

## Report EGS meeting, London September 2017.

### Definition Group

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#### Executive Summary

##### Background

There is no widely-agreed standard description of glaucoma that can be used for communication with patients, policy makers, payers and eye care professionals. To ensure the widest possible understanding of the goals of clinical and research activity in glaucoma, it is desirable to have a standard, recognisable phrase describing the condition. This phrase should be concise and describe the main features of glaucoma, which can be used as an introduction and followed by text expanding on concepts important for the main audience for each communication.

The tasks set for this workshop were to:

1. Agree a 'definition' paragraph
2. Agree diagnostic criteria

##### Task 1: To agree on a working definition of glaucoma

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Dr Quigley provided a 'straw man' definition of glaucoma (see workshop report, below) as a starting point:

- 93% agreed with that definition, with or without minor reservations

The main reservations were: too long/complex/ confusing, disagreement on IOP role, VF description and with 'bilateral'.

The group produced a synthesis definition:

"POAG is a chronic, progressive, potentially blinding, irreversible eye disease causing optic nerve rim and RNFL loss with related visual field defects. Angle appearance is normal, and major risk factors include the level of IOP and older age."

Relevant discussion points included:

- Consider making two definitions, one more technical and another one in plain language
- Whether or not to include 'optic neuropathy'
- Use the term eye 'condition' instead of 'disease'
- Use just 'IOP' instead of 'level of IOP'
- Use just 'age' instead of 'older age'
- Include treatment/prevention in the definition (more positive approach)

Following a final discussion, 69% of participants agreed with the synthesis definition. 83% were in agreement that 'treatable/preventable' should be added to the definition. In a post-meeting e-mail exchange, the proposed definition was suggested:

"POAG is a chronic, progressive, potentially blinding, irreversible eye disease causing optic nerve rim and RNFL loss with related visual field defects. Angle appearance is normal, and major risk factors include the level of IOP and older age. Visual disability is usually prevented by early diagnosis and treatment."

## Task 2: Assessing glaucoma diagnostic criteria

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To assist in identifying the key disease features considered to be diagnostic by the workshop participants, various clinical scenarios were presented. Group members were asked to classify twelve different clinical scenarios considering structure loss, function loss, and structure/function congruency, into one of the following categories: Definite, probable, or possible glaucoma. It was assumed that non-glaucomatous neuropathies had been excluded.

Summary:

- Definite glaucoma
  - 100% agreement that congruent, unequivocal structural and functional loss is 'definite glaucoma'
- Probable glaucoma

There was majority agreement that:

  - unequivocal structural and functional loss, without congruency, is 'probable glaucoma', with a minority considering it 'definite glaucoma'.
  - unequivocal structural loss and equivocal functional loss with congruency is 'probable glaucoma', with a small minority considering it 'definite glaucoma'. When there was no congruency, the majority still considered this 'probable glaucoma', with a small minority considering it 'possible glaucoma'.
- Possible glaucoma
  - There was majority agreement that unequivocal functional loss and a normal disc/RNFL was 'possible glaucoma', with a small minority considering it 'probable glaucoma'
  - There was 100% agreement that equivocal structural and functional loss without congruency was 'possible glaucoma'
- No consensus
  - 50% agreed that unequivocal functional loss and equivocal structural loss with congruency is 'probable glaucoma', with a larger minority considering it 'definite glaucoma' and a smaller minority considering it 'possible glaucoma'. When there was no congruency of damage, the majority considered it 'probable glaucoma', with a small minority considering it 'possible glaucoma'.
  - In a scenario in which structural loss was considered unequivocal, yet the visual field is normal, there was a 50/50 split between 'probable glaucoma' and 'possible glaucoma'.
  - In a scenario in which there was equivocal structural and functional loss and congruency, there was a 50/50 split between 'probable glaucoma' and 'possible glaucoma'.
  - Either unequivocal structural or unequivocal functional progression (in the absence of unequivocal structural or functional damage) was considered variously 'definite glaucoma', 'probable glaucoma' and 'possible glaucoma'.

