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A core outcome set for three ophthalmic conditions: a healthcare professional and patient consensus on Core Outcome Sets for Amblyopia, Ocular Motility and Strabismus (COSAMS study)

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Author contributions: FR and JJK contributed to conceptualising and designing the study. SJ was responsible for the day-to-day running of the project. All authors contributed to the review of the study design and to the review and analysis of study data. JJK drafted the manuscript. FR and SJ made major revisions. Due to the strong involvement of JJK and FR at several different stages of the study, all authors agreed to consider them joint senior. All authors read and approved the final manuscript.

Abstract

Objectives: Amblyopia, strabismus and ocular motility disorders are common conditions with significant impact on visual function, appearance and quality of life. The aim of this study is to establish a core set of outcomes for all treatment interventions for each of the three conditions for use in clinical trials and routine clinical practice.

Design: Prospective 3-stage core outcome set process.

Setting: UK-wide consultation.

Participants: Researchers, clinicians, patients and carers.

Methods and analysis: A comprehensive databank of outcomes was developed from a systematic review of the literature, and a series of focus groups with healthcare professionals, researchers, patients and carers. The databank of outcomes was then scored in a two-round Delphi survey completed by two stakeholder groups; healthcare professionals/ researchers and patients/carers. The results to the online Delphi were discussed at a face-to-face consensus meeting where the core outcome sets were finalised.

Results: For amblyopia, strabismus and ocular motility (40/42/33) participants contributed to both rounds of the Delphi and (6/9/7) voting members attended the consensus meetings respectively. Consensus was reached on ten core outcomes for both amblyopia and ocular motility and nine for strabismus. The core outcomes ocular alignment, vision-related quality-of-life, adverse events and cost were common to all three conditions.

Conclusions: The study used robust consensus methods to develop a core outcome set for three ophthalmic conditions. The implementation of these core outcome sets in

clinical trials and routine clinical practice will ensure that the outcomes that are being measured and reported are relevant to all stakeholders. This will enhance the relevance of study findings and enable results from different studies to be compared.

Keywords:

Core outcome set; Amblyopia; Strabismus; Ocular motility; Consensus; Delphi

Article summary:

Strengths and limitations of this study:

- We targeted amblyopia, strabismus and ocular motility disorders which are common ophthalmic conditions.
- We have developed three core outcome sets; one for each condition.
- The study included key stakeholders including researchers, clinicians, patients and carers.
- Use of these core outcome sets in future studies has the potential to enable comparison of the results across studies.
- Although developed in the UK, there is potential for these COS to be further developed and used more widely.

Introduction

Amblyopia (lazy eye) and strabismus (squint) occur in up to 5% of the general population [1,2]. It is unknown how prevalent ocular motility disorders (abnormal eye movements) are in the general population. These conditions often present in children and can lead to long-term problems for children and young adults such as blurred vision, double vision, low esteem and even blindness if not treated [3]. There are several approaches to the management of these conditions including occlusion, penalisation, spectacles, prisms, drugs, surgery, botulinum toxin, exercises, watchful waiting, or a combination of two or more of the above [4-20].

Interventional systematic reviews in this field of research have identified that there is considerable variation in the outcomes being measured and reported in primary research

studies, which impacts on the ability to compare and synthesise outcome results across studies. Moreover, it was noted that there is a paucity of outcome data available on important patient outcomes such as quality of life, long-term outcome as well as the cost of treatment [4-20]. To mitigate these issues and to increase the relevance of research, a core outcome set (COS) can be developed which represents an agreed standardised set of outcomes that should be measured and reporting in all studies for a specific area of health or healthcare. A search of the COMET (Core Outcome Measures in Effectiveness Trials) database revealed that there are several studies that have investigated important outcomes for eyes and vision disease; examples include cataracts and glaucoma but none have specifically looked at amblyopia, strabismus or ocular motility disorders [21].

The aim of this study was to develop core outcome sets for use in clinical trials and routine practice for all intervention types for the treatment of amblyopia, strabismus and ocular motility disorders in children and adults that includes input from all stakeholders. While we aim to develop three separate COS for each of the ophthalmic conditions, we anticipate that there could be considerable overlap in the importance of certain outcomes across these conditions.

Methods

The development of the COS study involved three stages (Figure 1): (1) the generation of a long list of outcomes; (2) a two- round online Delphi survey and (3) face- to- face consensus meetings to discuss the results of the Delphi survey and agree on the COS. The process considered the minimum standards for the design of a COS study (COS-STAD), which included careful consideration of the scope, stakeholders and the consensus process [22].

Outcome list generation

A databank of outcomes was generated from two sources: a systematic review of outcomes reported by researchers and clinicians in studies for the treatment of the conditions under evaluation, and, secondly using three separate focus groups (one for each condition) containing a mix of healthcare professionals, researchers, patients and

carers. The detailed search strategy, methods and results for the systematic review have been published elsewhere [23]. Outcomes from the systematic review and suggested outcomes from the recorded focus group meetings were extracted verbatim and grouped into suitable domains to facilitate easy classification. The final list was checked by experts in all three clinical conditions (SJ, FR), who also had the opportunity to use their clinical expertise to add additional outcomes to the list. In preparation for the Delphi survey, clinical assessment outcomes used only by healthcare professionals were either separated out (not to be scored by patients) or combined into a simplified outcome for patients to score. Each outcome was written using plain language and feedback sought from four researchers from the Health Service Research department, University of Liverpool and a clinician from a local hospital on the acceptability and their understanding of the wording used. The databank of outcomes can be found in Supplementary Table 1.

Online Delphi survey

The databank of outcomes was used to populate an online Delphi survey, which was administered using DelphiManager [24]. Participants were invited from two key stakeholder groups. The first group consisted of healthcare professionals involved in the care for people with one of the three conditions or researchers working within this field. Invitations to participate were sent by email flyers to national professional organisations including the British and Irish Orthoptic Society, Paediatric Ophthalmology networks, and local groups linked with the University of Liverpool. The second group included patients or carers of patients affected by at least one of the three conditions of interest. Patients and carers were invited to participate into the survey using flyers distributed on the University of Liverpool noticeboards, newsletters (via the professional Society), social media (twitter) and in ophthalmology departments in local hospitals including Aintree University Hospital, The Royal Liverpool University Hospital and Southport and Ormskirk hospitals. Through routine clinical practice, the study authors (SJ, FR) and healthcare professionals were also encouraged to distribute the patient survey links to their relevant patients if they showed an interest in the study.

Four surveys were set up, one for the healthcare professionals and researchers that contained the outcomes to be scored for all three conditions, and, three separate surveys

containing only the outcomes relevant to patients and carers associated with each individual condition. The Delphi process was completed using two rounds (hereafter referred to R1 and R2). In each round participants were presented with the list of outcomes and asked to score each outcome on how important it was to include in the COS, using a 9-point Likert scale, with 1-3 labelled 'not important', 4-6 labelled 'important but not critical', and 7-9 labelled as 'critically important' [25]. Participants had the option to indicate 'unable to score' on any outcome they felt unable to score, and at the end of R1, participants were invited to submit additional outcomes they thought were missing from the list. These outcomes were reviewed by the study authors (SJ, FR) and any outcomes that represented a new relevant outcome were added to the list to be scored in R2. Irrespective of participant scoring, no outcomes were removed from the list between R1 and R2. During R2, participants were shown the distribution of scores for both stakeholder groups for each outcome along with their own score from R1 and asked to score the outcome again, using the same scale, taking this extra information into account.

Consensus meeting

Separate face-to-face consensus meetings were held at the University of Liverpool, UK for each of the three conditions. Participants who either had an active role in the focus groups and/or completed both rounds of the Delphi survey were invited to attend, although others with an interest in the project were invited to ensure each meeting had a balanced mix of participants from both stakeholder groups. In advance of the meeting, participants received a copy of their scores from the online survey (if appropriate) and a consensus matrix (Supplementary Table 1) detailing the results of R1 and R2 by stakeholder group, and which outcomes had reached the a priori definition of consensus in, consensus out or no consensus (Table 1). The consensus definition is similar to that used in other COS development studies.

The meeting for amblyopia was chaired by a non-clinical researcher with expertise in COS development methodology (JJK) while the meeting for strabismus and ocular motility was chaired by a student investigator with a clinical background (SJ).

In order to facilitate the discussion all outcomes that had reached consensus 'in' after R2 for both stakeholder groups were presented first, followed by outcomes that reached consensus 'in' for only one stakeholder group. All outcomes that scored critical for inclusion for 50-69% of the participants for either both or one of the stakeholder groups in R2 were presented next followed by all other outcomes that were scored by both stakeholder groups. Outcomes that were only scored by healthcare professionals and researchers were discussed last. Results for each outcome from the Delphi were shown to the participants with more time allocated to discussing outcomes where there was more uncertainty on whether the outcome should be included in the COS or not. Views for and against inclusion in the COS were sought by the meeting chair, who also ensured that participants had equal opportunity to comment prior to voting. Voting was undertaken anonymously using Poll Everywhere [26] software which was linked to mobile and tablet devices. The definition of consensus used in the Delphi survey (Table 1) was applied to the consensus meeting. The final COS was presented at the end of the meetings.

Study registration, ethics and reporting guidance

The study was prospectively registered with the COMET Initiative (Core Outcome Measures in Effectiveness Trials) [27]. Ethical approval was obtained from the University of Liverpool institutional research ethics committee for the focus groups, online survey and the consensus meetings to be undertaken with healthcare professionals and patients (Ref. Nos. 2063 and 2260). Informed consent was obtained from participants. The study is reported in line with the Core Outcome Set – Standards for Reporting (COS-STAR) guidance [28].

Patient and Public Involvement

The study was supported by a patient advisory group which provided input to this research study. The patient advisory group met on a regular basis for the duration of the study. Patients contributed to the design of the study and were involved at all stages of the survey and consensus meetings.

Results

A summary of the COS development process is shown in Figure 1. The final COS contains ten, nine and ten outcomes across seven, six and seven domains for amblyopia, strabismus and ocular motility respectively (Table 2). Ocular alignment, vision-related quality-of-life, adverse events and cost were common to all three conditions.

Development of the databank of outcomes

The systematic review and focus groups of health care professionals, researchers, patients and carers identified 31, 61, and 78 individual outcomes for amblyopia, strabismus and ocular motility respectively. These were combined with a list of outcomes suggested by professional experts (SJ, FR) resulting in a total of 40, 70 and 106 outcomes for amblyopia, strabismus and ocular motility respectively. The outcomes were classified into 12 domains, (symptoms, visual function, refraction, oculomotor function, quality-of-life, treatment dependency, signs, investigations, long-term outcome, compliance, adverse events, cost) and outcomes that were not considered to be patient relevant were separated out or combined. As an example, 'refractive status', 'spherical and cylindrical refraction' and 'median spherical equivalence' were combined into a single outcome 'refractive status' for patients as they all have a similar meaning, but are often referred to separately by healthcare professionals. Details of all outcomes including domain classification, combined outcomes and plain language descriptions of outcomes is provided in Supplementary Table 1.

Online Delphi

Thirty three healthcare professionals / researchers scored all outcomes for both R1 and R2 of the amblyopia component of the online survey while 29 completed for strabismus and ocular motility. Three patients/carers completed both rounds for amblyopia while nine completed both rounds for strabismus and five for ocular motility (Figure 1). At the end of R1, five outcomes for amblyopia, 12 for strabismus and 23 for ocular motility reached consensus 'in' for both stakeholder groups. After a review of all additional outcomes suggested by participants in R1, three new outcomes were added to the strabismus survey in R2 (improvement in angle by a set amount (suggested by a

healthcare professional) and, immediate result post-surgery and long-term discomfort from scar tissue (both suggested by a patient)).

On completion of R2, ten outcomes reached consensus 'in' for amblyopia across both stakeholder groups while 17 and 32 outcomes reached the same criteria for strabismus and ocular motility respectively.

Consensus meeting

Six, nine and seven voting participants attended the consensus meeting for amblyopia, strabismus and ocular motility respectively with an even balance of healthcare professional/researchers and patients present (Figure 1).

Amblyopia

For amblyopia, *future functionality/long-term impact* and *adverse events* reached the consensus 'in' criteria for both stakeholder groups in both rounds of the Delphi and remained in the COS. Despite reaching consensus 'in' for both rounds of the Delphi for both stakeholder groups, intolerable diplopia and occlusion amblyopia (both adverse events) were not included in the final COS as it was felt that these could be captured under 'adverse events' and therefore were not critical for separate inclusion in the COS. Long-term outcome was also excluded following discussion as the group felt that there was currently no agreed set time for measuring long-term objective outcomes. *Best corrected visual acuity* and *compliance* marginally did not reach consensus 'in' during R2 of the Delphi but made the final COS after discussion. Following a discussion on the other visual function outcomes, *near visual acuity* was also added because it was noted that it was a good marker of early improvement for the treatment of amblyopia and important for children as it is important to their education. Refractive status reached consensus for both groups in R2 but following discussion this was replaced by *spherical and cylindrical refraction* (scored only by health care professionals in the Delphi) because it was successfully argued that this was a more precise measurement of refractive status. The list of outcomes within the quality of life domain were discussed simultaneously. While this was not listed specifically as an outcome in the Delphi, participants agreed to include *visual-related quality of life* in the core set as it was felt that a generic health-related quality of life outcome was not sensitive enough. Psychological impact of

treatment was scored only by healthcare professionals in the Delphi but reached consensus 'in' during R2. Following discussion led by a parent participant, the panel derived a new outcome to include *treatment-related impact* into the final COS in order to capture the effect of treatment, such as patching on children, which could be long lasting. For both Delphi rounds, cost outcomes did not reach consensus 'in' by either stakeholder groups, however, the consensus panellists successfully advocated for its inclusion as a core outcome as *cost* outcome data is vital information for contemporary health systems.

Strabismus

For strabismus, *symptoms* and *patient satisfaction* reached the consensus 'in' criteria for both stakeholder groups in both rounds of the Delphi and remained in the COS. Best corrected visual acuity also reached consensus 'in' for both rounds and groups in the Delphi although the consensus panel argued that any change in vision and/or loss of vision as an adverse event would be very significant and reportable as per the Royal College of Ophthalmology guidelines [29]. At the consensus meeting, participants noted that strabismus interventions aim to change the strabismus angle and visual acuity should not be affected by the intervention unless an adverse event occurred. Thus a change in visual acuity would be captured within adverse events. On this basis a decision was taken to exclude visual acuity from the core set. All remaining visual acuity tests were discussed simultaneously, and while the post-op diplopia test reached consensus 'in' during the Delphi exercise, the consensus panel voted in favour of including *binocular vision* as core, as it was more representative of a group of visual function related outcomes. Oculomotor function outcomes were discussed simultaneously and it was highlighted that *ocular movement* was critical to be reported in all strabismus types as a change caused by the intervention would be significant. Quantifying both the *ocular alignment* and *deviation* were also seen to be critical in the context of any strabismus type and were included as core outcomes. *Visual-related quality-of life*, *adverse events* and *cost* were also included in the COS for reasons discussed for amblyopia.

Ocular Motility

The discussions for ocular motility closely followed those of strabismus with the addition of clinical signs being added as an extra core outcome. Similar to adverse events, this outcome was a catch all for all clinical signs which were scored individually in the Delphi

exercise. This strategy was seen favourable by the meeting participants as many sub-conditions of ocular motility have specific signs associated with them. An example includes corneal exposure in the ocular motility condition of Thyroid Eye Disease but which is not relevant in other ocular motility disorders.

Discussion

This study has developed a set of core outcomes for the treatment of three ophthalmic conditions using a robust consensus process involving healthcare professionals, researchers, patients and carers. We recommend that, as a minimum, these core outcomes are used in future trials of interventions to treat amblyopia, strabismus and ocular motility disorders. We also advocate that these outcomes are recorded in routine clinical practice to ensure that the outcome data collected is meaningful and important. While these three core outcome sets were developed independently within the same study, there exists some parallels, and as a consequence, four outcomes (ocular alignment, vision-related quality-of-life, adverse events and cost) were common to all three conditions.

A strength of this study is that it was prospectively registered with the COMET Initiative and it was developed using the COS- STAD (Core Outcome Set - STAndards for Development) recommendations [22]. Engagement with patient participants was particularly challenging and we sought to improve patient input by offering paper copies of the Delphi survey with pre-paid return envelopes in orthoptic clinics, although this was later abandoned after a number of sessions when there was no uptake. As a consequence of a relatively low number of patients responding to the Delphi and attrition between the two rounds, there was concern that consensus was not being achieved at the end of the final round given the number of outcomes reaching consensus for both stakeholder groups had increased dramatically from R1. While measures were taken to ensure survey participation and retention was maximised (including sending reminders and extending deadlines for completion), it was felt that after several months of keeping the survey open our efforts became futile. In order to compensate for this we ensured that the consensus meetings where the final COS were ratified contained a good balance of healthcare professionals and patients. The main limitation of this study was that the consensus process was based using only participant's in the UK. However, as a starting

point, we have reason to believe that this COS could also be useful in other countries and settings.

Further consensus work is needed to establish the best measurement instruments to measure these core outcomes. To assist this process, the systematic review for generating the databank of outcomes also recorded the measurement instruments associated with each outcome [23]. The generalisability of the COS also needs to be reviewed in healthcare settings outside the UK. While the review of outcomes identified studies from around the world (with prominence from the United States, United Kingdom, China and other European countries), the formal consensus process was undertaken using only participants from the UK, and those attending the consensus meeting were mostly localised to the North West of England.

There are few reported COS in the literature that relate to the three conditions in this study. An attempt to utilise a COS is evident for the National Strabismus Data Set project (29). However, the choice of outcomes largely reflects routine clinical practice and there are no 'core' outcomes specified within the full outline of assessments that are specified for strabismic conditions. Chiu and colleagues recommended four outcomes for reporting results of surgery for intermittent exotropia (30). Their study aimed to explore the extent of standardisation of outcomes reported in surgical studies for the condition. However the study was limited by the extent of literature review (10-year literature search period) and lack of external consensus. A short narrative review of outcome measurements for size of deviation showed considerable variability across the tests available and the recommendations for their use. They suggested four core outcomes for all future studies: alignment, near stereoacuity, control score, and quality of life score. If assigning near stereoacuity and control score to 'binocular vision', their outcomes map to those reported in our COS for strabismus. Most recently a study aiming to define successful outcomes for strabismus surgery was published by Serafino et al (31). Although this study did not state an intention to develop a COS, there are a lot of similarities and overlap in the objectives and methodology used. A Delphi process was used to identify areas of consensus and disagreement among experts for the definition of success post strabismus surgery. The panel of experts in their study represented wide international geographic areas and included experts who were chosen based on their peer-reviewed publications, participation at international meetings and their surgical experience. The

study concluded the following: they achieved consensus on which strabismus types need their separate set of outcome criteria. They also identified the importance of “stereopsis” and “the range of single vision” for inclusion of success definition in some strabismus types. The study also found that there was no consensus on the length of time after surgery for determination of success, magnitude of deviation consistent with success, and whether manifest or latent deviation should be considered to define success. Limitations of the study were that their survey did not involve scoring of outcomes, there was no systematic search of literature of reported outcomes prior to survey construction, and patients or service users were not consulted in the process. A further study to evaluate outcome measures for use in clinical trials involving subjects with nystagmus is in the planning stage and registered within the COMET initiative database (32). This study aims to investigate the intra and inter-subject variability in a variety of putative outcome measures in children over time in order to evaluate the most suitable and robust outcome measures for future trials.

A search in the COMET initiative database in April 2020 did not reveal registration of Serafino’s study (31) or any further additions of similar studies in the database. Duplication of efforts and waste of research can result from failure to register COS studies of similar scopes and objectives.

Conclusion

The three COS developed from this study can be applied to future trials and routine data collection for all intervention types to treat the three ophthalmic conditions considered. There use will allow the comparison of outcome data to be made across studies and to better inform treatment decisions. Future work will include seeking consensus on how these outcomes should be measured and to evaluate the acceptability of the current COS to patients and professionals in other countries, particularly where healthcare systems differ from the UK.

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Figure 1 Study flowchart

Table 1: Definition of consensus

Consensus classification	**Description**	**Definition of consensus**
Consensus in	Consensus that the outcome should be included in the core set	≥70% of participants scoring the outcome as '7–9' (critically important)
Consensus out	Consensus that the outcome should *not* be included in the core set	≥70% of participants scoring the outcome as '1–3' (not important)
No consensus	Uncertainty about the importance of the outcomes	Anything else

Table 2: Outcomes included in the Amblyopia, Strabismus and Ocular Motility core outcome set

Outcome	Domain	Amblyopia	Strabismus	Ocular Motility
Best corrected visual acuity	Visual function	X		
Near visual acuity	Visual function	X		
Binocular vision	Visual function		X	X
Spherical and cylindrical refraction	Refractive status	X		
Ocular alignment	Oculomotor function	X	X	X
Deviation	Oculomotor function		X	X
Ocular movement	Oculomotor function		X	X
Symptoms	Symptoms		X	X
Clinical signs	Signs			X
Vision-related quality of life	Quality of life	X	X	X
Treatment-related impact	Quality of life	X		
Future functionality / long term impact	Quality of life	X		
Patient satisfaction	Quality of life		X	X
Compliance	Compliance	X		
Adverse events	Adverse events	X	X	X
Cost	Cost	X	X	X

Development of databank of outcomes

Systematic review of electronic bibliographic databases

2982 records screened
142 articles included: A:42*; S:33*; OM 68
(*one article considered both A and S)

Patient/carer and healthcare professional focus groups

A: 1 patient, 1 clinical orthoptist, 2 research orthoptists
S: 1 patient, 1 carer, 1 clinical orthoptist, 2 research orthoptists
OM: 3 patients, 1 carer, 3 clinical orthoptists, 2 research orthoptists

Systematic review

A: 24 outcomes
S: 47 outcomes
OM:68 outcomes

Focus groups

A: 7 outcomes
S: 14 outcomes
OM:10 outcomes

Professional opinion (study authors)

A: 9 outcomes
S: 9 outcomes
OM:28 outcomes

Outcomes following domain categorisation and consideration of patient suitability

A: 40 outcomes (40 HCP; 36 patients)
S: 70 outcomes (70 HCP; 57 patients)
OM:106 outcomes (106 HCP; 82 patients)

Online Delphi survey

Delphi round 1

A: 77 responses: 60 (11) HCP; 6 patients
S: 76 responses: 50 (10) HCP; 13 (3) patients
OM: 59 responses: 44 (6) HCP; 8 (1) patients

(numbers in parentheses denote partial responders)

Outcomes meeting consensus 'in' for both stakeholder groups / HCP only / patient only

A: both 5 / HCP 5 / patient 11
S: both 12 / HCP 11 / patient 11
OM: both 23 / HCP 13 / patient 14

Analysis of free text responses to additional outcomes question. Three outcomes added to strabismus survey:

1) improvement in angle by a set amount
2) immediate result post-surgery
3) long-term discomfort from scar tissue

1) was suggested by HCP (to be scored by HCP only in round 2)
2) + 3) suggested by patient (to be scored by patients only in round 2)

Delphi round 2

A: 40 responses: 33 (4) HCP; 3 patients
S: 42 responses: 29 (4) HCP; 9 patients
OM:33 responses: 29 HCP; 5 patients

(numbers in parentheses denote partial responders)

Outcomes scored in round 2

A: 40 outcomes (40 HCP; 36 patients)
S: 73 outcomes (71 HCP; 59 patients)
OM:106 outcomes (106 HCP; 82 patients)

Outcomes meeting consensus 'in' for both stakeholder groups / HCP only / patient only

A: both 10 / HCP 7 / patient 4
S: both 17 / HCP 19 / patient 10
OM: both 32 / HCP 14 / patient 13

Consensus meeting

Consensus meeting

A: 6 voting participants: 4 HCP; 3 patients
S: 9 voting participants: 5 HCP; 4 patients
OM: 7 voting participants: 4 HCP; 3 patients

Outcomes in the final core outcome set (Table 2)

A: 10 outcomes
S: 9 outcomes
OM: 10 outcomes

Supplementary Table 1: Long list of outcomes used in the Delphi survey and critical scoring in both rounds of the Delphi survey by stakeholder group

[Outcomes identified from: systematic review (SR), focus groups (FG) and professional opinion (PO)].

Percentages highlighted in red denote outcomes that reached the consensus 'in' criteria.

