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HYPOTHYROIDISM AND SOMATIZATION: RESULTS FROM E-MODE PATIENT SELF-ASSESSMENT OF THYROID THERAPY (E-MPATHY), A CROSS-SECTIONAL, INTERNATIONAL ONLINE PATIENT SURVEY

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Abstract:	Background Between 10-15% of hypothyroid patients experience persistent symptoms despite achieving biochemical euthyroidism. Unexplained persistent symptoms can be a sign of somatization. This is associated with distress and high healthcare resource use and can be classified as Somatic Symptom Disorder (SSD). Prevalence rates for SSD differ depending on classification criteria and how they are ascertained, varying between 4-25%. As this has not been studied in hypothyroid patients before, the aim of this study was to document somatization in people with hypothyroidism and explore associations with other patient characteristics and outcomes. Methods Online, multi-national, cross-sectional survey of individuals with self-reported, treated hypothyroidism, that included the validated patient health questionnaire-15 (PHQ-15) for assessment of somatization. Chi-

	squared tests with Bonferroni correction were used to explore outcomes for respondents with a PHQ-15 score >10 (probable somatic symptom disorder (pSSD)) versus <10 (absence of SSD). Results A total of 3915 responses were received, 3516 of which contained valid PHQ-15 data (89.8%). The median score was 11.3 (range 0-30, 95% CI 10.9-11.3). The prevalence of pSSD was 58.6%. Associations were found between pSSD and young age ($p<0.001$), women ($p<0.001$), not working ($p<0.001$), having below average household income ($p<0.001$), being treated with levothyroxine (rather than combination of levothyroxine and liothyronine, liothyronine alone, or desiccated thyroid extract) ($p<0.001$), expression of the view that the thyroid medication taken did not control the symptoms of hypothyroidism well ($p<0.001$), and with number of comorbidities ($p<0.001$). pSSD was associated with respondent attribution of most PHQ-15 symptoms to the hypothyroidism or its treatment ($p<0.001$), dissatisfaction with care and treatment of hypothyroidism ($p<0.001$), a negative impact of hypothyroidism on daily living ($p<0.001$) and with anxiety and low mood / depression ($p<0.001$). Conclusions This study demonstrates a high prevalence of pSSD among people with hypothyroidism and associations between pSSD and negative patient outcomes, including a tendency to attribute persistent symptoms to hypothyroidism or its treatment. SSD may be an important determinant of dissatisfaction with treatment and care among some hypothyroid patients.

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ABSTRACT

Background

Between 10-15% of hypothyroid patients experience persistent symptoms despite achieving biochemical euthyroidism. ~~Unexplained persistent symptoms are associated with distress and high healthcare resource use and may be due to somatization or Somatic Symptom Disorder (SSD), a diagnosis that affects 4-7% of the world population.~~ Unexplained persistent symptoms can be a sign of somatization. This is associated with distress and high healthcare resource use and can be classified as Somatic Symptom Disorder (SSD). Prevalence rates for SSD differ depending on classification criteria and how they are ascertained, varying between 4-25%. As this has not been studied in hypothyroid patients before, the aim of this study was to document somatization in people with hypothyroidism and explore associations ~~between SSD and~~ with other patient characteristics and outcomes.

Methods

Online, multi-national, cross-sectional survey of individuals with self-reported, treated hypothyroidism, that included the validated patient health questionnaire-15 (PHQ-15) for assessment of somatization. Chi-squared tests with Bonferroni correction were used to explore outcomes for respondents with a PHQ-15 score ≥10 (probable somatic symptom disorder (pSSD)) versus <10 (absence of SSD).

Results

A total of 3915 responses were received, 3516 of which contained valid PHQ-15 data (89.8%). The median score was 11.3 (range 0-30, 95% CI 10.9-11.3). The prevalence of pSSD was 58.6%. Associations were found between pSSD and young age (p<0.001), women (p<0.001), not working (p<0.001), having below average household income (p<0.001), being treated with levothyroxine (rather than combination of levothyroxine and liothyronine, liothyronine alone, or desiccated thyroid extract) (p<0.001), expression of the view that the thyroid medication taken did not control the symptoms of hypothyroidism well (p<0.001), and with number of comorbidities (p<0.001). pSSD was associated with respondent attribution of most PHQ-15 symptoms to the hypothyroidism or its treatment (p<0.001), dissatisfaction with care and treatment of hypothyroidism (p<0.001), a negative impact of hypothyroidism on daily living (p<0.001) and with anxiety and low mood / depression (p<0.001).

Conclusions

This study demonstrates a high prevalence of pSSD among people with hypothyroidism and associations between pSSD and negative patient outcomes, including a tendency to attribute persistent symptoms to hypothyroidism or its treatment. SSD may be an important determinant of dissatisfaction with treatment and care among some hypothyroid patients.

INTRODUCTION

Hypothyroidism is a common disorder affecting 1-7% of the population.[1-3] Over the past 20 years Persistent symptoms occur in have been reported among 10-15% of hypothyroid patients compared to controls people without hypothyroidism.[4-6] There are several Hypotheses for the cause of these symptoms include: (a) inability of L-T4 to emulate normal physiology and restore liothyronine (L-T3) at tissue level ("low tissue T3 hypothesis"); (b) confounding effects of comorbidities; (c) autoimmune inflammation; (d) L-T4 prescribed or taken by patients sub-optimally; (e) people with unexplained symptoms being more likely to be investigated and diagnosed with minor and incidental perturbations of thyroid dysfunction; (f) the impact of the diagnostic label of chronic disease; and (g) somatic symptom disorder (SSD).[7-9] Direct evidence to support the above propositions is unavailable, though it is likely that all these factors are contributary.

In the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-V), somatic symptom disorder (SSD) refers to persistent bodily symptoms associated with significant functional impairment, psychological distress, and high healthcare resource use.[10] SSD is thought to result from an exaggerated awareness of a variety of bodily sensations, interpreted as being indicative of underlying disease.[11, 12] The etiology of SSD is unclear, although associations with past traumatic experiences, personality traits, and psychosocial stresses have been described.[13, 14] Genetic factors predisposing to bodily distress, and to chronic pain may contribute to susceptibility.[15, 16] SSD occurs in about 4-7% of the world population, and is ten times more prevalent in women than men.[14,17] SSD is a diagnosis in up to 17% of patients presenting to primary care in developed countries[18] and often occurs in patients with fibromyalgia, irritable bowel syndrome and myalgic encephalomyelitis / chronic fatigue syndrome.[19] The patient health questionnaire-15 (PHQ-15) can be used to assess subjects for SSD. PHQ-15 was initially developed and validated in primary care and general hospital settings,[20] has a sensitivity of 78-83% and specificity of 42-71% for somatization[21,22] and is well suited for use in large-scale studies internationally.[23]

SSD is a relatively recent classification, introduced in 2013 in DSM-V.[10] Reviews describing prevalence rates of earlier classifications related to somatization (such as somatization disorder analysing 32 studies from 24 countries), reported a pooled

estimate of the point prevalence of 16.5%.[17] However, somatization disorder is a severe form of SSD, and is limited to distress related to medically unexplained symptoms. In contrast, SSD relates to distress associated with physical symptoms in known medical conditions and medically unexplained symptoms, and thus prone to have been underestimated. A systematic review reported prevalence rates for somatoform disorders in the general population to range from 11-21% in younger, 10-20% in the middle-aged, and 1.5-13% in older age groups.[18] A 2022 review of 59 studies found a mean prevalence of SSD of 12.9 % based on self-report.[19] A population-based study in over 3000 people in Taiwan reported a prevalence of SSD of 5%,[20] and a German study of 1780 general practitioners reported a prevalence of SSD among their patients of 7.7%.[21] Based on the above findings, we can surmise that the prevalence of SSD in the general population is between 5-25%.

Studying SSD in hypothyroidism may help to understand the nature of persistent symptoms. Furthermore, identifying SSD may avoid unnecessary and expensive investigations, reduce the risk of inappropriate and harmful therapies, [22-28] and direct patients and physicians to interventions shown to be helpful in SSD.[29] ~~The~~

In this study probable SSD (pSSD, defined as a score ≥10 using the PHQ-15 questionnaire) in patients with hypothyroidism was explored. The research questions were: what is the prevalence of pSSD among patients with hypothyroidism, and what is the relationship between (a) pSSD and respondent characteristics, and (b) pSSD and patient-reported outcomes?

METHODS

Study design

Multi-national, large-scale, cross-sectional, online questionnaire survey of people with a diagnosis of hypothyroidism. Some of the findings have been published.[30]

PHQ-15

PHQ-15 is a ~~brief short self-administered~~ questionnaire that is self-administered. It has been used in research and clinically as a screening test for somatization~~used for screening for somatization and monitoring somatic symptom severity in clinical practice and research~~.[31] It includes 15 symptoms, which comprise the most frequent

somatic complaints encountered in primary care. ~~It screens for 15 somatic symptoms that account for more than 90% of the somatic symptoms reported in the primary care setting.~~ High scores correlate closely with somatoform disorder, disability, functional impairment and use of healthcare resources. ~~High scores on the PHQ-15 are strongly associated with functional impairment, disability, healthcare use and with somatoform disorder.~~[31] This instrument has been validated and used extensively, ~~The PHQ-15 is a valid measure, which has been used in 40 studies so far in different health care settings.~~[32] is equivalent or better in performance to other tools and is ~~The PHQ-15 is equal or superior to other brief measures for assessing somatic symptoms and screening for somatoform disorders.~~[33] ~~It has been~~ recommended by the American Psychiatric Association.[10] ~~as an emerging measure of somatic symptoms in the general population~~ PHQ-15[20] has a sensitivity of 78-83% and specificity of 42-71% for somatization[21,22] and is well suited for use in large-scale studies internationally.[23] PHQ-15 lists 15 somatic symptoms, 13 of which are related to physical symptoms, while two (feeling tired or having little energy, and trouble sleeping) are associated with depression.[31, 34] Each symptom is scored as 0, 1 or 2 ("not bothered at all", "bothered a little", "bothered a lot", respectively). The sum score is used as a measure for symptom load. A score of ≥10 ~~or more~~ is associated with somatization equivalent to clinical disorder ~~level and can be regarded as indicative of SSD~~.[31] In this study, values of PHQ-15 were considered valid when the provided answers were undoubtedly ~~above or below~~ ≥10 or <10. Therefore, respondents with a PHQ-15 score of ≥10 were included even if they did not respond to all questions of PHQ-15 and categorized as having probable SSD (pSSD). Respondents whose scores could not exceed 9 even if the missing data scored maximally, were included and categorized as not having SSD. Respondents who had left out parts of PHQ-15 and could have attained a score indicating SSD were excluded as we could not undoubtedly attribute their responses. pSSD (score ≥10) was used as a research classification rather than a medical diagnosis of SSD.

