Image: 1<u>Review Article</u>2Post-stroke visual impairment: A systematic3literature review of types and recovery of visual4conditions

5 ABSTRACT

Aim: The aim of this literature review was to determine the reported incidence and prevalence of visual impairment due to stroke for all visual conditions including central vision loss, visual field loss, eye movement problems and visual perception problems. A further aim was to document the reported rate and extent of recovery of visual conditions post stroke.

Method: A systematic review of the literature was conducted including all languages and translations obtained. The review covered adult participants (aged 18 years or over) diagnosed with a visual impairment as a direct cause of a stroke. Studies which included mixed populations were included if over 50% of the participants had a diagnosis of stroke. We searched scholarly online resources and hand searched journals and registers of published, unpublished and ongoing trials. Search terms included a variety of MESH terms and alternatives in relation to stroke and visual conditions. The quality of the evidence was assessed using key reporting guidelines, e.g. STROBE, CONSORT. **Results:** Sixty-one studies (n=25,672) were included in the review. Overall prevalence of visual impairment early after stroke was estimated at 65%, ranging from 19% to 92%. Visual field loss reports ranged from 5.5% to 57%, ocular motility problems from 22% to 54%, visual inattention from 14% to 82% and reduced central vision reported in up to 70%. Recovery of visual field loss varied between 0% and 72%, with ocular motility between 7% and 92% and visual inattention between 29% and 78%.

Conclusion: The current literature provides a range of estimates for prevalence of visual impairment after stroke. Visual impairment post stroke is a common problem and has significant relevance to the assessment and care these patients receive. Prospective figures regarding incidence remain unknown.

- 6 Keywords: Incidence, Prevalence, Visual impairment, Stroke, Recovery, Review
- 7

8 1. BACKGROUND

9 Types of visual impairment following stroke can be complex including ocular as well as cortical 10 damage [1-6]. Visual impairment can have a wide ranging impact on activities of daily living, 11 independence and quality of life. Links with depression have also been found [7-11]. Many studies 12 provide information on prevalence of various visual conditions from their sample based on cross 13 section and case note observation studies [12-17]. Accurate estimates of prevalence or incidence of 14 visual impairment for stroke survivors remains unknown. Determination of prevalence of visual 15 impairment in a stroke unit is important in order to enable appropriate planning of efficacious referrals 16 to an eye specialist for assessment, treatment and targeted advice [6, 18, 19].

17 The aim of this systematic literature review was to provide a comprehensive synthesis and exploration 18 of reported evidence relating to visual problems after stroke with specific attention to incidence and 19 prevalence.

20

21 **1.1 Visual impairment definitions**

Visual impairment is a deficit of visual function and includes abnormalities of peripheral vision, central vision, eye movements and a variety of perception problems [1, 3, 4, 20].

Visual field loss is loss of a section of the field of vision and can either be central or peripheral. Following stroke visual field loss is frequently homonymous, with a loss in the same half of the visual field of both eyes. The types of visual field loss can include, hemianopia, quadrantanopia, constriction and scotomas [20, 21]. It is also possible to have a loss of the central area of vision. 28 There are a wide range of ocular motility problems which can occur as a result of stroke including 29 strabismus, cranial nerve palsies, gaze palsies, vergence abnormalities and nystagmus [22]. 30 Strabismus is the misalignment of the eyes, which can be longstanding from childhood or occur as a 31 result of an insult to the extra-ocular muscles or the cranial nerves supplying them. Eye movement 32 palsies or pareses following stroke can include cranial nerve palsy, horizontal gaze palsy and/or 33 vertical gaze palsy. Nystagmus is a continuous oscillatory movement of the eyes and is frequently associated in which both eyes move symmetrically. It may occur in every position of gaze or only be 34 35 present in certain gaze positions. A further consideration is that patients commonly have multiple 36 defects concurrently [23].

There are a number of different perceptual problems which can occur after stroke. The most recognised is visual inattention/neglect, in which the individual does not respond or attend to visual stimuli on the affected side. Other perceptual problems are also reported such as agnosia, visual hallucinations and image movement problems [24].

41

42 **2. METHODS**

43 We conducted an integrative review, aiming to bring together all evidence relating to incidence,

- 44 prevalence and recovery from stroke-related visual problems. The review observed and is reported
- 45 according to the PRISMA guidelines (additional file 1). This review was not registered with
- 46 PROSPERO [25].
- 47

48 2.1 Inclusion criteria for considering studies for this review

49 2.1.1 Types of studies

50 The following types of studies were included: randomised controlled trials, controlled trials, 51 prospective and retrospective cohort studies and observational studies. Case reports and case-52 controlled studies were excluded, as they specifically look at selected cases and are therefore unable 53 to report incidence or prevalence. All languages were included and translations obtained when 54 necessary.

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56 2.1.2 Types of participants

57 We included studies of adult participants (aged 18 years or over) diagnosed with a visual impairment 58 as a direct result of a stroke. Studies which included mixed populations were included if over 50% of 59 the participants had a diagnosis of stroke and data were available for this subgroup.

60 2.1.3 Types of outcome and data

We defined incidence as the number of new cases of any visual condition occurring during a certain period in a stroke survivor population. We defined prevalence as the number of cases of any visual condition present in a stroke survivor population at a certain time. We defined a measure of recovery as being present if prevalence figures were available at more than one time point post stroke. The visual impairments included are defined below.

66 **2.2 Visual impairment definitions**

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 vision, eye movements and a variety of perception problems [1, 3, 4, 20].

69 Visual field loss is loss of a section of the field of vision and can either be central or peripheral. 70 Following stroke visual field loss is frequently homonymous, with a loss in the same half of the visual 71 field of both eyes. The types of visual field loss can include, hemianopia, quadrantanopia, constriction 72 and scotomas [20, 21]. It is also possible to have a loss of the central area of vision.

73 There are a wide range of ocular motility problems which can occur as a result of stroke including 74 strabismus, cranial nerve palsies, gaze palsies, vergence abnormalities and nystagmus [22]. 75 Strabismus is the misalignment of the eyes, which can be longstanding from childhood or occur as a result of an insult to the extra-ocular muscles or the cranial nerves supplying them. Eye movement palsies or paresis following stroke can include cranial nerve palsy, horizontal gaze palsy and/or vertical gaze palsy. Nystagmus is a continuous oscillatory movement of the eyes and is frequently associated in which both eyes move symmetrically. It may occur in every position of gaze or only be present in certain gaze positions. A further consideration is that patients commonly have multiple defects concurrently [23].

There are a number of different perceptual problems which can occur after stroke. The most recognised is visual inattention/neglect, in which the individual does not respond or attend to visual stimuli on the affected side. Other perceptual problems are also reported such as agnosia, visual hallucinations and image movement problems [24].

86 **2.3 Search methods for identification of studies**

87 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 88 bibliographic databases (additional file 2). In an effort to identify further published, unpublished and 89 ongoing trials, we searched registers of ongoing trials, hand-searched journals and conference 90 91 transactions, performed citation tracking using Web of Science Cited Reference Search for all 92 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 93 excluded studies identified as possible preliminary or pilot work). Search terms included a 94 95 comprehensive range of MeSH terms and alternatives in relation to stroke and visual conditions 96 (additional file 2).

97 2.4 Selection of studies

98 The titles and abstracts identified from the search were independently screened by two authors (FR, 99 LH) using the pre-stated inclusion criteria. The full papers of any studies considered potentially 100 relevant were then considered and the selection criteria applied independently by two reviewers (FR, 101 LH). In the case of disagreement for inclusion of studies, an option was available to obtain a third 102 author opinion (CN).

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105 **2.5 Data Extraction**

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

109 2.6 Data analysis

Due to the heterogeneous nature of the studies, a narrative analysis was undertaken. The exception to this was a calculation to estimate the prevalence of overall visual impairment following stroke. Strict criteria of only studies using consecutive recruitment from a stroke population and reporting an overall prevalence for visual impairment were used for the mean prevalence calculation.

114 2.7 Quality Assessment

115 To assess the quality of the studies included in this review, two checklists were considered relevant to 116 the study designs in our inclusion criteria: the STROBE (Strengthening the Reporting of Observational 117 Studies in Epidemiology) checklist [26, 27]. The checklist was adapted as the original was designed 118 to assess the quality of reporting rather than the potential for bias within a study. There is currently no 119 'gold standard' guality assessment tool for observational studies [28]. The STROBE Statement covers 120 22 items covering the whole of the articles from introduction, method, results and discussion, which 121 are important to consider when assessing the quality of observation studies (including cohort, case-122 control and cross-sectional studies). The adapted version used in this review included 18 items; only 123 the information which is pertinent to quality appraisal of the studies was included. Using Boyle's 124 recommendations for the evaluation of prevalence studies, the items exclude which were not 125 considered relevant information, such as the title, abstract, background, setting and funding [29].

126 **3. RESULTS OF THE SEARCH**

127 The search results are outlined in appendix 1. Sixty-four articles (26,321 participants) were included. 128 Of the 64 included studies, none of which were RCTs, 52 were prospective observational studies and 129 12 were retrospective analyses. Consequently quality of study was assessed using the STROBE 130 checklist. Although none of the studies were RCTs, one study was a retrospective analysis of data 131 from an RCT archive [30]. Studies excluded from this review are outlined in appendix 2. Quality 132 appraisal using the adapted STROBE checklist is outlined in appendix 3.

