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Prevalence of Subclinical Thyroid Dysfunction and Its Relation to Socioeconomic Deprivation in the Elderly: A Community-Based Cross-Sectional Survey

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Context: Population-based screening has been advocated for subclinical thyroid dysfunction in the elderly because the disorder is perceived to be common, and health benefits may be accrued by detection and treatment.

Objective: The objective of the study was to determine the prevalence of subclinical thyroid dysfunction and unidentified overt thyroid dysfunction in an elderly population.

Design, Setting, and Participants: A cross-sectional survey of a community sample of participants aged 65 yr and older registered with 20 family practices in the United Kingdom.

Exclusions: Exclusions included current therapy for thyroid disease, thyroid surgery, or treatment within 12 months.

Outcome Measure: Tests of thyroid function (TSH concentration and free T_4 concentration in all, with measurement of free T_3 in those with low TSH) were conducted.

Explanatory Variables: These included all current medical diagnoses and drug therapies, age, gender, and socioeconomic deprivation (Index of Multiple Deprivation, 2004)

Analysis: Standardized prevalence rates were analyzed. Logistic regression modeling was used to determine factors associated with the presence of subclinical thyroid dysfunction

Results: A total of 5960 attended for screening. Using biochemical definitions, 94.2% [95% confidence interval (CI) 93.8–94.6%] were euthyroid. Unidentified overt hyper- and hypothyroidism were uncommon (0.3, 0.4%, respectively). Subclinical hyperthyroidism and hypothyroidism were identified with similar frequency (2.1%, 95% CI 1.8–2.3%; 2.9%, 95% CI 2.6–3.1%, respectively). Subclinical thyroid dysfunction was more common in females ($P < 0.001$) and with increasing age ($P < 0.001$). After allowing for comorbidities, concurrent drug therapies, age, and gender, an association between subclinical hyperthyroidism and a composite measure of socioeconomic deprivation remained.

Conclusions: Undiagnosed overt thyroid dysfunction is uncommon. The prevalence of subclinical thyroid dysfunction is 5%. We have, for the first time, identified an independent association between the prevalence of subclinical thyroid dysfunction and deprivation that cannot be explained solely by the greater burden of chronic disease and/or consequent drug therapies in the deprived population. **(*J Clin Endocrinol Metab* 91: 4809–4816, 2006)**

SUBCLINICAL THYROID DYSFUNCTION is a biochemical diagnosis, and patients have few, if any, clinical signs or symptoms of thyroid dysfunction (1). Subclinical hypothyroidism is defined by the finding of an elevated serum TSH concentration with serum free T_4 concentration being within the reference range, whereas subclinical hyperthyroidism is defined by a low serum TSH with serum free T_4 and free T_3 concentrations being within the reference range (1, 2).

The relationship between overt hypothyroidism and deficits in cognitive functioning (3) and other clinical end points is relatively well established (4). The potential consequences of subclinical hypothyroidism are much less well established, and although an elevated TSH in the elderly has been recently suggested as conferring a mortality advantage, (4), most of the literature refers to adverse consequences such as the possibility of cardiac dysfunction or adverse cardiac end points (including atherosclerotic disease and cardiovascular mortality) (5), elevation in total and low-density lipoprotein cholesterol (6), systemic or neuropsychiatric symptoms (7), and progression to overt symptomatic hypothyroidism (8). Approximately 4% per year of community-based patients found to have subclinical hypothyroidism are estimated to progress to overt hypothyroidism (8, 9). Subclinical hyperthyroidism may also be associated with adverse cardiac end points (10, 11) including atrial fibrillation (12), cardiac dysfunction, systemic and circulatory disease mortality (13), neuropsychiatric symptoms (14, 15), reduced bone mineral density, and fractures (16, 17). The evidence supporting the progression of subclinical hyperthyroidism to overt hyperthyroidism lacks consensus, available studies tending to be small with study populations having significant heterogeneity (9, 18–21).

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Abbreviations: CI, Confidence interval; IMD, Index of Multiple Deprivation; IQR, interquartile range; OR, odds ratio.

Estimates of the prevalence of subclinical thyroid dysfunction in elderly populations differ substantially and vary according to ethnic group, dietary iodine intake, and the prevalence of antithyroid antibodies (22–25). The prevalence of subclinical hypothyroidism has been estimated, in European and U.S. populations of elderly ambulatory participants, to vary 5-fold from 1.4% in rural Sweden (26) to 7.8% in the Framingham Heart Study (27). Subclinical hypothyroidism appears more common in females (7–18%) than males (2–15%) (22, 25, 28), and the Whickham survey (British survey of adults of all ages) demonstrated an increasing prevalence with age in women, reaching 18% in those aged 74 yr and older, compared with a relatively stable 2–5% in males regardless of age (29). There are fewer studies defining the prevalence of subclinical hyperthyroidism; however, those that are available also show significant variability, estimates in elderly populations ranging from 0.8% (9) to 5.8% (19), although typically quoted prevalences are 1.5% in women and 1% in men over the age of 60 yr (30). Robust estimates of the prevalence of both subclinical hypo- and hyperthyroidism are difficult to derive from the available data because there is significant heterogeneity in the sampling frames and biochemical definitions of subclinical thyroid dysfunction.

There has been a gradual trend toward widespread screening of elderly populations for thyroid dysfunction. Whereas the association between subclinical hyperthyroidism and atrial fibrillation is well established (12, 20, 31), robust data quantifying the association between subclinical hyperthyroidism and other clinical end points is relatively lacking (1). Likewise for subclinical hypothyroidism, evidence for associations with clinically significant end points is generally conflicting and inconclusive (1). Despite some studies indicating improvements in well-being and mental function (32), the results of the available treatment trials with T_4 are not definitive (1). Nevertheless, the existing data prompted some professional bodies to advocate screening for subclinical thyroid dysfunction and treating identified disease (33) in advance of a clear evidence base that demonstrates the efficacy and safety of such strategies (6).

Routine screening should not be introduced unless the benefits have been demonstrated to outweigh the costs (34). In determining the potential of routine screening, the priorities are to determine whether subclinical thyroid dysfunction is of sufficient clinical importance to warrant screening and whether, once these conditions are detected, therapy is justified. These factors are particularly important in the elderly in whom there is increased probability of abnormal results due to other drug therapy/illness and in whom the consequences of inappropriate therapy may be more severe. A variety of nonthyroidal illnesses and drug therapies are associated with abnormal thyroid function test results and recovery from nonthyroidal illness may be associated with a transient rise in TSH (35–38). The present study aimed to address these issues by determining the prevalence of subclinical thyroid dysfunction and unidentified overt thyroid dysfunction and allowing for the confounding effect of major comorbidities and drug therapies. The effect of these potential confounding factors has not been addressed in previous prevalence studies.