Eyes considered to have 'possible glaucoma' would be considered by the majority to have 'probable glaucoma' if a disc haemorrhage or glaucoma in the other eye were present.

Less disc or VF damage would be required by the majority to diagnose 'definite glaucoma' if a disc haemorrhage were present.

## Task 3: Criteria for loss

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At a population level, there was no agreement on an acceptable false positive rate for a diagnosis of 'definite glaucoma', with 20% of participants favouring 1/1000 and 36% favouring 1/100.

Quantitative criteria for disc rim/ RNFL loss when there is an unequivocal visual field defect, to achieve the desired false positive rate. Responses included:

- Any rim/RNFL damage if corresponding
- Rim/RNFL damage significant/progressive, even if in the range of normality
- Suspicious damage

Quantitative criteria for VF loss when there is unequivocal rim/RNFL loss, to achieve the desired false positive rate. Responses included:

- Any VF loss if corresponding with rim/RNFL loss
- A small cluster of significant depressed points (even if significance is rather low)
- Any unequivocal defect (scotoma definition)
- Repeatable GHT outside normal limits
- Reproducible corresponding VF/defects characterized by at least three contiguous points with  $p < 5\%$  or 2 contiguous points with  $p < 1\%$

In general, participants found it more straight-forward to identify quantitative criteria for VF loss than for structural damage.

## Workshop report

### Task 1: To agree on a working definition of glaucoma for clinical practice guidelines

Starting Point: Dr. Harry Quigley's Definition

“Primary open-angle glaucoma (POAG) is a chronic optic neuropathy in adults with multiple risk factors that is bilateral, but often asymmetric. It features thinning and undermining of the optic disc rim and deepening of its floor. Retinal ganglion cells (RGC) are the primary neuron affected, with a measurable loss of RGC bodies and axons in the retina, retinal nerve fiber layer, and disc rim. Injury to RGC axons at the optic disc causes differential damage of upper or lower visual field, respecting the horizontal midline and beginning in the mid-peripheral field. POAG eyes have no visible abnormality in an open anterior chamber angle by gonioscopic examination. Progressive worsening is related to the level of intraocular pressure (IOP), with many POAG eyes exhibiting IOP levels seen in non-POAG eyes. IOP lowering from the untreated level demonstrably slows the rate of damage. While complete blindness can occur, the majority of POAG eyes retain useful vision, though there can be limitation of function and quality of life”

The members of the group were asked about the agreement with this definition.

- 23 % Fully agreed with that definition
- **70% I can live with that definition, though I have a minor reservation**
- 7% I can't live with that definition – I have a significant reservation

The main reservations about this definition were as follow:

- 51.9% Too long/complex/confusing
- 12.5% Disagreement on IOP role
- 11.5% Disagreement on VF defect description
- < 5%
  - Not agreement with 'Bilateral'
  - Disagreement on OCT
  - Include 'Progression'
  - Optic nerve clinical assessment
  - Quality of life/refer to blindness
  - Specify pathophysiology

### The new definition “Workshop.”

The group members were divided into six different working groups, and they were asked to produce a new glaucoma definition. Then, they were merged into three groups, and they had to agree to obtain a new glaucoma definition. These were the three definitions obtained:

#### Definition 1

“POAG is a chronic, multifactorial, progressive optic neuropathy with characteristic thinning of the optic nerve rim and RNFL with corresponding VF defects. IOP is a proven treatable risk factor.”

## Definition 2

“Glaucoma is a progressive and irreversible disease of the optic nerve, that becomes more common with age. Patients often have no symptoms until late stages, but the disease can lead to blindness. **Worsening can be diminished or stopped by lowering the eye pressure.**”

## Definition 3

“POAG is a chronic, potentially blinding progressive optic neuropathy. It manifests as a neuroretinal loss at the optic nerve head with visual field loss. It is characterized by normal angle appearance, and major risk factors include level of IOP and older age.”

## SYNTHESIS DEFINITION

The whole group worked to produce a single **synthesis definition**:

“POAG is a chronic, progressive, potentially blinding, irreversible eye disease causing optic nerve rim and RNFL loss with related visual field defects. Angle appearance is normal, and major risk factors include the level of IOP and older age.”

