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Variation in the use of definitive treatment options in the management of Graves' disease – a UK clinician survey

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ABSTRACT

Background:

Graves' disease can be treated with antithyroid drugs (ATDs), radioiodine or surgery. Use of definitive treatments (radioiodine or surgery) varies widely across centres. Specific clinical circumstances, local facilities, patient and clinician preferences and perceptions will affect choice of treatment. Detailed understanding of UK clinicians' views and their rationale for different treatments is lacking.

Aims: To study the preferences and perceptions of UK clinicians on the role of surgery and radioiodine in the management of Graves' disease.

Methods: British Thyroid Association' (BTA), 'Society for Endocrinology' (SFE) and 'British Association of Endocrine and Thyroid Surgeons' (BAETS) members were invited to complete an online survey examining their management decisions in Graves' disease and factors that influenced their decisions.

Results: 158 responses from UK consultants were included. The ratio of physicians to surgeons was 11:5 and males to females was 12:4. Most clinicians would commence ATDs in uncomplicated first presentation of Graves' disease. A wide range of risk estimates on the effectiveness and risks of treatment was given by clinicians. Radioiodine was used most frequently in relapsed Graves' disease. However severe eye disease and pregnancy strongly influenced choice in favour of surgery. Surgeons underestimated the success of radioiodine ($P<0.01$) and were more likely to recommend thyroidectomy than physicians.

Conclusions: This survey demonstrates significant variation in clinicians' perceptions of risks of treatment and their choice of management options for relapsed Graves' disease. The variation appeared to be dependent on patient and disease specific factors as well as physician experience, gender and speciality.

Main messages

- The survey demonstrates s~~S~~ignificant variation in management of Graves' disease across UK
- Surgery was more likely to be recommended in patients with severe ~~Graves'~~ thyroid eye disease and pregnancy.
- Clinicians' perceptions of effectiveness and risk of treatment options in Graves' disease varied widely.~~Physicians and Surgeons' have different approaches to the management of relapsed Graves'disease.~~

Research Questions

- ~~Is relapsed Graves' disease treated appropriately?~~
- What are the outcomes (effectiveness and risks) following the use of various treatment options in ~~are the actual risks of G~~graves' disease~~s management~~ in the UK?
- How does surgery compare with radio-iodine in the management of Graves' disease overall and in specific subgroups?
- Should there be n~~N~~ational guidelines and would these improve ~~in the UK for~~ the management of Graves' disease in the UK?

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BACKGROUND

Graves' disease is the most frequent cause of hyperthyroidism in iodine-replete countries. The production of autoantibodies against the thyroid stimulating hormone receptor (TSH-receptor) results in hyperplasia and hypertrophy of thyroid follicles and subsequent increase in thyroxine synthesis and release. The clinical manifestations of Graves' disease include those due to hyperthyroidism (such as tachycardia, weight loss, diarrhoea, menstrual irregularities and sweating) as well as those specific to Graves' disease, including a diffuse goitre and signs and symptoms of infiltrative eye disease (such as periorbital oedema, proptosis, ophthalmoplegia).

Following a diagnosis of Graves' disease, antithyroid drugs (ATDs) including carbimazole and propylthiouracil are used to control hyperthyroidism. Although these are very effective, they are associated with high rates of relapse[1,2]. For patients with relapsed hyperthyroidism or disease uncontrolled with ATDs, alternative treatment options such as radioiodine (RAI) therapy and surgery (most commonly total thyroidectomy) are considered to offer definitive treatment; each with its risks and benefits.

The precise indications for these options have been debated and management practices are varied, particularly in the uncomplicated patient[3]. Patient preference also plays a large role in the decision to undergo either surgery or radioiodine. The rates of success, complication rates, severity of Graves' disease, availability of local facilities and expertise also influence decision making. However, the clinician's assessment of these factors and their perceptions and preferences will inevitably influence the patient's decision and the decision making process.

