

Supplemental Table 1: Characteristics of adult NHANES participants with normal TSH levels, by levothyroxine use.

	LT ₄ -treated (n=469)	Healthy Controls (n=9512)	p-value*
Age (years)	64.3 ± 14.1	46.8 ± 18.6	<0.0001
Female (%)	360 (77%)	4648 (49%)	<0.0001
Race (%)			
Non-Hispanic White	336 (71%)	4194 (44%)	<0.0001
Non-Hispanic Black	36 (8%)	1954 (21%)	
Hispanic	76 (16%)	2703 (28%)	
Other	21 (4%)	6661 (7%)	
Serum TSH (mIU/L)	2.13 ± 1.32	1.73 ± 0.96	<0.0001
Serum Free T ₃ (pg/mL)	2.85 ± 0.33	3.19 ± 0.46	<0.0001
Serum Total T ₃ (ng/mL)	97.56 ± 20.64	114.81 ± 23.21	<0.0001
Serum Free T ₄ (ng/mL)	0.94 ± 0.21	0.79 ± 0.13	<0.0001
Serum Total T ₄ (ug/dL)	9.14 ± 1.76	7.97 ± 1.57	<0.0001
Free T ₃ :Free T ₄ §	3.18 ± 0.80	4.14 ± 0.85	<0.0001
Total T ₃ : Free T ₄ §	109.59 ± 36.30	149.55 ± 40.73	<0.0001
Total T ₃ : Total T ₄ §	11.01 ± 2.85	14.73 ± 3.23	<0.0001

Data are mean ± SD, n (%). P-value by chi-square (categorical data) or student's t test (continuous data).

LT₄: levothyroxine; TSH: thyroid stimulating hormone; T₄: thyroxine; T₃ tri-iodothyronine. *For the comparison of LT₄-treated and healthy controls. †For the comparison of LT₄-treated and matched controls. §Multiplied x 1000.

Supplemental Table 2: Clinical parameters of adult NHANES participants with normal TSH levels

	LT ₄ -treated (n=469)	Healthy Controls (n=9512)	p-value*
Objective measures			
BMI (kg/m ²)	29.8 ± 6.7	28.5 ± 6.6	<0.0001
Systolic blood pressure (mm Hg)	131 ± 22	124 ± 19	<0.0001
Diastolic blood pressure (mm Hg)	68 ± 14	70 ± 13	<0.0001
Heart rate (beats per minute)	72 ± 12	73 ± 12	0.18
HbA _{1c} (%)	5.9 ± 0.9	5.7 ± 1.0	<0.0001
Fasting glucose (mg/dL)	106 ± 37	100 ± 38	<0.0001
Total cholesterol (mg/dL)	197 ± 41	195 ± 42	0.49
HDL (mg/dL)	54 ± 16	52 ± 16	<0.01
LDL (mg/dL)	115 ± 35 (n=175)	115 ± 36 (n=3618)	0.77
Triglyceride (mg/dL)	144 ± 86 (n=180)	135 ± 109 (n=3715)	0.30
C-reactive protein (mg/dL)	0.50 ± 0.64 (n=400)	0.41 ± 0.81 (n=8128)	0.03
Ferritin (ng/mL)	102 ± 106 (n=103)	81 ± 100 (n=3198)	0.03
Creatinine (mg/dL)	0.93 ± 0.53	0.89 ± 0.37	0.01
Creatine phosphokinase (IU/L)	118 ± 91 (n=69)	168 ± 196 (n=1561)	0.04
Medication use			
Beta-blocker (%)	175 (37%)	1161 (12%)	<0.0001
Statin (%)	111 (24%)	838 (9%)	<0.0001
Insulin (%)	20 (4%)	203 (2%)	<0.01
Oral hypoglycemic (%)	59 (45%)	668 (46%)	0.89
Anti-depressant (%)	101 (22%)	716 (8%)	<0.0001
Anti-anxiety (%)	30 (6%)	249 (3%)	<0.0001
Anti-psychotic (%)	5 (1%)	73 (1%)	0.47
Metabolic equivalents (METs)/Physical parameters			
Total MET (work and recreational activity)	2255 ± 3464	4887 ± 6829	<0.0001
Work/job requires vigorous activity (%)	42 (10%)	1629 (20%)	<0.0001
Vigorous work MET	3765 ± 4215	7168 ± 7205	<0.01
Work/job requires moderate activity (%)	115 (27%)	3063 (38%)	<0.0001
Moderate work MET	2000 ± 2429	3248 ± 3336	<0.0001
Walks/bikes for transportation (%)	75 (18%)	2311 (28%)	<0.0001
Transportation MET	826 ± 952	1484 ± 2146	<0.01
Participates in vigorous recreational activity (%)	43 (10%)	1822 (22%)	<0.0001
Vigorous recreational MET	658 ± 573	935 ± 833	0.03
Participates in moderate recreational activity (%)	173 (41%)	3129 (38%)	0.27
Moderate recreational MET	746 ± 595	905 ± 1084	0.05
Cognitive/Well-being parameters			
Stated health condition (%)			
Excellent	26 (6%)	948 (11%)	<0.0001
Very good	115 (26%)	2418 (28%)	
Good	185 (42%)	3520 (40%)	
Fair	81 (19%)	1601 (18%)	
Poor	31 (7%)	272 (3%)	
Number of days in the past month physical health was not good	5.6 ± 11.5	3.8 ± 8.6	<0.0001
Number of days in the past month mental health was not good	5.1 ± 11.6	4.1 ± 8.6	0.03
Number of days in the past month inactive due to physical or mental health	2.5 ± 7.7	1.9 ± 6.6	0.08
Physical, mental or emotional limitation kept from working (%)	82 (18%)	1062 (12%)	<0.0001
Experience confusion/memory problem (%)	62 (13%)	634 (7%)	<0.0001

