How effective is eccentric viewing training? A systematic literature review

Abbreviated Title: How effective is eccentric viewing training?

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DISCLOSURE

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ABSTRACT

Purpose: The global prevalence of age-related macular degeneration (AMD) and associated central vision loss (CVL) is rising. CVL hinders the performance of many activities of daily living (ADLs). Adaptive strategies such as eccentric viewing (EV) and steady eye strategy (SES) may be used to compensate for CVL. In order to establish the potential of these rehabilitation strategies, this systematic review evaluates current literature regarding the effectiveness of EV and SES training in people with CVL.

Recent Findings: The search strategies identified 2605 publications, 36 of which met the inclusion criteria for the review, but only three of which were randomised controlled trials. This literature shows that EV and SES training can improve near visual acuity, reading speed, and performance of ADLs in people with CVL. However, there was insufficient literature to establish a relationship between training and distance visual acuity or quality-of-life. There is no conclusive evidence to show that a particular model of EV training is superior to another, little clear evidence of a relationship between participant characteristics and training outcomes and no data regarding the cost effectiveness of training.

Summary: This report highlights the need for further robust research to establish the true potential and cost effectiveness of EV and SES training as a rehabilitation strategy for individuals with CVL.

INTRODUCTION

The prevalence of age-related macular degeneration (AMD) is reaching epidemic proportions. Globally, there are estimated to be approximately 2.85 million individuals with irreversible visual impairment caused by AMD.[1] Although developments in anti-angiogenic therapies have improved the prognosis for individuals diagnosed with neovascular AMD, [2-3] the majority of patients suffer from the dry form of the disease, [4] for which there is currently no treatment.

The end-stage of AMD is the development of a central scotoma,[5] which has a substantial detrimental impact on many visual functions, including visual acuity (VA) [6-7] and contrast sensitivity.[8-10] This hinders the performance of activities of daily living (ADLs) including reading, mobility, visual search and face recognition.[11-18] For these individuals, and others with untreatable central visual loss (CVL), the provision of eccentric viewing (EV) training and the prescription of low vision aids (LVAs) are important rehabilitative strategies.

With the loss of central vision, individuals are forced to use relatively healthy paracentral areas of retina to fixate objects.[19] Although this viewing strategy may initially feel unnatural, given time, most individuals with CVL will select a 'preferred retinal locus' (PRL) for eccentric viewing,[20-21] and a proportion of these individuals will select a number of PRLs, which they use for different purposes.[19, 21] However, some individuals do not select a PRL that maximises their visual ability.[22-23] In addition, the stability of fixation at the PRL is often variable,[24-26] which may also affect functional ability.[11, 27-29] Eccentric viewing training may help people with CVL to select a retinal locus that maximises their visual capability, known as a 'trained retinal locus' (TRL), or to effectively utilise their self-selected PRL.

A marked reduction in reading speed has been recorded in people with CVL.[11, 14, 30-31] In part, this is likely to be due to inefficient eye movements,[30] as well as a reduction in the size of the visual span and a reduction in the speed of visual processing.[32] A steady eye strategy (SES) may be used in conjunction with EV to overcome the difficulties experienced by individuals with CVL during reading. The PRL is initially directed towards a word, and the eyes held in a steady position, whilst the text is moved through this fixation point.[33] This strategy may also benefit individuals with a foveal island of residual vision, for whom EV is not necessary. The purpose of SES training is to remove the need for forward saccades. Alternatively, "eye movement training" programmes aim to optimise the ability of the saccadic eye movements to consistently place the image of the object of interest on the PRL.[34-38]

There are currently no comprehensive systematic reviews of EV and SES training. There is also limited evidence regarding the prevalence of EV and SES training, although reviews suggest that 40-50% of low vision services in America and Australia offer this type of therapy.[39-40] Given the expense of providing such training and the fact that 2.85 million individuals worldwide could benefit,[1] there is a need for a strong evidence base regarding the ability of different training strategies to achieve positive outcomes in people with CVL. This will become increasingly important in the coming decades as projected increases in the average age of the population [41] will lead to increases in the prevalence of age-related eye disease, and limitations in healthcare resources will increasingly necessitate evidence of the cost effectiveness of rehabilitation strategies. Consequently, the aim of this systematic review was to establish if EV and SES training improves outcomes in people

with CVL in comparison to 1) performance before training or, 2) another type of intervention / control group, in studies of any design.

