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Thyroid

Use of thyroid hormones in hypothyroid and euthyroid patients: A survey of members of the Endocrine Society of Australia

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Abstract

Objective: Hypothyroidism is a common endocrine condition usually managed with levothyroxine (LT4). However, controversy remains around the use of liothyronine (LT3). We aimed to investigate the practices of Australian endocrinologists when managing patients with hypothyroidism, their use of LT3 + LT4 combination therapy and use of thyroid hormones in euthyroid patients.

Design and Participants: Members of the Endocrine Society of Australia (ESA) were invited to participate in an online questionnaire.

Measurements: We analysed questionnaires that had complete demographic data.

Results: Eighty-seven questionnaires fulfilled the criteria. LT4 was used as first line treatment for hypothyroidism by all respondents. Only 45% reported that their patients were dispensed the brand of LT4 that they recommend. LT3 (alone or in combination) was prescribed by 44% in their clinical practice. Although 49% of respondents would consider LT3 + LT4 in patients with normal TSH who had ongoing symptoms of hypothyroidism, the inability of LT4 to restore normal physiology was ranked the least likely explanation for persistent symptoms and only 32% would consider it for themselves if they were diagnosed with hypothyroidism. The majority (55%), in accordance with evidence, would not prescribe thyroid hormone to euthyroid individuals but 39% would consider use in euthyroid female infertility with high levels of thyroid antibodies and 11% in euthyroid patients with a simple goitre growing over time. LT4 use in pregnancy was variable among members.

Conclusions: Australian endocrinologists mostly follow international guidelines when prescribing thyroid hormone therapy and many prescribe combination LT3 and LT4 therapy, particularly for patients who remain symptomatic on LT4 monotherapy. Prescribing practices are largely similar to other countries who have completed similar questionnaires.

KEYWORDS

Australia, endocrinologist, hypothyroidism, thyroxine, triiodothyronine

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1 | INTRODUCTION

Hypothyroidism is a common endocrine condition, with overt hypothyroidism being present in ~0.5% of Australians and a further ~5% having subclinical hypothyroidism (increased thyrotropin [TSH] and normal free thyroxine [fT4]).¹ The most common cause of hypothyroidism in Australia, a mostly iodine sufficient country, is Hashimoto's disease, an autoimmune condition characterised by lymphocytic infiltration of the thyroid gland and production of thyroid antibodies.¹

Levothyroxine (LT4) is the recommended treatment for patients with hypothyroidism with the aim of symptom resolution and normalisation of circulating TSH levels.² In the year 2021–2022, LT4 was the drug with the 44th highest total prescription volume in the Pharmaceutical Benefits Scheme (PBS) in Australia, accounting for 1,946,472 prescriptions in the year.³ At the time of the survey, four brands of LT4 were available in Australia: EutroxsigTM and OroxineTM which are identical, LevoxineTM, which is considered bioequivalent to the former two, and EltroxinTM, which is not bioequivalent.^{4,5} Most patients experience resolution of symptoms on LT4 therapy, but studies have shown residual symptoms in some people despite adequate biochemical control and the reason for this remains unclear.^{6,7}

Symptoms of hypothyroidism are nonspecific and are often seen in people without hypothyroidism.⁷ The use of liothyronine (LT3) in combination with LT4 remains controversial as several randomised controlled studies investigating the use of combination LT3 + LT4 therapy to improve symptoms have failed to demonstrate benefit.⁷ The only formulation of LT3 approved by the Therapeutic Goods Administration (TGA) in Australia is LT3 sodium 20 microgram tablets in the brand Tertroxin. Patients can obtain other formulations of LT3 and desiccated thyroid extract (DTE) from compounding pharmacies which are not approved by the TGA nor are they subject to TGA regulations. An ESA position statement published in 2011 recommended against routine use of DTE, combination of thyroid hormones or LT3 therapy.⁴ However, more recent international guidelines suggest considering the use of combination therapy in patients who remain symptomatic on LT4 despite adequate biochemical control and where no other cause is identified for their symptoms.^{2,6,8}

Our study aims to understand how Australian endocrinologists manage patients with hypothyroidism, their use of LT3 + LT4 combination therapy and their use of thyroid hormones in euthyroid patients.