Limited in activity due to physical, mental or emotional problem (%)	16 (6%)	214 (3%)	0.02
Social factors			
Smoked at least 100 cigarettes in lifetime (%)	219 (47%)	4158 (47%)	0.81
Currently smoking daily (%)	47 (21%)	1641 (40%)	<0.0001
Consumed at least 12 alcoholic drinks per year (%)	181 (64%)	3835 (71%)	0.02
Nutrient intake			
Calories consumed in 24 hour recall (kcal/day)	1761 ± 715	2145 ± 1040	<0.0001
Calories consumed, adjusted by body weight (kcal/day/kg)	23 ± 9	28 ± 15	<0.0001
% calorie intake compared to DRI for energy	90 ± 38	111 ± 59	<0.0001
Carbohydrate consumed (g)	217 ± 94	264 ± 134	<0.0001
Carbohydrate consumed (%)	50 ± 11	50 ± 11	0.88
Protein consumed (g)	67 ± 31	82 ± 43	<0.0001
Protein consumed (%)	16 ± 4	16 ± 5	0.84
Fat consumed (g)	68 ± 36	80 ± 47	<0.0001
Fat consumed (%)	34 ± 9	33 ± 9	0.05
Selenium intake (mcg)	52 ± 44	52 ± 81	0.99

Supplemental Table 3: Thyroid hormone levels of healthy controls, by serum TSH.

	Healthy Controls (n=9512)	
	TSH 0.24-1.74 (n=5733)	TSH 1.75-5.40 (n=3779)
Age (years)	44.5 ± 18.0	50.1 ± 18.9 *
Female (%)	2815 (49%)	1833 (49%)
Race/Ethnicity (%)		*
Non-Hispanic white	2244 (39%)	1950 (52%)
Non-Hispanic black	1410 (25%)	544 (14%)
Hispanic	1646 (28%)	1057 (28%)
Other	433 (8%)	228 (6%)
Serum TSH (mIU/L)	1.12 ± 0.37	2.67 ± 0.80 *
Serum Free T ₃ (pg/mL)	3.21 ± 0.51	3.16 ± 0.38 *
Serum Total T ₃ (ng/mL)	115.05 ± 23.15	114.43 ± 23.30
Serum Free T ₄ (ng/mL)	0.80 ± 0.14	0.78 ± 0.13 *
Serum Total T ₄ (ug/dL)	8.03 ± 1.58	7.88 ± 1.54 *
Free T ₃ :Free T ₄ §	4.13 ± 0.91	4.15 ± 0.76
Total T ₃ : free T ₄ §	148.55 ± 40.97	151.07 ± 40.34 *
Total T ₃ : total T ₄ §	14.65 ± 3.21	14.85 ± 3.26 *

The mean serum TSH level from the entire population was 1.75 mIU/L. Participants within each group were then classified as having serum TSH levels above or below this mean, and then thyroid function tests reassessed for each subgroup. Data are mean ± SD, n (%). P-value by chi-square (categorical data) or student's t test (continuous data). LT₄: levothyroxine; TSH: thyroid stimulating hormone; T₄: thyroxine; T₃ tri-iodothyronine. *For the comparison of LT₄-treated and healthy controls. †For the comparison of LT₄-treated and matched controls. §Multiplied x 1000.

Supplemental Table 4: Clinical parameters of participant groups, by serum TSH.

