

A multidisciplinary (MDT) approach to  
**Graves Orbitopathy (GO)**  
**Thyroid Eye disease (TED)**  
*the most common inflammatory disease of the orbit*

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Consultant Ophthalmic & Oculoplastic Surgeon

**TEAMeD**  
Thyroid Eye Disease Amsterdam Declaration  
Implementation Group UK

**BOPSS**  
BRITISH OCULOPLASTIC SURGERY SOCIETY

# One patient's journey

40+ year old NIDDM  
Asian lady  
Graves Hyperthyroidism  
2014 Thyroidectomy  
Normal TFT levels  
non smoker

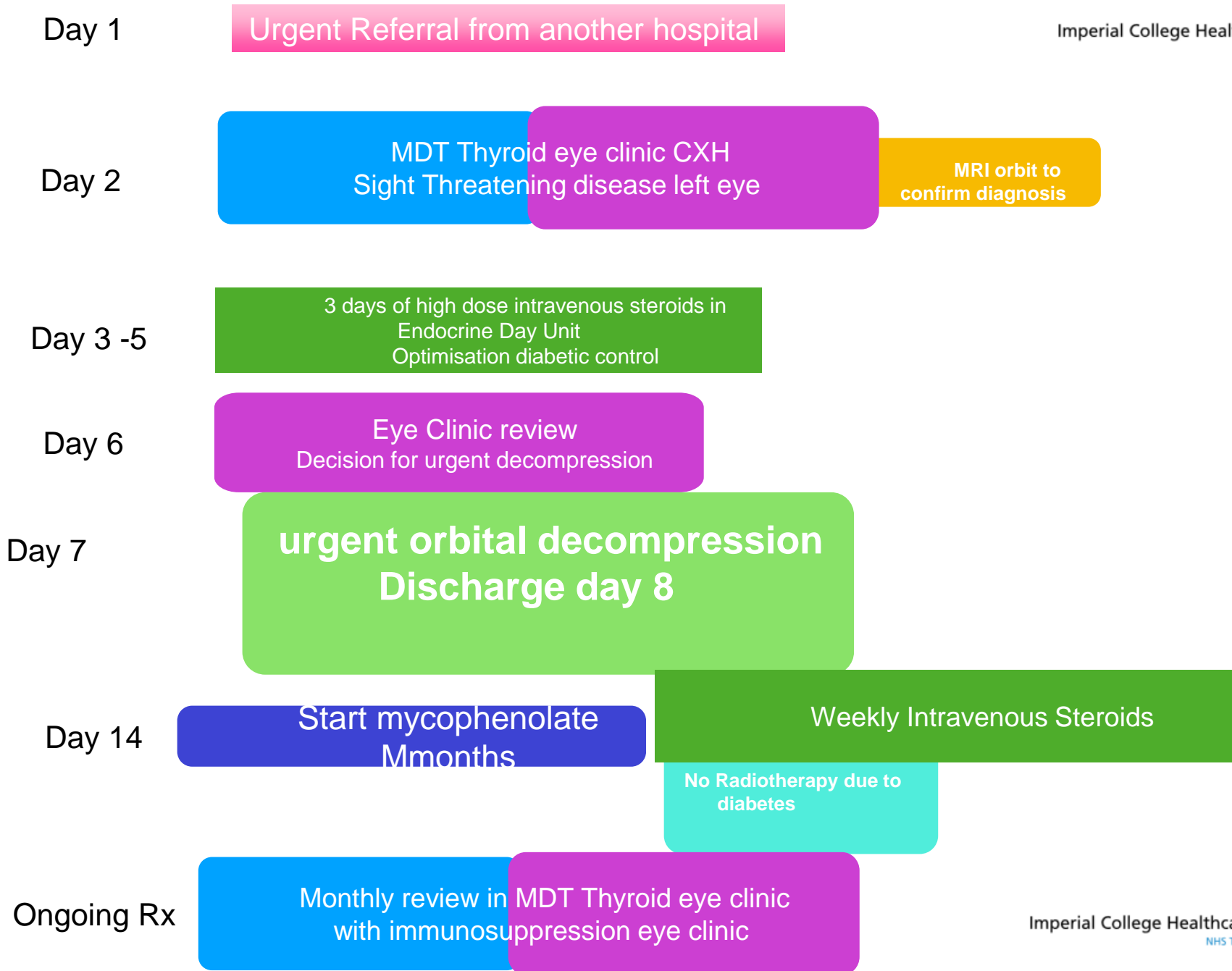
3 day history of intermittent  
sudden loss of vision  
pain and double vision



pain  
proptosis  
loss of left vision  
when trying to look up  
unable to move her eye  
constant double vision



Euthyroid Post thyroidectomy  
Uncontrolled NIDDM HbA1c >100





Day 1  
pain proptosis  
transient visual obscurations  
unable to move her eye  
constant double vision

Day 8  
no pain less proptosis  
no transient visual obscurations  
improved eye movements  
no double vision



6 months later  
Recurrence of pain proptosis  
transient visual obscurations  
pain on moving her eye  
constant double vision

Recurrence of orbital inflammation despite orbital decompression IVMP & ongoing immunosuppression with mycophenolate  
Decreasing vision increasing pain

Switched to prednisolone & ciclosporin to try to maintain her vision  
Poorly controlled diabetes, diabetic eye disease  
not suitable for radiotherapy

# Why are we talking about

Graves Orbitopathy GO  
Thyroid Associated orbitopathy TAO  
Thyroid eye disease TED

50% GD disease have clinically relevant GO

Can worsen despite good thyroid control

poor clinical outcome

Can blind or cause severe double vision

no effective medical cure

Disfigurement & Impact on QOL usually much worse than clinical severity

No animal model  
How is immune tolerance broken?

1 Aetiology & Pathogenesis

2 Risk Factors and how to modify them

3 Principles of management of Thyroid Eye Disease (including TEAMed 5 )

4 A case study to illustrate the need for a multidisciplinary approach

# Aetiology & Pathogenesis



60-80% of all cases of hyperthyroidism

Autoimmune condition stimulating the TSH receptor

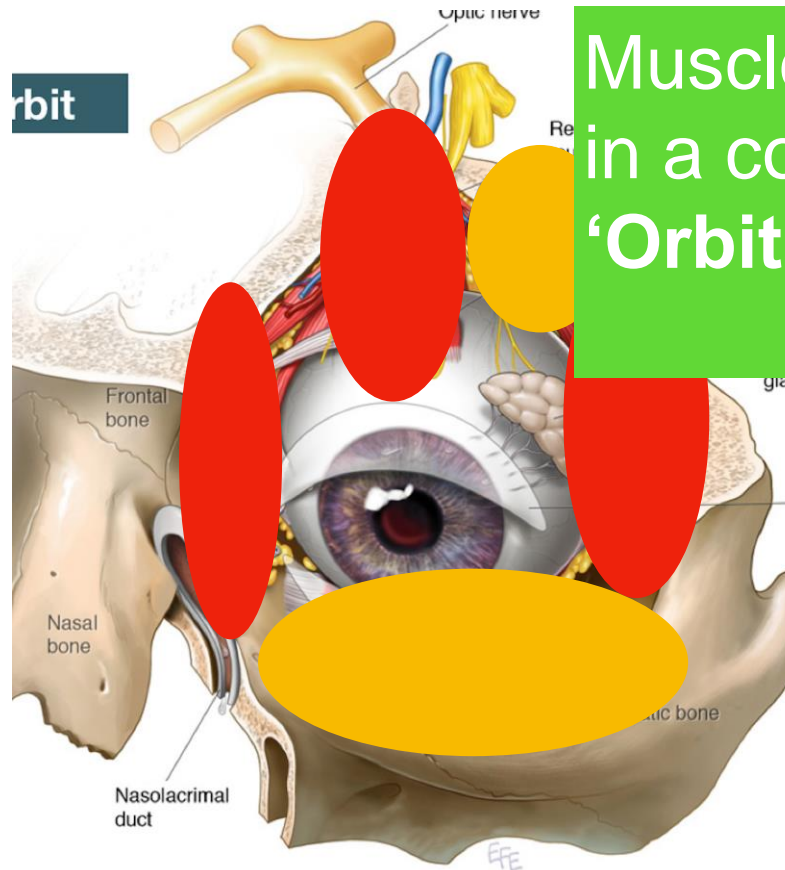
Defined typically by hyperthyroidism, TSH R antibody or diffuse uptake on a Tc NM scan