METHODS

The methodology for this review was based on the Cochrane Handbook for Systematic Reviews, and is consistent with guidance provided by Rudnicka and Owen.[42,43] A detailed description of the protocol for the review follows, however it has not previously been published elsewhere. The following databases were searched using the terms defined in Table 1 (search period 1950 to December 2013): Web of Science, EMBASE, Medline, Cochrane CENTRAL, Psychinfo, and Centre for Reviews and Dissemination (CRD). Additional literature was identified by hand searching the reference lists of all identified studies and relevant review articles [19, 44-47] and by asking the lead and senior authors of studies pertaining to EV and SES training to identify additional references. The abstracts of potentially relevant articles were independently assessed by two authors to identify studies that met the eligibility criteria. Eligible studies had to include participants with CVL (studies of simulated visual impairment were excluded); a comparison (between groups or before and after intervention); EV or SES training (those which included only the provision of prismatic spectacles were excluded); and be reported in English. Studies could be of any design, include any outcome measures and be of any length of follow up, but they had to be published in peer reviewed journals.

Relevant data extracted from all included studies were inputted into a table, which was a modified version of the Cochrane recommendation.[42] This table included details of study design and methods, eligibility criteria, participants, interventions, outcomes, results, key conclusions by the study authors and comments from the review authors. These data were

used to assimilate the key findings of the review and are included in summary form in the Supplementary Table.

Table 1. Search terms used in the literature review. Studies were required to match at least one search term from each category.

Group 1: Target population	**Group 2: Intervention**
"low vision" OR "vis* impair*" OR "sight impair*" OR "partial* sight*" OR "age-related macular degeneration" OR "age related maculopathy" OR “senile macular degeneration” OR “ARMD” OR “AMD” OR “SMD” OR "central scotoma" OR "central vision loss" OR "visual disability" OR "low-vision" OR “macular disease” OR “macular degeneration”	“eccentric viewing” OR “eccentric reading” OR “preferred retinal locus” OR “PRL” or “trained retinal locus” OR “TRL” or “fixation” OR “saccadic” OR “steady eye” OR “rapid serial visual presentation” OR “RSVP”

The studies included in this review incorporated a wide range of outcome measures, follow-up times and interventions, which rendered a meta-analysis unfeasible. To aid quantitative comparison of the outcomes of different studies, Cohen’s d effect sizes were calculated where possible.[48] Effect sizes of less than 0.20 were considered small, those of approximately 0.50 medium and those above 0.80 large.[48] If there were insufficient data to calculate the Cohen’s d effect size, a request for these data was submitted to the corresponding author.

The quality of identified studies was evaluated according to recommendations by the Cochrane Collaboration.[42] The results of this evaluation were presented in a risk of bias table (Table 2). The table considers 6 features recommended by the Cochrane Collaboration: sequence generation, allocation sequence concealment, masking, incomplete outcome data, selective outcome reporting, and other potential sources of bias. Additionally, the quality of all included studies was defined as ‘high’, ‘moderate’, ‘low’ or

'very low' using the approach described by the GRADE Working Group.[49] Throughout this paper, the quality of evidence for a given outcome measure is graded with respect to the highest quality publication cited.

RESULTS

Of the 2605 potentially relevant articles identified by the search, 36 met the inclusion criteria for the review (Figure 1). However, Fitzmaurice & Clarke (1993; 1994) [51, 52] presented the same data in two separate articles, and Nilsson & Nilsson (1994) [53] presented the same data as Nilsson (1990).[54] These pairs of data were each treated as a single entry and the earlier of the two publications cited throughout this review.[51, 54] Consequently, the final number of included studies was 34 (see Supplementary Table for a summary of included studies).

Quality of evidence

The quality of the 34 included publications was variable (Table 2). The majority of included studies used a relatively weak 'before and after' comparison design, without a control group. This often made it difficult to determine the effect of the intervention, as it was not possible to distinguish between treatment effects and disease-related changes in visual function over time. Three of the included studies presented the results of a randomised controlled trial (RCT).[54-56] However, these studies failed to meet the criteria for well-designed RCTs set out by the Cochrane Collaboration. In addition, many studies included in the review failed to report in sufficient detail the study design, the characteristics and recruitment of the participants, the nature of the intervention or the findings obtained.

