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Use of thyroid hormones in the treatment of hypothyroidism: Thesis questionnaire survey for Finnish specialists

BACKGROUND The standard treatment of hypothyroidism is levothyroxine (LT4). The aim of the study was to investigate Finnish endocrinologists' use of thyroid hormones in hypothyroid and euthyroid patients as part of the international Thesis study carried out in 28 European countries.

METHODS The survey was sent to all members of the Finnish Endocrine Society by email (n = 504) using the LimeSurvey platform.

RESULTS A total of 112 responding participants were specialists in endocrinology, paediatric endocrinology, or internal medicine. Ninety-nine percent of the specialists preferred LT4 tablets as the first-line treatment in hypothyroidism. According to 43% of the specialists, combined LT4 and liothyronine (LT3) treatment was indicated in patients with symptoms of hypothyroidism despite normal serum TSH. Thirty-four percent of the specialists never used thyroid hormones in euthyroid patients while 41% used them for growing goitre and 30% for female infertility with a high level of thyroid antibodies.

CONCLUSIONS LT4 was used as the first line treatment for hypothyroidism. LT4 was used almost exclusively in tablet form, and the use of liquid solution and capsules was extremely rare because these formulations are not reimbursed in Finland. Combined LT4 and LT3 treatment was commonly used in patients with normal serum TSH who still complained of symptoms suggestive of hypothyroidism.

Hypothyroidism is a condition where the thyroid gland doesn't create and release enough thyroid hormones. At the end of 2020, thyroid hormone preparations were used by 337,275 Finns (1). The number of patients has increased 1.6-fold in the last 12 years (Figure 1). Thyroid hormones without marketing authorization and used with special permission were taken by 3,210 patients, of whom 988 used desiccated animal thyroid products.

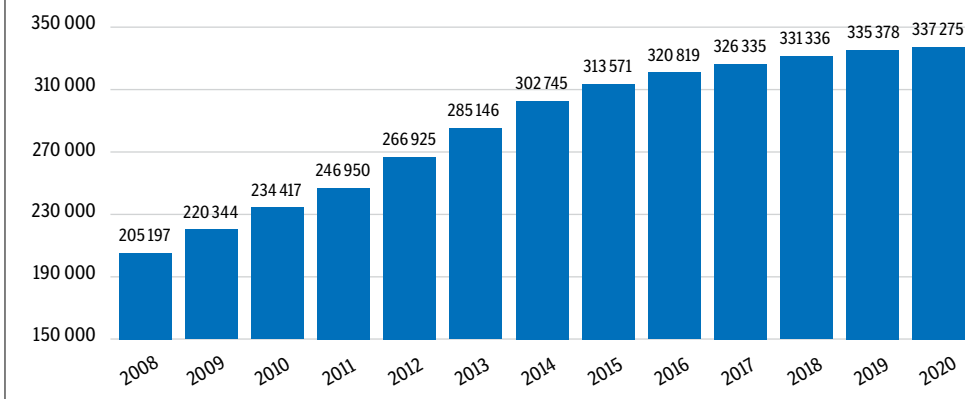
There are several recent Finnish reviews (2,3) and international treatment recommendations (4,5,6) on hypothyroidism diagnostics, medications and monitoring. According to these recommendations, the first-line treatment for hypothyroidism is levothyroxine (T4). The use of different thyroid hormone products is determined by the treatment guidelines, marketing authorization, prices, and reimbursement. Under the legislation governing medications all marketing of a preparation is forbidden if it does not have marketing authorization.

Two levothyroxine products with marketing authorization are available in Finland. They are included in the group of medications eligible for 100% reimbursement for those suffering from insufficient function of the pituitary gland and clinical hypothyroidism and in the 40% reimbursement group for subclinical hypothyroidism. Fimea has granted a special permit for some thyroid hormone products that have no marketing authorization in Finland to be released for consumption in individual cases for special therapeutic reasons. These levothyroxine (T4), liothyronine (T3) and T4+T3 combination products and animal-based desiccated thyroid products and their prices are presented in the Supplementary Table 1. Of the products with special permits only Liothyronin 20 µg-tablets are eligible for 40% reimbursement (7).