~~E-MPATHY~~ Questionnaire~~, cognitive testing, questionnaire translations and pilot~~

The questionnaire was cognitively tested in 30 English-speaking patients with hypothyroidism across five rounds in accordance with published methodology.[35] Minor changes were made ~~to question wording and answer options~~ to establish consistent comprehension. Translations of the English version of the questionnaire

were made into French, German, Italian, and Spanish. Each translation was performed by two certified native translators. Idioms were replaced with appropriate alternatives. ~~The online survey platform (Qualtrics, https://www.qualtrics.com) was used to host the questionnaireEnglish version and translations.~~ A pilot was conducted in English with 387 respondents (344 completed and 43 partially completed) for data validation, which demonstrated good face validity and response. The final version took 30-45 minutes to complete and was hosted online in Qualtrics (https://www.qualtrics.com) between 11/4/20-3/1/21. ~~4th November 2020 and 1st March 2021.~~

Dissemination ~~of survey~~

Advertisements and information sheets to explain the purpose of the survey were prepared in the aforementioned five languages and promoted through Thyroid Federation International, a global network of patient~~-oriented~~ thyroid disorder organisations, (https://thyroid-fed.org/) affiliates, and partners via social media, and web pages (Supplementary Figure 1). ~~shows the number potentially eligible individuals identified, number confirmed eligible, number included in the study, and number analyzed.~~

Inclusion criteria

Participants had to be ≥18 years and to be using medication for hypothyroidism.

Institutional Review Board waiver statement

The non-interventional nature of the survey and the fact that data were anonymized rendered the study exempt from Institutional Board approval. The study was conducted in accordance with Declaration of Helsinki as revised in 2013. All participants gave informed consent. ~~at the beginning of the survey.~~

Statistical analyses

The dataset was calculated to detect a delta 0.1 in proportions for z-tests, using GPower3.1.9 for a power of 95% and alpha set at 0.05, which calculated the number of participants to be around 1000 (1066). Chi-squared tests with Bonferroni correction were used, via Python 3.10. A binary PHQ-15 score <10 or ≥10 (corresponding to absence or presence of pSSD) was used as an independent variable and was compared against 10 dependent variables comprising demographic and other baseline characteristics (gender, age, marital status, employment, ethnicity, years in education, household income, comorbidities, cause of

hypothyroidism, treatment for hypothyroidism). In addition, the PHQ-15 binary score was compared against ~~4~~ 5 respondent outcomes :

a) **attribution of the PHQ-15 symptoms**:
for each of the symptoms ~~included~~ in PHQ-15, participants were asked whether they attributed the symptom to “the hypothyroidism or side-effects of the hypothyroidism medication”, or to “other causes”.

b) **control of symptoms of hypothyroidism by medication**:
participants were asked to respond to the statement “my hypothyroidism medication controls my symptoms well”, with the following response options: "strongly disagree", "tend to disagree", “neither agree nor disagree”, “tend to agree”, “strongly agree”, and “uncertain”.

c) **satisfaction with overall treatment and care for hypothyroidism**:
participants were asked “how satisfied are you with the overall care and treatment you have received for your hypothyroidism?”, with the following response options: “very satisfied”, “slightly satisfied”, “neither satisfied nor dissatisfied”, “slightly dissatisfied”, “very dissatisfied” and “don’t know”.

d) **impact of hypothyroidism on daily living**:
participants were asked to respond to the statement “my hypothyroidism has affected everyday activities that people my age usually do (e.g. exercise, household chores, etc.)”, with the following response options: "strongly disagree", "tend to disagree”, “neither agree nor disagree”, “tend to agree”, “strongly agree”, and “uncertain”.

e) Anxiety, low mood / depression:
participants were asked “during the past 4 weeks, how much have you been bothered by anxiety?” and “during the past 4 weeks, how much have you been bothered by low mood / depression?” with the following response options: “bothered a little or bothered a lot”, “not bothered at all”.

RESULTS

Respondent baseline characteristics

A total of 3915 responses were received, 3516 of which contained valid PHQ-15 data (89.8%) (Table 1). Women comprised 94.5% (3321/3516) of respondents. Most

respondents (87.2%; 3065/3516) were over 40 years old. Responses from the UK dominated (35.5%; 1250/3516). The majority of respondents were white (86.5%; 3040/3516), employed (71.8%; 2526/3516), had received more than 8 years of education (84.4%; 2968/3516), had comorbidities (72.8%; 2561/3516) and were being treated with L-T4 (75.8%; 2665/3516).

~~As a PHQ-15 score ≥10 has been shown to correlate closely with a clinical diagnosis of SSD,[31] pSSD is used synonymously with a PHQ-15 score ≥10.~~

Prevalence of pSSD

The median PHQ-15 score was 11.3 (range 0-30, 95% CI 10.9-11.3). Women respondents (n=3321) had higher PHQ-15 score than men (n=164) (mean 11.3, SD 5.8 vs mean 7.6, SD 5.6, respectively, p<0.001). Tiredness was the commonest symptom experienced by 90.2% (3163/3505) of respondents (Supplementary Table 1).

Associations between pSSD and demographic and other baseline characteristics

Significant associations with pSSD were found with age, gender, employment status, household income, treatment for hypothyroidism and number of comorbidities (Table 2). By binary categorization into PHQ-scores <10 and ≥10, the following groups were identified as having higher pSSD prevalence: aged 18-30, women, not working, having below average household income, being treated with L-T4 (as compared to combination of levothyroxine and liothyronine, liothyronine alone, or desiccated thyroid extract) (Table 2), and having one or more comorbidities (Figure 1). No associations were found between pSSD and marital status, years of education, cause of hypothyroidism, and ethnicity.

Associations between pSSD and respondent attributions of causes of symptoms

There was a significant association between pSSD and attribution of symptoms to the hypothyroidism or its treatment for 13 out of the 15 symptoms, the non-significant symptoms being “fainting spells”, and “pain or problems during intercourse” (Figure 2

and Table 3). Respondents with pSSD were equally likely to blame hypothyroidism or its treatment for typical hypothyroid symptoms (such as constipation, tiredness, or atypical symptoms ~~such as~~ (e.g. stomach pain, backache or dizziness.)[36, 37]

Association between pSSD and control of symptoms of hypothyroidism

pSSD was associated with the expression of the view by respondents that the thyroid medication taken did not control the symptoms of hypothyroidism well (Figure 3a and Table 2).

Association between pSSD and satisfaction with care and treatment of hypothyroidism

There was a significant association between pSSD and dissatisfaction with care and treatment of hypothyroidism (Figure 3b and Table 2).

Association between pSSD and impact of hypothyroidism on daily living

There was an association between a negative impact on daily living and pSSD (Figure 3c and Table 2).

Anxiety, low mood / depression

Both anxiety and low mood / depression were prevalent in respondents with pSSD (72.3%, 1689/2337 and 71.8%,1739/2422 respectively) and the association was statistically significant (Table 2).

DISCUSSION

SSD is common, associated with persistent symptoms, individual and societal burden, high levels of healthcare utilisation and economic cost. [38] Yet there is little information in the literature about SSD in hypothyroidism,[39, 40] while impaired quality of life and dissatisfaction with care and treatment are well documented.[41-44] We used the validated PHQ-15 questionnaire[31] to assess somatization and to test the hypothesis that SSD is a contributor to persistent symptoms and dissatisfaction. We have used pSSD as a research classification based on self-reported responses to a questionnaire, in order to gain insights on the nature of persistent symptoms in

hypothyroidism. It should be noted that this is not equivalent to a medical diagnosis of SSD (which requires individual assessment by an expert). Respondents' characteristics were similar to hypothyroid patient populations reported in the literature.[1, 2, 45-47] PHQ-15 has been used previously to screen for SSD,[31, 48, 49] study associations between somatic symptoms and demographic factors[50] and behaviors[51] and quantify somatic distress associated with specific diseases such as diabetes,[52] thus providing potentially useful insights.

The proportion of respondents with pSSD was higher (58.6%), than normative data (7.2%~~, p<0.001~~) (Supplementary Table 3) [33]. SSD is common among patients with chronic diseases,[53-55] thus it is not surprising this was also the case in hypothyroidism. The significance of this finding rests with how clinicians approach the common scenario of hypothyroid patients with persistent unexplained symptoms. Research in Europe conducted in 2019-2021[56-73 74, 75] shows that thyroid specialists usually offer pharmacological solutions to such patients in the form of combination therapy of L-T4 with L-T3, despite evidence from randomized controlled studies indicating no benefit from combination treatment compared to L-T4 alone.[9, 44] In the light of these ~~E-MPATHY~~ findings, a pharmacological approach is inappropriate for some of these patients, as their underlying psychosocial needs will not be addressed. The high prevalence of pSSD among participants demonstrated in this study does not support binary "mind" versus "body" dualism, which sometimes leads to dismissive attitudes by healthcare professionals towards patients with unexplained symptoms. On the contrary, the findings ~~of E-MPATHY~~ suggest that a biopsychosocial approach[76] to the conundrum of persistent symptoms despite euthyroid biochemistry may be appropriate. The experience of healthcare professionals who manage patients with unexplained persistent symptoms suggests that they may respond to empathetic listening, affirmation that their symptoms are real, explanations that physical and psychological symptoms are intimately integrated, avoidance of over-investigation and use of cognitive behavioral and other established psychological therapies, ideally in a multi-disciplinary setting.[77, 78]

In our study pSSD was associated with young age, women, low household income, employment status, and multiple comorbidities. Some of these variables are likely to be interdependent, however the above findings are in keeping with other studies of

SSD in general populations.[79-82] The association between pSSD and treatment with L-T4 as opposed to L-T3-containing treatments ~~is of interest. A possible explanation is~~ may indicate that hypothyroid patients treated with L-T3-containing medication become less symptomatic than those treated with L-T4, particularly if overtreated (e.g. observations of beneficial effects of high doses of L-T3 on mood in patients with resistant depression[22]). However, the association between pSSD and L-T4 treatment cannot be assumed to be causal, nor is it possible to infer from this data that L-T3-containing treatments should be used to provide relief from the symptoms of SSD.

