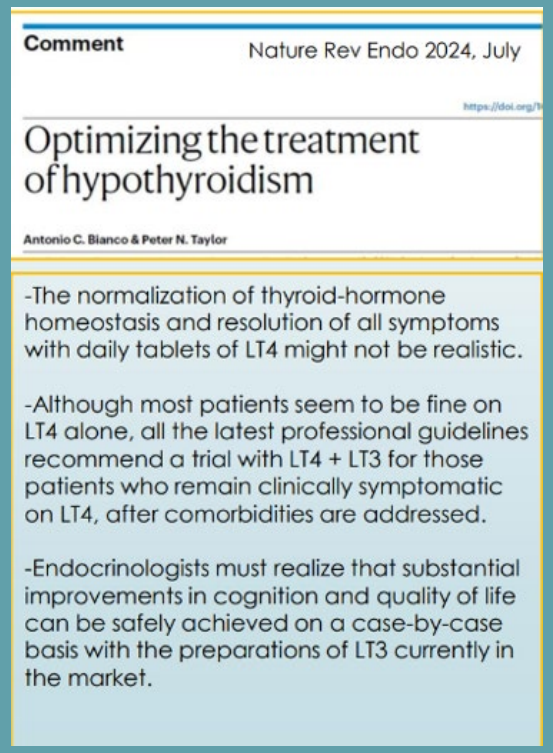
Objective: We undertook a multisource systematic review and meta-analysis of LT3 safety.

Data Sources: We searched PubMed for articles relating to death, adverse events (AEs), and cardiovascular outcomes in LT3 users. We also searched AEs data in the UK Yellow Card scheme and US Food and Drug Administration Adverse Reporting System (FAERS).

Data Extraction: Data was extracted independently by 2 reviewers. Out of 1814 articles identified, 52 studies were selected, comprising 21 randomized controlled trials (RCTs), 4 cohort studies, and 27 case reports. Meta-analyses were conducted for adverse outcomes in RCTs and cohort studies of combination vs monotherapy.

Data Synthesis: LT3-related AEs were only reported with unregulated LT3 use or pharmacy compounding errors. LT3 and LT4 showed similar adverse severity profiles in the Yellow Card scheme. Disproportionality analysis in the FAERS database showed no increased LT3 safety signals. A meta-analysis of RCTs (n = 2128) showed a similar AEs risk for combination vs monotherapy [relative risk (RR) 1.22, 95% confidence interval (CI) 0.66-2.25]. A cohort study meta-analysis (LT3 vs LT4-only users, n = 630 254) showed no increased risk of atrial fibrillation (RR 1.10, 95% CI 0.74-1.63), heart failure (RR 1.54, 95% CI 0.95-2.47), or strokes (RR 0.86, 95% CI 0.11-6.75), but reduced mortality risk was observed for LT3 (RR 0.70, 95% CI 0.62-0.78).

Conclusion: Our findings are reassuring that regulated LT3 use is not associated with the risk of death or serious AEs. More studies are needed to supplement existing data.



Comment Nature Rev Endo 2024, July

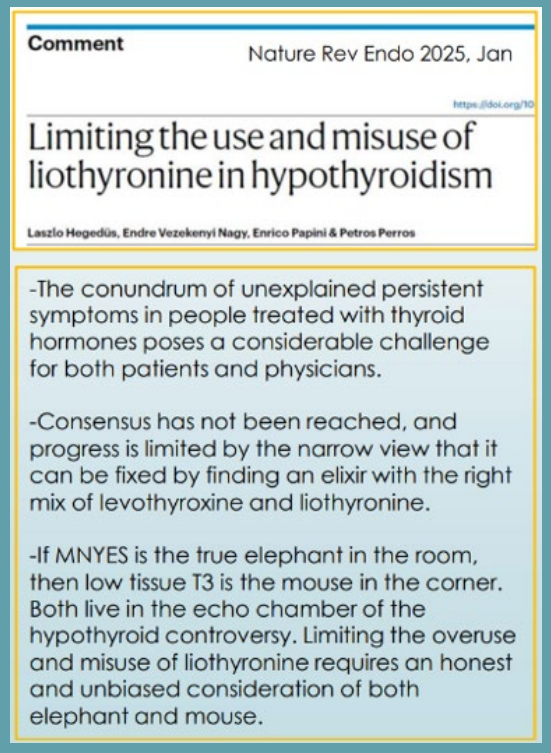
Optimizing the treatment of hypothyroidism

Antonio C. Bianco & Peter N. Taylor

-The normalization of thyroid-hormone homeostasis and resolution of all symptoms with daily tablets of LT4 might not be realistic.

