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Thyroid

Canadian Endocrinologists' Perspectives on Treatment With Thyroid Hormone Substitutions in Euthyroid and Hypothyroid Patients: A 2023 THESIS Questionnaire Survey

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ABSTRACT

Objective: The practice of treating hypothyroid and euthyroid patients with thyroid hormones varies between countries, as observed in the recent surveys of European thyroid experts, THESIS. As part of the THESIS initiative, we investigated Canadian endocrinologists' perspectives on this topic, focusing on combination therapy with either liothyronine (LT3) plus levothyroxine (LT4) or desiccated thyroid extract (DTE).

Design: Members of the Canadian Society of Endocrinology and Metabolism (CSEM) were invited to participate in an anonymous online survey.

Results: Out of 348 eligible CSEM members, 68 (19.5%) respondents were included in the analysis. All respondents used LT4 as the first-line treatment for hypothyroid patients. Many respondents (64.7%) would consider LT4 + LT3 for patients on LT4 with persistent symptoms, whereas fewer would consider DTE (16.2%). Most respondents attributed persistent symptoms in LT4-treated patients to psychosocial factors, comorbidities, or unrealistic expectations. Approximately half of the respondents stated that thyroid hormone therapy is never indicated for euthyroid patients. The remaining respondents considered thyroid hormones for euthyroid women with infertility and high thyroid antibody levels (36.8%), depression (13.2%), and growing goiter (7.4%).

Abbreviations: ATA, American thyroid association; CSEM, Canadian society of endocrinology and metabolism; DTE, desiccated thyroid extract; LT3, liothyronine; LT4, levothyroxine; LT4 + LT3, levothyroxine and liothyronine combination therapy; QoL, quality of life; T3, triiodothyronine; T4, thyroxine; TPOAb, thyroid peroxidase antibodies; TSH, thyroid stimulating hormone.

THESIS: Treatment of Hypothyroidism in Europe by Specialists: An International Survey.

Conclusions: Following current guidelines, LT4 tablet is the preferred treatment for hypothyroidism. Most respondents would consider triiodothyronine-containing therapy for patients with persistent symptoms, preferring LT4 + LT3 over DTE. The number of endocrinologists considering combination therapy for hypothyroid patients in Canada was higher than in Europe. Finally, at variance with current guidelines, a fraction of the respondents would consider thyroid hormones in patients with non-thyroidal conditions.

1 | Introduction

Overt hypothyroidism is a common condition, with a prevalence of 0.2–5.3% in Europe and 0.3–3.7% in the United States [1]. The variation in prevalence depends on the definition of hypothyroidism and the population [1]. In Canada, prescriptions of levothyroxine (LT4), the standard treatment for hypothyroidism, have consistently increased over time [2]. LT4 is available in generic and branded tablet forms. In contrast, many European countries have access to additional LT4 formulations, such as soft-gel capsules and liquid solutions, which may exhibit improved bioavailability compared to LT4 tablets in selected conditions [3, 4].

Despite achieving biochemical euthyroidism with LT4, some patients continue to experience symptoms [5, 6]. Much focus has been on potential inadequacies in restoring euthyroidism and relief by LT4 of symptoms compatible with hypothyroidism and less so on non-hormone related causes of persistent symptoms, or so-called "medically unexplained symptoms" (MUS) in biochemically euthyroid individuals [7]. Thus, attention to the potential role of psychological traits such as somatization [8] and type D personality has only recently surfaced [9].

Interventions such as ginger, L-carnitine, and total thyroidectomy (for those with high serum thyroid autoantibodies) have been investigated in hypothyroid patients with persistent symptoms without convincing evidence of improvement in symptoms or general health [10]. Further, a recent randomized controlled trial showed that selenium and placebo, as complementary supplements to LT4, were equally effective in improving quality of life (QoL) in patients with autoimmune thyroiditis [11].

There is ongoing controversy regarding whether patients with persistent symptoms may benefit from preparations containing triiodothyronine (T3) [7], which can be administered as a combination of LT4 and liothyronine (LT3) or as desiccated thyroid extract (DTE) that includes both thyroxine (T4) and T3. However, side effects due to possible iatrogenic thyrotoxicosis are a concern [12]. Given the lack of long-term safety data and no evidence of the superiority of combination therapy over LT4 monotherapy, combination therapy is not recommended for routine use. Still, it can be considered as a trial for patients with persistent symptoms despite LT4 treatment [6, 13].