2 | MATERIALS AND METHODS

We used the THESIS (Treatment of Hypothyroidism in Europe by Specialists; An International Survey) questionnaire, amended to fit the Australian clinical setting (Supporting Information: 1).^{9,10} The survey consisted of nine demographic questions and 18–21 questions on the respondents' approach to thyroid hormone use in

hypothyroid and euthyroid individuals. An invitation for consultant endocrinologists and advanced trainees in endocrinology to participate in this study was included in an ESA bulletin sent to members on 15 August 2022 with a reminder on 8 September 2022. Qualtrics was used to administer the survey anonymously. Repeat submissions using the same IP address were automatically blocked. Completion of the survey took approximately 8 min.

This study was approved by the University of Western Australia Ethics Committee (2022/ET000004).

2.1 | Statistical analysis

Questionnaires that had complete demographic data were included in analyses. Descriptive statistics are presented as absolute numbers and percentage of respondents for each question. Subgroup analysis used the Chi-squared test and Fisher's exact test to assess for associations between responses to each question and demographic variables. A two-sided $p < .05$ was considered significant. For the two questions in which respondents were asked to rank options from most likely to least likely, each option was scored from 1 being most likely down to least likely 7 or 8, respectively. Only results that scored all options were used. The mean score for each question was then ranked from lowest (most likely) to highest (least likely). We performed subgroup analyses for question 16 and 17 according to whether respondents prescribe T3 or T3 + T4 combination therapy. All analyses were performed using R version 4.2.1.

3 | RESULTS

3.1 | Response rate and respondents' characteristics

Ninety ESA members responded to the questionnaire and provided consent to participate. Of these, 87 completed all demographic questions and were included in further analyses. The number of clinicians who received the invitation is unknown, but the ESA currently has 850 financial members, of whom approximately 80% are thought to be clinicians. Although an exact response rate cannot be calculated, this suggests a response rate of approximately 13%.

The demographic data of respondents are summarised in Table 1. Seven of 87 (8%) were registrars (advanced trainees) and all others were consultant physicians (80/87; 92%). Nine of 87 (10%) were members of a thyroid association.

3.2 | Thyroid hormone use in the management of hypothyroidism

The responses are summarised in Table 2. Subgroup analysis showed a significant association between the number of hypothyroid patients treated by respondents per year and the likelihood of respondents

TABLE 1 Demographic characteristics of respondents.

| | n (%) |
|---|----------|
| Gender | |
| Female | 53 (61%) |
| Male | 34 (39%) |
| Age | |
| ≤40 years old | 28 (32%) |
| 41–50 years old | 28 (32%) |
| 51–60 years old | 20 (23%) |
| 61–70 years old | 7 (8%) |
| >70 years old | 4 (5%) |
| Years in practice | |
| 0–10 years | 19 (22%) |
| 11–20 years | 27 (31%) |
| 21–30 years | 26 (30%) |
| 31–40 years | 10 (11%) |
| >40 years | 5 (6%) |
| Specialty | |
| Endocrinology | 65 (75%) |
| Paediatric endocrinology | 3 (3%) |
| Dual trained endocrinology and other specialty | 17 (20%) |
| Internal medicine | 2 (2%) |
| Membership^a | |
| Endocrine Society of Australia | 86 (99%) |
| American Thyroid Association (ATA) | 6 (7%) |
| Asian and Oceania Thyroid Association (AOTA) | 5 (6%) |
| European Thyroid Association (ETA) | 1 (1%) |
| Place of practice^a | |
| Private practice | 49 (56%) |
| Regional Hospital | 12 (14%) |
| University hospital/teaching hospital | 64 (74%) |
| Frequency of management of patients with thyroid disease | |
| Rarely | 1 (1%) |
| Weekly | 40 (46%) |
| Daily | 46 (53%) |
| Frequency of management of patients with hypothyroidism | |
| Rarely | 1 (1%) |
| 10–50 patients per year | 28 (32%) |
| 51–100 patients per year | 27 (31%) |
| >100 patients per year | 31 (36%) |

^aLegend: respondents were able to select more than one option therefore sum of percentages exceeds 100%.