pSSD was associated with ~~a tendency to attribute~~ attribution of persistent symptoms to hypothyroidism or its treatment, including symptoms not recognized to be associated with hypothyroidism or thyroid hormone replacement. ~~(e.g. stomach pain, backache or dizziness).~~ Among the symptoms included in PHQ-15, tiredness and pain were the most frequently reported. This aligns with findings that somatization symptoms tend to cluster into four groups: fatigue, pain, cardiorespiratory and bowel symptoms [83]. The high prevalence of pain symptoms, especially back pain and headaches in this sample is consistent with the Global Burden of Disease study.[84] Patients with SSD who experience back pain and headaches that cluster with fatigue may attribute symptoms that occur frequently in the general population to ~~their thyroid condition~~ hypothyroidism. The above findings ~~of E-MPATHY~~ are consistent with insights from other studies relating to the symptomatology of hypothyroidism and how symptoms may be perceived by patients, particularly in view of the fact that most of the symptoms of hypothyroidism are non-specific and often experienced by the euthyroid population.[36] A study of patients with subclinical hypothyroidism who were not aware of their serum TSH levels, showed no difference in symptoms compared to euthyroid controls.[85] In another study, patient awareness that they had a thyroid diagnosis was associated with an increased prevalence of symptoms, and conversely, in patients ~~who were~~ not aware that they had a thyroid diagnosis a higher serum TSH was associated with fewer symptoms.[6] Self-knowledge of a diagnosis of hypothyroidism therefore seems to be an important factor in how symptoms are perceived and experienced ~~by patients~~. Another important factor is that recent studies indicate that the majority of patients diagnosed and started on thyroid hormone replacement have mild or subclinical hypothyroidism,[86, 87] or even transient elevation in serum TSH.[88] Furthermore, several studies and meta-analyses

show similar rates of symptoms in subclinical hypothyroid patients as in euthyroid controls.[44, 89]

An association was found between pSSD and respondent opinion that the thyroid medication taken did not control their symptoms of hypothyroidism well, which could be indicative of a patient belief that all or most persistent symptoms experienced are due to hypothyroidism. This is likely to be false given that persistent symptoms such as those included in the PHQ-15 questionnaire occur in the background general population and particularly in patients with comorbidities other than hypothyroidism. In this respect it is of interest that evidence from another survey of hypothyroid women indicates that patient beliefs about the nature of their illness may play a role in the development of symptoms such as depression, anxiety, and anger.[90]

The association between dissatisfaction with care and treatment of hypothyroidism and pSSD parallels those described for medically unexplained symptoms in general[91] and may reflect the frustrating nature of persistent symptoms and inadequacy of available services. Similarly, the association between pSSD and a negative impact of hypothyroidism on daily living ~~in E-MPATHY~~ was significant and may be subject to patients' attributions of symptoms to hypothyroidism. As SSD is usually established by the age of 30 years,[38] in most cases it precedes the onset of hypothyroidism by 1-2 decades[1] and therefore may be a causal contributor to the phenomenon of persistent symptoms in some patients who are given the diagnosis of hypothyroidism.

The prevalence of self-reported anxiety and low mood / depression among respondents with pSSD was high (72.3% and 71.8%, respectively). It should be noted that these were not medical diagnoses of anxiety or depression, but a research classification self-report. The fact that the survey was carried out during the COVID pandemic may have increased anxiety and low mood / depression and could explain the above high levels. However, an association between hypothyroidism and psychiatric morbidity (including use of anxiolytic and antidepressant medication) has been noted before and seems to hold true both before and after the diagnosis of hypothyroidism.[28] An association between SSD and anxiety and depression is well established in the general population.[92] Our findings suggest that hypothyroid

patients presenting with symptoms of SSD have a high likelihood of an underlying anxiety or mood disorder, which is important for clinicians managing patients with hypothyroidism to be aware of.

The cause of persistent symptoms in patients with hypothyroidism is still unknown, a causal relationship with SSD is not established and underlying biological explanations are also plausible. However, ~~the~~ our findings ~~of E-MPATHY~~ are of importance in the management of patients with hypothyroidism and indicate that somatization plays a significant role in the presentation of some of these patients.

~~Limitations of E-MPATHY included self-reported responses that could not be validated independently, over-representation of some countries, recruitment through patient networks and social media, sample heterogeneity, and evaluation of the impact on everyday living without using a validated thyroid specific quality of life instrument, such as the ThyPRO, absence of directly comparative data on prevalence of pSSD in a control population, and absence of thyroid biochemical data.~~ The study has limitations. Some nations were over-represented, the data were self-reported, respondents were invited via patient organizations and social media, there was some sample heterogeneity, the assessments of quality of life, anxiety and low mood / depression did not ulilize validated instruments, informative data on cause of hypothyroidism were unavailable in 28.5% of responses, directly comparative data on prevalence of pSSD in a control population were unavailable, and we had no access to thyroid biochemistry. The high percentage of pSSD needs to be taken in the context of the fact that only a minority (10-15%) of hypothyroid patients report impaired quality of life,[44] and dissatisfied patients are more likely to respond to surveys ~~such as E-MPATHY~~.[30, 41, 42] In mitigation of the above, ~~limitations~~ the large sample size, cognitive testing, piloting and inclusion of a patient representative in the research team, were strengths.

In conclusion, this study demonstrates a high prevalence of pSSD among people with hypothyroidism who responded to the survey, a tendency to attribute persistent symptoms to hypothyroidism or its treatment and associations between pSSD and negative patient outcomes. SSD may be an important determinant of dissatisfaction with treatment and care among some hypothyroid patients. Our findings require

independent confirmation with studies that focus on SSD and address the limitations outlined above. Close collaboration between the disciplines of thyroidology, psychology and sociology is likely to be key in progressing our understanding in this area.

FIGURE LEGENDS

Figure 1

Association between probable somatic symptom disorder (PHQ-15 score ≥10) and respondent characteristics: (a) age, (b) gender, (c) employment, (d) household income, (e) treatment for hypothyroidism, (f) number of comorbidities. The vertical axis shows the proportion (%) of respondents with PHQ-15 score <10 (white bars) and PHQ-15 score ≥10 (black bars), for each grouped category, so that the sum of percentages for each pair of bars (white and black) equals 100. All comparisons between groups were statistically significant at p<0.001. For each pair of bars, the number of observations (n) is provided. L-T4: levothyroxine; L-T3: liothyronine; DTE: desiccated thyroid extract.

Figure 2

Attribution of PHQ-15 symptoms by respondents to hypothyroidism or its treatment. Respondents were asked to indicate if they attributed the symptom to the hypothyroidism or its treatment, or to other causes. Data are shown for those respondents that attributed their symptoms to hypothyroidism or its treatment, by severity of somatization as expressed by the PHQ-15 score <10 (white bars) and ≥10 (black bars). For each pair of bars the number of observations (n) is also provided. Comparison between white and black bars was statistically significant at p<0.001 for all symptoms except “fainting spells” and “pain or problems during intercourse”. The figures in brackets shown in the horizontal axis indicate the number of respondents who had each symptom. The number of valid responses Chi=38.7, p=1.97e-8 (see Table 2) for each symptom is shown in Supplementary Figure 1.

Figure 3

Association between probable somatic symptom disorder (PHQ-15 score ≥10) and (a) respondent opinion on whether the hypothyroid medication taken controls symptoms of hypothyroidism well, (b) respondent satisfaction with care and treatment for hypothyroidism, (c) impact of hypothyroidism on daily living. The vertical axis shows the proportion (%) of respondents with PHQ-15 score <10 (white bars) and PHQ-15 score ≥10 (black bars). There was an association between somatic symptom and: respondent opinion that the hypothyroid medication did not control the symptoms of hypothyroidism well (p<0.001); dissatisfaction with care and

treatment of hypothyroidism (p<0.001); a negative impact of hypothyroidism on daily living (p<0.001). For each pair of bars the number of observations (n) is also provided.

Supplementary Figure 1

Flow diagram showing number potentially eligible individuals identified, number confirmed eligible, number included in the study, and number analyzed.

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Authorship confirmation/contribution statement

Petros Perros: Conceptualization (lead); methodology (equal), supervision (equal), writing -review & editing (lead).
Laszlo Hegedüs: Conceptualization (equal); funding acquisition (lead), methodology (equal), review & editing (equal).
Endre Vezekenyi Nagy: Conceptualization (equal), methodology (equal), review & editing (equal).
Enrico Papini: Conceptualization (equal), methodology (equal), -review & editing (equal).
Christina Maria Van Der Feltz-Cornelis: methodology (equal); review & editing (equal).
Anthony Peter Weetman: review & editing (equal).
Harriet Alexandra Hay: Data curation (equal), investigation (equal); methodology (equal), project administration (lead), supervision (equal), review & editing (equal).
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Megan Bilas: Investigation (equal), methodology (equal), project administration (equal), supervision (equal), review & editing (equal).

Peter Lakwijk: Resources (lead), methodology (equal), review & editing (equal), Investigation (equal)
Alan J Poots: Methodology - review & editing (equal); formal analysis (lead), review & editing (equal).

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Petros Perros reports honoraria from IBSA Institut Biochimique SA
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Anthony Peter Weetman reports honoraria from IBSA Institut Biochimique SA
Harriet Alexandra Hay reports no competing financial interests.
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TABLE 1
Baseline respondent characteristics.

	n	%
Number of respondents	3516	100
Gender		
Man	164	4.7
Woman	3321	94.5
Prefer to self-identify	13	0.4
Prefer not to say	16	0.5
Missing data	2	0.1
Age		
18-30	236	6.7
31-40	606	17.2
41-50	950	27.0
51-60	850	24.2
Over 60	659	18.7
Missing data	215	6.1
Top 10 Countries by respondent number		
United Kingdom	1250	35.6
France	591	16.8
Sweden	194	5.5
Finland	146	4.2
Australia	136	3.9
Italy	121	3.4
Germany	114	3.2
Norway	102	2.9
United States of America	100	2.8
Canada	104	3.0
Other countries	505	14.4
Missing data	153	4.4
Marital status		

Married/partnership	2320	66.0
Single/divorced	880	25.0
Prefer not to say	58	1.6
Other	39	1.1
Missing data	219	6.2
Employment status		
Working (full time, part time, student, carer)	2526	71.8
Not working	589	16.8
Prefer not to say	55	1.6
Other	127	3.6
Missing data	219	6.2
Ethnic background		
White	3040	86.5
Other	205	5.8
Prefer not to say	52	1.5
Missing data	219	6.2
Years of education		
8 years or less	260	7.4
More than 8 years	2968	84.4
Prefer not to say	71	2.0
Missing data	217	6.2
Household income		
Above average	1044	29.7
Average	1480	42.1
Below average	614	17.5
Prefer not to say	120	3.4
Missing data	258	7.3
Comorbidities		
Median (range)	2 (0-11)	72.8
Missing data	373	10.6
Time since diagnosis of hypothyroidism		

Less than 2 years	357	10.2
Two to 10 years	1294	36.8
More than 10 years	1787	50.8
Don't know / cannot remember	69	2.0
Missing data	9	0.3
Current treatment for hypothyroidism		
Levothyroxine (L-T4)	2665	75.8
Liothyronine (L-T3)	69	2.0
Desiccated Thyroid Extract (DTE)	262	7.5
Levothyroxine (LT-4) + Liothyronine (L-T3)	343	9.8
Missing data	177	5.0
Cause of hypothyroidism		
Hashimoto/autoimmune disease	~~1282~~ 1290	~~36.5~~ 36.7
Treatment for Graves' disease or hyperthyroidism	~~286~~ 326	~~8.1~~ 9.3
Treatment for thyroid cancer	~~454~~ 460	~~12.9~~ 13.1
Treatment for benign goiter	~~177~~ 219	5.0 6.2
Pregnancy related	~~136~~ 143	~~3.9~~ 4.1
Congenital hypothyroidism	51	1.5
Medications	34	1.0
Pituitary disease	31	0.9
Wilson's temperature syndrome	1	0.02
Not known	874	24.6
Variety of other answers provided as free text*	126	3.6
Missing data	4	0.1

*Causes in free text included: "radiation", "radiotherapy", "stress", "viral", "injury to the thyroid", "puberty", "menopause", "eating disorder", "none", "levothyroxine brand switch", "insulin resistance", "endocrine disruption", "fluoridation", "flu vaccine", "gallbladder surgery", "Hereditary", "genetic","hormonal contraceptive", "allergy", "aging", "leaky gut", 'hysterectomy", "mono", "quitting smoking", "sluggish thyroid", "antibiotics", "Yodo", "hypothyroidism".