N/A: not scored by stakeholder group (HCPs or patients)

Amblyopia

Domain	Source	Outcome	Lay-term summary	Delphi results							
				Round 1				Round 2			
				HCPs		Patients		HCPs		Patients	
				n	% (7-9)	n	% (7-9)	n	% (7-9)	n	% (7-9)
Symptoms	FG	1. Patient symptoms	*Symptoms or complaints related to vision or eyes*	67	34.3	4	50.0	37	37.8	3	66.7
Visual function	SR	2. Best corrected visual acuity	*Vision measured at distance corrected with glasses*	70	**98.6**	4	66.7	37	**100.0**	3	66.7
	SR	3. Near visual acuity	*Close up or reading vision*	70	65.7	4	50.0	37	**78.4**	3	66.7
	PO	4. Habitual visual acuity	*Vision measured in the usual preferred state for a person*	62	58.1	5	**80.0**	37	67.6	3	**100.0**
	SR	5. Uncorrected visual acuity	*Vision without glasses or contact lenses*	70	4.3	4	40.0	37	5.4	3	0.0
	FG	6. Suppression	*Testing if the person has developed "suppression" of one image to improve double vision which usually happens in childhood as a coping mechanism from the brain to improve visual development*	70	42.9	4	**75.0**	36	47.2	2	**100.0**
	FG	7. Fixation	*Testing if the person is using the central part of the retina to see with or alternatively using an eccentric part of the retina*	70	52.9	3	33.3	36	50.0	3	33.3

	FG	8. Contrast sensitivity	*Objects of varying brightness*	66	12.1		60.0	34	5.9	3	0.0
	SR	9. Visual evoked potentials	*Testing vision signals from the eyes to the brain with electrodiagnostics (visual evoked potentials/VEP)*	56	8.9		33.3	33	3.0	2	0.0
	SR	10. Binocularity	*to check if the eyes are working together to give any level of 3D vision or depth appreciation*	70	47.1		**80.0**	36	63.9	2	50.0
	SR	11. Stereoacuity	*Fine 3D vision or depth appreciation with both eyes or "stereo vision"*	70	37.1		**80.0**	35	34.3	2	**100.0**
	PO	12. Simultaneous perception	*Testing lower levels of 3D vision*	70	30.0		60.0	35	25.7	2	0.0
	PO	13. Retinal correspondence		70	31.4	N/A	N/A	35	11.4	N/A	N/A
Refraction	SR	14. Refractive status	*Testing the amount of prescription of glasses or contact lenses*	69	**84.1**		66.7	35	**94.3**	3	**100.0**
	SR	15. Spherical & cylindrical refraction		69	**79.7**	N/A	N/A	35	**91.4**	N/A	N/A
	SR	16. Median spherical equivalent		64	26.6	N/A	N/A	33	21.2	N/A	N/A
Oculomotor function	SR	17. Ocular alignment /deviation	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation*	68	63.2		66.7	35	**71.4**	3	**100.0**
	PO	18. Abnormal head posture	*The presence of a compensatory head posture to avoid double vision*	68	33.8		66.7	34	32.4	3	66.7
Quality of life	SR	19. Quality of life measures (in general)	*Health related quality of life (all relevant aspects)*	69	53.6		**100.0**	35	62.9	3	**100.0**
	FG	20. Psychological impact of the disorder	*Negative impact of lazy eye (amblyopia) on emotions and/or behaviour*	69	55.1		**83.3**	34	67.6	3	**100.0**
	SR	21. Psychological impact of treatment of disorder	*The psychological impact of treatment of lazy eye (amblyopia) on emotions and/or behaviour*	69	62.3	N/A	N/A	34	**73.5**	N/A	N/A
	PO	22. Self-esteem	*Negative impact of lazy eye (amblyopia) on self-esteem & confidence*	69	59.4		**100.0**	34	**70.6**	3	**100.0**
	SR	23. Social anxiety and social avoidance due to the disorder	*Negative impact of lazy eye (amblyopia) on social interaction or causing social stigma*	69	55.1		**83.3**	34	67.6	3	**100.0**
	SR	24. Academic/ occupation achievement in relation to the condition or its treatment	*Academic/ occupation achievement in relation to the condition or its treatment*	69	60.9		**83.3**	34	**76.5**	3	66.7
	SR	25. Activity of daily living (ADL)	*Negative impact of lazy eye (amblyopia) on normal daily activities*	68	52.9	6	**100.0**	33	**72.7**	3	**100.0**
	SR	26. Patient satisfaction from treatment	*Patient satisfaction from treatment*	68	61.8	6	**83.3**	34	**76.5**	3	**100.0**
	FG	27. Future functionality/long-term impact	*Future functionality/long-term impact (patient-reEOrted)*	69	**78.3**	6	**100**	34	**91.2**	3	**100.0**

	SR	28. Fear of losing better eye		69	**71.0**		66.7	33	**84.8**	3	66.7
Compliance	SR	29. Compliance	*How well the treatment is done*	69	**95.7**		66.7	33	**97.0**	3	66.7
Adverse events	SR	30. Adverse effects from treatment (any)	*Adverse effects from treatment (any)*	69	**73.9**		**80.0**	33	**87.9**	2	**100.0**
	SR	31. Intolerable diplopia	*Intolerable double vision as a side effect from treatment*	69	**89.9**		**83.3**	33	**100.0**	3	**100.0**
	SR	32. Occlusion amblyopia	*Development of lazy eye (amblyopia) in the better eye as a result of patching/penalisation treatment*	69	**76.8**		**100.0**	33	**87.9**	3	**100.0**
	SR	33. Visual disorientation	*Visual disorientation due to treatment with occlusion of better eye*	64	45.3		66.7	32	56.3	3	**100.0**
	PO	34. Disturbed distance estimation	*Disturbed distance estimation due to treatment with occlusion of better eye*	64	39.1		66.7	32	46.9	3	33.3
	SR	35. Skin irritation or allergy to patches	*Skin irritation or allergy from eye patches used to occlude the eye*	69	50.7		33.3	33	51.5	3	33.3
	PO	36. Atropine eye drops side effects	*Side effects of the eye drops used regularly at home for treatment of lazy eye (amblyopia)*	69	65.2		33.3	33	69.7	3	66.7
Cost	SR	37. Economic data (in general)	*Economic data (in general) including services and families/individuals*	54	24.1		16.7	30	20.0	3	0.0
	PO	38. Cost of treatment on services	*Cost of treatment on services*	55	25.5		16.7	31	32.3	3	0.0
	PO	39. Cost of treatment on families/individuals	*Cost of treatment on families/individuals*	54	37.0		33.3	30	50.0	3	0.0
Long-term	FG	40. Long-term outcomes	*Long-term outcomes (clinical outcomes)*	59	**84.7**		**100.0**	33	**93.9**	3	**100.0**

Strabismus

Domain	Source	Outcome	Lay-term summary	Delphi results							
				Round 1				Round 2			
				HCPs		Patients		HCPs		Patients	
				n	% (7-9)	n	% (7-9)	n	% (7-9)	n	% (7-9)
Symptoms	FG	1. Patient symptoms	*Symptoms or complaints related to vision or eyes*	60	**91.7**	16	**75.0**	33	**100.0**	9	**77.8**
	FG	2. Diplopia	*Improvement in double vision in general*	60	**95.0**	14	**85.7**	33	**100.0**	8	62.5
	FG	3. Appearance of strabismus	*Appearance of the squint*	60	**85.0**	15	46.7	33	**87.9**	9	33.3
	FG	4. Eye aesthetics as the patient perceives	*Appearance of the squint as the patient perceives*	60	**80.0**	15	40.0	33	**84.8**	9	44.4
	FG	5. Eye aesthetics as relatives and friends perceive	*Appearance of the squint as the relatives and friends perceive*	60	58.3	15	46.7	33	63.6	9	33.3
Visual function	SR	6. Best corrected visual acuity	*Vision measured at distance corrected with glasses*	60	**71.7**	11	**72.7**	33	**90.9**	7	**100.0**
	PO	7. Near visual acuity	*Close up or reading vision*	60	45.0	12	**75.0**	33	63.6	7	**71.4**
	PO	8. Habitual visual acuity	*Vision measured in the usual preferred state for a person*	53	41.5	10	**70.0**	32	59.4	7	**100.0**
	PO	9. Uncorrected visual acuity	*Vision without glasses or contact lenses*	60	8.3	12	58.3	33	3.0	7	**71.4**
	FG	10. Suppression	*Testing if the person has developed "suppression" of one image to improve double vision which usually happens in childhood as a coping mechanism from the brain to improve visual development*	60	65.0	10	**80.0**	32	**75.0**	8	**75.0**
	PO	11. Fixation	*Testing if the person is using the central part of the retina to see with or alternatively using an eccentric part of the retina*	60	46.7	9	33.3	32	46.9	7	42.9
	PO	12. Contrast sensitivity	*Objects of varying brightness*	59	6.8	8	37.5	32	0.0	8	37.5
	SR	13. Binocularity	*Testing "binocularity" which is to check if the eyes are working together to give any level of 3D vision or depth appreciation*	60	**76.7**	12	58.3	32	**75.0**	8	**87.5**

	SR	14. Stereoacuity at near	*Fine 3D vision or depth appreciation with both eyes measured for near*	60	60.0	12	58.3	32	62.5	8	**87.5**
	SR	15. Stereoacuity at near and distance (any strabismus type)	*Fine 3D vision or depth appreciation with both eyes measured for both near and distance*	59	44.1	12	58.3	32	46.9	8	**75.0**
	SR	16. Stereoacuity at near and distance (for certain strabismus types? please specify)	*Fine 3D vision or depth appreciation with both eyes measured for both near and distance for certain types of squint*	54	53.7	N/A	N/A	30	56.7	N/A	N/A
	SR	17. Field of binocular single vision	*Testing the extent of area of vision where there is no double vision while looking around with both eyes open*	60	46.7	12	66.7	32	53.1	8	62.5
	FG	18. Post op diplopia test	*Testing if a person is likely to get double vision after correcting the eye deviation with surgery*	59	**81.4**	11	**81.8**	32	**93.8**	9	**77.8**
	SR	19. Simultaneous perception	*Testing lower levels of 3D vision*	59	37.3	10	50.0	32	25.0	8	62.5
	PO	20. Retinal correspondence	*Testing lower levels of 3D vision*	60	43.3	N/A	N/A	32	37.5	N/A	N/A
	PO	21. Refractive status	*Testing the amount of prescription of glasses or contact lenses*	60	61.7	11	54.5	32	**75.0**	8	50.0
Oculomotor function	SR	22. Ocular alignment /deviation	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation*	60	**86.7**	12	**91.7**	32	**100.0**	8	50.0
	SR	23. Abnormal head posture	*The presence of a compensatory head EOsture to avoid double vision*	60	66.7	11	63.6	32	**84.4**	9	**77.8**
	FG	24. Ocular motor alignment at various positions especially where the deviation is greatest	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation at different EOsitions*	60	**75.0**	N/A	N/A	32	**87.5**	N/A	N/A
	SR	25. Presence of incomitance (any strabismus type)	*Testing if there is variation of the eye deviation in different EOsitions when looking around*	59	**71.2**	N/A	N/A	32	**78.1**	N/A	N/A
	SR	26. Presence of incomitance (for certain strabismus types? please specify)	*Testing if there is variation of the eye deviation in different EOsitions when looking around*	58	**75.9**	N/A	N/A	31	**80.6**	N/A	N/A
	SR	27. Control of deviation (any strabismus type)	*Measuring how well the person can control the eye turn*	59	**79.7**	12	**83.3**	32	**96.9**	9	55.6
	SR	28. Control of deviation (for	*Measuring how well the person can control the eye turn*	58	**81.0**	N/A	N/A	31	**93.5**	N/A	N/A

		certain strabismus types? please specify)									
	SR	29. Ocular movement	*How well eyes move as a person is looking around*	60	66.7	13	61.5	32	**71.9**	9	**77.8**
	SR	30. Presence of latent nystagmus (any strabismus type)	*Checking if there are involuntary rapid movements of the eyes when one eye is covered*	58	46.6	11	63.6	32	53.1	9	44.4
	SR	31. Presence of latent nystagmus (for certain strabismus types? please specify)	*Checking if there are involuntary rapid movements of the eyes when one eye is covered*	57	54.4	N/A	N/A	32	**71.9**	N/A	N/A
	SR	32. Presence of dissociated vertical deviation (DVD) (any strabismus type)	*Testing if there is tendency for the eye to move up and out +/- rotates when covered*	58	51.7	11	54.5	32	53.1	8	**37.5**
	SR	33. Presence of dissociated vertical deviation (DVD) (for certain strabismus types? please specify)	*Testing if there is tendency for the eye to move up and out +/- rotates when covered*	56	64.3	N/A	N/A	31	**71.0**	N/A	N/A
	SR	34. A or V pattern deviation	*Testing if there is a deviation that increases either on looking up or looking down*	60	60.0	N/A	N/A	32	**81.3**	N/A	N/A
	SR	35. Fusional vergence at near and distance /fusion amplitudes/prism fusion range	*Testing how well the eyes can control a deviation induced with prisms in clinic*	60	68.3	11	63.6	32	**81.3**	9	55.6
	SR	36. Near point of convergence (for any strabismus type)	*Testing if the eyes can normally look inwards to see a near object to an acceptable amount*	60	31.7	13	**76.9**	32	43.8	9	66.7
	SR	37. Near point of convergence (for certain strabismus types? please specify)	*Testing if the eyes can normally look inwards to see a near object to an acceptable amount*	58	51.7	N/A	N/A	32	62.5	N/A	N/A

	FG	38. Accommodation (for any strabismus type)	*Testing if the eyes can change their focus appropriately to see objects at varying distances*	60	23.3	13	61.5	32	18.8	9	44.4
	FG	39. Accommodation (for certain strabismus types? please specify)	*Testing if the eyes can change their focus appropriately to see objects at varying distances*	58	60.3	N/A	N/A	31	61.3	N/A	N/A
	SR	40. AC/A ratio (for any strabismus type)	*Testing the ratio between the ability of the eyes to look inwards and their ability to focus*	59	30.5	13	46.2	32	28.1	9	33.3
	SR	41. AC/A ratio (for certain strabismus types? please specify)	*Testing the ratio between the ability of the eyes to look inwards and their ability to focus*	58	65.5	N/A	N/A	31	67.7	N/A	N/A
	CLIN PART	42. Improvement in angle by a set amount e.g. >10^ *		N/A	N/A	N/A	N/A	31	51.6	N/A	N/A
	PT PART	43. Immediate result EOst-surgery**		N/A	N/A	N/A	N/A	N/A	N/A	8	12.5
Quality of life	SR	44. Quality of life measures (in general)	*Health related quality of life (all relevant aspects)*	53	**81.1**	13	69.2	31	**93.5**	9	66.7
	SR	45. Psychological impact of the disorder	*Negative impact of squint (strabismus) on emotions and/or behaviour*	53	**88.7**	13	69.2	30	**100.0**	9	**77.8**
	SR	46. Psychological impact of treatment of disorder	*EOsitive impact of treatment on emotions and/or behaviour*	53	**75.5**	13	**84.6**	30	**80.0**	9	**77.8**
	SR	47. Social anxiety and social avoidance due to the disorder	*Negative impact of squint (strabismus) on social interaction or causing social stigma*	53	**84.9**	14	**71.4**	30	**90.0**	9	66.7
	FG	48. Academic/ occupation achievement in relation to the condition or its treatment	*Academic/ occupation achievement in relation to the condition or its treatment*	52	69.2	13	69.2	30	**76.7**	9	66.7
	FG	49. Activity of daily living (ADL)	*Activity of daily living (ADL) such as driving*	52	67.3	14	**78.6**	29	**86.2**	9	**77.8**
	SR	50. Patient satisfaction from treatment	*Patient satisfaction from treatment*	53	**83.0**	14	**92.9**	29	**96.6**	9	**88.9**

	FG	51. Future functionality/long-term impact	*Future functionality/long-term impact (patient-reEOrted)*	52	**92.3**	11	**100.0**	29	**96.6**	9	**88.9**
Compliance	PO	52. Compliance	*How well the treatment is done*	52	63.5	12	**91.7**	29	62.1	8	**87.5**
Treatment dependency	SR	53. Successful discontinuation of lens therapy or "special glasses" (for any strabismus type)	*Successful discontinuation of lens therapy or "special glasses" such as bifocals or minus lenses*	49	40.8	4	**100**	28	46.4	6	**83.3**
	SR	54. Successful discontinuation of lens therapy or "special glasses" (for certain strabismus types? please specify)	*Successful discontinuation of lens therapy or "special glasses" such as bifocals or minus lenses*	49	51.0	N/A	N/A	28	64.3	N/A	N/A
	PO	55. Successful discontinuation of prism therapy	*Successful discontinuation of prism therapy*	52	46.2	4	**100.0**	29	51.7	6	**83.3**
Adverse events	SR	56. Adverse effects from treatment (any)	*Adverse effects from treatment (any)*	53	**83.0**	10	60.0	29	**93.1**	9	55.6
	FG	57. Adverse effect on vision from patches or prisms used to treat diplopia	*Adverse effect on vision from patches or prisms used to treat diplopia such as vision degradation or psychosocial effects*	53	67.9	7	42.9	29	**75.9**	6	**83.3**
	SR	58. Intolerable diplopia	*Intolerable double vision*	53	**98.1**	11	**81.8**	29	**96.6**	9	**77.8**
	SR	59. Induced ptosis (post toxin injection)	*Appearance of transient droopy eye lid as a result of using toxin injection to treat squint*	52	51.9	7	57.1	29	55.2	8	62.5
	SR	60. Induced subconjunctival haemorrhage	*Appearance of a bleed in the surface of the eye after squint surgery or injection*	52	32.7	9	33.3	29	20.7	8	37.5
	SR	61. Discomfort or abnormal sensation	*Discomfort or pain during/after treatment of squint*	53	28.3	9	44.4	29	17.2	8	37.5
	SR	62. Overcorrection or under correction of the deviation with surgery or injection	*Persistence of the squint at a lesser extent or appearance of deviation in the opEOsite direction*	52	**71.2**	9	55.6	29	**79.3**	9	66.7
	SR	63. Recurrence of deviation	*Reappearance of the squint after treatment*	53	66.0	9	**77.8**	29	**75.9**	9	**88.9**

	SR	64. Induced vertical deviation	*Appearance of a vertical squint after treatment of a horizontal deviation*	53	69.8	8	**75.0**	29	**82.8**	9	**77.8**
	SR	65. Induced A or V pattern	*Appearance of a deviation that increases either on looking up or looking down*	53	54.7	9	66.7	29	65.5	8	**75.0**
	SR	66. Development of DVD	*Appearance of a tendency for the eye to move up and out when covered*	50	46.0	6	16.7	29	34.5	8	37.5
	SR	67. Induced incomitance	*Development of variation of the eye deviation in different EOsitions when looking around*	53	56.6	7	**71.4**	29	62.1	7	**71.4**
	SR	68. Number of operations/procedures needed	*Number of operations/procedures needed*	53	66.0	9	66.7	29	65.5	8	62.5
Cost	SR	69. Economic data (in general)	*Economic data (in general) including services and families/individuals*	45	44.4	11	36.4	27	37.0	9	33.3
	SR	70. Cost of treatment on services	*Cost of treatment on services*	45	46.7	11	18.2	27	44.4	9	33.3
	SR	71. Cost of treatment on families/ individuals	*Cost of treatment on families/individuals*	45	40.0	11	45.5	26	38.5	9	22.2
Long-term outcomes	SR	72. Long-term outcomes	*Long-term outcomes (clinical outcomes)*	50	**88.0**	11	**90.9**	29	**96.6**	9	**88.9**
	PT PART	73. Long term discomfort from scar tissue **		N/A	N/A	N/A	N/A	N/A	N/A	9	55.6

Ocular motility disorders

Domain	Source	Outcome	Lay-term summary	Delphi results							
				Round 1				Round 2			
				HCPs		Patients		HCPs		Patients	
				n	% (7-9)	n	%	n	% (7-9)	n	% (7-9)
Symptoms	SR	1. Patient symptoms	*Symptoms or complaints related to vision or eyes*	50	**92.0**	9	**88.9**	29	**96.6**	5	**100.0**
	SR	2. Improvement in diplopia (in general)	*Improvement in double vision in general*	50	**90.0**	8	**100.0**	29	**100.0**	5	**100.0**
	SR	3. Improvement of diplopia in primary gaze	*Improvement of double vision when looking straight ahead*	50	**94.0**	8	**87.5**	29	**100.0**	5	**100.0**
	SR	4. Improvement in diplopia in primary and down gaze	*Improvement in double vision when looking straight ahead and down (reading position)*	50	**88.0**	7	**85.7**	29	**100.0**	5	**100.0**
	SR	5. Improvement in diplopia in primary and down gaze with prisms	*Improvement in double vision when looking straight ahead and down with prisms*	50	**86.0**	4	**75.0**	29	**96.6**	5	**100.0**
	SR	6. Severity and duration of visual symptoms/eye deviation	*Severity and duration of visual symptoms/eye deviation*	50	**78.0**	9	**77.8**	29	**79.3**	5	**100.0**
	SR	7. Appearance of the eye deviation	*Appearance of the eye deviation*	50	**74.0**	9	33.3	29	**79.3**	5	60.0
	SR	8. Reduction in pain (for certain types of ocular motility disorders? please specify)	*Reduction in pain*	49	**75.5**	4	50.0	29	**89.7**	4	**100.0**
	SR	9. Improvement in oscillopsia/blur and vertigo in adults (in nystagmus)	*Improvement in oscillopsia/blur and vertigo in adults (in nystagmus)*	50	**92.0**	6	66.7	29	**100.0**	5	**100.0**
	FG	10. Improvement in headaches (for certain types of ocular motility disorders? please specify)	*Improvement in headaches*	50	**80.0**	6	50.0	29	**79.3**	4	40.0
Visual function	SR	11. Best corrected visual acuity	*Vision measured at distance for one eye at a time corrected with glasses*	50	60.0	7	42.9	29	69.0	5	60.0

	SR	12. Near visual acuity	*Close up or reading vision*	50	44.0	8	62.5	29	48.3	5	60.0
	PO	13. Habitual visual acuity	*Vision measured in the usual preferred state for a person*	44	50.0	7	**71.4**	29	69.0	5	**80.0**
	PO	14. Uncorrected visual acuity	*Vision without glasses or contact lenses*	50	6.0	7	28.6	29	0.0	5	20.0
	SR	15. Binocular BCVA	*Vision measured at distance with both eyes open at the same time corrected with glasses*	49	57.1	5	**80.0**	28	**71.4**	5	**100.0**
	SR	16. Suppression	*Testing if the person has developed "suppression" of one image to improve double vision which usually happens in childhood as a coping mechanism from the brain to improve visual development*	50	46.0	3	33.3	29	48.3	3	66.7
	PO	17. Fixation	*Testing "fixation" which is if the person is using the central part of the retina to see with or alternatively using an eccentric part of the retina*	50	32.0	4	25.0	29	24.1	4	25.5
	PO	18. Contrast sensitivity	*Testing "contrast sensitivity" which is objects of varying brightness Contrast sensitivity*	49	6.1	3	33.3	28	0.0	3	20.0
	PO	19. Colour vision test (for any type of ocular motility disorder)	*Colour vision test*	50	8.0	5	60.0	29	0.0	5	20.0
	PO	20. Colour vision test (for certain types of ocular motility disorders? please specify)		49	36.7	N/A	N/A	29	31.0	N/A	N/A
	PO	21. Visual field test (for certain types of ocular motility disorders? please specify)	*Visual field test*	48	37.5	8	50.0	29	24.1	5	60.0
	SR	22. Broadening of the null region (in nystagmus)	*Broadening of the null region (in nystagmus)*	48	58.3	3	**100.0**	29	69.0	4	**100.0**
	SR	23. Reduce the amplitude of nystagmus (in nystagmus)	*Reduce the amplitude of nystagmus (in nystagmus)*	48	60.4	3	**100.0**	29	69.0	3	**100.0**
	SR	24. Stereo acuity	*Fine 3D vision or depth appreciation with both eyes or "stereo vision"*	50	62.0	8	**87.5**	29	**75.9**	5	**100.0**
	SR	25. Field of binocular single vision	*Testing the extent of area of vision where there is no double vision while looking around with both eyes open*	50	**70.0**	7	**71.4**	29	**86.2**	5	**80.0**
	PO	26. Post op diplopia test	*Testing if a person is likely to get double vision after correcting the eye deviation with surgery*	50	68.0	7	**100.0**	29	**82.8**	5	**100.0**
	SR	27. Simultaneous perception	*Testing lower levels of 3D vision*	50	48.0	7	42.9	29	41.4	5	60.0
	SR	28. Retinal correspondence		50	38.0	N/A	N/A	29	24.1	N/A	N/A
	SR	29. Refractive status (for any type of ocular motility disorder)	*Testing the amount of prescription of glasses or contact lenses*	50	46.0	6	50.0	29	37.9	5	40.0

