Why are GPs treating subclinical hypothyroidism?

Allport, Jack; McCahon, Deborah; Hobbs, Frederick; Roberts, Lesley M

DOI:
10.1017/S1463423612000230

Document Version
Publisher's PDF, also known as Version of record

Citation for published version (Harvard):
Allport, J, McCahon, D, Hobbs, F & Roberts, LM 2013, 'Why are GPs treating subclinical hypothyroidism? Case note review and GP survey', *Primary Health Care Research & Development*, vol. 14, no. 2, pp. 175-84. https://doi.org/10.1017/S1463423612000230

Primary Health Care Research & Development 2013; **14**: 175–184
doi:10.1017/S1463423612000230

RESEARCH

Why are GPs treating subclinical hypothyroidism? Case note review and GP survey

Jack Allport[1], **Deborah McCahon**[2], **F.D. Richard Hobbs**[3] and **Lesley M. Roberts**[4]

[1]Foundation Year Doctor, Care of Primary Care Clinical Sciences, School of Health and Population Sciences, University of Birmingham, UK
[2]Research Fellow, Primary Care Clinical Sciences, School of Health and Population Sciences, University of Birmingham, UK
[3]Head of Department, Department of Primary Health Care, University of Oxford, 2nd Floor, 23-38 Hythe Bridge Street, Oxford, UK
[4]Senior Lecturer, Primary Care Clinical Sciences, School of Health and Population Sciences, University of Birmingham, UK

Background: Subclinical hypothyroidism (SCHo) is a common biochemical diagnosis in older age. Evidence of impact is inconclusive and guidelines are inconsistent. With increasing numbers of thyroid function tests (TFTs) performed, GPs frequently have to make management decisions regarding this diagnosis. However, little is known about how SCHo is currently being managed in primary care. **Aim:** To explore management of SCHo in primary care and GP reported rationale for treatment of SCHo in older individuals. **Design:** Descriptive study using retrospective case note review and GP survey. **Setting:** Nineteen General Practices, Central England, UK. **Methods:** Follow-up of a large cohort with subsequent detailed review of individuals for whom therapy had been initiated following diagnosis of SCHo. Data on practice policies, and rationale behind treatment were collected via GP questionnaire. **Results:** Forty-two individuals were treated following identification of SCHo. Factors regarded as supporting instigation of therapy recorded by practitioners included symptoms, a positive antithyroid antibody test and history of radioiodine therapy. In all, 55% were registered at 3/19 practices suggesting significant between practice variation. Reasons for testing included chronic disease check-up ($n = 14$), presenting 'thyroid symptoms' ($n = 5$) and presenting other symptoms ($n = 9$). Reasons for therapy initiation were only recorded in 26 cases and included presence of symptoms, persistently high or increasing serum thyroid stimulating hormone concentration and patient request. Only 2/15 GPs reported having practice guidelines on management. **Conclusion:** Results suggest that GPs are uncertain how to interpret symptoms and TFT results in older individuals. There is considerable variation in management of SCHo between GPs with some GPs treating patients outside of all guideline recommendations.

Key words: aged; hypothyroidism; primary health care; thyroid function tests; thyroxine

Received 6 February 2012; revised 22 March 2012; accepted 16 April 2012; first published online 1 August 2012

Background

Subclinical hypothyroidism (SCHo) is a biochemical diagnosis characterised by a raised serum thyrotrophin concentration (thyroid stimulating hormone (TSH)) accompanied by a normal concentration of free thyroxine (FT4) and is found frequently in older age (Wiersinga, 1995; Ross, 2001; Wilson *et al*., 2006). Recent estimates suggest a UK prevalence of 2.6%–3.1% in individuals aged 65 years and above (Wilson *et al*., 2006). Diagnostic rates are unknown and are likely to rise due to both

Correspondence to: Dr Deborah McCahon, Primary Care Clinical Sciences, University of Birmingham, Birmingham, West Midlands B15 2TT, UK. Email: d.Mccahon@bham.ac.uk

an aging population and an increasing use of thyroid function tests (TFTs) to rule out thyroid dysfunction, with recent data showing that 10 million TFTs are performed each year in the United Kingdom with the majority of requests being generated in primary care (Association for Clinical Biochemistry, British Thyroid Association and British Thyroid Foundation, 2006).

The clinical manifestation and consequences of overt hypothyroidism are well established and can be successfully treated through administration of thyroxine replacement therapy. In contrast, there is a lack of consensus with respect to the pathophysiological consequences of SCHo particularly in older individuals. Although SCHo is essentially a biochemical diagnosis, some studies have reported a greater prevalence of symptoms in patients with SCHo compared with age matched euthyroid controls (Zulewski *et al*., 1997; Canaris *et al*., 2000; Meier *et al*., 2001).