-Although most patients seem to be fine on LT4 alone, all the latest professional guidelines recommend a trial with LT4 + LT3 for those patients who remain clinically symptomatic on LT4, after comorbidities are addressed.

-Endocrinologists must realize that substantial improvements in cognition and quality of life can be safely achieved on a case-by-case basis with the preparations of LT3 currently in the market.



Comment Nature Rev Endo 2025, Jan

Limiting the use and misuse of liothyronine in hypothyroidism

Laszlo Hegedüs, Endre Vezekenyi Nagy, Enrico Papini & Petros Perros

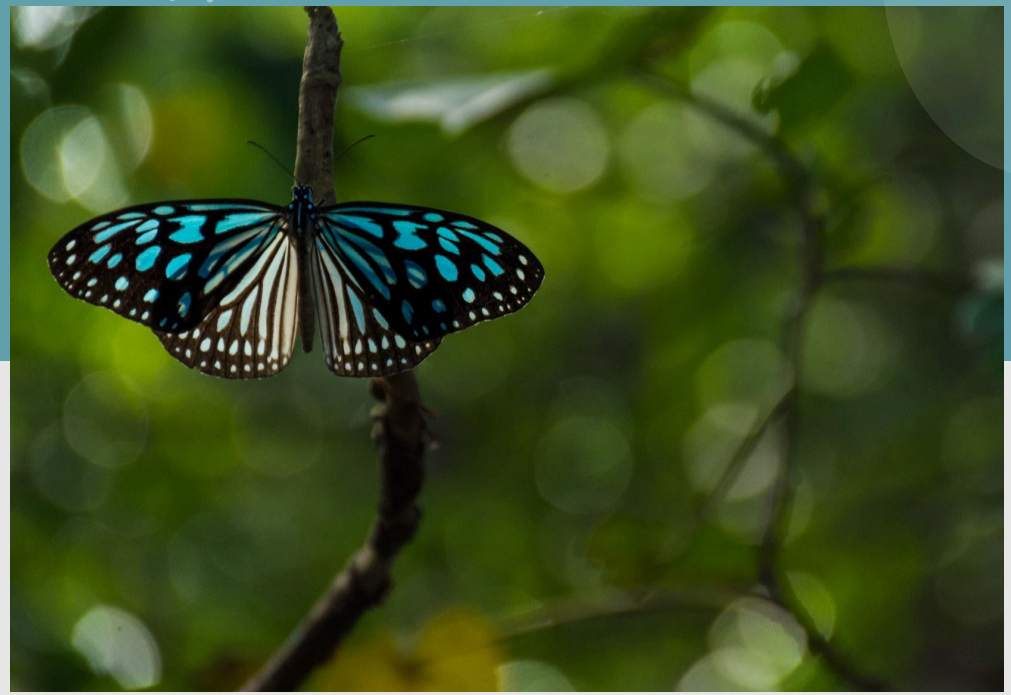
-The conundrum of unexplained persistent symptoms in people treated with thyroid hormones poses a considerable challenge for both patients and physicians.

-Consensus has not been reached, and progress is limited by the narrow view that it can be fixed by finding an elixir with the right mix of levothyroxine and liothyronine.

-If MNYES is the true elephant in the room, then low tissue T3 is the mouse in the corner. Both live in the echo chamber of the hypothyroid controversy. Limiting the overuse and misuse of liothyronine requires an honest and unbiased consideration of both elephant and mouse.