Seven of the studies (14,573 participants) reported on overall visual impairment. Nineteen of the studies (17,924 participants) reported on visual field defects; 22 of the studies (4330 participants) reported on ocular alignment and motility defects; nine of the studies (2097 participants) reported on central vision problems; and 13 of the studies (2885 participants) reported on types of perceptual visual deficits following stroke (including visual neglect/inattention, visual hallucinations, agnosia and reduced stereopsis). Several studies reported on two or more of these categories.

None of the studies included had a specific primary aim to calculate either prevalence or incidence of visual impairment following stroke. Fifty five studies were studies specifically investigated visual impairment following stroke, this included studies looking at specific visual problems such as visual inattention. The remaining 16 studies investigated symptoms and signs of stroke, which included reported visual impairment.

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145 **4. Quality of the evidence**

Three paper reported 100% of the items requested by the adapted STROBE checklist [31]. Sixteen papers reported 90% or more of the requested items, 51 papers reported 75% or more. Sixty-one reported 50% or more and three papers failed to reach 50%, achieving 17%, 33% and 39% [32-34]. Only 36% of papers reported limitations of their studies. Results from all papers were reported and the individual results for each paper are outlined in appendix 3

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153 **5. Prevalence and Incidence**

154 **5.1 Visual impairment**

Our search of the literature did not reveal any studies that specifically aimed to assess the incidence of visual impairment following stroke. We identified a number of studies that report an overall figure of prevalence for visual impairment. All these studies, however, were judged to have limitations relating to the methods of recruitment or assessment. Thus a calculation of incidence was not possible and estimates are calculated for prevalence.

160 Three prospective studies of stroke populations (n=709) report an average prevalence of visual 161 impairment post stroke of 65% ranging from 62-71% (table 1) [32, 33, 35]. These studies evaluated a 162 general stroke population including medical and orthoptic assessments undertaken during the acute 163 stroke phase within one week of onset to three months post stroke onset. Further to these three 164 studies of general stroke populations, one prospective study (n=915) recruited a sub population of 165 stroke survivors with suspected visual impairment who received full orthoptic assessment, typically 166 within 3 weeks of stroke onset [6]. They reported a prevalence of 92% visual impairment. It is 167 unknown what was missed from the general stroke population as not all individuals can report visual 168 symptoms and referrals were evaluated to be more accurate when visual symptoms were taken into 169 consideration in addition to ocular signs in comparison to ocular signs alone [36]. Ali et al., analysed 170 results from a database for stroke survivors recruited to a variety of stroke-related clinical trials and reported a baseline prevalence of 60% visual impairment [30]. This cohort would typically include 171 172 those who are able and willing to participate in a clinical trial and are therefore, not representative of 173 the whole population, for example individuals with cognitive impairment and aphasia are less likely to 174 be recruited [37].

175 **Table 1. Overall visual impairment prevalence**

Study	Design	Populatio n	Time of vision assessment	Sample size (n=)	Prevalenc e of visual issue (%)	Co- existent ocular conditio n	Method of visual assessment
1974; Isaeff et al.	Prospective observation	General stroke	Median within 3 months of onset	322	62	Yes	Medical
1987; Freem an &Rud ge	Prospective observation	General stroke	Median within 1 week of onset	247	63	Yes	Medical Orthoptic
1995; Clisby	Prospective observation	General stroke	Acute period on stroke unit	140	71	Yes	Orthoptic
2007; Barrett et al.	Prospective observation	General stroke	Unknown	505	19	Unknown	NIHSS and Questionnair e for verifying stroke-free status
2009; Rowe et al.	Prospective observation	Stroke survivors with suspected visual issues	Median within 3 weeks of onset	323	92	Yes	Orthoptic
2013; Ali et al.	Trial data	Acute stroke	Median within 1 week of stroke onset	11900	60	Unknown	NIHSS
2010; Gall et al.	Retrospecti ve	General stroke	Unknown	1136	25.9 23 – male 29 – female	Unknown	NIHSS

177 Three studies (n=13,541) used a stroke assessment tool (NIHSS ± status questionnaire) which only partly assesses visual function [30, 31, 38]. The National Institute of Health Stroke Scale (NIHSS) is 178 179 an assessment tool that only assesses for the presence of visual field loss and horizontal gaze 180 problems [39]. Thus it is not a full assessment of the possible visual problems which can manifest as a result of stroke. It can therefore be argued that the numbers presented by these studies are not a 181 182 true measure of overall incidence of visual impairment following stroke. In addition to the NIHSS, the Questionnaire for Verifying Stroke-free Status (QVSFS) was used. However this questionnaire only 183 asks the patient about painless complete or partial vision loss [40]. The range of overall incidence of 184 185 visual problems was 19-25.9% from these studies which was considerably less than studies with 186 more comprehensive vision assessment methods.

187 **5.2 Visual field loss**

The reported prevalence of visual field loss after stroke varies considerably in the literature from 5.5%
to 57% (table 2) and most probably due to its dependence on the type and affected area of a stroke,
inclusion criteria and the timing of assessments and the method of testing used [41-44].

191

192 Table 2. Visual field loss prevalence

	I					-	
Study	Design	Populati	Time of	Sampl	Prevalence	Co-	Method of
· · · · ,	3	•	vision			ovictort	vieual field
		on	vision	e size	of visual	existent	visual field

			assessme nt	(n=)	issue (%)	ocular conditio n	assessme nt
1973; Haerer et al.	Prospective observation	General stroke	Unknown	265	25 – homonymous hemianopia / quadrantanopi a	Unknow n	Confrontati on
1974; Isaeff et al.	Prospective observation	General stroke	Median within 3 months of onset	322	17 – visual field loss	Ocular patholog y	Confrontati on
1989; Gray et al.	Prospective observation	General stroke	Followed every 24 hours for 4 days and max to 28 days	174	56.9 – homonymous hemianopia 46.6 – hemianopia 10.3 – quadrantanopi a	Ocular patholog y	Confrontati on
1993; Benedett i et al.	Prospective observation	General stroke	Median within 48 hours of admission	94	19.1 – homonymous hemianopia	Unknow n	Unknown
1995; Clisby	Prospective observation	General stroke	Acute period on stroke unit	140	47 – visual field loss	Ocular patholog y	Confrontati on Campimetr y
1997; Agrell et al.	Prospective observation	General stroke	Median within 3 months of onset	67	30 – homonymous hemianopia	Visual inattenti on	Confrontati on
1997; Celesia et al.	Prospective observation	Stroke survivors with hemianop ia	Median within 24 hours of onset	32	100 – homonymous hemianopia 62 – asymptomatic	Unknow n	Kinetic perimetry
2000; Lotery et al.	Prospective observation	General stroke	Median within 3 months of onset	77	19.5 – visual field loss ¾ hemianopia	Ocular patholog y	Unknown
2001; Cassidy et al.	Prospective observation	General stroke	Median within 3 months of onset	148	50.6 - visual field loss	Ocular patholog y	Confrontati on Perimetry
2007; Townse nd et al.	Prospective observation	General stroke excluding receptive aphasia and cognitive impairme nt	Within 9 months of onset	61	16 – homonymous hemianopia	Unknow n	Static perimetry
2009; Rowe et al. (b)	Prospective observation	Stroke survivors with suspecte d visual issues	Median within 3 weeks of onset	915	49.5 – visual field loss 3⁄3 hemianopia 1/2 - asymptomatic	Ocular patholog y Visual inattenti on	Confrontati on Kinetic perimetry Static perimetry

		-			1		
2012; Tao et al.	Prospective observation	General stroke: anterior vs posterior circulatio n	Median within 3 months of onset	1174	6.9 – visual field loss Hemianopia: 4.3 – posterior circulation 1.3 – anterior circulation Quadrantanop ia: 1.3 – posterior corulcation	Unknow n	NIHSS Confrontati on
2013; Ali et al.	Prospective trial data	General stroke	Median within 1 week of stroke onset	11900	51 – visual field loss: majority hemianopia	Unknow n	NIHSS Confrontati on
2013c; Rowe et al	Prospective	Stroke survivors with suspecte d visual impairme nt	Variable over 2 weeks to 6 months	915	52.3 – visual field loss 54 – complete homonymous hemianopia 19.5 – partial homonymous hemianopia 15.2 – homonymous quadrantaopia 0.2 – temporal crescent 9.2 – constricted fields 5.1 – scotomas 1.7 – bilateral hemianopia	Yes	Confrontati on Static perimetry Kinetic perimetry
2014; Siong et al.	Prospective observation	General stroke	10 days to 26 years post stroke onset	113	26.5 – monocular defects 11.5 – binocular defect	Ocular patholog y	Confrontati on
2001; Lawrenc e et al.	Retrospecti ve	Stroke register	Median within 3 months of onset	1136	26.1 – visual field loss	Unknow n	Unknown
2002; Rathore et al.	Retrospecti ve	Database stroke cohort	Unknown	474	14.6 – homonymous hemianopia	Unknow n	Unknown
2005; Ng et al.	Retrospecti ve	Posterior circulatio n strokes	Unknown	89	53 – visual field loss	Unknow n	Unknown
2011; Jerath et al.	Retrospecti ve	General stroke Male vs female	Unknown	449	22.7 – visual field loss (female) 20.9 – visual field loss (male)	Unknow n	Neurology Accident & Emergency assessmen t Non- standardise

							d
2012; Searls et al.	Retrospecti ve	Posterior circulatio n stroke	Unknown	407	22 – visual field loss	Unknow n	Neurology assessmen t of signs and symptoms

Seven studies (n=1210) recruited stroke patients consecutively either as they were admitted to hospital acute stroke units or rehabilitation wards. Assessment of visual fields by confrontation and/or perimetry on admission after stroke onset detected visual field loss in up to 57% [32, 33, 41, 45-48]. The mean prevalence of visual field loss after stroke was calculated as 31% [32, 33, 41, 45-48]. These studies typically assessed patients in the acute phase with homonymous hemianopia or quadrantanopia defects most frequently detected.