Others have suggested an association between SCHo and raised serum lipids (Danese *et al*., 2000), cardiac dysfunction (Biondi *et al*., 1999; Monzani *et al*., 2001) and increased cardiac and all-cause mortality (Rodondi *et al*., 2010). However, other data show that raised TSH concentration confers a survival benefit in octogenarians (Gussekloo *et al*., 2004). The main argument advanced for treatment of SCHo is the risk of progression to overt hypothyroidism with progression rates varying from 2% to 17% (Gordin and Lamberg, 1981; Nystrom *et al*., 1988; Parle *et al*., 1993; Vanderpump *et al*., 1995). Risk of progression is further enhanced in the presence of antithyroid antibodies and with increasing serum thyrotrophin concentration (Surks *et al*., 2004). With respect to treatment of SCHo, trials have generally been small, with some reporting an improvement in symptoms and others failing to demonstrate any clinical benefits (Cooper *et al*., 1984; Nystrom *et al*., 1988; Jaeschke *et al*., 1996; Meier *et al*., 2001; Razvi *et al*., 2007; Parle *et al*., 2010). In older individuals the benefits of treatment must be balanced against the additional risks associated with polypharmacy.

Overall, evidence relating to SCHo remains inconclusive and deemed insufficient to justify population screening or routine treatment. Recommendations and guideline documents pertaining to management of SCHo are inconsistent, being based upon consensus opinion (see Table 1; Vanderpump *et al*., 1996; Adlin, 1998; Surks *et al*., 2004; Association for Clinical Biochemistry, British Thyroid Association and British Thyroid Foundation, 2006; Mayo Clinic, 2007; Villar *et al*., 2007; NHS Clinical Knowledge Summaries, 2010). Few data are available on how these recommendations are taken up in routine care or how SCHo is managed, and the aim of this study is therefore to describe these.

Methods

In 2002–2003, the Birmingham Elderly Thyroid Study (BETS) recruited 5881 individuals aged 65 years or more from 20 practices in central England. A few patients were excluded on the grounds of lack of capacity or serious illness, but in all other respects the cohort represents a community dwelling elderly population with 68% of invited individuals participating. Full details of the BETS cohort have been reported elsewhere (Wilson *et al*., 2006).

Follow-up and re-screening of thyroid function in this cohort (BETS2), excluding patients with overt thyroid dysfunction, was undertaken in 19 of the original 20 practices after an interval period of approximately five years. Overall, 3005 individuals from the baseline cohort participated in follow-up (BETS2).

Thyroid function was defined by the TFT results at re-screen or at initiation of thyroxine replacement therapy where this had occurred in the interval period between BETS1 and BETS2. TFTs were extracted from GP records and tests may have been performed in a variety of laboratories. Thyroid function was categorised as overt hyperthyroid, subclinical hyperthyroid, euthyroid, subclinical hypothyroid or overt hypothyroid in accordance with standard reference criteria of the main laboratory serving this GP area. Classification was based purely on TFT result and did not include consideration of symptoms. All BETS2 participants who had commenced thyroxine replacement therapy following a SCHo test result (defined by a TSH concentration above reference range and FT4 within reference range), in the period between screening for BETS1 and BETS2, were eligible for inclusion in the current study.

Review of guideline documents and statements of expert opinion informed development of the case report form and defined data to be extracted

Table 1 Summary of current guidelines

Guidelines/review	Screening	Diagnosis	Treatment	Factors to consider
British Thyroid Association (Association for Clinical Biochemistry, 2006)	Not in healthy population Case finding can be appropriate: women at menopause or with non-specific symptoms	Raised TSH and normal FT4, with repeat; 3–6/12 later	TSH > 10, treatment is recommended TSH > 10, monitor every three years or annually if antibody positive. A therapeutic trial of thyroxine can be considered	Goitre, pregnancy and rising TSH
ATA, AACE and Endocrine Society Consensus (Surks *et al.*, 2004)	Recommends against population screening Aggressive case finding: high-risk groups, symptomatic patients or goitre	Raised TSH and normal FT4	TSH > 10, treatment is reasonable TSH > 10, monitoring every 6–12 months Antibody testing not recommended as it does not alter management	Pregnancy
NHS Clinical Knowledge Summaries (NHS Clinical Knowledge Summaries, 2010)	Not in asymptomatic patients Case finding: goitre, sub-fertility, hyperlipidaemia or diabetes. Pregnant women with a family history Annually: radioiodine, thyroid surgery, Lithium or Amiodarone	Raised TSH and normal FT4, with repeat 3-6/12 later.	TSH > 10 treatment is recommended TSH > 10, treatment not recommended, a therapeutic trial may be appropriate in symptomatic patients	Goitre and rising TSH
RCP Consensus Statement (Vanderpump *et al.*, 1996)	Unjustified in general population Case finding: pregnant women with type 1 DM, radioiodine, thyroid surgery, Lithium or Amiodarone	Raised TSH and normal FT4 with no symptoms	Treatment recommended if antibody positive TSH > 10, monitoring is advised	
American Association of Family Practice (Adlin, 1998)	Patients >60 years should be screened	Raised TSH and normal FT4	TSH > 10, treat if symptomatic or antibody positive TSH > 10, monitor every six months	
Mayo Clinic (Mayo Clinic, 2007)	ATA suggests screening every five years for patients over 35 years of age ACP recommends screening women over 50 years of age	Raised TSH and normal FT4, after ruling out non-thyroidal illness	TSH > 10, expert opinion is to treat TSH > 10, treatment based on clinical judgement	Pregnancy, goitre, young, mood disorder, infertility, antibodies, rising TSH and hyperlipidaemia
Cochrane Review (Villar *et al.*, 2007)			Clinical judgement and patient preference remain the best manner to decide	

