



# Visual Impairment Following Stroke - The Impact on Quality of Life: A Systematic Review

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## Authors' contributions

*This work was carried out in collaboration between both authors. Author LRH ran searches, identified relevant studies, acted as first review author, extracted data, entered data, provided content expertise and co-wrote the final drafts. Author FJR led this review, provided methodological expertise, acted as a second review author. Both authors read and approved the final manuscript.*

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## ABSTRACT

**Background:** The visual impairments caused by stroke have the potential to affect the ability of an individual to perform activities of daily living. An individual with visual impairment may also have reduced level of independence. The purpose of this review was to investigate the impact on quality of life from stroke related visual impairment, using subjective patient reported outcome measures.

**Methods:** A systematic search of the literature was performed. The inclusion criteria required studies to have adult participants (aged 18 years or over) with a diagnosis of a visual impairment directly resulting from a stroke. Studies which included visual impairment as a result of other intracranial aetiology, were included if over half of the participants were stroke survivors. Multiple scholarly online databases and registers of published, unpublished and ongoing trials were searched, in addition articles were hand searched. MESH terms and alternatives in relation to stroke and visual conditions were used. Study selection was performed by two authors independently. Data was extracted by one author and verified by a second. The quality of the evidence was assessed using a quality appraisal tool and reporting guidelines.

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**Results:** This review included 11 studies which involved 5646 participants, the studies used a mixture of generic and vision-specific instruments. The seven instruments used by the included studies were the EQ-5D, LIFE-H, SF-36, NEI VFQ-25, VA LV VFQ-48, SRA-VFP and DLTV. **Conclusion:** A reduction in quality of life was reported by all studies in stroke survivors with visual impairment. Some studies used generic instruments, therefore making it difficult to extract the specific impact of the visual impairment as opposed to the other deficits caused by stroke. The majority of studies (8/11) primarily had participants with visual field loss. This skew towards visual field loss and no studies investigating the impact ocular motility prevented a comparison of the effects on quality of life due to different visual impairments caused by stroke. In order to fully understand the impact of visual impairment following stroke on quality of life, further studies need to use an appropriate vision-specific outcome measure and include all types of visual impairment which can result from a stroke.

*Keywords: Stroke; visual impairment; quality of life; impact; review.*

## 1. BACKGROUND

Visual impairment as a result of a stroke takes many different guises across four main categories: Central vision loss, visual field loss, visual perception problems and ocular motility defects. All these impairments have the potential to affect the ability of an individual to perform activities of daily living (ADLs) for example mobility, social interaction and self-care. An individual with visual impairment may also have reduced level of independence. A combination of limitations has the potential to have an effect on an individual's mood and motivation. These effects have been reported in populations with visual impairment [1-4].

The World Health Organisation (WHO) defines health as "a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity" [5]. The assessment of quality of life could be seen as a measurement of the subjective perceptions of an individual of how they are effected by their health state [1].

The analysis of utility values of diabetic retinopathy and age-related macular degeneration revealed the impact on quality of life was associated with the severity of impairment rather than the cause [6]. However, it has also been shown that there is not a consistent trend between severity of symptoms and reduction in quality of life. The individuals with the most severe visual impairment may not report the poorest quality of life but those with a slight impairment may [7]. This highlights the importance of patient reported outcomes as part of clinical and research assessments.

Stroke is a complex condition; an individual can be affected by a wide range of problems, for example physical disability (hemiplegia), communication disability (aphasia), feeding disability (dysphagia), cognitive disability, and visual impairment. It is important to establish the impact of the various components of stroke in order to evaluate interventions which are aimed at one of the specific disabilities [8].

The aim of this review is to summarise the impact of stroke related visual impairment on quality of life.

## 2. METHODS

We conducted an integrative review, aiming to bring together all evidence relating to impact of stroke-related visual problems.

### 2.1 Inclusion Criteria for Considering Studies for this Review

#### 2.1.1 Types of studies

The following types of studies were included: randomised controlled trials, controlled trials, prospective and retrospective cohort studies and observational studies. Case reports were excluded. All languages were included and translations obtained when necessary.

#### 2.1.2 Types of participants

We included studies of adult participants (aged 18 years or over) diagnosed with a visual impairment as a direct result of a stroke. Studies which included mixed populations were included if over 50% of the participants had a diagnosis of stroke and data were available for this subgroup.