Pathognomonic features, eye disease, thyroid bruit



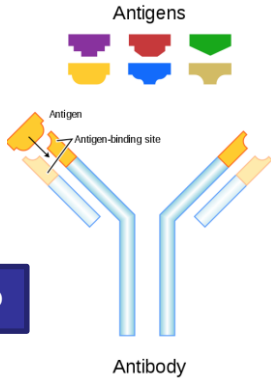


Orbit

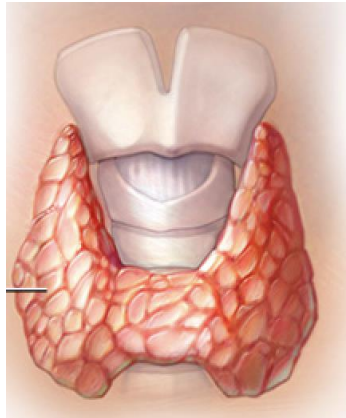


# Muscle & fat expansion in a confined space 'Orbital Cushings'

TrAb



gland

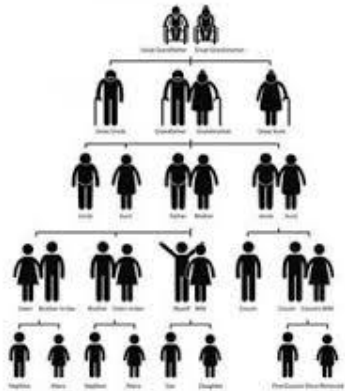


# Estimated Prevalence of GO

	PREVALENCE (per 10,000 population)	PROPORTION OF PATIENTS WITH VARIANT
(a)		
All cases of GO	8.97	-
	15.48	
Mild GO	5.83	65.0%
	11.03	72.8%
Moderate-to-severe	2.96–4.45	33.0–29.4%
Sight-threatening	0.18	2.0%
(b)		
Euthyroid/hypothyroid GO	0.02–1.10	0.2–11.0%
GO associated with dermopathy	0.15	1.5%
GO associated with myopathy		
Asymptomatic		
Unilateral		

1 in 10 will not have any thyroid hormone problems  
of these about half will go on to have thyroid hormone problems  
about 1 in 10 will only be affected in one eye socket

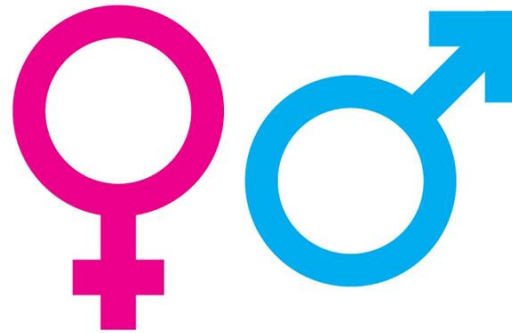
# Who is at risk?



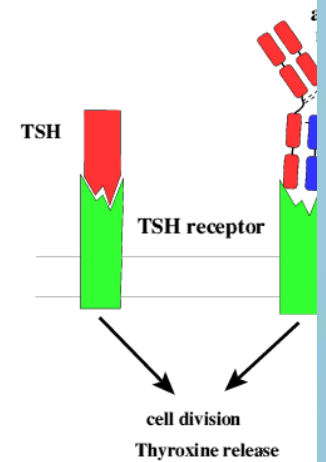
family history



age



gender



high TrAb anti  
(normal <1.75 IU  
high risk for progression



Radioiodine



thyroid control



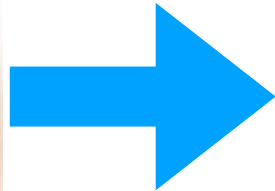
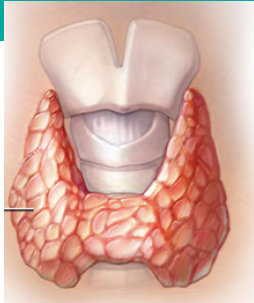
smoking

- Prummel & Wiersinga 1993
- x7 risk of visual loss
- Higher relapse rate on stopping anti-thyroid drugs
- x4 GO progression post I-131
- poorer response to immunosuppression

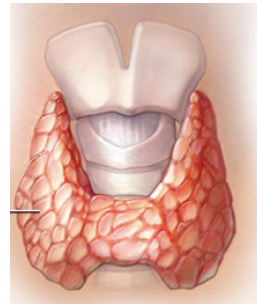
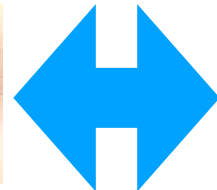


# GO does not necessarily parallel thyroid activity but important to render euthyroid

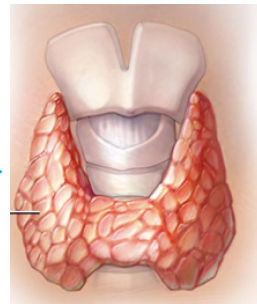
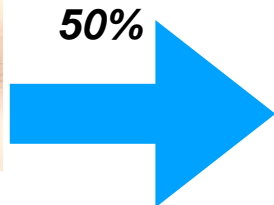
## Can worsen post radio iodine treatment