	LT ₄ -treated (n=469)		Healthy Controls (n=9512)		Matched Controls (n=469)	
	TSH 0.24-1.74 (n=208)	TSH 1.75-5.40 (n=247)	TSH 0.24-1.74 (n=5733)	TSH 1.75-5.40 (n=3779)	TSH 0.24-1.74 (n=210)	TSH 1.75-5.40 (n=259)
Objective measures						
BMI (kg/m ²)	29.6 ± 6.2	29.9 ± 7.1	28.0 ± 6.3	29.2 ± 7.0 *	27.6 ± 5.7	28.7 ± 6.6
Systolic blood pressure (mm Hg)	129 ± 21	132 ± 22	122 ± 19	126 ± 20 *	129 ± 21	133 ± 23
Diastolic blood pressure (mm Hg)	68 ± 13	67 ± 15	70 ± 13	71 ± 14 *	69 ± 13	68 ± 15
Heart rate (beats per minute)	73 ± 13	72 ± 12	73 ± 13	73 ± 13	73 ± 13	71 ± 12
HbA _{1c} (%)	5.9 ± 0.8	5.9 ± 1.0	5.7 ± 1.0	5.7 ± 1.0 *	5.8 ± 0.9	5.9 ± 0.9
Fasting glucose (mg/dL)	105 ± 34	108 ± 38	99 ± 39	102 ± 37 *	105 ± 38	102 ± 28
Total cholesterol (mg/dL)	195 ± 42	198 ± 41	194 ± 42	197 ± 42 *	206 ± 42	204 ± 43§
HDL (mg/dL)	56 ± 17	53 ± 15†	52 ± 16	51 ± 16 *	58 ± 17	56 ± 16
LDL (mg/dL)	108 ± 36 (n=75)	120 ± 33† (n=100)	116 ± 36 (n=2080)	115 ± 37 (n=1538)	121 ± 36 (n=72)	124 ± 38 (n=108)
Triglyceride (mg/dL)	126 ± 75 (n=76)	157 ± 91 † (n=104)	127 ± 102 (n=2142)	146 ± 118 * (n=1609)	127 ± 64 (n=72)	138 ± 70 (n=109)
CRP (mg/dL)	0.42 ± 0.52 (n=180)	0.57 ± 0.72† (n=220)	0.40 ± 0.83 (n=4737)	0.43 ± 0.78 (n=3205)	0.44 ± 0.82 (n=180)	0.54 ± 1.12 (n=222)
Ferritin (ng/mL)	99 ± 103 (n=41)	104 ± 109 (n=62)	78 ± 99 (n=2049)	87 ± 102 * (n=1104)	88 ± 91 (n=42)	90 ± 86 (n=59)
Creatinine (mg/dL)	0.93 ± 0.71	0.93 ± 0.31	0.87 ± 0.36	0.91 ± 0.38*	0.88 ± 0.38	0.92 ± 0.33
Creatinine phosphokinase (IU/L)	106 ± 64 (n=33)	129 ± 110 (n=36)	173 ± 206 (n=993)	160 ± 178 (n=568)	103 ± 72 (n=30)	115 ± 68 (n=37)
Medication use						
Beta-blocker (%)	68 (31%)	107 (42%) †	603 (11%)	558 (15%) *	49(23%)	61 (24%)
Statin (%)	64 (30%)	47 (18%) †	461 (8%)	377 (10%) *	35 (17%)	37 (14%)
Taking insulin (%)	7 (4%)	13 (6%)	111 (2%)	92 (2%)	5 (2%)	9 (3%)
Oral hypoglycemic (%)	38 (18%)	33 (14%)	429 (7%)	354 (9%)	24 (11%)	40 (15%)
Anti-depressant (%)	47 (22%)	54 (21%) †	372 (7%)	344 (9%) *	23 (11%)	46 (18%)
Anti-anxiety (%)	16 (8%)	14 (6%)	143 (3%)	106 (3%)	15 (7%)	14 (5%)
Anti-psychotic (%)	45 (1%)	1 (1%)	45 (1%)	28 (1%)	2(1%)	47 (1%)
Metabolic equivalent (METs)/Physical activity						
Total MET (work and recreational activity)	2407 ± 4048	2124 ± 2872	5139 ± 7107	4497 ± 6356 *	3084 ± 3942	3185 ± 5340
Work/job requires vigorous activity (%)	18 (10%)	24 (10%) †	1026 (21%)	603 (18%) *	31 (8%)	40 (9%)
Vigorous work MET	3840 ± 4677	3708 ± 3938	7489 ± 7337	6622 ± 6948 *	5280 ± 5606	6760 ± 8218
Work/job requires moderate activity (%)	57 (29%)	58 (25%)	1821 (38%)	1242 (38%)	125 (31%)	126 (27%)
Moderate work MET	2253 ± 2757	1750 ± 2051	3363 ± 3390	3081 ± 3249 *	2901 ± 2950	3071 ± 3734
Walks/bikes for transportation (%)	32 (16%)	43 (19%)	1455 (30%)	856(26%) *	79 (20%)	86 (18%)
Transportation MET	939 ± 1004	743 ± 914	1559 ± 2323	1355 ± 1799 *	1599 ± 2280	1192 ± 1629
Participates in vigorous recreational activity (%)	21 (10%)	22 (9%)	1169 (24%)	653 (20%) *	34 (9%)	49 (10%)