Thesis (Treatment of Hypothyroidism in Europe by Specialists: an international survey) is a questionnaire survey co-ordinated by the European Thyroid Association (ETA). It aims to

 **FIGURE 1.**

Patients taking hypothyroidism medications (H03A) in Finland 2008–20



study the availability of different thyroid preparations and the ways in which these are used in Europe.

Data and methods

The Thesis questionnaire study was implemented by the national endocrine societies of 28 European countries. In 2020, there were 509 members in the Finnish Endocrine Society including medical specialists in several fields, specialising physicians, nurses, researchers and students. The questionnaire was sent to 504 members who had consented to the use of their email. Responses were collected on the LimeSurvey platform. The questions were the same in all European countries (Appendix 1). The questionnaire was sent six times at weekly intervals during the period 29.9.–10.11.2020. Responses from the same IP address were excluded as duplicates. According to the Thesis study plan, only responses given by specialists in endocrinology, in paediatric endocrinology or in internal medicine were chosen to the study. Responses were analysed using SPSS (version 26). Pearson's χ^2 test was used for the comparison of variables to be classified. Level of statistical significance was set at $P < 0.05$.

Results

Responses were received from 141 members. Responses included in the study were those from specialists in endocrinology ($n = 66$; 5%),

paediatric endocrinology ($n = 18$; 16%) and internal medicine ($n = 28$; 25%) (Appendix 2). Of the endocrinologists 76% were also specialised in internal medicine. Of the 112 respondents, 86% were less than 70 years old, 71% had been in working life for over 20 years and 81% reported treating thyroid patients at least weekly. Eighty-three per cent of respondents were practising in hospitals. Twenty-eight per cent of medical specialists practiced in private clinics but of these 67% ($n = 21$) worked also in public hospitals (Table 1).

Ninety-nine per cent of respondents considered levothyroxine to be the first-line treatment for hypothyroidism while none of them considered T3-monotherapy or desiccated thyroid products to be the first-line treatment option for hypothyroidism and only one respondent considered T4+T3-combined treatment to be the first-line option. Twelve per cent of respondents did not respond to this question ($n = 11$) (Appendix 3).

Thirty-four per cent of respondents ($n = 38$) never prescribed thyroid medications for patients whose thyroid values were normal, but 41% ($n = 46$) prescribed these for the treatment of growing goitre. Thirty per cent ($n = 34$) prescribed thyroid medications for the treatment of infertility for women with normal thyroid tests but high levels of thyroid antibodies (TPO). Only few respondents prescribed thyroid medications as adjuvant treatment for fatigue (10%), obesity (5%), severe hypercholesterolemia (5%)

TABLE 1.

Characteristics of the endocrinologists, specialists in internal medicine and paediatric endocrinologists who responded to the questionnaire

Variables describing medical specialists	n	%
Men	47	42
Women	65	58
Age in years		
20–30	0	0
31–40	18	16
41–50	21	19
51–60	36	32
61–70	21	19
> 70	16	14
Years in working life		
< 20	32	29
21–40	56	50
> 40	24	21
Specialization		
Endocrinology	66	59
Endocrinology and internal medicine	50	
Endocrinology only	16	
Paediatric endocrinology	18	16
Internal medicine	28	25
Employer		
University hospital	50	45
Central or regional hospital	43	38
Private practice	31	28
General practice	4	4
Basic researcher	3	3
Treating thyroid patients		
Daily	35	31
Weekly	56	50
Seldom	15	13
No response	6	5
Number of hypothyroid patients treated		
Seldom	9	13
10–50 annually	44	39
51–100 annually	26	23
over 100 annually	27	24
No response	6	5

or depression (6%) despite of normal thyroid tests (Appendix 4).

Except for the treatment of infertility, age group, gender and field of specialisation did not affect above mentioned treatment decisions. For infertility, 27% of endocrinologists and four per cent of specialists in internal medicine initiated thyroid hormone despite thyroid tests within the reference values (treatment of infertility with thyroid medications vs. field of specialisation, $p < 0.01$).