There were some points of discussion:

- [Although the audiences had been specified in the Introductory talk and the pre-meeting reading material] Clarifying the audience to whom this definition is directed was recommended. It would be interesting to make two definitions, one more technical for glaucoma specialists and another one in plain language that would be more suitable for patients, non-experts and general population.
- Include ‘optic neuropathy’ or not in the definition.
- Use a more general approach or less negative using eye condition instead of disease.
- To take out ‘level of IOP’ from the definition, just say ‘IOP’
- Removing ‘older’ from the definition: Major risk factors include level of IOP and age.
- Include treatment/prevention in the definition

This synthesis definition was presented to all the meeting participants who were asked to share their opinion using a scale of agreement. The results collected were as follows:

- 19% Full agreement
- **50% Agreement with minor question, concern or reservation**
- 21% Disagree with minor question, concern or reservation
- 10% Disagree with major question, concern or reservation

Including treatment and prevention was a subject of discussion. If ‘treatable/preventable’ is added in the definition the group of agreement with minor question risen to 64%.

The three most commented aspects were:

1. **Include treatable in the definition (16%)**
2. **Take out ‘level of’ IOP (15%)**

### 3. Make two different definitions (11%)

We propose to include these three points as a starting point for further work in the definition.

## Task 2: Glaucoma Diagnostic Criteria

### Diagnostic Criteria Table exercise

In this workshop, members were divided into six groups, and they were asked to classify 12 different clinical scenarios into one of these three categories: Definite Glaucoma, Probable Glaucoma or Possible Glaucoma. Answers are displayed in the table below (each row represents a different group).

Definite glaucoma	Probable glaucoma	Possible glaucoma
3	4,5,8,9	1,2,6,7,10,11,12
1,2,3	4,5,6,7,8,9,10	11,12
3,4	1,5,6,7,11	2,8,9,10,12
1,2,3,5,8	4,6,7,9,11	10,12
3	2,4,5,6,8,9	1,7,10,11,12
3,4,8	1,5,6,9,11	2,7,10,12

In red, we have highlighted the clinical scenarios that had more consensus (80% agreement). We have considered these scenarios as 'easy' cases. The rest of cases, in which agreement among groups was not clear, have been considered as 'difficult'.

We will now investigate further the **easy cases** for each of the different categories:

### EASY CASES DEFINITE GLAUCOMA

Patient scenario 3

Disc rim/RNFL:	<b>Unequivocal loss</b>
Visual field:	<b>Unequivocal loss</b>
Structure/function congruency:	<b>Yes</b>

Patient scenario number 3 in which unequivocal loss was present both in disc rim/RNFL and in VF with structure-function congruency was classified as Definite glaucoma by 100% of the participants

### EASY CASES PROBABLE GLAUCOMA

Patient scenario 4

Disc rim/RNFL:	<b>Unequivocal loss</b>
Visual field:	<b>Unequivocal loss</b>
Structure/function congruency:	<b>No/uncertain</b>

Patient scenario 5

Disc rim/RNFL:	<b>Unequivocal loss</b>
Visual field:	<b>Suspect (no definite loss)</b>
Structure/function congruency:	<b>Yes</b>

Patient scenario 6

Disc rim/RNFL:	<b>Unequivocal loss</b>
Visual field:	<b>Suspect (no definite loss)</b>
Structure/function congruency:	<b>No/uncertain</b>

Patient scenario 9

Disc rim/RNFL:	<b>Suspect (no definite loss)</b>
Visual field:	<b>Unequivocal loss</b>
Structure/function congruency:	<b>No/uncertain</b>

Disc rim/RNFL unequivocal loss was the key feature to define this category. In case disc was suspect (not unequivocal loss) then an unequivocal visual field defect would also make the diagnosis of probable glaucoma for five of the six groups.