Table 2. See end of document

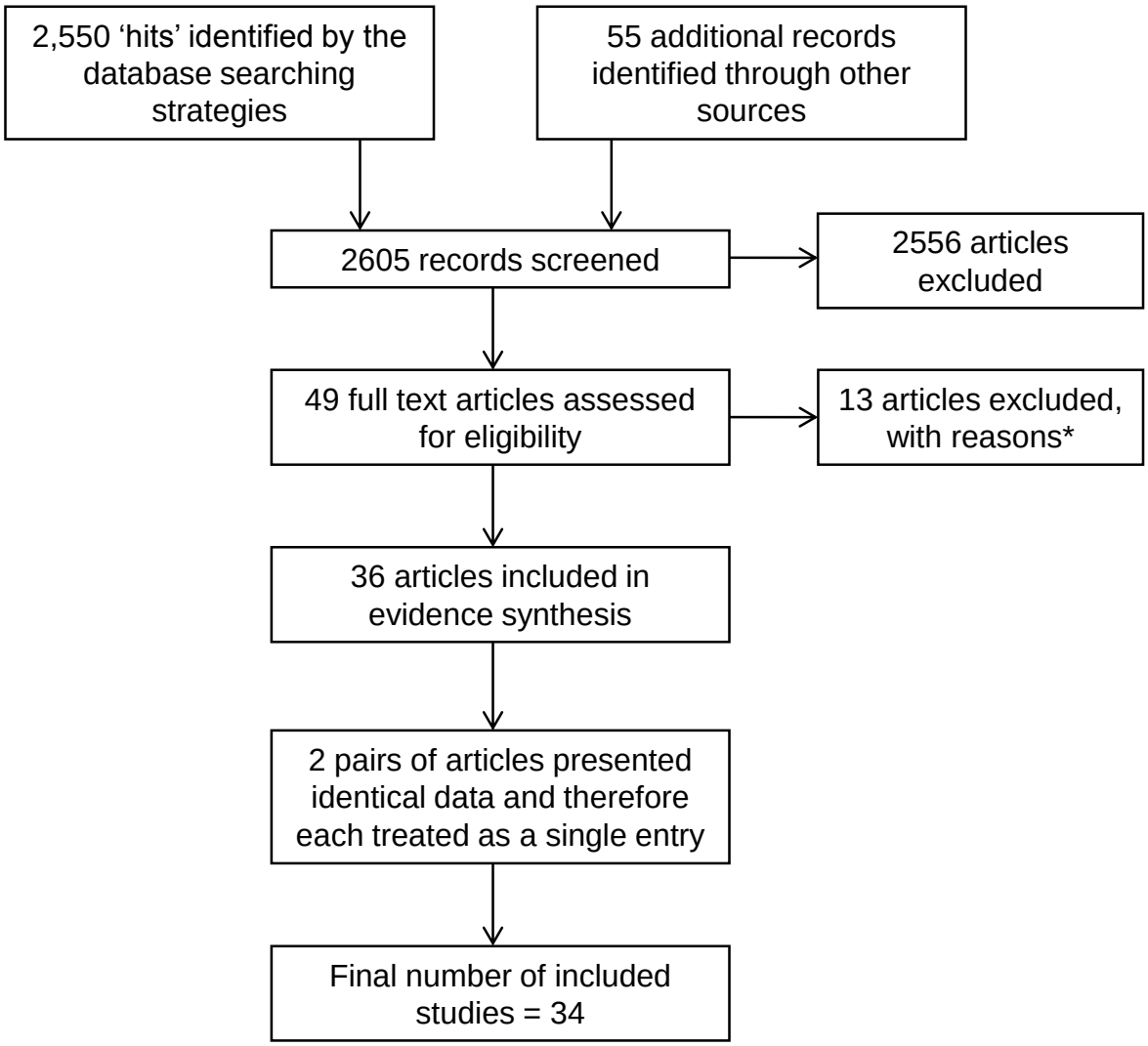

Figure 1. Modified PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram illustrating the identified studies and those included and excluded at each stage of the literature review.[50] Of the 13 articles excluded upon evaluation of the full text articles (*), six examined prismatic spectacles only; five included participants with simulated vision loss; one did not involve a comparison (between groups or before and after training); and one was not reported in English.