Previously published papers have demonstrated the wide variation in practice within Europe and the world relating to~~garding~~ the treatment of relapsed Graves' ~~D~~disease. In 2000, Escobar-Jimenez

et al[4] surveyed Endocrine units in Spain to explore their management of uncomplicated Graves' disease and relapsed patients looking at factors that influenced their decision making. Vaidya et al [5] reported on a UK survey of 698 clinicians~~(2008) discussed Graves' disease management in the UK~~ in the year 2008, but the study focussed primarily~~mainly concentrated~~ on the use of radio-iodine with little information regarding surgical practice.

~~Some studies have explored clinicians' views on the management of Graves' disease and have found significant variation in practices. In 2008 Vaidya et al[4] reported on a UK survey of 698 consultants involved in the management of thyroid disease. Various scenarios were discussed. In an uncomplicated thyrotoxic patient, 80% chose ATDs, 19% radioiodine, and 0.4% thyroidectomy. However in the presence of active thyroid eye disease, no respondent chose radioiodine. In patients with inactive eye disease, 46% would give radioiodine with steroid cover, and 26% would give radioiodine without steroid cover. Although the study was comprehensive for matters regarding radioiodine therapy, there is limited information on surgical preference.~~

~~In 2000, Escobar-Jimenez et al[5] reported the results of a survey of Endocrine units in Spain. Ten scenarios were presented, each of which varied in factors that could influence treatment. In patients presenting with uncomplicated Graves' disease, 98% chose ATDs as the initial treatment and 2% radioiodine. In patients with relapsed Graves' disease, 61% of responders preferred radioiodine except in pregnancy where 12% would use surgery and the remainder would use a further course of ATDs.~~

In 2011 a survey was conducted by Burch et al[3] to assess international practice in the diagnosis and management of Graves' disease amongst physicians and surgeons using various scenarios. The vast majority of the respondents ~~first case was of non-complicated Graves' disease. European responders chose between antithyroid drugs (85.7%), radioiodine (13.3%) and surgery (1%). This~~

~~practice differed to North America where the choice of ATD, radioiodine and surgery were made in 40.5%, 58.6% and 0.9% respectively. In the presence of eye disease or pregnancy, antithyroid drugs and thyroidectomy were preferred to radioiodine.~~majority of respondents (92.2%) ~~Of note, 92.2% of the respondents~~ were specialists in adult Endocrinology (92.2%), with only 0.6% in General Surgery and 2.2% in Nuclear Medicine[3]. This may have potentially influenced results in favour of medical treatment. In 2013, the same questionnaire as that used by Burch et al in 2011, was sent to the European Thyroid Association members [6]. They reported no significant changes from previous surveys conducted in Europe on the treatment of Graves' disease[7], but demonstrated~~ongoing~~ significant differences between North America and Europe[3]. In uncomplicated first presentation of Graves' disease, 83.8% of survey responders chose ATDs as first line treatment (similar to 1987 survey), 14.1% radioiodine and surgery in just 2.1%. Neither ~~Both~~ of these two studies ~~papers did not~~ addressed the management of relapsed Graves' disease.

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2.Which is the 1987 survey? If not sure, delete this…

To date, there are no national~~current British~~ guidelines for the treatment of Graves' disease or~~nor any~~ studies that explore ~~the~~ factors influencing choice of surgery and radioiodine in the definitive treatment of relapsed Graves' disease in the UK~~, particularly in the scenario of relapse~~. In addition, clinicians' preferences and perceptions of success and complication rates in this scenario are, as yet, unexplored.

The aim of this study was to survey the preferences and perceptions of UK clinicians on the role of surgery and RAI in the management of relapsed Graves' disease.

METHODS

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Between December 2013 and January 2014, a survey (see Appendix) was sent out to all Consultant members of the British Thyroid Association (BTA), Society of Endocrinology (SFE) and the British Association of Endocrine and Thyroid Surgeons (BAETS) involved in the treatment of Graves' disease. This was conducted using the online tool 'surveymonkey.com' and reminders sent 2 weeks later. To ensure anonymity, no names or personal details were requested. Information on speciality, year of graduation in Medicine, county of practice and gender was collected to enable us to detect duplicate responses and to evaluate if any of these demographic differences influenced clinicians' perceptions and preferences. The survey start times and IP addresses of respondents collected automatically were also used to detect duplicate responses made in error (such as pressing the "submit" button more than once).