An extensive survey conducted in twenty-eight European countries, known as THESIS (Treatment of Hypothyroidism in Europe by Specialists: An International Survey), examined endocrinologists' prescribing preferences for patients with persistent symptoms [14]. In some countries, up to 40% would consider LT4 + LT3 for patients with persistent hypothyroid symptoms despite normalization of thyrotropin (TSH). In contrast, only a few considered DTE in the treatment of hypothyroid patients [14]. Reasons for reluctance to prescribe DTE include the insufficient evidence demonstrating its superiority compared to LT4 therapy, the paucity of studies investigating potential adverse effects, both in the short and the long term, as well as DTE's unavailability in most European countries [12].

At variance with European countries, DTE is approved for use in Canada, which may influence local prescribing patterns. Therefore, we aimed to evaluate Canadian endocrinologists' perspectives regarding hypothyroidism treatment via a nationwide Canadian survey as part of the international THESIS project. Understanding physicians' treatment preferences is crucial as they affect patient experience and outcomes, contribute to data on practice variation, and identify areas for further research to improve the treatment of hypothyroidism.

2 | Methods

2.1 | Study Design

The original THESIS questionnaire was developed to evaluate European thyroid experts' attitudes regarding treating hypothyroidism and using thyroid hormones for non-hypothyroid indications. The present study included Canadian endocrinologists who treated patients with hypothyroidism. Eight questions about demographic data (Section A) were followed by 31 questions about treating hypothyroid and euthyroid patients (Section B) (Supporting Information 1). Before distributing the survey among Canadian endocrinologists, eight questions were added to the original questionnaire to highlight aspects of the use of LT4 + LT3 and DTE (The additional questions are marked with red in Supporting Information 1).

SurveyMonkey, an online survey platform, was utilized to create and distribute the questionnaire, which was estimated to take 15–20 min to complete. An e-mail containing an electronic link to the voluntary and anonymous questionnaire, along with a consent form, was sent to all members of the Canadian Society of Endocrinology and Metabolism (CSEM) on September 26, 2023. The initial invitation was followed by one reminder e-mail 3 weeks later and another reminder in the November 2023 newsletter for CSEM members. The survey was closed on December 26, 2023. Repeat submissions from the same IP address were automatically blocked. Survey responses were gathered and electronically stored by the SurveyMonkey service, where the data were accessible via password.

This survey was approved by the Western University Health Science Research Ethics Board in London, Ontario, Canada (Project ID: 122168; Reference: 2023-122168-79095).

2.2 | Statistical Analysis

Only respondents who completed all demographic questions were considered valid for statistical analysis. Descriptive statistics were prepared for responses to all questions. In all analyses, respondents stating that they did not know the answer to a specific question were grouped with those who did not provide an answer. The goodness of fit chi^2-test was used to compare frequencies between the categorical variables. Pearson's chi^2-test was used to assess if variables in the demographic data (Section A) were independent of the outcomes in questions in Section B. A two-sided p-value < 0.05 was considered statistically significant. All analyses were conducted using Stata software (V18.0; Stata-Corp, College Station, TX, USA).

3 | Results

3.1 | Sample Characteristics

Figure 1 illustrates the number of survey responses from CSEM members, and Table 1 compiles their demographic data. We could not demonstrate a relationship between demographic variables and answers to the questions regarding the use of thyroid hormones in the treatment of hypothyroid and euthyroid patients.

3.2 | Treatment Patterns for Patients with Hypothyroidism

All responding participants ($n = 60$, 88.2%) indicated that they recommended LT4 as the first-line treatment for hypothyroidism, while 11.8% ($n = 8$) did not respond. As a second-line treatment, 15 respondents (22.1%) recommended LT4 + LT3 before considering DTE therapy, and five respondents (7.4%) offered no preference regarding the order of LT4 + LT3 and DTE therapy.

In daily clinical practice, endocrinologists have several thyroid hormone substitutions available for treating patients with hypothyroidism. The respondents were asked which types they prescribed (question B3): 36.8% ($n = 25$) of respondents prescribed DTE, 57.4% ($n = 39$) prescribed LT4 + LT3, and 19.1% ($n = 13$) prescribed LT3. In contrast, 16.2% ($n = 11$) of respondents indicated they never prescribed LT4 + LT3, while 41.2% ($n = 28$) indicated they never prescribed DTE. Additionally, 45.6% ($n = 31$) and 66.2% ($n = 45$) of respondents, when prescribing DTE and LT4 + LT3, respectively, did so for less than 10% of their patients.

3.3 | Use of Different LT4 Formulations

Canadian endocrinologists were asked to answer five questions to explore their opinions on the potential benefits of different LT4 formulations, although only LT4 tablets are available in Canada (Supporting Information 2). Most respondents preferred LT4 tablets and did not anticipate a significant difference between tablets, soft-gel capsules, and liquid solutions in various clinical scenarios, including when patients take interfering drugs, are unable to take LT4 separately from food, have a possible malabsorptive condition, exhibit unexplained poor biochemical control, or experience persistent symptoms despite good biochemical control of hypothyroidism (Supporting Information 2; tablets and no significant difference expected vs. soft-gel capsules + liquid solution, $p < 0.01$).

