UK Thyroid Eye Disease Amsterdam Declaration Implementation Group

First Report – April 2014

This report is available at:
http://www.btf-thyroid.org/index.php/campaigns/teamed
Executive Summary

Thyroid Eye Disease (also known as Graves’ Orbitopathy [GO]) is a disfiguring condition that affects an estimated 50,000-100,000 people in the UK. Recent advances in our understanding of the predisposing factors and treatment have made it possible to reduce the incidence and severity of this disease but evidence suggests that this is not occurring in many parts of the UK.

In response to similar concerns in many countries, The Amsterdam Declaration (AD) to improve prevention, care and access to care for thyroid eye disease (TED) was signed by 86 national and international professional and patient-led organisations in 2009-10. The targets set by the AD include:

- halving the time from presentation to diagnosis,
- halving the time from diagnosis to referral to a centre of excellence,
- optimal treatment of thyroid disease including appropriate use of radioiodine, avoidance of hypothyroidism and vigorous anti-smoking measures in patients at risk of or with thyroid eye disease.

The UK Thyroid Eye Disease Amsterdam Declaration Implementation Group (TEAMeD) was formed in 2010 to take forward this initiative in the UK and comprises representatives of all the key stakeholder organisations: The Royal College of Physicians, British Thyroid Foundation, Royal College of Ophthalmologists, Scottish Ophthalmologists Club, Society for Endocrinology, British OculoPlastic Surgery Society, British Thyroid Association, and the Thyroid Eye Disease Charitable Trust.

This is the first TEAMeD report and describes progress so far and the plans for completion of other work streams over the next two years. Work to date includes a survey of recently diagnosed patients, a web survey of the specialist clinics for TED, analysis of referral rates for specialist procedures in TED care (orbital decompression), a clinical tool for detection and referral of TED in endocrine clinics and development of a smoking advice tool for use in clinics. The key points arising from the work of TEAMeD so far are (note that the current data for the first four points requires confirmation as it is based on a small UK sample (n=10)):

- There remains a significant delay (mean of five months) from the onset of symptoms to making the diagnosis with much variation between individuals (0-216 months). However this appears to represent some improvement on previous rates (> 6 months, Estcourt et al 2009).
- Many patients are not seen in specialist clinics: only 50% of patients are referred to a specialist clinic and only 20% are seen in a joint clinic. This is insufficient but also represents an improvement on previous rates (Estcourt et al 2009 – 25% attending a specialist clinic)
- Once referred, patients appear to be seen promptly in a specialist clinic (median delay to first appointment - 2 months).
- Awareness of smoking risks (making the disease more likely to occur, more severe and more resistant to treatment) once diagnosed seems high (100%), though smoking rates among patients who are newly referred to tertiary centres is still high.
• Around 26% of patients with Graves’ disease in endocrine clinics have thyroid eye disease and 8% would benefit from specific interventions not offered by endocrinologists. The use of a questionnaire screening tool can aid in identifying these patients.

• More than 30 centres in the UK treat moderate and severe thyroid eye disease.

• Of these, around 38% have clinics conducted jointly between an ophthalmologist and an endocrinologist. Patient activity varies widely across centres – 65% of centres see less than two severe cases of TED per year and 61% (47/77) of all severe cases were seen in three centres

• TEAMeD has published a review of decompression rates by PCT which also suggests that the provision of specialist procedures and rates of referral for TED specialist care for patients varies widely (more than 30-fold) by region.

• An advice leaflet on the risks of smoking based on the principles of information sharing and specifically designed for patients with TED was drafted by the Group. It contains practical advice and promotes shared decision making.

These findings suggest that care of patients with TED in specialist centres has improved in recent years. However, there is potential to further reduce delays in diagnosis, and to increase the number of patients seen in specialist clinics. The provision of specialist clinics, joint working with endocrinology, and reducing inequalities in workload, maintenance of specialist expertise and access to specialist services by region could also be improved.

Ongoing workstreams include an observational study and audit of the use of radioiodine in thyrotoxicosis across endocrine units, the development of best practice guidelines for referral of patients to specialist centres, preparation and dissemination through endocrine clinics of an eye disease awareness card for patients with Graves disease, a baseline audit of rates of optic neuropathy due to TED (severe disease) and an audit of the journey taken by patients arriving in specialist clinics.

TEAMeD is also leading a national group for defining specifications of centrally commissioned specialised services in England. In combination with best practice guidelines for referral and provision of specialist clinics and the implementation of measures to reduce the incidence rates of significant TED (appropriate use of radioiodine, early smoking advice), there is significant potential to achieve the goals set by the Amsterdam Declaration.