Vigorous recreational MET	805 ± 759	518 ± 257	936 ± 786	931 ± 911	655 ± 680	716 ± 829
Participates in moderate recreational activity (%)	76 (39%)	97 (43%)	1895 (39%)	1234 (37%)	133 (33%)	184 (39%)
Moderate recreational MET	741 ± 603	750 ± 591	909 ± 1110	898 ± 1042	755 ± 719	891 ± 918
Cognitive/well-being parameters						
Stated health condition (%)						
Excellent	11 (6%)	15 (6%)	578 (11%)	370 (10%)	20 (10%)	19 (7%)
Very good	52 (26%)	63 (26%)	1463 (28%)	955 (27%)	52 (27%)	59 (25%)
Good	90 (45%)	95 (40%)	2140 (40%)	1380 (39%)	75 (39%)	106 (44%)
Fair	37 (18%)	44 (19%)	930 (18%)	671 (19%)	33 (17%)	47(20%)
Poor	11(6%)	20(8%)	152 (3%)	120 (4%)	12 (6%)	10 (4%)
Number of days in the past month physical health was not good	5.9 ± 13.2	5.3 ± 9.7	3.8 ± 8.5	3.9 ± 8.9	5.6 ± 11.6	4.8 ± 8.9
Number of days in the past month mental health was not good	4.9 ± 12.5	5.1 ± 10.8	4.1 ± 8.4	4.0 ± 9.0	5.0 ± 11.7	5.0 ± 10.8
Number of days in the past month inactive due to physical or mental health	2.3 ± 8.6	2.6 ± 6.8	1.8 ± 6.5	1.9 ± 6.8	2.1 ± 7.5	2.3 ± 6.6
Physical, mental, or emotional limitation kept from working (%)	40 (19%)	42 (17%)	587 (11%)	475 (13%) *	38 (18%)	34 (13%)
Experience confusion/memory problem (%)	34 (16%)	28 (11%)	354 (7%)	280 (8%) *	21(10%)	24 (9%)
Limited in activity due to physical, mental or emotional problem (%)	7 (5%)	9 (6%)	128 (3%)	86 (3%)	11 (8%)	6 (3%)
Social factors						
Smoked at least 100 cigarettes in lifetime (%)	100 (47%)	119 (47%)	2567 (48%)	1591 (44%) *	99 (47%)	114 (45%)
Currently smoking daily (%)	21 (21%)	26 (22%)	1108 (43%)	533 (34%) *	28 (13%)	23 (9%)
Consumed at least 12 alcoholic drinks per year (%)	77 (65%)	104 (63%)	2251 (71%)	1584 (71%)	68 (56%)	110 (65%)
Number of alcoholic drinks consumed per day	1.9 ± 1.7	1.7 ± 1.3	3.1 ± 3.2	2.9 ± 3.4	2.0 ± 1.5	1.9 ± 1.2
Nutrient intake						
Calories consumed (kcal/day)	1701 ± 634	1811 ± 775	2180 ± 1063	2092 ± 1001 *	1677 ± 708	1831 ± 911
Calories adjusted by body weight (kcal/day/kg)	22 ± 8	23 ± 10	29 ± 15	27 ± 14 *	23 ± 10	24 ± 13
% calorie intake	89 ± 34	93 ± 41	115 ± 60	107 ± 57*	91 ± 39	96 ± 52
Carbohydrate consumed (g)	208 ± 85	225 ± 100	268 ± 135	258 ± 132 *	206 ± 91	228 ± 115
Carbohydrate consumed (%)	50 ± 11	50 ± 10	50 ± 11	50 ± 12	50 ± 11	51 ± 11
Protein consumed (g)	64 ± 26	70 ± 34 †	83 ± 44	80 ± 42 *	64 ± 30	69 ± 35
Protein consumed (%)	15 ± 4	16 ± 4	16 ± 5	16 ± 5	16 ± 5	15 ± 4
Fat consumed (g)	66 ± 34	69 ± 39	81 ± 48	78 ± 46 *	64 ± 34	69 ± 42
Fat consumed (%)	34 ± 9	33 ± 8	33 ± 9	33 ± 9	33 ± 9	34 ± 9
Selenium intake (mcg)	53 ± 43	52 ± 43	53 ± 95	52 ± 58	55 ± 49	51 ± 41

The mean serum TSH level from the entire population was 1.75 mIU/L. Participants within each group were then classified as having serum TSH levels above or below this mean, and then thyroid function tests reassessed for each subgroup. Data are mean \pm SD, n (%). P-value by chi-square (categorical data) or student's t test (continuous data). LT4: levothyroxine, TSH: thyroid stimulating hormone, T4: thyroxine, T3: tri-iodothyronine, BMI: body mass index, HbA_{1C}: hemoglobin A_{1C}, LDL: low-density lipoprotein cholesterol, HDL: high-density lipoprotein cholesterol, DRI: dietary reference intake. † For the comparison of LT4-treated. * For the comparison of healthy controls. §For the comparison of matched controls.

Supplemental Table 5: Correlations of clinical parameters with free T₃:free T₄.

	LT ₄ -treated (n=469)		Healthy Controls (n=9512)		Matched controls (n=469)	
	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value
Demographics						
Age (years)	-0.41	<0.0001	-0.25	<0.0001	-0.277	<0.0001
Female (%)	-0.15	<0.01	-0.08	<0.0001	-0.043	0.35
Race/Ethnicity (%)						
Non-Hispanic White	-0.09	0.05	-0.03	<0.0001	-0.073	0.12
Non-Hispanic Black	0.05	0.25	0.00	0.850	-0.025	0.59
Hispanic	0.08	0.08	0.09	<0.0001	0.131	<0.010.35
Other	-0.01	0.80	-0.09	<0.0001	-0.043	
Objective measures						
BMI (kg/m ²)	0.14	<0.01	0.05	<0.0001	0.14	<0.01
Systolic blood pressure (mm Hg)	-0.12	0.01	-0.07	<0.0001	-0.04	0.41
Diastolic blood pressure (mm Hg)	0.22	<0.0001	0.08	<0.0001	0.18	<0.0001
Heart rate (beats per minute)	0.10	0.03	0.06	<0.0001	0.02	0.64
HbA _{1c} (%)	0.01	0.92	-0.11	<0.0001	0.01	0.88
Fasting glucose (mg/dL)	-0.03	0.55	-0.10	<0.0001	0.02	0.74
Total cholesterol (mg/dL)	0.07	0.12	0.07	<0.0001	0.05	0.28
LDL (mg/dL)	0.04	0.64	0.05	<0.01	0.05	0.52
HDL (mg/dL)	-0.09	0.04	-0.09	<0.0001	-0.13	<0.01
Triglyceride (mg/dL)	0.30	<0.0001	0.14	<0.0001	0.29	<0.0001
C-reactive protein (mg/dL)	-0.03	0.61	-0.08	<0.0001	-0.08	0.10
Ferritin (ng/mL)	0.02	0.85	-0.03	0.09	0.16	0.12
Creatinine (mg/dL)	-0.14	<0.01	-0.12	<0.0001	-0.23	<0.0001
Creatinine phosphokinase (IU/L)	0.16	0.18	0.12	<0.0001	0.16	0.20
Medication use						
Beta-blocker (%)	-0.06	0.21	-0.11	<0.0001	-0.12	0.01
Statin (%)	0.01	0.76	-0.06	<0.0001	0.07	0.11
Insulin (%)	0.04	0.35	-0.06	<0.0001	-0.01	0.78
Oral hypoglycemic (%)	0.17	0.06	0.13	<0.0001	0.11	0.25
Anti-depressant (%)	0.12	<0.01	-0.01	0.93	0.02	0.71
Anti-anxiety (%)	-0.04	0.41	-0.01	0.20	-0.05	0.25
Anti-psychotic (%)	-0.03	0.52	-0.01	0.87	-0.04	0.45
Metabolic equivalents (METs)/Physical parameters						
Total MET (work and rec activity)	0.04	0.48	0.12	<0.0001	0.06	0.31
Work/job requires vigorous activity (%)	-0.01	0.956	-0.10	<0.0001	0.02	0.71
Vigorous work MET	-0.14	0.39	0.08	<0.01	0.25	0.21
Work/job requires moderate activity (%)	0.02	0.66	-0.07	<0.0001	-0.04	0.43
Moderate work MET	0.21	0.03	0.10	<0.0001	0.13	0.15
Walks/bikes for transportation (%)	-0.05	0.34	-0.04	<0.01	-0.02	0.67
Transportation MET	0.07	0.57	0.03	0.15	0.03	0.80
Participates in vigorous recreational activity (%)	-0.11	0.03	-0.04	<0.0001	-0.03	0.58
Vigorous recreational MET	-0.14	0.38	0.09	<0.0001	0.24	0.15
Participates in moderate recreational activity (%)	-0.03	0.54	-0.01	0.68	-0.05	0.29
Moderate recreational MET	-0.08	0.33	0.05	0.01	0.07	0.40
Cognitive/well-being parameters						
Number of days in the past month physical health was not good	0.10	0.04	-0.04	<0.01	-0.02	0.76
Number of days in the past month mental health was not good	0.07	0.16	0.02	0.04	0.01	0.85
Number of days in the past month inactive due to physical or mental health	0.08	0.08	-0.03	<0.01	0.02	0.67
Physical, mental or emotional limitation kept from working (%)	-0.03	0.55	0.06	<0.0001	-0.01	0.88
Experience confusion/memory problem (%)	-0.01	0.98	0.04	<0.0001	0.10	0.03
Limited in activity due to physical, mental or emotional problem (%)	0.11	0.08	0.02	0.05	-0.01	0.85
Social factors						
Smoked at least 100 cigarettes	-0.01	0.82	-0.02	0.12	0.01	0.79
Currently smoking daily	0.14	0.04	-0.10	<0.0001	0.05	0.50
Consumed at least 12 drinks per year	-0.12	0.04	-0.10	<0.0001	0.04	0.51