TABLE 2 Management of patients with hypothyroidism.

| | |
|--|-----------|
| Which thyroid hormones available for substitution therapy should be the first choice for the treatment of hypothyroid patients? | |
| LT4 | 82 (100%) |
| LT3 (alone or in combination with LT4) | 0 (0%) |
| Desiccated thyroid | 0 (0%) |
| Which of the following drugs are you prescribing in clinical practice? | |
| LT3 (alone or in combination with LT4) | 36 (44%) |
| Desiccated thyroid | 8 (10%) |
| How much control do you have over the formulation of LT4 dispensed for your patients? | |
| Most of my patients are dispensed the type of LT4 that I recommend | 37 (45%) |
| For most of my patients I have no control over the type of LT4 that they are dispensed | 31 (38%) |
| The type of dispensed LT4 is mostly chosen by general practitioners | 14 (17%) |
| Which would you prescribe for a patient established on LT4 who has unexplained poor biochemical control of hypothyroidism? | |
| I expect no major changes with different formulations | 45 (55%) |
| Tablets from another manufacturer | 26 (32%) |
| LT3 + LT4 combination | 10 (12%) |
| LT3 monotherapy | 1 (1%) |
| Desiccated thyroid | 0 (0%) |
| Which would you prescribe for a patient established on LT4 who has good biochemical control of hypothyroidism but continues to have symptoms? | |
| I expect no major changes with different formulations | 42 (51%) |
| LT4 from another manufacturer | 4 (5%) |
| LT3 + LT4 combination | 30 (37%) |
| Increase LT4 dose | 6 (7%) |
| LT3 monotherapy | 0 (0%) |
| Desiccated thyroid | 0 (0%) |
| When would you recheck TSH after commencement of LT4 therapy? | |
| 4–6 weeks | 61 (74%) |
| 8 weeks | 21 (26%) |
| In case of a switch to a different formulation or change from one manufacturer of LT4 to another, when do you recommend that serum TSH should be rechecked? | |
| 4–6 weeks | 47 (57%) |
| 8 weeks | 26 (32%) |
| No need to recheck TSH | 8 (10%) |
| Clinical evaluation only | 1 (1%) |

(Continues)

When do you think dietary supplements (such as selenium or iodine) in addition to thyroid hormone replacement in hypothyroidism may be used?

| | |
|--|----------|
| At the patient's request or as complementary treatment | 34 (41%) |
| Co-existing autoimmune thyroiditis | 15 (18%) |
| Subclinical hypothyroidism | 3 (4%) |
| Should never be used | 30 (37%) |

Abbreviations: LT4, levothyroxine; LT3, liothyronine; TSH, thyroid stimulating hormone.

prescribing LT3/LT3 + LT4 combination therapy ($p = .007$) (Figure 1) as well as their management of hypothyroid patients with good biochemical control on LT4 therapy with ongoing symptoms ($p = .04$). Most respondents who treat 10–50 patients with hypothyroidism per year did not expect any changes with different formulations (16/27; 59%) whereas those who treat more than 100 hypothyroid patients per year were more likely to prescribe LT3 + LT4 combination therapy (15/28; 54%) in this group. Respondents who reported being members of at least one thyroid association were more likely to prescribe DTE (3/9; 33%) compared to those who were not (5/73; 7%, $p = .039$). There was also a significant association between age group and management of patients with hypothyroidism on LT4 who had unexplained poor biochemical control ($p = .02$). Respondents who were younger than 40 years old were more likely to try LT4 from a different manufacturer (13/28; 46%), whereas most over 40 years old did not expect major changes with different formulations (32/54; 59%).

3.3 | Use of combination LT3 and LT4

Next, respondents were asked to choose in which of the following situations they would consider the use of LT3 + LT4 combination therapy. Forty (49%) would consider prescribing in patients with normal TSH who have ongoing symptoms of hypothyroidism, 19/82 (23%) would consider for a short period in patients recovering from protracted hypothyroidism, and only 4/82 (5%) would consider in patients with normal TSH who complain of unexplained weight gain. Twenty-four (29%) answered that due to low quality evidence, combined therapy should never be used. Subgroup analysis showed a significant association between the number of hypothyroid patients treated per year by the respondent and response to this question ($p = .04$). Those who saw 10–50 hypothyroid patients per year were more likely never to use combination therapy due to low quality evidence (13/27; 48%), whereas respondents who saw greater than 100 hypothyroid patients per year were most likely to consider use of LT3 + LT4 combination therapy for patients with ongoing symptoms despite normal TSH (17/28; 61%). There was no significant difference in use of combination LT3 + LT4 between respondents according to place of practice.