TABLE 2

Chi-squared analysis for independent variables against PHQ-15 scores <10 and ≥10. The adjusted threshold by Bonferroni method was for the p level of ~~0.001724~~ 0.001667.

Variable	**chi**	**p**	**Adjusted significance using Bonferroni correction**
Gender	44.3	$1.28e^{-09}$	Significant
Age	59.7	$5.18e^{-11}$	Significant
Marital status	3.1	0.37	Not significant
Employment	62.4	$1.76e^{-13}$	Significant
Ethnic background	9.8	0.007	Not significant
Years of education	5.5	0.06	Not significant
Household income	64.8	$2.87e^{-13}$	Significant
Cause of hypothyroidism	7.9	0.16	Not significant
Treatment for hypothyroidism	38.7	$1.97e^{-8}$	Significant
Number of comorbidities	~~244.2~~ 343.8	~~$9.41e^{-54}$~~ $8.32e^{-68}$	Significant
Control of hypothyroidism symptoms by medication	483.6	$2.36e^{-103}$	Significant
Dissatisfaction with overall care and treatment for hypothyroidism	255.2	$4.29e^{-53}$	Significant
Hypothyroidism has affected everyday activities negatively	499.6	$1.03e^{-104}$	Significant
Bothered by anxiety	546.2	$8.23e^{-121}$	Significant
Bothered by low mood or depression	565.7	$4.89e^{-125}$	Significant

TABLE 3

Attribution of respondents' symptoms to hypothyroidism or its treatment. Respondents who had one or more of the symptoms listed in the PHQ-15 questionnaire (scored as "bothered a little" or "bothered a lot"), were further asked to indicate whether they attributed the symptom to "hypothyroidism or its treatment", or to other causes. Respondents were categorized as not having somatic symptom disorder" (SSD) if their PHQ-15 score was <10 and as having probable SSD (pSSD) if their PHQ-15 score was ≥10. Comparisons in attribution of symptoms were made between respondents with pSSD with those without SSD by chi-squared tests with Bonferroni correction. The chi and p values for the comparisons are shown below. The adjusted threshold by Bonferroni method was for the p level of 0.001724.

Symptom	**Attribution of symptom**	**No SSD (n)**	**pSSD (n)**	**chi**	**P**	**Adjusted significance using Bonferroni correction**
Stomach pain	Hypothyroidism or its treatment	46	458	32.5	$1.19e^{-08}$	Significant
	Other	258	991			
Back pain	Hypothyroidism or its treatment	65	441	52.5	$4.39e^{-13}$	Significant
	Other	439	1070			
Pain in arms, legs or joints (knees, hips, etc)	Hypothyroidism or its treatment	297	1064	80.3	3.20^{e-19}	Significant
	Other	462	753			
Menstrual cramps or other problems with your	Hypothyroidism or its treatment	51	274	23.2	$1.48e^{-06}$	Significant
	Other	236	557			

periods (women only)						
Headaches	Hypothyroidism or its treatment	100	547	58.4	$2.17e^{-14}$	Significant
	Other	440	952			
Chest pain	Hypothyroidism or its treatment	27	341	10.3	0.001	Significant
	Other	79	466			
Dizziness	Hypothyroidism or its treatment	110	662	14.3	0.0001	Significant
	Other	158	564			
Fainting spells	Hypothyroidism or its treatment	13	175	2.3	0.130	Not significant
	Other	20	144			
Feeling the heart pound or race	Hypothyroidism or its treatment	196	835	14.8	0.0001	Significant
	Other	161	427			
Shortness of breath	Hypothyroidism or its treatment	126	712	26.2	$3.09e^{-07}$	Significant
	Other	208	617			
Pain or problems during intercourse	Hypothyroidism or its treatment	49	265	2.8	0.09	Not significant
	Other	93	357			
Constipation, loose bowels, or diarrhea	Hypothyroidism or its treatment	243	909	39.8	$2.83e^{-10}$	Significant
	Other	341	687			
Nausea, gas, or indigestion	Hypothyroidism or its treatment	109	743	82.5	$1.06e^{-19}$	Significant
	Other	347	806			
Feeling tired or having low	Hypothyroidism or its treatment	685	1528	120.2	$5.55e^{-28}$	Significant

energy	Other	393	341			
Trouble sleeping	Hypothyroidism or its treatment	266	1010	121.7	$2.72e^{-28}$	Significant
	Other	476	667			

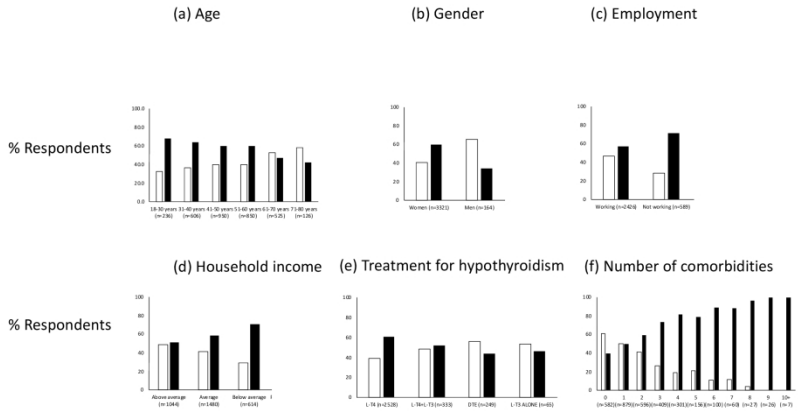

FIGURE 1

Association between probable somatic symptom disorder (PHQ-15 score >10) and respondent characteristics: (a) age, (b) gender, (c) employment, (d) household income, (e) treatment for hypothyroidism, (f) number of comorbidities. The vertical axis shows the proportion (%) of respondents with PHQ-15 score <10 (white bars) and PHQ-15 score >10 (black bars), for each grouped category, so that the sum of percentages for each pair of bars (white and black) equals 100. All comparisons between groups were statistically significant at $p<0.001$. For each pair of bars, the number of observations (n) is provided. L-T4: levothyroxine; L-T3: liothyronine; DTE: desiccated thyroid extract.

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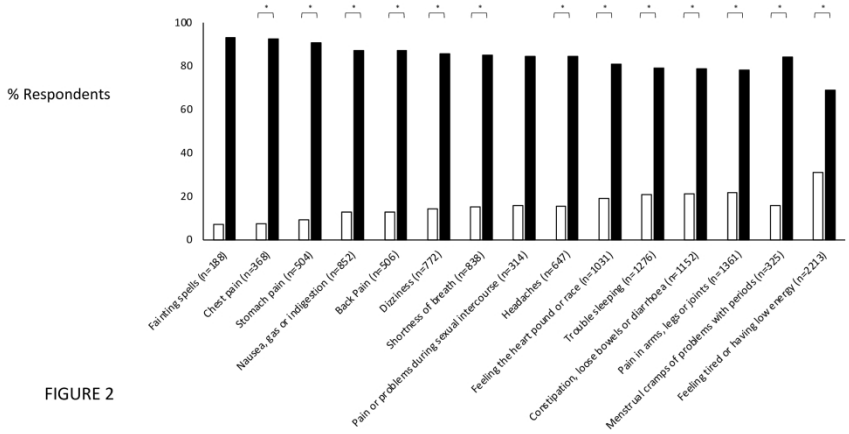

FIGURE 2

Attribution of PHQ-15 symptoms by respondents to hypothyroidism or its treatment. Respondents were asked to indicate if they attributed the symptom to the hypothyroidism or its treatment, or to other causes. Data are shown for those respondents that attributed their symptoms to hypothyroidism or its treatment, by severity of somatization as expressed by the PHQ-15 score <10 (white bars) and >10 (black bars). For each pair of bars the number of observations (n) is also provided. Comparison between white and black bars was statistically significant at $p<0.001$ for all symptoms except "fainting spells" and "pain or problems during intercourse". The figures in brackets shown in the horizontal axis indicate the number of respondents who had each symptom. The number of valid responses Chi=38.7, p=1.97e-8 (see Table 2) for each symptom is shown in Supplementary Figure 1.

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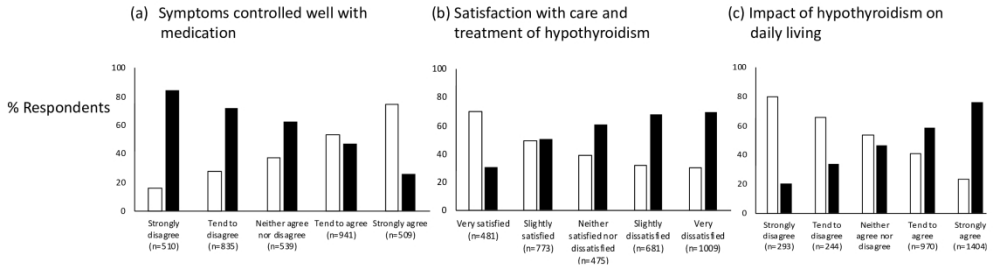

FIGURE 3

Association between probable somatic symptom disorder (PHQ-15 score >10) and (a) respondent opinion on whether the hypothyroid medication taken controls symptoms of hypothyroidism well, (b) respondent satisfaction with care and treatment for hypothyroidism, (c) impact of hypothyroidism on daily living. The vertical axis shows the proportion (%) of respondents with PHQ-15 score <10 (white bars) and PHQ-15 score >10 (black bars). There was an association between somatic symptom and: respondent opinion that the hypothyroid medication did not control the symptoms of hypothyroidism well ($p<0.001$); dissatisfaction with care and treatment of hypothyroidism ($p<0.001$); a negative impact of hypothyroidism on daily living ($p<0.001$). For each pair of bars the number of observations (n) is also provided.