Clinical specialities surveyed included Endocrinology, Endocrine Surgery, Head & Neck Surgery as well as Nuclear Medicine. The survey consisted of initial questions establishing the responders' status as UK consultants and then collecting information on speciality, geography, gender, year since graduation, and the number of Graves' patients seen per year. Subsequent questions explored reasons for commencing ATDs in newly diagnosed Graves' disease and what patient factors influenced clinicians' decisions on definitive treatment in relapsed Graves' disease. The side effects quoted to patients for either radioactive iodine or surgery and the clinicians' perception of what risks influenced patient decision-making was also examined. The final question asked what the clinicians' preference would be if they were the patient with relapsed, uncomplicated Graves' disease.

Questionnaires were completed on surveymonkey.com. The results were downloaded to a Microsoft Excel 2007 worksheet and exported to IBM SPSS version 21 statistical software for

further analysis. Evaluation for potential duplicate or multiple entries was performed, as explained above. For incomplete surveys, available answers were included in the analysis. In questions where ranges or open text answers were given, certain assumptions were made. Data presented as ratios were changed to percentages. Averages were calculated for data presented as ranges, unless the range was very wide (for eg. >25). If ">" or "<" was used to describe a value, 10% was added to or subtracted from the value. If two values were presented for different groups (i.e. male or female; young or old), the average was taken. If two values are given for immediate and later relapse, the total was taken (or the larger number if this was thought to incorporate those that have relapsed before). If personal results were presented alongside literature, the personal results were taken. If the response rates to first and second course of antithyroid drugs were presented, only the rates from the first course were included in the analysis.

Data on gender, specialty, county, and other categorical or ordinal responses to questions were reported as frequencies or percentages. Data on year since graduation, and other quantitative data were reported using median and range (as none of our quantitative variables were normally distributed). Answers in text were grouped into similar categories. For example, 30 responses related to voice (change in voice, vocal cord weakness, hoarseness, recurrent laryngeal nerve palsy etc.) and these were grouped in a specific category of 'voice change' for surgical complications. The responses were compared by specialty, region, gender, volume of Graves' disease seen and years since graduation where appropriate. Binary data between groups were compared using the Pearson chi square test with continuity correction (or Fisher's exact test). Continuous data was compared using the Mann-Whitney U test (for two groups) or Kruskal-Wallis test (for more than two groups). The significance was set at the 5% level (p=0.05).

The study received ethical approval from the University of Sheffield's 'University Research Ethics Committee'.

RESULTS

169 responses were received but 11 were excluded either for duplicate responses (n=4) or because the respondents were not practising consultants in the UK (n=7). The demographics of the respondents are displayed in Table 1.

Table 1. Demographic features of clinicians who responded to the survey

Demographic	Subcategory	Number (%)
Gender (n=154)	Male	115 (74.7%)
	Female	39 (25.3%)
Specialty (n=158)	Endocrinology	108 (68.4%)
	Surgery	50 (31.6%)
Region (n=156)	East Midlands	8 (5.1%)
	East of England	18 (11.5%)
	London	20 (12.8%)
	North East England	8 (5.1%)
	North West England	16 (10.3%)
	Northern Ireland	5 (3.2%)
	Scotland	17 (10.9%)
	South East England	21 (13.5%)
	South West England	15 (9.6%)
	Wales	5 (3.2%)
	West Midlands	6 (3.8%)
	Yorkshire and the Humber	17 (10.9%)
Volume of Graves' disease seen per year (n=156)	Less than 10	16 (10.3%)
	10 to 30	61 (39.1%)
	More than 30	79 (50.6%)

Note: regions grouped by Eurostat Nomenclature of Territorial Units for statistics (NUTS 1)