Medical specialists working in private clinics initiated treatment with thyroid medications statistically significantly more seldom than doctors employed only in the public hospitals for the treatment of fatigue (4 vs. 6%, $p < 0.01$), obesity (2 vs. 4%, $p < 0.01$), hypercholesterolemia (1 vs. 5%, $p < 0.01$), depression (1 vs. 5%, $p < 0.01$), infertility (9 vs. 21%, $p < 0.01$) and growing goitre (13 vs. 29%, $p < 0.01$).

Levothyroxine as drops and soluble tablets are available in Finland only with special permission from Fimea (Appendix 1). Finnish medical specialists did not believe that T4 in soft-gel capsules or liquid solution would help patients with suspected malabsorption, with adherence problems or with symptoms despite of normal thyroid values or whose thyroid test are not within the target with T4-tablets (Appendix 5).

Forty-three per cent of the respondents ($n = 48$) considered persistence of symptoms despite of normal TSH an indication to try T4 and T3 combined treatment. Twenty-nine per cent of respondents ($n = 33$) answered that due to the low quality of available evidence combined therapy should never be used (Appendix 6). Neither gender nor age affected significantly to attitudes to combined treatment.

Twenty-seven per cent of respondents estimated that in spite of normal TSH values symptoms persisted in 6–30% of patients (Table 2). Sixty per cent of respondents estimated that the numbers of such patients had increased or remained constant in the last five years. If a patient's TSH value was normal, but the symptoms persisted, more than half of respondents considered the symptoms to be likely attributable to psychosocial factors, to other concurrent conditions, chronic illness or burden of illness due to regular medication and the patients' unrealistic expectations with regard to the treatment of hypothyroidism (Table 2).

TABLE 2.

Patients having persistent symptoms of hypothyroidism despite of normal TSH value

How many of the patients have persistent symptoms despite of normal TSH value	n	%
< 5	52	46
6–10	21	19
11–30	9	8
> 30	1	1
Cannot say or no response	29	26
Has the number of patients increased in 5 years		
I encounter more such patients	39	35
I encounter fewer such patients	8	7
The number of such patients has remained as before	28	25
I cannot say or no response	37	33
Most likely reason for persistent symptoms despite of normal TSH		
Inability of levothyroxine to restore normal physiology	19	17
Psychosocial factors	70	63
Comorbidities	51	46
Chronic fatigue syndrome	34	30
Patients' unrealistic expectations	61	54
Inflammation due to autoimmune disease	21	19
Burden of disease due to chronic illness	48	43
The burden of having to take medication	29	26
I cannot say or no response	24	21

Discussion

Hypothyroidism affects approximately three per cent of the population (8). Thus, it is important to assess the cost-efficiency and efficacy of medications before embarking on their extensive use (9).

The first-line treatment for hypothyroidism is T4 in tablet form. It should be taken on an empty stomach half an hour before breakfast. If taken with food the absorption of the substance is impaired by 40–80% (2,4). An optimal treatment response requires a good adherence to the treatment. Several illnesses and medications affect the pharmacokinetics of thyroid hormone products (9). Not all patients' quality of life is optimal even if the treatment has been successfully administered (3,5,10). Numerous new thyroid medications have come onto the European markets in an attempt to resolve the problems of hypothyroidism. The evidence of the differences between these products in

pharmacokinetics, efficacy on the patients' symptoms and thyroid function tests remains to be inadequate (9).

The Thesis study elicited endocrinologists' practices in Europe in the treatment of hypothyroidism. Practices are influenced by evidence-based treatment guidelines, the range of products with marketing authorization, the price and reimbursement of the available products. There are so far no current care recommendations on hypothyroidism in Finland, but work on these is ongoing and it is expected to be completed in 2023.

T4 tablets are used as the front-line treatment for hypothyroidism in Finland. Liquid solution and soft-gel capsules are not considered an alternative if the patient is suspected of having malabsorption, problems in adherence to treatment or persistent symptoms despite levothyroxine treatment. With the exception of T4 tablets there are no other T4- products having marketing authorization in Finland. The prices of T4 products in other than tablet form are five to eight times higher than those having marketing authorization and reimbursement (Supplementary Table 1), and this probably restricts the use of such products in Finland. Compared to other results of the Thesis study, Finland's results corresponds to that of Denmark, while in Italy, Poland and Romania as many as 50–75% of respondents reported using T4 liquid solution and soft-gel capsules (11,12,13,14).