TEAMeD organised a meeting in May 2014, which brought UK and European experts on TED, patients, carers and the public together, in order to prioritise and promote research in this area.
## CONTENTS

1. Executive Summary 2
2. Background: The Amsterdam Declaration 5
3. The UK Thyroid Eye Disease Amsterdam Declaration Implementation Group (TEAMeD) 6
4. TEAMeD Workstreams 7
5. Results of Completed Workstreams 8
6. Next Steps 16
7. Appendices 28
1. Background: THE AMSTERDAM DECLARATION (VERSION2 18 June 09)

GRAVES’ ORBITOPATHY: IMPROVING OUTCOMES

Graves’ orbitopathy affects hundreds of thousands of people in the world every year. It causes pain, discomfort, double vision, disfigurement and sometimes blindness. Graves’ orbitopathy can lead to a poor quality of life and long-term psychosocial morbidity. Published data suggests that the quality of care received by the majority of people affected by this condition can be improved. Conventional treatments are effective when used appropriately and by centres with expertise. However, not all patients are offered effective treatments either because most are not referred early or at all. Furthermore, people at high risk of developing Graves’ orbitopathy can be identified and effective risk management can potentially lessen the severity of the disease.

In October 2009, international experts on Graves’ orbitopathy, representatives of professional organisations and patient representatives met in Amsterdam and unanimously agreed on the following (referred to as the “Amsterdam Declaration”):

Health care providers and professional organisations should recognise the need to improve the care of people with Graves’ orbitopathy and support plans for implementing better care and prevention.

The general objectives are:

- to minimise the morbidity associated with Graves’ orbitopathy and improve the patients’ experience and quality of life
- prevent the development of Graves’ orbitopathy in people at high risk

The 5-year targets are:

1. **Raise awareness** of this condition among health care professionals and managers
2. **Establish pathways** of referral and care
3. **Support existing centres** of excellence in management of this condition
4. **Create new centres** of excellence in localities where they are lacking
5. **Establish audit and monitoring** mechanisms of quality assurance of provision of care to people with Graves’ orbitopathy
6. **Implement measures** to reduce the incidence and morbidity of the disease by
   - 6.1 halving the time from presentation to diagnosis
   - 6.2 halving the time from diagnosis to referral to a centre of excellence
   - 6.3 appropriate management of thyroid dysfunction including use of radioiodine
   - 6.4 vigorous anti-smoking measures in patients at risk of or with Graves’ orbitopathy
7. **Improve the existing research** networks and develop further international collaborative research
2. The UK Thyroid Eye Disease Amsterdam Declaration Implementation Group (TEAMeD)

TEAMeD (UK) was formed in 2010, following letters of invitation to a wide range of stakeholder organisations. All agreed to provide representatives except the Royal College of General Practitioners.

The current representatives on the group are as follows:

<table>
<thead>
<tr>
<th>Group</th>
<th>Representative</th>
</tr>
</thead>
<tbody>
<tr>
<td>British Thyroid Foundation</td>
<td>Mrs Janis Hickey, Prof Geoff Rose, Mr Peter Foley (patient member)</td>
</tr>
<tr>
<td>Thyroid Eye Disease Charitable Trust</td>
<td>Prof Colin Dayan (Chair), Mrs Julie McLaren (patient member)</td>
</tr>
<tr>
<td>Royal College of Ophthalmologists</td>
<td>Mrs Jane Dickinson, replaced by Mr Dan Ezra Jan 2014.</td>
</tr>
<tr>
<td>Society for Endocrinology</td>
<td>Dr Petros Perros</td>
</tr>
<tr>
<td>Scottish Ophthalmologists Club</td>
<td>Prof Carrie MacEwen</td>
</tr>
<tr>
<td>British Oculoplastic Surgery Society</td>
<td>Mr Jimmy Uddin</td>
</tr>
<tr>
<td>British Thyroid Association</td>
<td>Dr Bijay Vaidya</td>
</tr>
<tr>
<td>Royal College of Physicians</td>
<td>Prof John Lazarus</td>
</tr>
</tbody>
</table>

Table 1: TEAMeD members

The group has been meeting every 1-2 months by teleconference since 2010 and agreed a series of workstreams.
### 3. TEAMeD workstreams