Patients and Methods

Participants and settings

The population was selected from 20 family practices within the greater Birmingham area of the United Kingdom, this geographical area being broadly representative of urban areas of England and Wales (39). Practice registers were searched to identify those aged 65 yr or older. To maximize generalizability to routine family practice, subjects taking drugs known to affect thyroid function, such as amiodarone or anticonvulsants, were included. Potential participants were excluded only if: 1) they were currently receiving T_4 (or other thyroid hormone preparation) or antithyroid therapy; 2) during the previous 12 months, they had thyroid surgery, radioiodine therapy, or antithyroid drugs; 3) their family doctor judged that contact was inappropriate (*e.g.* recent bereavement); or 4) they were unable to provide informed consent.

Invitation to participate was by letter; nonresponders received one reminder. A research nurse saw subjects at either the family practice or, for those unfit to travel to the practice, their home. Informed consent was obtained from all participants. The Multi-Center Research Ethics Committee and local research ethics committees provided ethical approval.

Screening assessments

A serum sample was obtained from each subject for testing of thyroid function. There were no restrictions on eating or requests to discontinue medication before testing, and samples were obtained during normal office hours. Serum TSH, free T_4, and free T_3 were measured by chemiluminescent immunoassay (Advia Centaur; Bayer Diagnostics, Newbury, UK). Serum TSH had a laboratory reference range of 0.4–5.5 mU/liter with an interassay coefficient of variation of 4.4–10.9% over the range 0.41–24.5 mU/liter, and the assay was calibrated against the second International Reference Preparation 80/558. The lower limit of reporting for the TSH assay was 0.1 mU/liter and the manufacturer's quoted mean functional sensitivity was 0.019 mU/liter. The laboratory reference range for free T_4 was 9.0–20.0 pmol/liter with an interassay coefficient of variation of 8.2–9.8% over the range 8.2–54.9 pmol/liter. Serum TSH and free T_4 concentrations were determined in all; in those with serum TSH below normal, serum free T_3 (reference range 3.5–6.5 pmol/liter, interassay coefficient of variation of 4.2–6.9% over the range 4.0–16.0 pmol/liter) was also measured. Subjects were categorized according to measurements of serum TSH and free thyroid hormone concentrations as follows: 1) overt hyperthyroidism [serum TSH $<$ 0.4 mIU/liter with raised free T_4 and free T_3 or raised free T_3 alone (T_3-toxicosis)]; 2) subclinical hyperthyroidism (serum TSH $<$ 0.4 mIU/liter with normal free T_4 and free T_3); 3) euthyroid (serum TSH 0.4–5.5 mIU/liter); 4) subclinical hypothyroidism (serum TSH $>$ 5.5 mIU/liter with normal free T_4); or 5) overt hypothyroidism (serum TSH $>$ 5.5 mIU/liter with low free T_4).

All major current medical diagnoses and current drug therapies were recorded based on patient reporting, with validation by inspection of routine family practice records. Diagnoses were then categorized in line with recognized major disease groupings. Similarly, drug therapies previously identified as influencing tests of thyroid function or being indicative of significant medical diagnoses were categorized.

The Index of Multiple Deprivation (IMD) 2004 (40) was used as a proxy measure of multiple deprivation at the small area level (continuous geography areas of ~1500 people). This model of multiple deprivation is based on the idea of distinct dimensions of deprivation, experienced by individuals living in an area that can be recognized and measured separately. People may be counted in one or more of the domains, depending on the number of types of deprivation that they experience. IMD 2004 scores are calculated for each subject based on their place of residence and encompass seven domains of deprivation over local areas of the United Kingdom: income, employment, health deprivation and disability, education skills and training, barriers to housing and services, crime, and living environment. The IMD 2004 is a weighted area level aggregation of these dimensions of deprivation. Lower IMD scores indicate less deprived areas of residence. Ranked data were converted to quartiles for analysis, quartile 1 representing the most affluent group and quartile 4 the most deprived.

Statistical methods

Analyses were undertaken using SAS (version 9.1; SAS Institute, Cary, NC) and STATA (version 7; StataCorp LP, College Station, TX). Prevalence rates were estimated using the observed age- and sex-specific proportions. Subjects were categorized on the basis of their thyroid function test results, as described above, and prevalence rates were directly standardized by age, sex, and deprivation (IMD 2004) to the West Midlands population (39). The categories of overt hyper- and overt hypothyroidism comprised insufficient subjects to enable standardization by deprivation, and therefore, standardization by age and sex alone was used for these categories.

χ^2 tests and Cochrane Armitage tests were used to examine the association and trends for categorical variables. The proportion of people in each of the subclinical hyperthyroid categories was compared with the euthyroid category by means of the binomial exact test of proportions. Kruskal-Wallis tests were used to compare the number of conditions and medications between the thyroid categories.

Logistic regression modeling was also used to predict the factors [age, sex, deprivation score (IMD 2004), major medical diagnoses, current drug therapies, smoking status)] associated with the presence of subclinical thyroid dysfunction. Colinearity and two-way interactions were assessed. Parsimonious models were identified using the backward elimination method.

Sample size

Assuming a prevalence of subclinical thyroid dysfunction of 5% or less, a sample of 5800 participants would enable a precise estimate of prevalence, within 0.6%, to be estimated with 95% confidence. Should the prevalence be as high as 10%, the precision would be within 0.8% with 95% confidence.

Results

Initial searches of the lists of participating family practices identified 17,271 persons aged 65 yr or older; 1,146 (6.6%) were excluded before mailing potential participants because of current or recent treatment for thyroid disease.

Response rates

Of the 16,125 patients invited to participate, 13,406 responded (85% of those eligible), and 6,159 of these (46%) indicated willingness to attend a screening appointment; 5,960 attended. Screening was completed for 5881 patients (Fig. 1), although for nine of these participants, thyroid status could not be categorized biochemically, leaving a final study population of 5,872 subjects.