Symptoms consistent with hypothyroidism, goitre and infertility are indications for initiating treatment in patients with subclinical hypothyroidism (6). However, thyroid replacement therapy is not indicated if thyroid function tests are normal (2,4,6). One third of respondents adhered to these recommendations, but 41% used thyroid medications for goiter growing over time and 30% for the treatment of infertility. Endocrinologists probably considered levothyroxine appropriate in the treatment of infertility at TSH level 2.5–4 mU/l because this is believed to ensure normal thyroid hormonal levels during pregnancy. Comparable findings were also obtained in other European countries (11,12,13,14) although there is no evidence that levothyroxine treatment improves fertility or prevents from pregnancy complications in euthyroid mothers (15). Doctors in Finland, Italy, Poland and Romania generally use thyroxine to

reduce goitre in euthyroidism patients, while it is rarely used in this indication in Denmark (11,12,13,14).

In the treatment of hypothyroidism TSH target is within the reference range (2,4) although for the elderly the TSH target should probably be higher (16). According to the treatment recommendations 5-10 per cent of patients on T4 treatment are not doing well even though the TSH value is on target (3,5). According to a recent questionnaire study as many as 77% of patients were dissatisfied with their treatment for hypothyroidism. However, such dissatisfaction was not explained by the thyroid medications used in the treatment but by other factors. The most important of these were patients' prior healthcare experiences and expectations for support and information. Focusing on enhancing the patient experience and clarifying expectations at diagnosis may improve satisfaction and quality of life (10).

Finnish endocrinologists have comprehended the significance of treating the patient holistically. In addition to hypothyroidism treatment, it is deemed necessary to ascertain and address psychosocial reasons, the patient's expectations of treatment, other concurrent conditions and the burden of disease caused by

chronic illness or regular medication. Almost half of the endocrinologists initiated combined T4 and T3 treatment if necessary (3,5).

Our study represents very well the medical specialists responsible for the treatment of Finns' hypothyroidism. According to the statistics of the Finnish Medical Association there were 67 endocrinologists under the age of 65 in Finland in 2019, and of these 67% were women (17). The Thesis study obtained responses from 66 endocrinologists, of whom 59 were less than 70 years old and 64% were women. In addition, 18 paediatric endocrinologists and 25 specialists in internal medicine responded to the questionnaire. The treatment of primary hypothyroidism in Finland is decentralised among the public primary care. Thus, the questionnaire study does not yield a picture of the treatment practices of all doctors involved in the treatment of hypothyroidism.

The treatment of hypothyroidism in Finland adheres to treatment recommendations and is consistent with the practices of other European countries. It is important for Finland to be involved in Europe-wide research co-operation when the efficacy and cost-effectiveness of medications of hypothyroidism are studied and treatment recommendations updated. ●



SUPPLEMENTARY TABLE 1.