### **2.1.3 Types of outcome and data**

A formal quality of life assessment using a patient reported outcome measure (PROM). Studies which are assessing an intervention and have used a PROMs before and after, were included if the results prior to treatment were available for comparison to other studies.

## **2.2 Search Methods for Identification of Studies**

We used systematic strategies to search key electronic databases and contacted known individuals conducting research in stroke and visual impairment. We searched Cochrane registers and electronic bibliographic databases (Appendix 1). In an effort to identify further published, unpublished and ongoing trials, we searched registers of ongoing trials, hand-searched journals and conference transactions, performed citation tracking using Web of Science Cited Reference Search for all included studies, searched the reference lists of included trials and review articles about vision after acquired brain injury and contacted experts in the field (including authors of included trials, and excluded studies identified as possible preliminary or pilot work). Search terms included a comprehensive range of MeSH terms and alternatives in relation to stroke and visual conditions (Appendix 1).

## **2.3 Selection of Studies**

The titles and abstracts identified from the search were independently screened by the two authors using the pre-stated inclusion criteria. The full papers of any studies considered potentially relevant were then considered and the selection criteria applied independently by the two authors.

## **2.4 Data Extraction**

A pre-designed data extraction form was used which gathered information on sample size, study design, quality of life instrument used, visual conditions reported and population type. Data was extracted and documented by one researcher (LH) and verified by another (FR).

## **2.5 Quality Assessment**

To assess the quality of the studies included in this review, an adapted version of a checklist

was used: The STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) checklist [9,10]. The checklist was adapted as the original was designed to assess the quality of reporting rather than the potential for bias within a study. There is currently no 'gold standard' quality assessment tool for observational studies [11]. The STROBE Statement covers 22 items covering introduction, method, results and discussion of observation studies (including cohort, case-control and cross-sectional studies) (Appendix 2). The adapted version used in this review included 18 items, only the information which is pertinent to quality appraisal of the studies was included. The items exclude which were not considered relevant information, such as the title, abstract, background, setting and funding.

## **3. RESULTS AND DISCUSSION**

### **3.1 Results of the Search**

The search results are outlined in Fig. 1. Eleven studies (5646 participants) were included. Of the 11 included studies, ten were prospective observational studies and one was a retrospective analyses. Seven different questionnaires were used in the included studies to report quality of life in stroke survivors with visual impairment.

### **3.2 Quality of the Evidence**

Two of the eleven papers reported 100% of the items requested by the STROBE checklist [12]. Eight of the eleven papers reported 90% or more of the requested items, ten of the eleven papers reported 75% or more. All eleven papers reported 73% or more. The majority of papers (81%) reported limitations of their studies. Results from all papers were reported and the individual results for each paper are outlined in Table 1.

### **3.3 Quality of Life Assessment for Stroke Survivors with Visual Impairment**

Eight studies investigating quality of life following stroke were focused on patients with visual field loss [12-19]. Homonymous hemianopia is the most common type of visual field loss following stroke. Other types of defect are possible including homonymous quadrantanopia, general constriction and scotomas [19]. Of the remaining

studies, Ali et al. [20] and Rowe et al. [21] address a combination of visual impairments following stroke while Beaudoin et al. [22] focused on visual perception problems.

The included studies used both generic health-related instruments and/or vision specific instruments which were administered to stroke survivors.