The median (range) time since graduation for the cohort (n=155) was 25 (12-43) years. The proportion of females was 28.6% in Endocrinology and 18.4% in Surgery. Regarding the rationale for initiating antithyroid drugs in patients with newly diagnosed Graves' disease, 60.2% of physicians and 63.6% surgeons commenced ATDs to make the patients euthyroid with subsequent remission expected on withdrawal of ATDs. 9.1% of surgeons, however, used ATDs in preparation to definitive surgery compared to only 1.9% of physicians. 38% and 27.3% of physicians and surgeons respectively answered they used ATDs for both definitive treatment as well as a bridge to surgery. Their reasons were patient preference (n=11), other comorbidities (n=7), presence of large goitre (n=7) or an older patient (n=7). All the physicians answered they would commence ATDs for the reasons discussed but over half of the (54%) either answered 'unsure/I am not involved in this stage' or left the question unanswered.

The second question determined the influence of clinical factors on recommendations for definitive treatment of relapsed Graves' disease. Overall, clinicians were more likely to recommend surgery than radioiodine in the presence of the factors mentioned other than mild eye disease. The influence of speciality on the recommendation for treatment in context of the described factors are summarised in a cluster bar chart (Figure 1). Surgeons were significantly more likely than physicians to recommend surgery in the presence of mild ($p<0.001$) and moderate eye disease ($p=0.002$), large goitre ($p<0.001$), children at work/home ($p=0.011$) and young women intending to start a family ($p<0.001$).

Similar analyses ~~(Figure 2)~~ were performed to look at the influence of gender on clinicians' preference for surgery or radioiodine. Female clinicians were significantly more likely than their

male counterparts to recommend surgery in the presence of severe eye disease (p=0.017) and lactation (p=0.008) (data not shown).

The experience of consultants (in terms of years since graduation) did not appear to influence preference for radioiodine or surgery in Graves' disease associated with the factors described (data not shown).

The ~~influence~~ ea~~a~~ffect of volume of Graves' disease seen by clinicians per year was also examined and assessed using Kruskal-Wallis test. ~~(Figure 3).~~ Although the majority of clinicians across all subgroups (by volume) would recommend surgery in the presence of all of the factors listed, clinicians who see high volumes of Graves' disease were significantly less likely to recommend surgery in patients with a large goitre (p<0.001) and in women intending to start a family (p=0.004).

Clinicians were then asked what they thought influenced patients' choices regarding their treatment. The majority of clinicians agreed that most of the factors suggested would influence patient decisions except for 'slow/unpredictable response to radioiodine'. The responses to this question were compared in subgroups defined by specialty (Figure 2~~4~~) and assessed with Mann-Whitney U test. Surgeons were less likely to agree that factors that related to surgery – fear of surgery (p=0.001) and complications of general anaesthesia (p=0.037) – influenced patient decisions with regards to definitive management. Endocrinologists were more likely to strongly disagree that the slow or unpredictable response with radioiodine (p<0.001) was a factor that patients may consider.

The survey also examined how clinical speciality may influence the risks mentioned to patients when discussing definitive management of Graves' disease i.e. surgery or radioactive iodine. As shown in Table 2, surgeons were more likely to quote a higher rate of failure (p=0.005) or relapse (p=0.003) with radioiodine and the risk of long-term hypocalcaemia (p=0.016) than physicians.

Table 2. Risks of failure and complications of treatments as quoted by clinicians by specialty

	Responses (n)	All clinicians – median % (range)	Physicians – median % (range)	Surgeons – median % (range)	P value (Mann-Whitney U test)
Relapse following ATD	132	50.0 (10.0-70.0)	50.0 (10.0-70.0)	50.0 (12.5-70.0)	0.151
Failure rate of first dose radioiodine	123	10.0 (0.9-60.0)	10.0 (0.9-60.0)	20.0 (4.5-50.0)	0.005
Relapse rate following first dose radioiodine	109	5.0 (0.0-50.0)	5.0 (0.0-33.3)	8.75 (1.5-50.0)	0.003
Risk of permanent laryngeal nerve injury	131	1.0 (0.0-8.0)	1.0 (0.4-5.0)	1.0 (0.0-8.0)	0.272
Risk of long-term hypocalcaemia	131	4.5 (0.2-30.0)	4.0 (0.2-30.0)	5.0 (0.5-15.0)	0.016

When questioned about what risks were quoted to patients when discussing surgery and radioactive iodine, answers varied widely. The main complications of radioiodine mentioned to patients were hypothyroidism, exacerbation of thyroid eye disease and radiation protection issues. When discussing surgical treatment, ~~the~~ risks discussed frequently were scarring, hypothyroidism and infection. Only 18.9% said they would mention risk of voice damage and only 12.6% mentioned risk of post-operative hypocalcaemia.