40%



40%



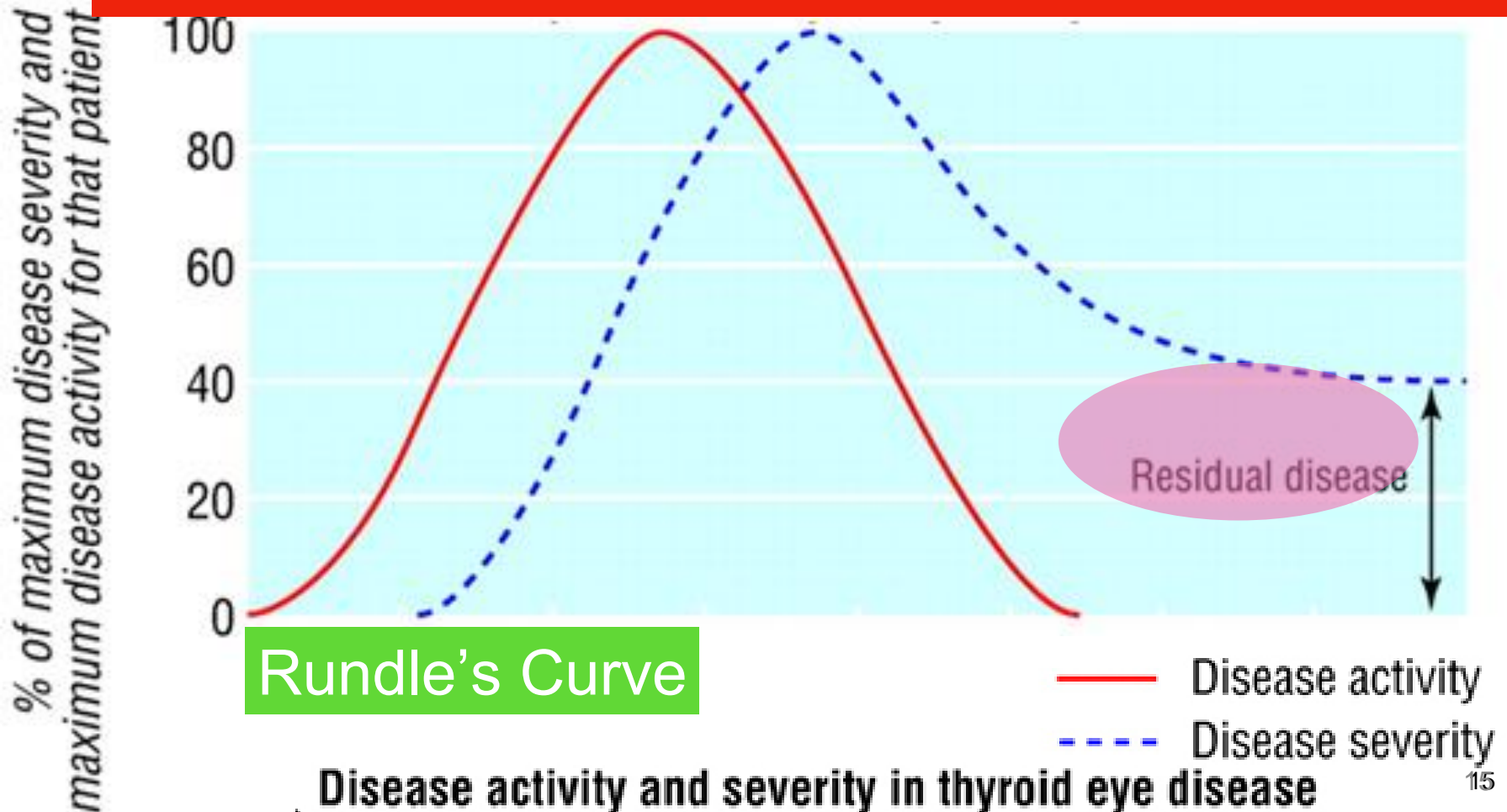
20%



**Do not give radio-iodine if there is significant eye disease**  
**cover high risk groups with oral steroids**

**75% eye and thyroid onset within the same year**

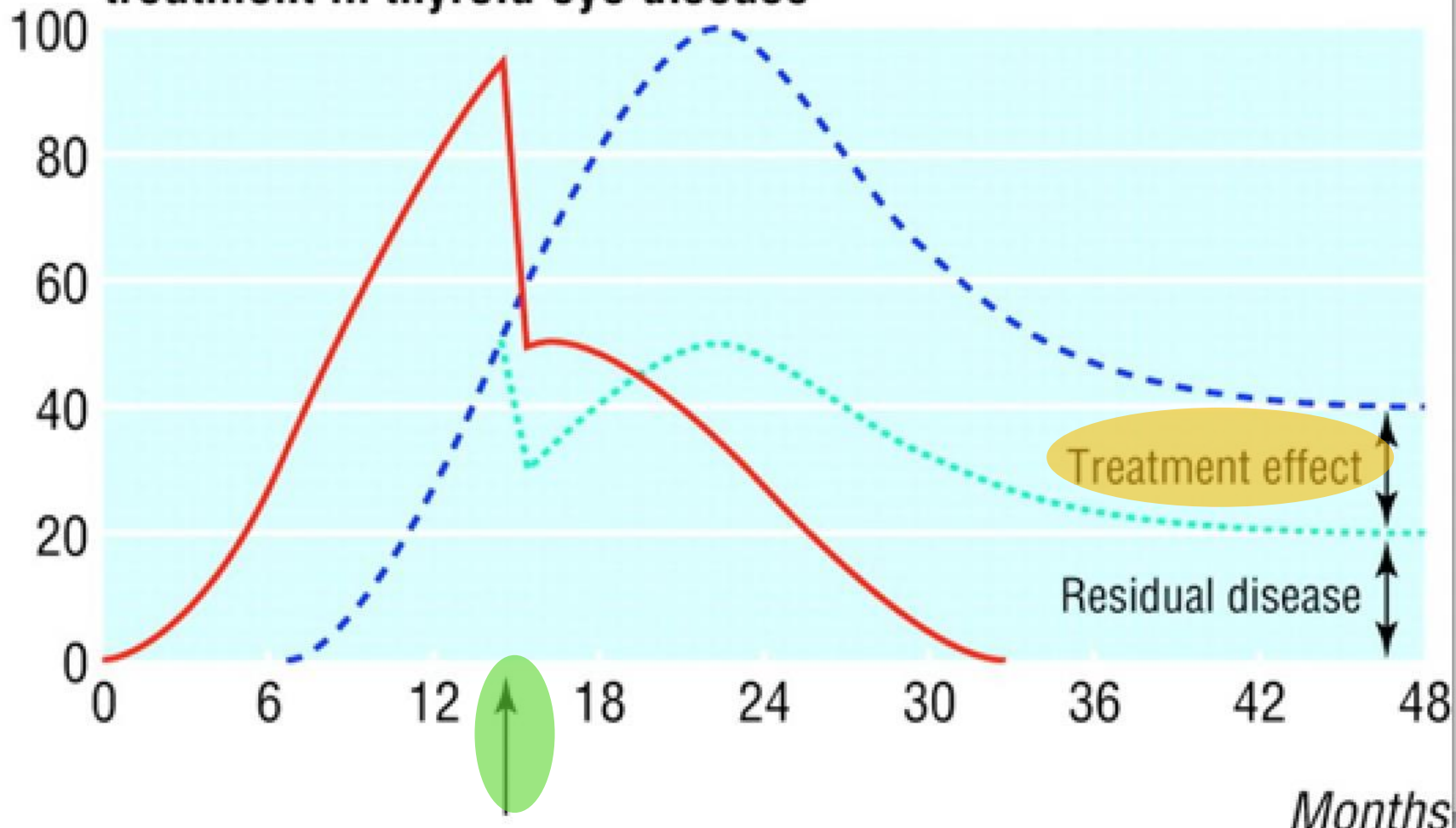
The disease does 'burn out'  
Lasts on average 1 yr in non smokers 2-3 yrs smokers  
Reactivation 5-10%  
Risk of blindness uncommon 2-5%



Prevent visual loss  
Modifying severity of  
residual disease with timely  
intervention

- Disease activity
- ⋯ Modified disease severity
- - - Unmodified disease severity