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SUPPLEMENTARY TABLE S1

Responses to individual components of PHQ-15 among respondents. Each symptom (shown in the left column) was scored as "not bothered at all", "bothered a little" or "bothered a lot".

Symptom	**Respondents selecting "bothered a little" and "bothered a lot" % (n)**
Fainting spells *(Missing data n=49)*	11.3 (392/3467)
Chest pain (Missing data n=77)	29.8 (1025/3439)
Stomach pain *(Missing data n=61)*	51.2 (1769/3455)
Nausea, gas or indigestion *(Missing data n=30)*	62.7 (2185/3486)
Back pain *(Missing data n=26)*	62.9 (2195/3490)
Dizziness *(Missing data n=39)*	47.0 (1634/3477)
Shortness of breath *(Missing data n=31)*	51.8 (1805/3485)
Pain or problems during sexual intercourse *(Missing data n=50)*	25.1 (870/3466)
Headaches (Missing data n=49)	64.3 (2230/3467)
Feeling the heart pound or race (Missing data n=42)	52.7 (1830/3474)
Trouble sleeping *(Missing data n=11)*	74.9 (2625/3505)
Constipation, loose bowels or diarrhoea *(Missing data n=16)*	66.8 (2338/3500)
Pain in arms, legs or joints	75.1 (2619/3489)

(Missing data n=27)	
Menstrual cramps or problems with periods *(Missing data n=71; men were excluded)*	36.9 (1200/3250)
Feeling tired or having low energy *(Missing data n=11)*	90.2 (3163/3505)

SUPPLEMENTARY TABLE 2

Distribution of PHQ-15 scores <10 and ≥10 by type of thyroid medication. Chi-squared analysis for the independent variable "treatment for hypothyroidism" against PHQ-15 scores <10 and >10 showed significance (Chi=38.7, $p=1.97e^{-8}$ (see Table 2).

	PHQ-15 <10 % (n)	**PHQ-15 ≥10 % (n)**
Treatment for hypothyroidism (%, n)		
L-T4 75.8% (2665/3516)	39.2 (1046/2665)	60.8 (1619/2665)
L-T3 alone 2.0% (69/3516)	53.6 (37/69)	46.4 (32/69)
DTE 7.5% (262/3516)	56.1 (147/262)	43.9 (115/262
Combination of L-T4 and L-T3 9.8% (343/3516)	48.1 (165/343)	51.9 (178/343)
Missing data 5.0% (117/3516)		

Abbreviations: L-T4: levothyroxine; L-T3: liothyronine; DTE: desiccated thyroid extract.

SUPPLEMENTARY TABLE 3

PHQ-15 scores of women and men respondents compared to normative data (34)*.

	E-MPATHY RESPONDENTS	NORMATIVE DATA	p
Women (n=3321)			
Mean (SD)	11.3 (5.8)	6.6 (4.8)	<0.001
Median (range)	11.0 (0-30)	6.0 (0-27)	
95% CI	11.3-11.5	6.4-6.8	
Men (n=164)			
Mean (SD)	7.6 (5.6)	5.0 (4.3)	<0.001
Median (range)	6.0 (0-25)	4.0 (0-28)	
95% CI	6.8-8.5	4.8-5.1	

*General population normative values (34) matched for age and sex were compared to E-MPATHY responses using unpaired t-tests.

Supplementary file. Hypothyroidism questionnaire (English version)
Please note that this survey is owned by Picker and should not be replicated, reproduced and/or used without prior written consent from Picker. Please contact *info@pickereurope.ac.uk* for further information about the survey or to request a licence to use the questions.

Hypothyroidism Patient Experience Survey

What is this questionnaire about?
This questionnaire is about your care experiences and support needs as someone who is being treated for **hypothyroidism** (e.g. due to an under-active thyroid, not having a thyroid, or treatments for hyperthyroidism). You may have taken part in the pilot version of this questionnaire a few months ago. Please note that we would still value your input even if you participated in an earlier pilot questionnaire. Results from the survey will be used to better understand the different experiences of those with hypothyroidism. More information is available here.

This questionnaire is sponsored by the pharmaceutical company, IBSA, with the involvement of Thyroid Federation International and an academic board. The purpose is non-commercial and the data will be used for publication in the medical press.

Who is this questionnaire for?

This questionnaire is for adults aged 18 years and over who are being treated for **hypothyroidism**.

Questions or help

If you have any questions about how to complete this questionnaire please email Harriet Hay at take_part@pickereurope.ac.uk and reference 'Hypothyroidism Patient Experience Survey' within the subject line. This survey will take approximately 30 minutes to complete. For ease of completion, we recommend completing this on a computer screen within one session. The care you received may have been impacted by the Coronavirus pandemic. Please answer based on your **typical** experience or according to date ranges mentioned in the question text, excluding any instances where your care may be atypical due to the pandemic. **Taking part in this survey is voluntary. Your answers will be anonymised and treated in confidence.**

You can access the Picker privacy notice for online surveys here.

R1 By completing this questionnaire, you are confirming that you are happy for Picker to use the anonymous data gathered. A summary of this information may be shared publicly for the benefit of others. Are you happy for your data to be shared?

- Yes, I am happy for my data to be shared anonymously (1)
- No, I do not want my data to be shared (2)

R0 If you close the questionnaire before the end of the survey, we would still like to use the responses that you give, even if you do not finish the survey. Are you happy for us to do so?

- Yes, you may use my responses if I only partly complete the survey (1)
- No, you may not use my responses unless I fully complete the survey (2)

End of Block: Cover

Start of Block: Screening 1

Description **About You**

A2 Are you 18 years of age or over?

- Yes (1)
- No (2)

A10 Are you currently taking anything to control symptoms of **hypothyroidism** (e.g. due to an under-active thyroid, not having a thyroid, or treatments for hyperthyroidism)? This may include prescribed medications, non-prescribed medications, and dietary supplements.

- Yes (1)
- No (2)
- Don't Know (99)

End of Block: Screening 1

Start of Block: About You 1

Description **About You**

A3 What is your gender?

- ○ Male (1)
- ○ Female (2)
- ○ Prefer to self-identify (3) _____
- ○ Prefer not to say (4)

A4 Where do you currently live?

▼ Afghanistan (1) ... Zimbabwe (195)

End of Block: About You 1

Start of Block: Diagnosis and Treatment

Description **Diagnosis and Treatment**

D1 When did you develop **hypothyroidism**?

- Don't Know/ Can't remember (99)
- Within the last year (1)
- More than 1 year but less than 2 years ago (2)
- More than 2 years but less than 5 years ago (3)
- More than 5 years but less than 10 years ago (4)
- More than 10 years ago (5)

D2 What is the likely cause of your **hypothyroidism**?

- Not known (99)
- Hashimoto/autoimmune disease (1)
- Treatment for Graves' disease or hyperthyroidism (2)
- Treatment for thyroid cancer (3)
- Treatment for benign goiter (4)
- Medications (5)
- Pituitary disease (6)
- Congenital disorder (e.g. born without a thyroid or with a defective thyroid) (7)
- Pregnancy related (8)
- Wilson's temperature syndrome (9)
- Other (Please specify) (10) _____

Description TSH stands for Thyroid Stimulating Hormone. A TSH test is a blood test that measures this hormone level.

D3a How long ago was your most recent TSH test?

- Don't know/ Can't remember (99)
- Within the last 2 months (1)
- Between 2-6 months ago (2)
- Between 6-12 months ago (3)
- More than 12 months ago (4)

D3b In what range was your current or most recently measured TSH test?

- Don't Know/ Can't remember (99)
- Under 0.1 (1)
- Between 0.1 and 0.4 (2)
- Over 0.4 but less than 2.5 (3)
- Between 2.5 and 4.0 (4)
- Between 4.0 and 10 (5)
- Between 10 and 20 (6)
- More than 20 (7)

D4 Thinking about your highest ever TSH level, in what range did it fall in?

- Don't Know/ Can't remember (99)
- Under 4.0 (1)
- Between 4.0 and 10 (2)
- Between 10 and 20 (3)
- More than 20 (4)

D5 What are you **currently** taking to treat your **hypothyroidism**? (Please select all that apply).

- ☐ **Levothyroxine** (e.g. Levoxyl, Synthroid, Euthyrox, Unithroid, Eltroxin, Levothyroid, Tyrosint, L Thyroxine, Levo T, Levoxine, Levothyroxine, T4) (1)
- ☐ **Liothyronine** (e.g. T3, Cytomel, Triostat, Tertroxin, Thybon) (2)
- ☐ **Desiccated Thyroid Extract** (e.g. Armour Thyroid, Nature-Throid, NP Thyroid, ERFA Thyroid, Westhroid) (3)
- ☐ Dietary supplements (4)
- ☐ Other treatment (Please specify) (5) _____
- ☐ Don't know/Prefer not to say (99)

D6 Have you ever taken Levothyroxine (e.g. Levoxyl, Synthroid, Euthyrox, Unithroid, Eltroxin, Levothyroid, Tyrosint, L Thyroxine, Levo T, Levoxine, Levothyroxine, T4) to treat your hypothyroidism?

- ○ Yes (1)
- ○ No (2)
- ○ Don't know/can't remember (99)

D7 How long did you take Levothyroxine (e.g. Levoxyl, Synthroid, Euthyrox, Unithroid, Eltroxin, Levothyroid, Tyrosint, L Thyroxine, Levo T, Levoxine, Levothyroxine, T4)?

- ○ Less than 1 year (1)
- ○ More than 1 year but less than 2 years (2)
- ○ More than 2 years but less than 5 years (3)
- ○ More than 5 years but less than 10 years (4)
- ○ 10 years or more (5)
- ○ Don't know/can't remember (99)

D8 How long have you been taking Levothyroxine (e.g. Levoxyl, Synthroid, Euthyrox, Unithroid, Eltroxin, Levothyroid, Tyrosint, L Thyroxine, Levo T, Levoxine, Levothyroxine, T4)?

- Less than 1 year (1)
- More than 1 year but less than 2 years (2)
- More than 2 years but less than 5 years (3)
- More than 5 years but less than 10 years (4)
- 10 years or more (5)
- Don't know/can't remember (99)

D9 What is the primary reason why you stopped taking Levothyroxine (e.g.Levoxyl, Synthroid, Euthyrox, Unithroid, Eltroxin, Levothyroid, Tyrosint, L Thyroxine, Levo T, Levoxine, Levothyroxine T4)? (Please select all that apply).