Effect of EV and SES training on clinical measures of visual function

There is moderate quality evidence that EV training incorporating SES or eye movement training improves near VA in participants with CVL.[55-57] For example, Vukicevic & Fitzmaurice (2009) [56] conducted an RCT to assess the effect of weekly EV training on near VA, over an eight week period, in 24 participants with an absolute central scotoma, compared to 24 control participants. All participants in the EV group demonstrated an improvement in near VA after training (from mean 1.42+/-0.18 to 1.00+/-0.18 logMAR), with a large Cohen's d effect size of 2.33. In contrast, there were no significant changes ($p>0.05$) in the near VA of the control group (mean 1.40+/-0.17 log MAR before and after training). However, although the participants were not told the group to which they were assigned, or how this would affect their treatment, the investigators were not masked and the outcome data were collected by the individual that administered the training. In addition, some of the individuals that took part in this study also participated in an earlier study involving EV training; therefore further compromising the integrity of these data. In another controlled trial, Verdina et al. (2013) demonstrated that 8 weekly 10 minute long sessions of EV training, using a microperimeter and audible feedback to encourage use of a TRL, caused a significant improvement in near VA from 0.67 +/- 0.18 to 0.56 +/- 0.16 logMAR in 12 patients with Stargardt disease at a 10 week follow up.[57] Six participants assigned to a control group showed a reduction in reading acuity over the same period of time. However, although a control group was included in this study, there was no evidence of random assignment of participants to groups, and it was not clear whether the individual providing the training was also collecting the outcome data.

Five of the studies included in the review report improvements in near VA after EV training delivered as part of a comprehensive low vision assessment. As these assessments also included the prescription of LVAs and / or other training, such as the provision of

lighting advice,[54, 58-61] it is not possible to determine the specific contribution of EV training to functional improvement. For example, Palmer et al. (2010) reported a significant improvement ($p<0.001$) in the near VA of 242 participants with CVL after three or four weekly low vision rehabilitation sessions in which LVAs were provided in conjunction with EV training.[61]

In contrast, Vukicevic and Fitzmaurice (2005) [55] conducted an RCT to compare the effect of EV training (n=22), magnifier provision (n=12), a combination of EV training and magnifier provision (n=12), and no intervention (n=12) on near VA. A significant improvement ($p=0.001$) in near VA was reported after training in all of the intervention groups. The greatest improvement occurred for the group that received both magnification and EV training (Cohen's d = 4.97 for the combination group and Cohen's d = 4.17 for the magnification only group), thus providing evidence that EV training is more effective than the provision of magnifiers alone for improving near VA in individuals with CVL. Moreover, this study also reassessed training outcomes six months after the training had finished and found that gains in near VA were sustained in the participants that had received EV training, but not in the group that had received magnification only. This provides evidence that improvements in near VA are sustained for longer after EV training than after the provision of magnifiers alone. However, the outcomes of this study are once again limited by the lack of masking of the investigators and the collection of outcome data by the individuals that administered the training. In addition, there was considerable overlap between the participants recruited to this study [55] and those recruited to the later study by these authors, in which the effect of EV training on near VA and performance of ADLs was assessed.[56]

It has been proposed that the assessment of reading speed provides a more valuable indication of visual performance in individuals with CVL than the assessment of VA alone, as it is a more demanding visual task.[62] With the exception of one small before and after study,[63] the 21 studies included in the review that used reading speed as an outcome measure reported increases in the reading speed of the participants after training. For example, in a before and after training comparison of 14 participants with bilateral CVL that completed a computer-based EV and SES training program, Kasten et al. (2010) found a significant increase ($p<0.05$) in mean reading speed after training (mean reading speed at baseline = 57.5+/-33.0 wpm, and mean reading speed after training = 77.3+/-52.0 wpm).[64] This was associated with a significant decrease ($p<0.05$) in the number of errors recorded during the reading period (mean number of errors at baseline = 0.77+/-0.98, and mean number of errors after training = 0.29+/0.29), with effect sizes of 0.46 for reading speed and 0.76 for the error rate. Similarly positive results were reported in a trial by Vingolo et al. (2013), which compared two types of biofeedback (acoustic and luminous) in training participants (n=15 per group, with bilateral neovascular AMD) to use a TRL.[65] Auditory and visual stimuli, respectively, were provided to indicate the proximity of fixation to the desired TRL. Training involved 10 minute training sessions administered using a microperimeter on a weekly basis for 12 weeks. There was a significant improvement in reading speed in both groups, with the luminous biofeedback group achieving a large effect size of 1.13. This trial lacked a control group, but was randomised, and outcome data were not collected by the individual carrying out the training.