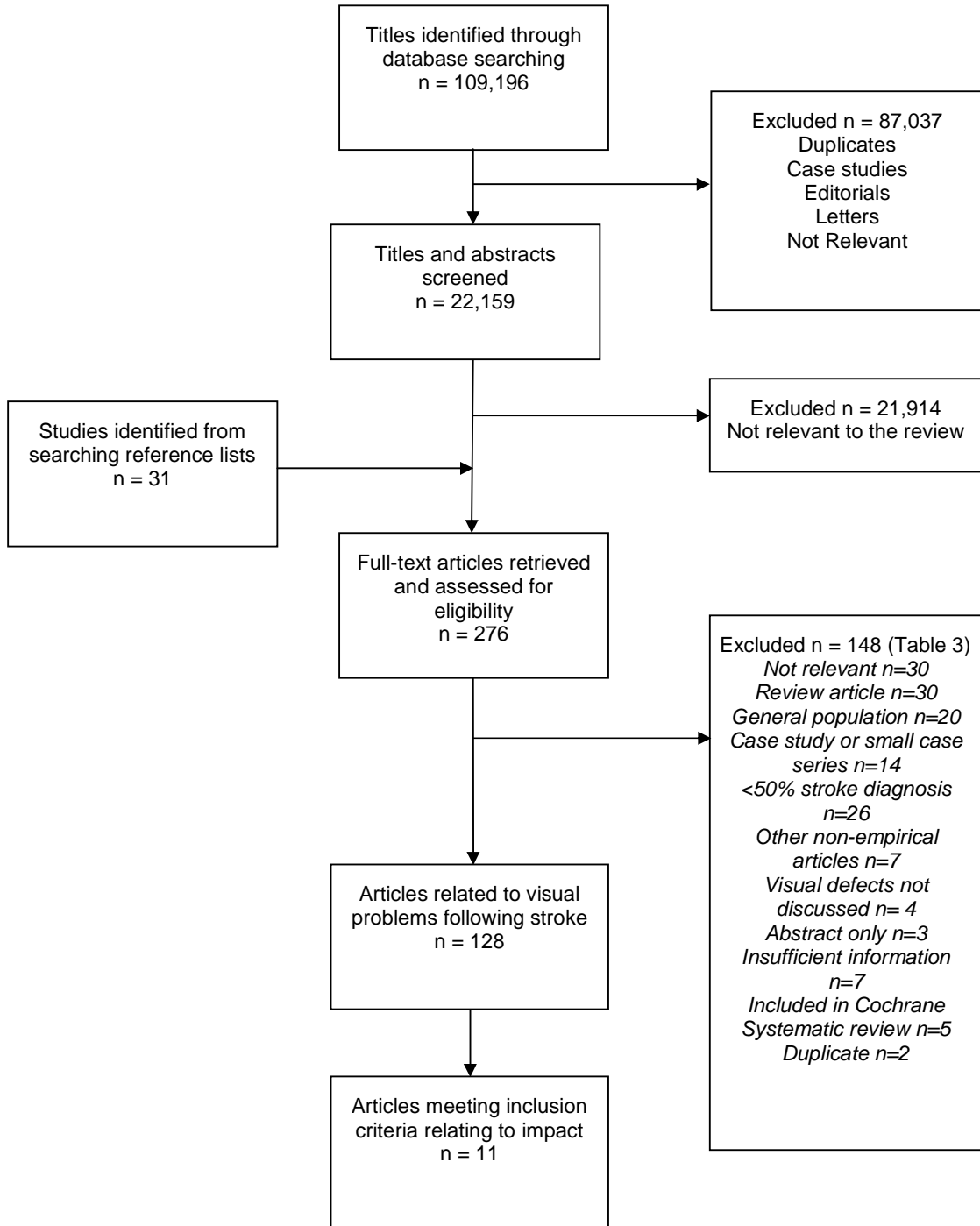


Fig. 1. Flowchart of the pathway for inclusion of articles

### **3.3.1 Generic Health-related Instruments**

The European Quality of Life Score (EQ-5D), the Medical-Outcome-Study Short-Form-36 Health Survey (SF-36) and the Assessment of Life Habits (LIFE-H) have been used to assess quality of life in individuals with visual impairment post-stroke. More details about these instruments can be viewed in Table 2. They are generic health-related instruments and are not vision specific. Generic instruments include items which are relevant to broad definition of health 'physical, mental and social well-being' (WHO, 1946). This allows comparisons to be made not only within a disease group but across difference disease groups; for example the EQ-5D is currently used in the NHS PROMs programme before and after four common surgeries (hip replacement, knee replacement, hernia repair and varicose vein surgery) [23]. However, they may not be sensitive to specific symptoms caused by visual impairment.

The EQ-5D was reported to show that participants (n=3,859) with visual impairment following stroke had a poorer quality of life at baseline assessment after adjustment for age, thrombolysis treatment, other stroke non-visual related impairment and other medical conditions [20]. Visual impairment was assessed by using the National Institute of Health Stroke Scale (NIHSS), which only tests for homonymous visual field loss and horizontal gaze defects. Therefore, it misses many other forms of visual impairment thus, it is not possible for this study to give an overview of the impact of visual impairment following stroke. It reported that participants with conjugate deviations had reduced scores in all domains with the exception of anxiety/depression. Participants with hemianopia were reported to have reduced scores in self-care and usual activities. If the visual impairment was persistent to 90 days post-stroke onset, those participants had poorer outcomes in all domains for participants with hemianopia and four out of five for participants with gaze palsies with the exception of pain and anxiety/depression [20].