- [ ] I wanted to take something more natural (1)
- [ ] I needed to change treatments due to a history of thyroid cancer (2)
- [ ] Levothyroxine wasn't controlling my symptoms well (3)
- [ ] Levothyroxine was interacting with other medications I take (4)
- [ ] I was experiencing unpleasant side effects (5)
- [ ] To avoid an ingredient in the medication (e.g. gelatine, lactose) (6)
- [ ] I was advised by my doctor to do so (7)
- [ ] Other (please specify) (8) _____
- [ ] Don't know/can't remember (99)

End of Block: Diagnosis and Treatment

Start of Block: Medication

Description **Medication**

M1 In what form do you **currently** take your Levothyroxine (e.g. Levoxyl, Synthroid, Euthyrox, Unithroid, Eltroxin, Levothyroid, Tyrosint, L Thyroxine, Levo T, Levoxine, Levothyroxine, T4)?

- Tablets (1)
- Capsules (2)
- Soft gels (3)
- Liquid (4)
- Don't Know (99)

M2 How many times do you take your Levothyroxine (e.g. Levoxyl, Synthroid, Euthyrox, Unithroid, Eltroxin, Levothyroid, Tyrosint, L Thyroxine, Levo T, Levoxine, Levothyroxine, T4)?

- Once a day (1)
- Twice a day (2)
- Three times per day (3)
- More than three times per day (4)
- Once a week (5)
- Other (Please specify) (6) _____
- Don't know (99)

M28 How many times do you take your Liothyronine (e.g. Cytomel, Triostat, Tertroxin, Thybon)?

- Once a day (1)
- Twice a day (2)
- Three times per day (3)
- More than three times per day (4)
- Other (Please specify) (5) _____

M29 How many times do you take your Desiccated Thyroid Extract (e.g. Armour Thyroid, Nature-Throid, NP Thyroid, ERFA Thyroid, Westhroid)?

- Once a day (1)
- Twice a day (2)
- Three times per day (3)
- More than three times per day (4)
- Other (Please specify) (5) _____

M25 Do you **currently** take alternate doses of your Levothyroxine medication (e.g. Levoxyl, Synthroid, Euthyrox, Unithroid, Eltroxin, Levothyroid, Tyrosint, L Thyroxine, Levo T, Levoxine, Levothyroxine, T4)?

For example, you might take 100 micrograms (mcg) on one day and 75 micrograms (mcg) the next day.

- Yes (1)
- No (2)
- Don't Know/can't remember (99)

M26 What is the total dose you are **supposed to take** each day you have your Levothyroxine (e.g. Levoxyl, Synthroid, Euthyrox, Unithroid, Eltroxin, Levothyroid, Tyrosint, L Thyroxine, Levo T, Levoxine, Levothyroxine, T4)?

(If you only take your dose once a week, please provide the weekly dosage).

- ○ Dose (enter number below in micrograms) (1) _____
- ○ Don't know/can't remember (99)

M27 You said that you take alternate doses when you have your Levothyroxine.

What are the two doses you are **supposed to take** each time you have your Levothyroxine (e.g. Levoxyl, Synthroid, Euthyrox, Unithroid, Eltroxin, Levothyroid, Tyrosint, L Thyroxine, Levo T, Levoxine, Levothyroxine, T4)?

- ☐ First dose (enter number below in micrograms) (1)

_____

- ☐ Second dose (enter number below in micrograms) (2)

_____

- ☐ Don't Know/can't remember (99)

M14 What is the total dose you are **supposed to take** each day you have your Liothyronine (e.g. Cytomel, Triostat, Tertroxin, Thybon)?

- ○ Less than 5 micrograms (1)
- ○ 5-20 micrograms (2)
- ○ 21-60 micrograms (3)
- ○ 61-120 micrograms (4)
- ○ More than 121 micrograms (5)

M15 What is the total number of grains/tablets you are **supposed to take** each day you have your Dessicated Thyroid Extract (e.g. Armour Thyroid, Nature-Throid, NP Thyroid, ERFA Thyroid, Westhroid)?

- Don't Know/can't remember (99)
- Less than 1 grain/tablet (1)
- 1 -2 grains/tablets (2)
- 2.25 - 3 grains/tablets (3)
- 3.25 grains/tablets or more (4)

M17 In the **past 12 months**, how many times has the dose of your hypothyroidism medication been adjusted?

- Never (1)
- Once (2)
- Twice (3)
- Three times (4)
- Four times (5)
- Five times or more (6)
- Don't know/can't remember (99)

M18 Thinking about taking your **hypothyroidism medication** in the **past 12 months**, how burdensome (if at all) have any of the following been?

Please select one option from each row. Select 'This does not apply to me' if you do not need to follow the guideline. Some statements may or may not apply to you. Select 'Not burdensome at all' if you do need to follow the guideline but do not find it burdensome.

	This does not apply to me (98)	Not burdensome at all (1)	Slightly burdensome (2)	Moderately burdensome (3)	Extremely burdensome (4)
Making sure that I take the correct dose at the right time (M18a)	○	○	○	○	○
Making sure that I take the dose on an empty stomach (M18b)	○	○	○	○	○
Making sure that I avoid drinking anything other than water for 30 minutes before and after taking my medication (M18c)	○	○	○	○	○
Making sure that I do not take any other medications that could interfere with my hypothyroidism medication (M18d)	○	○	○	○	○
Needing to alternate doses in order to get the right amount of levothyroxine (M18e)	○	○	○	○	○
Needing to split tablets in order to get the right dose (M18f)	○	○	○	○	○

M19 Still thinking about taking your **hypothyroidism medication** in the **past 12 months**, how burdensome (if at all) have any of the following been? Please select one option from each row. Select 'This does not apply to me' if you do not need to follow the guideline. Some statements may or may not apply to you. Select 'Not burdensome at all' if you do need to follow the guideline but do not find it burdensome.

	This does not apply to me (98)	Not burdensome at all (1)	Slightly burdensome (2)	Moderately burdensome (3)	Extremely burdensome (4)
Keeping track of my different hypothyroidism medications (M19a)	○	○	○	○	○
Having difficulty taking my medication because it tastes bad/does not look appealing (M19b)	○	○	○	○	○
Experiencing problems getting prescriptions from my doctor (M19c)	○	○	○	○	○
Making sure that I am getting blood tests done to make sure I am taking the right dose (M19d)	○	○	○	○	○
Getting used to taking a different dose of my medication (M19e)	○	○	○	○	○

M20 How often do you **typically miss or skip** taking a dose of your **hypothyroidism medication**?

- ○ Most days (1)
- ○ A few times per week (2)
- ○ Once a week (3)
- ○ A few times per month (4)
- ○ Once a month (5)
- ○ A few times per year (6)
- ○ Never (7)

M21 Why have you missed or skipped taking your medication? (Please select all that apply).

- ☐ I forgot (1)
- ☐ My routine was disrupted / I did not have the medication with me (2)
- ☐ I could not meet the food/drink requirements (3)
- ☐ I experienced unpleasant side effects (4)
- ☐ I wanted to avoid an ingredient in the medication (e.g. gelatine, lactose) (5)
- ☐ I didn't have any symptoms (6)
- ☐ I was afraid the medication would interact with other medication I had to take (7)
- ☐ I didn't think that the medication was working (8)
- ☐ I was feeling too ill to take it (9)
- ☐ I had concerns due to pregnancy (10)
- ☐ I ran out of medication (11)
- ☐ I needed additional information or support to take my medication (12)
- ☐ I could not afford the medication (13)
- ☐ Other (please specify) (14) _____

M22 How often do you **typically take more** of your **hypothyroidism medication** than what you have been prescribed?

- ○ Most days (1)
- ○ A few times per week (2)
- ○ Once a week (3)
- ○ A few times per month (4)
- ○ Once a month (5)
- ○ A few times per year (6)
- ○ Never (7)

M23 Why have you taken more of your hypothyroidism medication than what you have been prescribed? (Please select all that apply)

- ☐ I missed a dose and had to take more later (1)
- ☐ I forgot that I had already taken a dose and took it again (2)
- ☐ I felt like I needed to take more to control my symptoms (3)
- ☐ I had difficulty knowing how much to take (4)
- ☐ Other (please specify) (5) _____

M24 To what extent, if at all, do you agree or disagree with the following statements? (Please select one option from each row).

	Strongly agree (1)	Tend to agree (2)	Neither agree nor disagree (3)	Tend to disagree (4)	Strongly disagree (5)
My **hypothyroidism medication** controls my symptoms well (M24a)	○	○	○	○	○
My **hypothyroidism medication** is convenient to take (M24b)	○	○	○	○	○

End of Block: Medication

Start of Block: Treatment Expectations

Description **Treatment Expectations**

T1 When you first started taking levothyroxine for hypothyroidism, did you expect that your overall health would…

- Improve significantly (1)
- Improve slightly (2)
- Be about the same (3)
- I did not have any expectations (4)
- Don't know/can't remember (99)

T2 After you started taking levothyroxine for hypothyroidism, when did you expect the treatment to start working?

- Immediately (1)
- Within 1 - 3 months (2)
- Within 4 - 12 months (3)
- Within 13 months - 2 years (4)
- I did not have any expectations (5)
- Don't know/can't remember (99)

T3 How concerned were you about weight gain before starting treatment for hypothyroidism?

- Very concerned (1)
- Moderately concerned (2)
- A little concerned (3)
- Not at all concerned (4)
- Don't know/can't remember (99)

T4 How concerned are you about weight gain now?

- Very concerned (1)
- Moderately concerned (2)
- A little concerned (3)
- Not at all concerned (4)

T5A Thinking about your treatment for hypothyroidism, how did the introduction of ${D5/ChoiceDescription/2} make you feel?

- Very satisfied compared to before (1)
- A little more satisfied than before (2)
- Neither satisfied nor dissatisfied (3)
- A little less satisfied than before (4)
- Very dissatisfied compared to before (5)
- Don't know (99)

T5B Thinking about your treatment for hypothyroidism, how did the introduction of ${D5/ChoiceDescription/2} or ${D5/ChoiceDescription/3} make you feel?

- Very satisfied compared to before (1)
- A little more satisfied than before (2)
- Neither satisfied nor dissatisfied (3)
- A little less satisfied than before (4)
- Very dissatisfied compared to before (5)
- Don't know (99)

T5C Thinking about your treatment for hypothyroidism, how did the introduction of ${D5/ChoiceDescription/3} make you feel?

- Very satisfied compared to before (1)
- A little more satisfied than before (2)
- Neither satisfied nor dissatisfied (3)
- A little less satisfied than before (4)
- Very dissatisfied compared to before (5)
- Don't know (99)

End of Block: Treatment Expectations

Start of Block: Other conditions and medications

Description **Other conditions and medications**

C1 Do you have a current diagnosis of any of the following conditions? (Please select all that apply).

