Supplementary Data

SUPPLEMENTARY TABLE S1. TRIALS IN WHICH LT3+LT4 THERAPY WAS GIVEN ONCE DAILY TO TREAT HYPOTHYROID PATIENTS

Publications	*Study design*	*LT3 therapy duration (weeks)*	*Patients who received LT3* (n)	*Mean age (years)*	*LT3 dosage (mcg/day)*	*HR variation vs. LT4 (bpm)*	*SBP variation vs. LT4 (mmHg)*	*LT3-related ADR*
Bunevicius, *et al.* (S1)	Controlled, randomized, double-blind	10	33 (31 F)	46 ± 13[a]	12.5	+3	No change	None
Bunevicius and Prange (S2)	Controlled, randomized, double-blind	10	26 F	45 ± 9	12.5	N/A	N/A	No difference compared with the LT4 group
Bunevicius *et al.* (S3)	Crossover, double-blind	10	10 F	34	10	−8	N/A	No difference compared with the LT4 group
Walsh *et al.* (S4)	Crossover, randomized, double-blind	20	110 (101 F)	47 ± 11	10	−1.5	No change	2 pts withdrew due to worsening symptoms 1 pt withdrew due to palpitations
Siegmund *et al.* (S5)	Crossover, randomized, double-blind	24	23 (20 F)	23–69	6.5	No change	+7	1 pt withdrew due to AF (TSH <0.01)
Saravanan *et al.* (S6)	Controlled, randomized, double-blind	48	344 (286 F)	57 ± 11	10	+2.2	−6.4	No difference compared with the LT4 group
Rodriguez *et al.* (S7)	Crossover, randomized, double-blind	12	27 (23 F)	47	10	No change	No change	Headache, difficulty sleeping, and muscle weakness at least 10% more likely
Appelhof *et al.* (S8)	Controlled, randomized, double-blind	15	93 (79 F)	48.3 ± 9	1: 10 1:5 (T3:T4 molar)	+3.9 +7	+4 +12	Osteocalcin increased 1 pt had atrial premature beats
Escobar-morreale *et al.* (S9)	Crossover, randomized, double-blind	16	28 F	48 ± 11	5 or 7.5	−3	No change	No ADR reported in the paper
Regalbuto *et al.* (S10)	Nonrandomized, noncontrolled	28	20 (17 F)	46 ± 8	5.7 or 21.4	No change	No change	Osteocalcin increased
Slawik *et al.* (S11)	Crossover, double-blind	5	29 (8 F)	51 ± 2	13.4 (mean)	No change	No change	No difference compared with the LT4 group
Nygaard *et al.* (S12)	Crossover, randomized, double-blind	24	59 (55 F)	46	20	N/A	N/A	No difference compared with the LT4 group
Fadeyev *et al.* (S13)	Randomized, controlled	24	16 F	40	12.5	No change	N/A	Urine deoxypyridinoline increased
Trimboli *et al.* (S14)	Noncontrolled	6.4	21 (16 F)	43 ± 12	Liquid LT3 7.3 ± 3.4	N/A	N/A	No reported ADR
Kaminski *et al.* (S15)	Crossover, randomized, double-blind	16	32 (30 F)	42.6 ± 13.3	15	+3	No change	No reported ADR
Krysiak *et al.* (S16)	Quasi-randomized, single-blind	24	17 F	31 ± 6	8.8 ± 1.7	N/A	N/A	2 women withdrew due to tachycardia, nervousness, heat intolerance, and weight loss

[a]Mean ± SD.

ADR, adverse drug reactions; bpm, beat per minute; F, female number; HR, heart rate, LT3, liothyronine; SBP, systolic blood pressure.

SUPPLEMENTARY TABLE S2. TRIALS IN WHICH LT3+LT4 THERAPY WAS GIVEN TWICE DAILY TO TREAT HYPOTHYROID PATIENTS

Publications	*Study design*	*LT3 therapy duration (weeks)*	*Patients who received LT3* (n)	*Mean age (years)*	*LT3 dosage (mcg/twice daily)*	*HR variation Vs. LT4 (bpm)*	*SBP variations Vs. LT4 (mmHg)*	*LT3-related ADR*
Sawka *et al.* (S17)	Placebo, control, double-blind	15	20 (17 F)	25–75	12.5	N/A	N/A	No difference compared with the LT4 group
Clyde *et al.* (S18)	Controlled, randomized, double-blind	16	23 (19 F)	43 ± 11[a]	7.5	No change	No change	1 pt withdrew due to tremulousness, fatigue, and poor performance
Valizadeh *et al.* (S19)	Controlled, randomized, double-blind	16	30 (24 F)	39 ± 11	6.3	No change	No change	4 pts withdrew because of palpitation
Solter *et al.* (S20)	Open-label	36	15 (14 F)	31–55	10	N/A	N/A	None

[a]Mean ± SD.