The table below summarises the planned TEAMeD workstreams

<table>
<thead>
<tr>
<th>Workstream</th>
<th>Brief Description</th>
<th>Amsterdam Declaration issues addressed</th>
<th>Target Delivery Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Questionnaire</td>
<td>Survey of patients’ experience of their journey to specialist services</td>
<td>• Audit &amp; Monitoring (5)</td>
<td>July 2013 (Completed)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Raise awareness (1)</td>
<td></td>
</tr>
<tr>
<td>Endocrine Clinic Questionnaire</td>
<td>Development of a tool for patients and doctors in endocrine clinics to raise awareness of GO</td>
<td>• Raise Awareness (1)</td>
<td>Feb 2014 (Completed)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Reduce time to referral to specialist clinic (6.2)</td>
<td></td>
</tr>
<tr>
<td>Specialist Centre Questionnaire</td>
<td>Survey by specialist centres of patient journey prior to reaching them</td>
<td>• Audit and Monitoring (5)</td>
<td>Nov 2014</td>
</tr>
<tr>
<td>Commissioning Guideline</td>
<td>Guidance to commissioners especially in England on appropriate commission model for GO services</td>
<td>• Establish pathways of treatment and care (2)</td>
<td>Nov 2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Reduce time to referral to specialist clinic (6.2)</td>
<td></td>
</tr>
<tr>
<td>Joint Clinic Survey</td>
<td>Survey of the number of joint clinics in the UK</td>
<td>• Support existing specialist services (3)</td>
<td>Nov 2013 (Completed)</td>
</tr>
<tr>
<td>Publications</td>
<td>Relevant articles inc primary research</td>
<td>• Raise Awareness (1)</td>
<td>On going</td>
</tr>
<tr>
<td>Use of I-131 – Pragma study (A study by the Society for Endocrinology)</td>
<td>Survey of use of radioiodine in Graves’ disease across the UK</td>
<td>• Appropriate endocrine management (6.3)</td>
<td>March 2015</td>
</tr>
<tr>
<td>BOSU survey of optic neuropathy</td>
<td>Assessment of incidence of severe disease by reporting of cases</td>
<td>• Audit and Monitoring (5)</td>
<td>August 2015</td>
</tr>
<tr>
<td>Smoking cessation tool</td>
<td>Identification of an optimal tool to address this issue</td>
<td>• Vigorous antismoking measures (6.4)</td>
<td>Feb 2014 (Completed)</td>
</tr>
<tr>
<td>Thyroid Eye Disease awareness card</td>
<td>Wallet-sized warning card for issue to all Graves’ patients at diagnosis</td>
<td>• Halve time from presentation to diagnosis (6.1)</td>
<td>Dec 2014</td>
</tr>
<tr>
<td>RCP Best Practice guidelines</td>
<td>Evidence based guidelines to encourage early and appropriate referral to specialist service</td>
<td>• Establish pathways of treatment and care (2)</td>
<td>August 2014</td>
</tr>
</tbody>
</table>
4. Results of completed workstreams

5.1 Patient Questionnaire

**Description:** Patient Questionnaire – for completion by a sample of patients from the British Thyroid Foundation (BTF) and Thyroid Eye Disease Charitable Trust (TEDct) patient organisations who have been treated for TED in the last 12 months. Providing information on AD targets: delays in specialist review, percentages of patients being seen in joint clinics, use of radioiodine, awareness of smoking risks and advice given, but also types of treatment they have received and any blind/pairially sighted registrations.

The **UK questionnaire** was devised by the TEAMeD group and reviewed by BTF and TEDct. A note was placed on the websites of these two patients organisations and in their newsletters inviting people who had been diagnosed with TED in the last 12 months to take part. People who made contact to express interest were then sent a paper copy of the questionnaire to complete. Eleven questionnaires were completed between 1 Nov-2012 and 30 Apr-13. One was unusable as the subject was not diagnosed in the last 12 months. The full results are shown in appendix 7.1.

The **US questionnaire** was performed over a similar period (Sep-2012 to April-2013)

The key points from both surveys are summarised below

<table>
<thead>
<tr>
<th></th>
<th>UK survey</th>
<th>US survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers of respondents</td>
<td>10</td>
<td>262</td>
</tr>
<tr>
<td>Mean Age</td>
<td>53</td>
<td>49</td>
</tr>
<tr>
<td>Female respondents</td>
<td>9/10</td>
<td>202/262 (77%)</td>
</tr>
<tr>
<td>Age range</td>
<td>31-75</td>
<td>13-82</td>
</tr>
<tr>
<td>Troublesome disfigurement</td>
<td>8/10</td>
<td>N/A</td>
</tr>
<tr>
<td>Troublesome double vision</td>
<td>7/10</td>
<td>N/A</td>
</tr>
<tr>
<td>*Median time from first consultation on TED symptoms to diagnosis of TED</td>
<td>5 months (0 to 216 months)</td>
<td>3 months (0 - &gt; 12 months – exact time not recorded, 0-48 months) 48/240 (20%) &gt; 12 months</td>
</tr>
<tr>
<td>Referral to a TED specialist</td>
<td>5/10 (50%)</td>
<td>151/252 (40%)</td>
</tr>
<tr>
<td>Time from diagnosis to being seen by a specialist</td>
<td>2 months (3 weeks to 4 months)</td>
<td>1 month (1 month to longer than 12 months, (n=95))</td>
</tr>
<tr>
<td>Seen at joint clinic</td>
<td>2/10 (20%), only when necessary</td>
<td>N/A</td>
</tr>
<tr>
<td>Received treatment for over-active thyroid with radio-iodine (RAI)</td>
<td>2/8 (25%)</td>
<td>79/206 (38%)</td>
</tr>
<tr>
<td>TED deterioration after RAI</td>
<td>2/2 (100%) delayed</td>
<td>62/77 (81%)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>0/10 (0%)</td>
<td>49/248 (20%)</td>
</tr>
<tr>
<td>Aware of risk of smoking for TED</td>
<td>10/10 (100%)</td>
<td>224/247 (91%)</td>
</tr>
<tr>
<td>Aware that smoking reduces the effectiveness of TED treatment</td>
<td>7/10 (70%)</td>
<td>183/248 (74%)</td>
</tr>
</tbody>
</table>
**Table 2.** Summary of results from UK and US patient questionnaires (self-reported experience of patients diagnosed in the last 12 months)