3.4 | Persistent symptoms

Most respondents reported that fewer than 10% of patients with hypothyroidism in their practice have ongoing symptoms despite normal TSH and 49% reported that this trend has not changed in the last 5 years (Table 3). Subgroup analysis showed an association between the number of hypothyroid patients treated per year by the respondent and the percentage of hypothyroid patients with ongoing symptoms seen in their practice ($p = .002$) as well as the reported trend ($p = .01$). Respondents who saw more hypothyroid patients per year were more likely to report seeing a higher percentage of such patients and an increase in such cases over the past 5 years than those who saw less.

The opinions of respondents regarding possible factors that explain persistent symptoms of hypothyroidism despite normal TSH in patients treated with LT4 are presented in Figure 2 and Table 4. There were no significant differences in responses between respondents who prescribe LT3 (alone or in combination) and those who do not in their opinion of causes of persistent symptoms of hypothyroidism despite normal TSH.

3.5 | Use of thyroid hormone in biochemically euthyroid patients

Respondents were asked about indications for prescribing thyroid hormone in biochemically euthyroid patients and 44/80 (55%) replied that there is never an indication to prescribe thyroid hormone in this group. Female infertility with high levels of thyroid antibodies was the most common reason respondents would consider prescribing thyroid hormone in euthyroid patients (31/80; 39%), which was more common in those who work in private practice (23/47; 49% vs. 8/33; 24%, $p = .046$). The use of thyroid hormone in biochemically euthyroid patients with simple goitre growing over time (9/80; 11%), depression resistant to antidepressant medications (4/80; 5%), severe hypercholesterolaemia as a complementary therapy (3/80; 4%) and unexplained fatigue (2/80; 3%) was less common. None would consider thyroid hormone in obesity resistant to lifestyle interventions.

3.6 | Use of thyroid hormone in pregnancy

In women without a history of hypothyroidism and an uncomplicated obstetric history, 66/78 (85%) respondents would recommend LT4 in patients with TSH above the trimester specific reference range and positive thyroid antibodies and 33/78 (42%) would recommend LT4 in those with TSH above the trimester specific reference range with negative thyroid antibodies. LT4 would be recommended by 57/78 (73%) of respondents for those with TSH ≥ 4.0 mU/L and negative thyroid antibodies and by 43/78 (55%) for those with TSH ≥ 2.5 mU/L and positive thyroid antibodies. Eight respondents would prescribe LT4 for a low fT4 with a normal TSH.

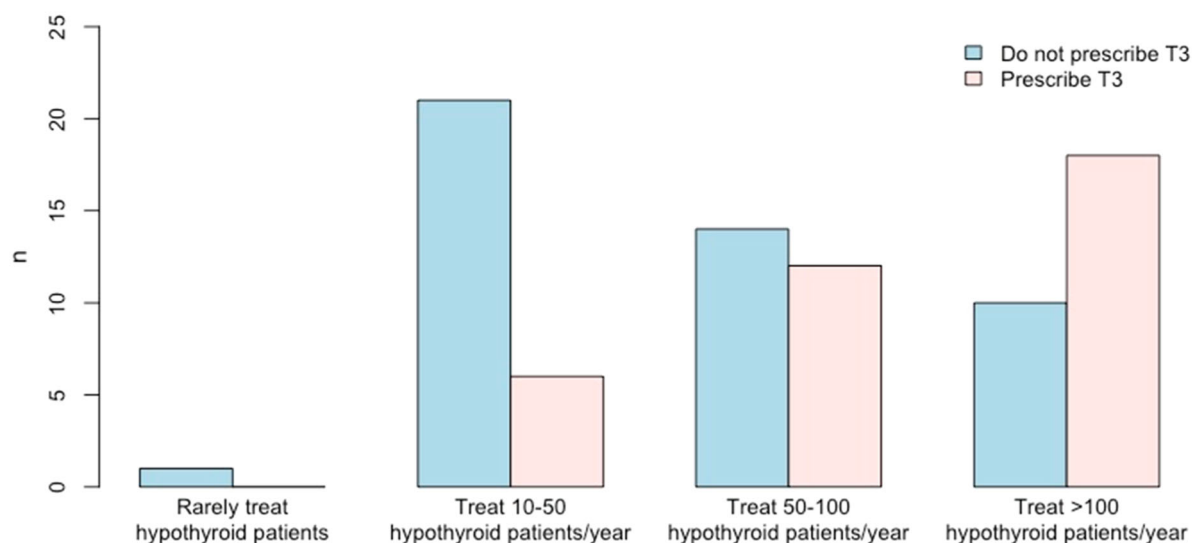


FIGURE 1 Respondents' response as to whether they prescribe LT3 or LT3 + LT4 combination therapy according to the number of patients with hypothyroidism treated per year. [Color figure can be viewed at wileyonlinelibrary.com]