## EASY CASES POSSIBLE GLAUCOMA

Patient scenario 10		Patient scenario 11	
Disc rim/RNFL:	<b>Normal</b>	Disc rim/RNFL:	<b>Suspect (no definite loss)</b>
Visual field:	<b>Unequivocal loss</b>	Visual field:	<b>Suspect (no definite loss)</b>
Structure/function congruency:	<b>N/A</b>	Structure/function congruency:	<b>Yes</b>
Patient scenario 12		Disc rim/RNFL:	<b>Suspect (no definite loss)</b>
Disc rim/RNFL:	<b>Suspect (no definite loss)</b>	Visual field:	<b>Suspect (no definite loss)</b>
Visual field:	<b>Suspect (no definite loss)</b>	Structure/function congruency:	<b>No/uncertain</b>
Structure/function congruency:	<b>No/uncertain</b>		

Unequivocal loss in visual field or structure/function congruency or the presence of changes both in discs and in visual fields were sufficient to diagnose possible glaucoma.

## DIFFICULT CASES

There was no clear consensus for scenarios 1, 2, 7 and 8. Tricky points were:

- Unequivocal progression in disc or visual field
- Intermediate situations with a suspect (not definite loss) in Disc rim/RNFL with unequivocal loss in visual field and a positive structure/function congruency, and unequivocal loss in Disc/rim/RNFL with normal visual field and N/A Structure/function congruency

After this task, some questions were asked to further investigate in these 'tricky' cases:

1-Suspect Glaucoma. Given an eye considered to have 'possible glaucoma' based on VF and disc/RNFL appearance, would any of the following shift your diagnosis to 'probable glaucoma'?

- IOP > 25 mmHg – 55%
- The presence of a disc haemorrhage – 75%
- **The presence of definite glaucoma in the other eye – 80%**
- A family history of glaucoma in a first-degree relative – 35 %
- None of the above – 0%

2-Definite glaucoma: Do you require less VF or disc/RNFL damage to diagnose definite glaucoma if risk factors are present? Which of the following influences your criteria for diagnosis of definite glaucoma?

- IOP > 25 mmHg – 35%
- **The presence of a disc haemorrhage – 75%**
- The presence of definite glaucoma in the other eye – 60%
- Family history for glaucoma in a first degree relative – 10%
- None of the above – 15%

3-Confirmation criteria: When assessing evidence for glaucoma, do you require confirmation of VF loss to make the diagnosis of definite glaucoma? Select all that apply.

- **Always – 62%**
- If there is a clear arcuate defect and definite, congruent, disc/RNFL damage – 10%
- If there is any VF defect and definite, congruent, disc/RNFL damage – 29%
- If there is a clear arcuate defect and definite disc/RNFL damage, even if not congruent – 24%
- If there is any VF defect and definite disc/RNFL damage, even if not congruent – 19%

4-Glaucoma affects about 1% of those over 50 yrs and 5% of those over 80yrs. Diagnostic criteria for glaucoma, therefore, need to have a low false positive rate. For 'definite glaucoma' diagnosis, what is an acceptable false positive rate?

- 0 – 4%
- <1 in 1000 – 21%
- 1 in 1000 – 21%
- 5 in 1000 – 18%
- **10 in 1000 – 36%**

## Task 3: Criteria for loss

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In this final workshop tasks, groups were asked to describe more specifically their criteria for loss.

### Quantitative criteria for disc rim/RNFL loss

Please describe the disc rim/RNFL criterion that, in the presence of definite VF loss, might have the desired specificity when making a diagnosis.

- Any rim/RNFL damage if corresponding
- Rim/RNFL damage significant/progressive/ even if in the range of normality
- Rim/RNFL damage independent of VF
- Suspicious

### Quantitative criteria for Visual Field loss

Please describe the VF criterion that, in the presence of definite disc rim/RNFL loss, might have the desired specificity when making a diagnosis

- Any VF loss if corresponding with rim/RNFL loss
- A small cluster of significant depressed points (even if significance is rather low)
- Any unequivocal defect (scotoma definition)
- Repeatable GHT outside normal limits
- Reproducible corresponding VF/defects characterized by at least three contiguous points with  $p < 5\%$  or 2 contiguous points with  $p < 1\%$