In summary, delay in diagnosis was very variable in the UK (immediate to 18 years) with a median of five months. Only 50% considered that they were referred to a specialist clinic and only 2/10 were aware of being seen in a joint clinic despite 7/10 having significant eye disease (“troublesome double vision”) and 8/10 reporting “troublesome disfigurement”. Patients were generally seen promptly in specialist clinics when referred. A significant proportion had received radioiodine (25%) and believed that their eye disease had deteriorated as a result. Awareness that smoking increases the risk of TED was high (100%), with a slightly lower awareness that it reduces the effectiveness of treatment (70%).

The limited numbers in the survey and the potential for bias mean that the results need to be interpreted with caution. However, the concordance with the US data is striking. Although patients in the US were referred more rapidly, only 40% considered that they had been referred for a specialties clinic for thyroid eye disease.

**Key points (UK data):**

- There is significant delay (5 months) from the onset of symptoms to making the diagnosis with much variation between individuals (0-216 months).
- Only 50% of patients are referred to a specialist clinic and only 20% are aware of being seen in a joint clinic.
- Once referred, patients are seen promptly in a specialist clinic (median 2 months)
- Awareness of smoking risks once diagnosed (already “in the system”) seems high (100%) so awareness raising may be best targeted to patients with Graves disease who have not yet developed TED.
- 25% of patients with TED have recently been treated with radioiodine.

**Conclusion:** There is room for improvement on the delay to diagnosis (AD target 6.1) and the number of patients referred to specialist clinics (AD target 6.2) though perhaps not the delay in referral for those who are referred. Many patients receive radioiodine, so this needs to be managed appropriately (AD target 6.3). Awareness of smoking (AD target 6.4) amongst patients already “in the system” is high, so awareness raising may be best targeted to patients with Graves’ disease who have not yet developed TED.

**5.2 Diagnostic tool for identifying referable Graves’ Orbitopathy in Endocrine Clinics (DiAGO-DiAgnosing Graves’ Orbitopathy)**

**Description:** DiAGO was designed by TEAMeD to raise awareness of TED and need for referral of patients from endocrine clinics to Ophthalmology – for completion partly by doctors, partly by patients. DiAGO is based on published EUGOGO and Vancouver Clinic questions to detect thyroid eye disease (Mohaseb et al 2008, Wiersinga et al 20006, Bartalena et al 2008). The full tool is provided in appendix 7.2.

5.3 Specialist Centre Questionnaire
As part of the work of TEAMeD, it was considered important to know how many joint thyroid eye disease clinics were currently being held in the UK and their location. A question comprising five parts was therefore drawn up by the group in April 2012.

However, the group was subsequently made aware that Ms Sally Ameen in collaboration with Miss V Lee at Central Middlesex Hospital was planning an overlapping survey via a websurvey to British Oculoplastic Surgical Society (BOPSS) members. The questions were reviewed by the group (appendix 1) and it was considered that there was sufficient overlap that (a) it would be over-burdensome to clinicians to perform both questionnaires separately and (b) sufficient data should be available from the web survey to provide the data that TEAMeD sought.

5.3.1 Methodology

The survey was sent out by Ms Ameen on the SurveyMonkey platform to members of BOPSS in June 2012. Results were initially collected in three cycles over a four-month period.

However, on review of the data in June 2013, it became apparent that there were five duplicate responses (from the same respondent e-mail address) and that there were no data from several major centres. The survey was then resent to seven major centres who had not responded (five replies received). Attempts were made to resolve the origin of the duplicate responses, but by this time, the primary data were no longer present on the website and it was no longer possible to re-analyse. Hence there are some inherent inaccuracies in the data and these are highlighted where appropriate below.

5.3.2 Results

Sixty surveys were sent to “working” e-mail addresses. It was reported initially that 38 responses were achieved, but only 30 separate respondents could be identified, suggesting that there may be eight duplicate or in some cases triplicate responses. Despite multiple efforts, it was not possible to identify and remove three of these multiplicate responses from the dataset and it is believed that five duplicate responses remain. Individual level data were only available at the time of final analysis from the last 12 responses.