The LIFE-H reported the participants' (n=93) quality of life to be persistently reduced in the presence of perceptual difficulties post-stroke compared to a group (n=96) without visuo-perceptual deficits [22]. This difference was still present when controlling for the use of a walking aid and previous stroke events. The greatest difference was in socialisation rather than activities of daily living. This was shown at all

three time points (n=57) of 18-24 days following discharge (baseline), then at three months and six months following baseline [22].

The domains relating to employment and education were not included as part of this study, however, with the increasing number stroke survivors of working age, these areas are critical to examining how a visual defect affects all areas of life.

The SF-36 has been used by three studies in conjunction with the NEI-VFQ and compared against healthy controls [12,16,17]. In each study stroke survivors with visual field defects were reported to have reduced scores in seven out of eight subscales (the exception being role limitation due to emotional problems). Participants with visual field defects were also reported to score better than general stroke survivors one month post-stroke without visual field defects [16]. However, when compared to general stroke survivors six months post-stroke without visual field defects, the participants with visual field defects had a reduced health-related quality of life [12,16]. When the composite scores of participants were compared with stroke survivors with different lesion ages (3, 6 and 12 months post-stroke onset), those with visual field defects scored better in the physical composite score and worse in the mental composite score [12]. Individuals with visual field defects in combination with reduced visual acuity are reported to have a further reduction of scores across four sub-scales: physical functioning, vitality, social functioning and emotional well-being [12]. The comparison groups used by these studies were from previously published data and therefore were not matched.

### **3.3.2 Vision-specific instruments**

The National Eye Institute Visual Function Questionnaire (NEI VFQ-25), the Veterans Low Vision Visual Function Questionnaire (VA LV VFQ-48), the Self-Reported Assessment of Functional Visual Performance (SRAFVP) and the Daily Living Tasks Dependent on Vision (DLTV) have been used to assess quality of life in individuals with visual impairment post-stroke. More details about these instruments can be viewed in Table 2. Vision-specific instruments come under the wider disease-specific instruments umbrella and are tailored to assess quality of life in individuals with visual impairment. They can be more clinically sensitive to changes in visual impairment than generic instruments [24].

Table 1. Quality appraisal of papers using the adapted STROBE checklist

	Intro		Methods							Results				Discussion				
	3 - Objectives	4 - Study design	6 - Participants	7 - Variables	8 - Data source	9 - Bias	10 - Study size	11 - Quantitative variables	12 - Statistical methods	13 - Participants	14 - Descriptive data	15 - Outcome data	16 - Main results	17 - Other analyses	18 - Key results	19 - Limitations	20 - Interpretation	21 - Generalisability
Ali et al. 2013 [20]	+	+	+	+	+	-	+	-	-	?	?	+	+	+	+	+	+	+
Beaudoin et al. 2013 [22]	+	+	+	+	+	+	-	+	-	+	+	+	+	+	+	+	+	+
Chen et al. 2009 [15]	+	+	+	+	+	-	-	+	+	+	+	+	+	n/a	+	-	+	+
Gall et al. 2008 [17]	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
Gall et al. 2009 [16]	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	+
Gall et al. 2010 [12]	+	+	+	+	+	+	+	+	+	+	+	+	+	n/a	+	+	+	+
George et al. 2011 [14]	+	+	+	+	+	-	-	+	+	+	+	+	+	+	+	+	+	+
Mennem et al. 2012 [13]	+	+	+	+	+	+	-	+	+	?	+	+	+	n/a	+	+	+	+
Papageorgiou et al. 2007 [18]	+	+	+	+	+	-	-	+	+	-	+	+	+	+	+	+	+	+
Rowe et al. 2013 [19]	+	+	+	+	+	-	+	+	+	-	+	+	+	n/a	+	+	+	+
Rowe et al. 2013 [21]	+	+	+	+	+	-	+	+	+	+	+	+	+	+	+	+	+	+