ATA = American Thyroid Association; AACE = American Association of Clinical Endocrinologists; RCP = Royal College Physicians; DM = Diabetes Mellitus; ACP = American College of Physicians; NHS = National Health Service; TSH = thyroid stimulating hormone; FT4 = free thyroxine.

from the primary care records. The data collection period was defined as the interval between baseline thyroid function screening (BETS1) and commencement of treatment. All consultations during this interval period were reviewed and data extracted. Data extraction focused upon 12 symptoms suggestive of overt hypothyroidism (muscle weakness, muscle cramps, weight gain, cold intolerance, constipation, lethargy, cognitive impairment, dry skin, poor memory, hoarse voice, deep voice and facial oedema) and nine other thyroid relevant patient factors or clinical characteristics (goitre, TSH concentration >10 mI/UL, depression, abnormal lipid concentrations, advancing age, high cardiovascular risk score, family history of hypothyroidism, positive test for antithyroid antibodies and patient requested TFT). TFT dates, results and entire records of the consultation that triggered requests for TFT and each subsequent discussion related to initiation of replacement therapy were extracted.

Consultations were classified as 'thyroid relevant' or not according to the reason for the consultation. Thyroid relevant consultations were further categorised on the basis of two key decisions (i) to perform a TFT or (ii) to commence thyroxine replacement therapy. Patient demographics, including age, gender and index of multiple deprivation (IMD score 2004; a measure of deprivation; Noble *et al*., 2010) were obtained from the original study database.

In addition to case note review, one GP (the research lead) in each of the participating BETS practices was invited to complete a study questionnaire. The GP questionnaire was devised specifically to ascertain whether differences in practice policies or routine procedures existed and to identify which symptoms and/or other patient characteristics were perceived to influence clinical decision making with respect to management of SCHo in older individuals. The questionnaire consisted of 10 questions with categorical options and a free text section for comments.

Statistical analysis

Data were entered into a Microsoft Access database and analysed using the Statistical Packages for Social Sciences (SPSS-17) Windows package. All free text was reviewed and coded to enable numerical content analysis. Data were summarised using means with standard deviation (SD) and corresponding range for data that were normally distributed and median with interquartile range (IQR) for data that were not normally distributed to describe current practice.

Results

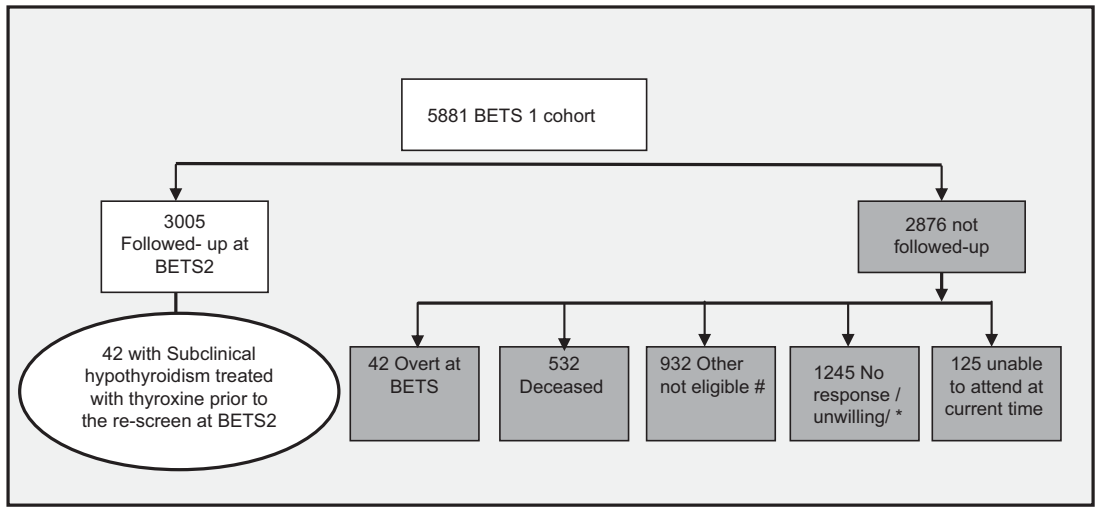
Of the 3005 individuals followed up, 42 had commenced thyroxine replacement therapy following an earlier test result indicating SCHo and were therefore eligible for inclusion in the current study (see Figure 1). These patients were registered at 14 of the 19 participating general practices with three practices accounting for 55% of such cases. Most (71.4%) were female and the mean age was 76.5 years (SD 5.49, range 66.8–88.3). Deprivation scores (IMD 2004 score) ranged from 3.8 (least deprived) to 60.8 (most deprived) with a median score of 14.6 (IQR 22.16).