5.3.2.1 Joint clinics.

<table>
<thead>
<tr>
<th>Are the GO patients managed in a multidisciplinary clinic?</th>
<th>First Round (n=29 responses)</th>
<th>Major centres (n=5 responses)</th>
<th>Combined (n=34)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>16</td>
<td>2</td>
<td>18</td>
</tr>
<tr>
<td>Yes</td>
<td>13</td>
<td>3</td>
<td>16 (47%)</td>
</tr>
<tr>
<td>If yes, other staff involved</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endocrinologist</td>
<td>10</td>
<td>3</td>
<td>13 (81%), 38% of all clinics</td>
</tr>
<tr>
<td>Immunosuppression specialist</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Specialist Nurse</td>
<td>6</td>
<td>2</td>
<td>8 (50%)</td>
</tr>
</tbody>
</table>

*Inc 5 duplicates
5.3.2.2 Use of GO classification.

A wide variety of GO classifications was used including CAS (~47%), EUGOGO, NOSPECS and VISA.

5.3.2.3 Severity of cases

All centres except one saw severe as well as moderate cases.

Figure 5.1 The distribution of moderate cases/year seen across centres (including five duplicates) is shown below. This suggests that around 15% (n=5) of centres see > 20 cases a year and ~60% of centres (n= 18) see > 10 cases per year.

Figure 5.2 The self-reported distribution of severe cases/year seen across centres (including five duplicates) is shown below. This suggests that around 15% (n=5) of centres see > 5 severe cases a year and ~35% of centres (n= 11) see > 2 cases per year. If the self-reported figures are correct, ~65% of all severe cases are seen in three centres out of the 31 where data were available.
5.3.2.4 Geographical distribution

Replies were received from clinics in 26 different locations:

<table>
<thead>
<tr>
<th>Locations of respondents to survey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birmingham</td>
</tr>
<tr>
<td>Bournemouth</td>
</tr>
<tr>
<td>Bradford</td>
</tr>
<tr>
<td>Brighton</td>
</tr>
<tr>
<td>Cardiff</td>
</tr>
<tr>
<td>Coventry</td>
</tr>
<tr>
<td>Dundee</td>
</tr>
<tr>
<td>Essex</td>
</tr>
<tr>
<td>Exeter</td>
</tr>
<tr>
<td>Glasgow</td>
</tr>
<tr>
<td>Kingston Upon Hull</td>
</tr>
<tr>
<td>Kingston Upon Thames</td>
</tr>
<tr>
<td>Lancashire</td>
</tr>
</tbody>
</table>

NB Specialist clinic in Manchester but no response received.

5.3.2.5 Use of different forms of treatment

Exact data for different forms of treatment used could not be extracted. However, around 65% of centres used radiotherapy, ~50% had tried rituximab in one or more patients, and 85% of centres used i/v steroids routinely.

5.3.2.6 Conclusions

The key conclusions of this survey are subject to the limitations that there was a ~50% response rate, only BOPSS members were surveyed, results are self-reported and not verified and the dataset contains five duplicates which could not be separated out. However, the responses still provide a useful “broad brush” picture of which the key points are as follows:

• More than 30 centres in the UK treat moderate and severe thyroid eye disease.
• Of these, around 38% have clinics conducted jointly between an ophthalmologist and an endocrinologist.
• For moderate cases, around 15% (n=5) of centres see > 20 cases a year and ~60% of centres (n=18) see > 10 cases per year.
• For severe disease, around 15% (n=5) of centres see > 5 severe cases a year and ~35% of centres (n=11) see > 2 cases per year.
• 61% (47/77) of all severe cases were seen in three centres

In summary, self-reported specialist clinics are present in most parts of the country, but less than half of these are joint clinics. Activity varies very widely between centres with three centres seeing
more than half of all specialist cases. This is consistent with the wide variation in decompression rates across the country we recently reported. The optimal number and configuration of clinics to ensure equity of access, expertise and convenience for patients attending multiple times needs to be determined.

5.4 Smoking Cessation Tool

An advice leaflet based on the principles of information sharing was drafted by the Group and reviewed. This is shown in appendix 7.5.

5.5 Publications

5.5.1 Orbital decompressions (Perros et al 2011)

To provide insight into the distribution of specialist care for TED across the country, data on orbital decompression (a specialist procedure only performed for TED) taking place in England over a two year period between 2007-2009 were derived from CHKS Limited, a Capita group company, and analysed by hospital and Primary Care Trust. Forty-four percent of these operations took place in hospitals with an annual workload of 10 or fewer procedures. Analysis of the same data by Primary Care Trust suggests an almost thirty-fold variance in the rates of decompression performed per unit population. These data are consistent with the specialist clinic survey activity data and in addition provide information on referral rates for specialist care (as the data are analysed by primary care trust). They suggest:

- Expertise available to patients with Graves’ orbitopathy varies significantly by region
- Rates of referral for TED specialist care in England appear to vary significantly by geographic location.