Few studies have examined the effect of training on other clinical measures of vision. However, the effect of training on distance VA has received some attention. An increase in distance VA was reported in two small before and after studies (n = 5 for each study), [35, 37]

one randomised trial,[65] and one case study.[66] A change in distance VA was found in another small controlled before and after study, but this failed to reach significance when Bonferroni correction was applied for multiple comparisons.[57] In the earliest of these studies, Deruaz et al. (2005) reported a significant improvement (p=0.022) in distance VA after EV training administered using a scanning laser ophthalmoscope, although the improvements recorded for individual participants did not exceed the test-retest repeatability.[35] In contrast, there is evidence from four studies that used a before and after design (n=14-20), that there is no improvement in distance VA with EV training.[34, 36, 64, 67] For example, Kasten et al. (2010) reported no significant change (p>0.05) in distance VA for 14 participants with CVL after computer-based training in EV & SES.[64] Clearly the evidence regarding the effect of EV training on distance VA is inconclusive.

Effect of EV and SES training on performance of ADLs and quality of life

There is moderate quality evidence that EV in conjunction with SES or eye movement training improves the ability of participants with CVL to perform ADLs.[55,56,68] For example, Vukicevic and Fitzmaurice (2005) [55] used the Melbourne Low Vision ADL Index in their RCT comparing the effect of EV training to that of training with magnifiers in participants with CVL. Those that received EV training exhibited the greatest improvement (p=0.001) on low acuity self-care tasks, such as eating and bathing, whereas those that received magnification training showed the greatest improvement (p=0.001) on high acuity tasks, such as reading a newspaper or recognising faces. This provides moderate quality evidence that EV training can significantly improve the performance of ADLs, particularly with respect to low-acuity self-care tasks.

In contrast, there is a paucity of evidence regarding the effect of EV and SES training on Quality of Life (QoL). There are no studies that assessed the effect of training on general health-related QoL and only one study assessed vision-related QoL after training.[67] Jeong & Moon (2011) [67] examined the effect of a home-based EV training program on vision-related QoL in 30 participants with CVL using 10 items selected from the Korean version of the Low Vision Quality-of-Life Questionnaire (LVQOL).[69] The LVQOL contains 25 items that are grouped into five sections. However, Jeong & Moon (2011) did not specify which 10 items were used to assess training outcomes in this study. Consequently, although a significant increase ($p=0.025$) in questionnaire score was recorded after training, it is unclear which aspects of QoL demonstrated these improvements.

It is notable that only three of the studies included in the review stated that the outcome data were collected by a different individual to the one who administered the training.[65, 67, 68,] As there is a strong risk that participants will be inclined to respond more positively when outcomes are measured by the service provider, this may have exaggerated the effects of training, particularly with respect to self-report items.

The effect of training model on outcomes

A broad range of training models were described by the studies in the review. These models comprised many different aims, training strategies, technologies, training materials and settings. A number of studies described training programmes combining computer-based training of a TRL with the use of printed training materials and LVAs.[33, 62, 64, 70-72] In recent years, training strategies based on acoustic or visual biofeedback have also increased in popularity.[36,37,38,57,65,66] However, there is insufficient evidence to conclude if a particular model of EV training is superior to another as only four studies compared the

effectiveness of different models alongside each other, using the same outcome measures.[65, 68, 73-74] In addition, seven of the 34 studies failed to describe the model used for training EV.[54, 58, 60, 67, 75-76]

There is evidence from eleven studies that training to use a TRL can improve reading ability and performance of ADLs in participants with CVL.[33, 38, 55-57, 62, 65,70-72, 77] However, there were no robust studies that recorded outcomes of a training program to optimise the use of an existing PRL, and no studies that directly compared the effect of retinal locus on outcomes.

Many of the studies failed to report key information regarding the training model, including the frequency and duration of the training, the setting of the training and the qualifications of the person administering training. However, based on the data available, there is little clear evidence of an association between training outcomes and dose of training, setting in which the training took place, the trainer or the training materials provided. For example, no relationship was demonstrated between the number of hours of EV training administered and the Cohen's d effect size (Figure 2).[33, 35, 38, 57, 62, 65, 67, 70, 77]

Twenty-three (71.9%) of the studies included in this review delivered EV and SES training in conjunction with other services, such as the provision of low vision aids (LVAs) Generally, positive training outcomes were reported by these studies.[54, 58-61] However, it is unclear what proportion of these outcomes may be attributed to EV training alone, as it is likely that the provision of magnifiers would have markedly improved near VA, even in the absence of EV training.