- = Not reported      ? = Unclear      + = Reported

**Table 2. Patient Reported Outcome Measures (PROMs) used with stroke survivors**

<b>Questionnaire</b>	<b>Type of instrument</b>	<b>Overview</b>	<b>References</b>
EQ-5D	Generic	5-item instrument, comprising of 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression with an additional health analogue scale.	Ali et al. 2013 [20]
LIFE-H	Generic	77-item instrument comprising of 12 domains split equally between daily activities and social roles.	Beaudoin et al. 2013 [22]
SF-36	Generic	36-item general health instrument consisting of 8 domains. Widely used in health research.	Gall et al. 2010 [12]
NEI-VFQ	Vision-specific	25-item short version instrument, composed of 11 vision-related subscales with an additional question for general health rating. Used to assess many different ocular conditions.	Chen et al. 2009 [15] Gall et al. 2008; 2009; 2010 [12,16,17] George et al. 2011 [14] Papageorgiou et al. 2007 [18]
SRA-FVP	Vision-specific	38 item instrument covering a range of activities of daily living.	Mennem et al. 2012 [13]
VA LV VFQ	Vision-specific	48 item instrument, composed of five domains: visual ability, reading, mobility, visual motor and visual information. Originally developed and validated with patients with ophthalmic pathology such as glaucoma, macular degeneration and diabetic retinopathy	Chen et al. 2009 [15] George et al. 2011 [14]
DLTV	Vision-specific	24-item instrument which are not categorised under named domains, but covers topics such as reading, mobility, self-care and recognition. Originally developed for individuals with macular degeneration.	Rowe et al. 2013 [19,21]

The most commonly used instrument is the NEI VFQ-25, and it is regarded to have good sensitivity to changes in visual impairment [25]. Six studies using the NEI VFQ-25 concentrated on visual field loss post-stroke [12,14-18]. Five studies compared the scores from the NEI VFQ-25 of individuals with visual field loss post stroke and a reference health population and reported a reduced quality of life for those with visual field loss [12,15-18]. Gall et al. [17] also compared the scores of individuals with visual field loss post-stroke to individuals diagnosed with glaucoma and reported the former group to have a poorer quality of life.

The studies reported reduction in several sub-scales in addition to the composite score. The number of affected sub-scales varied from seven up to all 12 sub-scales. Five subscales in common were found to have a significant difference between individuals with visual field loss post-stroke and healthy individuals: General health, general vision, near activities, vision-specific mental health, driving, and peripheral vision [12,15-18]. Chen et al. [15] performed a multivariate analysis, adjusting for visual acuity, reading ability, contrast sensitivity and any pre-existing ocular conditions which changed the sub-scales and were deemed significantly

different between the hemianopia and control group. Considering that the study had a very small sample size (n=10), following the multivariate analysis both the NEI VFQ-25 and VA LVQ-48 had a decreased in the number of subscales which were significantly affected, to five and one respectively. The factors adjusted for would not all be considered confounding factors but instead could also be a result of stroke and hemianopia, for example reduced reading ability [21]. The results following this multivariate analysis should be viewed as an assessment of quality of life with an isolated factor of hemianopia rather than visual impairment following stroke.

Five studies used a combination of instruments; two studies used the NEI-VFQ-25 in conjunction with the VA LV VFQ-48 [14,15]. A further three studies used the NEI-VFQ-25 in conjunction with the SF-36 [12,16,17].

Two of the studies investigated the effect of varying degrees of visual field loss post-stroke [12,17]. They reported that those with a greater area of spared central visual field had a better scores in the composite score and the following subscales: distance vision, social functioning and colour vision [12]. Individuals with a quadrantanopia had similar scores to individuals diagnosed with glaucoma, therefore, were less affected than those with hemianopia [17].

Several visual conditions can co-exist post stroke and this has the potential to have a larger impact on quality of life [26]. The presence of visual neglect has been shown to have a negative effect on the general health and mental health domains of the NEI VFQ-25 [16]. However, in the majority of domains participants with combined neglect and visual field loss were reported to have better quality of life than those with visual field loss without neglect. An explanation for this may be that those with visual neglect are less aware of their defect than those with visual field loss alone [21].

Two studies compared and reported the quality of life impact in individuals with visual field loss post-stroke with good visual acuity versus reduced visual acuity [12,16]. Individuals with reduced visual acuity in addition to visual field loss had lower scores (reduced quality of life) in the majority of domains with the exception of ocular pain, the following domains showed a significant reduction; general vision, near vision, distance vision, social functioning, mental health,

role difficulties, and dependency [12]. Furthermore, Gall et al. [16] reported a link between reduced scores for both reduced visual acuity and slower reading speeds.

