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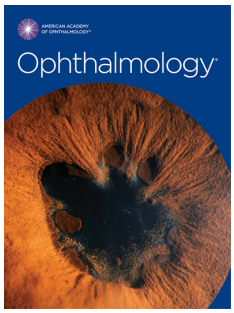

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Interventions for the management of computer vision syndrome: a systematic review and meta-analysis

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Running head: Interventions for computer vision syndrome.

Key words: Digital eye strain, Computer vision syndrome, Visual fatigue.

Abbreviations and Acronyms: CVS = computer vision syndrome; CFF = critical flicker-fusion frequency; CI = confidence interval; DHA = docosahexaenoic acid; DESS = Dry Eye Questionnaire and Scoring System; EPA = eicosapentaenoic acid; GRADE = grading of recommendations, assessment, development and evaluation; Hz = hertz; MD = mean difference; PRISMA = preferred reporting items for systematic reviews and meta analyses; RCT = randomized controlled trial; SMD = standardized mean difference, VDT = visual display terminal.

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Abstract

Topic: To evaluate the efficacy and safety of interventions for treating eye strain related to computer use relative to placebo or no treatment.

Clinical relevance: Computer use is pervasive and often associated with eye strain, referred to as “computer vision syndrome” (CVS). Currently, there are no clinical guidelines to help practitioners provide evidence-based advice about CVS treatments, many of which are directly marketed to patients. This systematic review and meta-analysis will help inform best practice for eye care providers.

Methods: Eligible randomized controlled trials (RCTs) were identified in Ovid MEDLINE, EMBASE, CENTRAL, and trial registries, searched from inception to November 23, 2021. Eligible studies were appraised for risk of bias, and synthesized. The certainty of the body of evidence was judged using GRADE. Standardized mean differences (SMD) were used when differently scaled measures were combined.

Results: Forty-five RCTs, involving 4497 participants, were included. Multifocal lenses did not improve visual fatigue scores compared to single-vision lenses (three RCTs, SMD: 0.11; 95% confidence interval (CI) -0.14 to 0.37; p=0.38). Visual fatigue symptoms were not reduced by blue-blocking spectacles (three RCTs), with evidence judged to be of low certainty. Relative to placebo, oral berry extract supplementation for 4 to 12 weeks did not improve visual fatigue (seven RCTs, SMD: -0.27; 95%CI -0.70 to 0.16; p=0.22), and dry eye symptoms (four RCTs, SMD: -0.10; 95%CI -0.54 to 0.33; p=0.65). Likewise, berry extract supplementation had no effect on critical flicker-fusion frequency (CFF) or accommodative amplitude. Oral omega-3 fatty acid supplementation for 45 days to 3 months improved dry eye symptoms (two RCTs, mean difference, MD: -3.36 units out of 18; 95%CI -3.63 to -3.10; p<0.00001) relative

to placebo. Oral carotenoid supplementation improved CFF (two RCTs, MD: 1.55 Hz; 95%CI 0.42 to 2.67; *p*=0.007) relative to placebo, although the clinical significance of this finding is unclear.

Conclusions: We found no high certainty evidence supporting the use of any of the therapies analyzed. There was low certainty evidence that oral omega-3 supplementation reduces dry eye symptoms in symptomatic computer users.

Introduction

Computer vision syndrome (CVS) describes a group of eye and vision related problems associated with prolonged computer use.[1] CVS affects 75 to 90% of computer users.[2] Its global prevalence is estimated at 60 million, with one million incident cases each year.[3] Common symptoms of CVS are eye strain, blurred vision, eye dryness, ocular redness, headache, and neck and shoulder pain.[4] Though these symptoms are usually temporary, they may not resolve at the end of the working day.[5] Given the typical chronicity of computer use, many of the symptoms of CVS are recurrent and/or prone to progression.[6]

In eye care practice, CVS is primarily diagnosed by surveying patients using a range of symptom-focused questions. Segui et al.[7] developed and validated a questionnaire that involved participants specifying the frequency and intensity of 16 symptoms associated with computer-induced eye strain. A score of six or more has been reported to be diagnostic of CVS;[7] this questionnaire has since been widely used in clinical studies to identify CVS.[8-10]

Established risk factors for CVS are extended periods of computer use (greater than four hours per day),[11] reflections and glare on the computer screen from surrounding lighting,[12] low humidity (<40%), and poor ergonomics with computer use.[13] Ocular symptoms in computer users may be associated with reduced blink rate, uncorrected refractive error, and/or accommodation anomalies.[14-17] Thorud et al.[18] studied the association between extraocular symptoms (such as pain around the eye) with computer use, using electromyography and photoplethysmography, and found a weakness in the orbicularis oculi muscles to be linked with CVS symptoms. In addition, blue (short wavelength visible) light emitted from computer screens has

been hypothesized to cause eye strain,[19] although this remains contentious given the lack of supporting evidence, the lack of a compelling biological mechanism through which blue light might directly cause eye strain, and the relatively low level of blue light emission from electronic devices.[20]

In terms of CVS management, a diversity of interventions has been investigated. A common clinical approach involves recommending an optimal ergonomic setup at the computer, and advising computer users to follow the “20-20-20 rule”, which involves viewing an object 20 feet away for a total of 20 seconds every 20 minutes.[21] Other interventions that have been considered include optical interventions (i.e., progressive addition spectacle lenses[22], and blue light-blocking spectacle lenses[19]), oral antioxidant and nutritional supplements,[23] omega-3 fatty acid supplements,[24] artificial tears,[4] and traditional medicines.[25] Optical aids, such as progressive addition lenses, are claimed to reduce symptoms of CVS by providing an optimal refractive correction for intermediate and near working distances.[22, 26] Blue light-blocking spectacle lenses have been promoted to reduce symptoms of eye strain by attenuating blue light emitted from computer screens,[27, 28] despite the lack of a compelling mechanism of action. Omega-3 fatty acids may reduce ocular surface inflammation by modulating systemic cytokine production levels, to reduce dry eye symptoms in computer users.[29] Artificial tears are considered to lubricate the ocular surface and to increase tear volume to reduce CVS symptoms.[21] The mechanism by which antioxidant and nutritional supplements might reduce eye strain symptoms is unclear. Despite this, both interventions are frequently advertised as potentially useful treatments for CVS.[30, 31] Many CVS interventions are directly marketed to patients, and so eye care providers need to be able to provide evidence-based advice to patients enquiring about the efficacy, or otherwise, of such interventions.

Although CVS has been extensively studied and a wide variety of interventions exist, currently there are no clinical guidelines to inform best practice. The aim of this systematic review was to identify, appraise and synthesize clinical evidence relating to the efficacy and safety of interventions for treating CVS, and thereby provide support to practitioners in providing evidence-based advice to their patients.

Methods

This review was prospectively registered on PROSPERO (CRD42020164092), conducted in accordance with the principles in the Cochrane Handbook, and reported according to the Preferred Reporting Items for Systematic Reviews and Meta Analyses (PRISMA) statement (see Appendix S1 in Supplement I, at http://www.aaojournal.org/).[32]

Eligibility criteria

Eligible for inclusion were randomized controlled trials (RCTs) that compared any intervention for managing signs or symptoms of CVS in humans, relative to an inactive control, placebo, sham or no treatment. Eligible studies had recruited male or female participants of any age, with a diagnosis of CVS, as defined by the study authors. Published conference abstracts, non-English studies, and non-human studies were excluded. Studies identified on clinical trial registries with sufficient details on interventions and outcomes (in the absence of a published manuscript) were included. The outcomes from the most recent publication for each study were included. For analysis, the interventions were grouped into the following categories: optical aids, complementary medicine and nutritional supplements, artificial tears, environmental modification, ergonomic adjustment, visual hygiene (e.g., blinking exercises, advice to follow the “20-20-20 rule”), binocular vision training, and other

interventions. Complementary medicine and nutritional supplements were further divided into six subcategories: oral berry extract supplements, polyunsaturated fatty acid supplements, antioxidant supplements, traditional medicines, combination supplements, and other interventions. Details on intervention group and relevant comparators are presented for each study in Appendix S2 (see Supplement I, at http://www.aaojournal.org/).