TABLE 3 Reported perception of patients in the respondents' practice.

| Proportion of patients with persistent symptoms despite normal serum TSH | n (%) |
|---|----------|
| ≤5% | 30 (37%) |
| 6–10% | 31 (38%) |
| 11–30% | 13 (16%) |
| >30% | 3 (4%) |
| Not sure | 5 (6%) |
| <i>Trend of proportion of patients with persistent symptoms over the past 5 years</i> | |
| Increase | 29 (35%) |
| No change | 40 (49%) |
| Decrease | 0 |
| Unsure | 13 (16%) |

3.7 | Endocrinologists with hypothyroidism

Four respondents had a diagnosis of hypothyroidism and only one experienced excessive fatigue and had tried LT3 + LT4 combination therapy, which they reported resolved their fatigue and brain fog. None had tried DTE. Of the respondents who did not have hypothyroidism, 23/72 (32%) would consider LT3 + LT4 combination treatment or DTE if they were diagnosed with hypothyroidism. Those who would consider LT3 + LT4 combination therapy for patients with normal TSH with ongoing symptoms of hypothyroidism were more likely to consider combination treatment or DTE if they had hypothyroidism themselves compared to those who would not (19/34; 56% and 4/38; 11% respectively, $p < .001$) as were respondents who prescribe LT3

(alone or in combination) compared to those who do not (16/33; 48% and 7/39; 18%, respectively, $p = .01$).

4 | DISCUSSION

This survey shows that ESA members prescribe LT4 as first line therapy for the management of hypothyroidism and monitor thyroid function after commencement of LT4 or after a change in dose or formulation according to international guidelines.^{2,11} LT4 therapy is effective for most patients and is safe however some patients remain dissatisfied with treatment.^{7,8} Like in other countries surveyed, most respondents reported seeing in their practice less than 10% of LT4 treated hypothyroid patients with ongoing symptoms despite a normal TSH, with a higher percentage of such patients in our study seen by those who saw more hypothyroid patients per year.^{10,12–22} Respondents perceived the percentage to be similar or increased compared to 5 years prior, again like other surveyed countries.^{10,12–17} This contrasted with most respondents from surveyed countries with high gross national income per capita including Denmark, Ireland and Sweden, that reported seeing more such cases over the past 5 years.^{18–20}

4.1 | Use of combination LT3/LT4 therapy

The use of LT3 + LT4 combination therapy remains controversial. There are several reasons which suggest that LT4 monotherapy may not constitute optimal physiological thyroid hormone replacement however most clinical trials have shown no convincing symptomatic benefit of LT3 + LT4 combination therapy over LT4 monotherapy and meta-analyses have found no symptomatic benefit.⁷ In 2011, the ESA published a statement which recommended against the use of LT3 in