3.4 | Treatment with Thyroid Hormones for Non-Hypothyroid Indications

Just under half (44.1%, $n = 30$) of the respondents indicated that treatment is never warranted in biochemically euthyroid patients (never indicated vs. others, $p = 1.00$). Conversely, 36.8% ($n = 25$) of respondents stated that thyroid hormones might be indicated for female infertility with high thyroid antibody levels, 13.2% ($n = 9$) for depression resistant to anti-depressant medications, 7.4% ($n = 5$) for a growing goiter, 4.4% ($n = 3$) as a complementary treatment for severe hypercholesterolemia, 2.9% ($n = 2$) for unexplained fatigue, and 1.5% ($n = 1$) for obesity resistant to lifestyle interventions. Eight individuals (11.8%) did not answer this question.

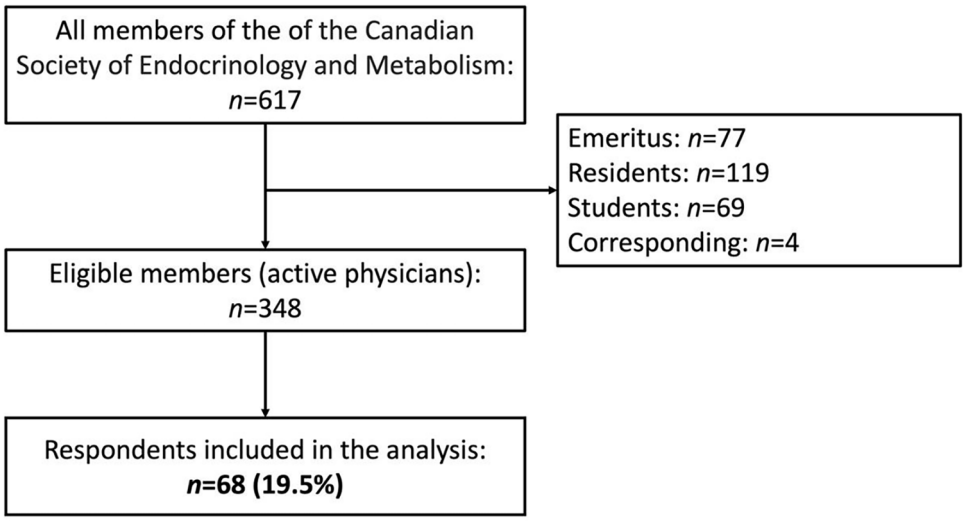

FIGURE 1 | Flowchart illustrating survey distribution and respondents.

TABLE 1 | Characteristics of survey respondents.

	n (%)
Sex	
Female	43 (63.2)
Male	25 (36.8)
Other/prefer not to say	0 (0)
Age, years	
20–30	3 (4.4)
31–40	26 (38.2)
41–50	19 (27.9)
51–60	14 (20.6)
61–70	5 (7.4)
> 70	1 (1.5)
Years in medical practice	
0–10	33 (48.5)
11–20	21 (30.9)
21–30	8 (11.8)
31–40	4 (5.9)
> 40	2 (2.9)
Specialty*	
Endocrinology	61 (89.7)
Internal medicine	6 (8.82)
Pediatric endocrinology	4 (5.9)
Other	1 (1.5)
Place of employment*	
University Center	43 (63.2)
Regional Hospital	13 (19.1)
Private Clinic	20 (29.4)
General Practice	6 (8.8)
Basic researcher	1 (1.5)
Frequency of treating thyroid patients	
Daily	49 (72.0)
Weekly	18 (26.5)
Rarely	1 (1.5)
Number of thyroid patients treated per year	
Rarely	1 (1.5)
10–50	17 (25.0)
51–100	25 (36.8)
> 100	25 (36.8)

*The sum of percentages exceeds 100% due to the option of several answers per respondent.

3.5 | Persistent Symptoms in LT4-treated Patients

Most respondents estimated that patients on LT4 who experienced persistent symptoms despite a normal TSH level comprised 6-10% ($n = 28$; 41.2%) or < 5% of their patients with hypothyroidism ($n = 15$; 22.1%). A minority of respondents estimated that such patients comprised 11-30% ($n = 11$; 16.2%) or greater than 30% ($n = 3$; 4.4%) ($\leq 10\%$ vs. > 10%, $p = 0.0001$). The remainder ($n = 11$; 16.2%) did not provide an answer.