Clinicians were also asked on the rates of different definitive treatment taken up by their patients. Their responses by specialty and geography are displayed in Table 3 and Figure 3~~5~~ respectively.

Table 3 shows a statistically significant difference in the perceived uptake of treatment between surgeons and physicians. However, it should be noted that there were only 109 responses to this question, of which only eight were surgeons.

Table 3. Rates of patients who undergo second-round antithyroid drugs, radioiodine and surgery as perceived by UK clinicians

	Total – median % (range)	**Physicians – median % (range)**	**Surgeons – median % (range)**	**P value (Mann-Whitney U test)**
Second round antithyroid drugs	25.0 (0.0-96.0)	20.0 (0.0-96.0)	25.0 (0.0-80.0)	0.815
Radioiodine	50.0 (4.0-97.0)	50.0 (0.0-97.0)	22.5 (10.0-80.0)	0.015
Surgery	10.0 (0.0-100.0)	10.0 (0.0-100.0)	27.5 (10.0-90.0)	0.018

When evaluated by region, the use of radioiodine did not appear to significantly vary between regions, but the choice of surgery and second round antithyroid therapy did. The vast majority of patients in Wales appeared to undergo radioiodine for relapsed Graves' disease, while this was least frequent in Scotland. Of the three options, surgery is used least frequently in most regions, particularly in Northern Ireland and Wales. The most frequent use of surgery is in the South East and East Midlands (25%). The significant differences in choice of second-round antithyroid treatment were demonstrated by the uncommon use in Wales (2%) compared to > 10% in many parts of England and > 50% in Scotland.

The final question asked the clinicians to decide treatment they would have if they were suffering from uncomplicated relapsed Graves' disease. The majority (n=95) chose radioiodine in this

situation; 37 chose antithyroid drugs and 17 surgery (of which 12 were surgeons). Seven were unsure, whilst two preferred not to say (Figure 46). Speciality was found to influence the choice of therapy in favour of the treatment in which the individual was involved (Pearson Chi-square p=0.001). Gender, volume and experience (median number of years since graduation) did not appear to influence their decision (Pearson's Chi-square test p=0.973; Pearson's Chi-square test p=0.161; and Spearman's correlation coefficient rho=0.066, p=0.425 respectively).

DISCUSSION

Current practices in the definitive treatment of Graves' disease in the UK are influenced by patients' choice, social circumstances and clinicians' experience. This is especially true for relapsed Graves' disease. Prior to this survey, these patterns have been explored in Europe[4,6]~~[5,6]~~ USA, and worldwide [3] but a detailed evaluation amongst UK consultants has not been performed.

Our survey revealed that the majority of clinicians would routinely start antithyroid medication with the aim of inducing remission in an uncomplicated, first presentation of Graves' disease. Only two physicians and two surgeons would start antithyroid medication as a bridge to definitive treatment in all of their patients. The reasons for adopting either of the two approaches in a selective manner in subgroups of patients were reviewed in Table 3. Patient preference seems to be a common influence on the policy of using antithyroid drugs in newly diagnosed Graves' disease as a bridge to definitive treatment. Comorbidity has also been quoted as a reason, which is similar to another UK-based survey on the use of radioiodine[5]~~[4]~~. This is reasonable given the relative need for more rapid and effective treatment of hyperthyroidism in some patients with cardiac comorbidity which has the potential to lead to heart failure and sudden cardiac death[8]. Large goitre was also considered as an indication for the early adoption of definitive treatment in other surveys[4,5]. The American Thyroid Association and American Association of Clinical Endocrinologists support using antithyroid medication as a bridge to definitive therapy in compressive/symptomatic goitres or goitres over 80 g[9]. Older age as a reason for using antithyroid drugs as a bridge to definitive treatment is debatable. Surveys have found a relatively greater preference for definitive treatment (primarily radioiodine) in the elderly[4,5]. In contrast, American guidelines suggest that antithyroid drugs should be favoured in older age, although this has been described in the context of risk of surgical complications[9]. Klein et al highlights that older patients are more likely to have more cardiac comorbidities, and are less likely to revert back