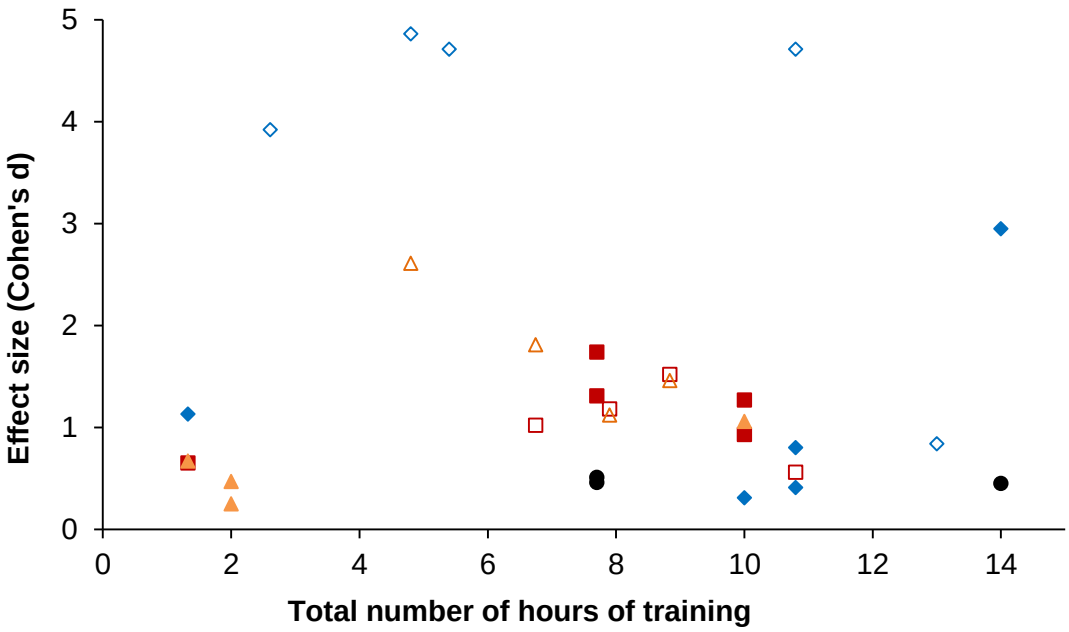

Figure 2. Effect size plotted as a function of "dose" in hours for studies in which effect sizes could be calculated, and where sufficient information regarding the intensity of intervention was provided. [33, 35, 38, 57, 62, 65, 67, 70, 77] When multiple outcomes were assessed, more than one effect size is shown per study. Diamonds = reading speed, squares = near VA, triangles = distance VA, and circles = functional outcomes. Filled symbols indicate studies in which the effect of EV training was assessed in isolation, whereas open symbols indicate those in which EV training was delivered alongside provision of magnification.

The effect of participant characteristics on the outcomes of training

With the exception of two studies,[73, 78] all of those reviewed reported the age of the participants that underwent training, and a median of 74 years (interquartile range: 54.26-76.78 years) was calculated. Within this age range the data are consistent with a slight increase in effect size for near VA with increasing age (Figure 3), although there were insufficient data from younger participants to establish any systematic relationship between age and training outcomes throughout adulthood.[33, 35, 38, 56, 57, 62, 64, 64-67, 70, 76, 79] Nevertheless, age was the only variable for which there were sufficient data to conduct a

meaningful analysis of the relationship between the participant characteristic and the Cohen's d effect size.