Approximately half of the respondents ($n = 29$; 42.6%) had observed an increase in the number of biochemically euthyroid patients with persistent symptoms over the past 5 years. In contrast, 33.8% ($n = 23$) reported no change (more cases vs. no change, $p = 0.41$), and 23.6% ($n = 16$) were unsure or did not provide a response.

Respondents were asked to provide their opinions on why LT4-treated patients with normal TSH levels might experience persistent symptoms (Figure 2). The most common answers included psychosocial factors, comorbidities, and patients' unrealistic expectations.

3.6 | Combination Therapy with LT4 and LT3

Most respondents ($n = 44$; 64.7%) would consider LT4 + LT3 therapy for patients who never felt well on LT4-monotherapy. Further, 32 respondents (47.1%) would consider LT4 + LT3 therapy for patients with normal serum TSH who still exhibit symptoms suggestive of hypothyroidism, and 28 respondents (41.2%) would consider it upon the patients' request (Figure 3).

For patients treated with LT4 + LT3, most endocrinologists estimated that 40% or fewer achieve improvements in persistent symptoms and quality of life (QoL) (Figure 4; $\leq 40\%$ vs. > 40%, $p = 0.01$). Specifically, 16.2% ($n = 11$) of respondents predicted improvements in < 10%, 27.9% ($n = 19$) in 11-40% of the patients, 13.2% ($n = 9$) in 41–70% of the patients, and 5.9% ($n = 4$) estimated that 71-99% of patients showed improvement. Additionally, 10.3% ($n = 7$) never prescribed LT4 + LT3, and 26.5% ($n = 18$) were unsure or did not answer (Figure 4).

3.7 | Therapy with Desiccated Thyroid Extract

Approximately half of the respondents ($n = 32$, 47.1%) would not consider prescribing DTE therapy due to the low quality of available evidence, and about 27 respondents (39.7%) would consider it upon patient request (Figure 3).

When asked whether they would prescribe DTE to hypothyroid patients with specific characteristics, 13.2% ($n = 9$) would consider it for patients with unstable TSH during treatment with LT4; 7.4% ($n = 5$) for patients over 65 years of age; 1.5% ($n = 1$) for patients with heart disease; and 5.9% ($n = 4$) for patients with osteoporosis or psychiatric disorders, respectively. Eighteen respondents (26.5%) would prescribe DTE but on other indications than those listed above.

For patients treated with DTE, most respondents estimated that 40% or fewer achieve improvements in persistent symptoms and QoL (Figure 4; $\leq 40\%$ vs. > 40%, $p = 0.001$). Specifically, 11.8% ($n = 13$) of respondents estimated improvements in fewer than 10% of patients, 19.1% ($n = 13$) answered 11-40%, 4.4% ($n = 3$) answered 41–70% of patients, and 1.5% ($n = 1$) estimate that all patients prescribed DTE showed improvements (Figure 4).

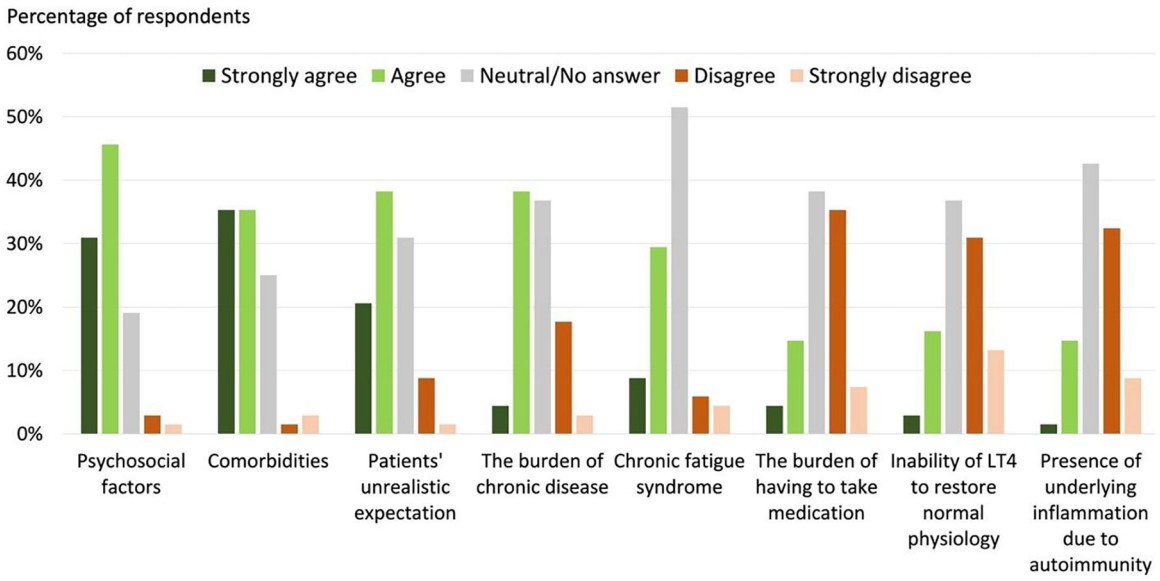

FIGURE 2 | Canadian endocrinologists' opinion concerning factors that may explain persistent symptoms of hypothyroidism despite biochemical euthyroidism in patients treated with levothyroxine (LT4). The figure ranks, from left to right, the most likely explanation for persistent symptoms, grouping "strongly agree and agree" together, progressing to the least likely causes, according to the opinions of Canadian endocrinologists.