Search methods

The following electronic databases were initially searched from inception to 12 December 2019, and were updated to 23 November 2021: Ovid MEDLINE, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), US National Institutes of Health Clinical Trials Registry (www.ClinicalTrials.gov), and the WHO International Clinical Trials Registry Platform (https://www.who.int/clinical-trials-registry-platform). Complete search strategies are provided in Appendix S3 (see Supplement I, at http://www.aaojournal.org/). Reference lists of included RCTs were screened for additional potentially relevant studies.

Selection of studies

Citations retrieved from electronic databases were compiled into an EndNote library. Following removal of duplicate citations, the library was imported into Covidence.[33] Two reviewers (SS [author] and one of LED [author], JHL or EM) independently screened citation titles and abstracts and decided whether they should be included, excluded or potentially included. Studies judged to be definitely or potentially eligible progressed to full-text screening. Two reviewers (SS and one of LED, JHL, or EM) independently screened the full-texts, based on pre-defined eligibility criteria. For studies excluded at the full-text screening stage, the primary reason for exclusion

was documented. Any disagreements between review authors were resolved by discussion, or by consulting a third review author if required.

Data extraction and management

Two reviewers (SS and one of LED, AJA [author], JHL, EM) independently extracted data; any discrepancies were resolved by discussion. Information extracted from each eligible study included: study details (author, title, journal, year of publication), methodology, participants, interventions, outcomes, and other details (e.g., sources of funding, conflicts of interest). For studies where missing outcome data were identified or additional information was required for statistical analysis, we attempted to contact the study authors via email for the information. If a response was not received within four weeks, or if the trial authors were unable to provide the information, the analysis was performed using details in the full-text publication.

Risk of bias assessment

Risk of bias was assessed for eligible studies according to guidance in the *Cochrane Handbook for Systematic Reviews of Interventions*.[34] The assessed risk of bias domains were: selection bias (random sequence generation and allocation concealment), performance bias (masking of study participants and personnel), detection bias (masking of outcome assessors), attrition bias (incomplete outcome data), reporting bias (selective outcome reporting), and other sources of bias (such as funding sources and conflicts of interest). Each study was judged to have low, high or unclear risk of bias in each domain. Two review authors independently performed the assessments, with any disagreements resolved by discussion.

Data synthesis and analysis

For all analyses in this review, the unit of analysis was defined as the study participant. Whenever possible, data for pre-specified primary (visual fatigue symptoms and CFF) and secondary outcomes (quality of life, dry eye symptoms, amplitude of accommodation, near point of convergence, blink rate, and overall patient satisfaction with the intervention) (Appendix S4 in Supplement I, at http://www.aaojournal.org/) were preferably extracted as change from baseline, otherwise data at the study end-point were extracted; this latter measure is a suitable substitute when comparing groups (under the assumption of randomized interventions).[35] In the absence of clinical guidelines to define best practice for CVS, the most widely reported outcomes being visual fatigue symptom scores[2, 5, 18, 36] and CFF[19, 37-39] were used as primary outcome measures.

When studies reported outcomes both before (pre) and after (post) computer use, following different durations of an intervention, we used data reported for the post-computer task at the final study visit for analysis. For studies that investigated multiple interventions, analyses were performed by comparing each intervention arm with the comparator group. As different scales were used to measure visual fatigue and dry eye scores across the studies, the standardized mean difference (SMD) was used to pool data.[40] Cohen[41] suggests a SMD of 0.2 represents a small effect, SMD of 0.5 a medium effect, and SMD of 0.8 a large effect. Further, as Cochrane advises not to combine mean change and endpoint outcome data, only studies with endpoint outcomes were pooled as this allowed the maximum number of studies to be included in our meta-analyses.[40] For studies that reported only change from baseline data, their individual study results were summarized. For the purpose of the analysis, data of cross-over trials were treated as like parallel-design studies as there was no

unit of analysis issue.[42] If data were not reported as a mean and standard deviation, guidance in Chapter 7 of *the Cochrane Handbook for Systematic Reviews of Interventions* was followed to convert the data into the required form.[35]

Meta-analyses were performed using Cochrane Review Manager (RevMan Version 5.4) software.[43] Mean differences were performed for the primary and secondary outcomes for each intervention subcategory, when deemed clinically meaningful (e.g., for studies where the intervention, participants and underlying clinical questions were similar). When fewer than three RCTs were included, a fixed-effect model was used, otherwise a random-effects model was adopted.[44, 45]

Clinical and methodological heterogeneity were assessed by considering trial design, baseline participant characteristics, and risk of bias judgements. Statistical heterogeneity was assessed using the I^2 statistic, which describes the percentage of total variation across all studies. An I^2 value >50% or a *p* value for Cochrane's Q statistic of <0.05 was used to define significant statistical heterogeneity.[46, 47] For comparisons where a meta-analysis was not possible (e.g., only one eligible study) or data pooling was considered inappropriate (e.g., I^2 value >50%), a descriptive summary of results was provided.

When sufficient data were available, subgroup analyses were performed for interventions with multiple subcategories (i.e., complementary medicines and nutritional supplements), as previously defined. As there were fewer than 10 trials for each of the intervention categories, funnel plots were not visually inspected to assess small study effects.[48]

Summary of findings table

The certainty of the body of evidence was assessed as high, moderate, low or very low, for the primary and secondary outcomes using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.[49] The reason(s) for downgrading the certainty estimates are reported in the 'Summary of findings' Tables 1 and 2 or Table S1 (see Supplement I, at http://www.aaojournal.org/).

Results

Characteristics of included studies

Electronic searches yielded 4891 citations (see PRISMA flow diagram, Figure 1). After removing duplicates (n=922), title and abstract screening was performed on 3969 citations. Of these, 296 records proceeded to full-text screening and 45 trials met the eligibility criteria; 43 were full-text articles,[19, 20, 22-25, 50-86] published between 1991 and 2021, and two studies[87, 88] were on clinical trial registries with available data (registered in 2016[88] and 2018[87]). In addition, 24 RCTs on trial registries were marked as ongoing (Table S2, see Supplement I, at http://www.aaojournal.org/). Supplementary Table S3 (see Supplement I, at http://www.aaojournal.org/) lists studies excluded after full-text screening, with the primary reason for exclusion.

The key characteristics of all eligible studies are provided in Table S4 (see Supplement I, at http://www.aaojournal.org/). Included RCTs were conducted in 11 countries: Japan (n=11),[23, 61-64, 66, 67, 75, 76, 79, 82] India (n=9),[24, 25, 50-53, 70, 72, 73] United States of America (n=6),[19, 54, 71, 74, 87, 88] Hong Kong (n=2),[22, 57] Korea (n=1),[68] China (n=1),[83] Saudi Arabia (n=1),[86] Australia (n=1),[20] Norway (n=1),[58] and Spain and the United Kingdom (n=1).[84] Eleven trials did not report the study location.[55, 56, 59, 60, 65, 69,

247 [77, 78, 80, 81, 85] Most RCTs (n=35) used a parallel arm design,[19, 20, 23-25, 50-53, 56-73, 76, 77, 79,
248 81-84, 86] and 10 studies used a cross-over design.[22, 54, 55, 74, 75, 78, 80, 85, 87, 88] In total,
249 4497 participants were recruited across the included 45 RCTs; sample sizes ranged
250 from 10 to 522 participants. Further details about the study characteristics are
251 provided in Supplementary Table S5 (see Supplement I, at
252 http://www.aaojournal.org/).

253 **Risk of bias assessment**

254 Figure 2 summarizes risk of bias assessments.[19, 20, 22-25, 50-88] No RCT was judged to
255 have low risk of bias in all seven Cochrane domains. The domain with the most
256 studies judged to be at low risk was attrition bias (30 studies,[17, 19, 20, 22-24, 50, 51, 56-61, 63-
257 66, 68, 70, 71, 76-78, 81-85, 88]). Domains with the greatest number of studies considered to
258 have a high risk were performance bias, relating to a lack of masking of participants
259 and/or personnel (17 studies,[19, 22, 25, 53-59, 70, 72, 73, 78, 86, 87, 89]); detection bias,
260 pertaining to the masking of outcome assessors (15 studies,[22, 25, 53-59, 69, 70, 78, 85-87]);
261 and other bias (Of sixteen studies judged high risk of bias, fifteen[19, 23, 61, 62, 64, 66, 67, 71,
262 76, 78, 79, 81-84] were due to industry funding and one[50] due to baseline differences
263 between participant groups).