In addition to the above studies, seven prospective studies (n=15,388) of stroke sub-populations report prevalence of visual field loss [21, 30, 43, 49-51]. These sub-populations typically include only stroke survivors with hemianopic or quadrantanopic field loss or with suspected visual impairment of any type, or do not recruit consecutively. Thus reported prevalence is not representative of the full stroke population.

205 Prevalence of visual field loss has been described based on symptom reporting by patients in four 206 studies (n=1362) ranging from 14.6 to 22.7% [42, 52-54]. These reports are considerably lower and 207 likely reflecting the poor reliability of detection by patient reported symptoms. In addition to those 208 formally diagnosed with visual field loss following stroke, it is important to consider how many patients 209 are unaware of their visual loss. Celesia et al. conducted a prospective observation study (n=32) to 210 investigate the presence of hemianopic anosognosia [54]. From a sample of thirty two patients with 211 homonymous visual field loss, 62% were unaware of their visual deficit. In a recent paper it was 212 reported that only 45% of participants with visual field loss reported symptoms of the visual field loss 213 [36]. It is important to note that not all patients had isolated visual field loss. Multiple visual 214 impairments caused by stroke were reported such as visual acuity loss, eye movement abnormalities 215 and perceptual difficulties. This discrepancy between those who do not complain of symptoms and have a diagnosis of visual field loss may highlight an under estimation in the incidence in this and 216 217 other studies.

For studies whose population samples have solely included patients with visual field loss post stroke, it is not possible to establish prevalence. However, several of these studies have shown almost equal numbers suffering right or left defects [34, 44, 55, 56].

221 5.3 Ocular motility/strabismus

Three prospective studies (n=1262) reported an average prevalence of all ocular motility problems as 33% (table 3) with a range from 22% to 54%, [18, 35, 57]. Assessments were usually within the acute period and two studies used detailed orthoptic evaluation of eye movements and binocular vision [18, 35]. Methods of ocular motility assessment are important to the accuracy of identification of eye movement abnormalities to ensure full detection of deficits in various gaze positions.

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Table 3. Eye movement disorder prevalence

Study	Design	Populatio n	Time of vision assessm ent	Samp le size (n=)	Prevalence of visual issue (%)	Co- existen t ocular conditi on	Method of assessmen t
1975; Yap et al.	Prospectiv e observatio n	General stroke	Median within 2 days of onset	100	44 – ocular motility disorders 28 – gaze palsy 11 – impaired	Unknow n	Unknown

		1			VOR		
					6 – cranial		
					nerve palsy		
1982;	Prospectiv	General	Follow-up	91	28 -	Unknow	NIHSS
De	e	stroke	every 3-4	-	horizontal	n	
Renzi et	observatio		days for 2		gaze palsy		
al.	n		weeks		7 - nystagmus		
			post onset				
1987;	Prospectiv	General	Median	247	22 – ocular	Yes	Medical
Freema n &	e observatio	stroke	within 1 week of		motility disorders		Orthoptic
Rudge	n		onset		35 –		
ridago			011001		strabismus		
					(additional 6%		
					pre-existent)		
					18 – palsies		
					(skew		
					deviation:3		
					1 ¹ / ₂ syndrome		
					o Horizontal		
					gaze palsy		
					57%		
					Vertical gaze		
					palsy 20%]		
					23 -		
1995;	Broopootiv	General	Acute	140	nystagmus 52 –	Ocular	Orthoptic
Clisby	Prospectiv e	stroke	period on	140	strabismus	patholo	Onnopric
Choby	observatio	oliono	stroke unit		44 – gaze	gy	
	n				palsy:	37	
					90 -		
					horizontal with		
					right		
					hemisphere stroke		
					73 –		
					horizontal with		
					left		
					hemisphere		
					stroke		
					39 – cranial		
					nerve palsy		
					(mainly III) 55- reduced		
					vergence and		
					stereoacuity		
1996;	Prospectiv	Mixed	Median	239	26 – stroke-	Unknow	Orthoptic
Fowler	е	neurologic	within 2	(54%	related	n	
et al.	observatio	alon	months of	stroke	strabismus		
	n	rehabilitati	admission)			
2000;	Prospectiv	on unit General	Median	77	2.6 – third	Yes	Ophthalmol
2000, Lotery	e	stroke	within 2	11	nerve palsy	162	ogy and
et al.	e observatio	SUORE	weeks of		norve paisy		optometric
5	n		onset				
2006;	Prospectiv	Sub	Within 6	116	26.7 –	Unknow	NIHSS
Singer	e	population	hours of		complete gaze	n	
et al.		excluding	onset		palsy		
		haemorrha			0.6 – partial		

		gic stroke and			gaze palsy		
		posterior circulation ischaemia					
2007; Rowe et al.	Prospectiv e observatio n	Stroke srvivors with suspected visual impairment	Median within 3 weeks of onset	243	54 – reduced convergence <6cms. 26 – reduced convergence <10cms.	Yes	Orthoptic
2008; Rowe et al.	Prospectiv e observatio n	Stroke survivors with suspected visual impairment	Median within 3 weeks of onset	323	12 – nystagmus N=2 – pre- existent N=18 – oscillopsia/ver tigo symptoms	Yes	Orthoptic
2009; Siddiqu e et al.	Prospectiv e	General stroke	Acute period	100	4 - nystagmus	Unknow n	Unspecified protocol
2009; Akhtar et al.	Prospectiv e	Posterior circulation stroke only	Acute period	116	48 – nystagmus	Unknow n	Unknown
2009; Rowe et al.	Prospectiv e observatio n	Stroke survivors with suspected visual impairment	Median within 3 weeks of onset	323	54 – reduced convergence <6cms 26 – reduced convergence <10cms	Yes	Orthoptic
2010; Rowe et al.	Prospectiv e observatio n	Stroke survivors with suspected visual imparment	Median within 3 weeks of onset	512	19 – strabismus 16.5 – new onset 2.5 – pre- existent	Yes	Orthoptic
2011a/b ; Rowe et al.	Prospectiv e observatio n	Stroke survivors with suspected visual impairment	Median within 3 weeks of onset	915	54 – ocular motility disorders 2/3 – diplopia 19 – strabismus (2.5% pre- existent) 10 – cranial nerve palsy (VI>III>IV) 58 – VI 26 - III	Yes	Orthoptic
2011; Baier & Dieteric h	Prospectiv e	Cerebellar stroke	Mean within 6 days	21	33 – nystagmus	Unknow n	Eye movement recording
2012; Maeshi ma et al.	Prospectiv e observatio n	Pontine stroke	Unknown	68	15.9 – diplopia	Unknow n	Unknown
2012; Tao et al.	Prospectiv e observatio	General stroke: Anterior vs	Acute period	1174	8 – diplopia: 7.3 posterior circulation	Unknow n	NIHSS

	n	posterior circulation stroke			0.7 anterior circulation 13.5 – gaze palsy:		
					11 – anterior circulation 2.6 – posterior circulation 4 – cranial nerve palsy: posterior circulation		
2013; Su & Young	Prospectiv e observatio n	Posterior fossa stroke: vertigo clinic	Unknown	70	31 – ocular motility disorders 45 – diplopia N=22 – nystagmus [45.5% multidirectiona I 54.5 unidirectional 86 - reduced OKN]	Unknow n	Nystagmus – eye movement recordings
2013b; Rowe et al.	Prospectiv e observatio n	Stroke survivors with suspected visual impairment	Median within 3 weeks of onset	915	23 – gaze defect: 15.9 – horizontal and vertical gaze palsy 69.7 – complete 13.5 – saccadic palsy 22.2 – smooth pursuit palsy 22.2 – impaired gaze holding 3.9 – Parinaud's syndrome 9.7 – INO 1.4 – one and a half syndrome	Yes	Orthoptic
2014; Siong et al.	Prospectiv e observatio n	General stroke	10 days to 26 years post stroke onset	113	53.1 – jerky eye movements 11.5 – restricted ocular motility 20 – reduced convergence (<15cm)	Yes	Optometrist
2011; Jerath et	Retrospecti ve	General stroke Male vs	Unknown	449	7.8 – diplopia (7.1% male, 0.7% female)	Unknow n	Neurology Accident & Emergency

		female			17.5 – nystagmus (4.6 male, 12.9 female)		assessment Non- standardise d
2012; Searls et al.	Retrospecti ve	Posterior circulation stroke	Unknown	407	20 – ocular motility disorders 15 – diplopia 25 – nystagmus	Unknow n	Neurology assessment of signs and symptoms

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231 5.3.1 Eye Alignment

232 Strabismus may occur as an isolated finding or in association with ocular motility problems and is 233 reported in 16.5% to 52% of stroke survivors recruited to three prospective observation studies 234 (n=626), with an average prevalence of 38% [32, 35, 58]. These studies used validated orthoptic assessments to detect presence of strabismus, increasing their accuracy of detection. In a sub-235 236 population prospective multi-centre observational study, 19% of the sample were identified with strabismus [23]. Pre-existing strabismus was acknowledged in 2.5%, thus 16.5% were considered to 237 be a direct result of stroke. The cause of the strabismus in 70% of cases was an ocular motility defect. 238 239 Only 36% were symptomatic with diplopia, which highlights an issue in relying purely on symptoms 240 alone. This study has a risk of under-estimating the prevalence, as the sample is not representative of 241 the whole stroke population.