Higher uptake rates were observed among males, in the younger age groups, and in those from affluent areas. These differential response rates resulted in a final study population that was slightly different from that of the West Midlands region and the United Kingdom as a whole (39) with respect to gender [proportion male: 49.1% (study) *vs.* 42.8% in West Midlands and 42.6% in England], age distribution [aged 65–69 yr: 32.75% (study) *vs.* 28.3% (West Midlands) *vs.* 27.7% (England)], and deprivation score [very affluent: 19.8% (study) *vs.* 19.4% (West Midlands) *vs.* 25.0% (England)].

Sample characteristics

Subject characteristics are shown in Table 1. Participants were aged 65–98 yr (mean 73.1 yr, SD 5.6) and 2980 (50.7%) were female. The majority (60.7%) of the sample lived in areas classified as socioeconomically deprived.

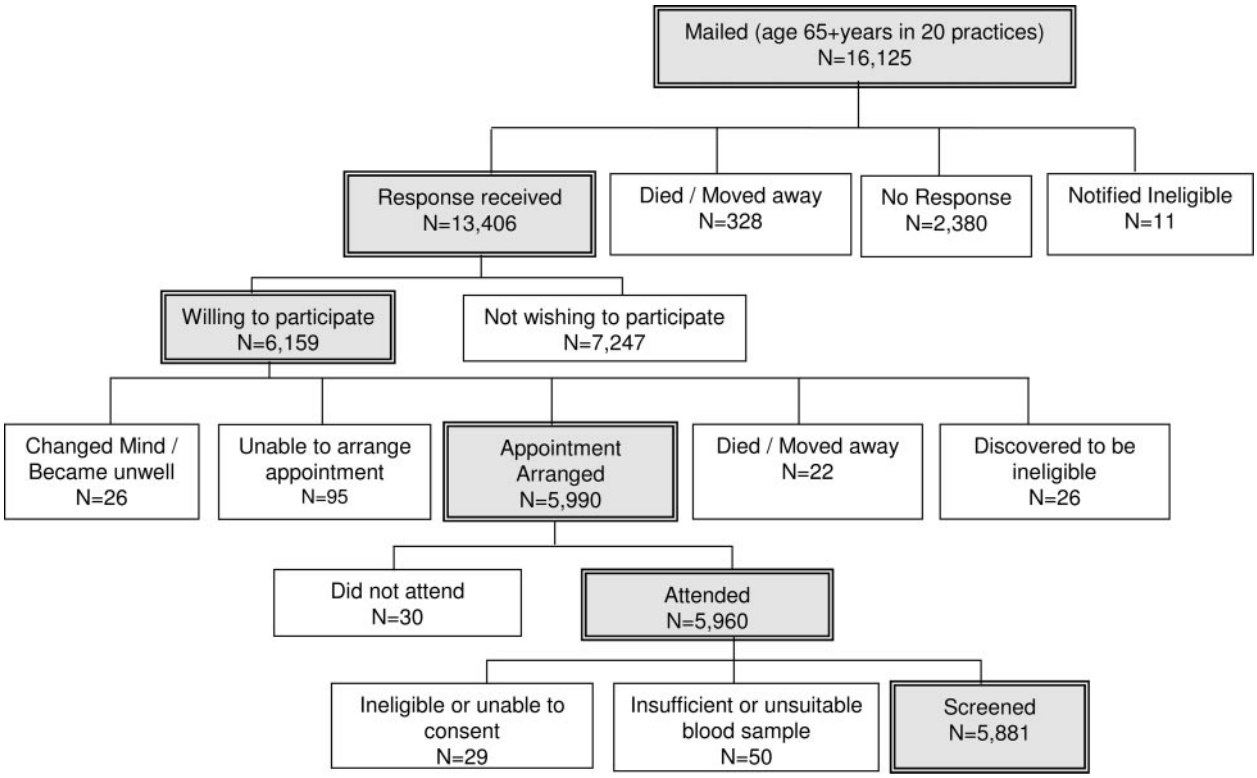

FIG. 1. Recruitment flow chart.

TABLE 1. Baseline characteristics of participants

Characteristics	All (n = 5872)
Age, yr	
Mean (range)	73.1 (65–98)
Median	72
Gender, n (%)	
Male	2892 (49.3)
Female	2980 (50.7)
IMD, n (%)	
Quartile 1 (least deprived)	1162 (19.8)
Quartile 2	1148 (19.6)
Quartile 3	1926 (32.8)
Quartile 4 (most deprived)	1636 (27.9)
Smoking status, n (%)	
Smoker	586 (10.0)
Nonsmoker	5286 (90.0)
Serum thyroid function, median (IQR)	
TSH (mIU/liter)	1.6 (1.1–2.4)
Free T_4 (pmol/liter)	14.2 (13.0–15.7)
Free T_3 (pmol/liter)	4.8 (4.4–5.3)
Major medical diagnoses, n (%)	
Cancer	183 (3.1)
Endocrine disease	607 (10.3)
Gastrointestinal disease	49 (0.8)
Hypertension	2777 (47.3)
Neurological disease	70 (1.2)
Psychiatric disease	248 (4.2)
Pulmonary disease	591 (10.1)
Renal disease	42 (0.7)
Rheumatic disease	115 (2.0)
Vascular disease	753 (12.8)
Current drug therapies	
Angiotensin-converting enzyme inhibitor	20 (0.3)
Amiodarone	30 (0.5)
Anticoagulant	181 (3.1)
Antidepressant	419 (7.1)
Anticonvulsant	74 (1.3)
β-Adrenergic blocker	1021 (17.4)
Calcium antagonist	59 (1.0)
Digoxin	163 (2.8)
Kelp	16 (0.3)
Lithium	10 (0.2)
Major tranquilizer	21 (0.4)
Minor tranquilizer	247 (4.2)
Morphine	96 (1.6)
Nonsteroidal antiinflammatory drug	2126 (36.2)
Glucocorticoids	121 (2.1)