264 **Effects of interventions**

265 Tables 1 and 2 provide Summary of Findings tables for the 'optical aids' and
266 'complementary medicine and nutritional supplement' intervention categories,
267 respectively. A sufficient number of studies (n≥2) were identified to perform meta-
268 analyses for two categories of interventions: i) optical aids, and ii) complementary
269 medicines or nutritional supplements.

1. Intervention category - optical aids

Ten trials (see Table 3 for details) investigated optical aids, consisting of: multifocal contact lenses,[87, 88] progressive (multifocal) addition spectacle lenses,[22, 58, 84] single-vision cylindrical lenses,[74] single-vision addition lenses,[80] and blue light-blocking spectacle lenses,[19, 20, 85] relative to control single-vision distance optical corrections,[22, 58, 84, 87, 88] placebo lenses,[74, 80] or non-blue light-blocking spectacle lenses.[19, 20, 85]

1.1. Primary outcome

Eight studies measured subjective visual fatigue, using a Likert scale[19, 22, 74, 84, 85] or visual analogue scale.[20, 87, 88] Pooling comparable data from three studies[22, 87, 88] provided no difference in visual fatigue with use of a multifocal relative to a single-vision distance correction (Figure 3; three studies, 262 participants; SMD: 0.11; 95% confidence interval (CI) -0.14 to 0.37; I^2 = 7%; p=0.38). Del Mar Segui-Crespo et al.[84] reported no difference for the change in visual fatigue scores with multifocals compared to single vision lenses (MD: -1.50 units; 95%CI –3.60 to 0.60, p=0.16). The certainty of evidence for this outcome was juded as very low.

In addition, Wiggins et al.[74] provided very low certainty evidence for reduced visual fatigue symptoms when correcting residual astigmatism in contact lens wearers, compared to having uncorrected residual astigmatism (Table S6, see Supplement I, at http://www.aaojournal.org/). For the other studies in this category,[19, 20, 85] no difference was found for the overall change in visual fatigue[19, 20] or average daily change in visual fatigue[85] with blue light-blocking lenses compared to non blue light-blocking lenses (Table S6).

Singh et al.[20] reported no difference for the change in CFF with use of blue light-blocking lenses compared to non blue light-blocking lenses (MD: -1.13 Hz; 95%CI –

3.00 to 0.74, *p*=0.240). In contrast, Lin et al.[19] described a less negative change in CFF (i.e., less visual fatigue) with high blue light-blocking lenses, compared to low blue-light blocking and non blue light-blocking lenses (Table S6).

The GRADE certainty of the evidence assessments for no effect on visual fatigue and little or no effect on CFF (blue light-blocking versus non blue light-blocking lenses) were both judged as low.

1.2. Secondary outcomes

Three studies considered dry eye symptoms. NCT02921087[88] reported very low certainty of evidence for no difference in symptom scores between multifocal and single-vision contact lenses after one week (44 participants; MD: 0.70 units; 95%CI -2.62 to 4.02, *p*=0.68), Two studies[20, 85] provided moderate certainty evidence for no improvement in dry eye symptoms with blue light-blocking lenses compared to non blue light-blocking lenses (Table S6).

For other secondary outcomes, Singh et al.[20] reported no difference between blue light-blocking and clear spectacle lenses for the change from baseline in near point of accommodation (MD: -0.30 D; 95%CI, -0.71 to 0.11, *p*=0.15), near point of convergence (MD: 0.29 cm; 95%CI, -0.28 to 0.86, *p*=0.32), and blink rate (MD: 1.37 blinks per minute; 95%CI, -0.44 to 3.18, *p*=0.14). The GRADE certainty of the evidence for each of these outcomes was judged as moderate.

1.3. Adverse events

Four trials[20, 84, 87,88] reported adverse event data. No adverse events were reported for two studies reporting spectacle lens interventions (blue light blocking (2-hours)[20] and multifocal lenses (6-months)[84]). Whilst one study[87] reported no adverse events

in two contact lens-wearing groups after one week, in another[88] two participants in a multifocal contact lens group, and one participant in a control (single vision contact lens) group had mild anterior eye adverse events after one week. Pooling data from three studies,[84, 87, 88] provided low certainty evidence for no difference in the risk of an adverse event between multifocal and single vision lenses (Figure S1, three studies, 180 participants; relative risk (RR): 2.09; 95% CI 0.20 to 21.45; *p*=0.53).

2. Intervention category - Complementary medicine and nutritional supplement

2.1. Intervention subcategory - Berry extract

Eight trials[23, 62, 66-68, 76, 79, 81] investigated forms of oral berry extract compared to placebo (bilberry extract, n=6[23, 62, 66, 67, 79, 81]; bog bilberry, n=1[68]; maqui berry, n=1[76]). Table 4 summarizes the characteristics of these studies.

2.1.1. Primary outcomes

Seven studies evaluated subjective visual fatigue.[23, 62, 66-68, 76, 79] Combining their data gave low certainty evidence for no improvement in visual fatigue score with oral berry extract supplementation relative to placebo (Figure 4; seven studies, 322 participants; SMD: -0.27 units; 95% CI -0.70 to 0.16; $I^2 = 70\%$; *p*=0.22); significant heterogeneity was observed due to divergent effects noted in one study[79] (Figure S2). Pooling data from three studies[23, 66, 76] provided low certainty for no difference in CFF with oral berry extract supplementation relative to placebo at the study endpoints (Figure 5; 193 participants; MD: -0.35 Hz; 95%CI -1.39 to 0.69; $I^2 = 29\%$; *p*=0.51).

2.1.2. Secondary outcomes

Yamashita et al.[76] provided very low certainty evidence for no difference in quality of life score after four weeks using oral maqui berry supplementation relative to placebo (74 participants; MD: 1.00 units; 95%CI -1.36 to 3.36, *p*=0.41). Pooling comparable data from four studies,[23, 62, 76, 79] provided no decrease in dry eye symptoms with oral berry extract supplements relative to placebo (Figure 6; four studies, 198 participants; SMD: -0.10 units; 95%CI -0.54 to 0.33; $I^2 = 50\%$; *p*=0.65). Park et al.[68] reported no difference for the change in dry eye scores with billberry extract supplement compared to placebo (MD: -0.69 units; 95%CI –1.41 to 0.03, *p*=0.006). The certainty of evidence for this outcome was juded as low.

Pooling data from two studies[23, 66] provided low certainty evidence for no difference in accommodative amplitude at the study endpoints with oral bilberry extract relative to placebo supplementation (Figure 7; two studies, 119 participants; MD: -0.06 D; 95%CI -0.64 to 0.53; $I^2 = 0\%$; *p*=0.85).

2.1.3. Adverse events

All eight studies,[23, 62, 66-68, 76, 79, 81] reported no adverse events in either the berry extract or placebo groups. The certainty of the evidence for this outcome was very low.

2.2. Intervention subcategory - Polyunsaturated fatty acids

Two parallel-arm trials[24, 50] evaluated oral long-chain omega-3 fatty acids (eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA)) compared to placebo.

2.2.1. Secondary outcomes

Pooling data from these studies,[24, 50] which had very high statistical heterogeneity (I^2 = 89%; Figure 8), there was moderate certainty for improved dry eye symptoms with oral omega-3 supplementation after 45 days to 3 months of follow-up (two studies, 978 participants; MD: -3.36 units; 95%CI -3.63 to -3.10; I^2 = 89%; p<0.00001) relative to placebo.

2.2.2. Adverse events

Although neither study explicitly reported adverse events, participants dropped out of the omega-3 fatty acid supplement group due to gastric intolerance (n=6[50] and n=26[24], over 45 days). Neither study reported if dropouts occurred in the placebo group. The certainty of evidence for this outcome was judged to be low.