Twenty-five (36.8%) had never prescribed DTE, and 26.5% ($n = 18$) did not answer or were unsure.

CSEM members were also asked how adverse events might differ between patients with hypothyroidism treated with DTE and those treated with LT4. While 10.3% ($n = 7$) believed that adverse events did not differ between the two treatment regimens, 38.2% ($n = 26$) thought patients treated with DTE experienced more symptoms consistent with thyrotoxicosis than those treated with LT4.

3.8 | Selenium and Iodine Supplements

Selenium was considered alongside thyroid hormone supplements upon patient request or as a complementary treatment by 52.9% ($n = 36$) of the respondents and to patients with autoimmune thyroiditis by 7.4% ($n = 5$). Nineteen respondents (27.9%) would never consider selenium supplements, and 11.8% ($n = 8$) did not provide an answer.

Regarding iodine supplements, fifteen (22.1%) of the respondents would consider them upon patient request or as a complementary treatment, while only one respondent would use such an approach for patients with autoimmune thyroiditis. Further, 64.7% ($n = 44$) would never consider them, and 11.8% ($n = 8$) did not provide an answer.

4 | Discussion

4.1 | Clinical Indications for Treatment with Thyroid Hormones

In line with international guidelines, this survey confirms that LT4 is the preferred treatment among Canadian endocrinologists for patients with hypothyroidism [15, 16].

Approximately half of the respondents believed that thyroid hormones are never warranted in treatment-naïve, biochemically euthyroid patients. However, one-third would consider thyroid hormone therapy for euthyroid women with infertility associated with high thyroid antibody levels. Similarly, 42% of thyroid experts across European countries would also support treatment in these patients [17]. This variation in practice may reflect the recommendation of the 2017 ATA guideline to consider low-dose LT4 treatment for thyroid peroxidase antibody (TPOAb)-positive euthyroid women undergoing assisted conception, given its potential benefits in improving pregnancy success compared to limited risk [18]. However, more recent systematic reviews and meta-analyses of randomized controlled trials have found no benefit of LT4 in euthyroid women with thyroid autoimmunity, whether pregnant or planning pregnancy, irrespective of the use of assisted conception [19, 20]. Furthermore, an ongoing discussion over the years on the definition of the reference range of thyroid function tests in pregnancy might also affect the response to this question [21]. International guidelines recommend local population- and pregnancy-specific reference intervals for TSH and free T4, according to the laboratory assays used, even though this is not feasible for most centers [18, 22]. Therefore, many centers use the nonpregnant TSH upper reference limit of 4.0 mU/L, a value that may not be applied uncritically to pregnant women [18].

A mere 7.4% of Canadian endocrinologists indicated prescribing LT4 for patients with a growing goiter, compared to one-third of European endocrinologists [23]. This different European attitude, more evident in its Eastern regions, could be due to the former presence of areas of low-iodine intake in which the treatment with thyroid hormones was reported as beneficial for nodular goiter. Accumulating evidence over the past decades has led to abandoning this