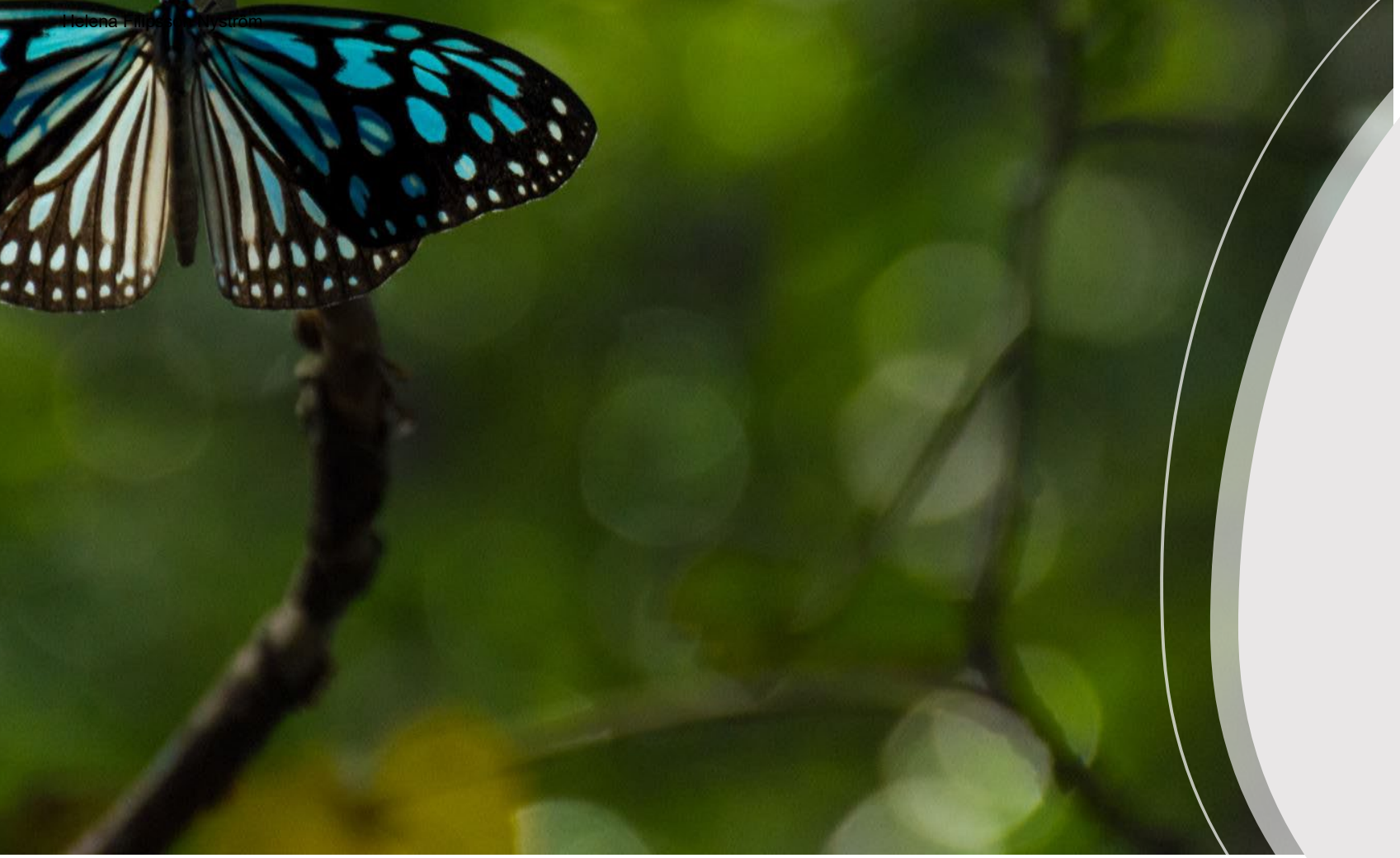
- Med enbart LT4 når vi inte samma serum-koncentrationer som hos friska
- Synen på kvarstående problem har vidgats
- Det är inte bara forskning på den optimala T3+T4 studien
- Kortverkande LT3 preparat användning är säker och kan kanske även ha bättre utfall än LT4
- Långverkande LT3 preparat prövas
-

Finns det en väg till en bättre behandling?



- För att handlägga dessa patienter – en väg framåt för en bättre vård
  - Rehabilitering
  - Se människorna som människor och inte som ett problem
  - Vård och stöd
  - Utbildning

- Mer Forskning behövs
    - LT3
    - Slow acting LT3
    - Personlighet
    - Coping
    - Immunologi
    - Person centrerad vård



Tack!

Frågor?