	SR	30. Refractive status (for certain types of ocular motility disorders? please specify)		47	48.9	N/A	N/A	29	51.7	N/A	N/A
Oculomotor function	SR	31. Ocular alignment / deviation	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation*	47	**91.5**	7	**71.4**	29	**100.0**	5	**80.0**
	SR	32. Abnormal head posture	*The presence of a compensatory head posture to avoid double vision*	47	**76.6**	6	66.7	29	**89.7**	5	**80.0**
	FG	33. Ocular motor alignment at various positions specially where the deviation is greatest	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation at different positions*	47	**80.9**	N/A	N/A	29	**89.7**	N/A	N/A
	SR	34. Presence of incomitance (for any type of ocular motility disorder)	*Variation of angle of deviation at different positions of gaze*	47	63.8	6	66.7	29	**79.3**	3	66.7
	SR	35. Presence of incomitance (for certain types of ocular motility disorders? please specify)		44	**72.7**	N/A	N/A	28	**75.0**	N/A	N/A
	PO	36. Control of deviation (any type)	*Measuring how well the person can control the eye turn*	47	**83.0**	6	**83.3**	29	**89.7**	5	**100.0**
	PO	37. Control of deviation (for certain types of ocular motility disorders? please specify)		43	**83.7**	N/A	N/A	29	**96.6**	N/A	N/A
	SR	38. Ocular movement	*How well eyes move as a person is looking around*	47	**85.1**	8	62.5	29	**93.1**	5	**100.0**
	SR	39. Forced duction test (for any type of ocular motility disorder)	*A test done to check eye muscle action passively using forceps*	45	31.1	N/A	N/A	29	24.1	N/A	N/A
	SR	40. Forced duction test (for certain types of ocular motility disorders? please specify)		44	65.9	N/A	N/A	27	66.7	N/A	N/A
	SR	41. Three step/head tilt test (for any type of ocular motility disorder)	*A test to check eye deviation with head tilt and head turn in addition to the straight-ahead EOsition*	44	20.5	N/A	N/A	29	10.3	N/A	N/A
	SR	42. Three step/head tilt test (for certain types of ocular motility disorders? please specify)		45	66.7	N/A	N/A	28	60.7	N/A	N/A
	PO	43. Presence of dissociated vertical deviation (DVD)	*Presence of a tendency for the eye to move up and out when covered*	47	46.8	N/A	N/A	29	44.8	N/A	N/A
	SR	44. A or V pattern deviation	*Testing if the deviation increases on looking up or looking down*	47	55.3	7	57.1	29	62.1	5	40.0

	PO	45. Fusional vergence at near and distance /fusion amplitudes/prism fusion range	*Testing how well the eyes can control a deviation induced with prisms in clinic*	47	53.2	7	57.1	29	62.1	4	**75.0**
	SR	46. Reading eye movements (for any type of ocular motility disorders)	*Checking if eye movements are normal during reading*	45	22.2	7	**71.4**	29	20.7	5	60.0
	SR	47. Reading eye movements (for certain types of ocular motility disorders? please specify)		42	42.9	N/A	N/A	29	48.3	N/A	N/A
	SR	48. Presence of a phoria (for any type of ocular motility disorders)	*A test done to check if there is a hidden small eye alignment problem*	46	54.3	7	42.9	29	58.6	5	20.0
	SR	49. Presence of a phoria (for certain types of ocular motility disorders? please specify)		41	56.1	N/A	N/A	28	**71.4**	N/A	N/A
	SR	50. Objective extortion (for any type of ocular motility disorders)	*Checking if the eye is rotated outwards due to a muscle problem (tested in clinic without the need of patient response)*	43	25.6	7	42.9	28	25.0	5	20.0
	SR	51. Objective extortion (for certain types of ocular motility disorders? please specify)		41	58.5	N/A	N/A	27	66.7	N/A	N/A
	SR	52. Subjective extortion (for any type of ocular motility disorders)	*Check if the eye is rotated outward due to a muscle problem (tested in clinic and results depend on patient response)*	44	50.0	7	42.9	28	60.7	4	25.0
	SR	53. Subjective extortion (for certain types of ocular motility disorders? please specify)		41	**73.2**	N/A	N/A	27	**92.6**	N/A	N/A
	SR	54. Near point of convergence (for any type of ocular motility disorders)	*Testing if the eyes can normally look inwards to see a near object to an acceptable amount*	47	34.0	8	50.0	29	34.5	5	40.0
	SR	55. Near point of convergence (for certain types of ocular motility disorders? please specify)		41	63.4	N/A	N/A	28	**78.6**	N/A	N/A
	SR	56. Accommodation (for any type of ocular motility disorders)	*Testing if the eyes can change their focus appropriately to see objects at varying distances*	46	15.2	8	62.5	29	13.8	5	60.0

	SR	57. Accommodation (for certain types of ocular motility disorders? please specify)		42	42.9	N/A	N/A	28	46.4	N/A	N/A
	SR	58. Dynamic retinoscopy (for certain types of ocular motility disorders? please specify)	*Changing refractive power of the eye with varying focus*	42	19.0	N/A	N/A	27	37.0	N/A	N/A
	SR	59. Pursuits (for certain types of ocular motility disorders? please specify)	*Testing a specific tracking slow movement of the eye for an object*	45	64.4	7	42.9	28	60.7	5	40.0
	SR	60. Saccades (for certain types of ocular motility disorders? please specify)	*Testing a specific rapid tracking eye movement for an object*	45	62.2	7	57.1	28	67.9	5	60.0
	SR	61. Optokinetic nystagmus (OKN)	*Special tracking eye movement using a striped drum*	46	34.8	N/A	N/A	29	31.0	N/A	N/A
Additional clinical signs	SR	62. Eye movement recordings (for certain types of ocular motility disorders? please specify)	*Eye movement recordings*	40	27.5	7	42.9	28	32.1	5	40.0
	SR	63. Palpebral fissure size/lid position (for certain types of ocular motility disorders? please specify)	*Checking eye lid position - whether it is droopy or elevated compared to normal*	44	63.6	5	40.0	29	65.5	5	40.0
	SR	64. Facial asymmetry (for 4th n palsy)	*Checking if the sides of the face are symmetrical or not to help diagnose some congenital motility disorders*	45	33.3	4	50.0	29	20.7	4	25.0
	SR	65. Pupil examination (for any type of ocular motility disorders)	*To check pupil size; reaction etc*	44	45.5	6	50.0	29	41.4	5	20.0
	SR	66. Pupil examination (for certain types of ocular motility disorders? please specify)		43	**74.4**	N/A	N/A	29	**79.3**	N/A	N/A
	SR	67. Proptosis/exophthalmos (for certain types of ocular motility disorders? please specify)	*Checking if the eyes are protruding out of their position*	44	**79.5**	4	**75.0**	29	**86.2**	5	60.0
	SR	68. Intraocular pressure (for certain types of ocular motility disorders? please specify)	*Check eye pressure*	43	48.8	5	**80.0**	28	42.9	4	**100.0**

	SR	69. Corneal exposure (for certain types of ocular motility disorders? please specify)	*Checking for corneal changes resulting from incomplete eyelid closure*	42	**76.2**	4	**75.0**	28	**96.4**	5	**80.0**
	SR	70. Corneal sensitivity (for certain types of ocular motility disorders? please specify)	*Checking if corneal nerve supply is intact*	39	66.7	4	**75.0**	28	67.9	5	**100.0**
	SR	71. Canthal displacement (for certain types of ocular motility disorders? please specify)	*Change in position of the eye contour*	32	28.1	N/A	N/A	23	21.7	N/A	N/A
	SR	72. Oculocardiac reflex (for certain types of ocular motility disorders? please specify)	*Slowing of the heart rate due to entrapped eye muscle*	28	32.1	N/A	N/A	22	36.4	N/A	N/A
	SR	73. Globe dystopia (for certain types of ocular motility disorders? please specify)	*Check the position of the eyeball in relation to the other eye and other parts of the face*	33	39.4	5	60.0	22	36.4	4	50.0
	SR	74. Enophthalmos (for certain types of ocular motility disorders? please specify)	*Checking if the eyes are sinking in from their normal position*	42	66.7	4	**75.0**	29	**82.8**	5	**80.0**
Clinical investigations	SR	75. Assessment for fractures and soft-tissue herniation for example inferior rectus muscle; fat; or connective tissue radiographically (for certain types of ocular motility disorders? please specify)	*Assessment for fractures and soft-tissue herniation for example inferior rectus muscle; fat; or connective tissue radiographically*	41	**87.8**	3	66.7	29	**96.6**	4	**75.0**
	SR	76. Assessment for muscle atrophy or absent nerve radiographically (for certain types of ocular motility disorders? please specify)	*Assessment for muscle atrophy or absent nerve radiographically*	35	65.7	5	60.0	26	69.2	4	**75.0**
	SR	77. Histologic examination of excised tissue (for certain types of ocular motility disorders? please specify)	*Histologic examination of excised tissue*	26	57.7	N/A	N/A	24	**75.0**	N/A	N/A
Quality of life	SR	78. Quality of life measures (in general)	*Health related quality of life (all relevant aspects)*	45	**82.2**	8	**87.5**	29	**93.1**	5	**100.0**

	FG	79. Psychological impact of the disorder	*Negative impact of eye motility problem on emotions and/or behaviour*	45	**84.4**	8	**100.0**	29	**96.6**	5	**100.0**
	FG	80. Psychological impact of treatment of disorder	*Positive impact of treatment on emotions and/or behaviour*	45	**77.8**	N/A	N/A	29	**93.1**	N/A	N/A
	FG	81. Social anxiety and social avoidance due to the disorder	*Negative impact of eye motility problem on social interaction or causing social stigma*	45	**77.8**	8	**100.0**	29	**89.7**	5	**100.0**
	FG	82. Academic/ occupation achievement in relation to the condition or its treatment	*Academic/ occupation achievement in relation to the condition or its treatment*	44	**72.7**	8	**87.5**	29	**79.3**	5	**80.0**
	FG	83. Activity of daily living (ADL)	*Activity of daily living (ADL) such as driving*	45	**80.0**	8	**100.0**	29	**93.1**	5	**100.0**
	SR	84. Patient satisfaction from treatment	*Patient satisfaction from treatment*	45	**82.2**	8	**87.5**	29	**93.1**	5	**80.0**
	FG	85. Future functionality/long-term impact	*Future functionality/long-term impact (patient-reported)*	44	**86.4**	8	**100.0**	29	**96.6**	5	**100.0**
Compliance	SR	86. Compliance	*How well the treatment is done*	42	54.8	7	**71.4**	29	65.5	5	**80.0**
Treatment dependency	PO	87. Successful discontinuation of glucocorticoids (in orbital inflammatory conditions such as thyroid eye disease)	*Successful discontinuation of lens therapy or* glucocorticoids *(in orbital inflammatory conditions such as thyroid eye disease)*	34	64.7	3	66.7	25	**76.0**	4	50.0
	PO	88. Successful discontinuation of lens therapy or "special glasses"	*Successful discontinuation of lens therapy or "special glasses" such as bifocals or minus lenses*	43	51.2	4	50.0	29	58.6	4	50.0
	PO	89. Successful discontinuation of prism therapy	*Successful discontinuation of prism therapy*	44	56.8	3	66.7	29	69.0	3	66.7
Adverse events	SR	90. Adverse effects from treatment (any)	*Adverse effects from treatment (any)*	44	**79.5**	8	**100.0**	29	**82.8**	5	**100.0**
	FG	91. Adverse effect on vision from patches or prisms used to treat diplopia	*Adverse effect on vision from patches or prisms used to treat diplopia such as vision degradation or psychosocial effects*	44	56.8	5	40.0	29	**82.8**	5	**80.0**
	PO	92. Intolerable diplopia	*Intolerable double vision*	44	**97.7**	7	**100.0**	29	**100.0**	5	**100.0**
	PO	93. Induced ptosis (Post toxin injection)	*Appearance of transient droopy eye lid as a result of using toxin injection to treat squint*	43	48.8	5	**80.0**	29	62.1	5	**80.0**
	PO	94. Induced subconjunctival haemorrhage	*Appearance of a bleed in the surface of the eye after squint surgery or injection*	44	34.1	7	57.1	28	32.1	5	**80.0**
	PO	95. Discomfort or abnormal sensation	*Discomfort or pain during/after treatment of squint*	43	39.5	7	**85.7**	29	48.3	5	**100.0**

	PO	96. Overcorrection or under correction of the deviation with surgery or injection	*Persistence of the squint at a lesser extent or appearance of deviation in the opposite direction*	44	**72.7**	6	**83.3**	29	**75.9**	5	60.0
	PO	97. Recurrence of deviation	*Reappearance of the squint after treatment*	44	**70.5**	8	**75.0**	29	**79.3**	5	**100.0**
	PO	98. Induced vertical deviation	*Appearance of a vertical squint after treatment of a horizontal deviation*	44	63.6	5	40.0	29	65.5	5	40.0
	PO	99. Induced A or V pattern	*Appearance of a deviation that increases either on looking up or looking down*	44	59.1	6	33.3	29	48.3	5	40.0
	PO	100. Development of DVD	*Appearance of a tendency for the eye to move up and out when covered*	44	31.8	5	60.0	29	27.6	5	40.0
	PO	101. Induced incomitance	*Development of variation of the eye deviation in different positions when looking around*	44	56.8	6	66.7	29	58.6	5	60.0
	PO	102. Number of operations needed	*Number of operations/procedures needed*	44	68.2	8	**87.5**	29	**75.9**	5	**80.0**
Cost	PO	103. Economic data (in general)	*Economic data (in general) including services and families/individuals*	39	48.7	8	**75.0**	27	59.3	5	**100.0**
	PO	104. Cost of treatment on services	*Cost of treatment on services*	39	46.2	8	50.0	27	51.9	5	60.0
	FG	105. Cost of treatment on families/individuals	*Cost of treatment on families/individuals*	39	41.0	8	**75.0**	27	48.1	5	**80.0**
Long-term	SR	106. Long-term outcomes	*Long-term outcomes (clinical outcomes)*	44	**88.6**	8	**87.5**	29	**96.6**	5	**100.0**

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A core outcome set for three ophthalmic conditions: a healthcare professional and patient consensus on Core Outcome Sets for Amblyopia, Ocular Motility and Strabismus (COSAMS study)

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Abstract

Objectives: Amblyopia, strabismus and ocular motility disorders are common conditions with significant impact on visual function, appearance and quality of life. We aimed to

establish a core set of outcomes for each of the three conditions for use in clinical trials and routine clinical practice.

Design: A comprehensive databank of outcomes was developed from a systematic review of the literature and a series of focus groups with healthcare professionals, researchers, patients and carers. The databank of outcomes was scored in a two-round Delphi survey completed by two stakeholder groups; healthcare professionals / researchers and patients / carers. Results of the online Delphi were discussed at a face-to-face consensus meeting where the core outcome sets were finalised.

Setting: UK-wide consultation.

Participants: Researchers, clinicians, patients and carers.

Outcome measures: Core Outcome Sets.

Results: For amblyopia, strabismus and ocular motility, 40/42/33 participants contributed to both rounds of the Delphi; 6/9/7 members attended consensus meetings, respectively. Consensus was reached on ten core outcomes for both amblyopia and ocular motility and nine for strabismus. All three conditions shared the core outcomes: *adverse events, cost, vision-related quality of life, and ocular alignment*. The strabismus and ocular motility disorder core sets included, in addition, *measuring the deviation, binocular vision, ocular movement, patient satisfaction and symptoms.* The amblyopia set, distinct from the sets for the other two conditions, included *best corrected distance and near visual acuity, spherical and cylindrical refraction, compliance, and treatment-related and functionality / long-term impacts*.

Conclusions: The study used robust consensus methods to develop a core outcome set for three ophthalmic conditions. Implementation of these core outcome sets in clinical trials and routine clinical practice will ensure that the outcomes being measured and reported are relevant to all stakeholders. This will enhance the relevance of study findings and enable comparison of results from different studies.

Keywords:

Core outcome set; Amblyopia; Strabismus; Ocular motility; Consensus; Delphi

Article summary:

Strengths and limitations of this study:

- This study followed robust methodology as guided by the Core Outcome Measures in Effectiveness Trials (COMET) Initiative.
- We targeted amblyopia, strabismus and ocular motility disorders which are common ophthalmic conditions.
- The study included key stakeholders including researchers, clinicians, patients and carers.
- Attrition rates in the Delphi process were moderate but similar to other COS studies.
- Larger response numbers, including international participants, would be preferrable for wider generalisability.

Introduction

Amblyopia (lazy eye) and strabismus (squint) occur in up to 5% of the general population [1 2]. It is unknown how prevalent ocular motility disorders (abnormal eye movements) are in the general population. These conditions often present in children and can lead to long-term problems for children and young adults such as blurred vision, double vision, low esteem and even blindness if not treated [3]. There are several approaches to the management of these conditions including occlusion, penalisation, spectacles, prisms, drugs, surgery, botulinum toxin, exercises, watchful waiting, or a combination of two or more of the above [4-20].

Interventional systematic reviews in this field of research have identified that there is considerable variation in the outcomes being measured and reported in primary research studies, which impacts on the ability to compare and synthesise outcome results across studies. Moreover, it was noted that there is a paucity of outcome data available on important patient outcomes such as quality of life, long-term outcome as well as the cost of treatment [4-20]. To mitigate these issues and to increase the relevance of research, a core outcome set (COS) can be developed which represents an agreed standardised set of outcomes that should be measured and reporting in all studies for a specific area of health or healthcare. A search of the COMET (Core Outcome Measures in Effectiveness Trials) database revealed that there are several studies that have investigated important

outcomes for eyes and vision disease; examples include cataract [21 22] ,glaucoma [23] and age-related macular degeneration [24] but none have specifically looked at amblyopia, strabismus or ocular motility disorders [25].

The aim of this study was to develop core outcome sets for use in clinical trials and routine practice for all intervention types for the treatment of amblyopia, strabismus and ocular motility disorders in children and adults that includes input from all stakeholders. While we aim to develop three separate COS for each of the ophthalmic conditions, we anticipate that there could be considerable overlap in the importance of certain outcomes across these conditions. This is due to the fact that the three conditions often overlap and co-exist in patients, are frequently targeted within the same research studies, and are usually managed by the same group of health care professionals.

Methods

The development of the COS study involved three stages (Figure 1): (1) the generation of a long list of outcomes; (2) a two- round online Delphi survey and (3) face- to- face consensus meetings to discuss the results of the Delphi survey and agree on the COS. The process considered the minimum standards for the design of a COS study (COS-STAD), which included careful consideration of the scope, stakeholders and the consensus process [26].

Outcome list generation

A databank of outcomes was generated from two sources: a systematic review of outcomes reported by researchers and clinicians in studies for the treatment of the conditions under evaluation, and, secondly using three separate focus groups (one for each condition) containing a mix of healthcare professionals, researchers, patients and carers. The detailed search strategy, methods and results for the systematic review have been published elsewhere [27]. Outcomes from the systematic review and suggested outcomes from the recorded focus group meetings were extracted verbatim and grouped into suitable domains to facilitate easy classification. The final list was checked by experts in all three clinical conditions (SJ, FR), who also had the opportunity to use their clinical expertise to add additional outcomes to the list. In preparation for the Delphi

survey, clinical assessment outcomes used only by healthcare professionals were either separated out (not to be scored by patients) or combined into a simplified outcome for patients to score. Each outcome was written using plain language and feedback sought from four researchers from the Health Service Research department, University of Liverpool and a clinician from a local hospital on the acceptability and their understanding of the wording used. The databank of outcomes can be found in Supplementary Table 1.

Online Delphi survey

The databank of outcomes was used to populate an online Delphi survey, which was administered using DelphiManager [28]. Participants were invited from two key stakeholder groups. The first group consisted of healthcare professionals involved in the care for people with one of the three conditions or researchers working within this field. Invitations to participate were sent by email flyers to national professional organisations including the British and Irish Orthoptic Society, Paediatric Ophthalmology networks, and local groups linked with the University of Liverpool. The second group included patients or carers of patients affected by at least one of the three conditions of interest. Patients and carers were invited to participate into the survey using flyers distributed on the University of Liverpool noticeboards, newsletters (via the professional Society), social media (twitter) and in ophthalmology departments in local hospitals including Aintree University Hospital, The Royal Liverpool University Hospital and Southport and Ormskirk hospitals. Through routine clinical practice, the study authors (SJ, FR) and healthcare professionals were also encouraged to distribute the patient survey links to their relevant patients if they showed an interest in the study.

Four surveys were set up, one for the healthcare professionals and researchers that contained the outcomes to be scored for all three conditions, and, three separate surveys containing only the outcomes relevant to patients and carers associated with each individual condition. The Delphi process was completed using two rounds (hereafter referred to R1 and R2). In each round participants were presented with the list of outcomes and asked to score each outcome on how important it was to include in the COS, using a 9-point Likert scale, with 1-3 labelled 'not important', 4-6 labelled 'important but not critical', and 7-9 labelled as 'critically important' [29]. Participants had the option to indicate 'unable to score' on any outcome they felt unable to score, and at the end of R1,

participants were invited to submit additional outcomes they thought were missing from the list. These outcomes were reviewed by the study authors (SJ, FR) and any outcomes that represented a new relevant outcome were added to the list to be scored in R2. Irrespective of participant scoring, no outcomes were removed from the list between R1 and R2. During R2, participants were shown the distribution of scores for both stakeholder groups for each outcome along with their own score from R1 and asked to score the outcome again, using the same scale, taking this extra information into account.

Consensus meeting

Separate face-to-face consensus meetings were held at the University of Liverpool, UK for each of the three conditions. Participants who either had an active role in the focus groups and/or completed both rounds of the Delphi survey were invited to attend, although others with an interest in the project were invited to ensure each meeting had a balanced mix of participants from both stakeholder groups. In advance of the meeting, participants received a copy of their scores from the online survey (if appropriate) and a consensus matrix (Supplementary Table 1) detailing the results of R1 and R2 by stakeholder group, and which outcomes had reached a priori definition of consensus in, consensus out or no consensus (Table 1). The consensus definition is similar to that used in other COS development studies.

The meeting for amblyopia was chaired by a non-clinical researcher with expertise in COS development methodology (JJK) while the meeting for strabismus and ocular motility was chaired by a student investigator with a clinical background (SJ).

In order to facilitate the discussion all outcomes that had reached consensus 'in' after R2 for both stakeholder groups were presented first, followed by outcomes that reached consensus 'in' for only one stakeholder group. All outcomes that scored critical for inclusion for 50-69% of the participants for either both or one of the stakeholder groups in R2 were presented next followed by all other outcomes that were scored by both stakeholder groups. Outcomes that were only scored by healthcare professionals and researchers were discussed last. Results for each outcome from the Delphi were shown to the participants with more time allocated to discussing outcomes where there was

more uncertainty on whether the outcome should be included in the COS or not. Views for and against inclusion in the COS were sought by the meeting chair, who also ensured that participants had equal opportunity to comment prior to voting. Voting was undertaken anonymously using Poll Everywhere [30] software which was linked to mobile and tablet devices. The definition of consensus used in the Delphi survey (Table 1) was applied to the consensus meeting. The final COS was presented at the end of the meetings.

Study registration, ethics and reporting guidance

The study was prospectively registered with the COMET Initiative (Core Outcome Measures in Effectiveness Trials)[31]. Ethical approval was obtained from the University of Liverpool institutional research ethics committee for the focus groups, online survey and the consensus meetings to be undertaken with healthcare professionals and patients (Ref. Nos. 2063 and 2260). Informed consent was obtained from participants. The study is reported in line with the Core Outcome Set – Standards for Reporting (COS-STAR) guidance [32].

Patient and Public Involvement

The study was supported by a patient advisory group which provided input to this research study. The patient advisory group met on a regular basis for the duration of the study. Patients contributed to the design of the study and were involved at all stages of the survey and consensus meetings.

Results

A summary of the COS development process is shown in Figure 1. The final COS contains ten, nine and ten outcomes across seven, six and seven domains for amblyopia, strabismus and ocular motility respectively (Tables 2-4). Ocular alignment, vision-related quality-of-life, adverse events and cost were common to all three conditions.

Development of the databank of outcomes

The systematic review and focus groups of health care professionals, researchers, patients and carers identified 31, 61, and 78 individual outcomes for amblyopia, strabismus and ocular motility respectively. These were combined with a list of outcomes suggested by professional experts (SJ, FR) resulting in a total of 40, 70 and 106 outcomes for amblyopia, strabismus and ocular motility respectively. The outcomes were classified into 12 domains, (symptoms, visual function, refraction, oculomotor function, quality-of-life, treatment dependency, signs, investigations, long-term outcome, compliance, adverse events, cost) and outcomes that were not considered to be patient relevant were separated out or combined. As an example, 'refractive status', 'spherical and cylindrical refraction' and 'median spherical equivalence' were combined into a single outcome 'refractive status' for patients as they all have a similar meaning, but are often referred to separately by healthcare professionals. Details of all outcomes including domain classification, combined outcomes and plain language descriptions of outcomes is provided in Supplementary Table 1.

Online Delphi

Thirty three healthcare professionals / researchers scored all outcomes for both R1 and R2 of the amblyopia component of the online survey while 29 completed for strabismus and ocular motility. Three patients/carers completed both rounds for amblyopia while nine completed both rounds for strabismus and five for ocular motility (Figure 1). At the end of R1, five outcomes for amblyopia, 12 for strabismus and 23 for ocular motility reached consensus 'in' for both stakeholder groups. After a review of all additional outcomes suggested by participants in R1, three new outcomes were added to the strabismus survey in R2 (improvement in angle by a set amount (suggested by a healthcare professional) and, immediate result post-surgery and long-term discomfort from scar tissue (both suggested by a patient)).

On completion of R2, ten outcomes reached consensus 'in' for amblyopia across both stakeholder groups while 17 and 32 outcomes reached the same criteria for strabismus and ocular motility respectively.

Consensus meeting

Six, nine and seven voting participants attended the consensus meeting for amblyopia, strabismus and ocular motility respectively with an even balance of healthcare professional/researchers and patients present (Figure 1).