242 Diplopia is reported as a symptom in many papers which is a result of a misalignment of the eyes and 243 a disruption of binocular vision. Other studies have highlighted the discrepancy between patients who 244 do or do not report diplopia in the presence of strabismus or ocular motility defects. There is a risk 245 that a proportion are not captured, if the symptom of diplopia is relied upon to identify ocular motility defects. The majority of studies reporting the incidence of diplopia limit recruitment to include strokes 246 affecting specific areas of the brain [43, 59, 60], are retrospective [42, 53] or required informed 247 248 consent [61]. These studies cannot be generalised to the whole stroke population and also carry a risk of under estimating the true prevalence of strabismus. 249

250 5.3.2 Eye movement palsy

Seven studies (n=2783) report figures for gaze palsies including horizontal and/or vertical gaze positions and have a mean prevalence following stroke of 26% (range 18-44%) [22, 32, 35, 43, 57, 62, 63]. These defects may occur in isolation or in conjunction with other visual problems, and are the most common of all ocular motility abnormalities [22, 57]. Horizontal gaze palsies are more prevalent than vertical and complete palsies more prevalence than partial [22, 32, 35, 63].

Cranial nerve palsies affecting the ocular motor muscles include third, fourth and sixth nerves with a mean post-stroke prevalence of 16% (range 3 to 39%) from three studies (n=2329) [32, 43, 57, 64]. Third nerve and sixth nerve palsies are reported as being more prevalent than fourth nerve palsies in these stroke populations [32, 64, 65]. Where ocular movement assessment only tests horizontal gaze (such as with the NIHSS screening tool) the identification of all ocular cranial nerve palsies is limited. It is likely that more subtle nerve palsies and those involving the vertical muscles may be missed.

262 5.3.3 Nystagmus

263 Following stroke, nystagmus is reported in an average of 11% (range 4 to 48%) in three studies 264 (n=438) [35, 62, 66]. In most prospective and retrospective studies reporting nystagmus, the specific 265 types of nystagmus are not reported. This, in addition to lack of information regarding the method of 266 assessment, makes it difficult to assess if the more subtle types, or nystagmus not present in primary position, have been missed. These factors increase the risk of an underestimation of prevalence. 267 268 When reported, common types of acquired nystagmus are gaze evoked, multi-vector and upbeat [67]. 269 The studies described to date, frequently report when the stroke has affected the posterior circulation, including the cerebellum [42, 60, 68, 69]. No studies have reported the prevalence of nystagmus in 270 271 anterior circulation strokes in isolation. It is, therefore not possible to estimate the proportion of cases 272 which are potentially missed by restricting populations to posterior circulation strokes only.

273 5.3.4 Vergence

Clisby (n=140) reported 55% of patients to have reduced convergence and/or stereopsis [32]. Rowe et al. (n=243) reported reduced convergence from the initial ten month data set of the Vision in Stroke (VIS) study [70]. Using the 'gold standard 'normal' attainment for convergence of 6cm, 54% were judged to have reduced convergence. However, they also reported that 26% had convergence reduced less than 10cm, which could be judged to be a more appropriate standard for an older group of patients. Siong et al. reported 21% of the recruited population to have convergence reduced less than 15cm [61].

281 5.4 Visual acuity and central vision deficit

282 Clinical assessment of visual acuity has been used to identify those with reduced vision and up to 283 70% of stroke survivors (table 4) have been noted to have poor central vision [32, 36, 65, 71]. The 284 mean prevalence of reduced visual acuity post-stroke was calculated from three studies (n=270) as 285 53% [32, 65, 71]. Methods include visual acuity assessment at near, a 3 or 6 metre distance. Further 286 retrospective studies (n=447) provide information on the prevalence of patients reporting symptoms 287 associated with a reduction of visual acuity [42, 53]. A key issue identified by three studies (n=1045) 288 related to patient glasses [36, 65, 71]. These were frequently reported as missing, or the glasses present were dirty, broken or the wrong prescription. 289

290

Study	Design	Population	Time of vision assessme nt	Sampl e size (n=)	Prevalence of visual issue (%)	Co- existent ocular conditio n	Method of assessment
1989; Bulens et al.	Prospective observation	General stroke	Days to years post onset	16	62 – reduced contrast sensitivity	No	Ophthalmolo gy
1995; Clisby	Prospective observation	General stroke	Acute period on stroke unit	140	58 – reduced visual acuity	Exclude d ocular patholog y	Orthoptic with adapaed visual acuity assessment for dysphasia
2000; Lotery et al.	Prospective observation	General stroke	Median within 2 weeks of onset	77	30 – visual acuity ≤6/12 27 – no glasses available, dirty or damaged lenses	Yes	Ophthalmolo gy and optometric
2006; Edward s et al.	Prospective observation	General stroke with exclusions if unable to hold a pencil or severe motor or language deficits	Median within 15 days of onset	53	70 – reduced visual acuity 30 – 6/7.5- 6/15 4 – 6/21- 6/30 36 – 6/60- 6/120 54 – no	Unknow n	Near visual acuity

291 Table 4. Central visual deficit prevalence

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					glasses available		
2011b; Rowe et al.	Prospective observation	Stroke survivors with suspected visual impairment	Median within 3 weeks of onset	915	19.3 – reading impairment: 61.6 – field loss 45.8 – reduced convergenc e 45 – saccadic defects 22.5 – reduced visual acuity 22 – perceptual defect	Yes	Orthoptic
2013a; Rowe et al.	Prospective observation	Stroke survivors with suspected visual impairment	Median within 3 weeks of onset	915	31 – reduced visual acuity	Yes	Orthoptic
2011; Jerath et al.	Retrospecti ve	General stroke Male vs female	Unknown	449	27 – loss of vision reported: 15.8 – male 10.3 - female 19 – visual disturbance reported: blurred vision, focus difficulty, photophobi a, visual hallunciatio ns	Unknow n	Neurology Accident & Emergency assessment Non- standardised
2012; Searls et al.	Retrospecti ve	Posterior circulation stroke	Unknown	407	20 – blurred vision	Unknow n	Neurology assessment of signs and symptoms
2012; dos Santos & Andrad e	Retrospecti ve	General stroke with haemorrha gic stroke excluded		40	100 – reduced contrast in comparison to controls	Exclude d ocular patholog y	Ophthalmolo gy
2014; Siong et al.	Prospective observation	General stroke	10 days to 26 years post stroke onset	113	29.8 – vision worse than 0.3 LogMAR	Yes	Optometrist

	11.5 – mild reduced vision (worse than 0.5 LogMAR) 1.8 – moderate reduced vision (worse than 1.0 LogMAR)	
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293 An important component of central visual function is contrast sensitivity, the reduction of which can 294 deform image perception. Contrast sensitivity function has been reported to be abnormal in 62% of 295 stroke patients (n=16) [72]. Different areas of the spectrum are impaired depending on the lesion site. 296 For example, participants with parietal and temporal lesions have been reported to have reduced 297 detection of low spatial frequencies whereas those with occipital and occipito-temporal lesions had 298 difficulty with medium to high spatial frequencies [72]. Furthermore, reduced contrast sensitivity in 299 stroke survivors, particularly those with severe functional difficulties, has been found to be associated 300 with reduced activities of daily living [73].

301 Central vision is key to activities such as reading. However, reading difficulties may be caused by a 302 wide range of visual impairments in addition to reduced visual acuity. Rowe et al. (n=915) reported 303 difficulties with reading occurred in 19.3% of the sample [19]. The three largest associations with reading difficulties were visual field loss (61.6%, the majority of which were complete homonymous 304 305 hemianopia), reduced convergence of less than 6cm (45.8%) and saccadic abnormalities (45.0%). 306 Other visual impairments associated with reading difficulties included reduced visual acuity (22.5%), 307 perceptual deficits (22%), including 16.5% with visual inattention, nystagmus (12.4%) and diplopia 308 (8.5%).

309

310 4.5 Visual perception abnormalities

The commonest form of visual perception disorder following stroke is visual neglect or inattention. The literature reporting the prevalence of visual neglect/inattention can be difficult to interpret. Often the different types of inattention (e.g. auditory, visual, and spatial) are not separated, so it is not always possible to isolate visual inattention.