Prevalence of thyroid dysfunction

Ninety-four percent of subjects (n = 5538) were euthyroid as indicated by their serum TSH concentration [median serum TSH 1.6 mU/liter, interquartile range (IQR) 1.1–2.3; median free T_4 14.3 pmol/liter, IQR 13.0–15.7]. Fifteen subjects [0.3%, 95% confidence interval (CI) 0.1–0.4] had previously undiagnosed overt hyperthyroidism (serum TSH < 0.1 mU/liter in all; median free T_4 24.7, IQR 18.4–28.7; median free T_3 7.9 pmol/liter, IQR 7.3–9.1). One hundred twenty-eight subjects (2.2%, 95% CI 1.8–2.6) had subclinical hyperthyroidism (median free T_4 15.4 pmol/liter, IQR 13.6–17.0; median free T_3 4.8 pmol/liter, IQR 4.4–5.3); serum TSH was undetectable (<0.1 mU/liter) in 27; TSH was reported as 0.1 mU/liter in 11 and was low but detectable (0.2–0.3 mU/liter) in the remaining 90. Median serum free T_4 was higher ($z = 4.53$, $P < 0.0001$) in those with subclinical hyperthyroid dysfunction than in the euthyroid category. One hundred sixty-eight (2.9%, 95% CI 2.5–3.3) had subclinical hypothyroidism (median serum TSH 6.8 mU/liter, IQR 6.0–8.8; median free T_4 12.6 pmol/liter, IQR 11.5–13.6), and 23 (0.4%, 0.3–0.6) were overtly hypothyroid (median serum TSH 40.6 mU/liter, IQR 16.7–52.2; median free T_4 7.5 pmol/liter, IQR 5.8–8.0) (Tables 2 and 3). Standardization of the crude prevalence rates to the West Midlands population by age, sex, and deprivation score (IMD 2004) had only a minor effect on estimates of prevalence (Tables 2 and 3).

The prevalence of subclinical hyperthyroidism was similar in males and females (1.9 and 2.2 per 100 population, respectively, $P = 0.42$), but subclinical hypothyroidism was almost twice as common in females (2.0 and 3.7 per 100 population in males and females, $P < 0.0001$). The prevalence of both subclinical hyperthyroidism and hypothyroidism increased with age [subclinical hyperthyroidism increasing with age for females (Cochran-Armitage test for trend $z = 3.4$, $P = 0.0006$); subclinical hypothyroidism increasing with age for males ($z = 2.9$, $P = 0.003$)].

Variability in the prevalence of subclinical thyroid dysfunction was also observed with respect to socioeconomic deprivation score; subclinical hyperthyroidism tended to be more common in those categorized as deprived and although no linear trend was observed, subclinical hypothyroidism tended to be more common in those categorized as affluent (Tables 2 and 3).

Association of thyroid dysfunction with deprivation, comorbidity, and medications

Only 46 (0.8%) participants had a previous diagnosis, up to 40 yr before screening, of thyroid disease (27 patients had a record of nonspecific thyroid disease and 19 were recorded in their family practice records as being previously thyrotoxic), which had not required treatment within the last 12 months. The number of other major current medical diagnoses recorded in the screened population ranged from 0 to 5 and was comparable in the euthyroid, subclinical hyperthyroid, and subclinical hypothyroid categories [median (IQR): 1.0 (0–1) *vs.* 1.0 (0–1.5) *vs.* 1.0 (0–1); $P = 0.70$]. Similarly, the number of significant current drug therapies ranged from 0 to 5 and was comparable in the euthyroid, subclinical hyperthyroid, and subclinical hypothyroid categories [median (IQR): 1.0 (0–1) *vs.* 1.0 (0–1) *vs.* 1.0 (0–1); $P = 0.65$]. Table 4 illustrates the distribution of participants with recorded current comorbidity and prescribed major drug therapies by thyroid function category. Although some differences were observed when comparing the proportion of participants with subclinical thyroid dysfunction with the euthyroid group, none of these achieved statistical significance ($P < 0.001$ used to denote statistical significance because of multiple testing). Of the 30 patients currently taking amiodarone, two had overt hyperthyroidism, two had overt hypothyroidism, two had subclinical thyroid dysfunction, and 24 were euthyroid (Table 4).

A significant association between deprivation category and the presence of chronic disease was observed [any chronic disease: 55.0% in IMD 1 (very affluent) to 69.3% in IMD 4 (very deprived), $\chi^2 = 66.35$, $P < 0.0001$]. This association of chronic disease with deprivation was observed for most of the common disease group, *i.e.* chronic pulmonary disease (7.0% of those

TABLE 2. Prevalence rates per 100 population and 95% CIs

	Male (n = 2892)	Female (n = 2980)	Overall (n = 5872)
Crude rates			
Overt hyperthyroid (n = 15)[a]	0.2 (0.1, 0.5)	0.3 (0.1, 0.6)	0.3 (0.1, 0.4)
Subclinical hyperthyroid (n = 128)	1.9 (1.5, 2.5)	2.4 (1.9, 3.0)	2.2 (1.8, 2.6)
Euthyroid (n = 5538)	95.4 (94.6, 96.1)	93.3 (92.3, 94.1)	94.3 (93.7, 94.9)
Subclinical hypothyroid (n = 168)	2.1 (1.6, 2.7)	3.6 (3.0, 4.4)	2.9 (2.5, 3.3)
Overt hypothyroid (n = 23)[a]	0.4 (0.2, 0.7)	0.4 (0.2, 0.7)	0.4 (0.3, 0.6)
Standardized rates			
Overt hyperthyroid[a,b]	0.2 (0.0, 0.4)	0.3 (0.1, 0.5)	0.3 (0.1, 0.4)
Subclinical hyperthyroid[c]	1.9 (1.6, 2.2)	2.2 (1.9, 2.6)	2.1 (1.8, 2.3)
Euthyroid[c]	95.4 (95.0, 95.9)	93.1 (92.5, 93.6)	94.2 (93.8, 94.6)
Subclinical hypothyroid[c]	2.0 (1.7, 2.3)	3.7 (3.3, 4.2)	2.9 (2.6, 3.1)
Overt hypothyroid[a,b]	0.4 (0.1, 0.6)	0.4 (0.2, 0.7)	0.4 (0.2, 0.6)

[a] Previously undiagnosed clinical disease.
[b] The categories of overt hyper- and hypothyroidism comprised insufficient subjects to enable standardization by deprivation, and therefore, standardization by age and sex alone was used.
[c] Standardized by age, gender, and deprivation.

living in areas classified as IMD 1, compared with 14.6% of those in IMD 4 ($\chi^2 = 55.9$, $P < 0.0001$), diabetes (6.9–11.3%, $\chi^2 = 19.52$, $P < 0.001$), heart failure (1.0–2.4%, $\chi^2 = 10.90$, $P < 0.05$), hypertension (40.5–54.3%, $\chi^2 = 55.01$, $P < 0.0001$), ischemic heart disease (4.7–7.9%, $\chi^2 = 12.60$, $P < 0.01$), chronic renal disease (0.7–1.3%, $\chi^2 = 11.16$, $P < 0.05$), and psychosis (0–0.4%, $\chi^2 = 7.97$, $P < 0.05$).