### Possible effect of early, effective anti-inflammatory treatment in thyroid eye disease

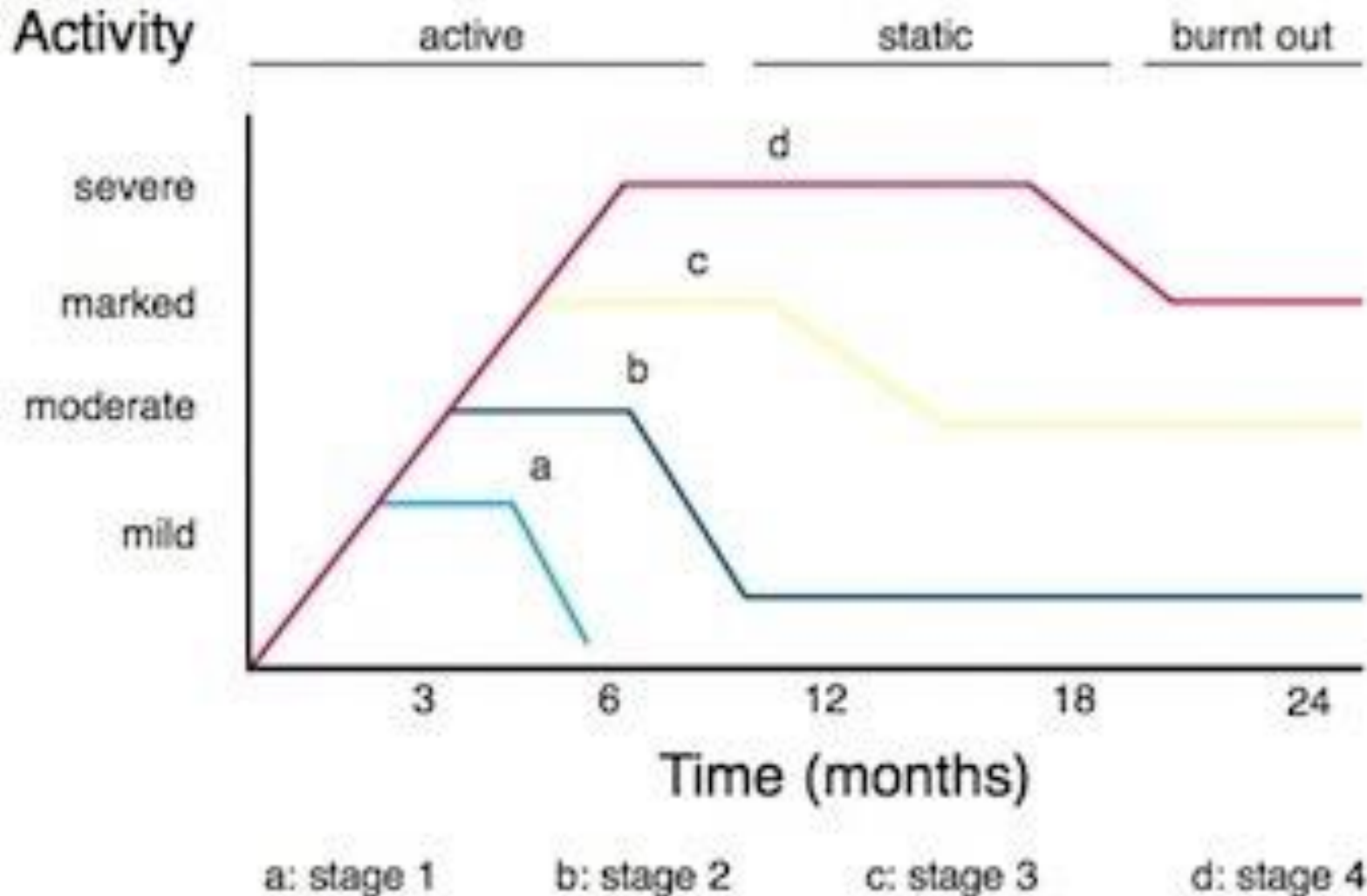




# Assessing Activity & Severity

<p><b>Sight threatening (2-5%)</b></p>	<p><b>Optic neuropathy/ corneal breakdown</b></p>	<p><b>Immediate treatment</b></p>
<p><b>Moderate to severe (29-33%)</b></p>	<p><b>Not sight threatening but sufficient impact on daily life Lid retraction <math>\geq 2</math>mm Moderate to severe soft tissue involvement <math>\geq 3</math>mm proptosis (corrected for race/gender) diplopia</b></p>	<p><b>Immunosuppression (If active) Surgery (if inactive)</b></p>
<p><b>Mild (65-73%)</b></p>	<p><b>Minor impact on daily life Minor lid retraction mild soft tissue involvement, &lt;3mm exophthalmos no diplopia</b></p>	<p><b>Lubricants and other simple measures</b></p>

is self limiting disease but you need to ask for every patient  
*which severity curve are they on ?*  
*where are they on their disease course?*



# Sight Threatening Disease

2-5%



**Corneal exposure keratopathy**



**dysthyroid Optic neuropathy  
DON**

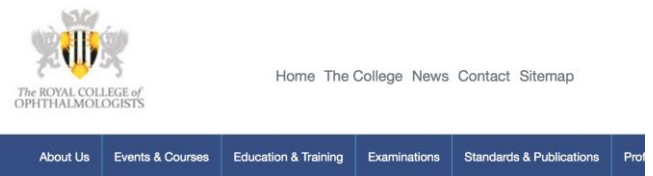
DON is a Clinical diagnosis  
no single gold standard sign

One study found that in patients with optic neuropathy  
**28% had other co-morbidities causing poor vision**  
25% CAS <3  
33% no proptosis

# Management

# Amsterdam Declaration for Thyroid Eye Disease 2009

- halving the time from presentation to diagnosis
- referral to a centre of excellence for optimal treatment of thyroid disease
- *appropriate use of radioiodine*
- *avoidance of hypothyroidism*
- *vigorous anti-smoking measures*



Home > News

## New Guidelines for Thyroid Eye Disease

22 July 2015



# TEAMeD

Thyroid Eye Disease Amsterdam  
Declaration Implementation Group UK



## TEAMeD-5 Improving outcomes in Thyroid Eye Disease



- 1. DIAGNOSE** Graves' disease accurately  
*- Measure TSH receptor antibody (TRab)*



- 2. SCREEN** all Graves' patients for TED  
*- Use the DiaGO clinical assessment tool*



- 3. ALERT** all Graves' patients to the risk of TED  
*- Give patients TEAMeD Early Warning Cards*



- 4. PREVENT** TED  
*- Encourage smoking cessation - Achieve and maintain euthyroidism rapidly  
- Avoid hypothyroidism after I-131 - Avoid I-131 in active TED*