Amblyopia

For amblyopia, *future functionality/long-term impact* and *adverse events* reached the consensus 'in' criteria for both stakeholder groups in both rounds of the Delphi and remained in the COS. Despite reaching consensus 'in' for both rounds of the Delphi for both stakeholder groups, intolerable diplopia and occlusion amblyopia (both adverse events) were not included in the final COS as it was felt that these could be captured under 'adverse events' and therefore were not critical for separate inclusion in the COS. Long-term outcome was also excluded following discussion as the group felt that there was currently no agreed set time for measuring long-term objective outcomes. *Best corrected visual acuity* and *compliance* marginally did not reach consensus 'in' during R2 of the Delphi but made the final COS after discussion. Following a discussion on the other visual function outcomes, *near visual acuity* was also added because it was noted that it was a good marker of early improvement for the treatment of amblyopia and important for children as it is important to their education. Refractive status reached consensus for both groups in R2 but following discussion this was replaced by *spherical and cylindrical refraction* (scored only by health care professionals in the Delphi) because it was successfully argued that this was a more precise measurement of refractive status. The list of outcomes within the quality of life domain were discussed simultaneously. While this was not listed specifically as an outcome in the Delphi, participants agreed to include *visual-related quality of life* in the core set as it was felt that a generic health-related quality of life outcome was not sensitive enough. Psychological impact of treatment was scored only by healthcare professionals in the Delphi but reached consensus 'in' during R2. Following discussion led by a parent participant, the panel derived a new outcome to include *treatment-related impact* into the final COS in order to capture the effect of treatment, such as patching on children, which could be long lasting. For both Delphi rounds, cost outcomes did not reach consensus 'in' by either stakeholder groups, however, the consensus panellists successfully advocated for its inclusion as a core outcome as *cost* outcome data is vital information for contemporary health systems.

Strabismus

For strabismus, *symptoms* and *patient satisfaction* reached the consensus 'in' criteria for both stakeholder groups in both rounds of the Delphi and remained in the COS. Best corrected visual acuity also reached consensus 'in' for both rounds and groups in the Delphi although the consensus panel argued that any change in vision and/or loss of vision as an adverse event would be very significant and reportable as per standard healthcare safety procedures [33]. At the consensus meeting, participants noted that strabismus interventions aim to change the strabismus angle and visual acuity should not be affected by the intervention unless an adverse event occurred. Thus a change in visual acuity would be captured within adverse events. On this basis a decision was taken to exclude visual acuity from the core set. All remaining visual function outcomes were discussed simultaneously, and while the post-op diplopia test reached consensus 'in' during the Delphi exercise, the consensus panel voted in favour of including *binocular vision* as core, as it was more representative of a group of visual function related outcomes. Oculomotor function outcomes were discussed simultaneously and it was highlighted that *ocular movement* was critical to be reported in all strabismus types as a change caused by the intervention would be significant. Quantifying both the *ocular alignment* and *deviation* were also seen to be critical in the context of any strabismus type and were included as core outcomes. *Visual-related quality-of life*, *adverse events* and *cost* were also included in the COS for reasons discussed for amblyopia.

Ocular Motility

The discussions for ocular motility closely followed those of strabismus with the addition of clinical signs being added as an extra core outcome. Similar to adverse events, this outcome was a catch all for all clinical signs which were scored individually in the Delphi exercise. This strategy was seen favourably by the meeting participants as many sub-conditions of ocular motility have specific signs associated with them. One example for this is corneal exposure in the ocular motility condition of Thyroid Eye Disease but which is not relevant in other ocular motility disorders.

Discussion

This study has developed a set of core outcomes for the treatment of three ophthalmic conditions using a robust consensus process involving healthcare professionals, researchers, patients and carers. Consensus was reached on what should be measured

in each of the three COS. They consisted of nine to ten outcomes distributed across six to seven domains to cover all important aspects related to treatment (objective clinical, adverse events, subjective or patient-reported outcomes, and health economics). While these three core outcome sets were developed independently, there are some parallels, and as a consequence, four outcomes (*ocular alignment, vision-related quality-of-life, adverse events and cost*) were common to all three conditions. The amblyopia COS captures the condition's unique features by reporting additionally on '*best corrected visual acuity', 'near visual acuity', 'compliance', 'spherical and cylindrical refraction', 'treatment-related impact' and 'future functionality/long-term impact'*, keeping in mind that children are the predominantly affected population. The COS for strabismus and ocular motility disorders, on the other hand, include '*binocular vision', 'ocular movement', 'measuring the deviation', 'symptoms' and 'patient satisfaction'*. The ocular motility disorder COS was unique in additionally reporting *'clinical signs'* related to the relevant conditions.

We recommend that, as a minimum, these core outcomes are used in future trials of interventions to treat amblyopia, strabismus and ocular motility disorders. We also advocate that these outcomes are recorded in routine clinical practice to ensure that the outcome data collected is meaningful and important. .

A strength of this study is that it was prospectively registered with the COMET Initiative and it was developed using the COS- STAD (Core Outcome Set - STAndards for Development) recommendations [26]. Engagement with patient participants was particularly challenging and we sought to improve patient input by offering paper copies of the Delphi survey with pre-paid return envelopes in orthoptic clinics, although this was later abandoned after a number of sessions when there was no uptake. As a consequence of a relatively low number of patients responding to the Delphi and attrition between the two rounds, there was concern that consensus was not being achieved at the end of the final round given the number of outcomes reaching consensus for both stakeholder groups had increased dramatically from R1. While measures were taken to ensure survey participation and retention was maximised (including sending reminders and extending deadlines for completion), it was felt that after several months of keeping the survey open, our efforts became futile. In order to compensate for this, we ensured that the consensus meetings where the final COS were ratified, contained a good

balance of healthcare professionals and patients. The main limitation of this study was that the consensus process was based using only participants in the UK. However, as a starting point, we have reason to believe that this COS could also be useful in other countries and settings.

Further consensus work is needed to refine and establish the best measurement instruments and time points for when to measure these core outcomes. To assist this process, the systematic review for generating the databank of outcomes also recorded the measurement instruments and timings associated with each outcome [27].Moreover, for some outcomes, the metric (e.g. change from baseline or inter-ocular difference (IOD) of BCVA), and method of aggregation (e.g. mean or median) [22] would need to be determined. Defining success criteria (e.g. 8 or 10 dioptres from orthophoria for alignment, for distance and/or near) is another aspect of outcome refining and definition to be done by further work. The generalisability of the COS also needs to be reviewed in healthcare settings outside the UK. While the review of outcomes identified studies from around the world (with prominence from the United States, United Kingdom, China and various European countries), the formal consensus process was undertaken using only participants from the UK, and those attending the consensus meeting were mostly localised to the North West of England.

There are few reported COS in the literature that relate to the three conditions in this study. Chiu et al. recommended four outcomes for reporting results of surgery for intermittent exotropia [34]. Their study aimed to explore the extent of standardisation of outcomes reported in surgical studies for the condition. However, the study was limited by the extent of literature review for this specific condition (10-year literature search period) and lack of external consensus. A short narrative review of outcome measurements for size of deviation showed considerable variability across the tests available and the recommendations for their use. They suggested four core outcomes for all future studies: alignment, near stereoacuity, control score, and quality of life score. If assigning near stereoacuity and control score to ‘binocular vision’, their outcomes map to those reported in our COS for strabismus.

Moreover, two recently published studies attempted to define criteria for success in treatment, one for amblyopia and the other for strabismus surgery, which could be

considered complementary to the COS and not alternatives because they essentially give more definitions of primary outcomes rather than suggesting a set of specific outcomes to be measured in research.

A report was published by Shoshany et al. [35] stating that the IRIS measures for amblyopia developed by the American Academy of Ophthalmology (IRIS7 [36], modified in 2019 to IRIS50 [35]) provide uniform criteria for defining amblyopia treatment success. Treatment was defined as 'successful' if corrected IOD was less than 0.23 logMAR 12–18 months after first diagnosis. IRIS50 considers improvement in VA, which may be relevant to patients who had dense amblyopia at baseline but nevertheless improved. Thus, IRIS50 may be a more practical reporting measure than IRIS7. In general, Shoshany et al. propose that these measures will allow more efficient reporting of quality metrics and rapid and objective assessment of new amblyopia treatments [35].

In addition, a study aiming to define successful outcomes for strabismus surgery was published by Serafino et al. [37]. Although this study did not state an intention to develop a COS, there are a lot of similarities and overlap in the objectives and methodology used. A Delphi process was used to identify areas of consensus and disagreement among experts for the definition of success post strabismus surgery. The panel of experts in their study represented wide international geographic areas and included experts who were chosen based on their peer-reviewed publications, participation at international meetings and their surgical experience. The study concluded the following: they achieved consensus on which strabismus types need their separate set of outcome criteria. They also identified the importance of ‘stereopsis’ and ‘the range of single vision’ for inclusion of success definition in some strabismus types, which interestingly could be mapped to ‘binocular vision’ in our strabismus COS. The study also found that there was no consensus on the length of time after surgery for determination of success, magnitude of deviation consistent with success, and whether manifest or latent deviation should be considered to define success, which the review of our study [27] has also found, and which we are advocating to define, by future work. Differences from our study is that their survey did not involve scoring of outcomes, there was no systematic search of literature

of reported outcomes prior to survey construction, and patients or service users were not consulted in the process.

A search in the COMET initiative database in April 2020 did not reveal registration of any further additions of similar studies in the database. It is advantageous to register COS studies in the database to facilitate collaborative work of similar scope, and to avoid duplication of efforts and waste of research.

Conclusion

The three COS developed from this study can be applied to future trials and routine data collection for all intervention types to treat the three ophthalmic conditions considered. Their use will allow the comparison of outcome data to be made across studies and to better inform treatment decisions. Future work will include seeking consensus on how these outcomes should be measured and to evaluate the acceptability of the current COS to patients and professionals in other countries, particularly where healthcare systems differ from the UK.

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Figure 1 Study flowchart

Table 1 Definition of consensus

Consensus classification	**Description**	**Definition of consensus**
Consensus in	Consensus that the outcome should be included in the core set	≥70% of participants scoring the outcome as '7–9' (critically important)
Consensus out	Consensus that the outcome should *not* be included in the core set	≥70% of participants scoring the outcome as '1–3' (not important)
No consensus	Uncertainty about the importance of the outcomes	Anything else

Table 2 Final COS for amblyopia

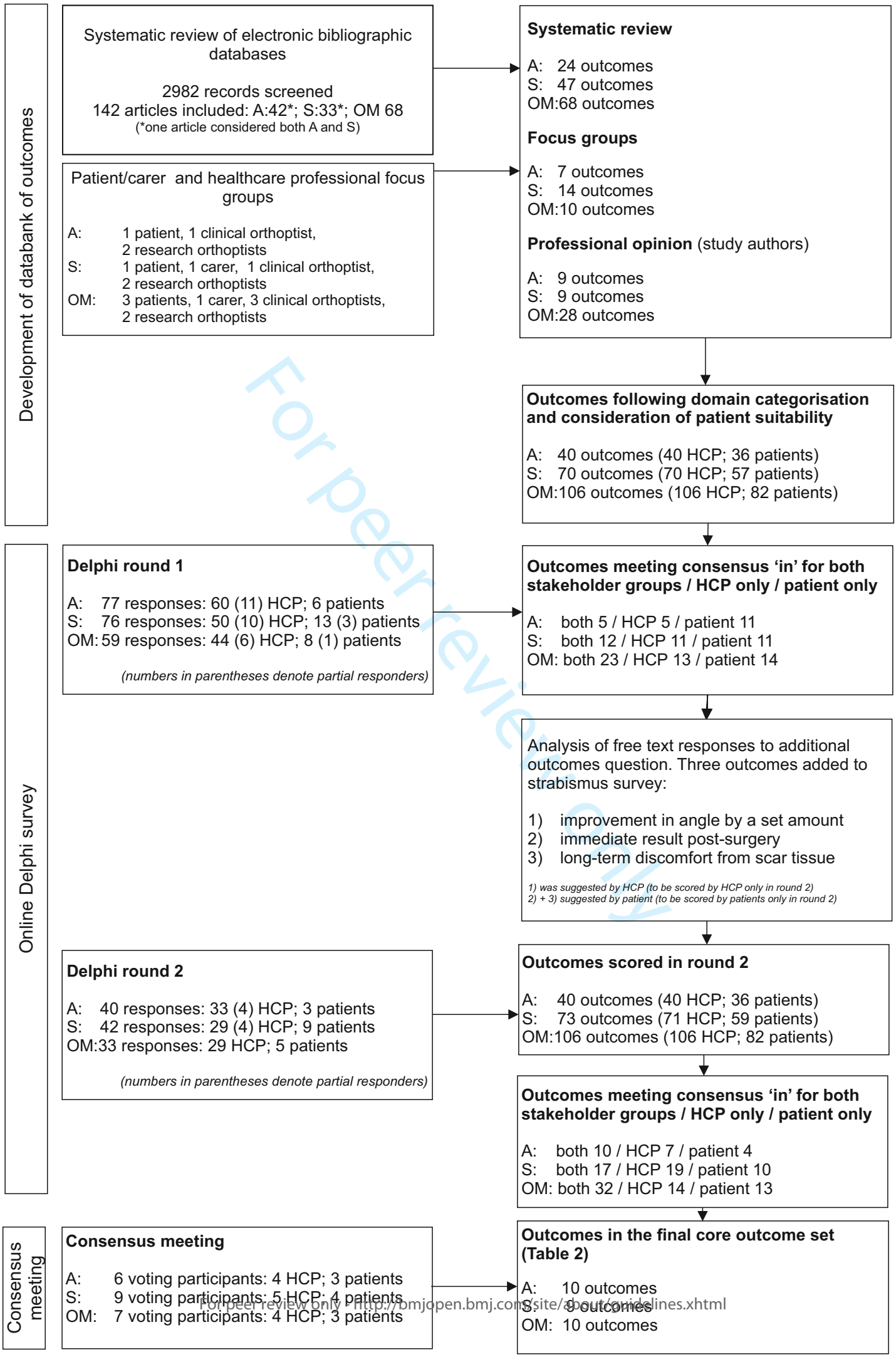
Domain	Outcome
Visual function	**1. Best corrected visual acuity**
	2. Near visual acuity
Refractive status	**3. Spherical and cylindrical refraction**
Oculomotor function	**4. Ocular alignment (is there an ocular deviation?)**
Quality of life	**5. Vision-related quality of life (for example, activities of daily living)**
	6. Treatment-related impact (for example, negative effects of patching on children during treatment)
	7. Future functionality / long-term impact
Compliance	**8. Compliance**
Adverse events	**9. Any adverse events (for example, intolerable diplopia, occlusion amblyopia)**
Cost	**10. Cost (for example, cost to services, families, and individuals)**

Table 3 Final COS for strabismus

Domain	Outcome
Symptoms	**1. Symptoms (for example, diplopia and appearance of the strabismus)**
Visual function	**2. Binocular vision (for example, stereoacuity and binocular single vision)**
Oculomotor function	**3. Ocular alignment (are the eyes straight?)**
	4. Measurement of deviation (what is the amount of deviation?)
	5. Ocular movement (specifically incomitance, latent nystagmus, DVD and A&V pattern)
Quality of life	**6. Vision-related quality of life; psychosocial aspects (such as self-esteem, confidence, behaviour, social interaction) and functional aspects (such as activities of daily living)**
	7. Patient satisfaction
Adverse events	**8. Any adverse events (for example, intolerable diplopia, recurrence of the deviation, overcorrection or under-correction of the deviation)**
Cost	**9. Cost (for example, cost to services, families, and individuals)**

Table 4 Final COS for ocular motility disorders

Domain	Outcome
Symptoms	**1. Symptoms (for example, diplopia and appearance of the eye deviation)**
Visual function	**2. Binocular vision (for example, stereoacuity, field of binocular single vision, and post-op diplopia test)**
Oculomotor function	**3. Ocular alignment (are the eyes straight?)**
	4. Measurement of deviation (what is the amount of deviation?)
	5. Ocular movement (specifically incomitance, latent nystagmus, DVD and A&V pattern)
Quality of life	**6. Vision-related quality of life; psychosocial aspects (such as self-esteem, confidence, behaviour, social interaction) and functional aspects (such as activities of daily living)**
	7. Patient satisfaction
Adverse events	**8. Any adverse events (for example, intolerable diplopia, recurrence of the deviation, and adverse effects from patches or prisms)**
Cost	**9. Cost (for example, cost to services, families, and individuals)**
Clinical signs	**10. Clinical signs (for example, corneal exposure, proptosis / exophthalmos, enophthalmos)**



Supplementary Table 1: Long list of outcomes used in the Delphi survey and critical scoring in both rounds of the Delphi survey by stakeholder group

[Outcomes identified from: systematic review (SR), focus groups (FG) and professional opinion (PO)].

Percentages highlighted in red denote outcomes that reached the consensus 'in' criteria.

N/A: not scored by stakeholder group (HCPs or patients)

Amblyopia

Domain	Source	Outcome	Lay-term summary	Delphi results							
				Round 1				Round 2			
				HCPs		Patients		HCPs		Patients	
				n	% (7-9)	n	% (7-9)	n	% (7-9)	n	% (7-9)
Symptoms	FG	1. Patient symptoms	*Symptoms or complaints related to vision or eyes*	67	34.3	4	50.0	37	37.8	3	66.7
Visual function	SR	2. Best corrected visual acuity	*Vision measured at distance corrected with glasses*	70	**98.6**	4	66.7	37	**100.0**	3	66.7
	SR	3. Near visual acuity	*Close up or reading vision*	70	65.7	4	50.0	37	**78.4**	3	66.7
	PO	4. Habitual visual acuity	*Vision measured in the usual preferred state for a person*	62	58.1	5	**80.0**	37	67.6	3	**100.0**
	SR	5. Uncorrected visual acuity	*Vision without glasses or contact lenses*	70	4.3	4	40.0	37	5.4	3	0.0
	FG	6. Suppression	*Testing if the person has developed "suppression" of one image to improve double vision which usually happens in childhood as a coping mechanism from the brain to improve visual development*	70	42.9	4	**75.0**	36	47.2	2	**100.0**
	FG	7. Fixation	*Testing if the person is using the central part of the retina to see with or alternatively using an eccentric part of the retina*	70	52.9	3	33.3	36	50.0	3	33.3

	FG	8. Contrast sensitivity	*Objects of varying brightness*	66	12.1		60.0	34	5.9	3	0.0
	SR	9. Visual evoked potentials	*Testing vision signals from the eyes to the brain with electrodiagnostics (visual evoked potentials/VEP)*	56	8.9		33.3	33	3.0	2	0.0
	SR	10. Binocularity	*to check if the eyes are working together to give any level of 3D vision or depth appreciation*	70	47.1		**80.0**	36	63.9	2	50.0
	SR	11. Stereoacuity	*Fine 3D vision or depth appreciation with both eyes or "stereo vision"*	70	37.1		**80.0**	35	34.3	2	**100.0**
	PO	12. Simultaneous perception	*Testing lower levels of 3D vision*	70	30.0		60.0	35	25.7	2	0.0
	PO	13. Retinal correspondence		70	31.4	N/A	N/A	35	11.4	N/A	N/A
Refraction	SR	14. Refractive status	*Testing the amount of prescription of glasses or contact lenses*	69	**84.1**		66.7	35	**94.3**	3	**100.0**
	SR	15. Spherical & cylindrical refraction		69	**79.7**	N/A	N/A	35	**91.4**	N/A	N/A
	SR	16. Median spherical equivalent		64	26.6	N/A	N/A	33	21.2	N/A	N/A
Oculomotor function	SR	17. Ocular alignment /deviation	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation*	68	63.2		66.7	35	**71.4**	3	**100.0**
	PO	18. Abnormal head posture	*The presence of a compensatory head posture to avoid double vision*	68	33.8		66.7	34	32.4	3	66.7
Quality of life	SR	19. Quality of life measures (in general)	*Health related quality of life (all relevant aspects)*	69	53.6		**100.0**	35	62.9	3	**100.0**
	FG	20. Psychological impact of the disorder	*Negative impact of lazy eye (amblyopia) on emotions and/or behaviour*	69	55.1		**83.3**	34	67.6	3	**100.0**
	SR	21. Psychological impact of treatment of disorder	*The psychological impact of treatment of lazy eye (amblyopia) on emotions and/or behaviour*	69	62.3	N/A	N/A	34	**73.5**	N/A	N/A
	PO	22. Self-esteem	*Negative impact of lazy eye (amblyopia) on self-esteem & confidence*	69	59.4		**100.0**	34	**70.6**	3	**100.0**
	SR	23. Social anxiety and social avoidance due to the disorder	*Negative impact of lazy eye (amblyopia) on social interaction or causing social stigma*	69	55.1		**83.3**	34	67.6	3	**100.0**
	SR	24. Academic/ occupation achievement in relation to the condition or its treatment	*Academic/ occupation achievement in relation to the condition or its treatment*	69	60.9		**83.3**	34	**76.5**	3	66.7
	SR	25. Activity of daily living (ADL)	*Negative impact of lazy eye (amblyopia) on normal daily activities*	68	52.9	6	**100.0**	33	**72.7**	3	**100.0**
	SR	26. Patient satisfaction from treatment	*Patient satisfaction from treatment*	68	61.8	6	**83.3**	34	**76.5**	3	**100.0**
	FG	27. Future functionality/long-term impact	*Future functionality/long-term impact (patient-reEOrted)*	69	**78.3**	6	**100**	34	**91.2**	3	**100.0**

	SR	28. Fear of losing better eye		69	**71.0**		66.7	33	**84.8**	3	66.7
Compliance	SR	29. Compliance	*How well the treatment is done*	69	**95.7**		66.7	33	**97.0**	3	66.7
Adverse events	SR	30. Adverse effects from treatment (any)	*Adverse effects from treatment (any)*	69	**73.9**		**80.0**	33	**87.9**	2	**100.0**
	SR	31. Intolerable diplopia	*Intolerable double vision as a side effect from treatment*	69	**89.9**		**83.3**	33	**100.0**	3	**100.0**
	SR	32. Occlusion amblyopia	*Development of lazy eye (amblyopia) in the better eye as a result of patching/penalisation treatment*	69	**76.8**		**100.0**	33	**87.9**	3	**100.0**
	SR	33. Visual disorientation	*Visual disorientation due to treatment with occlusion of better eye*	64	45.3		66.7	32	56.3	3	**100.0**
	PO	34. Disturbed distance estimation	*Disturbed distance estimation due to treatment with occlusion of better eye*	64	39.1		66.7	32	46.9	3	33.3
	SR	35. Skin irritation or allergy to patches	*Skin irritation or allergy from eye patches used to occlude the eye*	69	50.7		33.3	33	51.5	3	33.3
	PO	36. Atropine eye drops side effects	*Side effects of the eye drops used regularly at home for treatment of lazy eye (amblyopia)*	69	65.2		33.3	33	69.7	3	66.7
Cost	SR	37. Economic data (in general)	*Economic data (in general) including services and families/individuals*	54	24.1		16.7	30	20.0	3	0.0
	PO	38. Cost of treatment on services	*Cost of treatment on services*	55	25.5		16.7	31	32.3	3	0.0
	PO	39. Cost of treatment on families/individuals	*Cost of treatment on families/individuals*	54	37.0		33.3	30	50.0	3	0.0
Long-term	FG	40. Long-term outcomes	*Long-term outcomes (clinical outcomes)*	59	**84.7**		**100.0**	33	**93.9**	3	**100.0**

Strabismus

Domain	Source	Outcome	Lay-term summary	Delphi results							
				Round 1				Round 2			
				HCPs		Patients		HCPs		Patients	
				n	% (7-9)	n	% (7-9)	n	% (7-9)	n	% (7-9)
Symptoms	FG	1. Patient symptoms	*Symptoms or complaints related to vision or eyes*	60	**91.7**	16	**75.0**	33	**100.0**	9	**77.8**
	FG	2. Diplopia	*Improvement in double vision in general*	60	**95.0**	14	**85.7**	33	**100.0**	8	62.5
	FG	3. Appearance of strabismus	*Appearance of the squint*	60	**85.0**	15	46.7	33	**87.9**	9	33.3
	FG	4. Eye aesthetics as the patient perceives	*Appearance of the squint as the patient perceives*	60	**80.0**	15	40.0	33	**84.8**	9	44.4
	FG	5. Eye aesthetics as relatives and friends perceive	*Appearance of the squint as the relatives and friends perceive*	60	58.3	15	46.7	33	63.6	9	33.3
Visual function	SR	6. Best corrected visual acuity	*Vision measured at distance corrected with glasses*	60	**71.7**	11	**72.7**	33	**90.9**	7	**100.0**
	PO	7. Near visual acuity	*Close up or reading vision*	60	45.0	12	**75.0**	33	63.6	7	**71.4**
	PO	8. Habitual visual acuity	*Vision measured in the usual preferred state for a person*	53	41.5	10	**70.0**	32	59.4	7	**100.0**
	PO	9. Uncorrected visual acuity	*Vision without glasses or contact lenses*	60	8.3	12	58.3	33	3.0	7	**71.4**
	FG	10. Suppression	*Testing if the person has developed "suppression" of one image to improve double vision which usually happens in childhood as a coping mechanism from the brain to improve visual development*	60	65.0	10	**80.0**	32	**75.0**	8	**75.0**
	PO	11. Fixation	*Testing if the person is using the central part of the retina to see with or alternatively using an eccentric part of the retina*	60	46.7	9	33.3	32	46.9	7	42.9
	PO	12. Contrast sensitivity	*Objects of varying brightness*	59	6.8	8	37.5	32	0.0	8	37.5
	SR	13. Binocularity	*Testing "binocularity" which is to check if the eyes are working together to give any level of 3D vision or depth appreciation*	60	**76.7**	12	58.3	32	**75.0**	8	**87.5**