Subclinical hyperthyroidism was found to be associated with increasing age [for each additional year of age, there was a 5% increased probability of disease; odds ratio (OR) 1.05, 95% CI 1.02–1.08, $P < 0.001$] and IMD quartile (2-fold excess associated with IMD 2, 3, and 4) but not with gender, chronic medical condition, or medication (Table 5). Subclinical hypothyroidism was associated with an interaction between age and gender (*i.e.* probability of disease increased with age for men; OR 1.07, 95% CI 1.03–1.12, $P < 0.05$) and not smoking (OR 0.43, 95% CI 0.20–0.94, $P < 0.05$). Those on anticonvulsant medication were almost three times as likely to be categorized as having subclinical hypothyroidism; no association was observed with any other major medical diagnosis, current medication, or deprivation score.

Discussion

This large population-based survey provides comprehensive data on the prevalence of thyroid dysfunction and the distribution by age, gender, deprivation score, and comorbidity in the West Midlands region of the United Kingdom.

We identified only 38 cases of overt thyroid dysfunction (15 hyperthyroid, 23 hypothyroid) in the 5872 patients screened; this equates to a community prevalence of undiagnosed overt hyperthyroidism of 0.3% (males 0.2%; females 0.3%) and overt hypothyroidism of 0.4% (males 0.4%; females 0.4%). Undiagnosed overt thyroid dysfunction is therefore uncommon, probably because the majority of cases are identified during symptomatic presentation or routine care (6.6% of the potential study population were excluded from screening by their family practitioner because they were already known to have thyroid disease). Given the low prevalence of undiagnosed overt thyroid dysfunction and the low positive predictive value of TSH in detecting thyroid disease in family practice populations (0.24 for hyperthyroidism and 0.06 for hypothyroidism) (41), we suggest that routine population-based screening is not generally helpful in identifying overt thyroid disease. Nevertheless, this study demonstrated that factors such as socioeconomic deprivation, in addition to age and sex, may assist in the identification of groups at high risk of subclinical thyroid dysfunction. As further data become available to better enable the categorization of those at increased risk of subclinical dysfunction and better quantify the association of subclinical dysfunction with adverse outcomes, such as cardiovascular disease, it may eventually be possible to recommend a targeted approach to screening.

TABLE 3. Standardized rates by age and deprivation group

	Subclinical hyperthyroid (n = 128)	Subclinical hypothyroid (n = 168)
Standardized rates		
65–69 yr (n = 74)	1.4 (1.2, 1.8)	2.1 (1.8, 2.5)
70–74 yr (n = 78)	1.6 (1.2, 1.9)	2.8 (2.3, 3.3)
75–79 yr (n = 86)	3.7 (2.8, 4.1)	3.1 (2.6, 3.7)
80+ yr (n = 58)	2.7 (2.1, 3.4)	3.8 (3.1, 4.6)
Deprivation score (IMD 2004)		
Quartile 1 (least deprived) (n = 48)	1.1 (0.9, 1.5)	3.1 (2.5, 3.7)
Quartile 2 (n = 65)	2.1 (1.7, 2.6)	3.6 (3.0, 4.3)
Quartile 3 (n = 101)	2.4 (1.9, 2.9)	2.7 (2.3, 3.3)
Quartile 4 (most deprived) (n = 82)	2.7 (2.2, 3.2)	2.3 (1.9, 2.8)

The prevalence of subclinical hyperthyroidism was 2.1% and subclinical hypothyroidism was 2.9% in this study; these standardized rates are comparable with those reported in some other studies (9, 25, 42, 43), although they are considerably lower than those reported by others (8, 19, 29, 28). Prevalence is related to ethnic group, dietary iodine intake, and prevalence of antithyroid antibodies (22–24). Estimates of prevalence are also affected by the type of population accessed (*e.g.* community, hospitalized, nursing home), the proportion of subjects with concurrent comorbidity who may have abnormal TSH levels for reasons other than thyroid disease, and the TSH assay and cutoff values used (22). Previous studies used a variety of TSH assays and/or TSH cutoff concentrations (8, 9, 42), some relied only on TSH concentrations (and therefore also include overt thyroid dysfunction or patients with other illnesses or taking medications that affect TSH levels) (29), and some are based on small numbers of patients, (43) or describe prevalence within selected populations (43, 44).