Thyroid hormone preparations most commonly used in Finland

Thyroid hormone preparation	Trade name of the product	Marketing authorization	Price before reimbursement
Levothyroxin (T ₄), tablets	Thyroxin 25 and 100 µg	Yes	0,06 e / 100 µg
Levothyroxin (T ₄), tablets	Medithyrox 13, 25, 50, 62, 75, 88, 100, 125, 150, 175 and 200 µg	Yes	0,06 e / 100 µg
Levothyroxin (T ₄), suspension	Eferox 25, 50, 75, 100 and 125 µg	No	0,3 e / 100 µg
Levothyroxin (T ₄), drops 1 ml (28 drops) = 97,24 µg	Tirosint 100 µg/ml	No	0,5 e / 100 µg
Liothyronin (T ₃), tablets	Liothyronin 20 µg	No	0,2 e / 20 µg
Liothyronin (T ₃), tablets	Liothyronine Sodium 5 µg	No	5,5 e / 20 µg
Liothyronin (T ₃), tablets	Thybon Henning 20 µg	No	0,5 e / 20g
T ₄ +T ₃ -combination	Novothyral 100+20 µg and NovoThyral 75+15 µg	No	0,7 e / 100 µg T ₄ and 20 µg T ₃
T ₄ +T ₃ -combination	NP Thyroid 60 mg (T ₄ 38 µg and T ₃ 9 µg)	No	1,3 e / tabletti
Desiccated animal thyroid hormone preparation	Armour Thyroid 15, 30, 60 and 120 g	No	1,5 e / 60 mg = 1 grain
Desiccated animal thyroid preparation	Nature Thyroid 32,5, 65 and 130 mg	No	0,6 e / 65 mg
Desiccated animal thyroid preparation	Thyroid 30, 60, 125 mg	No	1,2 e / 60 mg = 1 grain

APPENDIX 1.

Survey on Current Use of thyroid hormone products in Europe

A: ABOUT YOU

A1. Sex

- a) Female
- b) Male

A2. Age (years) *[dropdown menu]*

- a) 20-30
- b) 31-40
- c) 41-50
- d) 51-60
- e) 61-70
- f) 70+

A3. Years in medical practice *[dropdown menu]*

- a) 0-10
- b) 11-20
- c) 21-30
- d) 31-40
- e) More than 40

A4. Specialty *[check all that apply]*

- a) Endocrinology
- b) Internal Medicine
- c) Pediatric Endocrinology
- d) Nuclear Medicine
- e) Surgery
- f) Family Medicine
- g) Gynecology
- h) Other

A5. Member of... *[check all that apply]*

- a) ETA (European Thyroid Association)
- b) ATA (American Thyroid Association)
- c) LATS (Latin American Thyroid Association)
- d) AOTA (Asian and Oceanian Thyroid Association)
- e) National Endocrine Societies
- f) None of the above

A6. Where do you practice? *[check all that apply]*

- a) University centre
- b) Regional hospital
- c) Private clinic
- d) General Practice
- e) Basic researcher
- f) Specialist Practice

A6bis. Are you clinically active?

- a) Yes
- b) no

A7. Do you treat thyroid patients on a regular basis (daily or weekly)?

- a) Yes, daily
- b) Yes, weekly
- c) No, I rarely treat thyroid patients

A8. Do you treat patients with hypothyroidism?

- a) Yes, from 10 to 50 patients/year
- b) Yes, from 51 to 100 patients/year
- c) Yes, > 100 patients/year
- d) No, I rarely treat hypothyroid patients

B. HYPOTHYROIDISM

B1. Thyroid hormones may be indicated in biochemically euthyroid patients with: *[check all that apply]*

- 1) unexplained fatigue
- 2) obesity resistant to life-style interventions
- 3) severe hypercholesterolemia, as a complementary treatment
- 4) depression resistant to anti-depressant medications
- 5) female infertility with high level of thyroid antibodies
- 6) simple goiter growing over time*
- 7) no, treatment is never indicated for these patients

**If this is ever an indication, even under specific circumstances (eg taking into account age and comorbidities) then it should be ticked.*

B2. Which thyroid hormones available for substitution therapy should be the first choice for the treatment of hypothyroid patients?

- 1) LT4
- 2) LT3
- 3) Desiccated thyroid
- 4) LT4 and LT3 combination

B3. Which of the following drugs are you prescribing in clinical practice? [check all that apply]

- 1) LT4
- 2) LT3
- 3) Desiccated thyroid
- 4) LT4 and LT3 combination

B4. How much control do you have over the formulation of LT4 dispensed for your patients? Please choose the option the best applies to your practice

- 1) most of my patients are dispensed the type of LT4 that I recommend
- 2) I have control over the type of LT4, but I have to justify it to the regulatory authorities every time I recommend it
- 3) the type of dispensed thyroxine is mostly chosen by general practitioners
- 4) for most of my patients I have no control over the type of LT4 that they are dispensed

B5. Interfering drugs may influence the stability of therapy. Which LT4 preparation is in your experience least likely to be subject to variable absorption?