Nutrient Intake						
Calories consumed in 24 hour recall (kcal/day)	0.19	<0.0001	0.16	<0.0001	0.11	0.02
Calories consumed, adjusted by body weight (kcal/day/kg)	0.06	0.24	0.10	<0.0001	0.02	0.68
% calorie intake compared to DRI for energy	0.06	0.24	0.10	<0.0001	0.02	0.68
Carbohydrate consumed (g)	0.13	<0.01	0.14	<0.0001	0.08	0.09
Carbohydrate consumed (%)	-0.06	0.21	-0.02	0.05	0.04	0.35
Protein consumed (g)	0.20	<0.0001	0.11	<0.0001	0.07	0.15
Protein consumed (%)	0.01	0.87	-0.05	<0.0001	-0.11	0.02
Fat consumed (g)	0.15	<0.01	0.12	<0.0001	0.09	0.06
Fat consumed (%)	0.02	0.93	-0.01	0.74	-0.04	0.38
Selenium intake (mcg)	0.01	0.98	0.02	0.47	-0.09	0.35

Data are Pearson's correlation coefficient (r) and corresponding p-value. T₄: thyroxine; T₃: tri-iodothyronine, BMI: body mass index, HbA_{1C}: hemoglobin A_{1C}, LDL: low-density lipoprotein cholesterol, HDL: high-density lipoprotein cholesterol, DRI: dietary reference intake.

Supplemental Table 6: Correlations of clinical parameters with free T₃.