We did not anticipate comparable prevalence rates to other

TABLE 4. Participant characteristics by category of thyroid status

Characteristics	Overt hyperthyroid (n = 15)	Subclinical hyperthyroid (n = 128)	P^a	Euthyroid (n = 5538)	Subclinical hypothyroid (n = 168)	P^a	Overt hypothyroid (n = 23)
Age, yr							
Mean	73.1	74.7		73.0	74.0		73.3
Range	65–84	65–88		65–98	65–94		65–80
Median	73	75		72.0	73.5		75.0
Gender							
Male	6 (40.0)	56 (43.8)		2759 (49.8)	60 (35.7)		11 (47.8)
Female	9 (60.0)	72 (56.2)		2779 (50.2)	108 (64.3)		12 (52.2)
IMD							
Quartile 1 (least deprived)	3 (20.0)	13 (10.2)		1107 (20.0)	35 (20.8)		4 (17.4)
Quartile 2	2 (13.3)	24 (18.7)		1073 (19.4)	41 (24.4)		8 (34.8)
Quartile 3	4 (26.7)	47 (36.7)		1818 (32.8)	54 (32.1)		3 (13.0)
Quartile 4 (most deprived)	6 (40.0)	44 (34.4)		1540 (27.8)	38 (22.6)		8 (34.8)
Smoking status							
Smoker	4 (26.7)	9 (7.0)		563 (10.2)	7 (4.2)		3 (13.0)
Nonsmoker	11 (73.3)	119 (93.0)		4975 (89.8)	161 (95.8)		20 (87.0)
Serum thyroid function							
TSH, mIU/liter, median (IQR)	0.05 (0.05,0.05)	0.2 (0.1,0.3)		1.6 (1.1,2.3)	6.8 (6.0,8.8)		40.6 (16.7,52.2)
Free T_4, pmol/liter, median (IQR)	27.7 (18.4,28.7)	15.5 (13.6,16.9)		14.3 (13.0,15.7)	12.6 (11.5,13.6)		7.5 (5.8,8.0)
Free T_3, pmol/liter, median (IQR)	7.9 (7.3, 9.1)	4.8 (4.4, 5.3)		Not recorded	Not recorded		Not recorded
Major medical diagnoses							
Cancer	0 (0)	3 (2.3)	0.62	174 (3.1)	6 (3.6)	0.51	0 (0)
Endocrine disease	4 (26.7)	12 (9.4)	0.77	578 (10.4)	10 (6.0)	0.05	3 (13.0)
Gastrointestinal disease	0 (0)	0 (0)	0.36	46 (0.8)	3 (1.8)	0.11	0 (0)
Hypertension	7 (46.7)	57 (44.5)	0.48	2623 (47.4)	78 (46.4)	0.76	12 (52.2)
Neurological disease	0 (0)	2 (1.6)	0.42	64 (1.2)	4 (2.4)	0.09	0 (0)
Psychiatric disease	1 (6.7)	8 (6.3)	0.18	227 (4.1)	12 (7.1)	0.05	0 (0)
Pulmonary disease	0 (0)	20 (15.6)	0.04	557 (10.1)	13 (7.7)	0.30	1 (4.3)
Renal disease	1 (6.7)	1 (0.8)	0.40	37 (0.7)	3 (1.8)	0.07	0 (0)
Rheumatic disease	1 (6.7)	2 (1.6)	0.99	108 (2.0)	4 (2.4)	0.42	0 (0)
Vascular	2 (13.3)	19 (14.8)	0.43	710 (12.8)	18 (10.7)	0.41	4 (17.4)
Current drug therapies							
ACE inhibitor	0 (0)	0 (0)	0.99	19 (0.3)	1 (0.6)	0.28	0 (0)
Amiodarone	2 (13.3)	0 (0)	0.99	24 (0.4)	2 (1.2)	0.11	2 (8.7)
Anticoagulant	1 (6.7)	5 (3.9)	0.45	170 (3.1)	4 (2.4)	0.66	1 (4.3)
Antidepressant	0 (0)	8 (6.3)	0.73	392 (7.1)	17 (10.1)	0.10	2 (8.7)
Anticonvulsant	0 (0)	1 (0.8)	0.99	67 (1.2)	6 (3.6)	0.01	0 (0)
β-Adrenergic blocker	4 (26.7)	19 (14.8)	0.41	969 (17.5)	26 (15.5)	0.47	3 (13.0)
Calcium antagonist	0 (0)	0 (0)	0.38	55 (1.0)	3 (1.8)	0.17	1 (4.3)
Digoxin	0 (0)	3 (2.3)	0.99	153 (2.8)	7 (4.2)	0.17	0 (0)
Kelp	0 (0)	0 (0)	0.99	15 (0.3)	1 (0.6)	0.23	0 (0)
Lithium	0 (0)	0 (0)	0.99	10 (0.2)	0 (0)	0.99	0 (0)
Major tranquilizer	0 (0)	1 (0.8)	0.23	20 (0.4)	0 (0)	0.99	0 (0)
Minor tranquilizer	0 (0)	5 (3.9)	0.99	234 (4.2)	7 (4.2)	0.99	1 (4.3)
Morphine	1 (6.7)	4 (3.1)	0.10	86 (1.6)	5 (3.0)	0.12	0 (0)
NSAID	7 (46.7)	42 (32.8)	0.41	2011 (36.3)	59 (35.1)	0.75	7 (30.4)
Glucocorticoids	1 (6.7)	5 (3.9)	0.12	113 (2.0)	2 (1.2)	0.58	0 (0)

Figures presented are n (%) unless stated otherwise. ACE, Angiotensin-converting enzyme; NSAID, nonsteroidal antiinflammatory drug.
[a] Comparison of independent binomial proportions in subclinical and euthyroid categories.

populations with differing iodine status (*e.g.* parts of continental Europe with relative iodine deficiency). The median urinary iodine levels for the United Kingdom are estimated to be 141 μg/liter, with newborn TSH levels being comparable with other iodine-sufficient regions and an average daily intake of 255 μg/person·d (45). Our data should therefore be typical of other iodine-replete areas. A previous screening study in the same geographical area, conducted during 1988–1989, in one family practice also included in this present study, reported a substantially higher prevalence of subclinical hypothyroidism of 6.3% (95% CI 5.0–7.8%) and subclinical hyperthyroidism of 5.8% (95% CI 4.5–7.3%) but a substantially lower prevalence (1.4%) of known overt thyroid dysfunction than the data reported here (19). Subgroup analyses confirmed that the present prevalence of subclinical dysfunction within this family practice is comparable with that observed in our larger study population [subclinical hyperthyroidism: study population 2.1% (95% CI 1.8–2.3%) *vs.* 2.1% in single practice; subclinical hypothyroidism: study population 2.9% (95% CI 2.6–3.1%) *vs.* 3.8% in single practice]. The reasons for our more recent data demonstrating a substantially lower prevalence than some previous studies are likely to be multifactorial and include the use of different assays and cutoffs, that the current elderly population are generally healthier (as indicated by increasing life expectancy) (46), and increased testing of thyroid status in routine family practice with the consequent removal of patients with borderline subclinical thyroid dysfunction and overt thyroid dysfunction from the study population.

This is the first study to provide evidence of an association between socioeconomic deprivation and subclinical thyroid dysfunction that persists after adjusting for the effects of age,

TABLE 5. Results of logistic regression modeling

Variable	OR	95% CI	*P* value
Logistic model to predict subclinical hyperthyroidism			
Age (yr)	1.05	1.02–1.08	0.001
IMD quartile			
1 (very affluent)	1.00		
2 (moderately affluent)	1.95	1.08–3.52	0.03
3 (moderate deprived)	2.13	1.20–3.80	0.01
4 (very deprived)	2.30	1.30–4.08	0.001
Logistic model to predict subclinical hypothyroidism			
Age (yr) × males	1.07	1.01–1.14	0.90
Age (yr) × females	1.00	0.97–1.04	0.002
Smoker	0.43	0.20–0.94	0.03
IMD quartile			
1 (very affluent)	1.00		
2 (moderately affluent)	0.94	0.62–1.43	0.76
3 (moderate deprived)	0.79	0.52–1.22	0.29
4 (very deprived)	0.79	0.51–1.24	0.31
Anticonvulsant drug	2.92	1.24–6.88	0.01

gender, comorbidity, and current drug therapies. It is well recognized that low serum TSH may reflect drug therapies and/or nonthyroidal illnesses. However, median serum free T_4 was higher in those with subclinical hyperthyroid dysfunction than in the euthyroid category, consistent with their low serum TSH reflecting mild thyroid hormone excess rather than nonthyroidal illness or drug therapies. Unexpected and contradictory results were observed with respect to the association between the prevalence of subclinical hyper- and hypothyroidism and deprivation score (IMD 2004). A 2-fold excess of subclinical hyperthyroidism was seen in patients resident in the most deprived quartile, compared with those in the most affluent quartile. Conversely, subclinical hypothyroidism was 33% more common in patients resident in the most affluent quartile, compared with those in the most deprived quartile. Logistic regression identified the IMD 2004 to be a better predictor of the prevalence of subclinical thyroid dysfunction than comorbidity or current medication alone.