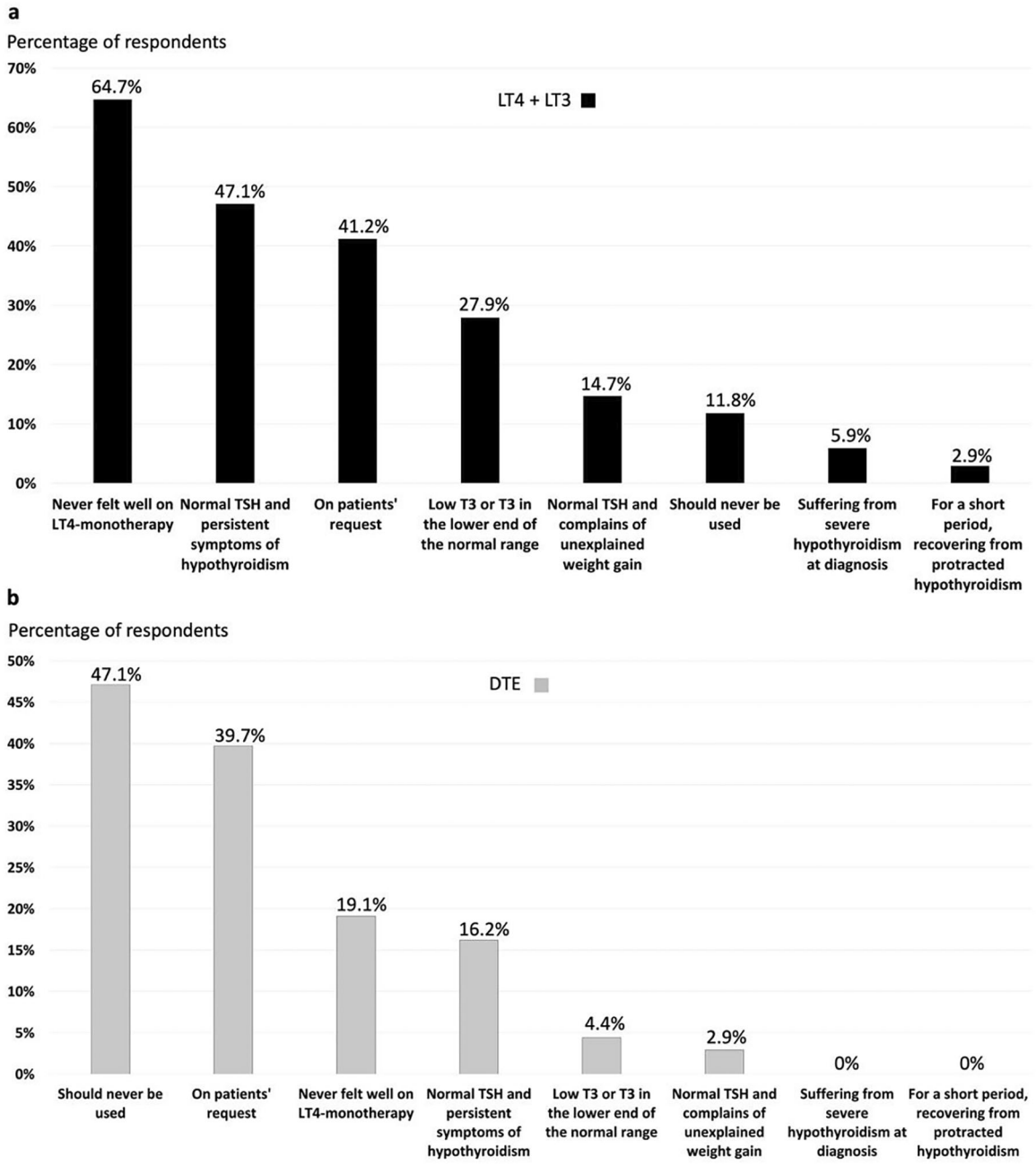

FIGURE 3 | Canadian endocrinologists' opinion on when to consider combination therapy with levothyroxine and liothyronine (LT4 + LT3; 3a) or desiccated thyroid extract (DTE; 3b) for treating hypothyroidism. There were 11.7% who did not answer this question; these respondents are not illustrated in the figure.

treatment option based on a lack of clinically significant efficacy [24, 25].

Overall, treating euthyroid individuals with LT4 has potential risks, and previous studies have shown associations with suppressed TSH in hypothyroid individuals and increased morbidity and mortality [26, 27]. Several factors might explain why physicians adhere to outdated treatment practices, including healthcare resources, patient-related factors (expectations, age, and culture), and physician characteristics (age, gender, and work institution) [14]. This emphasizes the need for a greater focus on disseminating the latest research and guidelines to encourage physicians to follow evidence-based practices.

4.2 | T3-containing Treatments

Current guidelines do not recommend DTE for the treatment of hypothyroidism, and LT4 + LT3 is not recommended for routine use [15, 16]. These recommendations are based on evidence for the lack of superiority of combination therapy over LT4 therapy and concerns about supraphysiologic serum T3 levels potentially leading to adverse effects [15]. However, the 2012 European guideline suggests that a trial of LT4 + LT3 therapy may be considered for LT4-treated patients with persistent symptoms despite achieving biochemical euthyroidism, importantly, provided that interfering comorbidities are excluded [16].