Visual inattention has been reported on average in 32% (range 14% to 82%) (table 5) of stroke

316 survivors from five studies (n=1800) [56, 74-77]. These studies have recruited participants

consecutively and have used a range of tests or tools for visual inattention including cancellation tests
 and the Behavioural Inattention Test. Studies (n=1335) using cancellation tests alone reported

319 prevalence of 15% to 26% [74, 76, 78]. Those using a variety of assessments (n=991) for visual

inattention reported a prevalence of 14% to 82% [56, 75, 79-82]. Discrepancies in the wide range of

320 Inattention reported a prevalence of 14% to 82% [56, 75, 79-82]. Discrepancies in the wide range of 321 prevalence figures typically related to the timing of assessment plus inclusion/exclusion criteria of left

prevalence right sided stroke lesions and severe cognitive and/or communication deficits. As expected,

- there was a greater provalence of left versus right sided inattention
- there was a greater prevalence of left versus right sided inattention.
- 324

Table 5. Visual perceptual impairment prevalence

Study	Design	Populatio n	Time of vision assessme nt	Sampl e size (n=)	Prevalence of visual issue (%)	Co- existent ocular conditio n	Method of assessmen t
1987;	Prospective	General	Median	247	79 –	Yes	Orthoptic

Freeman	observation	stroke	within 1		reduced		[]
& Rudge			week of		stereoacuity		
1000	D		onset				
1993; Stone et al.	Prospective	General stroke	Median within 3 days of onset	171	82 - visual neglect [right hemisphere] 65 - visual neglect [left hemisphere] 28 - anosognosi a [right hemisphere] 5 - anosognosi a [left hemisphere]	Unknow n	Modified behavioural inattention test
1997; Pederse n et al.	Prospective	General stroke	At admission	1014	23 – visual neglect [42 – right hemisphere , 8 – left hemisphere 1	Unknow n	Cancellation tasks
1998; Cassidy et al.	Prospective	General stroke with left hemispher e lesions excluded	Within 7 days and monthly follow-up	66	40.9 – visual neglect 74 – visual field loss	Unknow n	Behavioural inattention test
1999; Cassidy et al.	Prospective	General stroke with left hemispher e lesions excluded	Within 7 days and monthly follow-up	44	61.4 – visual neglect	Unknow n	Behavioural inattention test
2002; Appleros et al.	Prospective retrospectiv e cases	General stroke	Unknown	279	279 23 – visual neglect [62 – right hemisphere] 74 – anosognosi a		Test battery
2006; Linden et al.	Prospective	General stroke	At 20 months of onset	243	15 – visual neglect	Unknow n	Star cancellation
2007; Becker & Karnath	Prospective	General stroke	Median within 3 days of onset	93	26.2 – visual neglect [right hemisphere] 24.3 – visual	Unknow n	Cancellation tasks

2009; Lee et al.	Prospective	General stroke Left hemispher e excluded	Median within 2 months of onset	138	extinction 2.4 – visual neglect [left hemisphere] 4.9 – visual extinction 58 – visual neglect 22.5 – neglect dyslexia	Unknow n	Test battery
2009; van Nes et al.	Prospective	General stroke Excluded aphasia, gaze palsy, cognitive issues	Median within 2 weeks of onset	78	21.8 – visual neglect 88 – right hemisphere	Gaze paresis excluded	Cancellation tasks
2009a/b; Rowe et al.	Prospective	Stroke survivors with suspected visual defect	Median within 3 weeks of onset	323	14 – visual neglect 4 – visual hallucinatio ns 2.5 – visual agnosia	Yes	Test battery
2013; Beaudoi n et al.	Prospective longitudinal	General stroke	At discharge to home	189	49.2 – visual perceptual defect	Unknow n	Motor-free visual perceptual test-vertical version
2014; Chechlac z et al.	Prospective observation al	Sub-acute stroke	2.5 – 27.3 days	454	9.1 – left visual extinction 4.6 right visual extinction	Unknow n	Confrontatio n extinction
2014; Siong et al.	Prospective observation al	General stroke	10 days to 26 years post stroke onset	113	5.3 visual neglect	Yes	Line bisection
2014; Yang et al.	Prospective obsevation al	Brainstem infarction	Less than 10 days post symptom onset	82	50 – pathologic subjective visual vertical tilt (>3 ⁹) 76 – ipsiversive 24 – contraversiv e 54.7 – abnormal torsion	Unknow n	Computeris ed assessment

327 In addition to visual neglect/inattention, the prevalence of other perceptual deficits are reported in the 328 literature. Perceptual deficits, such as object agnosia, colour detection difficulties have been reported 329 in the literature in very small numbers [19, 23, 82, 83]. Our literature search found four studies reporting an estimated prevalence for different visual perceptual deficits following stroke [82]. 330 331 Beaudoin et al. (n=189) reported an overall prevalence of visual perception deficits as 49.2% [84]. 332 Rowe et al. (n=323) estimated the prevalence as 20%, of which the prevalence of visual 333 hallucinations after stroke was 4% and visual agnosia was 2.5% [82]. It was reported that patients 334 with visual hallucinations and other perceptual deficits frequently do not disclose these symptoms. 335 This, in addition to the method of recruitment could result in an under-estimation of the true 336 prevalence. Yang et al. (n=82) reported 50% of participants had pathologic (>3°) subjective visual 337 vertical tilt following brainstem stroke [85]. Chechlacz et al. (n=454) reported 28% of participants with 338 right hemisphere stroke showed left visual extinction versus 6.8% of participants with left hemisphere 339 stroke showed right visual extinction [86].

Freeman and Rudge reported 79% of participants to have defective stereopsis [35]. Stereopsis was only tested in the pilot study (n=26), therefore the number of participants tested was limited to 19. It was also purposely not tested on participants with manifest strabismus even those which were a direct result of the stroke. The majority of those with strabismus would not demonstrate any stereopsis. This would result in an underestimation of those suffering reduced or absent stereopsis as a direct result of stroke.

346

347 6. Recovery of visual function

348 Our literature search identified just one study that appears to report the recovery of overall visual 349 problems following stroke (table 6). The majority that report recovery do so for visual field loss (table 350 7). Ali et al. had the largest sample for tracking recovery of multiple visual problems following stroke 351 [30]. However, not all visual problems were included due to the use of the NIHSS which limits 352 assessment to visual field loss and horizontal gaze paresis. There was a variable sample size at the 353 three time points used (baseline, 30 days and 90 days post stroke). The authors reported a reduction 354 of visual problems to 28.2% at 30 days and a further reduction to 20.5% at 90 days, compared to the 355 initial 60.5% at baseline. The sample size considerably decreased between baseline (n=11.900) to 30 356 davs post stroke (n=4.965).

Study	Design	Population	Time of vision assessment	Sample size (n=)	Prevalence of visual issue (%)	Assessment
2013; Ali et al.	Prospective	Stroke trial database	Baseline, 30 days and 90 days	11900 at baseline 4965 at follow-up	28.2 – visual impairment at 30 days 20.5 – visual impairment at 90 days Versus 60.6 at baseline	NIHSS

357 Table 6. Recovery of visual impairment

358

359 6.1 Visual field loss

Recovery of visual field loss is reported by a number of studies but across variable time periods (table 7). The percentage of patients recovering from visual field loss ranges from 0% to 44% for complete recovery and up to 72.2% for partial recovery (n=6656) [30, 35, 41, 46, 55, 87-89]. Variability in recovery rates appears to be dependent on time of baseline assessment and length of follow-up, accuracy of visual field assessment methods and their sensitivity to detection of change, prospective versus retrospective studies and exclusions of severe neurological and communication defects.

366Table 7Recovery of visual field loss

Study Design Population Time of Sample Prevalence Assessme

			vision assessmen t	size (n=)	of visual issue (%)	
1987; Freeman & Rudge	Prospective	General stroke	Mean 73 day follow- up 1 week to 6 months	247	33 – improvemen t (22 full, 11 partial) 25 – stable field	Confrontatio n
1989; Gray et al.	Prospective	General stroke	Followed every 24 hours for 4 days and max to 28 days	174	Complete hemianopia: 17 – full resolution within 2-10 days 27 – partial imprivement 39 – stable field Partial hemianopia: 44 – full resolution within 48 hours 28 – full resolution within 14 days 17 – stable field	Confrontatio n
1991; Tiel & Kolmel	Prospective	Posterior circulation stroke Excluded communicatio n difficulty and severe neurological deficits	Daily follow- up within 3 weeks of onset	125	47.8 – improvemen t within 6-25 days 56.5 for right heianopia 56.3 – macula involved with 72.2 improvemen t of this 34.4 – recovery of lower quadrant 25 – full recovery 21.9 – recovery of upper quadrant 18.7 – partial recovery	Confrontatio n
2001; Cassidy et al.	Prospective	General stroke	4 week intervals up to 12 weeks	19	15.8 – full recovery at 4 weeks 42.1 –	Perimetry