The mean interval period between baseline thyroid function screening (BETS1) and initiation of thyroxine replacement therapy was 2.52 years (range 0.17–4.45 years), giving a total follow-up of 105.8 patient years. During the interval period between baseline screening and commencement of therapy, a total of 854 consultations were recorded for these individuals; 17.4% ($n = 149$) of these consultations were deemed to be 'thyroid relevant', with a median number of 3.0 (IQR 3, range 1–14) thyroid relevant consultations being recorded per patient. Overall, 119 tests were undertaken between baseline screen and initiation of thyroxine therapy with 59 of these being repeat tests after an initial subclinical result had been received by the practice, equating to 1.4 confirmatory tests per patient before initiation of treatment.

Requests for thyroid function testing

Indications for the index TFT (the test that first indicated SCHo) were identified and recorded (see Table 2). The BETS baseline screening TFT was the index TFT for eight individuals and no justification for conducting the index TFT was recorded for 4/42 patients (Table 2).

Repeat TFTs were requested with a median interval of 102 days (IQR 157.5, range 4–803) following a result indicating euthyroid function



Includes participants of BETS1 follow on trial who were subject to intervention outside of usual practice, patients with unclassifiable thyroid function, patients excluded by their GP, 1 practice that did not participate in follow-up screening and patients no longer registered with participating practices.

*Includes not available for follow-up (non-responding, non-contactable, unwilling to participate and non-consenting patients)

Figure 1 Consort diagram defining study population. BETS = Birmingham Elderly Thyroid Study.

and 96 days (IQR 136.5, range 4–412) after a result indicating SCHo. Documented reasons for repeating TFTs are presented in Table 2.

Initiation of thyroxine replacement therapy

Thyroxine replacement therapy was initiated in 32 (76%) patients following two TFTs confirming SCHo. In 10 patients, replacement therapy was initiated on the basis of a single TFT. TSH concentrations at the point of initiation of therapy are presented in Figure 2. Median TSH was 7.1 mIU/L (IQR 3.25, range 4.55–79.7) and median FT4 was 12.4 pmol/L (IQR 3.38, range 10.0–20.3). Reasons for initiation of thyroxine therapy were only documented for 26 of the 42 patients (61.9%) and are presented in Table 2. Prior to initiation of thyroxine replacement therapy measurement of antithyroid antibody was undertaken for six patients (five having a positive antibody titre).

GP questionnaire

Overall 15/19 (79%) GPs representing 15 practices, completed and returned the study questionnaire. Two (13%) GPs reported having practice guidelines for management of SCHo. Most GPs (67%; 10/15), however, reported discussing management strategies with colleagues, with 6/15 (40%) reporting having general discussion to clarify usual practice and/or regarding specific patients.

Of the 12 symptoms suggestive of overt hypothyroidism that could trigger a request for TFT or influence the decision to initiate thyroxine, 91% of GPs stated that presence of cold intolerance and 82% that cognitive dysfunction or weight gain would trigger a TFT request (Table 3). Combinations of symptoms increased likelihood of GPs requesting a TFT and are presented in Table 3. One GP reported that TFT was routinely conducted in patients aged 65 years of age or more. When asked about their prescribing practice, 12 (80%) GPs reported 'sometimes' prescribing thyroxine replacement therapy for SCHo. Three responded that they had 'never' initiated treatment for SCHo, however, three GPs (20%) reported being aware of other GPs who routinely treated this borderline state (see Table 3).

Twelve (92%) GPs reported that a serum TSH concentration >10 mIU/L would influence their decision to commence treatment for SCHo. The

Table 2 Documented reasons for performing TFTs and initiation of thyroxine replacement therapy

Reasons for performing TFTs	Index TFT (diagnosing subclinical hypothyroidism; $n = 42$ (%))	Reason for subsequent TFTs ($n = 59$ (%))
Missing/no specific reason documented	4 (9.5)	4 (6.7)
Baseline screening TFT in BETS I	8 (19.0)	N/A
Presence of symptoms suggestive of hypothyroidism	5 (11.8)	4 (6.7)
Presence of non-specific symptoms	9 (21.4)	6 (10.2)
Routine chronic disease review clinic	14 (33.3)	9 (15.3)
Monitoring of prescribed iodine rich medication	1 (2.4)	3 (5.1)
Monitoring of subclinical hypothyroidism	N/A	33 (56.0)
Family history	1 (2.4)	N/A
Reasons for initiation of thyroxine replacement therapy (documented for 26/42 patients)	TSH < 10 mIU/L (19 patients; *n* (%))	TSH > 10 mIU/L (7 patients; *n* (%))
Symptomatic (thyroid related symptoms)	12 (63.2)	4 (57.1)
Therapeutic trial	6 (31.6)	–
FT4 'low normal'	5 (26.3)	–
TSH 'rising'	4 (21.1)	–
Positive antithyroid antibody test	3 (15.8)	–
Patient request	2 (10.5)	1 (14.3)
TSH 'persistently raised'	2 (10.5)	1 (14.3)
History of radioiodine therapy	1 (5.3)	1 (14.3)
On Amiodarone	1 (5.3)	1 (14.3)
Other	2 (10.5)	2 (28.6)

TFT = thyroid function test; BETS = Birmingham Elderly Thyroid Study; TSH = thyroid stimulating hormone; FT4 = free thyroxine.

presence of antithyroid antibodies (77%, $n = 10$), raised serum lipid concentrations (62%, $n = 8$), goitre (39%, $n = 5$), family history (39%, $n = 5$) and depression (31%, $n = 4$) were also factors reported to be likely to effect GP decision making. Seven GPs reported that patient requests for treatment were important considerations and two suggested that decision making is influenced by age >80 years and presence of cardiovascular disease.