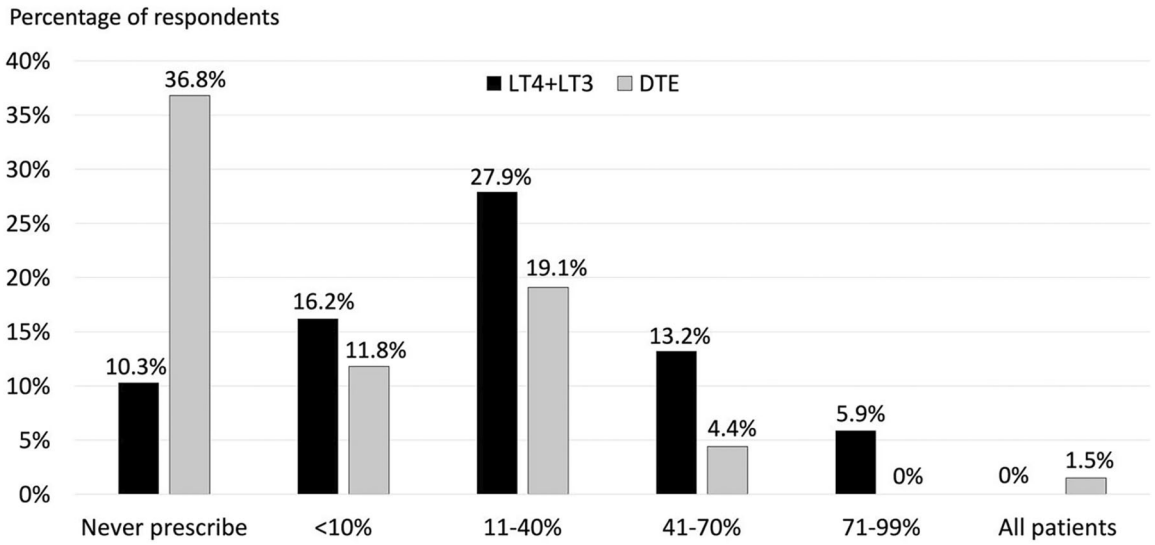

FIGURE 4 | Canadian endocrinologists' opinion on how many hypothyroid patients treated with levothyroxine and liothyronine (LT4 + LT3) or desiccated thyroid extract (DTE) experience improvement in symptoms and quality of life. There were 26.5% who did not answer this question or were unsure; these respondents are not illustrated in the figure.

The recommendation against offering DTE to hypothyroid patients is reflected in the low prescribing rates among thyroid experts in many European countries: Denmark (2.6%), Poland (0%), Romania (0%), Germany (4.9%), Belgium (0%), UK (5.4%), Portugal (0.9%), Czech Republic (0.6%) and France (0.2%) [28–36]. In contrast, 36.8% of Canadian endocrinologists reported prescribing DTE, which may reflect its greater availability than many European countries.

Additionally, the varying costs of T3-containing preparations and the lack of standardization between preparations to ensure uniform hormonal activity might also influence prescribing patterns among countries [37].

Canadian endocrinologists were more inclined to prescribe LT4 + LT3 for patients who never felt well on LT4 monotherapy (64.7%) or for those with persistent symptoms of hypothyroidism (47.1%). This proportion exceeds the 39.7% of nearly 6,000 European national Endocrine Society members [14]. However, there is considerable variation in LT4 + LT3 use among European countries, highlighting the controversial nature of this issue [14, 28–36, 38–51]. Although many Canadian respondents would prescribe DTE or LT4 + LT3, none consider it a first-line treatment option.

Most respondents estimated that 40% or fewer of their patients taking DTE experienced symptom improvements. These results reflect the lack of evidence that DTE is superior to LT4 treatment for hypothyroid patients. Indeed, data from two randomized controlled trials did not show significant differences in QoL or symptom scores between DTE and other thyroid hormone formulations [52, 53]. However, a post hoc subgroup analysis from the three-armed RCT found that the most symptomatic third of patients on LT4 had significant improvements in QoL-scores after switching to DTE or LT4 + LT3, with TSH remaining within the reference range, which warrants further investigation in this subpopulation of patients who remain symptomatic on LT4 [53].

It has been postulated that thyroid hormone signaling in a minority of patients on LT4 remains subnormal and can be improved with T3-containing therapy, though this remains unproven [54]. However, most Canadian respondents believed that persistent symptoms on LT4 are not due to the inability of LT4 to restore normal physiology but rather to psychosocial factors, comorbidities, and unrealistic expectations, aligning with opinions from all other THESIS surveys [14].

Most respondents believed persistent symptoms were due to psychosocial factors, which is paradoxical given the high prescription rates of combination therapy and their expectation that it benefits fewer than 40% of patients. This investigation emphasizes that patients' demands sometimes affect physicians' prescription patterns, even though evidence does not support this. Social media and the immediate availability of information, both true and untrue, on the internet, might negatively affect the interaction and communication between patients and physicians.