- ☐ No long-term condition (17)
- ☐ Autoimmune disease (other than thyroid) (1)
- ☐ Heart disease (e.g. angina, coronary artery disease, congenital heart disease) (2)
- ☐ Lung disease (e.g. asthma, COPD) (3)
- ☐ Diabetes (4)
- ☐ Joint problem (e.g. arthritis or other rheumatic disease) (5)
- ☐ Osteoporosis (6)
- ☐ Bone/muscle disease (e.g. fibromyalgia) (7)
- ☐ Gastrointestinal (GI) disease (e.g. irritable bowel syndrome, celiac disease) (8)
- ☐ Mental health condition (e.g. depression, anxiety) (9)
- ☐ Cancer (10)
- ☐ Chronic pain (e.g. back pain) (11)
- ☐ Fatigue syndrome (e.g. chronic fatigue, myalgic encephalomyelitis) (12)
- ☐ Adrenal disease (e.g. adrenal fatigue, Addison's disease) (13)
- ☐ Food allergy (e.g. gluten intolerance) (14)
- ☐ Sleep apnoea (15)
- ☐ Other long-term condition (16)

C2 Do you take prescribed medications for any condition other than hypothyroidism?

- ○ Yes (1)
- ○ No (2)

C3 In addition to hypothyroidism, how many conditions do you take prescribed medicine for?

▼ 1 (1) ... Over 10 (11)

End of Block: Other conditions and medications

Start of Block: Health Status

Description **Health Status**

H1 In a **typical** week, how many hours do you spend doing physical activity, which is enough to raise your breathing rate? (This may include sport, exercise, and brisk walking or cycling for recreation or to get to and from places, but should NOT include housework or physical activity that may be part of your job).

- None (1)
- Less than 1 hour a week (2)
- 1 to 3 hours a week (3)
- 3 to 6 hours a week (4)
- 6 to 10 hours a week (5)
- 10 to 15 hours a week (6)
- More than 15 hours a week (7)

H2 Given your age and height, would you say that you are about the right weight, too heavy, or too light?

- I am about the right weight (2)
- I am too heavy (3)
- I am too light (1)
- Don't know (99)

H3 During the **past 4 weeks**, how much have you been bothered by any of the following problems?

	Not bothered at all/Not applicable (0)	Bothered a little (1)	Bothered a lot (2)
Stomach pain (H3a)			
Memory problems (H3b)			
Weight loss (H3c)			
Menstrual cramps or other problems with your periods (H3d)			
Sensitivity to the cold (H3e)			
Shaking, usually of the hands (H3f)			
Headaches (H3g)			
Dry/itchy skin (H3h)			
Flushing or sweating a lot (H3i)			
Chest pain (H3j)			
Pins and needles in the fingers and hands (H3k)			
Mood swings (H3l)			
Feeling your heart pound or race (H3m)			

H4 You mentioned that you were bothered by the following problems during the **past 4 weeks**. What do you think is the **main cause or causes** of each of these problems?	My hypothyroidism or side effects from my hypothyroidism medication (1)	Another condition or its medication (2)	Ageing (3)	Lifestyle (e.g. diet, exercise, work) (4)	Short term illness (e.g. cold/ flu/ allergies) (5)	Other (6)	Don't know (99)
Stomach pain (H4a)	☐	☐	☐	☐	☐	☐	☐
Memory problems (H4b)	☐	☐	☐	☐	☐	☐	☐
Weight loss (H4c)	☐	☐	☐	☐	☐	☐	☐
Menstrual cramps or other problems with your periods (H4d)	☐	☐	☐	☐	☐	☐	☐
Sensitivity to the cold (H4e)	☐	☐	☐	☐	☐	☐	☐
Shaking, usually of the hands (H4f)	☐	☐	☐	☐	☐	☐	☐
Headaches (H4g)	☐	☐	☐	☐	☐	☐	☐
Dry/itchy skin (H4h)	☐	☐	☐	☐	☐	☐	☐
Flushing or sweating a lot (H4i)	☐	☐	☐	☐	☐	☐	☐

Chest pain (H4j)	☐	☐	☐	☐	☐	☐	☐
Pins and needles in the fingers and hands (H4k)	☐	☐	☐	☐	☐	☐	☐
Mood swings (H4l)	☐	☐	☐	☐	☐	☐	☐
Feeling your heart pound or race (H4m)	☐	☐	☐	☐	☐	☐	☐

H5 During the **past 4 weeks**, how much have you been bothered by any of the following problems?

	Not bothered at all/Not applicable (0)	Bothered a little (1)	Bothered a lot (2)
Weight gain (H5n)	○	○	○
Irritability (H5o)	○	○	○
Constipation, loose bowels, or diarrhoea (H5p)	○	○	○
Slow speech, movements, or thoughts (H5q)	○	○	○
Feeling tired or having low energy (H5r)	○	○	○
Low mood or depression (H5s)	○	○	○
Anxiety (H5t)	○	○	○
Trouble sleeping (H5u)	○	○	○
Difficulty concentrating (H5v)	○	○	○
Nervousness (H5w)	○	○	○
Back pain (H5x)	○	○	○
Dry hair/nails (H5y)	○	○	○
Feeling restless (H5z)	○	○	○

H6 You mentioned that you were bothered by the following problems during the **past 4 weeks**. What do you think is the **main cause or causes** of each of these problems?	My hypothyroidism or side effects from my hypothyroidism medication (1)	Another condition or its medication (2)	Ageing (3)	Lifestyle (e.g. diet, exercise, work) (4)	Short term illness (e.g. cold/ flu/ allergies) (5)	Other (6)	Don't know (99)
Weight gain (H6n)	☐	☐	☐	☐	☐	☐	☐
Irritability (H6o)	☐	☐	☐	☐	☐	☐	☐
Constipation, loose bowels, or diarrhea (H6p)	☐	☐	☐	☐	☐	☐	☐
Slow speech, movements, or thoughts (H6q)	☐	☐	☐	☐	☐	☐	☐
Feeling tired or having low energy (H6r)	☐	☐	☐	☐	☐	☐	☐
Low mood or depression (H6s)	☐	☐	☐	☐	☐	☐	☐
Anxiety (H6t)	☐	☐	☐	☐	☐	☐	☐
Trouble sleeping (H6u)	☐	☐	☐	☐	☐	☐	☐
Difficulty concentrating (H6v)	☐	☐	☐	☐	☐	☐	☐
Nervousness (H6w)	☐	☐	☐	☐	☐	☐	☐

Back pain (H6x)	☐	☐	☐	☐	☐	☐	☐
Dry hair/nails (H6y)	☐	☐	☐	☐	☐	☐	☐
Feeling restless (H6z)	☐	☐	☐	☐	☐	☐	☐

H7 During the **past 4 weeks**, how much have you been bothered by any of the following problems?

	Not bothered at all/Not applicable (0)	Bothered a little (1)	Bothered a lot (2)
Pain in your arms, legs, or joints (knees, hips, etc.) (H7a)	○	○	○
Hoarse/croaky voice (H7b)	○	○	○
Thinning hair (H7c)	○	○	○
Dizziness (H7d)	○	○	○
Puffy face/bags under eyes (H7e)	○	○	○
Low sex drive (H7f)	○	○	○
Fainting spells (H7g)	○	○	○
Hearing loss (H7h)	○	○	○
Muscle weakness/cramps/aches (H7i)	○	○	○
Shortness of breath (H7j)	○	○	○
Nausea, gas, or indigestion (H7k)	○	○	○
Pain or problems during sexual intercourse (H7l)	○	○	○

H8 You mentioned that you were bothered by the following problems during the **past 4 weeks**. What do you think is the **main cause or causes** of each of these problems?

	My hypothyroidism or side effects from my hypothyroidism medication (1)	Another condition or its medication (2)	Ageing (3)	Lifestyle (e.g. diet, exercise, work) (4)	Short term illness (e.g. cold/ flu/ allergies) (5)	Other (6)	Don't know (99)
Pain in your arms, legs, or joints (knees, hips, etc.) (H8a)	☐	☐	☐	☐	☐	☐	☐
Hoarse/croaky voice (H8b)	☐	☐	☐	☐	☐	☐	☐
Thinning hair (H8c)	☐	☐	☐	☐	☐	☐	☐
Dizziness (H8d)	☐	☐	☐	☐	☐	☐	☐
Puffy face/bags under eyes (H8e)	☐	☐	☐	☐	☐	☐	☐
Low sex drive (H8f)	☐	☐	☐	☐	☐	☐	☐
Fainting spells (H8g)	☐	☐	☐	☐	☐	☐	☐
Hearing loss (H8h)	☐	☐	☐	☐	☐	☐	☐
Muscle weakness/cramps/aches (H8i)	☐	☐	☐	☐	☐	☐	☐
Shortness of breath (H8j)	☐	☐	☐	☐	☐	☐	☐
Nausea, gas, or indigestion (H8k)	☐	☐	☐	☐	☐	☐	☐
Pain or problems during sexual intercourse (H8l)	☐	☐	☐	☐	☐	☐	☐

End of Block: Health Status

Start of Block: Healthcare Staff

S5 Have you been seen by healthcare staff in the past 12 months about your hypothyroidism?

- Yes (1)
- No (2)

Description
Healthcare Staff

Thinking about the care you have received for your hypothyroidism over the **past 12 months from the healthcare staff who you primarily see for your thyroid...**

S1
Do you have confidence and trust in the healthcare staff treating your hypothyroidism?

- Yes, always (1)
- Yes, sometimes (2)
- No (3)

S2
Do the healthcare staff that you see for your hypothyroidism know enough about the condition?

- Yes, definitely (1)
- Yes, to some extent (2)
- No (3)

S3
Do you have enough time to talk and interact with healthcare staff about your hypothyroidism?

- Yes, definitely (1)
- Yes, to some extent (2)
- No (3)

S4
Do healthcare staff talk to you about your care and treatment in a way that you can understand?

- Yes, definitely (1)
- Yes, to some extent (2)
- No (3)

End of Block: Healthcare Staff

Start of Block: Managing your condition

Description **Managing your condition**

Thinking about managing your condition over the **past 12 months**...

SM1 Have you been given enough information about when and how to take your hypothyroidism medication?

- Yes, enough information (1)
- Some, but not enough information (2)
- Little or no information (3)
- I did not need any information (4)

SM2 Have you been given enough information about the side effects of your hypothyroidism medication and any interactions with other medications and supplements?

- Yes, enough information (1)
- Some, but not enough information (2)
- Little or no information (3)
- I did not need any information (4)

SM3 Are you involved enough in decisions about your condition and treatment?

- Yes, definitely (1)
- Yes, to some extent (2)
- No, but I would like this (3)
- I do not want or need to be (4)

End of Block: Managing your condition

Start of Block: Overall Satisfaction

Description **Overall Satisfaction**

O1 How satisfied are you with the overall care and treatment you have received for your hypothyroidism?