These data have been published:

Figure 5.3: Decompression procedures by PCT (2007-9) – rates per 100,000 population per year

5.3.3 Retrospective data on patients being seen in specialist clinics (Estcourt et al 2009)

This survey was conducted in 2008 in association with the Thyroid Eye Disease Charitable Trust (TEDct) and the British Thyroid Foundation (BTF). A postal questionnaire was sent to 395 members of these two patients support organisations.

The response rate was 67%. The majority of responders were females (91%) and aged above 45 (74%). Note that in contrast to the Patient Questionnaire in section 5.1 above, 99% were diagnosed more than 1 year previously, and 41% more than 10 years. Hence the data around diagnosis do not necessarily reflect the present situation.

In 26% of responders, the time from the first symptoms to the diagnosis of TED was over 12 months. There was a wide variation in the type of clinic and healthcare professionals involved in the treatment of TED. Only 25% of the responders attended a specialist TED clinic. Out of these, 33% waited over 6 months from the first consultation with a doctor to being seen at a specialist TED clinic. Only 56% of responders were satisfied with the treatment they received for TED. More responders who had attended a specialist TED clinic were satisfied with the treatment than those who had not attended a specialist clinic (67 vs 52%, P<0.05).

Comments: Comparison with the recently diagnosed patients in the Patients Questionnaire suggests there have been improvements in recent years. It seems that the delay in diagnosis has reduced, twice as many people are seen in specialist clinics (25% vs 50%) and the wait to be seen once referred has reduced markedly.

## Next steps

The table below indicates the current workstreams of the TEAMeD group.

<table>
<thead>
<tr>
<th>Workstream</th>
<th>Brief Description</th>
<th>Amsterdam Declaration issues addressed</th>
<th>Target Delivery Date</th>
</tr>
</thead>
</table>
| DiAGO                             | Further development and dissemination of tool for patients and doctors in endocrine clinics to raise awareness of GO | • Raise Awareness (1)  
• Reduce time to referral to specialist clinic (6.2) | Feb 2015 |
| Specialist Centre Questionnaire   | Survey by specialist centres of patient journey prior to reaching them            | • Audit and Monitoring (5)                                                   | Nov 2014 |
| Commissioning Guideline           | Guidance to commissioners esp in England on appropriate commission model for GO services | • Establish pathways of treatment and care (2)  
• Reduce time to referral to specialist clinic (6.2) | Nov 2014 |
| Use of I-131 – Pragma study        | Survey of use of radioiodine in Graves’ disease across the UK                      | • Appropriate endocrine management (6.3)                                     | March 2015 |
| BOSU survey of optic neuropathy   | Assessment of incidence of severe disease by reporting of cases                    | • Audit and Monitoring (5)                                                   | August 2015 |
| Thyroid Eye Disease awareness card| Wallet-sized warning card for issue to all Graves’ patients at diagnosis via endocrine clinics | • Halve time from presentation to diagnosis (6.1)                            | Feb 2015 |
| Improved smoking awareness tool   | Improved web based information tool to promote cessation of smoking               | • Vigorous antismoking measures (6.4)                                        | Feb 2015 |
| RCP Best Practice guidelines      | Evidence based guidelines to encourage early and appropriate referral to specialist service | • Establish pathways of treatment and care (2)                              | August 2014 |
In addition there is a need to extend the baseline assessment of care of patients with TED in the UK and these measures will provide tools to improve the process. Implementation will need to focus on using the commissioning network, referral guidelines, radioiodine data and smoking and early detection tools to expedite the care of patients with TED in specialist services and reduce incidence rates. Separate measures will be needed to reduce delays in diagnosis in patients not currently under endocrine services.
7 Appendices

7.1 Summary of responses from UK patient questionnaire survey

1. The survey was completed between 1 Nov-2012 and 30 Apr-13
2. There were 10 respondents all of whom were diagnosed with TED in the past 12 months; and one respondent who had not been diagnosed with TED in the past 12 months.
3. All were living in the UK
4. The median age was 53 (range 31 to 78)
5. 9/10 respondents were female with a median age of 49 (range 31 to 75) and 1/10 male (age 78)
6. The median time from onset of symptoms to diagnosis was 5 months (range immediate to 216 months)
7. Only 50% (5 out of 10) respondents were referred to a specialist centre for thyroid eye disease, and that referral took from 3 weeks to 4 months
8. 2/10 respondents were seen at a joint clinic and, if so, only when necessary
9. 8/10 respondents have been treated for an overactive thyroid, and the range of time from diagnosis to normal blood tests was 3 to 36 months, including 2/8 whose blood tests were still not normal; hyperthyroidism reoccurred in 5/8 of these treated patients (including 2 out of those 8 whose blood tests were still not normal)
10. 4/10 respondents have had spells of hypothyroidism, including 2 out of those 8 experiencing periods of hyperthyroidism
11. 2/8 of those respondents experiencing hyperthyroidism were treated with radioactive iodine, and both had resultant symptoms of hypothyroidism and delayed worsening of thyroid eye disease
12. 2/10 respondents had been smokers, and both had ceased prior to diagnosis
13. 10/10 respondents were aware that smoking increases the chance of TED worsening
14. 7/10 respondents were aware that treatments were more effective in non-smokers
15. 6/10 respondents were aware that antithyroid drug treatment of Graves’ was more likely to be successful in non-smokers
16. The severity of the disease was ranked: troublesome swelling of the eyelids (10/10), troublesome disfigurement (8/10), troublesome double vision (7/10), and pressure on optic nerve affecting vision (5/10)
17. 2/10 respondents mentioned treatment with steroids, 1/10 also mentioned radiotherapy, and 1/10 had eye lid surgery
18. No respondent was registered blind because of TED
19. No respondent was registered partially sighted because of TED.
7.2 Endocrine clinic questionnaire