2013; Ali et al.	Prospective	Stroke trial database	Baseline, 30 days and 90 days	11900 at baselin e 4965 at follow- up	central recovery 11.1 - stable Complete hemianopia: 13 at 30 days 10 at 90 days Versus 35% at baseline Partial hemianopia: 11 at 90 days Versus 14.5% at baseline	NIHSS Confrontatio n
2006b; Zhang et al.	Retrospectiv e	Mixed population	Median 3 months of onset Change at 3 and 6 months	254	3 – full recovery 34 – partial 63 – stable field	Perimetry Central 30 or 24 degrees
2007; Schmiela u & Wong	Prospective	Mixed population	Change at 1 through to 105 months post onset	20	61.5 – improvemen t	Kinetic perimetry
2007; Kedar et al.	Retrospectiv e	Mixed population	Median 3 days post onset	852	Congruous hemianopia: 38.1 – improvemen t 58.5 – stable field 3.4 – deteriorated Incongruous hemianopia: 39.6 – improvemen t 41.5 – stable field 18.9 – deteriorated	Perimetry Central 30 or 24 degrees
2013c; Rowe et al	Prospective	Stroke survivors with suspected visual impairment	Variable over 2 weeks to 6 months	915	7.5 – full recovery 39.2 – partial recovery 1 – deterioration 52.3 – static	Confrontatio n Static perimetry Kinetic perimetry

Gray et al. (n=174) documented recovery in 47.8% of their sample, with a slightly higher proportion of 56.5% who had suffered a right hemianopia [41]. The macula was involved in 56.3% of the sample;

72.2% seeing an improvement in this and surrounding areas. They noted four different patterns of 370 371 recovery, the most common (34.4%) of which was recovery of the lower quadrant. This was followed 372 by complete recovery (25%), recovery of the upper quadrant (21.9%) and finally improvement in both 373 quadrants with some residual defect (18.7%). They found that most improvement occurred between 6 374 and 25 days post stroke. Cassidy et al. (n=19) reported that of those patients who demonstrated some recovery, only 15.8% achieved complete recovery at 4 weeks [46]. The majority of 42.1% had 375 376 some central recovery and the remainder had quadrantic recovery. For a patient with complete 377 homonymous hemianopia the recovery of the macula area can appear to be only a small recovery. 378 However, this can have a considerable functional impact such as with reading ability. They were also 379 able to demonstrate the reduced sensitivity of the confrontation method at detecting areas of 380 recovery. Variances in reports related to whether the baseline visual field loss was complete or partial 381 and/or congruous versus incongruous loss along with stroke-specific or mixed populations.

382 **6.2 Ocular motility abnormalities and strabismus**

Less has been reported on the recovery of ocular alignment and motility problems following a stroke (table 8). The percentage of patients which were reported to recover ranged from 7% to 28.5% for full recovery and up to 92% for partial recovery (n=6047) [22, 30, 35, 62, 64, 67]. The greatest recovery was for reduced stereoacuity at 92% [35]. Sixth nerve palsies were reported to have the highest incidence of complete recovery of cranial nerve palsies at 28.5% [64]. At least one third showed no recovery across ocular motility conditions of gaze palsy, nystagmus, cranial nerve palsy and strabismus [19, 35, 64, 67].

390

Study	Design	Population	Time of vision assessment	Sample size (n=)	Prevalence of visual issue (%)	Assessment
1982; De Renzi et al.	Prospective	General stroke	Follow-up every 3-4 days for 2 weeks post onset	91	8.6 days - mean duration to improvement with left stroke 14.9 – mean duration to improvement with right stroke	NIHSS
1987; Freeman & Rudge	Prospective	General stroke	Up to 12 months post onset	76	7 – full improvement 50 – partial improvement 43 – stable 92 – improvement in stereoacuity within 1 month	Orthoptic
2011a; Rowe et al.	Prospective	Stroke survivors with suspected visual impairment	Variable over 2 weeks to 6 months	915	Cranial nerve palsy: 22.5 – full improvement 43 – partial improvement 3.5 – deterioration Nystagmus:	Orthoptic

Table 8. Recovery of eye movement deficits

					42 – partial improvement 24 – stable Gaze palsy: 4 – full improvement 66 – partial improvement 30 - stable	
2013; Ali et al.	Prospective	Stroke trial database	Baseline, 30 days and 90 days	11900 at baseline 4965 at follow-up	Complete gaze palsy: 1.1 – at 30 days Versus 14.5% at baseline Partial gaze palsy: 9 – at 30 days Versus 31% at baseline	NIHSS Confrontation

393 6.3 Visual acuity and central vision deficit

Little is reported on the recovery of vision following stroke (table 9). We found one study (n=247) that outlined the recovery of reduced vision following stroke [35]. The majority (71%) showed some recovery. It is not clear from this paper what extent of recovery was made and whether this had been achieved at the one or six month follow-up.

398 Table 9. Recovery of central vision deficit

Study	Design	Population	Time of vision assessment	Sample size (n=)	Prevalence of visual issue (%)	Assessment
1987; Freeman & Rudge	Prospective observation	General stroke	Median within 1 week of onset	247	71 – improvement	Medical Orthoptic
2011; Rowe et al. (b)	Prospective	Stroke survivors with suspected visual impairment	Variable over 2 weeks to 6 months	915	10.5 – full improvement 43.4 – partial improvement 44.7 – stable 1.3 - deteriorated	Orthoptic

399

Rowe et al. (n=915) reported the recovery rates for a group of participants suffering reading difficulties [19]. The data from follow-up visits was available for 42.9% of the participants. Of these, 10.5% had complete resolution of their symptoms, and 43.4% showed some improvement. A similar proportion of 403 44.7% saw no change in their symptoms and only 1.3% experienced deterioration in their condition.

404 **6.4 Visual Perception abnormalities**

405 6.4.1 Visual inattention

Four studies (n=5286) have reported recovery of visual neglect/inattention [30, 35, 80, 90]. The percentage of recovery reported in the literature ranges from 29% to 78% (table 10). In contrast to other visual impairments, patients suffering with visual neglect were more likely to require a longer stay in hospital and have a poorer prognosis for recovering function [74]. Recovery is mostly seen 410 within 3 months post onset [30, 35, 80] with approximately 10% full recovery within the first 2 weeks

411 [90].

Study	Design	Population	Time of vision assessment	Sample size (n=)	Prevalence of visual issue (%)	Assessment
1987; Freeman & Rudge	Prospective	General stroke	Up to 4 months post onset	247	Visual neglect: 29 – complete recovery 57 - stable	Medical Orthoptic
1998; Cassidy et al.	Prospective	General stroke with left hemisphere lesions excluded	Monthly follow-up	66	9.1 – visual neglect at 3 months Versus 40.9% at baseline	Behavioural inattention test
2004; Farne et al.	Prospective	R hemisphere only	Follow-up at 2 weeks and 3 months post onset	33 at baseline 8 at 3 months	43 – improvement at 2 weeks [9 – full] 63 – improvement at 3 months	Behavioural inattention test
2007; Poggel et al.	Prospective Retrospective questionnaire	Post- geniculate lesions Mixed population	Mean 36 months (7- 189 months), up to 6 months follow-up. Up to 6 months follow-up	19 121	Visual hallucinations persisted for several days/weeks and then gradually subsided Mean duration of 28 days	Interview Questionnaire
2013; Ali et al.	Prospective	Stroke trial database	Baseline, 30 days and 90 days	11900 at baseline 4965 at follow-up	0.6 – visual neglect at 90 days Versus 27.7% at baseline	NIHSS Confrontation

412 Table 10. Recovery of visual perceptual impairment

413

414 6.4.2 Other perceptual deficits

415 One study (n=140) was found to report the recovery of visual hallucinations [91]. The authors reported 416 that visual hallucinations (Charles Bonnet syndrome) persisted for several days or weeks after the 417 onset of stroke before gradually subsiding. The median duration of visual hallucinations was 28 days 418 and they stated that the first 90 days is when spontaneous recovery is most likely to occur.

419

420 7. Limitations and recommendations for future incidence, prevalence and recovery 421 studies

422 None of the studies provided information about stroke survivors who were not admitted to a stroke
 423 unit/ward/rehabilitation unit. It is acknowledged that a proportion of stroke survivors have visual
 424 impairment only (usually occipital infarcts) but the numbers of these remain unknown.

The time of visual examination post stroke has a direct effect on the estimate of prevalence of visual problems that occur due to stroke. As recovery of visual conditions can occur rapidly in some cases during the first weeks post stroke, studies that assess visual function later than this early two week period are likely to detect those with persistent visual impairment. The extent of visual impairment for those with persistent visual conditions may also be misrepresented as these individuals may have had substantial improvement with only partial deficits remaining. Thus there is considerable potential for an underestimation of stroke related visual impairment.

Accuracy of non-specialist vision assessments and accuracy of screening tools and scores is likely to impact on reported prevalence figures. Where basic screening is undertaken, it is possible to miss subtle visual problems whose ocular signs are not included in the screening assessment. Thus there is the potential for underdiagnoses when the assessment is performed by the stroke team rather than an eye team specialist or where screening tools are used which only measure specific features of vision, e.g. detection of hemianopia or horizontal gaze defects only as with the NIHSS, or reliance on basic confrontation assessment rather than detailed confrontation or perimetry assessment.

439 Studies that report sub populations of stroke survivors are also prone to reporting bias for visual 440 problems. Despite large sample sizes in studies that have included sub populations of stroke 441 survivors, such as the VIS study of those already suspected of having visual impairment or studies of 442 clinical trial databases, these studies are unlikely to be representative of the general stroke population 443 [6, 30]. These estimates are potential under- or over-representations of the true prevalence of visual 444 problems across all stroke survivors.

The time of the baseline assessment is crucial for studies tracking the recovery of visual impairment. If the baseline assessment is delayed, complete or partial recovery may have already taken place. Furthermore, it has not yet been accurately established at what time point recovery of each visual problem following stroke can be expected. If a study only has short period of follow-up, recovery could continue after the participant has completed the study. Both factors result in under-estimation of recovery of stroke-related visual impairment.