	LT ₄ -treated (n=469)		Healthy Controls (n=9512)		Matched controls (n=469)	
	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value
Demographics						
Age (years)	-0.33	<0.0001	-0.34	<0.0001	-0.29	<0.0001
Female (%)	-0.09	0.06	-0.18	<0.0001	-0.02	0.609
Race/Ethnicity (%)						
Non-Hispanic White	-0.13	<0.010.90	-0.08	<0.0001	-0.12	0.008
Non-Hispanic Black	0.01	<0.010.88	-0.04	<0.0001	-0.06	0.165
Hispanic	0.16		0.12	<0.0001	0.19	<0.0001
Other	-0.01		-0.01	0.95	0.02	0.678
Objective measures						
BMI (kg/m ²)	0.12	0.01	0.03	<0.01	0.19	<0.0001
Systolic blood pressure (mm Hg)	-0.13	<0.01	-0.10	<0.0001	-0.15	<0.01
Diastolic blood pressure (mm Hg)	0.16	<0.01	0.06	<0.0001	0.10	0.04
Heart rate (beats per minute)	0.08	0.11	0.06	<0.0001	0.05	0.27
HbA _{1c} (%)	-0.09	0.05	-0.08	<0.0001	-0.01	0.86
Fasting glucose (mg/dL)	-0.07	0.13	-0.05	<0.0001	0.05	0.30
Total cholesterol (mg/dL)	-0.10	0.03	-0.05	<0.0001	-0.03	0.48
LDL (mg/dL)	-0.11	0.13	-0.02	0.32	0.01	0.87
HDL (mg/dL)	-0.16	<0.0001	-0.17	<0.0001	-0.21	<0.0001
Triglyceride (mg/dL)	-0.01	0.94	0.07	<0.0001	0.08	0.27
C-reactive protein (mg/dL)	-0.06	0.25	-0.06	<0.0001	-0.09	0.07
Ferritin (ng/mL)	0.05	0.63	0.01	0.41	0.12	0.20
Creatinine (mg/dL)	-0.27	<0.0001	-0.10	<0.0001	-0.25	<0.0001
Creatinine phosphokinase (IU/L)	-0.02	0.89	0.13	<0.0001	-0.06	0.66
Medication use						
Beta-blocker (%)	-0.06	0.17	-0.13	<0.0001	-0.07	0.15
Statin (%)	-0.04	0.42	-0.09	<0.0001	-0.05	0.29
Insulin (%)	-0.03	0.58	-0.05	<0.0001	-0.02	0.64
Oral hypoglycemic (%)	0.01	0.88	0.10	<0.0001	0.13	0.20
Anti-depressant (%)	-0.04	0.41	-0.10	<0.0001	-0.04	0.38
Anti-anxiety (%)	-0.10	0.04	-0.04	<0.0001	-0.01	0.76
Anti-psychotic (%)	-0.04	0.45	-0.03	<0.01	-0.03	0.48
Metabolic equivalents (METs)/Physical parameters						
Total MET (work and rec activity)	-0.04	0.50	0.12	<0.0001	0.07	0.298
Work/job requires vigorous activity (%)	-0.07	0.14	-0.10	<0.0001	0.04	0.469
Vigorous work MET	-0.35	0.02	0.07	0.01	-0.02	0.91
Work/job requires moderate activity (%)	0.03	0.50	-0.07	<0.0001	-0.04	0.42
Moderate work MET	0.04	0.67	0.09	<0.0001	0.18	0.05
Walks/bikes for transportation (%)	-0.08	0.10	-0.07	<0.0001	-0.09	0.07
Transportation MET	0.01	0.99	0.01	0.64	0.06	0.57
Participates in vigorous recreational activity (%)	-0.05	0.27	-0.09	<0.0001	-0.06	0.21
Vigorous recreational MET	-0.04	0.79	0.16	<0.0001	0.26	0.12
Participates in moderate recreational activity (%)	-0.08	0.10	0.01	0.54	-0.01	0.96
Moderate recreational MET	0.04	0.58	0.04	0.02	0.25	<0.01
Cognitive/well-being parameters						
Number of days in the past month physical health was not good	0.02	0.69	-0.06	<0.0001	-0.07	0.18
Number of days in the past month mental health was not good	-0.06	0.23	0.01	0.87	0.07	0.16
Number of days in the past month inactive due to physical or mental health	-0.01	0.79	-0.05	<0.0001	0.01	0.99
Physical, mental or emotional limitation kept from working (%)	0.07	0.13	0.06	<0.0001	-0.07	0.12
Experience confusion/memory problem (%)	0.08	0.22	0.05	<0.0001	0.07	0.13
Limited in activity due to physical, mental or emotional problem (%)	0.05	0.44	0.03	0.04	-0.01	0.96
Social factors						
Smoked at least 100 cigarettes	0.05	0.27	-0.02	0.15	-0.01	0.82
Currently smoking daily	0.06	0.40	0.12	<0.0001	0.06	0.41
Consumed at least 12 drinks per year	-0.07	0.27	-0.09	<0.0001	-0.01	0.92

Nutrient Intake						
Calories consumed in 24 hour recall (kcal/day)	0.13	0.01	0.15	<0.0001	-0.01	0.91
Calories consumed, adjusted by body weight (kcal/day/kg)	0.02	0.64	0.10	<0.0001	-0.10	0.03
% calorie intake compared to DRI for energy	0.02	0.64	0.10	<0.0001	-0.10	0.03
Carbohydrate consumed (g)	0.08	0.09	0.14	<0.0001	-0.02	0.61
Carbohydrate consumed (%)	-0.04	0.35	0.01	0.31	0.04	0.40
Protein consumed (g)	0.12	0.01	0.11	<0.0001	-0.02	0.73
Protein consumed (%)	-0.02	0.66	-0.05	<0.0001	-0.08	0.08
Fat consumed (g)	0.12	0.01	0.11	<0.0001	0.01	0.97
Fat consumed (%)	0.06	0.21	-0.01	0.30	-0.01	0.76
Selenium intake (mcg)	-0.09	0.26	-0.01	0.80	-0.15	0.11

Data are Pearson's correlation coefficient (r) and corresponding p-value. T₄: thyroxine; T₃: tri-iodothyronine, BMI: body mass index, HbA_{1C}: hemoglobin A_{1C}, LDL: low-density lipoprotein cholesterol, HDL: high-density lipoprotein cholesterol, DRI: dietary reference intake.

Supplemental Table 7: Correlations of clinical parameters with free T₄.