SECTION 1- TO BE FILLED IN BY PATIENT

Please answer the following questions

1. Do you have redness in your eyes or eyelids? Y/N
2. Do you have swelling or feeling of fullness in
   one or both of your upper eyelids Y/N
3. Do you have bags under the eyes? Y/N
4. Do your eyes seem to be too wide open? Y/N
5. Is your vision blurry (even with glasses/contacts?) Y/N
6. Please have a look at the small print below, with your reading glasses on if you
   normally them. First cover your right eye and read using your left eye. Then
   repeat using your right eye to read.

   And he has taught you the habit of answering questions in a grand and bold style, which becomes
   those who know, and is the style in which he himself answers all comers

   Were you able to read the small print with either eye? Y/N
7. Please have a look at the red dot below, first with your right eye while covering
   the other eye with your hand. Then switch and cover your right eye and look at
   the red dot with your left eye. Keep switching between left and right eye while
   looking at the red dot.
Do you think there is a difference in the intensity of the red colour between your two eyes? Y/N
8. Are your eyes abnormally sensitive to light? Y/N
9. Are your eyes excessively gritty? Y/N
10. Do you have pain in or behind the eyes? Y/N
11. Has the appearance of the eyes and/or eyelids changed over the past 1–2 months? Y/N
12. Does the appearance of your eyes cause you concern? Y/N
13. Can you see two separate images when there should only be one? Y/N

SECTION 2- TO BE FILLED IN BY DOCTOR

Does the patient have any of the following:

14. Upper eyelid retraction? Y/N
15. A history of thyroid dysfunction? Y/N
16. Abnormal swelling or redness of eyelid(s) or conjunctiva(e)? Y/N
17. Restriction of eye movements? Y/N
18. Tilting of the head to avoid double vision? Y/N
19. Exophthalmos? Y/N
20. Obvious corneal opacity visible to the naked eye? Y/N
21. Papilloedema? Y/N

SECTION 3 - ACTION TO BE TAKEN BY DOCTOR

If the answers to all questions above (1-21) are “no”, the patient does not need to be referred and he/she should have usual follow-up in the endocrine clinic.

Refer to the Joint Thyroid Eye Clinic URGENTLY if any of the answers to questions 5, 6, 7, 20, 21 are “Yes”, as the patient may have sight-threatening Graves’ orbitopathy.

Refer all other patients to the Joint Thyroid clinic routinely, as they may have significant Graves’ orbitopathy and may benefit from treatment.
7. 3 Joint/Specialist clinic web survey questions

1. Are the GO patients managed in a multidisciplinary clinic?
   If Yes please indicate the other clinical staff involved

   ☐ No
   ☐ Yes
   ☐ Endocrinologist
   ☐ Immunosuppression Specialist
   ☐ Specialist nurse

   Other healthcare professionals (please specify)

2. Have you encountered difficulties with managerial/other health professionals supporting your GO service?

   ☐ No
   ☐ Yes

   If yes, please specify

3. Which GO classification(s) do you use?

   ☐ None
   ☐ NOSPECS
   ☐ CAS
   ☐ VISA

   Other (please state)

4. Please estimate the category and number of patients a year treated with the different types of immunosuppressive agents
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Peribulbar</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moderately active GO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe GO / optic nerve compression</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
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<tr>
<td>Steroids</td>
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<td>Azathioprine</td>
<td></td>
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<tr>
<td>Methotrexate</td>
<td></td>
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<tr>
<td>Mycophenolate Mofetil (MMF/CellCept,Myfortic)</td>
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<td>Cyclosporin</td>
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<td>Tacrolimus</td>
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<td>Rituximab</td>
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<td>IV immunoglobulins</td>
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<tr>
<td>Other</td>
<td></td>
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</tbody>
</table>