	SR	14. Stereoacuity at near	*Fine 3D vision or depth appreciation with both eyes measured for near*	60	60.0	12	58.3	32	62.5	8	**87.5**
	SR	15. Stereoacuity at near and distance (any strabismus type)	*Fine 3D vision or depth appreciation with both eyes measured for both near and distance*	59	44.1	12	58.3	32	46.9	8	**75.0**
	SR	16. Stereoacuity at near and distance (for certain strabismus types? please specify)	*Fine 3D vision or depth appreciation with both eyes measured for both near and distance for certain types of squint*	54	53.7	N/A	N/A	30	56.7	N/A	N/A
	SR	17. Field of binocular single vision	*Testing the extent of area of vision where there is no double vision while looking around with both eyes open*	60	46.7	12	66.7	32	53.1	8	62.5
	FG	18. Post op diplopia test	*Testing if a person is likely to get double vision after correcting the eye deviation with surgery*	59	**81.4**	11	**81.8**	32	**93.8**	9	**77.8**
	SR	19. Simultaneous perception	*Testing lower levels of 3D vision*	59	37.3	10	50.0	32	25.0	8	62.5
	PO	20. Retinal correspondence	*Testing lower levels of 3D vision*	60	43.3	N/A	N/A	32	37.5	N/A	N/A
	PO	21. Refractive status	*Testing the amount of prescription of glasses or contact lenses*	60	61.7	11	54.5	32	**75.0**	8	50.0
Oculomotor function	SR	22. Ocular alignment /deviation	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation*	60	**86.7**	12	**91.7**	32	**100.0**	8	50.0
	SR	23. Abnormal head posture	*The presence of a compensatory head EOsture to avoid double vision*	60	66.7	11	63.6	32	**84.4**	9	**77.8**
	FG	24. Ocular motor alignment at various positions especially where the deviation is greatest	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation at different EOsitions*	60	**75.0**	N/A	N/A	32	**87.5**	N/A	N/A
	SR	25. Presence of incomitance (any strabismus type)	*Testing if there is variation of the eye deviation in different EOsitions when looking around*	59	**71.2**	N/A	N/A	32	**78.1**	N/A	N/A
	SR	26. Presence of incomitance (for certain strabismus types? please specify)	*Testing if there is variation of the eye deviation in different EOsitions when looking around*	58	**75.9**	N/A	N/A	31	**80.6**	N/A	N/A
	SR	27. Control of deviation (any strabismus type)	*Measuring how well the person can control the eye turn*	59	**79.7**	12	**83.3**	32	**96.9**	9	55.6
	SR	28. Control of deviation (for	*Measuring how well the person can control the eye turn*	58	**81.0**	N/A	N/A	31	**93.5**	N/A	N/A

		certain strabismus types? please specify)									
	SR	29. Ocular movement	*How well eyes move as a person is looking around*	60	66.7	13	61.5	32	**71.9**	9	**77.8**
	SR	30. Presence of latent nystagmus (any strabismus type)	*Checking if there are involuntary rapid movements of the eyes when one eye is covered*	58	46.6	11	63.6	32	53.1	9	44.4
	SR	31. Presence of latent nystagmus (for certain strabismus types? please specify)	*Checking if there are involuntary rapid movements of the eyes when one eye is covered*	57	54.4	N/A	N/A	32	**71.9**	N/A	N/A
	SR	32. Presence of dissociated vertical deviation (DVD) (any strabismus type)	*Testing if there is tendency for the eye to move up and out +/- rotates when covered*	58	51.7	11	54.5	32	53.1	8	**37.5**
	SR	33. Presence of dissociated vertical deviation (DVD) (for certain strabismus types? please specify)	*Testing if there is tendency for the eye to move up and out +/- rotates when covered*	56	64.3	N/A	N/A	31	**71.0**	N/A	N/A
	SR	34. A or V pattern deviation	*Testing if there is a deviation that increases either on looking up or looking down*	60	60.0	N/A	N/A	32	**81.3**	N/A	N/A
	SR	35. Fusional vergence at near and distance /fusion amplitudes/prism fusion range	*Testing how well the eyes can control a deviation induced with prisms in clinic*	60	68.3	11	63.6	32	**81.3**	9	55.6
	SR	36. Near point of convergence (for any strabismus type)	*Testing if the eyes can normally look inwards to see a near object to an acceptable amount*	60	31.7	13	**76.9**	32	43.8	9	66.7
	SR	37. Near point of convergence (for certain strabismus types? please specify)	*Testing if the eyes can normally look inwards to see a near object to an acceptable amount*	58	51.7	N/A	N/A	32	62.5	N/A	N/A

	FG	38. Accommodation (for any strabismus type)	*Testing if the eyes can change their focus appropriately to see objects at varying distances*	60	23.3	13	61.5	32	18.8	9	44.4
	FG	39. Accommodation (for certain strabismus types? please specify)	*Testing if the eyes can change their focus appropriately to see objects at varying distances*	58	60.3	N/A	N/A	31	61.3	N/A	N/A
	SR	40. AC/A ratio (for any strabismus type)	*Testing the ratio between the ability of the eyes to look inwards and their ability to focus*	59	30.5	13	46.2	32	28.1	9	33.3
	SR	41. AC/A ratio (for certain strabismus types? please specify)	*Testing the ratio between the ability of the eyes to look inwards and their ability to focus*	58	65.5	N/A	N/A	31	67.7	N/A	N/A
	CLIN PART	42. Improvement in angle by a set amount e.g. >10^ *		N/A	N/A	N/A	N/A	31	51.6	N/A	N/A
	PT PART	43. Immediate result EOst-surgery**		N/A	N/A	N/A	N/A	N/A	N/A	8	12.5
Quality of life	SR	44. Quality of life measures (in general)	*Health related quality of life (all relevant aspects)*	53	**81.1**	13	69.2	31	**93.5**	9	66.7
	SR	45. Psychological impact of the disorder	*Negative impact of squint (strabismus) on emotions and/or behaviour*	53	**88.7**	13	69.2	30	**100.0**	9	**77.8**
	SR	46. Psychological impact of treatment of disorder	*EOsitive impact of treatment on emotions and/or behaviour*	53	**75.5**	13	**84.6**	30	**80.0**	9	**77.8**
	SR	47. Social anxiety and social avoidance due to the disorder	*Negative impact of squint (strabismus) on social interaction or causing social stigma*	53	**84.9**	14	**71.4**	30	**90.0**	9	66.7
	FG	48. Academic/ occupation achievement in relation to the condition or its treatment	*Academic/ occupation achievement in relation to the condition or its treatment*	52	69.2	13	69.2	30	**76.7**	9	66.7
	FG	49. Activity of daily living (ADL)	*Activity of daily living (ADL) such as driving*	52	67.3	14	**78.6**	29	**86.2**	9	**77.8**
	SR	50. Patient satisfaction from treatment	*Patient satisfaction from treatment*	53	**83.0**	14	**92.9**	29	**96.6**	9	**88.9**

	FG	51. Future functionality/long-term impact	*Future functionality/long-term impact (patient-reEOrted)*	52	**92.3**	11	**100.0**	29	**96.6**	9	**88.9**
Compliance	PO	52. Compliance	*How well the treatment is done*	52	63.5	12	**91.7**	29	62.1	8	**87.5**
Treatment dependency	SR	53. Successful discontinuation of lens therapy or "special glasses" (for any strabismus type)	*Successful discontinuation of lens therapy or "special glasses" such as bifocals or minus lenses*	49	40.8	4	**100**	28	46.4	6	**83.3**
	SR	54. Successful discontinuation of lens therapy or "special glasses" (for certain strabismus types? please specify)	*Successful discontinuation of lens therapy or "special glasses" such as bifocals or minus lenses*	49	51.0	N/A	N/A	28	64.3	N/A	N/A
	PO	55. Successful discontinuation of prism therapy	*Successful discontinuation of prism therapy*	52	46.2	4	**100.0**	29	51.7	6	**83.3**
Adverse events	SR	56. Adverse effects from treatment (any)	*Adverse effects from treatment (any)*	53	**83.0**	10	60.0	29	**93.1**	9	55.6
	FG	57. Adverse effect on vision from patches or prisms used to treat diplopia	*Adverse effect on vision from patches or prisms used to treat diplopia such as vision degradation or psychosocial effects*	53	67.9	7	42.9	29	**75.9**	6	**83.3**
	SR	58. Intolerable diplopia	*Intolerable double vision*	53	**98.1**	11	**81.8**	29	**96.6**	9	**77.8**
	SR	59. Induced ptosis (post toxin injection)	*Appearance of transient droopy eye lid as a result of using toxin injection to treat squint*	52	51.9	7	57.1	29	55.2	8	62.5
	SR	60. Induced subconjunctival haemorrhage	*Appearance of a bleed in the surface of the eye after squint surgery or injection*	52	32.7	9	33.3	29	20.7	8	37.5
	SR	61. Discomfort or abnormal sensation	*Discomfort or pain during/after treatment of squint*	53	28.3	9	44.4	29	17.2	8	37.5
	SR	62. Overcorrection or under correction of the deviation with surgery or injection	*Persistence of the squint at a lesser extent or appearance of deviation in the opEOsite direction*	52	**71.2**	9	55.6	29	**79.3**	9	66.7
	SR	63. Recurrence of deviation	*Reappearance of the squint after treatment*	53	66.0	9	**77.8**	29	**75.9**	9	**88.9**

	SR	64. Induced vertical deviation	*Appearance of a vertical squint after treatment of a horizontal deviation*	53	69.8	8	**75.0**	29	**82.8**	9	**77.8**
	SR	65. Induced A or V pattern	*Appearance of a deviation that increases either on looking up or looking down*	53	54.7	9	66.7	29	65.5	8	**75.0**
	SR	66. Development of DVD	*Appearance of a tendency for the eye to move up and out when covered*	50	46.0	6	16.7	29	34.5	8	37.5
	SR	67. Induced incomitance	*Development of variation of the eye deviation in different EOsitions when looking around*	53	56.6	7	**71.4**	29	62.1	7	**71.4**
	SR	68. Number of operations/procedures needed	*Number of operations/procedures needed*	53	66.0	9	66.7	29	65.5	8	62.5
Cost	SR	69. Economic data (in general)	*Economic data (in general) including services and families/individuals*	45	44.4	11	36.4	27	37.0	9	33.3
	SR	70. Cost of treatment on services	*Cost of treatment on services*	45	46.7	11	18.2	27	44.4	9	33.3
	SR	71. Cost of treatment on families/ individuals	*Cost of treatment on families/individuals*	45	40.0	11	45.5	26	38.5	9	22.2
Long-term outcomes	SR	72. Long-term outcomes	*Long-term outcomes (clinical outcomes)*	50	**88.0**	11	**90.9**	29	**96.6**	9	**88.9**
	PT PART	73. Long term discomfort from scar tissue **		N/A	N/A	N/A	N/A	N/A	N/A	9	55.6

Ocular motility disorders

Domain	Source	Outcome	Lay-term summary	Delphi results							
				Round 1				Round 2			
				HCPs		Patients		HCPs		Patients	
				n	% (7-9)	n	%	n	% (7-9)	n	% (7-9)
Symptoms	SR	1. Patient symptoms	*Symptoms or complaints related to vision or eyes*	50	**92.0**	9	**88.9**	29	**96.6**	5	**100.0**
	SR	2. Improvement in diplopia (in general)	*Improvement in double vision in general*	50	**90.0**	8	**100.0**	29	**100.0**	5	**100.0**
	SR	3. Improvement of diplopia in primary gaze	*Improvement of double vision when looking straight ahead*	50	**94.0**	8	**87.5**	29	**100.0**	5	**100.0**
	SR	4. Improvement in diplopia in primary and down gaze	*Improvement in double vision when looking straight ahead and down (reading position)*	50	**88.0**	7	**85.7**	29	**100.0**	5	**100.0**
	SR	5. Improvement in diplopia in primary and down gaze with prisms	*Improvement in double vision when looking straight ahead and down with prisms*	50	**86.0**	4	**75.0**	29	**96.6**	5	**100.0**
	SR	6. Severity and duration of visual symptoms/eye deviation	*Severity and duration of visual symptoms/eye deviation*	50	**78.0**	9	**77.8**	29	**79.3**	5	**100.0**
	SR	7. Appearance of the eye deviation	*Appearance of the eye deviation*	50	**74.0**	9	33.3	29	**79.3**	5	60.0
	SR	8. Reduction in pain (for certain types of ocular motility disorders? please specify)	*Reduction in pain*	49	**75.5**	4	50.0	29	**89.7**	4	**100.0**
	SR	9. Improvement in oscillopsia/blur and vertigo in adults (in nystagmus)	*Improvement in oscillopsia/blur and vertigo in adults (in nystagmus)*	50	**92.0**	6	66.7	29	**100.0**	5	**100.0**
	FG	10. Improvement in headaches (for certain types of ocular motility disorders? please specify)	*Improvement in headaches*	50	**80.0**	6	50.0	29	**79.3**	4	40.0
Visual function	SR	11. Best corrected visual acuity	*Vision measured at distance for one eye at a time corrected with glasses*	50	60.0	7	42.9	29	69.0	5	60.0

	SR	12. Near visual acuity	*Close up or reading vision*	50	44.0	8	62.5	29	48.3	5	60.0
	PO	13. Habitual visual acuity	*Vision measured in the usual preferred state for a person*	44	50.0	7	**71.4**	29	69.0	5	**80.0**
	PO	14. Uncorrected visual acuity	*Vision without glasses or contact lenses*	50	6.0	7	28.6	29	0.0	5	20.0
	SR	15. Binocular BCVA	*Vision measured at distance with both eyes open at the same time corrected with glasses*	49	57.1	5	**80.0**	28	**71.4**	5	**100.0**
	SR	16. Suppression	*Testing if the person has developed "suppression" of one image to improve double vision which usually happens in childhood as a coping mechanism from the brain to improve visual development*	50	46.0	3	33.3	29	48.3	3	66.7
	PO	17. Fixation	*Testing "fixation" which is if the person is using the central part of the retina to see with or alternatively using an eccentric part of the retina*	50	32.0	4	25.0	29	24.1	4	25.5
	PO	18. Contrast sensitivity	*Testing "contrast sensitivity" which is objects of varying brightness Contrast sensitivity*	49	6.1	3	33.3	28	0.0	3	20.0
	PO	19. Colour vision test (for any type of ocular motility disorder)	*Colour vision test*	50	8.0	5	60.0	29	0.0	5	20.0
	PO	20. Colour vision test (for certain types of ocular motility disorders? please specify)		49	36.7	N/A	N/A	29	31.0	N/A	N/A
	PO	21. Visual field test (for certain types of ocular motility disorders? please specify)	*Visual field test*	48	37.5	8	50.0	29	24.1	5	60.0
	SR	22. Broadening of the null region (in nystagmus)	*Broadening of the null region (in nystagmus)*	48	58.3	3	**100.0**	29	69.0	4	**100.0**
	SR	23. Reduce the amplitude of nystagmus (in nystagmus)	*Reduce the amplitude of nystagmus (in nystagmus)*	48	60.4	3	**100.0**	29	69.0	3	**100.0**
	SR	24. Stereo acuity	*Fine 3D vision or depth appreciation with both eyes or "stereo vision"*	50	62.0	8	**87.5**	29	**75.9**	5	**100.0**
	SR	25. Field of binocular single vision	*Testing the extent of area of vision where there is no double vision while looking around with both eyes open*	50	**70.0**	7	**71.4**	29	**86.2**	5	**80.0**
	PO	26. Post op diplopia test	*Testing if a person is likely to get double vision after correcting the eye deviation with surgery*	50	68.0	7	**100.0**	29	**82.8**	5	**100.0**
	SR	27. Simultaneous perception	*Testing lower levels of 3D vision*	50	48.0	7	42.9	29	41.4	5	60.0
	SR	28. Retinal correspondence		50	38.0	N/A	N/A	29	24.1	N/A	N/A
	SR	29. Refractive status (for any type of ocular motility disorder)	*Testing the amount of prescription of glasses or contact lenses*	50	46.0	6	50.0	29	37.9	5	40.0

	SR	30. Refractive status (for certain types of ocular motility disorders? please specify)		47	48.9	N/A	N/A	29	51.7	N/A	N/A
Oculomotor function	SR	31. Ocular alignment / deviation	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation*	47	**91.5**	7	**71.4**	29	**100.0**	5	**80.0**
	SR	32. Abnormal head posture	*The presence of a compensatory head posture to avoid double vision*	47	**76.6**	6	66.7	29	**89.7**	5	**80.0**
	FG	33. Ocular motor alignment at various positions specially where the deviation is greatest	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation at different positions*	47	**80.9**	N/A	N/A	29	**89.7**	N/A	N/A
	SR	34. Presence of incomitance (for any type of ocular motility disorder)	*Variation of angle of deviation at different positions of gaze*	47	63.8	6	66.7	29	**79.3**	3	66.7
	SR	35. Presence of incomitance (for certain types of ocular motility disorders? please specify)		44	**72.7**	N/A	N/A	28	**75.0**	N/A	N/A
	PO	36. Control of deviation (any type)	*Measuring how well the person can control the eye turn*	47	**83.0**	6	**83.3**	29	**89.7**	5	**100.0**
	PO	37. Control of deviation (for certain types of ocular motility disorders? please specify)		43	**83.7**	N/A	N/A	29	**96.6**	N/A	N/A
	SR	38. Ocular movement	*How well eyes move as a person is looking around*	47	**85.1**	8	62.5	29	**93.1**	5	**100.0**
	SR	39. Forced duction test (for any type of ocular motility disorder)	*A test done to check eye muscle action passively using forceps*	45	31.1	N/A	N/A	29	24.1	N/A	N/A
	SR	40. Forced duction test (for certain types of ocular motility disorders? please specify)		44	65.9	N/A	N/A	27	66.7	N/A	N/A
	SR	41. Three step/head tilt test (for any type of ocular motility disorder)	*A test to check eye deviation with head tilt and head turn in addition to the straight-ahead EOsition*	44	20.5	N/A	N/A	29	10.3	N/A	N/A
	SR	42. Three step/head tilt test (for certain types of ocular motility disorders? please specify)		45	66.7	N/A	N/A	28	60.7	N/A	N/A
	PO	43. Presence of dissociated vertical deviation (DVD)	*Presence of a tendency for the eye to move up and out when covered*	47	46.8	N/A	N/A	29	44.8	N/A	N/A
	SR	44. A or V pattern deviation	*Testing if the deviation increases on looking up or looking down*	47	55.3	7	57.1	29	62.1	5	40.0

	PO	45. Fusional vergence at near and distance /fusion amplitudes/prism fusion range	*Testing how well the eyes can control a deviation induced with prisms in clinic*	47	53.2	7	57.1	29	62.1	4	**75.0**
	SR	46. Reading eye movements (for any type of ocular motility disorders)	*Checking if eye movements are normal during reading*	45	22.2	7	**71.4**	29	20.7	5	60.0
	SR	47. Reading eye movements (for certain types of ocular motility disorders? please specify)		42	42.9	N/A	N/A	29	48.3	N/A	N/A
	SR	48. Presence of a phoria (for any type of ocular motility disorders)	*A test done to check if there is a hidden small eye alignment problem*	46	54.3	7	42.9	29	58.6	5	20.0
	SR	49. Presence of a phoria (for certain types of ocular motility disorders? please specify)		41	56.1	N/A	N/A	28	**71.4**	N/A	N/A
	SR	50. Objective extortion (for any type of ocular motility disorders)	*Checking if the eye is rotated outwards due to a muscle problem (tested in clinic without the need of patient response)*	43	25.6	7	42.9	28	25.0	5	20.0
	SR	51. Objective extortion (for certain types of ocular motility disorders? please specify)		41	58.5	N/A	N/A	27	66.7	N/A	N/A
	SR	52. Subjective extortion (for any type of ocular motility disorders)	*Check if the eye is rotated outward due to a muscle problem (tested in clinic and results depend on patient response)*	44	50.0	7	42.9	28	60.7	4	25.0
	SR	53. Subjective extortion (for certain types of ocular motility disorders? please specify)		41	**73.2**	N/A	N/A	27	**92.6**	N/A	N/A
	SR	54. Near point of convergence (for any type of ocular motility disorders)	*Testing if the eyes can normally look inwards to see a near object to an acceptable amount*	47	34.0	8	50.0	29	34.5	5	40.0
	SR	55. Near point of convergence (for certain types of ocular motility disorders? please specify)		41	63.4	N/A	N/A	28	**78.6**	N/A	N/A
	SR	56. Accommodation (for any type of ocular motility disorders)	*Testing if the eyes can change their focus appropriately to see objects at varying distances*	46	15.2	8	62.5	29	13.8	5	60.0

	SR	57. Accommodation (for certain types of ocular motility disorders? please specify)		42	42.9	N/A	N/A	28	46.4	N/A	N/A
	SR	58. Dynamic retinoscopy (for certain types of ocular motility disorders? please specify)	*Changing refractive power of the eye with varying focus*	42	19.0	N/A	N/A	27	37.0	N/A	N/A
	SR	59. Pursuits (for certain types of ocular motility disorders? please specify)	*Testing a specific tracking slow movement of the eye for an object*	45	64.4	7	42.9	28	60.7	5	40.0
	SR	60. Saccades (for certain types of ocular motility disorders? please specify)	*Testing a specific rapid tracking eye movement for an object*	45	62.2	7	57.1	28	67.9	5	60.0
	SR	61. Optokinetic nystagmus (OKN)	*Special tracking eye movement using a striped drum*	46	34.8	N/A	N/A	29	31.0	N/A	N/A
Additional clinical signs	SR	62. Eye movement recordings (for certain types of ocular motility disorders? please specify)	*Eye movement recordings*	40	27.5	7	42.9	28	32.1	5	40.0
	SR	63. Palpebral fissure size/lid position (for certain types of ocular motility disorders? please specify)	*Checking eye lid position - whether it is droopy or elevated compared to normal*	44	63.6	5	40.0	29	65.5	5	40.0
	SR	64. Facial asymmetry (for 4th n palsy)	*Checking if the sides of the face are symmetrical or not to help diagnose some congenital motility disorders*	45	33.3	4	50.0	29	20.7	4	25.0
	SR	65. Pupil examination (for any type of ocular motility disorders)	*To check pupil size; reaction etc*	44	45.5	6	50.0	29	41.4	5	20.0
	SR	66. Pupil examination (for certain types of ocular motility disorders? please specify)		43	**74.4**	N/A	N/A	29	**79.3**	N/A	N/A
	SR	67. Proptosis/exophthalmos (for certain types of ocular motility disorders? please specify)	*Checking if the eyes are protruding out of their position*	44	**79.5**	4	**75.0**	29	**86.2**	5	60.0
	SR	68. Intraocular pressure (for certain types of ocular motility disorders? please specify)	*Check eye pressure*	43	48.8	5	**80.0**	28	42.9	4	**100.0**

	SR	69. Corneal exposure (for certain types of ocular motility disorders? please specify)	*Checking for corneal changes resulting from incomplete eyelid closure*	42	**76.2**	4	**75.0**	28	**96.4**	5	**80.0**
	SR	70. Corneal sensitivity (for certain types of ocular motility disorders? please specify)	*Checking if corneal nerve supply is intact*	39	66.7	4	**75.0**	28	67.9	5	**100.0**
	SR	71. Canthal displacement (for certain types of ocular motility disorders? please specify)	*Change in position of the eye contour*	32	28.1	N/A	N/A	23	21.7	N/A	N/A
	SR	72. Oculocardiac reflex (for certain types of ocular motility disorders? please specify)	*Slowing of the heart rate due to entrapped eye muscle*	28	32.1	N/A	N/A	22	36.4	N/A	N/A
	SR	73. Globe dystopia (for certain types of ocular motility disorders? please specify)	*Check the position of the eyeball in relation to the other eye and other parts of the face*	33	39.4	5	60.0	22	36.4	4	50.0
	SR	74. Enophthalmos (for certain types of ocular motility disorders? please specify)	*Checking if the eyes are sinking in from their normal position*	42	66.7	4	**75.0**	29	**82.8**	5	**80.0**
Clinical investigations	SR	75. Assessment for fractures and soft-tissue herniation for example inferior rectus muscle; fat; or connective tissue radiographically (for certain types of ocular motility disorders? please specify)	*Assessment for fractures and soft-tissue herniation for example inferior rectus muscle; fat; or connective tissue radiographically*	41	**87.8**	3	66.7	29	**96.6**	4	**75.0**
	SR	76. Assessment for muscle atrophy or absent nerve radiographically (for certain types of ocular motility disorders? please specify)	*Assessment for muscle atrophy or absent nerve radiographically*	35	65.7	5	60.0	26	69.2	4	**75.0**
	SR	77. Histologic examination of excised tissue (for certain types of ocular motility disorders? please specify)	*Histologic examination of excised tissue*	26	57.7	N/A	N/A	24	**75.0**	N/A	N/A
Quality of life	SR	78. Quality of life measures (in general)	*Health related quality of life (all relevant aspects)*	45	**82.2**	8	**87.5**	29	**93.1**	5	**100.0**