- 1) tablets
- 2) soft-gel capsules
- 3) liquid solution
- 4) I expect no major changes with different formulations

B6. Which of the following preparations of LT4 would you prescribe in case of first diagnosis of hypothyroidism when the patient self-reports intolerance to various foods raising the possibility of celiac disease, malabsorption, lactose intolerance, or intolerance to common excipients

- 1) tablets
- 2) soft-gel capsules
- 3) liquid solution
- 4) I expect no major changes with the different formulations

B7. Which of the following preparations of LT4 would you prescribe for a patient established on LT4 who has unexplained poor biochemical control of hypothyroidism?

- 1) tablets from another manufacturer
- 2) soft-gel capsules
- 3) liquid solution
- 4) I expect no major changes with the different formulations

B8. Which of the following preparations of LT4 would you prescribe for a patient with poor biochemical control who is unable (due to busy lifestyle) to take LT4 fasted and separate from food/drink?

- 1) tablets
- 2) soft-gel capsules
- 3) liquid solution
- 4) I expect no major changes with the different formulations

B9. Which of the following preparations of LT4 would you prescribe for a patient established on LT4 tablets who has good biochemical control of hypothyroidism but continues to have symptoms?

- 1) tablets from another manufacturer
- 2) soft-gel capsules
- 3) liquid solution
- 4) I expect no major changes with the different formulations

B10. After the start of LT4 replacement therapy, when would you re-check serum TSH:

- 1) after 2 weeks
- 2) after 4 – 6 weeks
- 3) after 8 weeks
- 4) no, I mostly rely on clinical evaluation

B11. In case of a switch to a different formulation or change from one manufacturer's LT4 tablet to another, when do you recommend that the serum TSH should be re-checked:

- 1) after 4 to 6 weeks
- 2) after 8 weeks
- 3) on the basis of clinical evaluation
- 4) no, there is no need of TSH control after preparation changes if the dosage is the same

B12. Dietary supplements (such as selenium or iodine) are proposed for patients with thyroid disease. Do you think that they may be used in addition to thyroid hormone replacement in hypothyroidism?

- 1) when there is coexisting autoimmune thyroiditis
- 2) in subclinical hypothyroidism
- 3) at the patient's request or as a complementary treatment
- 4) no, dietary supplements should never be used

B13. The use of combined replacement therapy, with administration of both LT4 and LT3, is generally not recommended. Do you think that may be considered:

- 1) for a short period, in patients recovering from protracted hypothyroidism
- 2) in patients with normal serum TSH who still complain of symptoms suggestive of hypothyroidism
- 3) in hypothyroid patients with normal serum TSH who complain of unexplained weight gain
- 4) due to the low quality of available evidence, combined therapy should never be used.

B14. It has been reported that some patients with hypothyroidism treated with levothyroxine continue to experience persistent symptoms despite normal serum TSH. The following three questions refer to such patients.

In your clinical practice how common is this phenomenon?

- 1) less than 5% of patients
- 2) 6-10%
- 3) 11-30%
- 4) More than 30%
- 5) Not sure

B15. It has been reported that some patients with hypothyroidism treated with levothyroxine continue to experience persistent symptoms despite normal serum TSH.

In your experience what has been the trend over the past 5 years?

- 1) I am seeing more such cases
- 2) I am seeing fewer such cases
- 3) No change
- 4) Not sure

B16. In most patients treated with levothyroxine who achieve normal serum TSH, persistent symptoms are due to:

- 1) inability of levothyroxine to restore normal physiology
strongly disagree/disagree/neutral/agree/strongly agree
- 2) psychosocial factors
strongly disagree/disagree/neutral/agree/strongly agree
- 3) comorbidities
strongly disagree/disagree/neutral/agree/strongly agree
- 4) chronic fatigue syndrome
strongly disagree/disagree/neutral/agree/strongly agree
- 5) patient unrealistic expectation
strongly disagree/disagree/neutral/agree/strongly agree
- 6) presence of underlying inflammation due to autoimmunity
strongly disagree/disagree/neutral/agree/strongly agree
- 7) the burden of chronic disease
strongly disagree/disagree/neutral/agree/strongly agree
- 8) the burden of having to take medication
strongly disagree/disagree/neutral/agree/strongly agree

B17. Using your experience with patients treated with levothyroxine who achieve normal serum TSH, but continue to experience symptoms like fatigue, please rank them from 1-8, where 1 is the most likely and 8 the least likely explanation in your opinion. [Attribute a score from 1 (most likely) to 8 (least likely) to each item.]