Future studies are required to establish the incidence for post-stroke visual impairment in the early acute period within the first week of onset. Such studies should involve a full stroke cohort with no exclusions so that visual impairment rates are comprehensively evaluated. These patients require follow-up at regular time intervals to plot change in visual impairment over the first week, first month and longer term after stroke onset to provide information on trajectory of improvement, if any, and rates for full, partial or no recovery. At baseline and follow-up visits, full specialist assessment is required such that subtle visual deficits that can cause visual impairment are not missed.

458

459 8. CONCLUSIONS

460 The literature currently available for review does not include any studies whose primary aim was to 461 determine incidence or prevalence of visual impairment post stroke. Thus, this review can only 462 provide estimates of prevalence for individual stroke related visual problems. The estimation of the 463 overall prevalence of visual impairment was approximately 65% at baseline assessment. A reduction 464 to approximately 20% is seen by three month post stroke, due to factors such as recovery, adaptation 465 and death. The figures reported cover a wide range of prevalence for each visual problem. A variety 466 of factors may be the cause of this wide range of figures including; the different study aims, research 467 methods used, baseline assessments being conducted at different time points and different methods 468 assessment. The prevalence is reported as being highest for eye movement defects, visual field loss 469 and visual inattention. The existing literature regarding the recovery of visual problems following 470 stroke is scarce for both individual deficits and overall visual recovery. Further prospective studies are 471 required to establish the incidence of post-stroke visual impairment, the prevalence at various time 472 periods post stroke and trajectory of improvement.

473

474 **REFERENCES**

Pollock, A., et al., *Interventions for disorders of eye movement in patients with stroke.* Cochrane
 Database of Systematic Reviews, 2011. 10.

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477	2.	Pollock, A., et al., Interventions for visual field defects in patients with stroke. Cochrane Database
478		of Systematic Reviews, 2011. 10.
479	3.	Pollock, A., et al., Interventions for age-related visual problems in patients with stroke. Cochrane
480		Database of Systematic Reviews, 2012. 3.
481	4.	Bowen, A., et al., <i>Cognitive rehabilitation for spatial neglect following stroke</i> . Cochrane Database
482		of Systematic Reviews, 2013. 7.
483	5.	Jones, S.A. and R.A. Shinton, <i>Improving outcome in stroke patients with visual problems</i> . Age &
484		Ageing, 2006. 35(6): 560-5.
485	6.	Rowe, F., et al., Visual impairment following stroke: do stroke patients require vision
486	•	assessment? Age & Ageing, 2009. 38(2): 188-93.
487	7.	Granger, C.V., et al., Functional assessment scales: a study of persons after stroke. Archives of
488	7.	Physical Medicine & Rehabilitation, 1993. 74(2): 133-8.
489	8.	Nelles, G., et al., Compensatory visual field training for patients with hemianopia after stroke.
490	0.	Neuroscience Letters, 2001. 306(3): 189-92.
490	9.	Ramrattan, R.S., et al., Prevalence and causes of visual field loss in the elderly and associations
	9.	
492		with impairment in daily functioning: The Rotterdam Study. Archives of Ophthalmology, 2001.
493	4.0	119(12): 1788-1794.
494	10.	West, C.G., et al., Is vision function related to physical functional ability in older adults? Journal
495		of the American Geriatrics Society, 2002. 50(1): 136-45.
496	11.	Tsai, S.Y., et al., Association between visual impairment and depression in the elderly. Journal of
497		the Formosan Medical Association, 2003. 102(2): 86-90.
498	12.	Maberley, D.A.L., et al., <i>The prevalence of low vision and blindness in Canada</i> . Eye, 2006. 20(3):
499		341-346.
500	13.	Hyman, L., et al., Prevalence and causes of visual impairment in the Barbados eye study1.
501		Ophthalmology, 2001. 108(10): 1751-1756.
502	14.	Hsu, WM., et al., Prevalence and causes of visual impairment in an elderly Chinese population
503		in Taiwan1: The Shihpai Eye Study. Ophthalmology, 2004. 111(1): 62-69.
504	15	Rodriguez, J., et al., Causes of blindness and visual impairment in a population-based sample of
505		U.S. Hispanics. Ophthalmology, 2002. 109(4): 737-743.
506	16	Klein, R., B.E.K. Klein, and K.E. Lee, <i>Changes in Visual Acuity in a Population.</i> Ophthalmology,
507	10.	1996. 103(8): 1169-1178.
	17	
508	17.	Marmamula, S., et al., A cross-sectional study of visual impairment in elderly population in
509		residential care in the South Indian state of Andhra Pradesh: a cross-sectional study. BMJ Open,
510		2013. 3(3).
511	18.	Rowe, F., Prevalence of ocular motor cranial nerve palsy and associations following stroke. Eye,
512		2011. 25(7): 881-887.
513	19.	Rowe, F., et al., Reading difficulty after stroke: ocular and non ocular causes. International
514		Journal of Stroke, 2011. 6(5): 404-11.
515	20.	Pollock, A., et al., Interventions for visual field defects in patients with stroke. Stroke, 2012. 43(4):
516		e37-e38.
517	21.	Rowe, F., et al., A prospective profile of visual field loss following stroke: prevalence, type,
518		rehabilitation and outcome. BioMed Research International, 2013.
519	22.	Rowe, F., et al., Profile of gaze dysfunction following cerebrovascular accident. ISRN
520		Ophthalmology, 2013.
521	23.	
522	24.	
523	25.	
523	20.	register of systematic reviews. 2013 27 January 2015]; Available from:
525		http://www.crd.york.ac.uk/PROSPERO/.
	00	
526	26.	
527		(STROBE): Guidelines for reporting observational studies. PLOS Medicine, 2007. 4(10): 1623-
528	a -	1627.
529	27.	Vandenbroucke, J.P., et al., Strengthening the reporting of observational studies in epidemiology
530		(STROBE): Explanation and elaboration. PLOS Medicine, 2007. 4(10): 1628-1654.
531	28.	Sanderson, S., I.D. Tatt, and J.P. Higgins, <i>Tools for assessing quality and susceptibility to bias in</i>
532		observational studies in epidemiology: a systematic review and annotated bibliography.
533		International Journal of Epidemiology, 2007. 36(3): 666-676.
534	29.	
535		1(2): 37-39.

536 30. Ali, M., et al., Recovery from poststroke visual impairment: evidence from a clinical trials 537 resource. Neurorehabilitation & Neural Repair, 2013. 27(2): 133-41. 538 31. Gall, S.L., et al., Sex differences in presentation, severity, and management of stroke in a 539 population-based study. Neurology, 2010. 74(12): 975-981. 540 32. Clisby, C., Visual assessment of patients with cerebrovascular accident on the elderly care 541 wards. British Orthoptic Journal, 1995. 52: 38-41. 542 Isaeff, W.B., P.H. Wallar, and G. Duncan, Ophthalmic findings in 322 patients with a cerebral 33. 543 vascular accident. Annals of Ophthalmology, 1974. 6(10): 1059-1064. 544 34. Trobe, J.D., M.L. Lorber, and N.S. Schlezinger, Isolated homonymous hemianopia. A review of 545 104 cases. Archives of Ophthalmology, 1973. 89(5): 377-81. 546 35. Freeman, C.F. and N.B. Rudge. The orthoptist's role in the management of stroke patients. in 6th 547 International Orthoptic Congress. 1987. Harrogate, UK. 548 36. Rowe, F., et al., Symptoms of stroke-related visual impairment. Strabismus, 2013. 21(2): 150-549 154. 550 37. Rothwell, P.M., External validity of randomised controlled trials: "To whom do the results of this 551 trial apply?". The Lancet. 2005. 365(9453): 82-93. 552 38. Barrett, K.M., et al., Sex differences in stroke severity, symptoms, and deficits after first-ever 553 ischemic stroke. Journal of Stroke & Cerebrovascular Diseases, 2007. 16(1): 34-39. 554 39. Lyden, P., et al., Underlying Structure of the National Institutes of Health Stroke Scale: Results of 555 a Factor Analysis. Stroke, 1999. 30(11): 2347-2354. 556 40. Jones, W.J., L.S. Williams, and J.F. Meschia, Validating the Questionnaire for Verifying Stroke-557 Free Status (QVSFS) by Neurological History and Examination. Stroke, 2001. 32(10): 2232-558 2236. 559 41. Gray, C.S., et al., Recovery of visual fields in acute stroke: Homonymous hemianopia associated 560 with adverse prognosis. Age and Ageing, 1989. 18(6): 419-421. 561 Searls, D.E., et al., Symptoms and signs of posterior circulation ischemia in the new England 42. 562 medical center posterior circulation registry. Archives of Neurology, 2012. 69(3): 346-51. 563 43. Tao, W.D., et al., Posterior versus anterior circulation infarction: how different are the 564 neurological deficits? Stroke, 2012. 43(8): 2060-5. 565 44. Zhang, X., et al., Homonymous hemianopias: clinical-anatomic correlations in 904 cases. 566 Neurology, 2006. 66(6): 906-10. 567 45. Agrell, B.M., O.I. Dehlin, and C.J. Dahlgren, Neglect in elderly stroke patients: A comparison of 568 five tests. Psychiatry and Clinical Neurosciences, 1997. 51(5): 295-300. 569 46. Cassidy, T.P., D.W. Bruce, and C.S. Gray, Visual field loss after stroke: Confrontation and 570 perimetry in the assessment of recovery. Journal of Stroke and Cerebrovascular Diseases, 2001. 571 10(3): 113-117. 572 47. Haerer, A.F., Visual field defects and the prognosis of stroke patients. Stroke, 1973. 4(2): 163-573 168. 574 Benedetti, M.D., et al., Short term prognosis of stroke in a clinical series of 94 patients. The 48. 575 Italian Journal of Neurological Sciences, 1993. 14(2): 121-127. 576 Lawrence, E.S., et al., Estimates of the prevalence of acute stroke impairments and disability in a 49. 577 multiethnic population. Stroke, 2001. 32(6): 1279-1284. 578 50. Ng, Y.S., et al., Clinical characteristics and rehabilitation outcomes of patients with posterior 579 cerebral artery stroke. Archives of Physical Medicine and Rehabilitation, 2005. 86(11): 2138-580 2143. 581 51. Townend, B.S., et al., Perimetric homonymous visual field loss post-stroke. Journal of Clinical 582 Neuroscience, 2007. 14(8): 754-6. 583 Rathore, S.S., et al., Characterization of incident stroke signs and symptoms: findings from the 52. 584 atherosclerosis risk in communities study. Stroke, 2002. 33(11): 2718-21. 585 53 Jerath, N.U., et al., Gender differences in presenting signs and symptoms of acute ischemic 586 stroke: a population-based study. Gender Medicine, 2011. 8(5): 312-9. 587 54. Celesia, G.G., M.G. Brigell, and M.S. Vaphiades, Hemianopic anosognosia. Neurology, 1997. 588 49(1): 88-97. 589 55. Kedar, S., et al., Congruency in Homonymous Hemianopia. American Journal of Ophthalmology, 590 2007. 143(5): 772-780. 591 56. Stone, S.P., P.W. Halligan, and R.J. Greenwood, The incidence of neglect phenomena and 592 related disorders in patients with an acute right or left hemisphere stroke. Age & Ageing, 1993. 593 22(1): 46-52. 594 57. Yap, M.H.L., S.C. Loong, and I.P. Nei, Eve signs in strokes. Annals of the Academy of Medicine 595 Singapore, 1975. 4(2): 133-137.