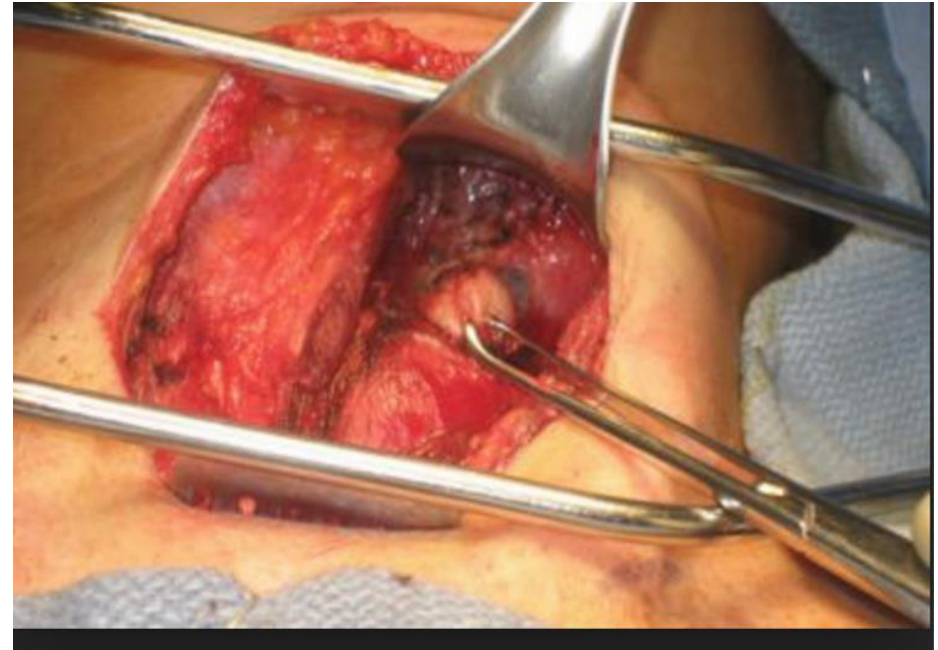
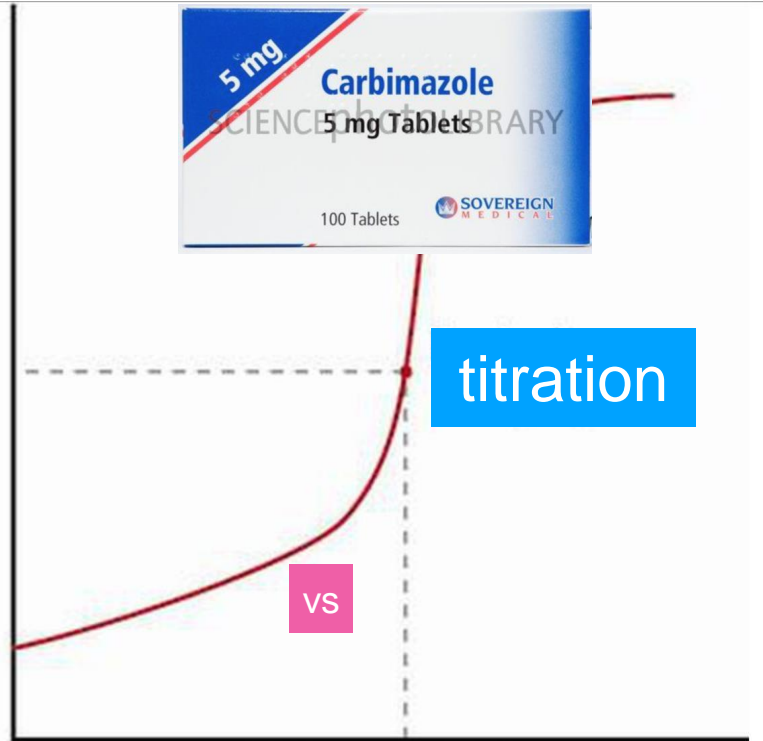
- 5. REFER** to a specialist clinic early  
*- Refer patients with TED to a specialist multidisciplinary joint thyroid-eye clinic*

Poster endorsed by:

For more information, visit: <http://www.btf-thyroid.org/teamed-5>



# Achieve & maintain Euthyroidism



Thyroidectomy







## 2. SCREEN all Graves' patients for TED

- Use the *DiaGO* clinical assessment tool

### DiaGO - GRAVES' ORBITOPATHY CLINICAL ASSESSMENT TOOL

#### SECTION 1 - TO BE ANSWERED BY PATIENT

1. Do you have redness in your eyes/eyelids? Yes  No
2. Do you have swelling or a feeling of fullness in one/both of your upper eyelids? Yes  No
3. Do you have bags under the eyes? Yes  No
4. Do your eyes seem to be too wide open? Yes  No
- 5a. Is your vision blurry even if you are wearing your usual glasses/contacts lenses? Yes  No   
*(if "No" go to 6)*
- 5b. Do you think that blinking/covering one or the other eye improves your vision? Yes  No
6. Please read the text below, covering one eye at a time  
  
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 corners  
  
Were you able to read the small print with either eye? Yes  No   
*(if "Yes" go to 8)*
7. If you cannot see the small print, do you think this deterioration in your sight is recent? Yes  No
8. Are your eyes abnormally sensitive to light? Yes  No
9. Are your eyes excessively gritty? Yes  No
10. Do you have pain in/behind the eyes? Yes  No
11. Has the appearance of the eyes and/or eyelids changed over the past 1-2 months? Yes  No
12. Does the appearance of your eyes concern you? Yes  No
13. Can you see two separate images when there should only be one? Yes  No

#### SECTION 2 - TO BE FILLED IN BY DOCTOR

14. Global assessment: Do the eyes look abnormal? Yes  No   
Does the patient have any of the following:
15. Upper eyelid retraction? Yes  No
16. Abnormal eyelid/conjunctiva swelling/redness? Yes  No
17. Restriction of eye movements? Yes  No
18. Exophthalmos? Yes  No
19. Cornea/sclera still visible when the eye is closed? Yes  No
20. Obvious corneal reflex? Yes  No

#### SECTION 3 - ACTION

- Refer to specialist
  - Refer to specialist
  - Refer to specialist
- Print more

TeaMed  
DiaGO

20 questions  
13 Q patient  
7 Q doctor

- Refer all other significant

Table 1: Vancouver Orbitopathy Rule (VOR) – A positive response to question 1 or 2 and one of 3, 4 or 5

1. Swelling or feeling of fullness in one or both of your upper eyelids?

2. Bags under the eyes?

3. Redness in your eyes or eyelids?

4. Do you eyes seem to be too wide open?

5. Is your vision blurry (even with glasses/contacts)?

Vancouver Orbitopathy  
Rule (VOR)



### 3. **ALERT** all Graves' patients to the risk of TED *- Give patients TEAMeD Early Warning Cards*

**For more information on TED go to**  
**[www.btf-thyroid.org/teamed](http://www.btf-thyroid.org/teamed)**  
or visit  
Thyroid Eye Disease Charitable Trust  
**[www.TEDct.org.uk](http://www.TEDct.org.uk)**  
British Thyroid Foundation  
**[www.btf-thyroid.org](http://www.btf-thyroid.org)**

TEAMeD EWC 321

### **Thyroid Eye Disease Early Warning Card**

If you have been diagnosed with **Graves' Disease** (an overactive thyroid gland) you have a 20% chance of developing **Thyroid Eye Disease (TED)**.

©TEAMeD Thyroid Eye Disease Amsterdam  
Declaration Implementation Group UK

#### **Common symptoms are:**

- Redness in the eyes or lids
- Swelling or feeling of fullness in one or both upper eyelids
- Bags under the eyes
- Eyes seem to be too wide open
- Pain in or behind the eyes
- Gritty eyes; sensitivity to light
- Blurred vision or double vision

**TED may develop months or even years after Graves' disease has been diagnosed.**

**Smoking increases the risk of TED.**

If you develop any of these symptoms contact:

Name .....

Tel .....