Rank (1-8)

- 1) the burden of having to take medication
- 2) patient unrealistic expectations
- 3) inability of levothyroxine to restore normal physiology
- 4) psychosocial factors
- 5) presence of underlying inflammation due to autoimmunity
- 6) comorbidities
- 7) chronic fatigue syndrome
- 8) the burden of chronic disease

B18. Do you, yourself have a diagnosis of hypothyroidism requiring thyroid hormone treatment?

1. Yes
2. No

B19. *(it will appear only in respondents who answered “yes” to question B18)* **Do you experience excessive tiredness/fatigue?**

1. Yes
2. No

B20. *(it will appear only in respondents who answered “yes” to question B18)* **Have you tried L-T4 and L-T3 combination treatment?**

1. Yes
2. No

B21. *(it will appear only in respondents who answered “yes” to question B18)* **Have you tried desiccated thyroid treatment?**

1. Yes
2. No

B22. *(it will appear only in respondents who answered “yes” to question B20 or B21)* **If you have tried of L-T4 and L-T3 combination treatment or desiccated thyroid, please describe your experience** (eg how effective compared with L-T4 monotherapy, whether you continue to take it, side-effects, long-term concerns).

(Space for free text)

B23. *(it will appear only in respondents who answered “No” to question B18)* **Would you consider L-T4 and L-T3 combination treatment or desiccated thyroid for yourself if you were to develop hypothyroidism?**