Additionally, many respondents were unsure or perceived DTE to be associated with increased adverse events compared to LT4 therapy. Although more long-term studies on the adverse effects of DTE are required, short-term data suggest potential iatrogenic thyrotoxicosis [12], in which case there is abundant evidence of an increase in somatic [55] as well as psychiatric co-morbidity [56] leading to an increase in mortality [27]. Therefore, it is also paradoxical that few of the respondents considered T3-containing preparations for patients with osteoporosis, heart disease, and psychiatric comorbidities.

4.3 | Use of Different LT4 Formulations

Limited evidence suggests potential improved bioavailability with LT4 as soft-gel capsules and liquid solutions compared to tablets [3]. In line with this, most Canadian respondents do not anticipate a significant difference between these formulations in various clinical situations that could affect absorption. Notably,

LT4 formulations other than tablets are unavailable in Canada. In the European THESIS surveys, the preference for soft-gel and liquid LT4 formulations in these clinical scenarios was higher in countries where these formulations were available [14]. However, even in these countries, only one-third or fewer respondents favored such formulations. The differing practices reflect the need for controlled long-term outcome studies to support their use in such scenarios, as well as potential cost differences between formulations [3].

4.4 | Strengths and Limitations

The endocrinologists who responded to our survey frequently treat patients with hypothyroidism, making their opinions on controversial areas particularly valuable. Given that many patients with hypothyroidism in Canada are treated by primary care physicians, respondents to this survey are most likely a subset of endocrinologists who manage a relatively higher proportion of patients dissatisfied with standard LT4 therapy.

Our survey has a response rate of 19.5%, which is relatively low compared to other national THESIS surveys, but it is higher than the response rate of 13% from Australia and 18.2% from South America [44, 45]. The low absolute number of respondents among CSEM members and Canadian endocrinologists may limit the generalizability of our results. Further, the respondents are predominantly women within their first ten years of practice and working at university centers. This stands in contrast to the fact that many patients with hypothyroidism are treated in primary care settings. Some questions in the survey, particularly those regarding unavailable LT4 formulations, are less relevant to Canadian general practitioners.

In conclusion, Canadian endocrinologists generally adhere to current guidelines for the treatment of hypothyroidism, favoring LT4 tablets as the first choice of therapy. However, a considerable number of them also prescribe DTE and LT4 + LT3 upon patient request or for those with persistent symptoms on LT4 monotherapy, despite a lack of supporting evidence. DTE use in this survey is notably higher than in European surveys, possibly due to its increased availability in Canada. Consistent with European THESIS results, most Canadian endocrinologists believe that persistent symptoms on LT4 are mainly due to psychosocial factors, comorbidities, and unrealistic expectations rather than the inability of LT4 to restore normal physiology. A substantial minority consider LT4 therapy for biochemically euthyroid women with thyroid autoimmunity and infertility despite recent evidence suggesting no benefit. In line with current evidence, only a minority use thyroid hormones in the treatment of obesity or a growing goiter. This survey emphasizes the need for further research on possible adverse effects of combination therapy, especially DTE, and possible non-thyroidal explanations for persistent symptoms in biochemically euthyroid patients.

Author Contributions

Conceptualization, methodology, project administration, and supervision: Steen J.Bonnema, Anna Liu, Kamilla R. Riis, Deric Morrison, Birte Nygaard, Laszlo Hegedüs, Petros Perros, Enrico Papini, Endre V. Nagy, Roberto Negro, Roberto Attanasio. Data curation, visualization, and writing of the original draft: Kamilla R. Riis, Anna Liu. Data collection, validation, review and editing: Kamilla R. Riis. Formal analysis, visualization: Kamilla R. Riis, Anna Liu. Writing, review and editing: all authors. All authors read and approved the final manuscript.

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Ethics Statement

This survey was approved by the Western University Health Science Research Ethics Board in London, Ontario, Canada (Project ID: 122168; Reference: 2023-122168-79095).

Conflicts of Interest

A.L., K.R.R., D.M., S.V.U., S.B., and B.N. do not have competing interests. Consulting fees: E.V.N., L.H., P.P. from IBSA; E.P. from IBSA and Terumo; L.H. from Horizon. Payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing or educational events: PP from IBSA; L.H. from IBSA, Berlin-Chemie, and Merck. Support for attending meetings and/or travel: P.P., E.P., and R.A. from IBSA; L.H. from IBSA, Berlin-Chemie, and Merck. Participation on a Data Safety Monitoring Board or Advisory Board: E.P., E.V.N., L.H., and P.P. were members of the IBSA scientific board. IBSA was not involved in the survey design, data analyses, data presentation and interpretation, or manuscript writing.

Data Availability Statement

The datasets used and analyzed during the current study are available from the corresponding author on request.

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Supporting Information

Additional supporting information can be found online in the Supporting Information section.
Supplementary 1. Supplementary 2.