5. If you use steroid treatment, please estimate the annual number of patients treated and the regimen used.

Peribulbar

Average no of injections per patient

Oral

Please state regimen used
Intravenous

Please state regimen used e.g. Kahaly

6. Who is the primary clinician responsible for the immunosuppression/IV steroid treatment?

- [ ] Ophthalmologist
- [ ] Endocrinologist
- Other (please specify)

7. Please estimate the annual number of GO patients you refer for orbital radiotherapy.

For moderately active GO

For severe/sight threatening GO

8. Please tell us of any comments you wish to add with regards to your management of GO
7.4 Smoking cessation tool

GRAVES’ DISEASE, THYROID EYE DISEASE AND SMOKING:
INFORMATION FOR PATIENTS

Graves’ disease is the most common cause of hyperthyroidism – an over-active thyroid. It is caused by antibodies that attack the thyroid gland.

About a third of people with Graves’ disease develop thyroid eye disease (TED). TED is caused by the body’s immune system stimulating the tissues inside the eye socket to increase in size. TED can happen at any time. It can develop before, during, or after the over-active thyroid disorder is diagnosed. In most cases the eye disease is mild, but it can be a distressing and disfiguring complication that can be difficult to treat.

Cigarette smoking is known to have a major influence on Graves’ disease.

- Smokers with Graves’ disease are about three times more likely to develop thyroid eye disease (1).
- If you develop TED and you continue to smoke you are more likely to suffer the more severe forms of the disease than if you quit (2).
- If you need any specific treatment for your eyes (such as steroids, radiotherapy or surgery), the treatment will not work as well if you continue to smoke (3, 4).

- Apart from the effects of smoking on the eyes of people with Graves’ disease, smoking reduces the chance of a cure of the thyroid over-activity after a course of tablets (4).

BENEFITS OF STOPPING SMOKING

The good news is that if you quit smoking, the chances are that your eyes will improve (2). There are of course many other reasons why you should quit, apart from the beneficial effects on thyroid eye disease. We know that stopping smoking reduces the risk of premature death. In fact benefits are seen straight away. As you can see from the diagram below, within twenty minutes after smoking your last cigarette, your body begins a series of changes that continue for years. Passive smoking may also have a detrimental effect, especially for children, and avoidance of passive smoking is likely to be beneficial.

AFTER...

Quitting is not easy but if you have Graves’ disease there is now one more reason why you should quit - to protect your eyes.

**HOW TO STOP SMOKING**

Deciding you want to quit is the first step. You can get support to help you arrive at a decision and choose the treatment option that is right for you.

Help is available from the NHS – all help, support and advice is free. You are four times more likely to be successful in stopping smoking using NHS support services and treatment than trying to stop on your own.

The NHS has a Shared Decision Making Programme, which takes you through the treatment options for you to consider: continuing to smoke; or reduction or quitting by self-management, health professional assistance or alternative therapy. The effects and the pros and cons of each treatment option are described.

To access Shared Decision Making help, visit [http://sdm.rightcare.nhs.uk/pda/smoking-cessation/](http://sdm.rightcare.nhs.uk/pda/smoking-cessation/) or call the Decision Support service on 0845 450 5851 to speak to a trained Health Coach.

Your doctor, pharmacist, or health visitor can also give advice and will be able to refer you to NHS stop smoking services in your area. You can find your local NHS Stop Smoking Service here: [http://smokefree.nhs.uk/ways-to-quit/local-nhs-stop-smoking-service/](http://smokefree.nhs.uk/ways-to-quit/local-nhs-stop-smoking-service/)

Even if you do not give up completely, or for ever, cutting down the amount you smoke is still worthwhile and will have a beneficial effect on your eyes. You may find that nicotine replacement and other treatments can help you to cut down or quit. Even though you have a thyroid condition you can use these products. Your doctor will be able to give you full information about the choices available and whether you are exempt from prescription charges.

Further information is available on the following websites:

[http://www.nhs.uk/Livewell/smoking/Pages/Motivateyourself.aspx](http://www.nhs.uk/Livewell/smoking/Pages/Motivateyourself.aspx)

Information is available in other languages on the above website by clicking on the ‘Translate’ link at the top of the page

For pregnant women seeking help in stopping smoking: [http://www.quit.org.uk/pregnant.php](http://www.quit.org.uk/pregnant.php)

**References**


TEAMed (Thyroid Eye Disease Amsterdam Declaration) Implementation Group UK is working to improve the patient experience for people with thyroid eye disease. Its activities are supported by the British Thyroid Foundation, TEDct, the Royal College of Physicians, the Royal College of Ophthalmologists, the Scottish Ophthalmologists Club, the Society for Endocrinology, the British OculoPlastic Surgery Society and the British Thyroid Association. For further information see [www.tedd-thyroid.org/index.php/campaigns/thyroid-eye-disease/learned](http://www.tedd-thyroid.org/index.php/campaigns/thyroid-eye-disease/learned)

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