	LT ₄ -treated (n=469)		Healthy Controls (n=9512)		Matched controls (n=469)	
	Correlation coefficient	p-value	Correlation coefficient	p-value	Correlation coefficient	p-value
Demographics						
Age (years)	0.28	<0.0001	0.03	0.001	0.118	0.01
Female (%)	0.11	0.02	-0.05	<0.0001	0.031	0.51
Race/Ethnicity (%)						
Non-Hispanic White	0.04	0.38	-0.04	0.001	-0.022	0.63
Non-Hispanic Black	-0.04	0.38	-0.03	0.007	-0.007	0.87
Hispanic	-0.02	0.61	0.01	0.874	-0.020	0.57
Other	0.01	0.88	0.11	<0.0001	0.093	0.05
Objective measures						
BMI (kg/m ²)	-0.10	0.04	-0.04	<0.0001	-0.01	0.78
Systolic blood pressure (mm Hg)	0.08	0.10	0.01	0.54	-0.06	0.19
Diastolic blood pressure (mm Hg)	-0.14	<0.01	-0.05	<0.0001	-0.12	0.01
Heart rate (beats per minute)	-0.06	0.18	-0.02	0.13	0.04	0.46
HbA _{1c} (%)	-0.04	0.40	0.07	<0.0001	-0.01	0.92
Fasting glucose (mg/dL)	0.01	0.81	0.08	<0.0001	0.02	0.61
Total cholesterol (mg/dL)	-0.14	<0.01	-0.13	<0.0001	-0.08	0.08
LDL (mg/dL)	-0.09	0.24	-0.078	<0.0001	-0.05	0.47
HDL (mg/dL)	0.01	0.71	-0.03	<0.01	0.01	0.97
Triglyceride (mg/dL)	-0.27	<0.0001	-0.11	<0.0001	-0.23	<0.01
C-reactive protein (mg/dL)	0.02	0.67	0.07	<0.0001	0.05	0.29
Ferritin (ng/mL)	0.07	0.46	0.05	<0.01	-0.08	0.43
Creatinine (mg/dL)	0.02	0.69	0.07	<0.0001	0.08	0.08
Creatinine phosphokinase (IU/L)	-0.12	0.34	-0.04	0.12	-0.22	0.07
Medication use						
Beta-blocker (%)	0.03	0.49	0.04	<0.0001	0.09	0.05
Statin (%)	-0.05	0.30	0.01	0.50	-0.12	0.01
Insulin (%)	-0.05	0.26	0.04	<0.0001	0.01	0.87
Oral hypoglycemic (%)	-0.22	0.01	-0.62	0.02	-0.05	0.60
Anti-depressant (%)	-0.16	<0.0001	-0.07	<0.0001	-0.05	0.31
Anti-anxiety (%)	0.01	0.96	-0.02	0.02	0.05	0.30
Anti-psychotic (%)	-0.01	0.98	-0.01	<0.01	0.02	0.60
Metabolic equivalents (METs)/Physical parameters						
Total MET (work and rec activity)	-0.08	0.2	-0.06	<0.0001	-0.04	0.50
Work/job requires vigorous activity (%)	-0.11	0.48	0.04	<0.0001	0.01	0.85
Vigorous work MET	-0.03	0.50	-0.05	0.04	-0.28	0.16
Work/job requires moderate activity (%)	-0.01	0.86	0.04	<0.0001	0.04	0.45
Moderate work MET	-0.21	0.03	-0.04	0.01	-0.01	0.94
Walks/bikes for transportation (%)	-0.01	0.82	-0.01	0.34	-0.05	0.32
Transportation MET	-0.02	0.84	-0.04	0.09	-0.03	0.82
Participates in vigorous recreational activity (%)	0.10	0.04	-0.02	0.10	0.01	0.82
Vigorous recreational MET	0.12	0.44	0.02	0.42	0.02	0.92
Participates in moderate recreational activity (%)	0.03	0.53	0.02	0.15	0.08	0.12
Moderate recreational MET	0.09	0.24	-0.02	0.24	0.09	0.29
Cognitive/well-being parameters						
Number of days in the past month physical health was not good	-0.11	0.03	0.01	0.90	-0.02	0.63
Number of days in the past month mental health was not good	-0.11	0.02	-0.03	0.02	0.04	0.36
Number of days in the past month inactive due to physical or mental health	-0.10	0.03	0.01	0.75	-0.02	0.62
Physical, mental or emotional limitation kept from working (%)	0.08	0.08	-0.03	<0.01	0.04	0.42
Experience confusion/memory problem (%)	0.03	0.53	-0.02	0.10	-0.08	0.09
Limited in activity due to physical, mental or emotional problem (%)	-0.08	0.19	-0.01	0.49	-0.02	0.69
Social factors						
Smoked at least 100 cigarettes	0.04	0.44	0.01	0.45	-0.04	0.39
Currently smoking daily	-0.11	0.10	-0.04	0.01	-0.01	0.84
Consumed at least 12 drinks per year	0.10	0.09	0.04	<0.01	-0.04	0.47

Nutrient Intake						
Calories consumed in 24 hour recall (kcal/day)	-0.14	<0.01	-0.07	<0.0001	-0.12	0.01
Calories consumed, adjusted by body weight (kcal/day/kg)	-0.05	0.34	-0.04	<0.0001	-0.09	0.07
% calorie intake compared to DRI for energy	-0.05	0.34	-0.04	<0.0001	-0.09	0.07
Carbohydrate consumed (g)	-0.10	0.05	-0.06	<0.0001	-0.10	0.05
Carbohydrate consumed (%)	0.06	0.242	0.04	<0.01	-0.02	0.66
Protein consumed (g)	-0.14	<0.01	-0.05	<0.0001	-0.08	0.07
Protein consumed (%)	-0.01	0.89	0.02	0.03	0.06	0.18
Fat consumed (g)	-0.10	0.04	-0.06	<0.0001	-0.09	0.05
Fat consumed (%)	0.01	0.95	-0.01	0.53	0.03	0.51
Selenium intake (mcg)	-0.06	0.48	-0.02	0.39	0.02	0.83

Data are Pearson's correlation coefficient (r) and corresponding p-value. T₄: thyroxine; T₃: tri-iodothyronine, BMI: body mass index, HbA_{1C}: hemoglobin A_{1C}, LDL: low-density lipoprotein cholesterol, HDL: high-density lipoprotein cholesterol, DRI: dietary reference intake.