## 4. PREVENT TED

- Encourage *smoking cessation* - Achieve and maintain *euthyroidism* rapidly
- Avoid *hypothyroidism* after I-131 - Avoid I-131 in active TED



Referral to smoking cessation  
services  
Discourage passive smoking



## 4. PREVENT TED

- Encourage *smoking cessation* - Achieve and maintain *euthyroidism rapidly*
- Avoid *hypothyroidism after I-131* - Avoid *I-131 in active TED*



# RAI

*Can worsen GO*  
*Prummel & Wiersinga 1993*

Do not give radio-iodine to patients with significant eye disease requiring immunosuppression

Good evidence that oral steroid cover and rapid treatment of post RAI hypothyroidism mitigates risk in patients with low risk of GO / mild GO



## 5. REFER to a specialist clinic early

- Refer patients with TED to a specialist multidisciplinary joint thyroid-eye clinic

# MDT speeds up GO Diagnosis

Downloaded from <http://bjpo.bmj.com/> on June 6, 2017 - Published by group.bmj.com

Clinical science

**PREGO (presentation of Graves' orbitopathy) study: changes in referral patterns to European Group On Graves' Orbitopathy (EUGOGO) centres over the period from 2000 to 2012**

Petros Perros,<sup>1</sup> Miloš Žarković,<sup>2</sup> Claudio Azzolini,<sup>3</sup> Göksun Ayvaz,<sup>4</sup> Lelio Baldeschi,<sup>5</sup> Luigi Bartalena,<sup>6</sup> Antonella Boschi,<sup>5</sup> Claire Bournaud,<sup>7</sup> Thomas Heiberg Brix,<sup>8</sup> Danila Covelli,<sup>9</sup> Slavica Ćirić,<sup>2</sup> Chantal Daumerie,<sup>10</sup> Anja Eckstein,<sup>11</sup> Nicole Fichter,<sup>12</sup> Dagmar Führer,<sup>13</sup> Laszlo Hegedüs,<sup>8</sup> George J Kahaly,<sup>14</sup> Onur Konuk,<sup>15</sup> Jürg Lareida,<sup>12</sup> John Lazarus,<sup>16</sup> Marenza Leo,<sup>17</sup> LEMONIA Mathiopoulos,<sup>18</sup> Francesca Menconi,<sup>17</sup> Daniel Morris,<sup>19</sup> Onyebuchi Okosieme,<sup>16</sup> Jaques Orgiazzi,<sup>20</sup> Susanne Pitz,<sup>21</sup> Mario Salvi,<sup>9</sup> Cristina Vardanian-Vartin,<sup>22</sup> Wilmar Wiersinga,<sup>23</sup> Martine Bernard,<sup>24</sup> Lucy Clarke,<sup>25</sup> Nicola Currò,<sup>26</sup> Colin Dayan,<sup>16</sup> Jane Dickinson,<sup>25</sup> Miroslav Knežević,<sup>27</sup> Carol Lane,<sup>19</sup> Claudio Marcocci,<sup>17</sup> Michele Marinò,<sup>17</sup> Lars Möller,<sup>13</sup> Marco Nardi,<sup>28</sup> Christopher Neoh,<sup>25</sup> Simon Pearce,<sup>1</sup> George von Arx,<sup>12</sup> Fosun Baloş Törüner<sup>4</sup>

**PREGO demonstrates that MDT clinic setup improves time to diagnosis (6 vs 16 months), time from first symptoms to first consultation (9 vs 16 months)**

**UK Multicentre audit (Orbit 2017) demonstrates similar findings**



## 5. REFER to a specialist clinic early

- Refer patients with TED to a specialist multidisciplinary joint thyroid-eye clinic

Number of ophthalmologists BOPSS surveyed who work in Thyroid MDT clinic

Are the TED patients managed in a multidisciplinary based

Not enough ophthalmologists work in thyroid Eye MDT clinics in the UK  
There are not enough clinics to accommodate this recommendation

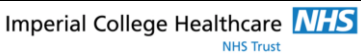
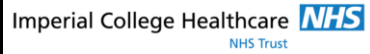


# MDT Thyroid Eye Network

@ Central Middlesex Hospital (since 2011)

@ Western Eye Hospital (since 2015)

@ Charing Cross Hospital (starting Jan 2018)



Endocrinologist

Oculoplastic Surgeon

MDT Clinic

*Radiotherapist*  
Orbital Radiotherapy

*Radiologist*  
DWI MRI

*Thyroid surgeons*  
Thyroidectomy

*Oculoplastic Surgeon*  
Functional Decompression  
surgery

immunosuppression  
specialist

Sight saving  
urgent orbital  
decompression  
(ENT/ Eyes)

Squint  
+ lid surgery

active

inactive



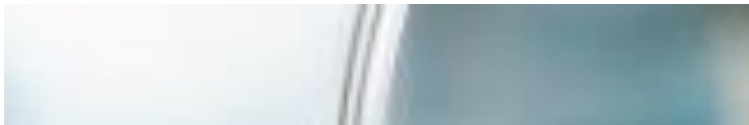
Mild disease 60%+

# Tear Supplements + Selenium





# Moderate to Sight Threatening Disease



There is currently no available treatment to effectively reverse the protruding eyes in the acute stage

ession  
se



radiotherapy

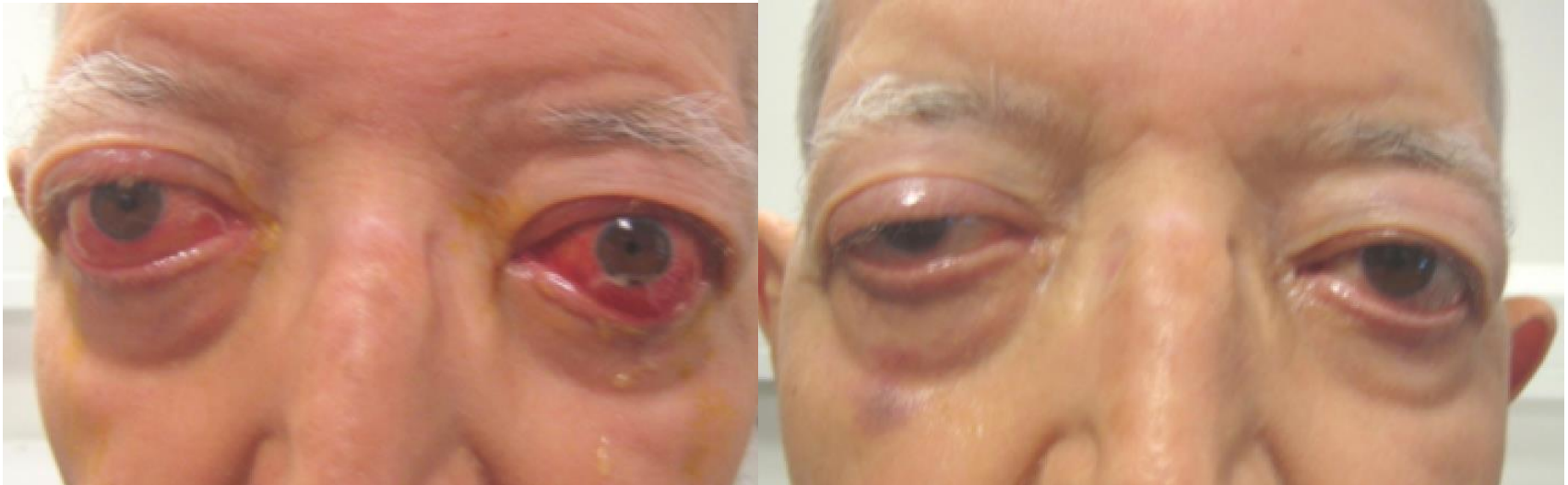


Second line immunosuppression  
eg mycophenolate

Intravenous steroids

# Immunosuppression reduces

Soft tissue inflammation (70-80%)  
Double vision (55%)  
DON (77%)