- ○ Very satisfied (1)
- ○ Slightly satisfied (2)
- ○ Neither satisfied nor dissatisfied (3)
- ○ Slightly dissatisfied (4)
- ○ Very dissatisfied (5)
- ○ Don't know (99)

End of Block: Overall Satisfaction

Start of Block: Quality of Life

Description **Quality of Life**

*The care you received may have been impacted by the Coronavirus pandemic. Please answer based on your **typical** experience or according to date ranges mentioned in the question text, excluding any instances where your care may be atypical due to the pandemic.*

Thinking about how your **hypothyroidism** has affected your day-to-day life in the **past 12 months**...

Q1 To what extent, if at all, do you agree or disagree with each of the following statements? (Please select one option from each row).

	Strongly agree (1)	Tend to agree (2)	Neither agree nor disagree (3)	Tend to disagree (4)	Strongly disagree (5)	Don't know/can't recall (99)	This does not apply to me (98)
My **hypothyroidism** has affected everyday activities that people my age usually do (e.g. exercise, household chores, etc.) (Q1a)	○	○	○	○	○	○	○
Managing treatment or medications for my **hypothyroidism** has had a significant impact on my day-to-day life (Q1b)	○	○	○	○	○	○	○
My **hypothyroidism** has negatively impacted on my holiday/ vacation/travel plans (Q1c)	○	○	○	○	○	○	○
I have been unable to work/had to change my job or working pattern because of my **hypothyroidism** (Q1d)	○	○	○	○	○	○	○
My **hypothyroidism** has had a negative impact on my financial situation (Q1e)	○	○	○	○	○	○	○

Q2 Still thinking about the **past 12 months**...
To what extent, if at all, do you agree or disagree with each of the following statements? (Please select one option from each row)

	Strongly agree (1)	Tend to agree (2)	Neither agree nor disagree (3)	Tend to disagree (4)	Strongly disagree (5)	Don't know/can't recall (99)	This does not apply to me (98)
My **hypothyroidism** has created problems with my partner, close friends or relatives (Q2a)	○	○	○	○	○	○	○
My **hypothyroidism** has had a negative impact on my social life (Q2b)	○	○	○	○	○	○	○
My **hypothyroidism** has negatively impacted on my confidence and self-esteem (Q2c)	○	○	○	○	○	○	○

End of Block: Quality of Life

Start of Block: Personality

Description
Personality

We are interested in exploring whether there is any relationship between hypothyroidism and certain personality traits. Below are a number of statements that people often use to describe themselves. Please read each statement and then choose the most appropriate answer.

There are no right or wrong answers: Your own impression is the only thing that matters.

*Some statements may be affected by social distancing measures due to the Coronavirus pandemic. Please answer based on your **typical** experience, not based on measures you may have needed to take due to the pandemic.*

P1 I make contact easily when I meet people

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P2 I often make a fuss about unimportant things

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P3 I often talk to strangers

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P4 I often feel unhappy

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P5 I am often irritated

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P6 I often feel inhibited in social interactions

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P7 I take a gloomy view of things

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P8 I find it hard to start a conversation

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P9 I am often in a bad mood

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P10 I am a closed kind of person

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P11 I would rather keep other people at a distance

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P12 I often find myself worrying about something

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P13 I am often down in the dumps

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

P14 When socializing, I don't find the right things to talk about

- False (0)
- Rather false (1)
- Neutral (2)
- Rather true (3)
- True (4)

End of Block: Personality

Start of Block: Information about Hypothyroidism

Q135
Information

We are interested in exploring your views on topics that often appear within patient forums.

*Some statements may be affected by social distancing measures due to the Coronavirus pandemic. Please answer based on your **typical** experience, not based on measures you may have needed to take due to the pandemic.*

I1 Please indicate whether you think the following statements are true or false. Please answer based on your own opinion. Note that the following statements **ARE NOT** medical statements. You should always follow the advice of your doctor. Experts have varying opinions about the statements that follow. We would like to hear yours.

	True (1)	False (2)	Don't know (99)
Untreated hypothyroidism can cause daily fluctuations of symptoms (I1a)	○	○	○
A patient with a normal thyroid blood test does not need to be treated with thyroid hormones (even if they have positive thyroid antibodies and symptoms) (I1b)	○	○	○
It's safe to be slightly over-treated with thyroid hormones (e.g. having a TSH below the normal range) (I1c)	○	○	○
Body temperature is the best method for diagnosing hypothyroidism (I1d)	○	○	○
Most patients with untreated hypothyroidism also have problems with their adrenal glands (I1e)	○	○	○

Q124
The correct answers to the questions that you were asked about on the previous page are below.

TITLE ANSWER Untreated hypothyroidism can cause daily fluctuations of symptoms FALSE A patient with a normal thyroid blood test does not need to be treated with thyroid hormones (even if they have positive thyroid antibodies and symptoms) TRUE It's safe to be slightly over-treated with thyroid hormones (e.g. having a TSH below the normal range) FALSE Body temperature is the best method for diagnosing hypothyroidism FALSE Most patients with untreated hypothyroidism also have problems with their adrenal glands FALSE

I2 Please indicate whether you think the following statements are true or false. Please answer based on your own opinion. Note that the following statements **ARE NOT** medical statements. You should always follow the advice of your doctor. Experts have varying opinions about the statements that follow. We would like to hear yours.

	True (1)	False (2)	Don't know (99)
Hypothyroid patients need to take iodine supplements even if they are already taking thyroid hormone (I2a)	○	○	○
Having untreated hypothyroidism weakens the immune system and makes people prone to infection (I2b)	○	○	○
Hypothyroid patients can lose weight if adequately treated (I2c)	○	○	○
You can manage your hypothyroidism without medication, just by watching what you eat (I2d)	○	○	○
Hypothyroidism is an infectious disease (I2e)	○	○	○

Q125
The correct answers to the questions that you were asked about on the previous page are below.

TITLE ANSWER Hypothyroid patients need to take iodine supplements even if they are already taking thyroid hormone FALSE Having untreated hypothyroidism weakens the immune system and makes people prone to infection FALSE Hypothyroid patients can lose weight if adequately treated TRUE You can manage your hypothyroidism without medication, just by watching what you eat FALSE Hypothyroidism is an infectious disease FALSE

I3 To what extent do you use social media and the internet to find out information about your **hypothyroidism**?

- Daily (1)
- Once or twice a week (2)
- Once a month (3)
- Less than once a month (4)
- Never (5)

End of Block: Information about Hypothyroidism

Start of Block: About you 2

Description **About you**

Q123 How old are you?

- 18-30 years (1)
- 31-40 years (2)
- 41-50 years (3)
- 51-60 years (4)
- 61-70 years (5)
- 71-80 years (6)
- 81 years or over (7)

A5 Please indicate your household status.

- Married/in a civil partnership/living with a partner (1)
- Single/divorced/widowed and living alone (2)
- Single/divorced/widowed and living with others (e.g. my parents, my children, and/or other adults) (3)
- Other (Please specify) (4) _____
- Prefer not to say (5)

A6 Which statement best describes your employment status? If you are retired, disabled, or a student and are also working, then please choose the option 'Working (full time or part time)'.

- Working (full time, part time) (1)
- On maternity/parental leave (2)
- Not working - looking for work (3)
- Not working - retired (4)
- Not working - disabled/ on long-term sickness (5)
- Not working - Other (6)
- Full time carer (7)
- Student (8)
- Prefer not to say (9)
- Other (Please specify (10) _____

A7 Which of these best describes your ethnic background?

- White (1)
- Mixed/multiple ethnic groups (2)
- Asian (3)
- Black/African/Afro-Caribbean (4)
- Middle Eastern/Arab (5)
- Latino (descended from Latin America) (6)
- Native American/Pacific Islander (7)
- Other (Please specify) (8) _____
- Prefer not to say (9)

A8 How many years of education have you obtained? (Please include all education from primary/elementary through any secondary, vocational, university, and post-graduate education).

- Under 4 years (1)
- 4-8 years (2)
- 9-12 years (3)
- 13-16 years (4)
- 17-20 years (5)
- Over 20 years (6)
- Prefer not to say (7)

A9 How would you rate your household economic status (e.g. income, living conditions) compared to your country's average?

- Well above average (1)
- Above average (2)
- Average (3)
- Below average (4)
- Well below average (5)
- Don't know (6)
- Prefer not to say (7)

End of Block: About you 2

Start of Block: Optional Feedback

E1 If you would like to share any additional thoughts or feedback about your hypothyroidism treatment and care, please enter your comments in the box below.

Otherwise, please click to the next page in order to submit your responses and complete this survey.

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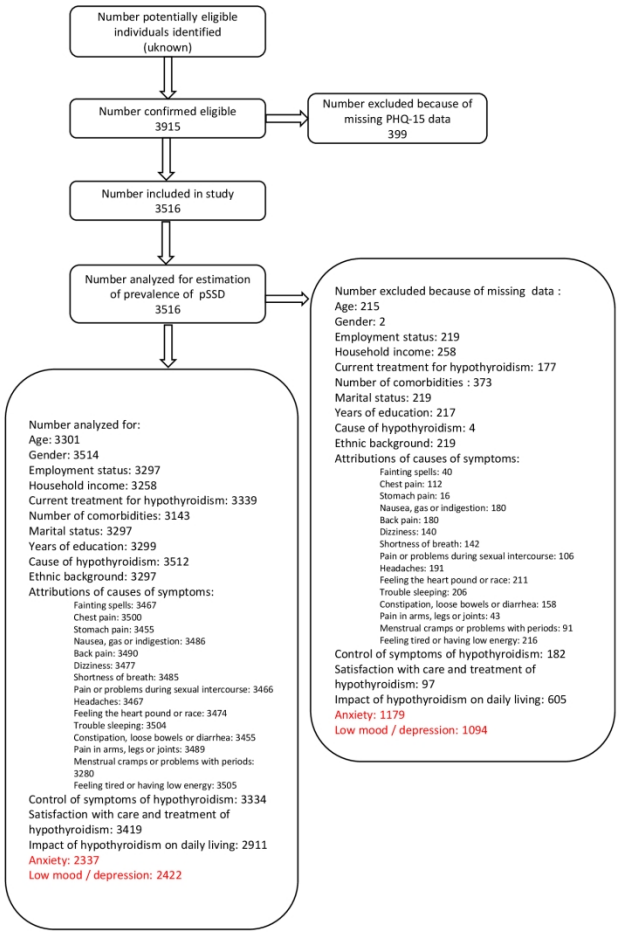

Supplementary Figure 1

Flow diagram showing number potentially eligible individuals identified, number confirmed eligible, number included in the study, and number analyzed.

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