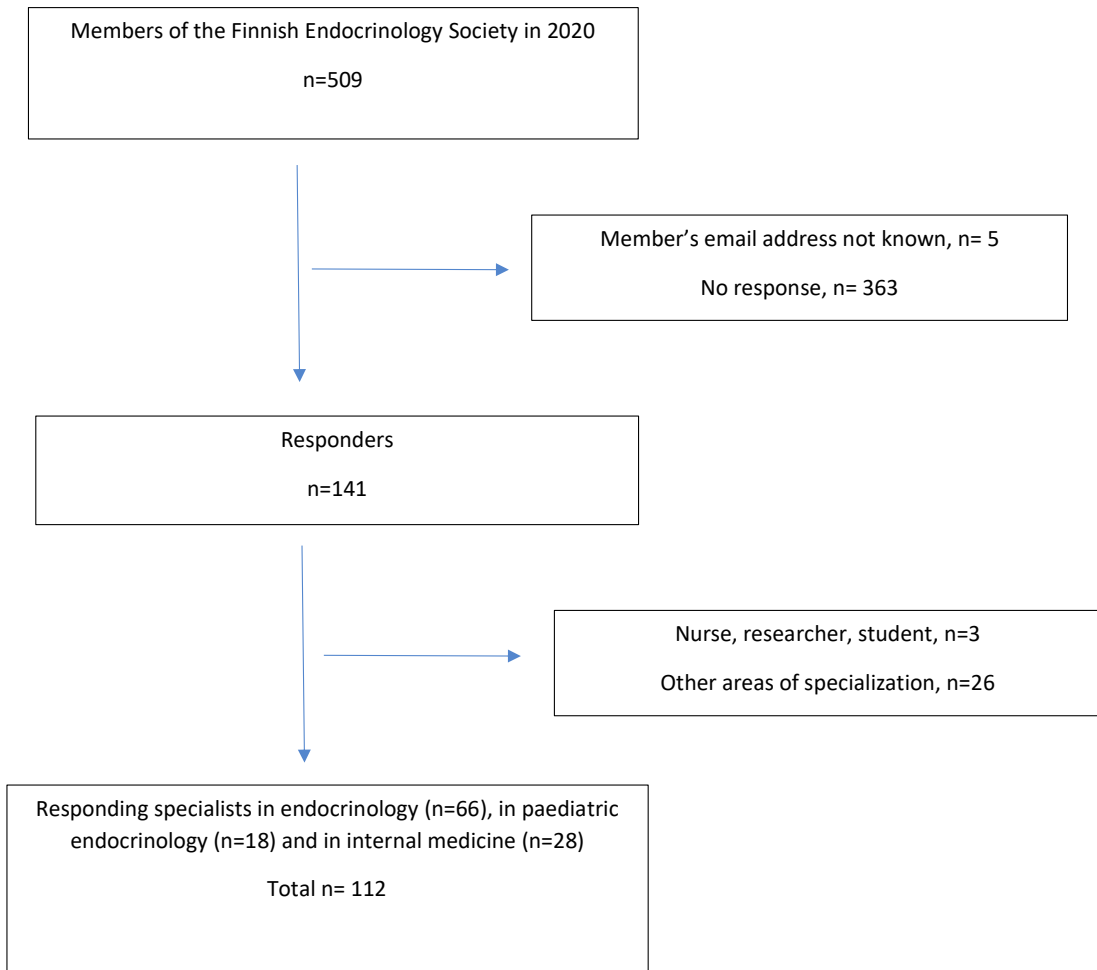
1. Yes
2. No

B24. **Please add comments (eg why you would or would not choose to take L-T4 and L-T3 combination treatment or desiccated thyroid for yourself)**

(Space for free text)

APPENDIX 2.

Thesis study flowchart



APPENDIX 3.

What thyroid preparation should be used as the first-line option in the treatment of hypothyroidism

Thyroid preparation	n	%
Levothyroxin (T ₄)	99	88
Liothyronin (T ₃)	0	0
Desiccated thyroid	0	0
Synthetic combination treatment T ₄ +T ₃	1	1
No response	12	11

APPENDIX 4.

Indications for thyroid preparation use in euthyroid patients, i.e. those with normal thyroid function tests

Indication	n	%
Unexplained fatigue	11	10
Obesity resistant to lifestyle changes	6	5
Adjuvant treatment in severe hypercholesterolemia	6	5
Depression unresponsive to medication	7	6
Infertility in women with high TPO antibody level	34	30
Simple goiter growing over time	46	41
Treatment is never indicated for these patients	38	34
No response	12	11

APPENDIX 5.

Selection of various levothyroxin preparations in clinical situations

Preparation	n	%
	Patient self-reports intolerance to various foods raising the possibility of celiac disease, malabsorption, lactose intolerance, or intolerance to common excipients	
Tablets	78	70
Soft-gel capsules	0	0
Liquid solution	0	0
I expect no major changes with the different formulations	20	18
No response	14	13
	Patient established on LT4 who has unexplained poor biochemical control of hypothyroidism	
Tablets by some other manufacturer	42	38
Soft-gel capsules	0	0
Liquid solution	1	1
I expect no major changes with the different formulations	54	48
No response	15	13
	Poor biochemical control who is unable (due to busy lifestyle) to take LT4 fasted and separate from food/drink?	

Tablets	38	34
Soft-gel capsules	3	3
Liquid solution	1	1
I expect no major changes with the different formulations	38	34
No response	15	13
	Patient established on LT4 tablets who has good biochemical control of hypothyroidism but continues to have symptoms?	
Tablets from another manufacturer	28	25
Soft-gel capsules	0	0
Liquid solution	0	0
I expect no major changes with the different formulations	67	60
No response	17	15

APPENDIX 6.

Indications for T₄ and T₃ combination treatment in patients with hypothyroidism

Indications for LT4 and LT3 combination treatment	n	%
For a short period, in patients recovering from protracted hypothyroidism	9	8
In patients with normal serum TSH who still complain of symptoms suggestive of hypothyroidism	48	43
In hypothyroid patients with normal serum TSH who complain of unexplained weight gain	1	1
Due to the low quality of available evidence, combined LT4 and TT3 therapy should never be used	33	29
No response	21	19