Discussion

Summary of the main findings

This study reviewed the routine primary care records of 42 elderly patients prescribed thyroxine replacement therapy in response to a TFT result suggestive of SCHo to identify all thyroid relevant consultations and examine indications for TFT and initiation of treatment. Eight hundred and fifty-four individual consultations were reviewed to capture all relevant data. A survey was also conducted to further explore GP rationale for diagnosing and managing SCHo in patients aged 65 years or more.

The study showed considerable variation in routine practice and between practices in the way GPs manage elderly patients with SCHo, with five practices not having initiated treatment on the basis of a subclinical result for any patient within the cohort and three practices accounting for 55% (23/42) of treated cases. This study is unable to comment on whether symptom burdens do differ between practices and this may in part account for the variation in practice. Importantly, GP responses suggest that GPs are uncertain how to manage SCHo in older individuals and that management strategies are largely intuitive due to a lack of clear evidence-based guidance to support decision making, highlighting an important training need.

In the current study, opportunistic thyroid function testing, undertaken during routine chronic disease clinics or due to presence of no specific symptoms lead to diagnosis of SCHo in more than

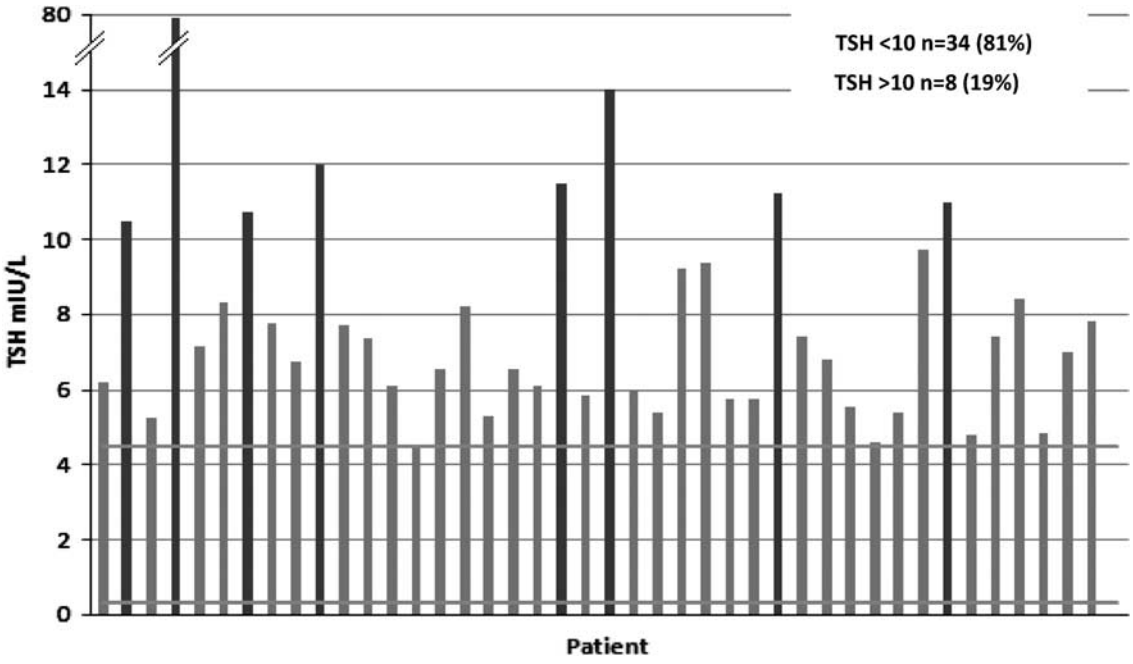


Figure 2 Serum thyrotrophin concentrations immediately prior to initiation of thyroxine replacement therapy. TSH = thyroid stimulating hormone.