Supplementary Table S3. Trials in Which LT3 Therapy Was Given Daily as Adjuvant in Psychiatric Patients

Publication	*Study design*	*LT3 therapy duration (weeks)*	*Patients who received LT3* (n)	*Mean age (years)*	*LT3 dosage (mcg/day)*	*HR variation (bpm)*	*SBP variation (mmHg)*	*LT3-related ADR*
Coppen *et al.* (S21)	Placebo, controlled	2	14 (7 F)	56 ± 4[a]	25	N/A	N/A	2 out of 3 bipolar patients experienced manic symptoms
Gitlin *et al.* (S22)	Crossover, randomized, double-blind	4	16 (7 F)	41	25	No change	No change	Some reported muscle twitching and insomnia
Joffe (S23)	Crossover, double-blind	5	22 (13 F)	38.3 ± 11	25-37.5	N/A	N/A	None
Joffe and Singer (S24)	Randomized, double-blind	3	17 (9 F)	34.5	37.5	N/A	N/A	None
Appelhof *et al.* (S25)	Placebo, controlled, randomized, double-blind	8	60(36 F)	46 ± 11	25 or 50	N/A	N/A	4 patients had palpitations, sweating, nervousness, and tremor 10 pts on LT3 50 mcg had severe function limiting symptoms
Nierenberg *et al.* (S26)	Randomized, nonblinded	14	73 (41 F)	43 ± 11	45.2 ± 11.4 (mean)	N/A	N/A	No difference compared with the other non-LT3 group
Abraham *et al.* (S27)	Noncontrolled, nonblinded	3.5	12 (8 F)	48 ± 17	25–50	N/A	N/A	1 pt withdrew due to increased anxiety and agitation
Cooper-Kazaz *et al.* (S28)	Placebo, controlled, double-blind, randomized	8	53 (29 F)	45.15	20–50	N/A	N/A	No difference compared with the other non-LT3 group (palpitations, sweating, and nervousness)
Posternak *et al.* (S29)	Placebo, controlled, double-blind, randomized	6	23 (13 F)	40 ± 9	25	N/A	N/A	No difference compared with the other non-LT3 group
Garlow *et al.* (S30)	Placebo, controlled, double-blind, randomized	8	76 (44 F)	43 ± 10	25–50	N/A	N/A	No difference compared with the other non-LT3 group (tremulousness, sweating, feeling jittery, palpitations, chest pain, and feeling hot)
Mohagheghi *et al.* (S31)	Controlled, double-blind	8	30 (23 F)	34 ± 8	50	N/A	N/A	None
Walshaw *et al.* (S32)	Placebo, controlled, double-blind	16	10 (6 F)	37 ± 7	LT3 titrated T3-resin uptake = 0.65–1.36 units	N/A	N/A	No difference compared with the other non-LT3 group

[a]Mean ± SD.

SUPPLEMENTARY TABLE S4. TRIALS IN WHICH LT3 WAS GIVEN FOR METABOLIC PURPOSES

Publication	*Study design*	*LT3 therapy duration (weeks)*	*Patients who received LT3* (n)	*Mean age (years)*	*LT3 dosage (mcg/day)*	*HR variation (bpm)*	*SBP variation (mmHg)*	*LT3-related ADR*
Gwinup and Poucher (S33)	Controlled, randomized	30	8	N/A	275 (mean)	+18	+9	2 pts dropped out due to nervousness and high HR 1 pt developed hyperglycemia
Hollingsworth *et al.* (S34)	Placebo controlled, randomized, double-blind	12	9 (2 F)	27–68	225	+ (8–32)	No constant pattern	All pts developed tachycardia 1 pt had AFIB 1 pt noted nervousness, palpitations, and weakness 6 were aware of a mild tremor
Bray *et al.* (S35)	Crossover, randomized, double-blind	10	12 (6 F)	17-50	225	+7.5 ± 2	No change	Weight loss primarily was from lean body tissue Only 6 patients had unspecific symptoms
Gardner *et al.* (S36)	Nonrandomized, noncontrolled	0.47	7 males	19–37	5 mcg LT3 every 3 hours × 20	N/A	N/A	Urea excretion was 9.1% higher in patients receiving LT3 during fasting
Moore *et al.* (S37)	Placebo, controlled, double-blind	12	8	N/A	60	N/A	N/A	4 patients left the study due to side effects
Koppeschaar *et al.* (S38)	Placebo, controlled	2	10	N/A	150	N/A	N/A	Nitrogen losses increased markedly during LT3 treatment, and they increased insulin resistance
Pasquali *et al.* (S39)	Placebo, controlled	11	14 (8 F)	37	40	N/A	N/A	None
Rosenbaum *et al.* (S40)	Crossover, randomized, single-blind,	5	22 (13 F)	32.2 ± 8[a]	25	+2	No change	Increased norepinephrine excretion

[a]Mean ± SD.

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