2.3. Intervention subcategory – Carotenoid supplement

Nagaki et al.[65] and Stringham et al.[71] evaluated oral carotenoid supplements relative to placebo.

2.3.1. Primary outcomes

Nagaki et al.[65] provided low certainty evidence for reduced visual fatigue with oral carotenoid relative to placebo supplements; numeric data were not provided. Pooling data from both studies[65, 71] provided very low certainty of an improvement in CFF with oral carotenoid supplementation relative to placebo (Figure 9; two studies, 74 participants; MD: 1.55 Hz; 95%CI 0.42 to 2.67; I^2 = 0%; p=0.007).

2.3.2. Secondary outcomes

Stringham et al.[71] did not measure any of the secondary outcomes. Nagaki et al.[65] provided very low certainty evidence for no difference in amplitude of

accommodation after four weeks of carotenoid supplementation relative to placebo (26 participants; MD: 0.50 D; 95%CI -0.56 to 1.56, *p*=0.35).

2.3.3. Adverse events

Only Nagaki et al.[65] (n=26) reported adverse events, finding none in either the carotenoid supplement or placebo groups. The certainty of evidence for this outcome was judged as low.

2.4. Intervention subcategory - Traditional medicines

Six parallel-arm RCTs[25, 51-53, 59, 70] investigated traditional medicines relative to a placebo; study details are summarized in Table S4.

2.4.1. Primary outcome

Joshi and Ujwale[59] provided very low certainty evidence for no difference in visual fatigue with use of Tila Taila Padabhyanga traditional medicine (foot massage with sesame oil) relative to placebo (60 participants; MD: -0.70 units; 95%CI -1.52 to 0.12, *p*=0.09).

2.4.2. Adverse events

Three studies,[51-53] involving 270 participants, reported no adverse events in the traditional medicine or placebo groups, over one month[53] to six weeks.[51, 52] The certainty of evidence for this outcome was judged to be moderate.

2.5. Intervention subcategory - Combination supplements

Five studies[60, 61, 75, 82, 83] investigated combination oral supplements relative to placebo (Table S4).

2.5.1. Primary outcomes

2.5.1.1. Visual fatigue score

Four studies[60, 61, 82, 83] reported on visual fatigue, however data were not pooled as the studies evaluated different supplement combinations (Table S4). Kan et al.[83] reported reduced visual fatigue symptoms with a combination supplement of lutein ester, zeaxanthin, and extracts of blackcurrant, chrysanthemum and goji berry after four weeks (303 participants; MD: -2.83 units; 95%CI -3.56 to -2.10, *p* <0.001) relative to placebo. Three studies[60, 61, 82] reported no improvement in symptoms of visual fatigue with combination supplements compared to placebo (see Table S6 for details). The certainty of the evidence was judged as very low.

2.5.2. Secondary outcomes

Kan et al.[83] reported improved dry eye symptom scores with the combination supplement after four weeks, relative to placebo (303 participants; MD: -0.52 units; 95%CI -0.74 to -0.30, *p*<0.001), Futher, two studies[60, 82] reported no difference in dry eye symptom scores with combination supplements compared to placebo (see Table S6 for details).

There was very low certainty evidence for no difference in amplitude of accommodation with the combination supplement (see Table 2 for details) investigated by Kondo and Sawano[61], relative to placebo (110 participants; MD: -0.29 D; 95%CI -0.94 to 0.36, *p*=0.38). Likewise, there was very low certainty evidence for no difference in eye blink rate between the combination supplement evaluated by Yagi et al.[75] relative to a placebo supplement.

2.5.3. Adverse events

Two studies[82, 83] reported no adverse events in either the combination supplement or placebo groups. Kondo and Sawano[61], studying 110 participants, reported 15 adverse events in the combination supplement group and 19 in the placebo group, over 12 weeks; all were self-reported and deemed unrelated to the intervention by the study medical investigator. The certainty of evidence for this outcome was judged to be very low.

2.6. Intervention subcategory - other

Three parallel-arm trials[63, 64, 77] investigated other types of complementary medicines or nutritional supplements relative to a placebo supplement. The interventions that were evaluated were Yabukita (group I) and Sunrouge (group II) green tea extracts,[63] an oral probiotic[64] and an oral taurine supplement

2.6.1. Primary outcomes

Two studies reported visual fatigue data.[63, 64] Morita et al.[64] reported no difference with probiotics relative to placebo (59 participants; MD: -3.00 units; 95%CI -13.06 to 7.06, *p*=0.56). Similarly, Maeda-Yamamoto et al.[63] found no difference between Sunrouge, Yabukita and placebo green tea extracts; numeric data were not reported.

For CFF, Morita et al.[64] reported no difference between oral probiotics and placebo (59 participants; MD: 0.03 Hz; 95%CI 1.60 to 1.66, *p*=0.97). Zhang et al.[77] observed no difference between taurine and placebo supplements (25 participants; MD: -4.00 Hz; 95%CI -10.65 to 2.65, *p*=0.24).

The certainty of evidence for visual fatigue scores was judged to be low, and for CFF was judged as very low.

2.6.2. Secondary outcomes

Morita et al.[64] provided very low certainty evidence for no difference in dry eye symptom score between oral probiotics and placebo (59 participants; MD: 2.20 units; 95%CI -7.11 to 11.51; *p*=0.64).

Two studies[64, 77] evaluated accommodative amplitude. Morita et al.[64] found no difference with oral probiotics relative to placebo (59 participants; MD: 0.27D; 95%CI -1.17 to 1.71, *p*=0.71). Maeda-Yamamoto et al.[63] performed a subgroup analysis and described that, in a group aged less than 45 years, there was an increase in amplitude of accommodation with Sunrouge green tea extract (n=8), relative to a placebo (n=10); no numeric data were provided. The certainty of evidence for this outcome was judged to be very low.

2.6.3. Adverse events

Maeda-Yamamoto et al.[63], studying 114 participants, reported no adverse events in the green tea extract or placebo groups. The certainty of evidence was judged as moderate.

3. Intervention category – Artificial tears

Guillon et al.[78] investigated 2% povidone preservative-free lubricating eye drops, using three dosing regimens, compared to no intervention.

3.1. Primary outcomes

Visual fatigue was measured, although no numeric data were provided; the study provided very low certainty evidence for reduced symptoms with the eye drops using all three instillation frequencies, compared to no intervention.

3.2. Adverse events

Adverse events were not reported.

4. Intervention category – Environmental modifications

Two parallel-arm studies investigated environmental modifications,[56, 57] comprising a moist cool air device[56] and computerized risk assessment systems[57].

4.1. Primary outcome

Hirayama et al.[56] found no difference in visual fatigue score with a moist cool air device after five days, relative to no intervention (20 participants; MD: -0.20 units; 95% CI -2.70 to 2.30, *p*=0.88). Ho et al.[57] reported reduced visual fatigue in participants who received workplace modification advice per the recommendations generated by a software system, relative to participants who received a delayed intervention after two weeks (111 participants; MD: -1.47 units; 95%CI -2.35 to -0.59, *p*=0.001). After modifying the software to be web-based, no significant improvement in visual fatigue score was observed in participants who received the work modification advice immediately, compared to those who received it after a two week delay (75 participants; MD: -0.78 units; 95%CI -1.83 to 0.27, *p*=0.15). The certainty of evidence was judged as very low for this outcome.

4.2. Secondary outcomes

Hirayama et al.[56] provided very low certainty evidence for no difference in dry eye symptom score and blink rate with a moist cool air device, relative to no intervention, for five days (Table S6).

4.3. Adverse events

Hirayama et al.[56] (n=20) reported no adverse events with either the moist cool air device or no intervention. The certainty of evidence was judged to be very low.

5. Intervention category – Ergonomic adjustment

Robertson et al. [69] investigated office ergonomic training compared to minimal training. None of the primary or secondary outcomes were measured, nor were adverse events documented.

6. Invervention category – Visual hygiene

Alrasheed and Alghamdi[86] investigated whether the 20/20/20 rule reduced symptoms associated with computer use compared to a placebo involving advice to drink water.