596	58.	Fowler, M.S., et al., Squints and diplopia seen after brain damage. Journal of Neurology, 1996.
597		243(1): 86-90.
598	59.	Maeshima, S., et al., Functional outcome in patients with pontine infarction after acute
599		rehabilitation. Neurological Sciences, 2012. 33(4): 759-764.
600	60.	
601		posterior fossa stroke. Acta Oto-Laryngologica, 2013. 133(9): 916-923.
602	61.	Siong, K.H., et al., Prevalence of visual problems among stroke survivors in Hong Kong Chinese.
603	~~	Clinical and Experimental Optometry, 2014. 97: 433-441.
604 605	62.	De Renzi, E., et al., Conjugate gaze paresis in stroke patients with unilateral damage. An
605 606	60	unexpected instance of hemispheric asymmetry. Archives of Neurology, 1982. 39(8): 482-6. Singer, O.C., et al., <i>Conjugate eye deviation in acute stroke: Incidence, hemispheric asymmetry</i> ,
606 607	63.	and lesion pattern. Stroke, 2006. 37(11): 2726-2732.
608	64	Rowe, F., et al., Prevalence of ocular motor cranial nerve palsy and associations following
609	04.	stroke. Eye, 2011. 25(7): 881-7.
610	65.	Lotery, A.J., et al., Correctable visual impairment in stroke rehabilitation patients. Age and
611		Ageing, 2000. 29(3): 221-222.
612	66.	Siddique, M.A.N., et al., <i>Clinical presentation and epidemiology of stroke - A study of 100 cases.</i>
613		Journal of Medicine, 2009. 10(2): 86-89.
614	67.	Rowe, F., et al., The spectrum of nystagmus following cerebro-vascular accident. British and Irish
615		Orthoptic Journal, 2008. 5: 22-25.
616	68.	Baier, B. and M. Dieterich, Incidence and anatomy of gaze-evoked nystagmus in patients with
617		cerebellar lesions. Neurology, 2011. 76(4): 361-5.
618	69.	Akhtar, N., et al., Ischaemic posterior circulation stroke in State of Qatar. European Journal of
619	70	Neurology, 2009. 16(9): 1004-1009.
620	70.	Rowe, F., et al. Visual impairment in stroke survivors: a prospective multi-centre trial. in 31st
621 622	71	European Strabismological Association. 2007. Mykonos, Greece.
622 623	71.	Edwards, D.F., et al., <i>Screening patients with stroke for rehabilitation needs: Validation of the post-stroke rehabilitation guidelines.</i> Neurorehabilitation and Neural Repair, 2006. 20(1): 42-48.
624	72	Bulens, C., et al., Spatial contrast sensitivity in unilateral cerebral ischaemic lesions involving the
625	12.	posterior visual pathway. Brain, 1989. 112(Pt 2): 507-20.
626	73.	dos Santos, N.A. and S.M. Andrade, Visual contrast sensitivity in patients with impairment of
627		functional independence after stroke. BMC Neurology, 2012. 12: 90.
628	74.	Pedersen, P.M., et al., Hemineglect in acute strokeincidence and prognostic implications. The
629		Copenhagen Stroke Study. American Journal of Physical Medicine & Rehabilitation, 1997. 76(2):
630		122-7.
631	75.	Appelros, P., et al., Neglect and anosognosia after first-ever stroke: incidence and relationship to
632		disability. Journal of Rehabilitation Medicine, 2002. 34(5): 215-20.
633	76.	Linden, T., et al., Visual neglect and cognitive impairment in elderly patients late after stroke.
634		Acta Neurologica Scandinavica, 2005. 111(3): 163-168.
635	11.	Becker, E. and H.O. Karnath, Incidence of visual extinction after left versus right hemisphere
636	70	stroke. Stroke, 2007. 38(12): 3172-4.
637 638	78.	van Nes, I.J., et al., <i>Is visuospatial hemineglect really a determinant of postural control following stroke? An acute-phase study.</i> Neurorehabilitation & Neural Repair, 2009. 23(6): 609-14.
639	70	Lee, B.H., et al., Neglect dyslexia: Frequency, association with other hemispatial neglects, and
640	13.	lesion localization. Neuropsychologia, 2009. 47(3): 704-710.
641	80	Cassidy, T.P., S. Lewis, and C.S. Gray, <i>Recovery from visuospatial neglect in stroke patients.</i>
642	00.	Journal of Neurology, Neurosurgery & Psychiatry, 1998. 64(4): 555-7.
643	81.	Cassidy, T.P., et al., The association of visual field deficits and visuo-spatial neglect in acute
644		right-hemisphere stroke patients. Age & Ageing, 1999. 28(3): 257-60.
645	82.	Rowe, F., et al., Visual perceptual consequences of stroke. Strabismus, 2009. 17(1): 24-8.
646	83.	Shrestha, G.S., et al., Ocular-visual defect and visual neglect in stroke patients - A report from
647		Kathmandu, Nepal. Journal of Optometry, 2012. 5(1): 43-49.
648	84.	Beaudoin, A.J., et al., Visuoperceptual deficits and participation in older adults after stroke.
649		Australian Occupational Therapy Journal, 2013. 60(4): 260-266.
650	85.	Yang, TH., et al., <i>Topology of brainstem lesions associated with subjective visual vertical tilt.</i>
651	00	Neurology, 2014. 82: 1968-1975.
652 653	86.	Chechlacz, M., et al., <i>The frequency and severity of extinction after stroke affecting different vascular territories</i> . Neuropsychologia, 2014. 54: 11-17.
035		vascular territories. Neuropsychologia, 2014. 54. 11-17.

- Tiel, K. and H.W. Kolmel, *Patterns of recovery from homonymous hemianopia subsequent to infarction in the distribution of the posterior cerebral artery.* Neuro-Ophthalmology, 1991. 11(1):
 33-39.
- 88. Schmielau, F. and E.K. Wong Jr, *Recovery of visual fields in brain-lesioned patients by reaction perimetry treatment.* Journal of NeuroEngineering and Rehabilitation, 2007. 4.
- 659 89. Zhang, X., et al., *Natural history of homonymous hemianopia*. Neurology, 2006. 66: 901-905.
- Farne, A., et al., *Patterns of spontaneous recovery of neglect and associated disorders in acute right brain-damaged patients.* Journal of Neurology, Neurosurgery & Psychiatry, 2004. 75(10):
 1401-10.
- 663 91. Poggel, D.A., et al., *Visual hallucinations during spontaneous and training-induced visual field* 664 *recovery.* Neuropsychologia, 2007. 45(11): 2598-2607.

666 **APPENDIX**

- 667 Appendix 1 PRISMA 2009 Checklist
- 668 Appendix 2 Search options and search terms
- 669 Appendix 3 Flowchart of pathway for inclusion of articles
- 670 Appendix 4 Excluded articles
- 671 Appendix 5 Quality appraisal of papers using the STROBE checklist

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