	FG	79. Psychological impact of the disorder	*Negative impact of eye motility problem on emotions and/or behaviour*	45	**84.4**	8	**100.0**	29	**96.6**	5	**100.0**
	FG	80. Psychological impact of treatment of disorder	*Positive impact of treatment on emotions and/or behaviour*	45	**77.8**	N/A	N/A	29	**93.1**	N/A	N/A
	FG	81. Social anxiety and social avoidance due to the disorder	*Negative impact of eye motility problem on social interaction or causing social stigma*	45	**77.8**	8	**100.0**	29	**89.7**	5	**100.0**
	FG	82. Academic/ occupation achievement in relation to the condition or its treatment	*Academic/ occupation achievement in relation to the condition or its treatment*	44	**72.7**	8	**87.5**	29	**79.3**	5	**80.0**
	FG	83. Activity of daily living (ADL)	*Activity of daily living (ADL) such as driving*	45	**80.0**	8	**100.0**	29	**93.1**	5	**100.0**
	SR	84. Patient satisfaction from treatment	*Patient satisfaction from treatment*	45	**82.2**	8	**87.5**	29	**93.1**	5	**80.0**
	FG	85. Future functionality/long-term impact	*Future functionality/long-term impact (patient-reported)*	44	**86.4**	8	**100.0**	29	**96.6**	5	**100.0**
Compliance	SR	86. Compliance	*How well the treatment is done*	42	54.8	7	**71.4**	29	65.5	5	**80.0**
Treatment dependency	PO	87. Successful discontinuation of glucocorticoids (in orbital inflammatory conditions such as thyroid eye disease)	*Successful discontinuation of lens therapy or* glucocorticoids *(in orbital inflammatory conditions such as thyroid eye disease)*	34	64.7	3	66.7	25	**76.0**	4	50.0
	PO	88. Successful discontinuation of lens therapy or "special glasses"	*Successful discontinuation of lens therapy or "special glasses" such as bifocals or minus lenses*	43	51.2	4	50.0	29	58.6	4	50.0
	PO	89. Successful discontinuation of prism therapy	*Successful discontinuation of prism therapy*	44	56.8	3	66.7	29	69.0	3	66.7
Adverse events	SR	90. Adverse effects from treatment (any)	*Adverse effects from treatment (any)*	44	**79.5**	8	**100.0**	29	**82.8**	5	**100.0**
	FG	91. Adverse effect on vision from patches or prisms used to treat diplopia	*Adverse effect on vision from patches or prisms used to treat diplopia such as vision degradation or psychosocial effects*	44	56.8	5	40.0	29	**82.8**	5	**80.0**
	PO	92. Intolerable diplopia	*Intolerable double vision*	44	**97.7**	7	**100.0**	29	**100.0**	5	**100.0**
	PO	93. Induced ptosis (Post toxin injection)	*Appearance of transient droopy eye lid as a result of using toxin injection to treat squint*	43	48.8	5	**80.0**	29	62.1	5	**80.0**
	PO	94. Induced subconjunctival haemorrhage	*Appearance of a bleed in the surface of the eye after squint surgery or injection*	44	34.1	7	57.1	28	32.1	5	**80.0**
	PO	95. Discomfort or abnormal sensation	*Discomfort or pain during/after treatment of squint*	43	39.5	7	**85.7**	29	48.3	5	**100.0**

	PO	96. Overcorrection or under correction of the deviation with surgery or injection	*Persistence of the squint at a lesser extent or appearance of deviation in the opposite direction*	44	**72.7**	6	**83.3**	29	**75.9**	5	60.0
	PO	97. Recurrence of deviation	*Reappearance of the squint after treatment*	44	**70.5**	8	**75.0**	29	**79.3**	5	**100.0**
	PO	98. Induced vertical deviation	*Appearance of a vertical squint after treatment of a horizontal deviation*	44	63.6	5	40.0	29	65.5	5	40.0
	PO	99. Induced A or V pattern	*Appearance of a deviation that increases either on looking up or looking down*	44	59.1	6	33.3	29	48.3	5	40.0
	PO	100. Development of DVD	*Appearance of a tendency for the eye to move up and out when covered*	44	31.8	5	60.0	29	27.6	5	40.0
	PO	101. Induced incomitance	*Development of variation of the eye deviation in different positions when looking around*	44	56.8	6	66.7	29	58.6	5	60.0
	PO	102. Number of operations needed	*Number of operations/procedures needed*	44	68.2	8	**87.5**	29	**75.9**	5	**80.0**
Cost	PO	103. Economic data (in general)	*Economic data (in general) including services and families/individuals*	39	48.7	8	**75.0**	27	59.3	5	**100.0**
	PO	104. Cost of treatment on services	*Cost of treatment on services*	39	46.2	8	50.0	27	51.9	5	60.0
	FG	105. Cost of treatment on families/individuals	*Cost of treatment on families/individuals*	39	41.0	8	**75.0**	27	48.1	5	**80.0**
Long-term	SR	106. Long-term outcomes	*Long-term outcomes (clinical outcomes)*	44	**88.6**	8	**87.5**	29	**96.6**	5	**100.0**

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A core outcome set for three ophthalmic conditions: a healthcare professional and patient consensus on Core Outcome Sets for Amblyopia, Ocular Motility and Strabismus (COSAMS study)

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Ethics statement: Ethical approval was obtained from the University of Liverpool institutional research ethics committee for the focus groups, online survey and the consensus meetings to be undertaken with healthcare professionals and patients (Ref. Nos. 2063 and 2260). Informed consent was obtained from participants.

Abstract

Objectives: Amblyopia, strabismus and ocular motility disorders are common conditions with significant impact on visual function, appearance and quality of life. We aimed to establish a core set of outcomes for each of the three conditions for use in clinical trials and routine clinical practice.

Design: A comprehensive databank of outcomes was developed from a systematic review of the literature and a series of focus groups with healthcare professionals, researchers, patients and carers. The databank of outcomes was scored in a two-round Delphi survey completed by two stakeholder groups; healthcare professionals / researchers and patients / carers. Results of the online Delphi were discussed at a face-to-face consensus meeting where the core outcome sets were finalised.

Setting: UK-wide consultation.

Participants: Researchers, clinicians, patients and carers.

Outcome measures: Core Outcome Sets.

Results: For amblyopia, strabismus and ocular motility, 40/42/33 participants contributed to both rounds of the Delphi; 6/9/7 members attended consensus meetings, respectively. Consensus was reached on ten core outcomes for both amblyopia and ocular motility and nine for strabismus. All three conditions shared the core outcomes: *adverse events, cost, vision-related quality of life, and ocular alignment*. The strabismus and ocular motility disorder core sets included, in addition, *measuring the deviation, binocular vision, ocular movement, patient satisfaction and symptoms.* The amblyopia set, distinct from the sets for the other two conditions, included *best corrected distance and near visual acuity, spherical and cylindrical refraction, compliance, and treatment-related and functionality / long-term impacts*.

Conclusions: The study used robust consensus methods to develop a core outcome set for three ophthalmic conditions. Implementation of these core outcome sets in clinical trials and routine clinical practice will ensure that the outcomes being measured and reported are relevant to all stakeholders. This will enhance the relevance of study findings and enable comparison of results from different studies.

Keywords:

Core outcome set; Amblyopia; Strabismus; Ocular motility; Consensus; Delphi

Article summary:

Strengths and limitations of this study:

- This study followed robust methodology as guided by the Core Outcome Measures in Effectiveness Trials (COMET) Initiative.
- We targeted amblyopia, strabismus and ocular motility disorders which are common ophthalmic conditions.
- The study included key stakeholders including researchers, clinicians, patients and carers.
- Attrition rates in the Delphi process were moderate but similar to other COS studies.
- Larger response numbers, including international participants, would be preferable for wider generalisability.

Introduction

Amblyopia (lazy eye) and strabismus (squint) occur in up to 5% of the general population [1, 2]. It is unknown how prevalent ocular motility disorders (abnormal eye movements) are in the general population. These conditions often present in children and can lead to long-term problems for children and young adults such as blurred vision, double vision, low esteem and even blindness if not treated [3]. There are several approaches to the management of these conditions including occlusion, penalisation, spectacles, prisms, drugs, surgery, botulinum toxin, exercises, watchful waiting, or a combination of two or more of the above [4-20].

Interventional systematic reviews in this field of research have identified that there is considerable variation in the outcomes being measured and reported in primary research studies, which impacts on the ability to compare and synthesise outcome results across studies. Moreover, it was noted that there is a paucity of outcome data available on important patient outcomes such as quality of life, long-term outcome as well as the cost of treatment [4-20]. To mitigate these issues and to increase the relevance of research, a

core outcome set (COS) can be developed which represents an agreed standardised set of outcomes that should be measured and reporting in all studies for a specific area of health or healthcare. A search of the COMET (Core Outcome Measures in Effectiveness Trials) database revealed that there are several studies that have investigated important outcomes for eyes and vision disease; examples include cataract [21, 22] ,glaucoma [23] and age-related macular degeneration [24] but none have specifically looked at amblyopia, strabismus or ocular motility disorders [25].

The aim of this study was to develop core outcome sets for use in clinical trials and routine practice for all intervention types for the treatment of amblyopia, strabismus and ocular motility disorders in children and adults that includes input from all stakeholders. While we aim to develop three separate COS for each of the ophthalmic conditions, we anticipate that there could be considerable overlap in the importance of certain outcomes across these conditions. This is due to the fact that the three conditions often overlap and co-exist in patients, are frequently targeted within the same research studies, and are usually managed by the same group of health care professionals.

Methods

The development of the COS study involved three stages (Figure 1): (1) the generation of a long list of outcomes; (2) a two- round online Delphi survey and (3) face- to- face consensus meetings to discuss the results of the Delphi survey and agree on the COS. The process considered the minimum standards for the design of a COS study (COS-STAD), which included careful consideration of the scope, stakeholders and the consensus process [26].

Outcome list generation

A databank of outcomes was generated from two sources: a systematic review of outcomes reported by researchers and clinicians in studies for the treatment of the conditions under evaluation, and, secondly using three separate focus groups (one for each condition) containing a mix of healthcare professionals, researchers, patients and carers. The detailed search strategy, methods and results for the systematic review have been published elsewhere [27]. Outcomes from the systematic review and suggested

outcomes from the recorded focus group meetings were extracted verbatim and grouped into suitable domains to facilitate easy classification. The final list was checked by experts in all three clinical conditions (SJ, FR), who also had the opportunity to use their clinical expertise to add additional outcomes to the list. In preparation for the Delphi survey, clinical assessment outcomes used only by healthcare professionals were either separated out (not to be scored by patients) or combined into a simplified outcome for patients to score. Each outcome was written using plain language and feedback sought from four researchers from the Health Service Research department, University of Liverpool and a clinician from a local hospital on the acceptability and their understanding of the wording used. The databank of outcomes can be found in Supplementary Table 1.

Online Delphi survey

The databank of outcomes was used to populate an online Delphi survey, which was administered using DelphiManager [28]. Participants were invited from two key stakeholder groups. The first group consisted of healthcare professionals involved in the care for people with one of the three conditions or researchers working within this field. Invitations to participate were sent by email flyers to national professional organisations including the British and Irish Orthoptic Society, Paediatric Ophthalmology networks, and local groups linked with the University of Liverpool. The second group included patients or carers of patients affected by at least one of the three conditions of interest. Patients and carers were invited to participate into the survey using flyers distributed on the University of Liverpool noticeboards, newsletters (via the professional Society), social media (twitter) and in ophthalmology departments in local hospitals including Aintree University Hospital, The Royal Liverpool University Hospital and Southport and Ormskirk hospitals. Through routine clinical practice, the study authors (SJ, FR) and healthcare professionals were also encouraged to distribute the patient survey links to their relevant patients if they showed an interest in the study.

Four surveys were set up, one for the healthcare professionals and researchers that contained the outcomes to be scored for all three conditions, and, three separate surveys containing only the outcomes relevant to patients and carers associated with each individual condition. The Delphi process was completed using two rounds (hereafter referred to R1 and R2). In each round participants were presented with the list of

outcomes and asked to score each outcome on how important it was to include in the COS, using a 9-point Likert scale, with 1-3 labelled 'not important', 4-6 labelled 'important but not critical', and 7-9 labelled as 'critically important' [29]. Participants had the option to indicate 'unable to score' on any outcome they felt unable to score, and at the end of R1, participants were invited to submit additional outcomes they thought were missing from the list. These outcomes were reviewed by the study authors (SJ, FR) and any outcomes that represented a new relevant outcome were added to the list to be scored in R2. Irrespective of participant scoring, no outcomes were removed from the list between R1 and R2. During R2, participants were shown the distribution of scores for both stakeholder groups for each outcome along with their own score from R1 and asked to score the outcome again, using the same scale, taking this extra information into account.

Consensus meeting

Separate face-to-face consensus meetings were held at the University of Liverpool, UK for each of the three conditions. Participants who either had an active role in the focus groups and/or completed both rounds of the Delphi survey were invited to attend, although others with an interest in the project were invited to ensure each meeting had a balanced mix of participants from both stakeholder groups. In advance of the meeting, participants received a copy of their scores from the online survey (if appropriate) and a consensus matrix (Supplementary Table 1) detailing the results of R1 and R2 by stakeholder group, and which outcomes had reached a priori definition of consensus in, consensus out or no consensus (Table 1). The consensus definition is similar to that used in other COS development studies.

The meeting for amblyopia was chaired by a non-clinical researcher with expertise in COS development methodology (JJK) while the meeting for strabismus and ocular motility was chaired by a student investigator with a clinical background (SJ).

In order to facilitate the discussion all outcomes that had reached consensus 'in' after R2 for both stakeholder groups were presented first, followed by outcomes that reached consensus 'in' for only one stakeholder group. All outcomes that scored critical for inclusion for 50-69% of the participants for either both or one of the stakeholder groups in

R2 were presented next followed by all other outcomes that were scored by both stakeholder groups. Outcomes that were only scored by healthcare professionals and researchers were discussed last. Results for each outcome from the Delphi were shown to the participants with more time allocated to discussing outcomes where there was more uncertainty on whether the outcome should be included in the COS or not. Views for and against inclusion in the COS were sought by the meeting chair, who also ensured that participants had equal opportunity to comment prior to voting. Voting was undertaken anonymously using Poll Everywhere [30] software which was linked to mobile and tablet devices. The definition of consensus used in the Delphi survey (Table 1) was applied to the consensus meeting. The final COS was presented at the end of the meetings.

Study registration, ethics and reporting guidance

The study was prospectively registered with the COMET Initiative (Core Outcome Measures in Effectiveness Trials)[31]. Ethical approval was obtained from the University of Liverpool institutional research ethics committee for the focus groups, online survey and the consensus meetings to be undertaken with healthcare professionals and patients (Ref. Nos. 2063 and 2260). Informed consent was obtained from participants. The study is reported in line with the Core Outcome Set – Standards for Reporting (COS-STAR) guidance [32] (Supplementary Table 2).

Patient and Public Involvement

The study was supported by a patient advisory group which provided input to this research study. The patient advisory group met on a regular basis for the duration of the study. Patients contributed to the design of the study and were involved at all stages of the survey and consensus meetings.

Results

A summary of the COS development process is shown in Figure 1. The final COS contains ten, nine and ten outcomes across seven, six and seven domains for amblyopia, strabismus and ocular motility respectively (Tables 2-4). Ocular alignment,

vision-related quality-of-life, adverse events and cost were common to all three conditions.

Development of the databank of outcomes

The systematic review and focus groups of health care professionals, researchers, patients and carers identified 31, 61, and 78 individual outcomes for amblyopia, strabismus and ocular motility respectively. These were combined with a list of outcomes suggested by professional experts (SJ, FR) resulting in a total of 40, 70 and 106 outcomes for amblyopia, strabismus and ocular motility respectively. The outcomes were classified into 12 domains, (symptoms, visual function, refraction, oculomotor function, quality-of-life, treatment dependency, signs, investigations, long-term outcome, compliance, adverse events, cost) and outcomes that were not considered to be patient relevant were separated out or combined. As an example, 'refractive status', 'spherical and cylindrical refraction' and 'median spherical equivalence' were combined into a single outcome 'refractive status' for patients as they all have a similar meaning, but are often referred to separately by healthcare professionals. Details of all outcomes including domain classification, combined outcomes and plain language descriptions of outcomes is provided in Supplementary Table 1.

Online Delphi

Thirty three healthcare professionals / researchers scored all outcomes for both R1 and R2 of the amblyopia component of the online survey while 29 completed for strabismus and ocular motility. Three patients/carers completed both rounds for amblyopia while nine completed both rounds for strabismus and five for ocular motility (Figure 1). At the end of R1, five outcomes for amblyopia, 12 for strabismus and 23 for ocular motility reached consensus 'in' for both stakeholder groups. After a review of all additional outcomes suggested by participants in R1, three new outcomes were added to the strabismus survey in R2 (improvement in angle by a set amount (suggested by a healthcare professional) and, immediate result post-surgery and long-term discomfort from scar tissue (both suggested by a patient)).

On completion of R2, ten outcomes reached consensus 'in' for amblyopia across both stakeholder groups while 17 and 32 outcomes reached the same criteria for strabismus and ocular motility respectively.

Consensus meeting

Six, nine and seven voting participants attended the consensus meeting for amblyopia, strabismus and ocular motility respectively with an even balance of healthcare professional/researchers and patients present (Figure 1).

Amblyopia

For amblyopia, *future functionality/long-term impact* and *adverse events* reached the consensus 'in' criteria for both stakeholder groups in both rounds of the Delphi and remained in the COS. Despite reaching consensus 'in' for both rounds of the Delphi for both stakeholder groups, intolerable diplopia and occlusion amblyopia (both adverse events) were not included in the final COS as it was felt that these could be captured under 'adverse events' and therefore were not critical for separate inclusion in the COS. Long-term outcome was also excluded following discussion as the group felt that there was currently no agreed set time for measuring long-term objective outcomes. *Best corrected visual acuity* and *compliance* marginally did not reach consensus 'in' during R2 of the Delphi but made the final COS after discussion. Following a discussion on the other visual function outcomes, *near visual acuity* was also added because it was noted that it was a good marker of early improvement for the treatment of amblyopia and important for children as it is important to their education. Refractive status reached consensus for both groups in R2 but following discussion this was replaced by *spherical and cylindrical refraction* (scored only by health care professionals in the Delphi) because it was successfully argued that this was a more precise measurement of refractive status. The list of outcomes within the quality of life domain were discussed simultaneously. While this was not listed specifically as an outcome in the Delphi, participants agreed to include *visual-related quality of life* in the core set as it was felt that a generic health-related quality of life outcome was not sensitive enough. Psychological impact of treatment was scored only by healthcare professionals in the Delphi but reached consensus 'in' during R2. Following discussion led by a parent participant, the panel derived a new outcome to include *treatment-related impact* into the final COS in order to

capture the effect of treatment, such as patching on children, which could be long lasting. For both Delphi rounds, cost outcomes did not reach consensus 'in' by either stakeholder groups, however, the consensus panellists successfully advocated for its inclusion as a core outcome as *cost* outcome data is vital information for contemporary health systems.

Strabismus

For strabismus, *symptoms* and *patient satisfaction* reached the consensus 'in' criteria for both stakeholder groups in both rounds of the Delphi and remained in the COS. Best corrected visual acuity also reached consensus 'in' for both rounds and groups in the Delphi although the consensus panel argued that any change in vision and/or loss of vision as an adverse event would be very significant and reportable as per standard healthcare safety procedures [33]. At the consensus meeting, participants noted that strabismus interventions aim to change the strabismus angle and visual acuity should not be affected by the intervention unless an adverse event occurred. Thus a change in visual acuity would be captured within adverse events. On this basis a decision was taken to exclude visual acuity from the core set. All remaining visual function outcomes were discussed simultaneously, and while the post-op diplopia test reached consensus 'in' during the Delphi exercise, the consensus panel voted in favour of including *binocular vision* as core, as it was more representative of a group of visual function related outcomes. Oculomotor function outcomes were discussed simultaneously and it was highlighted that *ocular movement* was critical to be reported in all strabismus types as a change caused by the intervention would be significant. Quantifying both the *ocular alignment* and *deviation* were also seen to be critical in the context of any strabismus type and were included as core outcomes. *Visual-related quality-of life*, *adverse events* and *cost* were also included in the COS for reasons discussed for amblyopia.

Ocular Motility

The discussions for ocular motility closely followed those of strabismus with the addition of clinical signs being added as an extra core outcome. Similar to adverse events, this outcome was a catch all for all clinical signs which were scored individually in the Delphi exercise. This strategy was seen favourably by the meeting participants as many sub-conditions of ocular motility have specific signs associated with them. One example for this is corneal exposure in the ocular motility condition of Thyroid Eye Disease but which is not relevant in other ocular motility disorders.

Discussion

This study has developed a set of core outcomes for the treatment of three ophthalmic conditions using a robust consensus process involving healthcare professionals, researchers, patients and carers. Consensus was reached on what should be measured in each of the three COS. They consisted of nine to ten outcomes distributed across six to seven domains to cover all important aspects related to treatment (objective clinical, adverse events, subjective or patient-reported outcomes, and health economics). While these three core outcome sets were developed independently, there are some parallels, and as a consequence, four outcomes (*ocular alignment, vision-related quality-of-life, adverse events and cost*) were common to all three conditions. The amblyopia COS captures the condition's unique features by reporting additionally on '*best corrected visual acuity', 'near visual acuity', 'compliance', 'spherical and cylindrical refraction', 'treatment-related impact' and 'future functionality/long-term impact'*, keeping in mind that children are the predominantly affected population. The COS for strabismus and ocular motility disorders, on the other hand, include '*binocular vision', 'ocular movement', 'measuring the deviation', 'symptoms' and 'patient satisfaction'*. The ocular motility disorder COS was unique in additionally reporting *'clinical signs'* related to the relevant conditions.

We recommend that, as a minimum, these core outcomes are used in future trials of interventions to treat amblyopia, strabismus and ocular motility disorders. We also advocate that these outcomes are recorded in routine clinical practice to ensure that the outcome data collected is meaningful and important.

A strength of this study is that it was prospectively registered with the COMET Initiative and it was developed using the COS- STAD (Core Outcome Set - STAndards for Development) recommendations [26]. Engagement with patient participants was particularly challenging and we sought to improve patient input by offering paper copies of the Delphi survey with pre-paid return envelopes in orthoptic clinics, although this was later abandoned after a number of sessions when there was no uptake. As a consequence of a relatively low number of patients responding to the Delphi and attrition between the two rounds, there was concern that consensus was not being achieved at

the end of the final round given the number of outcomes reaching consensus for both stakeholder groups had increased dramatically from R1. While measures were taken to ensure survey participation and retention was maximised (including sending reminders and extending deadlines for completion), it was felt that after several months of keeping the survey open, our efforts became futile. In order to compensate for this, we ensured that the consensus meetings where the final COS were ratified, contained a good balance of healthcare professionals and patients. The main limitation of this study was that the consensus process was based using only participants in the UK. However, as a starting point, we have reason to believe that this COS could also be useful in other countries and settings.

Further consensus work is needed to refine and establish the best measurement instruments and time points for when to measure these core outcomes. To assist this process, the systematic review for generating the databank of outcomes also recorded the measurement instruments and timings associated with each outcome [27].Moreover, for some outcomes, the metric (e.g. change from baseline or inter-ocular difference (IOD) of BCVA), and method of aggregation (e.g. mean or median) [22] would need to be determined. Defining success criteria (e.g. 8 or 10 dioptres from orthophoria for alignment, for distance and/or near) is another aspect of outcome refining and definition to be done by further work. The generalisability of the COS also needs to be reviewed in healthcare settings outside the UK. While the review of outcomes identified studies from around the world (with prominence from the United States, United Kingdom, China and various European countries), the formal consensus process was undertaken using only participants from the UK, and those attending the consensus meeting were mostly localised to the North West of England.

There are few reported COS in the literature that relate to the three conditions in this study. Chiu et al. recommended four outcomes for reporting results of surgery for intermittent exotropia [34]. Their study aimed to explore the extent of standardisation of outcomes reported in surgical studies for the condition. However, the study was limited by the extent of literature review for this specific condition (10-year literature search period) and lack of external consensus. A short narrative review of outcome measurements for size of deviation showed considerable variability across the tests available and the recommendations for their use. They suggested four core outcomes for

all future studies: alignment, near stereoacuity, control score, and quality of life score. If assigning near stereoacuity and control score to 'binocular vision', their outcomes map to those reported in our COS for strabismus.

Moreover, two recently published studies attempted to define criteria for success in treatment, one for amblyopia and the other for strabismus surgery, which could be considered complementary to the COS and not alternatives because they essentially give more definitions of primary outcomes rather than suggesting a set of specific outcomes to be measured in research.