6.1. Primary outcome

Alrasheed and Alghamdi[86] provided very low certainty evidence for no improvement in visual fatigue symptoms with the 20/20/20 rule, relative to drinking water, at the end of a 20 day follow up period (40 participants; MD: 0.80 units; 95% CI -0.59 to 2.19, *p*=0.26).

Secondary outcomes

This study[86] provided very low certainty evidence for reduced dry eye symptoms with implementing the 20/20/20 rule relative to placebo (40 participants; MD: -2.60 units; 95% CI -4.51 to -0.69, *p*=0.008). There was also very low certainty evidence for no difference in blink rate between the study groups at the study end point (40 participants; MD: 0.85 blinks; 95% CI -3.47 to 5.17, *p*=0.70). Adverse events were not reported.

7. Intervention category - Other

Four studies investigated other interventions (Table S4).[54, 55, 72, 73] Galinsky et al.[55] evaluated the effects of supplementary workplace rest breaks compared to

519 conventional workplace breaks. Another study from the same group[54] evaluated
520 supplementary breaks with stretching exercises, compared with conventional breaks.
521 Two parallel-arm studies by the same lead author (Telles 2006, 2006a)[72, 73]
522 evaluated the effects of yoga relative to no exercise.

523 **7.1. Primary outcome**

524 Two studies reported visual fatigue data.[54, 73] Telles et al.[73] described reduced visual
525 fatigue with yoga relative to recreational activity (118 participants; MD -0.80 units;
526 95% CI -1.04 to -0.56, p<0.0001). Galinsky et al.[54] described less visual fatigue with
527 supplementary breaks compared to conventional breaks, but did not provide numeric
528 data. Both studies were judged to provide very low certainty evidence for this
529 outcome. Neither study measured any of the secondary outcomes or documented
530 adverse events.

531 **Discussion**

532 This is the first systematic review to investigate the efficacy and safety of
533 interventions for CVS. Forty-five RCTs, with sample sizes ranging from 10 to 522
534 participants and post-intervention follow up periods ranging between <24 hours to
535 one year, were identified. Of these trials, most investigated complementary
536 medicines or nutritional supplements (58%) or optical aids (22%). Overall, there were
537 limited quantitative data relating to the efficacy or safety of CVS interventions. The
538 certainty of evidence for the prespecified outcome measures, across all
539 interventions, was judged as moderate, low or very low. The two most common
540 reasons for downgrading the certainty of the evidence were risk of bias (participant
541 and outcome assessor not being masked, or industry funding) and imprecision (small
542 sample size). This uncertainty about the potential effect(s) of interventions on

outcomes relevant to CVS should be considered when making clinical management decisions.

This review found very low certainty evidence for no effect on visual fatigue with a multifocal, compared to single-vision distance, optical correction based on findings from three RCTs over intervention durations of one week to 6 months. There was low certainty for no reduction in visual fatigue with oral berry extract supplementation compared to placebo over four to 12 weeks, based on data from seven RCTs. There was also low certainty for berry extract supplementation not improving CFF relative to placebo. Regarding the trial follow-up periods relative to the time that might be expected for particular interventions to modulate outcome measures, the exposure period for optical aids is likely appropriate given that the time to derive any benefit is relatively short. However, for nutritional supplementation a minimum follow-up period of 12 weeks might be necessary based on their proposed systemic mechanism of action.[90]

Substantial risk of performance, detection, and other biases were identified in several studies. Specifically, 35% of eligible studies did not mask participants or study personnel to the intervention, including 33% where outcome assessors were not masked. Larger effect sizes have been associated with studies without masking relative to those with masking.[91] Confidence in estimates from studies that were neither single- nor double-masked is thus reduced. A further consideration is that one in three included studies had industry funding, a factor that has been associated with more favorable conclusions in relation to the efficacy of an intervention compared to non-industry funded trials.[92]

Of the 45 included RCTs, two-thirds did not provide trial registration details, resulting in limited capacity to assess selective outcome reporting. Two-thirds of included trials did not report sample size calculations, raising concerns about whether these studies were adequately powered to detect the intended treatment effects.

Overall completeness and applicability of the evidence

Optical aids are commonly used to manage CVS. A recent survey of 372 Australian optometrists found that most practitioners (87%) used spectacle lens corrections for CVS management.[93] Assuming a proportion of these corrections involved multifocal lenses for pre-presbyopic patients, the findings in this review suggest that such multifocal lens prescribing is unlikely to provide benefit, relative to single-vision correction, for managing CVS symptoms.

The potential use of blue light-blocking spectacle lenses for treating CVS has gained attention in recent years.[94, 95] Despite this, only three RCTs investigating these lenses were identified.[19, 20, 85] All three studies reported no benefit on eye strain with blue light-blocking lenses compared to no blue light-blocking lenses. Lin et al.[19] did not provide numeric data, but described a benefit (i.e., less negative change in CFF) with obviously brown-colored high blue light-blocking lenses, compared to both low blue light-blocking and no-blue light blocking lens groups. However, use of CFF as a measure of visual fatigue has been questioned, as not all studies measuring CFF have found a correlation between a decrease in CFF and symptoms of eye strain.[96-98] Furthermore, the findings of Lin et al.[19] should be viewed in the context of the study receiving industry funding, not being prospectively registered, having a moderate sample size (n=36) and a lack of outcome assessor masking. In contrast, the double-masked RCT by Singh et al.,[20] involving 120 participants, found no

significant between-group difference (blue light-blocking versus no blue light-blocking) in CFF, as a measure of visual fatigue.

The other major intervention category was oral berry extract. Pooled data from seven trials[23, 62, 66-68, 76, 79] showed no reduction in visual fatigue with berry extract supplements compared to placebo in study populations without established dietary deficiences. Use of this intervention also did not improve dry eye symptom scores. For both visual fatigue and subjective dry eye measures, a range of questionnaires and scales were used. SMD was used to meta-analyze relevant study data, but this parameter is not as readily interpretable with respect to clinical significance as absolute mean differences. Unfortunately, absolute mean differences can only be derived when consistent scales allow data to be directly pooled. For future RCTs, it is recommended that an agreed set of validated questionnaires are adopted by trialists to measure symptoms of CVS[5] and dry eye.[99]

Although some controversy remains as to their benefit, oral omega-3 fatty acid supplements have also gained attention with respect to their potential utility to improve ocular surface health, via mechanisms that may involve modulating tear homeostasis.[100, 101] Recent data suggest that omega-3 fatty acid supplements are a common recommendation amongst eye care practitioners for treating tear dysfunction.[102] In the current review, pooled data from two studies[24, 50] provided low certainty evidence for reduced dry eye symptoms in individuals with CVS assigned to oral omega-3 supplements compared to placebo. Both studies used the Dry Eye Questionnaire and Scoring System (DESS) score to quantify symptoms,[103] which does not have a defined minimal clinically important difference (MCID). However, converting the observed between-group mean difference in DESS score to a

percentage improvement (MD/maximum questionnaire score), indicates a 20% reduction in symptoms, which has been proposed to be clinically important for other validated dry eye symptom scales.[104]

High statistical heterogeneity was evident for the pooled analysis of symptom scores for the two studies,[24, 50] by the same research group, evaluating omega-3 fatty acid supplements, although the direction of effect was consistent. This finding may relate to use of different omega-3 doses in the studies. In practice, practitioners should also be mindful of potential adverse events associated with oral omega-3 fatty acid supplementation.[105] Bhargava et al.[24] had greater participant dropout, due to gastric intolerance, in the group prescribed the higher dose of omega-3 fatty acids (n=26, 1440mg EPA + 960mg DHA) compared to the lower dose[50] (720mg EPA + 480mg DHA). Gastric intolerance is a common side effect of oral omega-3 supplementation.[100, 106]

For oral carotenoid supplementation, pooled data from two studies,[65, 71] involving 74 participants, provided very low certainty evidence for an improvement in CFF with the carotenoid intervention relative to placebo. However, it is unclear if the observed between-group difference of 2 Hz is clinically meaningful, if indeed CFF is a useful measure of visual fatigue at all.[96-98] Further, the potential mechanism of action of carotenoid supplementation in reducing eye strain is unknown, and the study population did not appear to have been assessed (at baseline) with respect to a potential systemic deficiency that might provide some justification for the benefit of oral supplementation.