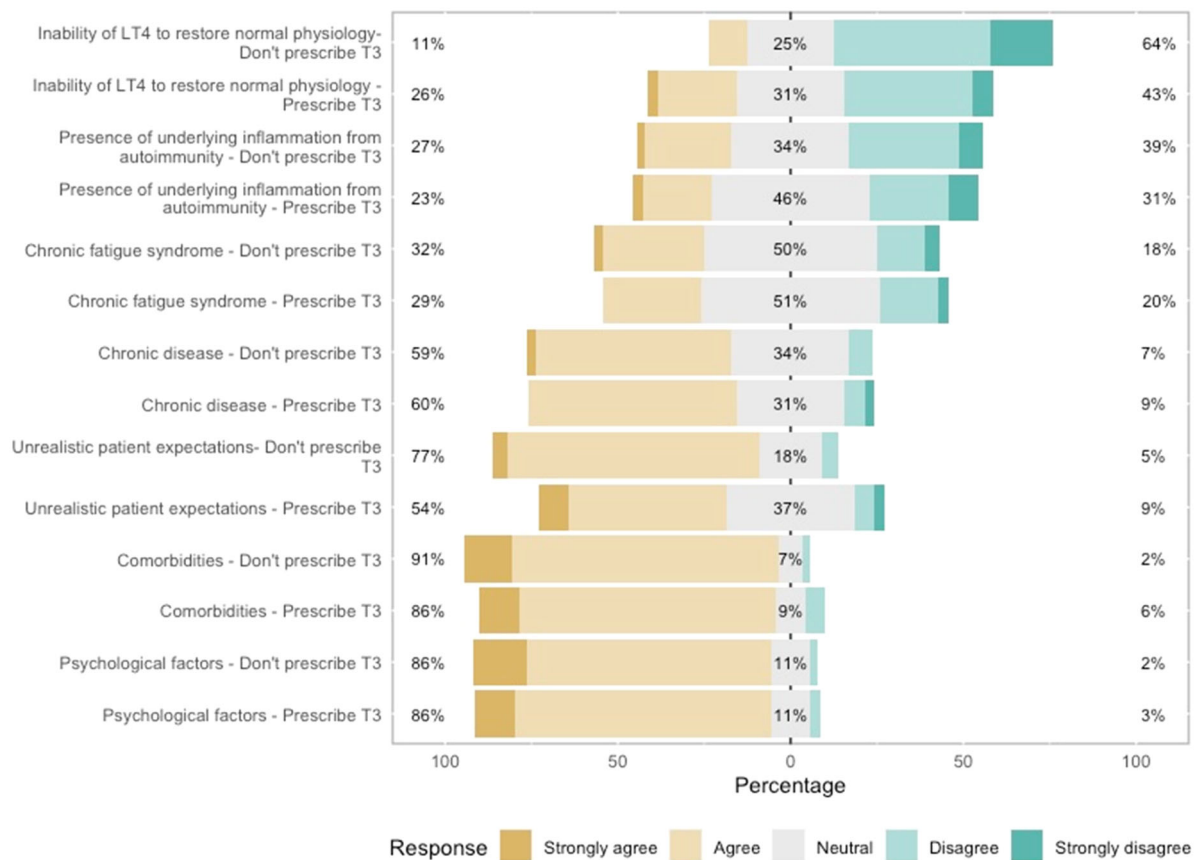


FIGURE 2 Opinion of respondents regarding causes of persistent symptoms in patients with hypothyroidism with a normal serum TSH stratified by T3/T3 + T4 combination prescribing practices. [Color figure can be viewed at wileyonlinelibrary.com]

the management of hypothyroidism.²³ Due to limitations of the clinical trials performed to date, in recent years international societies have included in their guidelines that LT3 + LT4 combination therapy can be considered in patients with normal TSH on LT4 who remain symptomatic without other cause identified for their symptoms, in discussion with the patient.^{2,8,24}

In our study, 44% of surveyed members of the ESA report prescribing LT3 containing medication (alone or in combination) in their clinical practice, with respondents treating more patients with hypothyroidism per year more likely to prescribe LT3. Although 44% of survey respondents are prescribing LT3 (alone or in combination), only 48% of those who are prescribing LT3 would consider it for themselves if they developed hypothyroidism and 44% of respondents who would not consider it for themselves would consider prescribing it to patients with normal TSH and ongoing symptoms of hypothyroidism, which is similar to the findings in Serbia.²¹

While 49% of respondents would consider prescribing LT3 in patients with ongoing symptoms of hypothyroidism with normal TSH on LT4, most respondents believe ongoing symptoms despite adequate biochemistry are due to psychosocial factors, comorbidities, patients' unrealistic expectations, and burden of chronic disease, rather than the inability of LT4 to restore normal physiology. These beliefs appear to be consistent with surveys of endocrinologists in

other countries across the world suggesting that many endocrinologists do not believe that different preparations are likely to benefit symptomatic patients.^{12,13,15,16,18,22,25} A recent international patient questionnaire has highlighted the discord between the views of patients and physicians regarding reasons for dissatisfaction with treatment,²⁶ but also that dissatisfaction is significantly associated with patients' personality traits.²⁷ However, many continue to prescribe LT3 + LT4 combination therapy for this group. It is likely that this group represents a heterogeneous group of patients and many of the reasons listed above may apply to different subgroup of patients and treatment of the appropriate cause is critical.⁶ A joint consensus document has recently been published by members of the ATA, BTA and ETA to help guide development of trials to clarify the role of LT3 + LT4 therapy in the management of hypothyroidism, which may guide practitioners in the future regarding appropriate patient selection and dosing.²⁸