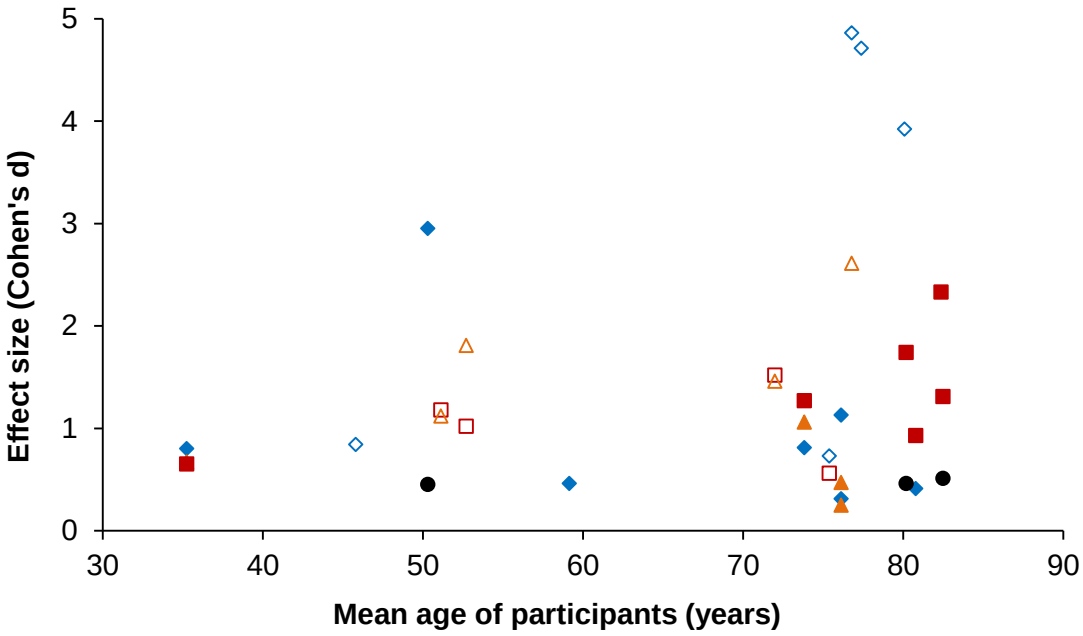

Figure 3. Effect size plotted as a function of age, in years, for studies in which effect sizes could be calculated. [33, 35, 38, 56, 57, 62, 64, 64-67, 70, 76, 79] When multiple outcomes were assessed, more than one effect size is shown per study. When multiple outcomes were assessed, more than one effect size is shown per study. Diamonds = reading speed, squares = near VA, triangles = distance VA, and circles = functional outcomes. Filled symbols indicate studies in which the effect of EV training was assessed in isolation, whereas open symbols indicate those in which EV training was delivered alongside provision of magnification.

In general, the duration and characteristics of the participants' vision loss were poorly specified by the studies in the review. None of the studies included individuals with newly diagnosed CVL, and none specifically examined the relationship between training outcomes and the duration and characteristics of the vision loss, such as the size and density of the scotoma.

Cost effectiveness of EV and SES training

The studies included in this review provide no data about the cost effectiveness of EV and SES / eye movement training. There were no studies that included an economic evaluation of EV provision and only two studies acknowledged the source of their funding.[33, 61]

DISCUSSION

Overall, there is a lack of high quality evidence regarding the effectiveness of EV and SES or eye movement training in individuals with CVL. Only three studies included in the review presented the results of a RCT,[54-56] and these failed to meet the criteria for well-designed RCTs set out by the Cochrane Collaboration, due to issues including, a lack of information regarding the randomisation of participants,[55-56] a lack of masking of the investigators / collection of outcome data by the individual providing the training,[54-56] and failure to separate the effects of EV training from those of LVAs.[54] The majority of studies used a relatively weak 'before and after' comparison design, and few incorporated a control group. Many studies failed to provide an adequate description of the training programme and the training outcomes were not always fully reported. Additionally, a lack of consensus regarding measurement of training outcomes limited the comparison of outcomes between different studies. This lack of high quality evidence is a feature of low vision research more generally; a recent review evaluating the effectiveness of low vision service provision as a whole reported a paucity of high quality evidence in this field.[80]

The available data did provide moderate quality evidence that EV in conjunction with SES or eye movement training improved near VA and reading speed in individuals with CVL. There was also moderate quality evidence that EV and SES / eye movement training led to

improvements in the performance of ADLs in people with CVL. However, more data are required to assess the impact of training on distance VA, QoL and vision-related QoL. Such data would be of significant value to healthcare providers and funding bodies in determining the optimal approach to low vision rehabilitation in patients with CVL.

Generally, EV and SES or eye movement training strategies, administered in isolation or in conjunction with a broader low vision rehabilitation program, were associated with positive outcomes in individuals with CVL. However, there were insufficient data to determine if a particular training strategy, or characteristic of a training strategy, was more effective than another. Similarly, as the characteristics of the participants' vision loss were poorly specified by many studies, it was difficult to establish any relationship with training outcomes.

There were no studies within the review that included an economic evaluation of the EV training program; therefore it is not possible to draw any conclusions about the cost effectiveness of EV training. This lack of evidence poses a significant problem to the development of an economic case for the use of EV training in the rehabilitation of individuals with CVL.

A literature review always carries a certain risk of bias, conferred by the opinions of the review authors, the risk of missing potentially relevant studies, and the bias intrinsic to the included studies themselves. This review has attempted to minimise these potential sources of bias in the review process by following a predefined protocol specifying the research question, review methods and eligibility criteria. The exclusion of studies that were not reported in English was a potential source of bias. However, the independent screening of

abstracts for eligibility by two individuals, and the consultation of lead and senior authors of studies pertaining to EV and SES training to identify additional references was designed to minimise the risk of excluding potentially relevant studies. To minimise the impact of bias introduced by the studies themselves, Table 2 summarises the risk of bias of all included studies. Methodological issues are highlighted in the review text, and the potential implications of these issues addressed.