Supplemental Table 8: Univariate regression analysis of clinical parameters and the serum free T₃:free T₄ ratio.

	Healthy Controls (n=9512)	
	Regression Coefficient	p-value
Demographics variables		
Age (5 year increase)	-0.06	<0.0001
Female	-0.14	<0.0001
Hispanic	0.16	<0.0001
Non-Hispanic White	-0.05	<0.01
Non-Hispanic Black	-0.01	0.85
Other race/ethnicity	-0.29	<0.0001
Objective measures		
BMI (5 kg/m ² increase)	0.04	<0.0001
Systolic blood pressure (mm Hg)	-0.01	<0.0001
Diastolic blood pressure (mm Hg)	0.01	<0.0001
Heart rate (beats per minute)	0.01	<0.0001
HgbA _{1c} (%)	-0.09	<0.0001
Fasting glucose (50 mg/dL increase)	-0.11	<0.0001
Total cholesterol (50 mg/dL increase)	0.07	<0.0001
LDL (50 mg/dL increase)	0.05	<0.01
HDL (50 mg/dL increase)	-0.23	<0.0001
Triglyceride (50 mg/dL increase)	0.05	<0.0001
C-reactive protein (mg/dL)	-0.08	<0.0001
Ferritin (50 ng/dL increase)	-0.02	0.09
Creatinine (0.5 mg/dL increase)	-0.13	<0.0001
Creatinine phosphokinase (50 IU/L increase)	0.02	<0.0001
Medication use		
Beta-blocker	-0.30	<0.0001
Statin	-0.19	<0.0001
Insulin	-0.35	<0.0001
Oral hypoglycemic	0.20	<0.0001
Anti-depressant	-0.03	0.34
Anti-anxiety	-0.07	0.20
Anti-psychotic	-0.02	0.87
Metabolic equivalents (METs)/physical parameters		
1000 MET activity (work and rec activity)	0.01	<0.0001
Work/job requires vigorous activity (%)	-0.22	<0.0001
1000 Vigorous work MET	0.01	<0.01
Work/job requires moderate activity (%)	-0.13	<0.0001
1000 Moderate work MET	0.02	<0.0001
Walks/bikes for transportation (%)	-0.07	<0.01
1000 Transportation MET	0.01	0.15
Participates in vigorous recreational activity (%)	-0.09	<0.0001
1000 Vigorous recreational MET	0.01	<0.0001
Participates in moderate recreational activity (%)	-0.01	0.68
1000 Moderate recreational MET	0.03	0.01
Cognitive/Well-being parameters		
Excellent/good stated health condition	-0.01	0.60
Poor stated health condition	-0.12	0.02
Number of days in the past month physical health was not good	-0.01	<0.01
Number of days in the past month mental health was not good	0.01	0.04
Number of days in the past month inactive due to physical or mental health	-0.01	<0.01
Physical, mental or emotional limitation kept from working	0.16	<0.0001
Experience confusion/memory problem	0.14	<0.0001
Limited in activity due to physical, mental or emotional problem	0.12	0.05

Social factors		
Smoked at least 100 cigarettes	-0.03	0.12
Currently smoking daily	0.16	<0.0001
Consumed at least 12 drinks per year	-0.13	<0.0001
Number of alcoholic drinks consumed per day	0.01	0.82
Nutrient intake		
1000 calories consumed in 24 hour recall	0.13	<0.0001
Calories consumed, adjusted by body weight (kcal/day/kg)	0.01	<0.0001
% calorie intake compared to DRI for energy	0.01	<0.0001
100 grams carbohydrate consumed	0.09	<0.0001
Carbohydrate consumed (%)	-0.02	0.05
50 grams protein consumed	0.11	<0.0001
Protein consumed (%)	-0.01	<0.0001
50 grams fat consumed	0.11	<0.0001
Fat consumed (%)	0.01	0.74
Selenium intake (mcg)	0.01	0.47

LT₄: levothyroxine, BMI: body mass index, HbA_{1C}: hemoglobin A_{1C}, LDL: low-density lipoprotein

cholesterol, HDL: high-density lipoprotein cholesterol, DRI: dietary reference intake.

Supplemental Table 9: Multivariate regression analysis identifies clinical parameters associated with the serum free T₃:free T₄ ratio.

	Healthy Controls (n=9709)	
	Regression Coefficient	p-value
Age (5 year increase)	-0.10	0.005
Female	-0.24	0.05
BMI (5 kg/m ² increase)	0.04	0.02
Total cholesterol (50 mg/dL increase)	0.13	0.03
Triglyceride (50 mg/dL increase)	0.04	0.02
Creatinine (0.5 mg/dL increase)	-0.09	0.04
1000 MET activity (work and recreation)	--	ns
1000 calories consumed	--	ns
Beta-blocker prescription	--	ns
Currently smoking daily	--	ns
Number of alcoholic drinks consumed per day	--	ns

Age was scaled to 5 years, BMI scaled to 5 kg/m², total cholesterol scaled to 50 mg/dL, triglyceride scaled to 50 mg/dL, creatinine scaled to 0.5 mg/dL, beta-blocker use, current smoker, number of alcohol drinks consumed per day, total METs scaled to 1000 MET, and calorie intake scaled to 1000 calories.

HDL and LDL were omitted due to multicollinearity with total cholesterol. BMI: body mass index, MET: metabolic equivalent