4.2 | Control over thyroxine brand

Of note, 38% of respondents reported not having control over the brand of LT4 dispensed to their patients which is much lower than other surveyed countries but similar to the United Kingdom and

TABLE 4 Mean ranked perceptions of respondents regarding possible explanations.

| Using your experience with patients treated with LT4 who achieved normal serum TSH but continue to experience symptoms like fatigue, please rank 1–8 (1 is most likely and 8 least likely explanation) in your opinion | |
|--|-----------------|
| Reason | Mean score ± SD |
| Psychosocial factors | 2.1 ± 1.5 |
| Comorbidities | 2.9 ± 1.7 |
| Patient unrealistic expectations | 3.3 ± 1.9 |
| Burden of chronic disease | 4.9 ± 1.8 |
| Presence of underlying inflammation due to autoimmunity | 5.3 ± 1.6 |
| Burden of having to take medication | 5.8 ± 1.6 |
| Chronic fatigue syndrome | 5.8 ± 1.9 |
| Inability of LT4 to restore normal physiology | 5.8 ± 2.3 |
| Some patients treated with supraphysiological doses of thyroid hormone (leading to suppressed serum TSH and elevated serum T4) report significant improvement in symptoms such as fatigue. What is the most likely explanation (rate from 1 (most likely) to 7 (least likely)) | |
| Reason | Mean score ± SD |
| Placebo effect | 3.0 ± 1.6 |
| Patients feel better because physicians that prescribe such medications also spend a lot of time listening to their complaints and take them seriously | 3.4 ± 1.3 |
| High doses are euphoric for some patients | 3.5 ± 1.9 |
| Such patients have low tissue T3 despite normal serum TSH and require high doses of thyroid hormone to restore normal health | 3.9 ± 2.0 |
| Improvement in symptoms is usually because high doses of thyroid hormones help patients lose weight | 4.6 ± 1.5 |
| I don't know | 4.8 ± 2.4 |
| I have never witnessed a significant improvement in symptoms in relation to over-treatment with thyroid hormones | 4.8 ± 2.2 |

Ireland.^{10,12–22} EltroxinTM is not considered bioequivalent and therefore is not interchangeable by pharmacists. However, LevoxineTM is bioequivalent and therefore interchangeable with EutroxigTM and OroxineTM. To demonstrate bioequivalence, a single large dose of LT4 is administered to healthy euthyroid subjects and T4 pharmacokinetic parameters are used to establish bioequivalence. This has been criticised by many endocrine and thyroid societies as it fails to take into account the initial T4 concentration, the effect at steady state and the effect on TSH, which is the measure used in clinical practice.^{23,29,30} Guidelines suggest rechecking after change in preparation and most respondents would do so, however given

pharmacists are able to change preparations without consultation with doctors and many endocrinologists feel that they do not have control over formulation dispensed, patient education is important as it may lead to suboptimal LT4 dosing.² Since the survey was conducted, a further 5 brands of LT4 have been approved in Australia, with the potential to cause further concerns on the part of patients and clinicians regarding consistency of treatment.

4.3 | Use of dietary supplements in hypothyroidism

The majority of endocrinologists in this study would never consider dietary supplements but 41% would consider them at patients' request and 18% would use it in the setting of coexisting autoimmune thyroiditis. This is despite Australia being an iodine sufficient country and, although there is evidence of a reduction in thyroid antibody levels with selenium, studies have not demonstrated clinical benefit in Hashimoto's disease with selenium use.^{31,32}

4.4 | Use of thyroid hormone in euthyroid individuals

Most endocrinologist in this study would not prescribe thyroid hormones in euthyroid individuals for any reason. Nevertheless, 39% would consider it for women with infertility with high levels of thyroid antibodies despite a recent randomised clinical trial demonstrating no benefit.³³ This is similar to results from other countries, such as Ireland, Denmark, Belgium, Greece and France, while some countries had much higher proportions, including Poland and Czech Republic.^{13–19}

Only eleven percent of respondents considered prescribing thyroid hormones for a simple goitre growing over time, which is consistent with clinically insignificant benefit and the risks associated with lowering TSH.³⁴ This number was lower than most surveyed European countries and similar to Latin America, Denmark and the United Kingdom.^{10,12–22} Reassuringly, use of thyroid hormone for euthyroid patients with depression, severe hypercholesterolaemia and unexplained fatigue were not considered by most respondents.