Previous narrative reviews that focused on CVS management[4, 15, 21, 107] have recommended optical interventions, artificial tears, ergonomic optimization, adequate

lighting, and frequent rest breaks to reduce CVS. In contrast, the present systematic review found no benefit with multifocal lenses compared to a single vision-distance spectacles for managing CVS. There were limited data to draw conclusions about the value of traditional medicines, environmental modifications, ergonomic adjustment, or artificial tears. Although limited data were available to assess the role of artificial tears in reducing CVS symptoms, dry eye is commonly associated with CVS[15], and artificial tears are a prevalent dry eye management approach.[108, 109] Furthermore, though advising computer users to use the “20-20-20” rule is a popular recommendation,[21, 107] only one RCT[86] evaluating this approach was identified. This study[86] found no benefit in modifying visual fatigue symptoms using the 20/20/20 rule compared to placebo intervention involving water intake, as required.

The current review included all interventions investigated for CVS, to provide a comprehensive evidence synthesis that can assist practitioners with clinical management decisions. It is acknowledged that only studies published in English were included, and — due to an insufficient number of trials within each intervention category — the potential reason(s) for heterogeneity could not be analyzed using meta-regression. Data extracted from clinical trial registry entries (n=2, both in the optical aids category) and included in the quantitative syntheses should be interpreted with caution as, compared to results from published studies, registry results have not undergone a peer review process. Further, among included trials, participant eligibility criteria varied considerably. The breadth of populations evaluated in different studies included healthy individuals, computer users, self-reported symptomatic computer users, and participants who performed computer tasks for a specific duration per day. This variability in study population may affect the generalizability of the findings. Another consideration is that, to optimize the

evidence capture, we did not exclude studies judged as having a high risk of bias based on the Cochrane Risk of Bias tool, however risk of bias has been factored into our GRADE evidence certainty assessments for each outcome. Therefore, such certainty assessments apply only to the evidence in aggregate, and should not be applied to individual studies making up this aggregate, which may differ substantially in their individual evidence certainties (for example, Lin et al.[19] vs Singh et al.[20] noted previously, with regards to blue light-blocking spectacles). It should be noted that two studies[72, 73] that investigated yoga from the same research groups had multiple similarities – like publication year (2016), recruited same sample size (n=291), and provided participants with similar intervention/comparator. Hence, the conclusion regarding yoga intervention needs to be treated with additional caution. In relation to the meta-analyses, the use of SMD restricted our ability to combine both change from baseline and endpoint outcome data. The presentation of single studies in the sub-group analysis of the forest plots (Figures 3 & 6) could be a potential limitation. In these situations, interpretation of these sub-group analyses must be treated with particular caution, and greater weight should be given to the total effect that represents an analysis of multiple studies.

Ten out of 45 studies included in this review did not report,[25, 53, 58, 59, 62, 70, 85] or only partially reported,[52, 75, 77] the age of the included participants. Some of the outcome measures we analyzed might be impacted by age (for example, CFF and amplitude of accommodation) and so a limitation of our evaluation is that differences in outcomes between studies could be the result of unreported differences between the age of the cohorts studied, rather than difference in the effectiveness of the interventions per se. Further, with inclusion of unadjusted estimates in the meta-analysis, any differences in confounding factors (such as age) between intervention

groups may be a potential source of confounding bias. Finally, a further potential limitation is that quantitative data provided purely in graphical, rather than numeric, form was not considered by this review.

Recommendations for future clinical trials

This review identified substantial inter-study variations in methodology and outcome measure selection. These findings indicate there would be benefit in developing a core outcome set for CVS trials, to standardize reporting in future studies and thus enable enhanced data synthesis in systematic reviews and meta-analyses; this would enable a clearer determination of the relative efficacy and safety of interventions, to better inform clinical practice. The need for a similar set of agreed core outcome measures, for evaluation in intervention trials, has been identified in other areas of ophthalmic research, including dry eye disease,[110] cataract surgery,[111] age-related macular degeneration,[112] and uveitis.[113]

Further to the findings in this review, the following recommendations are pertinent to future CVS RCTs: 1) for general considerations relating to the robust design, conduct, and reporting of RCTs, guidance outlined in the Consolidated Standards of Reporting Trials (CONSORT) should be followed.[114]; 2) symptomatic computer users should be enrolled, as they comprise the relevant population for evaluating CVS interventions; 3) the presence of CVS should be confirmed in the study population using an agreed validated questionnaire, such as the CVS questionnaire,[7] to provide a consistent measure of baseline symptom severity; 4) when measuring visual fatigue symptoms (the most common outcome measure reported in studies included in this review), use of a standardized questionnaire[5] is recommended; 5) outcome measure data should be reported in numeric form and include all relevant details

(e.g., means and standard deviations, or similar), either within the main paper itself or supplementary materials; 6) experimental studies measuring the change both before and after computer use, should ideally report the experimental workstation, type of computer task, task duration, computer screen brightness and contrast, and room temperature and humidity.

Conclusion

This systematic review finds low certainty evidence for a possible role of omega-3 fatty acid supplementation in managing dry eyes symptoms associated with CVS. There was low certainty evidence for oral berry extract supplementation to not reduce visual fatigue or dry eye symptoms. Likewise, low certainty evidence for blue-light blocking lenses being ineffective in reducing symptoms of visual fatigue was noted. For other interventions, there was insufficient evidence to establish their efficacy or safety with certainty. The review also highlights a range of frequent limitations in the design and reporting of RCTs investigating treatments for CVS and provides recommendations for how these shortcomings might be addressed in future studies.

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Figure legends

Figure 1: Flow diagram of studies included in this systematic review (1991-2021).

Figure 2: Risk of bias assessment in included studies, for each domain in the Cochrane Risk of Bias tool. Green, red and yellow circles indicate low, high or unclear risk of bias, respectively.

Figure 3: Forest plot of comparison: Active optical aid (spectacle or contact lens) vs. control. Outcome: Visual fatigue or asthenopia score, measured using a subjective questionnaire or visual analogue scale. Data are reported at the end of the study follow-up period: from 1 week (NCT03585790[87] and NCT02921087[88]; multifocal contact lenses) to 1 month (Kee et al.[22]; progressive addition spectacle lenses). For Kee et al.[22], data were combined from two separately reported age groups (18 to 35 years, n=19, and 30 to 40 years, n=45). For NCT03585790[87], the presented data were calculated from the median and inter-quartile range. For Kee et al.[22] mean scores were converted to ensure that higher scores indicated more symptoms, for consistency. For all studies presented here, higher scores indicate more severe symptoms.

Figure 4: Forest plot of comparison: Oral berry extract (bilberry and maqui berry) vs. placebo supplementation. Outcome: Visual fatigue or asthenopia score, measured using a subjective questionnaire or visual analogue scale. For Park et al.[68] (bilberry: 1000mg/day), Okamoto et al.[66] (bilberry: 60mg/day), and Sekikawa et al.[79] (bilberry: 43.2mg/day), data are reported at the end of the study follow up period, which were week 4,[68] week 6,[79] and week 12[66]. For Ozawa et al.[23] (bilberry: 3 x 160mg capsules per day), Liang et al.[62] (bilberry: 160mg/day), Okamoto et al.[67] (bilberry: 60mg/day), and Yamashita et al.[76] (dextrin 120 mg/day + maqui berry

extract 60mg/day), data are reported after VDT load at the end of the follow up period, which were week 4[76], week 6[62], week 8[23], and week 12[67].. Presented data were calculated from the standard error of the mean for Ozawa et al.[23], and median and inter-quartile range for both Yamashita et al.[76] and Sekikawa et al.[79] For Yamashita et al.[76] mean scores were converted to ensure that higher scores indicated more symptoms, for consistency. For all studies presented here, higher scores indicate more severe symptoms.