Table 3 GP responses to questions relating to symptoms influencing management decisions

Proportion of GPs reporting that in a patient aged 65 years or more they would	request a TFT based upon presence of the symptom in isolation, % (*n*)	request a TFT based upon presence of the symptom accompanied by any other symptom, % (*n*)	initiate T4 based upon the presence of the symptom accompanied by any other symptom, % (*n*)
Cognitive impairment	81.8 (9)	100 (14)	81.8 (9)
Poor memory	72.7 (8)	100 (14)	63.6 (7)
Weight gain	81.8 (9)	92.9 (13)	63.6 (7)
Lethargy	63.6 (7)	92.9 (13)	81.8 (9)
Cold intolerance	90.9 (10)	92.9 (13)	54.5 (6)
Constipation	45.5 (5)	85.7 (12)	45.5 (5)
Muscle weakness	54.5 (6)	78.6 (11)	36.4 (4)
Hoarse voice	54.5 (6)	78.6 (11)	45.5 (5)
Dry skin	45.5 (5)	78.6 (11)	54.5 (6)
Deep voice	36.4 (4)	71.4 (10)	36.4 (4)
Facial oedema	36.4 (4)	57.1 (8)	36.4 (4)
Muscle cramps	36.4 (4)	42.9 (6)	36.4 (4)
Any of the above if impacting on quality of life	N/A	N/A	54.5 (6)

TFT = thyroid function test.

50% of cases. In only 12% of cases, the index TFT diagnosing SCHo was triggered by the presence of symptoms suggestive of hypothyroidism. Following this biochemical diagnosis, GPs used a combination of monitoring and treatment to manage SCHo. TFTs were frequently and repeatedly requested

during the interval period between initial diagnosis and initiation of treatment with an average of 1.4 additional TFTs being conducted per patient during a mean interval period of 2.5 years. Repeated tests were triggered by a variety of patient factors, with monitoring of SCHo being the reason for 56% of the TFTs performed and presentation of symptoms. In terms of frequency of TFTs, shorter interval periods between TFTs were observed following results indicating higher serum concentration of thyrotrophin compared with results demonstrating borderline concentrations.

These findings are consistent with data reported in other studies. Following examination of data from a large healthcare database, Meyerovitch *et al.* reported an average frequency of three GP requested TFTs per person during a period of five years with an increased rate of testing with advancing age (Meyerovitch *et al.*, 2007). In a similar study, a range of between 0 and 5 requests for TFTs were observed over a period of 12 months in individuals with SCHo (Gibbons *et al.*, 2010). This is in line with the median repeat interval of 96 days after an initial subclinical result observed in this study.

Few GPs in the current study reported using practice guidelines for routine management of SCHo. Most reported that their decision to initiate thyroxine replacement therapy was made on a case-by-case basis, driven predominantly by presence of symptoms suggestive of overt hypothyroidism. However, on the basis of the case review, only 12% of patients had thyroid symptoms recorded prior to the initial TFT. Unsurprisingly given the lack of consistency in guideline and recommendation papers, GP's decision making in this study appears to reflect a lower threshold for treating than intended by guidelines, for example, in 81% of cases GPs chose to initiate thyroxine therapy based upon a serum thyrotrophin concentration below 10 mIU/L and treatment was frequently initiated on the basis of a single subclinical result (24%). Findings from focus group research in New Zealand suggests that in the absence of guidelines or evidence to direct testing and treatment, GPs management decisions were based on a host of factors, including patient wishes, maintenance of a good doctor–patient relationship and medicolegal issues, and were not always based on symptom presentations or other clinical factors (Gibbons *et al.*, 2009). Data from the current study demonstrate that UK GPs adopt a similar non-evidence-based approach to management of SCHo in elderly individuals.

Limitations

The primary limitation of this study is the reliance upon retrospective routine clinical data recorded in the patient's medical records (Mistry *et al.*, 2005). Full data capture for some patients was not possible because the reasons for the test request or initiation of treatment were not documented. Furthermore, data may be inaccurate and/or incomplete due to documentation of only those factors considered relevant to the investigation or treatment undertaken. Inclusion of the GP questionnaire however enhanced data collection and corroborated findings of the case note review.

This study did not aim to systematically identify why GPs treat some patients with SCHo and not others, but it is likely that recording in consultations where treatment is initiated differs from recording in consultations where prescribing does not occur. Bias introduced by such a retrospective comparison is likely to have restricted the value of a control group. Identification of all individuals who had TFTs in the interval period could have enabled further consideration of this issue. This does not detract from the main findings of significant practitioner variability, little adherence to published recommendations in determining treatment decisions and a clear call from GPs for unified and consistent guidelines.

Routine practice with respect to TFT and management of SCHo within these 19 practices may be atypical as all participating practices had previously taken part in a larger programme of research exploring thyroid dysfunction in the elderly and therefore had interest in the research topic. The significant variation observed between practices suggest this is unlikely to be the case, but arguably interested practices are likely to be demonstrating more informed practice and the observed lack of adherence to recommendations is likely to be even more evident elsewhere. Follow-up of this cohort was not planned when the initial 2002–2003 study was undertaken. We therefore feel that management of patients in the interval period has been conducted in a largely naturalistic setting and the variation between practices is a real observation.

Conclusion

GPs are uncertain how to manage SCHo in older individuals and strategies for management of SCHo in the community therefore vary. Repeat tests are conducted with varying frequency, which is not informed by evidence, and thyroxine is prescribed for varying reasons with limited scientific rationale. These findings further demonstrate a clear need for definitive evidence-based guidelines to support GP decision making and to standardise management of SCHo in the community.