A report was published by Shoshany et al. [35] stating that the IRIS measures for amblyopia developed by the American Academy of Ophthalmology (IRIS7 [36], modified in 2019 to IRIS50 [35]) provide uniform criteria for defining amblyopia treatment success. Treatment was defined as 'successful' if corrected IOD was less than 0.23 logMAR 12–18 months after first diagnosis. IRIS50 considers improvement in VA, which may be relevant to patients who had dense amblyopia at baseline but nevertheless improved. Thus, IRIS50 may be a more practical reporting measure than IRIS7. In general, Shoshany et al. propose that these measures will allow more efficient reporting of quality metrics and rapid and objective assessment of new amblyopia treatments [35].

In addition, a study aiming to define successful outcomes for strabismus surgery was published by Serafino et al. [37]. Although this study did not state an intention to develop a COS, there are a lot of similarities and overlap in the objectives and methodology used. A Delphi process was used to identify areas of consensus and disagreement among experts for the definition of success post strabismus surgery. The panel of experts in their study represented wide international geographic areas and included experts who were chosen based on their peer-reviewed publications, participation at international meetings and their surgical experience. The study concluded the following: they achieved consensus on which strabismus types need their separate set of outcome criteria. They also identified the importance of 'stereopsis' and 'the range of single vision' for inclusion of success definition in some strabismus types, which interestingly could be mapped to 'binocular vision' in our strabismus COS. The study also found that there was no

consensus on the length of time after surgery for determination of success, magnitude of deviation consistent with success, and whether manifest or latent deviation should be considered to define success, which the review of our study [27] has also found, and which we are advocating to define, by future work. Differences from our study is that their survey did not involve scoring of outcomes, there was no systematic search of literature of reported outcomes prior to survey construction, and patients or service users were not consulted in the process.

A search in the COMET initiative database in April 2020 did not reveal registration of any further additions of similar studies in the database. It is advantageous to register COS studies in the database to facilitate collaborative work of similar scope, and to avoid duplication of efforts and waste of research.

Conclusion

The three COS developed from this study can be applied to future trials and routine data collection for all intervention types to treat the three ophthalmic conditions considered. Their use will allow the comparison of outcome data to be made across studies and to better inform treatment decisions. Future work will include seeking consensus on how these outcomes should be measured and to evaluate the acceptability of the current COS to patients and professionals in other countries, particularly where healthcare systems differ from the UK.

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Figure 1 Study flowchart

Table 1 Definition of consensus

Consensus classification	Description	Definition of consensus
Consensus in	Consensus that the outcome should be included in the core set	≥70% of participants scoring the outcome as '7–9' (critically important)
Consensus out	Consensus that the outcome should *not* be included in the core set	≥70% of participants scoring the outcome as '1–3' (not important)
No consensus	Uncertainty about the importance of the outcomes	Anything else

Table 2 Final COS for amblyopia

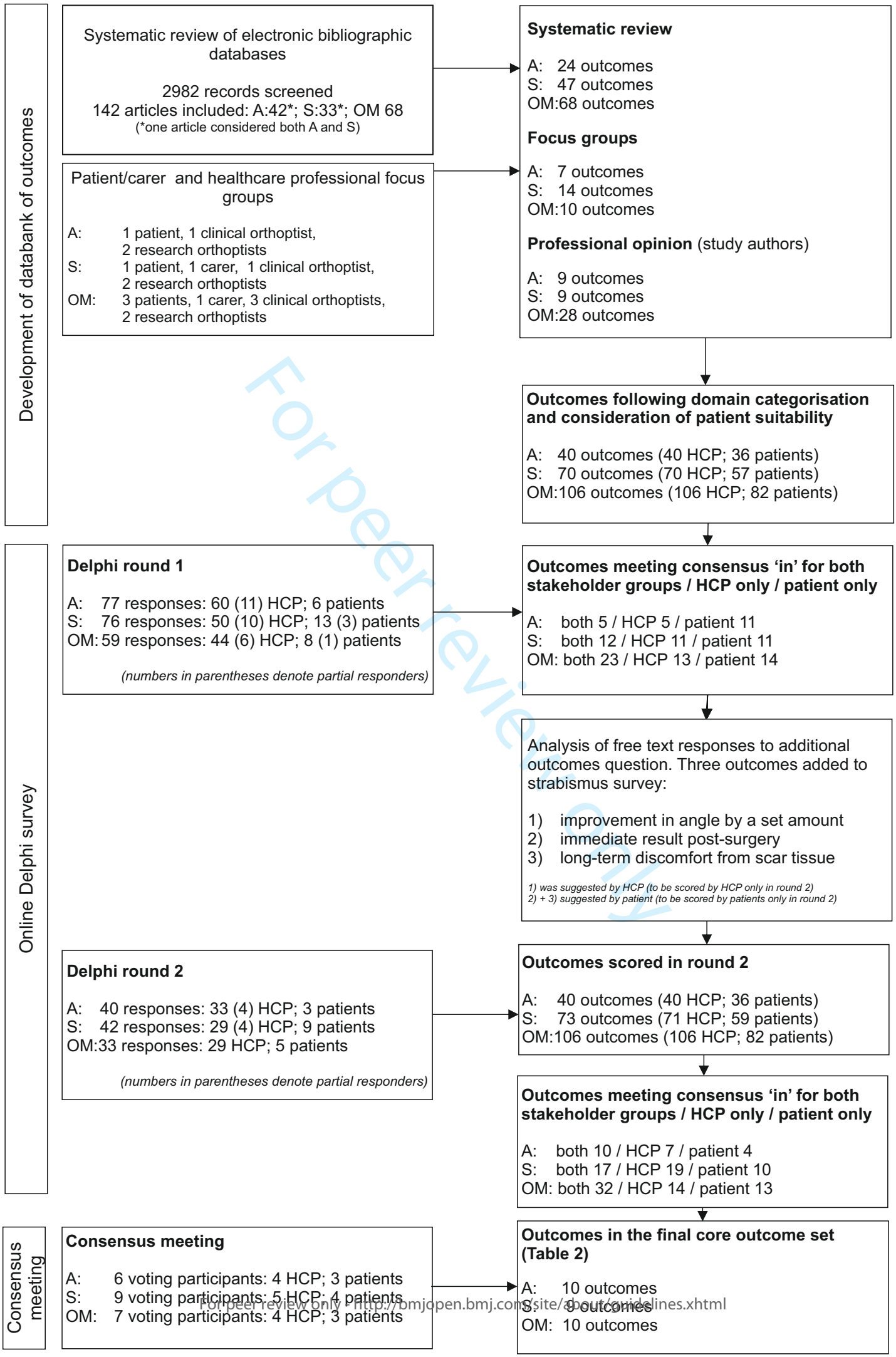
Domain	Outcome
Visual function	**1. Best corrected visual acuity**
	2. Near visual acuity
Refractive status	**3. Spherical and cylindrical refraction**
Oculomotor function	**4. Ocular alignment (is there an ocular deviation?)**
Quality of life	**5. Vision-related quality of life (for example, activities of daily living)**
	6. Treatment-related impact (for example, negative effects of patching on children during treatment)
	7. Future functionality / long-term impact
Compliance	**8. Compliance**
Adverse events	**9. Any adverse events (for example, intolerable diplopia, occlusion amblyopia)**
Cost	**10. Cost (for example, cost to services, families, and individuals)**

Table 3 Final COS for strabismus

Domain	Outcome
Symptoms	**1. Symptoms (for example, diplopia and appearance of the strabismus)**
Visual function	**2. Binocular vision (for example, stereoacuity and binocular single vision)**
Oculomotor function	**3. Ocular alignment (are the eyes straight?)**
	4. Measurement of deviation (what is the amount of deviation?)
	5. Ocular movement (specifically incomitance, latent nystagmus, DVD and A&V pattern)
Quality of life	**6. Vision-related quality of life; psychosocial aspects (such as self-esteem, confidence, behaviour, social interaction) and functional aspects (such as activities of daily living)**
	7. Patient satisfaction
Adverse events	**8. Any adverse events (for example, intolerable diplopia, recurrence of the deviation, overcorrection or under-correction of the deviation)**
Cost	**9. Cost (for example, cost to services, families, and individuals)**

Table 4 Final COS for ocular motility disorders

Domain	Outcome
Symptoms	**1. Symptoms (for example, diplopia and appearance of the eye deviation)**
Visual function	**2. Binocular vision (for example, stereoacuity, field of binocular single vision, and post-op diplopia test)**
Oculomotor function	**3. Ocular alignment (are the eyes straight?)**
	4. Measurement of deviation (what is the amount of deviation?)
	5. Ocular movement (specifically incomitance, latent nystagmus, DVD and A&V pattern)
Quality of life	**6. Vision-related quality of life; psychosocial aspects (such as self-esteem, confidence, behaviour, social interaction) and functional aspects (such as activities of daily living)**
	7. Patient satisfaction
Adverse events	**8. Any adverse events (for example, intolerable diplopia, recurrence of the deviation, and adverse effects from patches or prisms)**
Cost	**9. Cost (for example, cost to services, families, and individuals)**
Clinical signs	**10. Clinical signs (for example, corneal exposure, proptosis / exophthalmos, enophthalmos)**



Supplementary Table 1: Long list of outcomes used in the Delphi survey and critical scoring in both rounds of the Delphi survey by stakeholder group

[Outcomes identified from: systematic review (SR), focus groups (FG) and professional opinion (PO)].

Percentages highlighted in red denote outcomes that reached the consensus 'in' criteria.

N/A: not scored by stakeholder group (HCPs or patients)

Amblyopia

Domain	Source	Outcome	Lay-term summary	Delphi results							
				Round 1				Round 2			
				HCPs		Patients		HCPs		Patients	
				n	% (7-9)	n	% (7-9)	n	% (7-9)	n	% (7-9)
Symptoms	FG	1. Patient symptoms	*Symptoms or complaints related to vision or eyes*	67	34.3	4	50.0	37	37.8	3	66.7
Visual function	SR	2. Best corrected visual acuity	*Vision measured at distance corrected with glasses*	70	**98.6**	4	66.7	37	**100.0**	3	66.7
	SR	3. Near visual acuity	*Close up or reading vision*	70	65.7	4	50.0	37	**78.4**	3	66.7
	PO	4. Habitual visual acuity	*Vision measured in the usual preferred state for a person*	62	58.1	4	**80.0**	37	67.6	3	**100.0**
	SR	5. Uncorrected visual acuity	*Vision without glasses or contact lenses*	70	4.3	4	40.0	37	5.4	3	0.0
	FG	6. Suppression	*Testing if the person has developed "suppression" of one image to improve double vision which usually happens in childhood as a coping mechanism from the brain to improve visual development*	70	42.9	4	**75.0**	36	47.2	2	**100.0**
	FG	7. Fixation	*Testing if the person is using the central part of the retina to see with or alternatively using an eccentric part of the retina*	70	52.9	3	33.3	36	50.0	3	33.3

	FG	8. Contrast sensitivity	*Objects of varying brightness*	66	12.1		60.0	34	5.9	3	0.0
	SR	9. Visual evoked potentials	*Testing vision signals from the eyes to the brain with electrodiagnostics (visual evoked potentials/VEP)*	56	8.9		33.3	33	3.0	2	0.0
	SR	10. Binocularity	*to check if the eyes are working together to give any level of 3D vision or depth appreciation*	70	47.1		**80.0**	36	63.9	2	50.0
	SR	11. Stereoacuity	*Fine 3D vision or depth appreciation with both eyes or "stereo vision"*	70	37.1		**80.0**	35	34.3	2	**100.0**
	PO	12. Simultaneous perception	*Testing lower levels of 3D vision*	70	30.0		60.0	35	25.7	2	0.0
	PO	13. Retinal correspondence		70	31.4	N/A	N/A	35	11.4	N/A	N/A
Refraction	SR	14. Refractive status	*Testing the amount of prescription of glasses or contact lenses*	69	**84.1**		66.7	35	**94.3**	3	**100.0**
	SR	15. Spherical & cylindrical refraction		69	**79.7**	N/A	N/A	35	**91.4**	N/A	N/A
	SR	16. Median spherical equivalent		64	26.6	N/A	N/A	33	21.2	N/A	N/A
Oculomotor function	SR	17. Ocular alignment /deviation	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation*	68	63.2		66.7	35	**71.4**	3	**100.0**
	PO	18. Abnormal head posture	*The presence of a compensatory head posture to avoid double vision*	68	33.8		66.7	34	32.4	3	66.7
Quality of life	SR	19. Quality of life measures (in general)	*Health related quality of life (all relevant aspects)*	69	53.6		**100.0**	35	62.9	3	**100.0**
	FG	20. Psychological impact of the disorder	*Negative impact of lazy eye (amblyopia) on emotions and/or behaviour*	69	55.1		**83.3**	34	67.6	3	**100.0**
	SR	21. Psychological impact of treatment of disorder	*The psychological impact of treatment of lazy eye (amblyopia) on emotions and/or behaviour*	69	62.3	N/A	N/A	34	**73.5**	N/A	N/A
	PO	22. Self-esteem	*Negative impact of lazy eye (amblyopia) on self-esteem & confidence*	69	59.4		**100.0**	34	**70.6**	3	**100.0**
	SR	23. Social anxiety and social avoidance due to the disorder	*Negative impact of lazy eye (amblyopia) on social interaction or causing social stigma*	69	55.1		**83.3**	34	67.6	3	**100.0**
	SR	24. Academic/ occupation achievement in relation to the condition or its treatment	*Academic/ occupation achievement in relation to the condition or its treatment*	69	60.9		**83.3**	34	**76.5**	3	66.7
	SR	25. Activity of daily living (ADL)	*Negative impact of lazy eye (amblyopia) on normal daily activities*	68	52.9	6	**100.0**	33	**72.7**	3	**100.0**
	SR	26. Patient satisfaction from treatment	*Patient satisfaction from treatment*	68	61.8	6	**83.3**	34	**76.5**	3	**100.0**
	FG	27. Future functionality/long-term impact	*Future functionality/long-term impact (patient-reEOrted)*	69	**78.3**	6	**100**	34	**91.2**	3	**100.0**

	SR	28. Fear of losing better eye		69	**71.0**		66.7	33	**84.8**	3	66.7
Compliance	SR	29. Compliance	*How well the treatment is done*	69	**95.7**		66.7	33	**97.0**	3	66.7
Adverse events	SR	30. Adverse effects from treatment (any)	*Adverse effects from treatment (any)*	69	**73.9**		**80.0**	33	**87.9**	2	**100.0**
	SR	31. Intolerable diplopia	*Intolerable double vision as a side effect from treatment*	69	**89.9**		**83.3**	33	**100.0**	3	**100.0**
	SR	32. Occlusion amblyopia	*Development of lazy eye (amblyopia) in the better eye as a result of patching/penalisation treatment*	69	**76.8**		**100.0**	33	**87.9**	3	**100.0**
	SR	33. Visual disorientation	*Visual disorientation due to treatment with occlusion of better eye*	64	45.3		66.7	32	56.3	3	**100.0**
	PO	34. Disturbed distance estimation	*Disturbed distance estimation due to treatment with occlusion of better eye*	64	39.1		66.7	32	46.9	3	33.3
	SR	35. Skin irritation or allergy to patches	*Skin irritation or allergy from eye patches used to occlude the eye*	69	50.7		33.3	33	51.5	3	33.3
	PO	36. Atropine eye drops side effects	*Side effects of the eye drops used regularly at home for treatment of lazy eye (amblyopia)*	69	65.2		33.3	33	69.7	3	66.7
Cost	SR	37. Economic data (in general)	*Economic data (in general) including services and families/individuals*	54	24.1		16.7	30	20.0	3	0.0
	PO	38. Cost of treatment on services	*Cost of treatment on services*	55	25.5		16.7	31	32.3	3	0.0
	PO	39. Cost of treatment on families/individuals	*Cost of treatment on families/individuals*	54	37.0		33.3	30	50.0	3	0.0
Long-term	FG	40. Long-term outcomes	*Long-term outcomes (clinical outcomes)*	59	**84.7**		**100.0**	33	**93.9**	3	**100.0**

Strabismus

Domain	Source	Outcome	Lay-term summary	Delphi results							
				Round 1				Round 2			
				HCPs		Patients		HCPs		Patients	
				n	% (7-9)	n	% (7-9)	n	% (7-9)	n	% (7-9)
Symptoms	FG	1. Patient symptoms	*Symptoms or complaints related to vision or eyes*	60	**91.7**	16	**75.0**	33	**100.0**	9	**77.8**
	FG	2. Diplopia	*Improvement in double vision in general*	60	**95.0**	14	**85.7**	33	**100.0**	8	62.5
	FG	3. Appearance of strabismus	*Appearance of the squint*	60	**85.0**	15	46.7	33	**87.9**	9	33.3
	FG	4. Eye aesthetics as the patient perceives	*Appearance of the squint as the patient perceives*	60	**80.0**	15	40.0	33	**84.8**	9	44.4
	FG	5. Eye aesthetics as relatives and friends perceive	*Appearance of the squint as the relatives and friends perceive*	60	58.3	15	46.7	33	63.6	9	33.3
Visual function	SR	6. Best corrected visual acuity	*Vision measured at distance corrected with glasses*	60	**71.7**	11	**72.7**	33	**90.9**	7	**100.0**
	PO	7. Near visual acuity	*Close up or reading vision*	60	45.0	12	**75.0**	33	63.6	7	**71.4**
	PO	8. Habitual visual acuity	*Vision measured in the usual preferred state for a person*	53	41.5	10	**70.0**	32	59.4	7	**100.0**
	PO	9. Uncorrected visual acuity	*Vision without glasses or contact lenses*	60	8.3	12	58.3	33	3.0	7	**71.4**
	FG	10. Suppression	*Testing if the person has developed "suppression" of one image to improve double vision which usually happens in childhood as a coping mechanism from the brain to improve visual development*	60	65.0	10	**80.0**	32	**75.0**	8	**75.0**
	PO	11. Fixation	*Testing if the person is using the central part of the retina to see with or alternatively using an eccentric part of the retina*	60	46.7	9	33.3	32	46.9	7	42.9
	PO	12. Contrast sensitivity	*Objects of varying brightness*	59	6.8	8	37.5	32	0.0	8	37.5
	SR	13. Binocularity	*Testing "binocularity" which is to check if the eyes are working together to give any level of 3D vision or depth appreciation*	60	**76.7**	12	58.3	32	**75.0**	8	**87.5**

	SR	14. Stereoacuity at near	*Fine 3D vision or depth appreciation with both eyes measured for near*	60	60.0	12	58.3	32	62.5	8	**87.5**
	SR	15. Stereoacuity at near and distance (any strabismus type)	*Fine 3D vision or depth appreciation with both eyes measured for both near and distance*	59	44.1	12	58.3	32	46.9	8	**75.0**
	SR	16. Stereoacuity at near and distance (for certain strabismus types? please specify)	*Fine 3D vision or depth appreciation with both eyes measured for both near and distance for certain types of squint*	54	53.7	N/A	N/A	30	56.7	N/A	N/A
	SR	17. Field of binocular single vision	*Testing the extent of area of vision where there is no double vision while looking around with both eyes open*	60	46.7	12	66.7	32	53.1	8	62.5
	FG	18. Post op diplopia test	*Testing if a person is likely to get double vision after correcting the eye deviation with surgery*	59	**81.4**	11	**81.8**	32	**93.8**	9	**77.8**
	SR	19. Simultaneous perception	*Testing lower levels of 3D vision*	59	37.3	10	50.0	32	25.0	8	62.5
	PO	20. Retinal correspondence	*Testing lower levels of 3D vision*	60	43.3	N/A	N/A	32	37.5	N/A	N/A
	PO	21. Refractive status	*Testing the amount of prescription of glasses or contact lenses*	60	61.7	11	54.5	32	**75.0**	8	50.0
Oculomotor function	SR	22. Ocular alignment /deviation	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation*	60	**86.7**	12	**91.7**	32	**100.0**	8	50.0
	SR	23. Abnormal head posture	*The presence of a compensatory head EOsture to avoid double vision*	60	66.7	11	63.6	32	**84.4**	9	**77.8**
	FG	24. Ocular motor alignment at various positions especially where the deviation is greatest	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation at different EOsitions*	60	**75.0**	N/A	N/A	32	**87.5**	N/A	N/A
	SR	25. Presence of incomitance (any strabismus type)	*Testing if there is variation of the eye deviation in different EOsitions when looking around*	59	**71.2**	N/A	N/A	32	**78.1**	N/A	N/A
	SR	26. Presence of incomitance (for certain strabismus types? please specify)	*Testing if there is variation of the eye deviation in different EOsitions when looking around*	58	**75.9**	N/A	N/A	31	**80.6**	N/A	N/A
	SR	27. Control of deviation (any strabismus type)	*Measuring how well the person can control the eye turn*	59	**79.7**	12	**83.3**	32	**96.9**	9	55.6
	SR	28. Control of deviation (for	*Measuring how well the person can control the eye turn*	58	**81.0**	N/A	N/A	31	**93.5**	N/A	N/A

		certain strabismus types? please specify)									
	SR	29. Ocular movement	*How well eyes move as a person is looking around*	60	66.7	13	61.5	32	**71.9**	9	**77.8**
	SR	30. Presence of latent nystagmus (any strabismus type)	*Checking if there are involuntary rapid movements of the eyes when one eye is covered*	58	46.6	11	63.6	32	53.1	9	44.4
	SR	31. Presence of latent nystagmus (for certain strabismus types? please specify)	*Checking if there are involuntary rapid movements of the eyes when one eye is covered*	57	54.4	N/A	N/A	32	**71.9**	N/A	N/A
	SR	32. Presence of dissociated vertical deviation (DVD) (any strabismus type)	*Testing if there is tendency for the eye to move up and out +/- rotates when covered*	58	51.7	11	54.5	32	53.1	8	**37.5**
	SR	33. Presence of dissociated vertical deviation (DVD) (for certain strabismus types? please specify)	*Testing if there is tendency for the eye to move up and out +/- rotates when covered*	56	64.3	N/A	N/A	31	**71.0**	N/A	N/A
	SR	34. A or V pattern deviation	*Testing if there is a deviation that increases either on looking up or looking down*	60	60.0	N/A	N/A	32	**81.3**	N/A	N/A
	SR	35. Fusional vergence at near and distance /fusion amplitudes/prism fusion range	*Testing how well the eyes can control a deviation induced with prisms in clinic*	60	68.3	11	63.6	32	**81.3**	9	55.6
	SR	36. Near point of convergence (for any strabismus type)	*Testing if the eyes can normally look inwards to see a near object to an acceptable amount*	60	31.7	13	**76.9**	32	43.8	9	66.7
	SR	37. Near point of convergence (for certain strabismus types? please specify)	*Testing if the eyes can normally look inwards to see a near object to an acceptable amount*	58	51.7	N/A	N/A	32	62.5	N/A	N/A

	FG	38. Accommodation (for any strabismus type)	*Testing if the eyes can change their focus appropriately to see objects at varying distances*	60	23.3	13	61.5	32	18.8	9	44.4
	FG	39. Accommodation (for certain strabismus types? please specify)	*Testing if the eyes can change their focus appropriately to see objects at varying distances*	58	60.3	N/A	N/A	31	61.3	N/A	N/A
	SR	40. AC/A ratio (for any strabismus type)	*Testing the ratio between the ability of the eyes to look inwards and their ability to focus*	59	30.5	13	46.2	32	28.1	9	33.3
	SR	41. AC/A ratio (for certain strabismus types? please specify)	*Testing the ratio between the ability of the eyes to look inwards and their ability to focus*	58	65.5	N/A	N/A	31	67.7	N/A	N/A
	CLIN PART	42. Improvement in angle by a set amount e.g. >10^ *		N/A	N/A	N/A	N/A	31	51.6	N/A	N/A
	PT PART	43. Immediate result EOst-surgery**		N/A	N/A	N/A	N/A	N/A	N/A	8	12.5
Quality of life	SR	44. Quality of life measures (in general)	*Health related quality of life (all relevant aspects)*	53	**81.1**	13	69.2	31	**93.5**	9	66.7
	SR	45. Psychological impact of the disorder	*Negative impact of squint (strabismus) on emotions and/or behaviour*	53	**88.7**	13	69.2	30	**100.0**	9	**77.8**
	SR	46. Psychological impact of treatment of disorder	*EOsitive impact of treatment on emotions and/or behaviour*	53	**75.5**	13	**84.6**	30	**80.0**	9	**77.8**
	SR	47. Social anxiety and social avoidance due to the disorder	*Negative impact of squint (strabismus) on social interaction or causing social stigma*	53	**84.9**	14	**71.4**	30	**90.0**	9	66.7
	FG	48. Academic/ occupation achievement in relation to the condition or its treatment	*Academic/ occupation achievement in relation to the condition or its treatment*	52	69.2	13	69.2	30	**76.7**	9	66.7
	FG	49. Activity of daily living (ADL)	*Activity of daily living (ADL) such as driving*	52	67.3	14	**78.6**	29	**86.2**	9	**77.8**
	SR	50. Patient satisfaction from treatment	*Patient satisfaction from treatment*	53	**83.0**	14	**92.9**	29	**96.6**	9	**88.9**