As the average age of the population rises over the coming decades,[41] there will be a corresponding increase in the prevalence of age-related eye diseases such as AMD. Consequently, there is an urgent need for robust trials to establish the true potential and cost effectiveness of EV as a rehabilitative strategy for individuals with CVL.

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Table 2. Assessment of risk of bias for studies included in the literature review (where: NR = non-randomised study; NC = no untreated control group; OT = outcome data collected by trainers; PD = participant drop-out not reported; SS = single training session; QD = qualitative data only, EI = unable to determine effect of EV in isolation; O = other)

Study	Study design	Risk of bias assessment	GRADE quality rating
Arditi, 1999 [73]	Before and after study	NR, NC, PD, OT, SS, O (participants all had prior experience of one training method)	Very low
Chung, 2011 [79]	Before and after study	NR, NC, PD, OT, O (50% of participants had prior experience of training method)	Very low
Deruaz et al., 2006 [35]	Before and after study	NR, NC, OT	Very low
Epstein et al., 1981 [78]	Qualitative	NR, NC, PD OT, QD	Very low
Feely et al., 2007 [76]	Qualitative	NR, NC, PD, OT, QD	Very low
Fitzmaurice & Clarke, 1993/1994 [51-52]	Before and after study	NR, NC, OT	Very low
Fitzmaurice & Clarke, 2008 [81]	Case study	NR, NC, PD, OT	Very low
Frennesson et al., 1995 [70]	Before and after study	NR, NC, PD, OT, O (distance VA not reassessed after training)	Very low
Gustafsson & Inde, 2004 [33]	Before and after study	NR, NC, OT, O (participants selected due to high motivation)	Very low
Holcomb & Goodrich, 1976 [82]	Before and after study	NR, PD, OT	Very low
Jeong & Moon, 2011 [67]	Before and after study	NR, NC, O (training program poorly described)	Very low
Kasten et al., 2010 [64]	Before and after study	NR, NC, PD, OT, O (50% already used PRL prior to training)	Very low
Nguyen et al., 2011 [74]	Between technique comparison	NR, NC, OT, O (adherence to home-based training unclear)	Very low

Nilsson et al., 1986a [58]	Before and after study	NR, NC, OT, EI	Very low
Nilsson et al., 1986b [59]	Before and after study	NR, NC, OT, EI	Very low
Nilsson et al., 1989 [60]	Before and after study	NR, NC, OT, EI	Very low
Nilsson, 1990 / Nilsson & Nilsson, 1994 [53-54]	RCT	PD, OT, EI	Low
Nilsson et al., 1998 [71]	Before and after study	NR, NC, PD, OT	Very low
Nilsson et al., 2000 [72]	Case study	NR, NC, PD, OT	Very low
Nilsson et al., 2003 [62]	Before and after study	NR, NC, OT	Very low
Palmer et al., 2010 [61]	Before and after study	NR, NC, OT EI	Low
Salvatore et al., 2011 [66]	Case study	NR, NC, PD, OT	Very low
Seiple et al., 2005 [34]	Before and after study	NR, NC, PD, OT	Very low
Seiple et al., 2011 [68]	Randomised trial	PD, O (method of assessment likely to favour RSVP)	Moderate
Tarita-Nistor et al., 2009 [38]	Before and after study	NR, NC, OT, O (unable to establish if using TRL)	Very low
Verdina et al., 2013 [57]	Controlled before and after study	NR, OT	Low
Vingolo et al., 2007 [36]	Before and after study	NR, NC, OT	Very low
Vingolo et al., 2009 [37]	Before and after study	NR, NC, OT	Very low
Vingolo et al., 2013 [65]	Randomised trial	NC	Low

Vukicevic & Fitzmaurice, 2002 [77]	Randomised trial	NR, NC, PD, OT	Low
Vukicevic & Fitzmaurice, 2005 [55]	RCT	PD, OT (overlap in participants recruited with [56])	Moderate
Vukicevic & Fitzmaurice, 2009 [56]	RCT	PD, OT (overlap in participants recruited with [55])	Low
Watson et al., 2006 [63]	Before and after study	NR, NC, OT, O (unable to establish if using TRL)	Very low
Woo & Calder, 1987 [75]	Case study	NR, NC, PD, OT, QD	Very low