George et al. [14] reported correlations between the objective assessments of the Behaviour Inattention Test (BIT) and the Mayo-Portland Adaptability Inventory (MPAI) and the subjective NEI VFQ-25 in participants with homonymous hemianopia. The BIT demonstrated the participants did not have attention deficits and it correlated well with eight out of twelve domains of the NEI VFQ-25. The instrument had a good association with both the participation and ability/adjustment scales of the MPAI. The participants (n=24) involved in this study performed well on objective testing, however the details of the patient reported outcome were not discussed [14]. The raw composite score of the NEI VFQ-25 in this study are comparable with those reported by Chen et al. [15], Papageorgiou et al. [18] and Gall et al. [12,16,17], all of these studies investigated participants with homonymous hemianopia.

The Veterans Low Vision Visual Function Questionnaire (VA LV VFQ-48) has been used by two studies investigating quality of life post-stroke in individuals with homonymous hemianopia [14,15]. Chen et al. [15] reported that initially the scores showed that individuals with hemianopia (n=10) had more difficulty with visual ability, mobility and visual motor functioning when compared to healthy controls. The differences for the reading and visual information subscales were found to be much smaller. When visual acuity, contrast sensitivity and the presence of pre-existing ocular conditions were controlled for, the only remaining significant difference was mobility. George et al. [14] reported the correlations between the objective assessments of the Behaviour Inattention Test (BIT) and the Mayo-Portland Adaptability Inventory (MPAI) and the subjective VA LV VFQ-48 for participants with homonymous hemianopia without any attention deficits. The BIT correlated well with four out of five domains of the VA LV VFQ-48. The instrument had a good association with both the participation and ability/adjustment scales of the MPAI [14]. The raw scores for the VA LV VFQ-48 in this study are comparable with those reported by Chen et al. [15].

The Self-Reported Assessment of Functional Visual Performance (SRAFVP) was used in a



preliminary prospective observational study with the aim of validating the instrument with individuals with homonymous hemianopia (n=30) [13]. They reported that functional mobility tasks were less difficult to perform than reading and eye-hand co-ordination tasks. Participants without macular sparing had significantly more problems with reading. This study reported good reliability and validity of the SRAFP [13]. However, the study had several limitations including a small sample size, the majority of the sample were male (29:1) and individuals with inattention, aphasia and other ocular pathology were excluded.

The Daily Living Tasks Dependent on Vision (DLTV) was used in a large cohort study involving individuals with a wide variety of different visual impairments following stroke [21]. Not all patients within the study completed the questionnaire as it was not a compulsory assessment. Two papers relating to visual symptoms and visual field loss report the findings of from the DLTV [21,27]. No significant difference in scores was found between those with visual impairment that reported symptoms and those that did not. Across all the symptom types and an asymptomatic group a wide range of scores was noted. Scores were reported to be reduced in individuals with visual impairment following stroke irrespective if any symptoms were reported [21]. Quality of life was shown to be reduced in individuals with multiple visual impairments when compared to individuals without visual impairment. The reduced score with multiple visual impairments was not significantly different to those diagnosed only with visual field loss [27].

#### **4. CONCLUSION**

Issues exist when extracting the specific impact of visual impairment following stroke from the impact of other sequelae of stroke, such as physical and cognitive impairments [8]. The wording of the NEI VFQ aids this task. All questions ask the participant specifically about the impact of vision. However, generic PROMs ask about the impact of their current health state on a particular aspect of health related quality of life. Consequently, the individual's current health state could include any of the sequelae of stroke. This renders it impossible to establish how much of the impact on quality of life is as a result of visual impairment. Studies which adjust for multiple factors have shown that when adjusting for confounders, participants have a poorer

quality of life. This is an important consideration for researchers when choosing PROMs for future studies in this area.

Regardless of the instrument used, all studies similarly report that visual impairment following stroke results in a reduced quality of life. There are some differences in the areas of quality of life affected, relating in part to the range of instruments used and the sub-scales of these.

Eight of the eleven included studies focused on visual field loss following stroke. One of the eleven was found to assess the impact of a specific ocular motility defect (horizontal gaze palsy) occurring following stroke. There is currently no literature reporting the impact of a wider range of ocular motility defects following stroke. Due to this skew towards visual field loss and lack of studies investigating the impact of ocular motility, it was not possible to compare the effects on quality of life due to different visual impairments caused by stroke.