	FG	51. Future functionality/long-term impact	*Future functionality/long-term impact (patient-reEOrted)*	52	**92.3**	11	**100.0**	29	**96.6**	9	**88.9**
Compliance	PO	52. Compliance	*How well the treatment is done*	52	63.5	12	**91.7**	29	62.1	8	**87.5**
Treatment dependency	SR	53. Successful discontinuation of lens therapy or "special glasses" (for any strabismus type)	*Successful discontinuation of lens therapy or "special glasses" such as bifocals or minus lenses*	49	40.8	4	**100**	28	46.4	6	**83.3**
	SR	54. Successful discontinuation of lens therapy or "special glasses" (for certain strabismus types? please specify)	*Successful discontinuation of lens therapy or "special glasses" such as bifocals or minus lenses*	49	51.0	N/A	N/A	28	64.3	N/A	N/A
	PO	55. Successful discontinuation of prism therapy	*Successful discontinuation of prism therapy*	52	46.2	4	**100.0**	29	51.7	6	**83.3**
Adverse events	SR	56. Adverse effects from treatment (any)	*Adverse effects from treatment (any)*	53	**83.0**	10	60.0	29	**93.1**	9	55.6
	FG	57. Adverse effect on vision from patches or prisms used to treat diplopia	*Adverse effect on vision from patches or prisms used to treat diplopia such as vision degradation or psychosocial effects*	53	67.9	7	42.9	29	**75.9**	6	**83.3**
	SR	58. Intolerable diplopia	*Intolerable double vision*	53	**98.1**	11	**81.8**	29	**96.6**	9	**77.8**
	SR	59. Induced ptosis (post toxin injection)	*Appearance of transient droopy eye lid as a result of using toxin injection to treat squint*	52	51.9	7	57.1	29	55.2	8	62.5
	SR	60. Induced subconjunctival haemorrhage	*Appearance of a bleed in the surface of the eye after squint surgery or injection*	52	32.7	9	33.3	29	20.7	8	37.5
	SR	61. Discomfort or abnormal sensation	*Discomfort or pain during/after treatment of squint*	53	28.3	9	44.4	29	17.2	8	37.5
	SR	62. Overcorrection or under correction of the deviation with surgery or injection	*Persistence of the squint at a lesser extent or appearance of deviation in the opEOsite direction*	52	**71.2**	9	55.6	29	**79.3**	9	66.7
	SR	63. Recurrence of deviation	*Reappearance of the squint after treatment*	53	66.0	9	**77.8**	29	**75.9**	9	**88.9**

	SR	64. Induced vertical deviation	*Appearance of a vertical squint after treatment of a horizontal deviation*	53	69.8	8	**75.0**	29	**82.8**	9	**77.8**
	SR	65. Induced A or V pattern	*Appearance of a deviation that increases either on looking up or looking down*	53	54.7	9	66.7	29	65.5	8	**75.0**
	SR	66. Development of DVD	*Appearance of a tendency for the eye to move up and out when covered*	50	46.0	6	16.7	29	34.5	8	37.5
	SR	67. Induced incomitance	*Development of variation of the eye deviation in different EOsitions when looking around*	53	56.6	7	**71.4**	29	62.1	7	**71.4**
	SR	68. Number of operations/procedures needed	*Number of operations/procedures needed*	53	66.0	9	66.7	29	65.5	8	62.5
Cost	SR	69. Economic data (in general)	*Economic data (in general) including services and families/individuals*	45	44.4	11	36.4	27	37.0	9	33.3
	SR	70. Cost of treatment on services	*Cost of treatment on services*	45	46.7	11	18.2	27	44.4	9	33.3
	SR	71. Cost of treatment on families/ individuals	*Cost of treatment on families/individuals*	45	40.0	11	45.5	26	38.5	9	22.2
Long-term outcomes	SR	72. Long-term outcomes	*Long-term outcomes (clinical outcomes)*	50	**88.0**	11	**90.9**	29	**96.6**	9	**88.9**
	PT PART	73. Long term discomfort from scar tissue **		N/A	N/A	N/A	N/A	N/A	N/A	9	55.6

Ocular motility disorders

Domain	Source	Outcome	Lay-term summary	Delphi results							
				Round 1				Round 2			
				HCPs		Patients		HCPs		Patients	
				n	% (7-9)	n	%	n	% (7-9)	n	% (7-9)
Symptoms	SR	1. Patient symptoms	*Symptoms or complaints related to vision or eyes*	50	**92.0**	9	**88.9**	29	**96.6**	5	**100.0**
	SR	2. Improvement in diplopia (in general)	*Improvement in double vision in general*	50	**90.0**	8	**100.0**	29	**100.0**	5	**100.0**
	SR	3. Improvement of diplopia in primary gaze	*Improvement of double vision when looking straight ahead*	50	**94.0**	8	**87.5**	29	**100.0**	5	**100.0**
	SR	4. Improvement in diplopia in primary and down gaze	*Improvement in double vision when looking straight ahead and down (reading position)*	50	**88.0**	7	**85.7**	29	**100.0**	5	**100.0**
	SR	5. Improvement in diplopia in primary and down gaze with prisms	*Improvement in double vision when looking straight ahead and down with prisms*	50	**86.0**	4	**75.0**	29	**96.6**	5	**100.0**
	SR	6. Severity and duration of visual symptoms/eye deviation	*Severity and duration of visual symptoms/eye deviation*	50	**78.0**	9	**77.8**	29	**79.3**	5	**100.0**
	SR	7. Appearance of the eye deviation	*Appearance of the eye deviation*	50	**74.0**	9	33.3	29	**79.3**	5	60.0
	SR	8. Reduction in pain (for certain types of ocular motility disorders? please specify)	*Reduction in pain*	49	**75.5**	4	50.0	29	**89.7**	4	**100.0**
	SR	9. Improvement in oscillopsia/blur and vertigo in adults (in nystagmus)	*Improvement in oscillopsia/blur and vertigo in adults (in nystagmus)*	50	**92.0**	6	66.7	29	**100.0**	5	**100.0**
	FG	10. Improvement in headaches (for certain types of ocular motility disorders? please specify)	*Improvement in headaches*	50	**80.0**	6	50.0	29	**79.3**	4	40.0
Visual function	SR	11. Best corrected visual acuity	*Vision measured at distance for one eye at a time corrected with glasses*	50	60.0	7	42.9	29	69.0	5	60.0

	SR	12. Near visual acuity	*Close up or reading vision*	50	44.0	8	62.5	29	48.3	5	60.0
	PO	13. Habitual visual acuity	*Vision measured in the usual preferred state for a person*	44	50.0	7	**71.4**	29	69.0	5	**80.0**
	PO	14. Uncorrected visual acuity	*Vision without glasses or contact lenses*	50	6.0	7	28.6	29	0.0	5	20.0
	SR	15. Binocular BCVA	*Vision measured at distance with both eyes open at the same time corrected with glasses*	49	57.1	5	**80.0**	28	**71.4**	5	**100.0**
	SR	16. Suppression	*Testing if the person has developed "suppression" of one image to improve double vision which usually happens in childhood as a coping mechanism from the brain to improve visual development*	50	46.0	3	33.3	29	48.3	3	66.7
	PO	17. Fixation	*Testing "fixation" which is if the person is using the central part of the retina to see with or alternatively using an eccentric part of the retina*	50	32.0	4	25.0	29	24.1	4	25.5
	PO	18. Contrast sensitivity	*Testing "contrast sensitivity" which is objects of varying brightness Contrast sensitivity*	49	6.1	3	33.3	28	0.0	3	20.0
	PO	19. Colour vision test (for any type of ocular motility disorder)	*Colour vision test*	50	8.0	5	60.0	29	0.0	5	20.0
	PO	20. Colour vision test (for certain types of ocular motility disorders? please specify)		49	36.7	N/A	N/A	29	31.0	N/A	N/A
	PO	21. Visual field test (for certain types of ocular motility disorders? please specify)	*Visual field test*	48	37.5	8	50.0	29	24.1	5	60.0
	SR	22. Broadening of the null region (in nystagmus)	*Broadening of the null region (in nystagmus)*	48	58.3	3	**100.0**	29	69.0	4	**100.0**
	SR	23. Reduce the amplitude of nystagmus (in nystagmus)	*Reduce the amplitude of nystagmus (in nystagmus)*	48	60.4	3	**100.0**	29	69.0	3	**100.0**
	SR	24. Stereo acuity	*Fine 3D vision or depth appreciation with both eyes or "stereo vision"*	50	62.0	8	**87.5**	29	**75.9**	5	**100.0**
	SR	25. Field of binocular single vision	*Testing the extent of area of vision where there is no double vision while looking around with both eyes open*	50	**70.0**	7	**71.4**	29	**86.2**	5	**80.0**
	PO	26. Post op diplopia test	*Testing if a person is likely to get double vision after correcting the eye deviation with surgery*	50	68.0	7	**100.0**	29	**82.8**	5	**100.0**
	SR	27. Simultaneous perception	*Testing lower levels of 3D vision*	50	48.0	7	42.9	29	41.4	5	60.0
	SR	28. Retinal correspondence		50	38.0	N/A	N/A	29	24.1	N/A	N/A
	SR	29. Refractive status (for any type of ocular motility disorder)	*Testing the amount of prescription of glasses or contact lenses*	50	46.0	6	50.0	29	37.9	5	40.0

	SR	30. Refractive status (for certain types of ocular motility disorders? please specify)		47	48.9	N/A	N/A	29	51.7	N/A	N/A
Oculomotor function	SR	31. Ocular alignment / deviation	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation*	47	**91.5**	7	**71.4**	29	**100.0**	5	**80.0**
	SR	32. Abnormal head posture	*The presence of a compensatory head posture to avoid double vision*	47	**76.6**	6	66.7	29	**89.7**	5	**80.0**
	FG	33. Ocular motor alignment at various positions specially where the deviation is greatest	*Assessing if the eyes are straight or deviated and measuring the amount of eye deviation at different positions*	47	**80.9**	N/A	N/A	29	**89.7**	N/A	N/A
	SR	34. Presence of incomitance (for any type of ocular motility disorder)	*Variation of angle of deviation at different positions of gaze*	47	63.8	6	66.7	29	**79.3**	3	66.7
	SR	35. Presence of incomitance (for certain types of ocular motility disorders? please specify)		44	**72.7**	N/A	N/A	28	**75.0**	N/A	N/A
	PO	36. Control of deviation (any type)	*Measuring how well the person can control the eye turn*	47	**83.0**	6	**83.3**	29	**89.7**	5	**100.0**
	PO	37. Control of deviation (for certain types of ocular motility disorders? please specify)		43	**83.7**	N/A	N/A	29	**96.6**	N/A	N/A
	SR	38. Ocular movement	*How well eyes move as a person is looking around*	47	**85.1**	8	62.5	29	**93.1**	5	**100.0**
	SR	39. Forced duction test (for any type of ocular motility disorder)	*A test done to check eye muscle action passively using forceps*	45	31.1	N/A	N/A	29	24.1	N/A	N/A
	SR	40. Forced duction test (for certain types of ocular motility disorders? please specify)		44	65.9	N/A	N/A	27	66.7	N/A	N/A
	SR	41. Three step/head tilt test (for any type of ocular motility disorder)	*A test to check eye deviation with head tilt and head turn in addition to the straight-ahead EOsition*	44	20.5	N/A	N/A	29	10.3	N/A	N/A
	SR	42. Three step/head tilt test (for certain types of ocular motility disorders? please specify)		45	66.7	N/A	N/A	28	60.7	N/A	N/A
	PO	43. Presence of dissociated vertical deviation (DVD)	*Presence of a tendency for the eye to move up and out when covered*	47	46.8	N/A	N/A	29	44.8	N/A	N/A
	SR	44. A or V pattern deviation	*Testing if the deviation increases on looking up or looking down*	47	55.3	7	57.1	29	62.1	5	40.0

	PO	45. Fusional vergence at near and distance /fusion amplitudes/prism fusion range	*Testing how well the eyes can control a deviation induced with prisms in clinic*	47	53.2	7	57.1	29	62.1	4	**75.0**
	SR	46. Reading eye movements (for any type of ocular motility disorders)	*Checking if eye movements are normal during reading*	45	22.2	7	**71.4**	29	20.7	5	60.0
	SR	47. Reading eye movements (for certain types of ocular motility disorders? please specify)		42	42.9	N/A	N/A	29	48.3	N/A	N/A
	SR	48. Presence of a phoria (for any type of ocular motility disorders)	*A test done to check if there is a hidden small eye alignment problem*	46	54.3	7	42.9	29	58.6	5	20.0
	SR	49. Presence of a phoria (for certain types of ocular motility disorders? please specify)		41	56.1	N/A	N/A	28	**71.4**	N/A	N/A
	SR	50. Objective extortion (for any type of ocular motility disorders)	*Checking if the eye is rotated outwards due to a muscle problem (tested in clinic without the need of patient response)*	43	25.6	7	42.9	28	25.0	5	20.0
	SR	51. Objective extortion (for certain types of ocular motility disorders? please specify)		41	58.5	N/A	N/A	27	66.7	N/A	N/A
	SR	52. Subjective extortion (for any type of ocular motility disorders)	*Check if the eye is rotated outward due to a muscle problem (tested in clinic and results depend on patient response)*	44	50.0	7	42.9	28	60.7	4	25.0
	SR	53. Subjective extortion (for certain types of ocular motility disorders? please specify)		41	**73.2**	N/A	N/A	27	**92.6**	N/A	N/A
	SR	54. Near point of convergence (for any type of ocular motility disorders)	*Testing if the eyes can normally look inwards to see a near object to an acceptable amount*	47	34.0	8	50.0	29	34.5	5	40.0
	SR	55. Near point of convergence (for certain types of ocular motility disorders? please specify)		41	63.4	N/A	N/A	28	**78.6**	N/A	N/A
	SR	56. Accommodation (for any type of ocular motility disorders)	*Testing if the eyes can change their focus appropriately to see objects at varying distances*	46	15.2	8	62.5	29	13.8	5	60.0

	SR	57. Accommodation (for certain types of ocular motility disorders? please specify)		42	42.9	N/A	N/A	28	46.4	N/A	N/A
	SR	58. Dynamic retinoscopy (for certain types of ocular motility disorders? please specify)	*Changing refractive power of the eye with varying focus*	42	19.0	N/A	N/A	27	37.0	N/A	N/A
	SR	59. Pursuits (for certain types of ocular motility disorders? please specify)	*Testing a specific tracking slow movement of the eye for an object*	45	64.4	7	42.9	28	60.7	5	40.0
	SR	60. Saccades (for certain types of ocular motility disorders? please specify)	*Testing a specific rapid tracking eye movement for an object*	45	62.2	7	57.1	28	67.9	5	60.0
	SR	61. Optokinetic nystagmus (OKN)	*Special tracking eye movement using a striped drum*	46	34.8	N/A	N/A	29	31.0	N/A	N/A
Additional clinical signs	SR	62. Eye movement recordings (for certain types of ocular motility disorders? please specify)	*Eye movement recordings*	40	27.5	7	42.9	28	32.1	5	40.0
	SR	63. Palpebral fissure size/lid position (for certain types of ocular motility disorders? please specify)	*Checking eye lid position - whether it is droopy or elevated compared to normal*	44	63.6	5	40.0	29	65.5	5	40.0
	SR	64. Facial asymmetry (for 4th n palsy)	*Checking if the sides of the face are symmetrical or not to help diagnose some congenital motility disorders*	45	33.3	4	50.0	29	20.7	4	25.0
	SR	65. Pupil examination (for any type of ocular motility disorders)	*To check pupil size; reaction etc*	44	45.5	6	50.0	29	41.4	5	20.0
	SR	66. Pupil examination (for certain types of ocular motility disorders? please specify)		43	**74.4**	N/A	N/A	29	**79.3**	N/A	N/A
	SR	67. Proptosis/exophthalmos (for certain types of ocular motility disorders? please specify)	*Checking if the eyes are protruding out of their position*	44	**79.5**	4	**75.0**	29	**86.2**	5	60.0
	SR	68. Intraocular pressure (for certain types of ocular motility disorders? please specify)	*Check eye pressure*	43	48.8	5	**80.0**	28	42.9	4	**100.0**

	SR	69. Corneal exposure (for certain types of ocular motility disorders? please specify)	*Checking for corneal changes resulting from incomplete eyelid closure*	42	**76.2**	4	**75.0**	28	**96.4**	5	**80.0**
	SR	70. Corneal sensitivity (for certain types of ocular motility disorders? please specify)	*Checking if corneal nerve supply is intact*	39	66.7	4	**75.0**	28	67.9	5	**100.0**
	SR	71. Canthal displacement (for certain types of ocular motility disorders? please specify)	*Change in position of the eye contour*	32	28.1	N/A	N/A	23	21.7	N/A	N/A
	SR	72. Oculocardiac reflex (for certain types of ocular motility disorders? please specify)	*Slowing of the heart rate due to entrapped eye muscle*	28	32.1	N/A	N/A	22	36.4	N/A	N/A
	SR	73. Globe dystopia (for certain types of ocular motility disorders? please specify)	*Check the position of the eyeball in relation to the other eye and other parts of the face*	33	39.4	5	60.0	22	36.4	4	50.0
	SR	74. Enophthalmos (for certain types of ocular motility disorders? please specify)	*Checking if the eyes are sinking in from their normal position*	42	66.7	4	**75.0**	29	**82.8**	5	**80.0**
Clinical investigations	SR	75. Assessment for fractures and soft-tissue herniation for example inferior rectus muscle; fat; or connective tissue radiographically (for certain types of ocular motility disorders? please specify)	*Assessment for fractures and soft-tissue herniation for example inferior rectus muscle; fat; or connective tissue radiographically*	41	**87.8**	3	66.7	29	**96.6**	4	**75.0**
	SR	76. Assessment for muscle atrophy or absent nerve radiographically (for certain types of ocular motility disorders? please specify)	*Assessment for muscle atrophy or absent nerve radiographically*	35	65.7	5	60.0	26	69.2	4	**75.0**
	SR	77. Histologic examination of excised tissue (for certain types of ocular motility disorders? please specify)	*Histologic examination of excised tissue*	26	57.7	N/A	N/A	24	**75.0**	N/A	N/A
Quality of life	SR	78. Quality of life measures (in general)	*Health related quality of life (all relevant aspects)*	45	**82.2**	8	**87.5**	29	**93.1**	5	**100.0**

	FG	79. Psychological impact of the disorder	*Negative impact of eye motility problem on emotions and/or behaviour*	45	**84.4**	8	**100.0**	29	**96.6**	5	**100.0**
	FG	80. Psychological impact of treatment of disorder	*Positive impact of treatment on emotions and/or behaviour*	45	**77.8**	N/A	N/A	29	**93.1**	N/A	N/A
	FG	81. Social anxiety and social avoidance due to the disorder	*Negative impact of eye motility problem on social interaction or causing social stigma*	45	**77.8**	8	**100.0**	29	**89.7**	5	**100.0**
	FG	82. Academic/ occupation achievement in relation to the condition or its treatment	*Academic/ occupation achievement in relation to the condition or its treatment*	44	**72.7**	8	**87.5**	29	**79.3**	5	**80.0**
	FG	83. Activity of daily living (ADL)	*Activity of daily living (ADL) such as driving*	45	**80.0**	8	**100.0**	29	**93.1**	5	**100.0**
	SR	84. Patient satisfaction from treatment	*Patient satisfaction from treatment*	45	**82.2**	8	**87.5**	29	**93.1**	5	**80.0**
	FG	85. Future functionality/long-term impact	*Future functionality/long-term impact (patient-reported)*	44	**86.4**	8	**100.0**	29	**96.6**	5	**100.0**
Compliance	SR	86. Compliance	*How well the treatment is done*	42	54.8	7	**71.4**	29	65.5	5	**80.0**
Treatment dependency	PO	87. Successful discontinuation of glucocorticoids (in orbital inflammatory conditions such as thyroid eye disease)	*Successful discontinuation of lens therapy or* glucocorticoids *(in orbital inflammatory conditions such as thyroid eye disease)*	34	64.7	3	66.7	25	**76.0**	4	50.0
	PO	88. Successful discontinuation of lens therapy or "special glasses"	*Successful discontinuation of lens therapy or "special glasses" such as bifocals or minus lenses*	43	51.2	4	50.0	29	58.6	4	50.0
	PO	89. Successful discontinuation of prism therapy	*Successful discontinuation of prism therapy*	44	56.8	3	66.7	29	69.0	3	66.7
Adverse events	SR	90. Adverse effects from treatment (any)	*Adverse effects from treatment (any)*	44	**79.5**	8	**100.0**	29	**82.8**	5	**100.0**
	FG	91. Adverse effect on vision from patches or prisms used to treat diplopia	*Adverse effect on vision from patches or prisms used to treat diplopia such as vision degradation or psychosocial effects*	44	56.8	5	40.0	29	**82.8**	5	**80.0**
	PO	92. Intolerable diplopia	*Intolerable double vision*	44	**97.7**	7	**100.0**	29	**100.0**	5	**100.0**
	PO	93. Induced ptosis (Post toxin injection)	*Appearance of transient droopy eye lid as a result of using toxin injection to treat squint*	43	48.8	5	**80.0**	29	62.1	5	**80.0**
	PO	94. Induced subconjunctival haemorrhage	*Appearance of a bleed in the surface of the eye after squint surgery or injection*	44	34.1	7	57.1	28	32.1	5	**80.0**
	PO	95. Discomfort or abnormal sensation	*Discomfort or pain during/after treatment of squint*	43	39.5	7	**85.7**	29	48.3	5	**100.0**

	PO	96. Overcorrection or under correction of the deviation with surgery or injection	*Persistence of the squint at a lesser extent or appearance of deviation in the opposite direction*	44	**72.7**	6	**83.3**	29	**75.9**	5	60.0
	PO	97. Recurrence of deviation	*Reappearance of the squint after treatment*	44	**70.5**	8	**75.0**	29	**79.3**	5	**100.0**
	PO	98. Induced vertical deviation	*Appearance of a vertical squint after treatment of a horizontal deviation*	44	63.6	5	40.0	29	65.5	5	40.0
	PO	99. Induced A or V pattern	*Appearance of a deviation that increases either on looking up or looking down*	44	59.1	6	33.3	29	48.3	5	40.0
	PO	100. Development of DVD	*Appearance of a tendency for the eye to move up and out when covered*	44	31.8	5	60.0	29	27.6	5	40.0
	PO	101. Induced incomitance	*Development of variation of the eye deviation in different positions when looking around*	44	56.8	6	66.7	29	58.6	5	60.0
	PO	102. Number of operations needed	*Number of operations/procedures needed*	44	68.2	8	**87.5**	29	**75.9**	5	**80.0**
Cost	PO	103. Economic data (in general)	*Economic data (in general) including services and families/individuals*	39	48.7	8	**75.0**	27	59.3	5	**100.0**
	PO	104. Cost of treatment on services	*Cost of treatment on services*	39	46.2	8	50.0	27	51.9	5	60.0
	FG	105. Cost of treatment on families/individuals	*Cost of treatment on families/individuals*	39	41.0	8	**75.0**	27	48.1	5	**80.0**
Long-term	SR	106. Long-term outcomes	*Long-term outcomes (clinical outcomes)*	44	**88.6**	8	**87.5**	29	**96.6**	5	**100.0**

SECTION/TOPIC	ITEM No.	CHECKLIST ITEM	REPORTED ON PAGE #
TITLE/ABSTRACT			
Title	1a	Identify in the title that the paper reports the development of a COS	1
Abstract	1b	Provide a structured summary	2-3
INTRODUCTION			
Background and objectives	2a	Describe the background and explain the rationale for developing the COS	3-4
	2b	Describe the specific objectives with reference to developing a COS	4
Scope	3a	Describe the health condition(s) and population(s) covered by the COS	4
	3b	Describe the intervention(s) covered by the COS	4
	3c	Describe the setting(s) in which the COS is to be applied	4
METHODS			
Protocol/Registry Entry	4	Indicate where the COS development protocol can be accessed, if available and/or the study registration details	7
Participants	5	Describe the rationale for stakeholder groups involved in the COS development process, eligibility criteria for participants from each group and a description of how the individuals involved were identified	5
Information sources	6a	Describe the information sources used to identify an initial list of outcomes	4-5
	6b	Describe how outcomes were dropped/combined, with reasons (if applicable)	5-6
Consensus process	7	Describe how the consensus process was undertaken	5-7
Outcome scoring	8	Describe how outcomes were scored and scores summarised	6-7
Consensus definition	9a	Describe the consensus definition	Table 1
	9b	Describe the procedure for determining how outcomes were included or excluded from consideration during the consensus process	7
Ethics and consent	10	Provide a statement regarding the ethics and consent issues for the study	7
RESULTS			
Protocol deviations	11	Describe any changes from the protocol (if applicable), with reasons, and a describe what impact these changes have on the results	N/A

Participants	12	Present data on the number and relevant characteristics of the people involved at all stages of COS development	8-9
Outcomes	13a	List all outcomes considered at the start of the consensus process	Supplementary Table 1
	13b	Describe any new outcomes introduced and any outcomes dropped, with reasons, during the consensus process	8-9
Core outcome set	14	List the outcomes in the final core outcome set	11 & Table 2
DISCUSSION			
Limitations	15	Discuss any limitations in the COS development process	11
Conclusions	16	Provide an interpretation of the final COS in the context of other evidence, and implications for future research	12-13
OTHER INFORMATION			
Funding	17	Describe sources of funding, role of funders	1
Conflicts of interest	18	Describe any conflicts of interest within the study team and how these were managed	1