Acknowledgements

The authors would like to thank the patients and GPs who participated and also the general practice staff who facilitated collection of data. The co-investigators for BETS1 and/or BETS2 are Prof. Jayne Franklyn, Dr Michael Gammage, Dr Sayeed Haque, Mr Roger Holder, Prof. James Parle, Dr Helen Pattison, Mrs Andrea Roalfe and Prof. Sue Wilson. The study was designed by L.M.R., J.A. and DM and funding was secured by L.M.R. and F.D.R.H. J.A. and D.M. undertook management of the study, including overseeing data collection and management and quality assurance. J.A. undertook all analyses. All authors contributed to data interpretation. JA wrote the first draft of this paper and all authors were responsible for subsequent critical revision of the manuscript. D.M. is the corresponding author for this paper. This study was funded by the NIHR via the National School for Primary Care Research. J.A. was supported via funding from the Intercalated BMedSc Research Funding provided by the College of Medical and Dental Sciences, University of Birmingham and also from the Primary Care Research Trust. North Staffordshire Research Ethics Committee Ref. 07/H1204/136.

Reference

Adlin, V. 1998: Subclinical hypothyroidism: deciding when to treat. *American Family Physician* 57, 776–80.

Association for Clinical Biochemistry, British Thyroid Association and **British Thyroid Foundation.** 2006: UK Guidelines for the use of thyroid function tests [online]. Retrieved April 2012 from http://www clinbiochem.info/tftguide2006 pdf

Biondi, B., Fazio, S., Palmieri, E.A., Carella, C., Panza, N., Cittadini, A., Bone, F., Lombardi, G. and **Sacca, L.** 1999: Left ventricular diastolic dysfunction in patients with subclinical hypothyroidism. *Journal of Clinical Endocrinology & Metabolism* 84, 2064–67.

Canaris, G.J., Manowitz, N.R., Mayor, G. and **Ridgway, E.C.** 2000: The Colorado thyroid disease prevalence study. *Archives of Internal Medicine* 160, 526–34.

Cooper, D.S., Halpern, R., Wood, L.C., Levin, A.A. and **Ridgway, E.C.** 1984: L-Thyroxine therapy in subclinical hypothyroidism. A double-blind, placebo-controlled trial. *Annals of Internal Medicine* 101, 18–24.

Danese, M.D., Ladenson, P.W., Meinert, C.L. and **Powe, N.R.** 2000: Clinical review 115: effect of thyroxine therapy on serum lipoproteins in patients with mild thyroid failure: a quantitative review of the literature. *Journal of Clinical Endocrinology & Metabolism* 85, 2993–3001.

Gibbons, V., Lillis, S., Conaglen, J. and **Lawrenson, R.** 2009: The reality of subclinical hypothyroidism in general practice. *Journal of Primary Health Care* 1, 215–21.

Gibbons, V., Conaglen, J.V. and **Lawrenson, R.** 2010: A raised thyroid stimulating hormone result – a 12-month follow-up study in general practice. *Journal of Primary Health Care* 2, 29–34.

Gordin, A. and **Lamberg, B.A.** 1981: Spontaneous hypothyroidism in symptomless autoimmune thyroiditis. A long-term follow-up study. *Clinical Endocrinology (Oxford)* 15, 537–43.

Gussekloo, J., van Exel, E., de Craen, A.J., Meinders, A.E., Frolich, M. and **Westendorp, R.G.** 2004: Thyroid status, disability and cognitive function, and survival in old age. *Journal of the American Medical Association* 292, 2591–99.

Jaeschke, R., Guyatt, G., Gerstein, H., Patterson, C., Molloy, W., Cook, D., Harper, S., Griffith, L. and **Carbotte, R.** 1996: Does treatment with L-thyroxine influence health status in middle-aged and older adults with subclinical hypothyroidism? *Journal of General Internal Medicine* 11, 744–49.

Mayo Clinic. 2007: Practical approach to the treatment of subclinical hypothyroidism [online]. Retrieved April 2012 from http://www.mayoclinic.org/mcitems/mc5000-mc5999/mc5810-1206.pdf

Meier, C., Staub, J.J., Roth, C.B., Guglielmetti, M., Kunz, M., Miserez, A.R., Drewe, J., Huber, P., Herzog, R. and **Muller, B.** 2001: TSH-controlled L-thyroxine therapy reduces cholesterol levels and clinical symptoms in subclinical hypothyroidism: a double blind, placebo-controlled trial (Basel Thyroid Study). *Journal of Clinical Endocrinology & Metabolism* 86, 4860–66.

Meyerovitch, J., Rotman-Pikielny, P., Sherf, M., Battat, E., Levy, Y. and **Surks, M.I.** 2007: Serum thyrotropin measurements in the community: five-year follow-up in a large network of primary care physicians. *Archives of Internal Medicine* 167, 1533–38.

Mistry, H., Buxton, M., Longworth, L., Chatwin, J. and **Peveler, R.** 2005: Comparison of general practitioner records and patient self-report questionnaires for estimation of costs. *European Journal of Health Economics* 6, 261–66.