Figure 5: Forest plot of comparison: Oral berry extract (bilberry and maqui berry) vs. placebo supplementation. Outcome: Critical flicker-fusion frequency (CFF), measured in Hertz (Hz). For Okamoto et al.[66] (bilberry: 60mg/day), and Yamashita et al.[76] (dextrin 120 mg/day + maqui berry extract 60mg/day), data are reported at the end of the follow up period, which are week 4[76] and week 12[66]. For Ozawa et al.[23] (bilberry: 3 x 160mg capsules per day), data reported after VDT load at the end of the 8 week follow up period. Presented data were calculated from the standard error of the mean. For all studies presented here, more negative values indicate a greater improvement in visual fatigue.

Figure 6: Forest plot of comparison: Oral berry extract (bilberryand maqui berry) vs. placebo supplementation. Outcome: Dry eye symptom score, measured using a questionnaire or rating scale. For Yamashita et al.[76] (dextrin 120 mg/day + maqui berry extract 60mg/day) and Sekikawa et al.[79] (bilberry: 43.2mg/day), data are reported at the end of the study follow up period, which were week 4[68, 76] and week 6[79]. For Yamashita et al.[76] and Sekikawa et al.[79], data were calculated from the median and inter-quartile range. For Ozawa et al.[23] (bilberry: 3 x 160mg capsules per day) and Liang et al.[62] (bilberry: 160mg/day) data are reported after VDT load at

the end of the follow up period, which were week 6[62] and week 8.[23] For Ozawa et al.[23] data were calculated from the standard error of the mean. For all studies presented here, higher scores indicate more severe dry eye symptoms.

Figure 7: Forest plot of comparison: Oral bilberry extract vs. placebo supplementation. Outcome: Amplitude of accommodation, measured in dioptres (D). For Okamoto et al.[66] (bilberry: 60mg/day), data are reported at the end of the 12 week follow-up period. For Ozawa et al.[23] (bilberry: 3 x 160mg capsules per day), data are reported after VDT load at the end of the 8 week follow up period. Presented data were calculated from the standard error of the mean. For both Okamoto et al.[66] and Ozawa et al.,[23] more negative values indicate a greater improvement.

Figure 8: Forest plot of: Oral omega-3 fatty acid vs. placebo supplementation. Outcome: Dry eye symptoms, measured using a questionnaire or rating scale. For both studies (Bhargava et al. (2015)[50]: oral omega-3 fatty acid dose: 4 x 180mg EPA + 120mg DHA capsules per day; Bhargava et al. (2016)[24]: 8 x 180mg EPA + 120 mg DHA capsules per day), data are reported at the end of the follow up period (45 days for Bhargava et al. (2016)[24] and 3 months for Bhargava et al. (2015)[50]). Higher scores indicate more severe dry eye symptoms, measured with the Dry Eye Scoring System (/18).[103] The symptom severity schema is 0–6 mild, 6.1–12 moderate, 12.1–18 severe.

Figure 9: Forest plot of comparison: Oral carotenoid vs. placebo supplementation. Outcome: Critical flicker-fusion frequency (CFF), measured in Hertz (Hz). For Nagaki et al.[65] (carotenoid supplement: 5mg/day), and Stringham et al.[71] (macular carotenoid supplement: 24mg/day), data are at the end of the study

follow-up period (4 weeks[65] and 6 months[71]). For both studies, more positive values indicate a greater improvement.

Table 1. Summary of findings table, including Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessments for the certainty of the body of evidence, for optical interventions for managing computer vision syndrome.

Intervention vs comparator	Outcome measure	No. of participants (no. of studies)	Certainty of the evidence (GRADE)	Estimate (95% CI)		Comments
				with placebo / control	with active intervention	
Multifocal vs single-vision correction lenses	Visual fatigue score, measured using a Likert scale or VAS, with follow-up ranging from 1wk to 6m.	352 (4 RCTs)	⨁⊖⊖⊖[a] Very low	The pooled summary estimate from three studies[22, 87, 88] indicated little to no increase in visual fatigue score with the multifocal intervention relative to a single-vision correction: SMD: 0.11 units higher (0.14 lower to 0.37 higher). Del Mar Segui-Crespo et al.[84] reported no significant difference between multifocal and single vision correction: MD: 1.50 units lower (3.60 lower to 0.60 higher).		Kee et al. (2018)[22] and Del Mar Segui-Crespo et al.[84] measured visual fatigue using a Likert scale; NCT03585790[86] and NCT02921087[87] quantified visual fatigue using a VAS. Estimates are presented as SMD.
	Dry eye symptom score, measured using a questionnaire or rating scale at 1wk follow-up.	44 (1 RCT)	⨁⊖⊖⊖[b] Very low	One study (NCT02921087[88]) reported no significant difference between intervention arms: MD relative to placebo: 0.70 units lower (2.62 lower to 4.02 higher).		NCT02921087[88] measured dry eye symptoms using the Contact Lens Dry Eye Questionnaire-8 (/37).
	Adverse event rate, measured at follow-up ranging from 1wk to 6m.	180 (3 RCTs)	⨁⨁⊖⊖[c] Low	The pooled summary estimate from three studies[84, 87, 88] indicated little to no difference in adverse event rate with a multifocal relative to a single-vision correction: RR: 2.09 higher (0.20 lower to 21.45 higher).		None.
Residual astigmatism correction vs no correction lenses	Visual fatigue symptom score, measured using a questionnaire or rating scale at 25 minutes follow-up.	12 (1 RCT)	⨁⊖⊖⊖[d] Very low	Wiggings et al.[74] reported significant difference between intervention arms, but did not provide quantitative data.		Wiggings et al.[74] quantified visual fatigue symptoms using a Likert scale.

Blue light blocking vs. non blue light blocking lenses	Visual fatigue score, measured using a Likert scale or VAS, with follow-up ranging from <1d to 5d.	166 (3 RCTs)	⊕⊕⊖⊖[e] Low	Singh et al.[20] reported no significant difference between intervention arms; MD relative to placebo: 9.76 units higher (33.95 lower to 53.47 higher). Two other studies[19, 85] reported no significant difference between intervention arms.	Singh et al.[20] quantified visual fatigue using a VAS. Dabrowiecki et al.[85] and Lin et al.[19] measured visual fatigue using a Likert scale.
	CFF, measured in Hz, with follow up 2h.	156 (2 RCTs)	⊕⊕⊖⊖[f] Low	Singh et al.[20] reported no significant difference between intervention arms; MD relative to placebo: 1.13 Hz lower (3.00 lower to 0.74 higher). Lin et al.[19] reported a significant difference between intervention arms, but did not provide numeric data.	None.
	Dry eye symptom score, measured using a Likert scale or VAS, with follow-up ranging from <1d to 5d.	2 RCTs (130)	⊕⊕⊕⊖[g] Moderate	Singh et al.[20] reported no significant difference between intervention arms; MD relative to placebo: 1.31 units lower (10.39 lower to 7.77 higher). Dabrowiecki et al.[85] reported no significant difference between intervention arms, but data were reported as daily average change rather than change from baseline or endpoint data.	Singh et al.[20] quantified dry eye symptoms using a VAS. Dabrowiecki et al.[84] measured dry eye symptoms using a Likert scale.
	Amplitude of accommodation, measured in D, with a follow-up of 2h.	1 RCT (120)	⊕⊕⊕⊖[h] Moderate	Singh et al.[20] reported no significant difference between intervention arms; MD relative to placebo: 0.30 D lower (0.71 lower to 0.11 higher).	None.

	Near point of convergence, measured in cm, with a follow-up 2h.	1 RCT (120)	⨁⨁⨁⊖[h] Moderate	Singh et al.[20] reported no significant difference between intervention arms; MD relative to placebo: 0.29 cm higher (0.28 lower to 0.86 higher).	None.
	Blink rate, measured as the number of blinks per minute, with a follow-up of 2h.	1 RCT (120)	⨁⨁⨁⊖[h] Moderate	Singh et al.[20] reported no significant difference between intervention arms; MD relative to placebo: 1.37 blinks/minute higher (0.44 lower to 3.18 higher).	None.
	Adverse events, measure at 2h of follow-up.	1 RCT (120)	⨁⨁⨁⊖[h] Moderate	Singh et al.[20] reported no adverse events.	None.