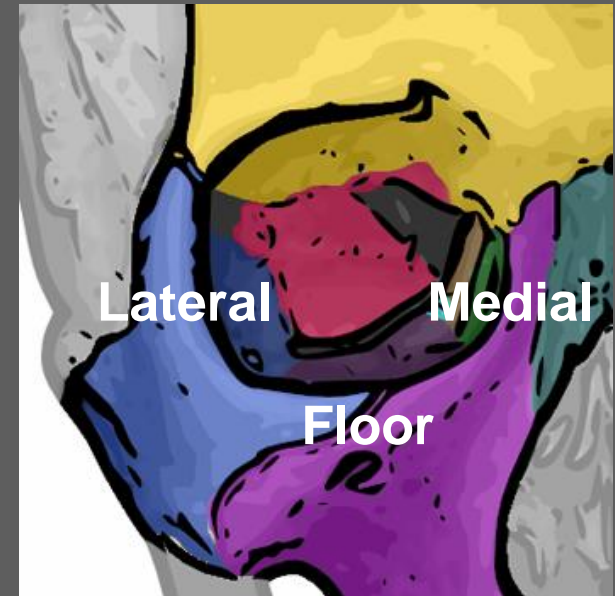
little change in proptosis

## treats proptosis and can save vision

### Urgent sight threatening disease

DON unresponsive to IV steroids  
Ulceration or infection of the cornea

Removal of walls of the orbit to expand the orbital volume to ease pressure or allow tissues to settle back into the orbit



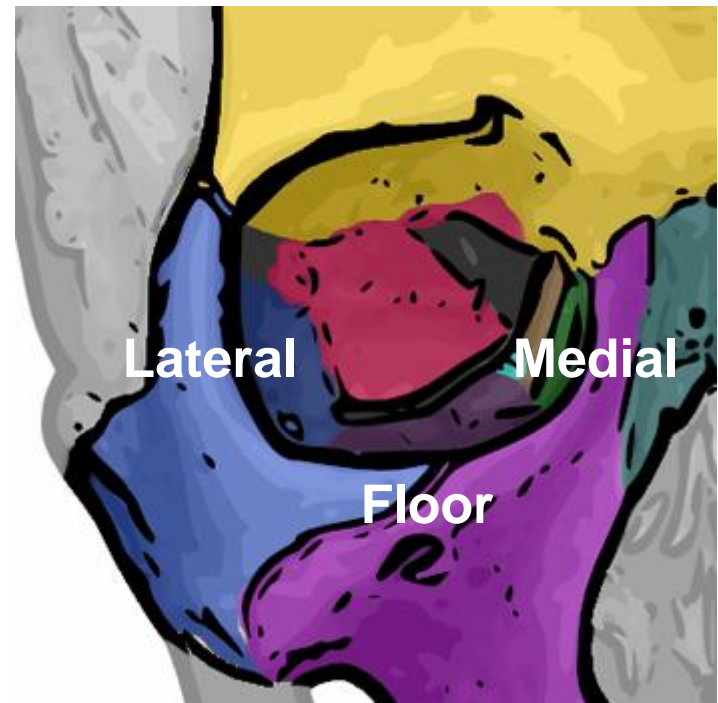
### Rehabilitation

Severe proptosis (disease should be inactive)  
Generally post thyroidectomy

- **Blindness**
- **Haemorrhage**
- **Double vision**
- **Periorbital numbness**
- **Sinusitis**
- **Asymmetry**
  - **globe malposition**
  - **lid malposition**



Post single medial wall decompression



## QOL

MY DOCTOR SAYS I'M DOING FINE . .

A study among 250 consecutive GO patients seen in an interdisciplinary thyroid-eye clinic in Germany reports significant occupational disability

36% were on sick leave

28% were disabled

5% had gone into early retirement

3% had lost their jobs

*Ponto et al 2009*

Many GO patients are unhappy and this may not reflect our clinical impressions of disease activity / severity





only 1 in 5 units  
treating TED in  
a UK wide survey  
collect QOL data



**TED-QOL questionnaire**

This questionnaire is designed to assess quality of life in thyroid eye disease.  
Please answer by **circling the number that best describes your position.**



1) How is your eye disease currently interfering with your overall quality of life?

 0 1 2 3 4 5 6 7 8 9 10   
Does not interfere Completely interferes

2) How is your eye disease currently affecting your ability to carry out daily activities?

 0 1 2 3 4 5 6 7 8 9 10   
Does not interfere Completely interferes

3) How is your eye disease currently affecting your satisfaction with your appearance?

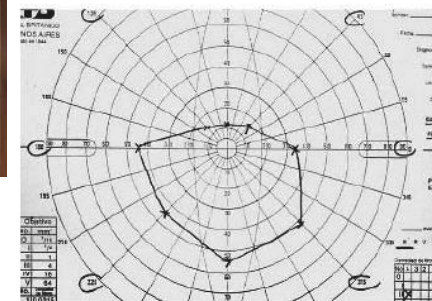
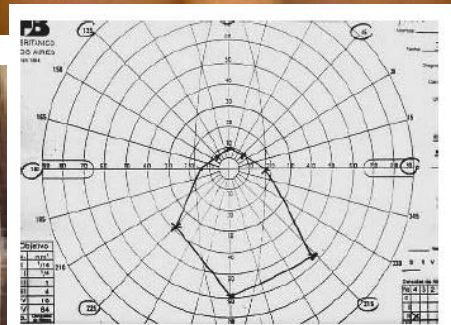
 0 1 2 3 4 5 6 7 8 9 10   
Does not interfere Completely interferes