4.5 | In pregnancy

There appears to be a lack of consensus in the use of LT4 in pregnant women without known hypothyroidism. The latest ATA guideline published in 2017 provides several options on TSH cut offs for clinicians to consider starting LT4.³⁵ This leads to differing practices among endocrinologists, as seen in our study. Since the publication of these guidelines, further studies have not identified benefit of LT4 therapy in pregnant patients with TSH below 4.0 mU/L.³⁶ Because of this evidence and to standardise practice, a Melbourne public hospital consensus was published in 2019 which recommends LT4 therapy in

pregnant women with TSH above the trimester specific range, or TSH greater than 4.0 mIU/L if not available, irrespective of antibody status.³⁷ Similar recommendations have recently been published by the Korean Thyroid Association.³⁶ Given the large differences in prescribing practices by Australian endocrinologists, it may be helpful to have updated local or international guidelines in line with current evidence to standardise treatment and advice.

4.6 | Strengths and limitations

This study provides insight into current clinical practice of endocrinologists managing hypothyroidism in Australia. A strength of the study is the use of a questionnaire which has now been utilised in multiple countries and allows comparison with practice elsewhere.

A limitation is that we could not accurately calculate the response rate from clinical endocrinologists. The invitation to participate was sent to the entire ESA membership, which includes non-clinicians (laboratory scientists), clinicians in fields other than endocrinology (chemical pathology, gynaecology, endocrine surgery) and endocrinologists who are no longer in clinical practice. Members are not required to provide this information for the membership database. For the purposes of this study, and after discussion with the ESA, we estimated that ~80% of financial ESA members are clinicians, but this may be an over-estimate; the calculated 13% response rate is conservative but does appear lower than in several previous surveys.⁹ That said, previous surveys differed in the methods used to identify and contact potential participants, as well as in the calculation of response rates; in one study, the denominator for the response rate was not the number of invitations initially e-mailed out, but rather the number of members who initially agreed to participate in response to that invitation.¹⁸ This makes comparisons of response rates difficult. Nevertheless, the demographic data from the respondents of our study is similar to other studies, with a wide range of years in practice, places of practice and number of patients with hypothyroidism managed.^{9,12,19} This suggests that the responses from our study are from a diverse group of practitioners and reflects a broad spectrum of clinical practice.

5 | CONCLUSION

Prescribing practices by Australian endocrinologists who are members of the Endocrine Society of Australia (ESA) largely follow international guidelines and are similar to other countries. Thyroid hormone continues to be used in euthyroid females with positive thyroid antibodies and infertility despite lack of evidence, but most would not prescribe them for other indications in euthyroid individuals. More up to date guidelines for the management of hypothyroidism in pregnancy based on recent data may help standardise prescribing practices for pregnant women with maternal hypothyroidism.

Many prescribe LT3+LT4 combination therapy in their clinical practice and would consider prescribing for patients on LT4 with ongoing symptoms, despite many not considering it for themselves if they were to

develop hypothyroidism. There seems to be a discordance between endocrinologists' beliefs around causes of persistent symptoms in this subpopulation and prescribing practices, highlighting the importance of improving our understanding of the causes of ongoing symptoms in these patients. Many questions regarding the treatment of patients with hypothyroidism with adequate biochemical control but ongoing symptoms remain including the benefits and risks of LT3+LT4 combination therapy. Further research in this area, including that of nonmedication related factors,²⁷ will help guide management of a very common condition and allow us to avoid low value treatments.

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CONFLICT OF INTEREST STATEMENT

P. P., E. P., E. V. N. and L. H. are members of the scientific board for, and have received consultancy fees from IBSA, Institute Biochimique S. A. and L. H. has received consultancy fees from Merck, Berlin-Chemie, Horizon Therapeutics and Bracco Imaging. The remaining authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data sets generated and analysed during this study are not publicly available but may be accessed through the corresponding author on reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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