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to sinus rhythm with treatment of hyperthyroidism[8]. They therefore suggest that more effective control over thyrotoxicosis may be preferable to trial of antithyroid medication treatment that has a ~~potential~~ relapse rate of approximately 60-70%[10].

This survey has found that surgery is the preferred option for the majority of consultants in relapsed Graves' disease complicated by the presence of any of the clinical and social features described (Table 3). Mild eye disease may be an exception to this trend - 42.7% have a slight or strong preference for surgery, and 47.1% were either unsure or had no preference. This survey was different to other studies in that it looked predominantly at factors influencing treatment of recurrent Graves' disease, rather than at initial presentation. Although recurrence was described in Burch and Vaidya et al[3,5], factors exploring choice of treatment in those studies were in relation to initial presentation. Escobar-Jimenez et al[4] looked at recurrence after previous ATD and surgery as well as that complicated by pregnancy. Certain findings were comparable across these previous studies. Eye disease influences choice away from radioiodine[3,5]; however if eye disease is inactive, 46% of clinicians would feel comfortable treating with radioiodine with the addition of steroids[5]. This is similar to the results of our survey. Large goitre was more often treated with surgery in the initial presentation of Graves' disease in Spain. For pregnant patients with relapse, antithyroid medication was the preferred option for the vast majority of patients[4]. In our survey, in which antithyroid medication was not an option, 73% had a strong ~~surgical~~ preference for surgery in pregnant patients.

The majority of consultants considered that complications of surgery or anaesthesia and fear of surgery could influence patients in their decision, although surgeons were less likely to agree that this was the case (p=0.037 and p=0.001 respectively). 80.8% of all consultants agreed that the radiation risk to children and other vulnerable people was likely to influence the patient's decision

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for definitive therapy. Fear of radioiodine with regards to cancer, and slow or unpredictable response with radioiodine was also considered to be influential, although to a lesser extent.

Although preference for recommending definitive treatment option in patients with relapsed, but uncomplicated Graves' disease was not explored, the personal preference of consultants surveyed was examined. 60.5% would undergo radioiodine as their preferred ~~therapy~~ choice of therapy. The significant influence of speciality on the preference ($p<0.001$) provides an interesting insight into personal choice of treatment. Only 4.6% of endocrinologists would prefer to have surgery, compared to 24.5% of surgeons. It needs to be emphasised that the scenario ~~specifically~~ excluded factors that may influence choice of treatment and that these preferences may be different in the presence of the variables that have been explored previously.

The perceived numbers of patients who undergo the three treatments following relapse (Table 3) shows a significant difference in treatment pathways across the UK. Radioiodine is considered to be used in 50.0% (median; range 4.0-97.0) of cases of relapse; second round antithyroid medication is used by 25.0% (0.0-96.0) and surgery in 10.0% (0.0-100.0). Preference for radioiodine in relapsed Graves' disease is also illustrated in other studies including physicians in the UK [5] and mainland Europe[4]. Seven consultants said that less than 5% of patients would undergo a second round treatment with antithyroid drugs in their centre (an additional four did not provide an answer for antithyroid drugs but a total of 100% was provided for radioiodine plus surgery). In contrast, eleven said that 80% or more would choose antithyroid drugs~~this option~~. The total of all answers provided in these questions had a total of 90-110%, (where some interpretation of ranges or 'more/less than' answers may account for differences), other than from one responder. This establishes that the majority of consultants interpreted the question correctly and considered second round antithyroid drug treatment to be a separate regime from

that which is used to prepare patients for radioiodine or surgery. The use of radioiodine did not differ between the regions (p=0.125), while repeat treatment with antithyroid drugs (p=0.022) and surgery (p=0.011) differed significantly. This is illustrated in Figure 5.