The association between deprivation and prevalence was investigated using the IMD 2004, which encompasses a broader definition of poverty than income alone. By combining more specific forms of deprivation (*e.g.* the domains of income, employment, health, education), the possibility that these specific forms of deprivation may interact and have more impact if found in certain combinations is allowed for. However, such composite indicators have the disadvantage that the relative effect of each form of deprivation is not established, and, as appears likely with respect to the prevalence of subclinical thyroid dysfunction, some important aspects of socioeconomic deprivation may not be included. Our regression analyses demonstrated that, once IMD had been allowed for, comorbidity or current medication alone was no longer an important predictor of the prevalence of subclinical disease. This suggests that deprivation (including factors we did not measure, such as material deprivation, ethnicity, nutritional status, access to or use of health services) may be associated with the development of both chronic disease and subclinical thyroid dysfunction.

Although the response rate to our initial mailing was 83%, only 45% of responders accepted the invitation to screening; this indicates the potential for bias in the estimation of prevalence. If those presenting for screening were less frail individuals and less likely to have subclinical thyroid dysfunction, bias may have been introduced, although the availability of home screening aimed to minimize the potential for selection bias. We are also aware that, should a routine screening program be introduced in the future, a proportion of the population would not participate. The 5% prevalence of subclinical thyroid dysfunction identified in this study is therefore likely to be a reasonable estimation of the potential yield from such population-based screening. Comparison of morbidity data from our screened population with prevalence estimates for the U.K. population (47) suggests that selection bias was not in fact a significant factor because the level of comorbidity among participants was generally comparable with the general population (*e.g.* diabetes: 11.5 and 7.3% in males and females aged 65–74 yr in the screened population, compared with 8.5 and 6.4% generally; coronary heart disease: 17.2 and 5.6% in males and females aged 65–75 yr compared with 18.4 and 11.2%, respectively) (47). Written materials for the study were only available in English; this may have reduced the extent of participation from some ethnic minorities. Data on the ethnic origin of participants were not collected. Differential response rates did result in a study sample that had a greater proportion of males and a smaller proportion of the very elderly than is typical of the population in the United Kingdom. The proportion of the study sample that was from affluent areas was representative of the West Midlands region and, as expected for this region, was less than in the United Kingdom as a whole. Nevertheless, standardization ensured that the estimates achieved are an accurate reflection of the frequency of disease.

Conclusions

Very few cases of overt thyroid dysfunction were identified; this suggests that most patients with significant thyroid dysfunction who present in primary care are appropriately diagnosed. In the present study, the prevalence of subclinical thyroid dysfunction is significantly lower than some previous studies, often performed in selected populations and conducted during the 1980s, have suggested. Given the lack of robust evidence demonstrating significant morbidity in this group of patients, these data provide further evidence to support recommendations that routine screening for subclinical thyroid dysfunction is unnecessary (1).