# Rehabilitation Surgery improves QOL

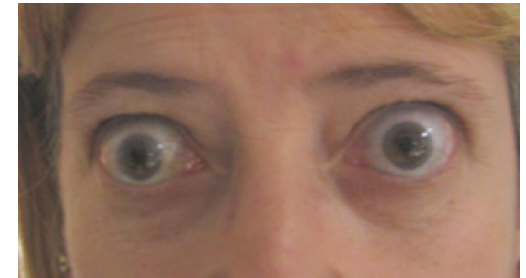
1 Orbital Decompression



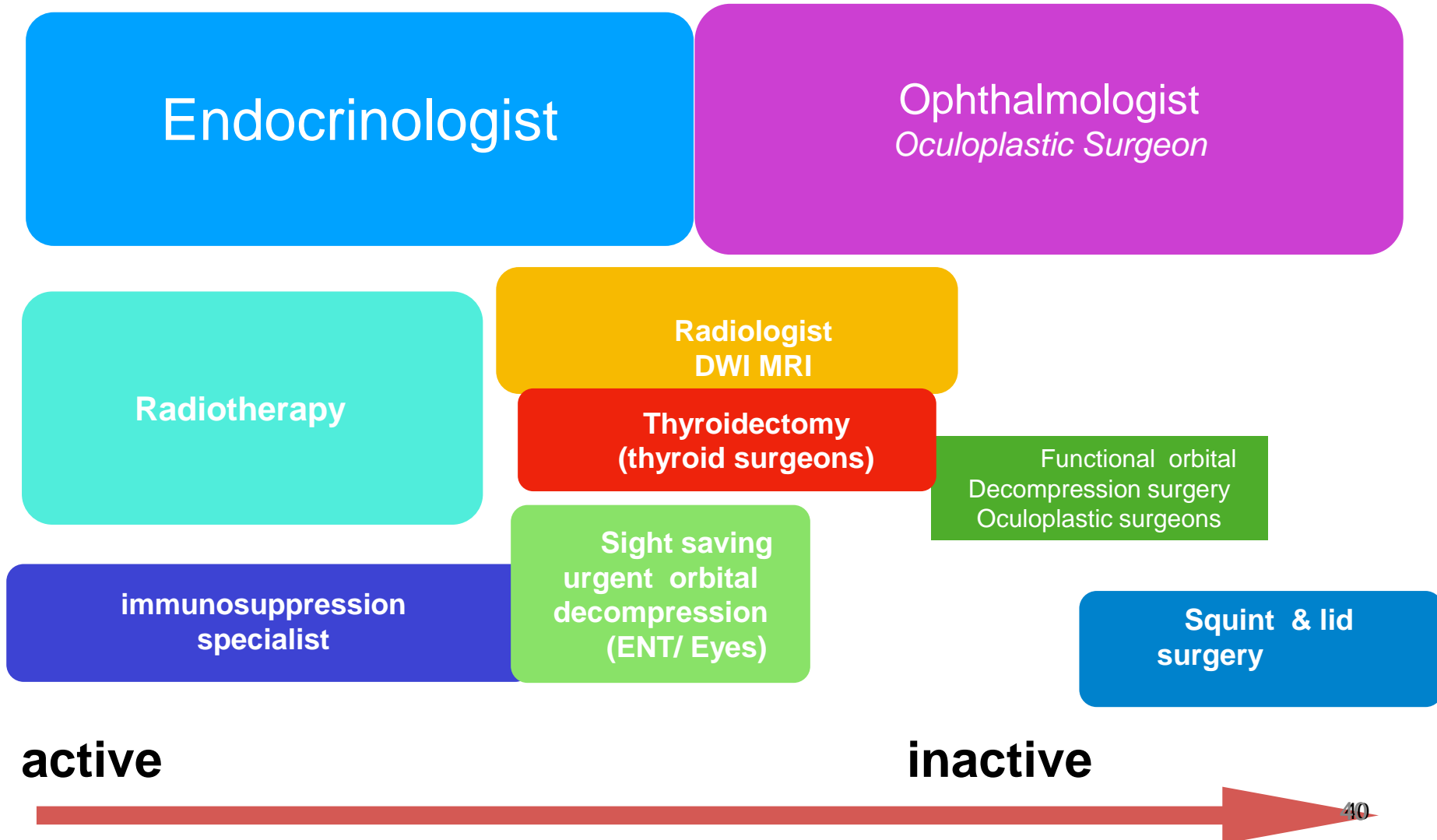
2 Squint Surgery



3 Eyelid surgery

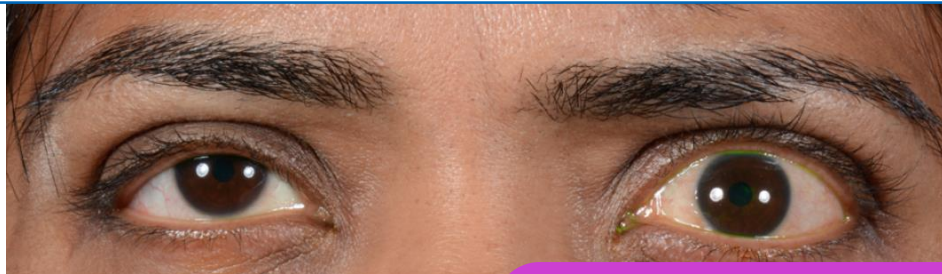


# MDT approach improves diagnosis and optimises management





# One patient many specialists



Endocrinologist

Ophthalmologist  
*Oculoplastic Surgeon*

Radiologist  
DWI MRI

Thyroidectomy  
(thyroid surgeons)

Functional orbital  
Decompression surgery  
Oculoplastic surgeons

immunosuppression  
specialist

Sight saving  
urgent orbital  
decompression  
(ENT/ Eyes)

Squint & lid  
surgery

**active disease**

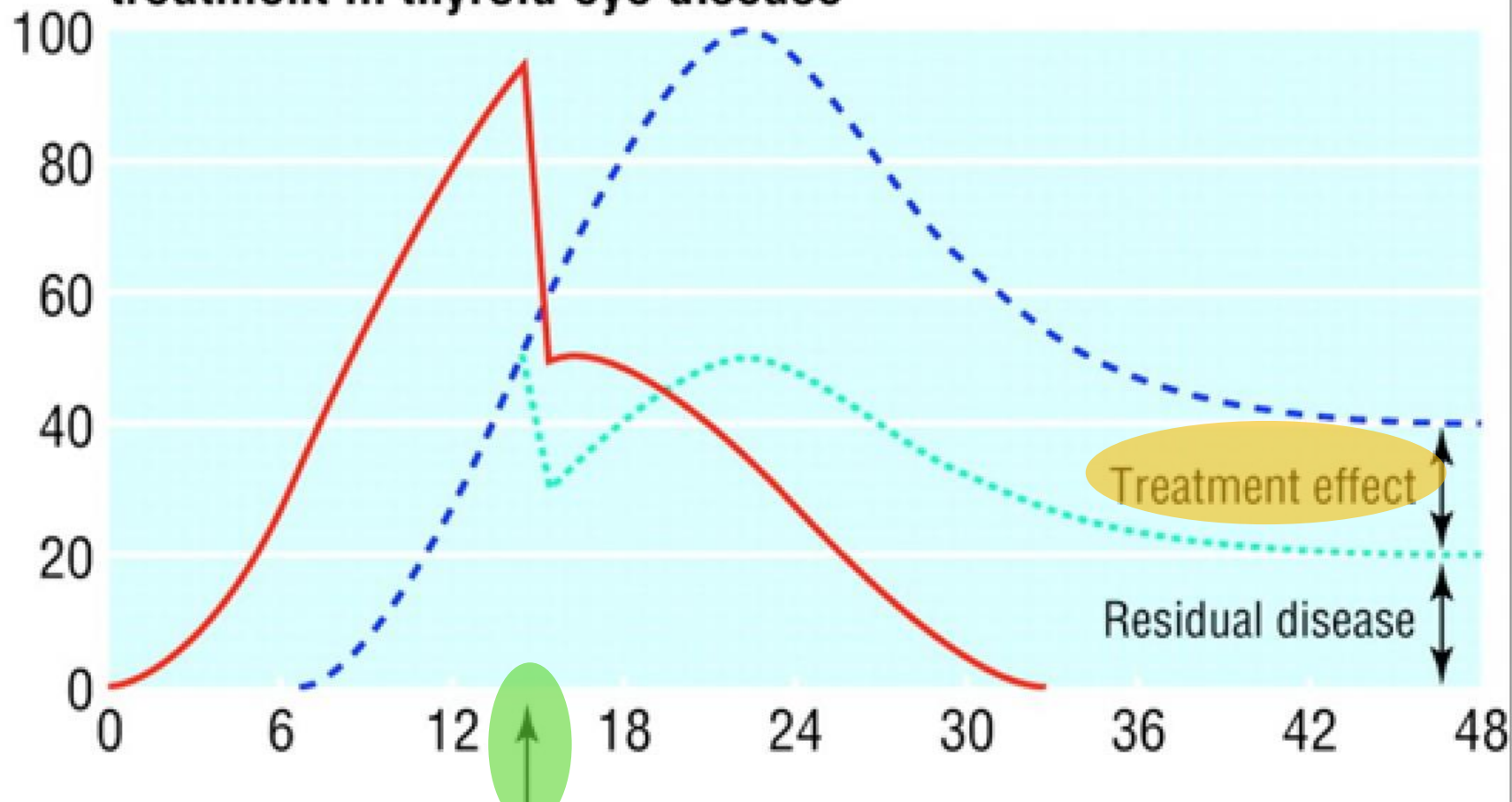
**inactive disease**



Prevent visual loss  
Modifying severity of residual disease with timely intervention

- Disease activity
- ⋯ Modified disease severity
- - - Unmodified disease severity

Possible effect of early, effective anti-inflammatory treatment in thyroid eye disease



**CMH Endocrinology**

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Mike Perry  
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**CMH Botulinum toxin**

*clinic* Dhannie  
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Emma Hatfield

**CXH Radiotherapy**

Sarah Partridge  
Simon Stewart

**CXH ENT**

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Hesham Saleh

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Neil Tolley  
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