Both endocrinologists and surgeons consider that 50.0% (median; range 10.0-70.0) of patients will relapse following antithyroid medication. However, widely ranging rates of failure and relapse with radioiodine, permanent laryngeal nerve injury and long-term hypocalcaemia were quoted by clinicians across the UK (Table 2). Risk of permanent laryngeal nerve injury did not differ by specialty, and was considered to be around 1.0% (0.0-8.0). Two surgeons considered that relapse following radioiodine was ten times higher than the median value provided by all consultants. Other than for relapse following antithyroid medication, the~~all~~ highest values stated by consultants were more than six times the median value. Although the surgical risks were described as 'permanent', consultants may have assumed that this was for 'transient' or total values. The differences in the perceptions of risk for complications, failure and relapse in Graves' disease treatments across the UK strengthen the case for the need for empiric data from the UK population.

The clinician's speciality was strongly associated with personal choice and preference for specific treatments in the presence of specific patient- and disease-related factors. Surgeons had more positive views of surgery.

Other interesting findings from this study were that female clinicians were more likely to recommend surgery in the presence of severe eye disease (p=0.017) and lactation (p=0.008); and high volume consultants were less likely to strongly recommend surgery in patients with a large goitre (p<0.001) or those intending to start a family (p=0.004). Given the exploratory nature of this

study, these should only be considered as preliminary findings. However, it is clear that clinician related factors can significantly influence treatment recommendations.

As with surveys in general, there are a few limitations, which may influence the conclusions of this study. Despite piloting the study locally, there was a suggestion of misinterpretation of some of the questions by a number of respondents from the comments in the free text area. In addition, we asked consultants for their interpretation of practice within their centre, which may not correlate with actual practice. Occasionally, the respondents used ratios, ranges, and text answers for questions requiring percentages. In these cases, we used a set of 'rules' to attempt to summarise the responses. However, this may have introduced bias in interpretation of the answers. The same limitation applies to the attempt to group some of the responses into themes. The response rate is not ascertainable given the overlap of membership between the three societies surveyed. The response rate may have been higher with posted questionnaires, or with a financial incentive; however this was not logistically or financially feasible. Given the size of the memberships emailed, the number of responses obtained seems adequate.

In conclusion, within the UK, most clinicians treat new onset Graves' disease with a course of antithyroid medication in the hope of achieving remission. Approximately 50% of patients are thought to have a relapse following treatment. Definitive treatment in the form of radioiodine is the preferred choice for 50% of patients (median; range 4.0-97.0); however clinicians are inclined to recommend surgery in the presence of moderate eye disease, large goitre, cold nodule, patients with children at home or young female patients intending to start a family. In the context of pregnancy, lactation, or severe eye disease, the majority of consultants would strongly recommend surgical treatment to their patients. The perceived complication and relapse rates of therapy varied significantly across consultants that responded to the questionnaire. Empiric data

on failure and complication rates in the UK population is required. Discussion about the need for national guidelines on the management of Graves' disease should also be considered.

Competing interests: none

Figures

Figure 1. Comparison of preferences of physicians and surgeons for surgery or radioiodine in the treatment of Graves' disease in the presence of specific clinical and social factors. (Mann-Whitney U test)

~~Figure 2. Comparison of preferences of male and female clinicians for surgery or radioiodine in the treatment of Graves' disease in the presence of specific clinical and social factors (Mann-Whitney U test)~~

~~Figure 3. Comparison of preferences for surgery or radioiodine of clinicians stratified by volume of Graves' disease seen per year in the presence of specific clinical and social factors (Kruskal-Wallis test)~~

Figure 2. Comparison of the perceptions of factors that influence patient decision in regards to definitive therapy by specialty (Mann-Whitney U test)

Figure 3. Schematic diagram of frequency of choice of second line treatment in patients with relapsed Graves' disease across regions in the UK

Figure 4. Personal treatment choice of physicians and surgeons for uncomplicated Graves' disease at relapse

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