Monzani, F., Di Bello, V., Caraccio, N., Bertini, A., Giorgi, D., Giusti, C. and **Ferrannini, E.** 2001: Effect of levothyroxine on cardiac function and structure in subclinical hypothyroidism: a double blind, placebo-controlled study. *Journal of Clinical Endocrinology & Metabolism* 86, 1110–15.

National Health Service (NHS) Clinical Knowledge Summaries. 2010: Hypothyroidism [online]. Retrieved April 2012 from http://www.cks.nhs.uk/hypothyroidism

Noble, M., Wright, G. and **Dibben, C.** 2010: The English indices of deprivation 2004 (revised) [online]. Retrieved April 2012 from http://www.communities.gov.uk/documents/communities/pdf/131209.pdf

Nystrom, E., Caidahl, K., Fager, G., Wikkelso, C., Lundberg, P.A. and **Lindstedt, G.** 1988: A double-blind cross-over 12-month study of L-thyroxine treatment of women with 'subclinical' hypothyroidism. *Clinical Endocrinology* 29, 63–75.

Parle, J.V., Franklyn, J.A., Cross, K.W., Jones, S.R. and **Sheppard, M.C.** 1993: Thyroxine prescription in the community: serum thyroid stimulating hormone level assays as an indicator of under treatment or over treatment. *British Journal of General Practice* 43, 107–109.

Parle, J., Roberts, L., Wilson, S., Pattison, H., Roalfe, A., Haque, MS., Heath, C., Sheppard, M., Franklyn, J.A. and **Hobbs, F.D.** 2010: A randomised controlled trial of the effect of thyroxine replacement on cognitive function in community dwelling elderly subjects with subclinical hypothyroidism: the Birmingham Elderly Study. *Journal of Clinical Endocrinology & Metabolism* 95, 3623–32.

Razvi, S., Ingoe, L., Keeka, G., Oates, C., McMillan, C. and **Weaver, J.U.** 2007: The beneficial effect of L-thyroxine on cardiovascular risk factors, endothelial function, and quality of life in subclinical hypothyroidism: randomised, crossover trial. *Journal of Clinical Endocrinology & Metabolism* 92, 1715–23.

Rodondi, N., den Elzen, W.P., Bauer, D.C., Cappola, A.R., Razvi, S., Walsh, J.P., Asvold, B.O., Iervasi, G., Imaizumi, M., Collet, T.H., Bremner, A., Maisonneuve, P., Sgarbi, J.A., Khaw, K.T., Vanderpump, M.P., Newman, A.B., Cornuz, J., Franklyn, J.A., Westendorp, R.G., Vittinghoff, E., and **Gussekloo, J., Thyroid Studies Collaboration.** 2010: Subclinical hypothyroidism and the risk of coronary heart disease and mortality. *Journal of the American Medical Association* 304, 1365–74.

Ross, D.S. 2001: Serum thyroid-stimulating hormone measurement for assessment of thyroid function and disease. *Endocrinology and Metabolism Clinics of North America* 30, 245–64, vii.

Surks, M.I., Ortiz, E., Daniels, G.H., Sawin, C.T., Col, N.F., Cobin, R.H., Franklyn, J.A., Hershman, J.M., Burman, K.D., Denke, M.A., Gorman, C., Cooper, K.S. and **Weissman, N.J.** 2004: Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. *Journal of the American Medical Association* 291, 228–38.

Vanderpump, M.P., Tunbridge, W.M., French, J.M., Appleton, D., Bates, D., Clark, F., Grimely Evans, J., Hasan, D.M., Rodgers, H. and **Tunbridge, F.** 1995: The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham Survey. *Clinical Endocrinology* 43, 55–68.

Vanderpump, M.P., Ahlquist, J.A., Franklyn, J.A. and **Clayton, R.N.** 1996: Consensus statement for good practice and audit measures in the management of hypothyroidism and hyperthyroidism. The Research Unit of the Royal College of Physicians of London, the Endocrinology and Diabetes Committee of the Royal College of Physicians of London, and the Society for Endocrinology. *British Medical Journal* 313, 539–44.

Villar, H.C., Saconato, H., Valente, O. and **Atallah, A.N.** 2007: Thyroid hormone replacement for subclinical hypothyroidism. *Cochrane Database System Review* CD003419.

Wilson, S., Parle, J.V., Roberts, L.M., Roalfe, A.K., Hobbs, F.D., Clark, P., Sheppard, M.D., Pattison, H.M. and **Franklyn, J.A.** 2006: Prevalence of subclinical thyroid dysfunction and its relation to socioeconomic deprivation in the elderly: a community-based cross-sectional survey. *Journal of Clinical Endocrinology & Metabolism* 91, 4809–16.

Wiersinga, W.M. 1995: Subclinical hypothyroidism and hyperthyroidism. I. Prevalence and clinical relevance. *The Netherlands Journal of Medicine* 46, 197–204.

Zulewski, H., Muller, B., Exer, P., Miserez, A.R. and **Staub, J.J.** 1997: Estimation of tissue hypothyroidism by a new clinical score: evaluation of patients with various grades of hypothyroidism and controls. *Journal of Clinical Endocrinology & Metabolism* 82, 771–76.