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References

1. **Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, Franklyn JA, Hershman JM, Burman KD, Denke MA, Gorman C, Cooper RS, Weissman NJ** 2004 Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA 291:228–238
2. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. National Guideline Clearinghouse. (http://www.guideline.gov/summary/summary.aspx?ss=15&doc_id=5916&nbr=3902); accessed 11 Aug 2005
3. **Leentjens AFG, Kappers EJ** 1995 Persistent cognitive defects after corrected hypothyroidism. Psychopathology 28:235–237
4. **Gussekloo J, van Exel E, de Craen AJ, Meinders AE, Frolich M, Westendorp, RG** 2004 Thyroid status, disability and cognitive function, and survival in old age. JAMA 292:2591–2599
5. **Hak AE, Pols HAP, Visser TJ, Drexhage HA, Hofman A, Witteman JC** 2000 Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: the Rotterdam study. Ann Intern Med 132:270–278
6. **Danese MD, Ladenson PW, Meinert CL, Powe NR** 2000 Clinical review 115: effect of thyroxine therapy on serum lipoproteins in patients with mild thyroid failure: a quantitative review of the literature. J Clin Endocrinol Metab 85: 2993–3001
7. **Haggerty Jr JJ, Stern RA, Mason GA, Beckwith J, Morey CE, Prange Jr AJ** 1993 Subclinical hypothyroidism: a modifiable risk factor for depression? Am J Psychiatry 150:508–510
8. **Vanderpump MP, Tunbridge WM, French JM, Appleton D, Bates D, Clark F, Grimley-Evans J, Hasan DM, Rodgers H, Tunbridge F, Young ET** 1995 The incidence of thyroid disorders in the community: a twenty-year follow-up of the Whickham survey. Clin Endocrinol (Oxf) 43:55–68
9. **Pirich C, Mullner M, Sinzinger H** 2000 Prevalence and relevance of thyroid dysfunction in 1922 cholesterol screening participants. J Clin Epidemiol 53: 623–629
10. **Rodondi N, Newman AB, Vittinghoff E, de Rekeneire N, Satterfield S, Harris TB, Bauer DC** 2005 Subclinical hypothyroidism and the risk of heart failure, other cardiovascular events, and death. Arch Intern Med 165:2460–2466
11. **Walsh JP, Bremner AP, Bulsara MK, O'Leary P, Leedman PJ, Feddema P, Michelangeli V** 2005 Subclinical thyroid dysfunction as a risk factor for cardiovascular disease. Arch Intern Med 165:2467–2472
12. **Cappola AR, Fried LP, Arnold AM, Danese MD, Kuller LH, Burke GL, Tracy RP, Ladenson PW** 2006 Thyroid status, cardiovascular risk, and mortality in older adults. JAMA 295:1033–1041
13. **Parle JV, Maisonneuve P, Sheppard MC, Boyle P, Franklyn JA** 2001 Prediction of all-cause and cardiovascular mortality in elderly people from one low serum thyrotropin result: a 10-year cohort study. Lancet 358:861–865
14. **Bommer M, Eversmann T, Pickardt R, Leonhardt A, Naber D** 1990 Psychopathological and neuropsychological symptoms in patients with subclinical and remitted hyperthyroidism. Klin Wochenschr 68:552–558
15. **de Escobar GM, Obregón MJ, del Rey FE** 2000 Is neuropsychological development related to maternal hypothyroidism or to maternal hypothyroxinemia? J Clin Endocrinol Metab 85:3975–3987
16. **Faber J, Galloe AM** 1994 Changes in bone mass during prolonged subclinical hyperthyroidism due to L-thyroxine treatment: a meta-analysis. Eur J Endocrinol 130:350–356
17. **Bauer DC, Browner WS, Cauley JA, Orwoll ES, Scott JC, Black DM, Tao JL, Cummings SR** 1993 Factors associated with appendicular bone mass in older women. The Study of Osteoporotic Fractures Research Group. Ann Intern Med 118:657–665
18. **Tenerz A, Forberg R, Jansson R** 1990 Is a more active attitude warranted in patients with subclinical thyrotoxicosis? J Intern Med 228:229–233
19. **Parle JV, Franklyn JA, Cross KW, Jones SC, Sheppard MC** 1991 Prevalence and follow-up of abnormal thyrotropin (TSH) concentrations in the elderly in the United Kingdom. Clin Endocrinol (Oxf) 34:77–83
20. **Sawin CT** 1992 Thyroid dysfunction in older persons. Adv Intern Med 37: 223–248
21. **Stott DJ, McLellan AR, Finlayson J, Chu P, Alexander WD** 1991 Elderly patients with suppressed serum TSH but normal free thyroid hormone levels usually have mild thyroid overactivity and are at increased risk of developing overt hyperthyroidism. Q J Med 78:77–84
22. **Samuels MH** 1998 Subclinical thyroid disease in the elderly. Thyroid 8:803–813
23. **Surks MI, Ocampo E** 1996 Subclinical thyroid disease. Am J Med 10092:217–223
24. **Ayala AR, Wartofsky L** 1997 Minimally symptomatic (subclinical) hypothyroidism. Endocrinologist 7:44–50
25. **Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA, Braveman LE** 2002 Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANESIII). J Clin Endocrinol Metab 87:489–499
26. **Falkenberg M, Kagedal B, Norr A** 1983 Screening of an elderly female population for hypo- and hyper-thyroidism by use of a thyroid hormone panel. Acta Med Scand 214:361–365
27. **Sawin CT, Castelli WP, Hershman JM, McNamara P, Bacharach P** 1985 The aging thyroid: thyroid deficiency in the Framingham study. Arch Intern Med 145:1386–1388
28. **Canaris GJ, Manowitz NR, Mayor G, Ridgway EC** 2000 The Colorado thyroid disease prevalence study. Arch Intern Med 160:526–534
29. **Tunbridge WM, Evered DC, Hall R, Appleton D, Brewis M, Clark F, Grimley Evans J, Young E, Bird T, Smith PA** 1977 The spectrum of thyroid disease in a community: the Wickham survey. Clin Endocrinol (Oxf) 7:481–493
30. **Helfand M, Redfern C** 1998 Clinical guideline, part 2. Screening for thyroid disease: an update. American College of Physicians. Ann Intern Med 129: 144–158
31. **Auer J, Scheibner P, Mische T, Langsteger W, Eber O, Eber B** 2001 Subclinical hyperthyroidism as a risk factor for atrial fibrillation. Am Heart J 142:838–842
32. **Weetman AP** 1997 Hypothyroidism: screening and subclinical disease. BMJ 314:1175–1178
33. 2002 American Association of Clinical Endocrinologists (AACE) medical guidelines for clinical practice for the evaluation and treatment of hyperthyroidism and hypothyroidism. Endocr Pract 8:457–469
34. **Wilson JMG, Junger G** 1968 Principles and practice of screening for disease. Geneva: World Health Organization
35. **Spencer CA, LoPresti JS, Patel A, Guttler RB, Eigen A, Shen D, Gray D, Nicoloff JT** 1990 Applications of new chemiluminometeric thyrotropin assay to subnormal measurement. J Clin Endocrinol Metab 70:453–460
36. **Franklyn JA, Black EG, Betteridge J, Sheppard M** 1994 Comparison of second and third generation methods for measurement of serum thyrotropin in patients with overt hyperthyroidism, patients receiving thyroxine therapy, and those with nonthyroidal illness. J Clin Endocrinol Metab 78:1368–1371
37. **Surks MI, Sievert R** 1995 Drugs and thyroid function. N Engl J Med 333: 1688–1694
38. **Van den Berghe G, de Zegher F, Lauwers P** 1994 Dopamine and the sick euthyroid syndrome in critical illness. Clin Endocrinol (Oxf) 41:731–737
39. Office for National Statistics. Mid-2003 population estimates T12: quinary age groups and sex for health areas in England and Wales; estimated resident population. http://www.statistics.gov.uk
40. Office of the Deputy Prime Minister. Indices of deprivation 2004—summary (revised). http://www.communities.gov.uk/index.asp?id=1128444 (accessed July 11, 2006)
41. **Attia J, Margetts P, Guyatt PL** 1999 Diagnosis of thyroid disease in hospitalised patients: a systematic review. Arch Intern Med 159:658–665
42. **Kanaya AM, Harris F, Volpato S, Perez-Stable EJ, Harris T, Bauer DC** 2002 Association between thyroid dysfunction and total cholesterol level in an older biracial population: the health, aging, and body composition study. Arch Intern Med 162:773–779
43. **Smithson J** 1998 Screening for thyroid dysfunction in a community population of diabetic patients. Diabet Med 15:148–150
44. **Luboshitzky R, Oberman AS, Kaufman N, Reichman N, Flatau E** 1996 Prevalence of cognitive dysfunction and hypothyroidism in an elderly community population. Isr J Med Sci 32:60–65
45. The Network for Sustained Elimination of Iodine Deficiency. http://206.191.51.240/countries/UK.html (accessed August 15, 2006)
46. Office for National Statistics. Government Actuary's Department for expectation of life data. ONS for healthy life expectancy data. http://www.statistics.gov.uk/cci/nugget.asp?id=934 (accessed July 10, 2006)
47. **Office for National Statistics** 2000 Key Health Statistics from General Practice 1998. London: National Statistics