This review highlights the need for further research into the impact of visual impairment following stroke on quality of life using appropriate vision-specific outcome measures.

#### **CONSENT**

It is not applicable.

#### **ETHICAL APPROVAL**

It is not applicable.

#### **DISCLAIMER**

This manuscript was presented in the conference.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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## APPENDIX

### Appendix 1. Search options and search terms

#### Databases:

- Cochrane Stroke Group Trials Register
- The Cochrane Eyes and Vision Group Trials Register
- The Cochrane Central Register of Controlled Trials (CENTRAL) (*The Cochrane Library*, latest issue);
- MEDLINE (1950 to May 2014);
- EMBASE (1980 to May 2014);
- CINAHL (1982 to May 2014);
- AMED (1985 to May 2014);
- PsycINFO (1967 to May 2014);
- Dissertations & Theses (PQDT) database (1861 to May 2014);
- British Nursing Index (1985 to May 2014);
- PsycBITE (Psychological Database for Brain Impairment Treatment Efficacy, [www.psycbite.com](http://www.psycbite.com)).

#### Registers:

- ClinicalTrials.gov (<http://clinicaltrials.gov/>);
- Current Controlled Trials ([www.controlledtrials.com](http://www.controlledtrials.com));
- Trials Central ([www.trialscentral.org](http://www.trialscentral.org));
- Health Service Research Projects in Progress ([www.cfm.nih.gov/hsr\\_project/home\\_proj.cfm](http://www.cfm.nih.gov/hsr_project/home_proj.cfm));
- National Eye Institute Clinical Studies Database (<http://clinicalstudies.info.nih.gov/cgi/protinstitute.cgi?NEI.0.html>)
- British and Irish Orthoptic Journal, Australian Orthoptic Journal, and proceedings of the European Strabismological Association (ESA), International Strabismological Association (ISA), International Orthoptic Association (IOA) ([http://pcwww.liv.ac.uk/~rowef/index\\_files/Page646.htm](http://pcwww.liv.ac.uk/~rowef/index_files/Page646.htm))
- Proceedings of Association for Research in Vision and Ophthalmology ([www.arvo.org](http://www.arvo.org));

#### Terms:

Cerebrovascular disorders/ Brain ischaemia/ Intracranial Arterial Disease Intracranial Arteriovenous Malformations/ "Intracranial Embolism and Thrombosis*/ Stroke/	Eye Movements/ Eye/ Eye Disease/ Visually Impaired Persons/ Vision Disorders/ Blindness/ Diplopia/ Vision, Binocular/ Vision, Monocular/ Visual Acuity/ Visual Fields/ Vision, Low/ Ocular Motility Disorders/ Blindness, Cortical/ Hemianopsia/ Abducens Nerve Diseases/ Abducens Nerve/ Oculomotor Nerve/ Trochlear Nerve/ Visual Perception/	Quality of Life Impact
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Nystagmus  
strabismus  
smooth pursuits  
saccades  
depth perception  
stereopsis  
gaze disorder  
internuclear ophthalmoplegia  
Parinaud's syndrome  
Weber's syndrome  
skew deviation  
conjugate deviation  
oscillopsia  
visual tracking  
agnosia  
hallucinations

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OR

OR

OR

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AND

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**Appendix 2. STROBE statement [9,10]**

	<b>Item no</b>	<b>Recommendation</b>
<b>Title and abstract</b>	1	(a) Indicate the study's design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found
<b>Introduction</b>		
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
Objectives	3	State specific objectives, including any pre-specified hypotheses
<b>Methods</b>		
Study design	4	Present key elements of study design early in the paper
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
Participants	6	(a) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants (b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
Data sources/measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
Bias	9	Describe any efforts to address potential sources of bias
Study size	10	Explain how the study size was arrived at
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (d) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy (e) Describe any sensitivity analyses
<b>Results</b>		
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram

	<b>Item no</b>	<b>Recommendation</b>
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders (b) Indicate number of participants with missing data for each variable of interest (c) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time <i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure <i>Cross-sectional study</i> —Report numbers of outcome events or summary measures
Main results	16	(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included (b) Report category boundaries when continuous variables were categorized (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses
<b>Discussion</b>		
Key results	18	Summarise key results with reference to study objectives
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
Generalisability	21	Discuss the generalisability (external validity) of the study results
<b>Other information</b>		
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

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