Abbreviations: CFF, critical flicker-fusion frequency; CI, confidence interval; D, dioptres; d, days; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; h, hours; m, months; MD, mean difference; RCT, randomized controlled trial; RR, relative risk; SMD, standardized mean difference; VAS, visual analogue scale; wk, weeks. *Only outcome measures evaluated by at least one study are listed in this table.

[a]Downgraded two levels due to risk of bias and one level due to inconsistency, as participants and outcome assessors were not masked in two studies,[22, 87] one study[84] had industry sponsorship, and one study[87] had divergent effects.
[b]Downgraded three levels due to imprecision, as one study[88] had a small sample size.
[c]Downgraded two levels for risk of bias, as in one study[87] participants and outcome assessors were not masked and one study[84] had industry sponsorship.
[d]Downgraded three levels due to imprecision, as one study[74] had a small sample size.
[e]Downgraded two levels for risk of bias, as in one study[85] outcome assessors were not masked and one study[19] had industry sponsorship.
[f]Downgraded one level for each of risk of bias and inconsistency, as one study[19] had industry sponsorship, and one study[20] showed no inter-group differences while the other[19] reported a positive effect with the blue light-blocking intervention.
[g]Downgraded one levels due to risk of bias, as in one study[85] outcome assessors were not masked.
[h]Downgraded one level due to imprecision, as results derived from a single study, at low risk of bias.[20]

Table 2. Summary of findings table, including Grading of Recommendations, Assessment, Development and Evaluation (GRADE) assessments for the certainty of the body of evidence, for complementary medicine and nutritional supplements for managing computer vision syndrome.

Intervention vs comparator	Outcome measure	No. of participants (no. of studies)	Certainty of the evidence (GRADE)	Estimate (95% CI)		Comments
				with placebo / control	with active intervention	
Oral berry extract vs placebo	Visual fatigue score measured using a Likert scale or VAS with follow-up ranging from 4 to 12wk.	322 (7 RCTs)	⨁⨁⨀⨀[a] Low	The pooled summary estimate from seven studies[23, 62, 66-68, 76, 79] indicated no difference in visual fatigue score with the berry extract relative to the placebo supplement: SMD: 0.27 units lower (0.70 lower to 0.16 higher).		In the seven studies, visual fatigue was quantified using either a Likert scale[62, 68, 79] or VAS[23, 66, 67, 76] Estimates are presented as SMD.
	CFF, measured in Hz, with follow-up ranging from 4 to 12wk.	193 (3 RCTs)	⨁⨁⨀⨀[b] Low	The pooled estimate from three studies[23, 66, 76] indicated little to no decrease in CFF with the oral berry extract relative to placebo: MD: 0.35 Hz lower (1.39 lower to 0.69 higher).		Doses ranged from 60mg/day to 160mg/day. Two studies[23, 66] evaluated bilberry extract and one study[76] evaluated maqui berry. Estimates are presented as MD.
	Quality of life measured using a questionnaire or rating scale at 4wk of follow up.	74 (1 RCT)	⨁⨀⨀⨀[c] Very low	One study[76] reported no significant difference between intervention arms: MD relative to placebo: 1.00 units higher (1.36 lower to 3.36 higher).		Yamashita et al.[76] measured quality of life using the Dry Eye Questionnaire Score (/100).
	Dry eye symptom score, measured using a Likert scale or VAS, with follow-up ranging from 4 to 8wk.	248 (5 RCTs)	⨁⨁⨀⨀[d] Low	The pooled estimate from four studies[23, 62, 76, 79] indicated no improvementin dry eye symptoms with the oral berry extract relative to placebo: SMD: 0.10 units lower (0.54 lower to 0.33 higher). Park et al.[68] reported no improvement in dry eye score with billberry extract compared to placebo: 0.69 units lower (1.41 lower to 0.03 higher)		Dry eye score was quantified using either a Likert scale[62, 68, 76, 79] or VAS[23] (/100). Estimates are presented as SMD.

	Amplitude of accommodation, measured in D, with follow-up ranging from 8 to 12wk.	119 (2 RCTs)	⨁⨁⊖⊖[e] Low	The pooled estimate from two studies[23, 66] indicated little to no decrease in amplitude of accommodation with the oral berry extract relative to placebo: MD: 0.06 D lower (0.64 lower to 0.53 higher).	Both studies evaluated oral bilberry extract. Estimates are presented as MD.
	Adverse event rate, measured at follow-up ranging from 4wk to 12wk.	8 RCTs (440)	⨁⊖⊖⊖[f] Very low	Eight studies[23, 62, 66-68, 76, 79, 81] reported no adverse events.	None.
Oral omega-3 fatty acids vs placebo	Dry eye symptom score, measured using a Likert scale or VAS, at 45d of follow-up.	978 (2 RCTs)	⨁⨁⊖⊖[g] Low	The pooled summary estimate from two studies[24, 50] indicated a reduction in dry eye score with oral omega-3 fatty acids relative to placebo: MD: 3.36 units lower (3.63 lower to 3.10 higher).	Both studies measured dry eye using Dry Eye Questionnaire and Scoring System (/18).[103] Estimates are presented as MD.
	Adverse event rate, measured at 45d of follow-up.	978 (2 RCTs)	⨁⨁⊖⊖[h] Low	Two studies[24, 50] did not explicitly report adverse events, but did mention that participants dropped out of the omega-3 fatty acid supplement group due to gastric intolerance.	None.
Oral carotenoid supplement vs placebo	Visual fatigue score measured using a questionnaire or rating scale at 4wk of follow-up.	39 (1 RCT)	⨁⊖⊖⊖[i] Very low	Nagaki et al.[65] reported no significant difference between intervention arms.	None.
	CFF, measured in Hz, with follow-up ranging from 4wk to 6m.	74 (2 RCTs)	⨁⊖⊖⊖[j] Very low	The pooled estimate from two studies[65, 71] indicated no significant improvement in CFF with the oral berry extract relative to placebo: MD: 1.55 Hz higher (0.42 lower to 2.67 higher).	The dose of carotenoids ranged from 5mg/day[65] to 24mg/day[71]. Estimates are presented as MD.
	Amplitude of accommodation, measured in D, at 4wk of follow-up.	26 (1 RCT)	⨁⊖⊖⊖[k] Very low	One study[65] reported no significant difference between the intervention arms: MD relative to placebo: 0.50 D higher (0.56 lower to 1.56 higher).	None.

	Adverse event rate, measured at 4wk of follow-up.	26 (1 RCT)	⊕⊕⊖⊖[l] Low	Nagaki et al.[65] reported no adverse events.	None.
Traditional medicine vs placebo	Visual fatigue score measured using a Likert scale or VAS, at 60d of follow-up.	60 (1 RCT)	⊕⊖⊖⊖[m] Very low	One study[59] reported no significant difference between the intervention arms: MD relative to placebo: 0.70 units lower (1.52 lower to 0.12 higher).	Joshi and Ujwale. (2016)[59] measured visual fatigue using a VAS (/10).
	Adverse event rate, measured at follow-up ranging from 1m to 6wk.	270 (3 RCTs)	⊕⊕⊖⊖[n] Low	Three studies[51-53] reported no adverse events.	None.
Combination of oral supplements vs placebo	Visual fatigue score measured using a questionnaire or rating scale, with follow-up ranging from 4wk to 12wk.	475 (4 RCTs)	⊕⊖⊖⊖[o] Very low	Kan et al.[83] reported significant difference between interventions: MD relative to placebo: 2.83 units lower (3.56 lower to 2.10 higher). Kawabata and Tsuji[60] reported no significant difference between the intervention arms: MD relative to placebo: 0.40 units lower (1.20 lower to 0.40 higher). Kondo and Sawano[61] reported no significant difference between the intervention arms: MD relative to placebo: 0.40 units lower (2.20 lower to 1.40 higher). Kizawa et al.[82] reported no significant difference between the intervention arms: MD relative to placebo: 0.00 units (0.65 lower to 0.65 higher).	All studies quantified visual fatigue using a Likert scale.

	Dry eye symptom score, measured using a Likert scale or VAS, with follow-up ranging from 4 to 12wk.	365 (3 RCTs)	⊕⊕⊖⊖[p] Low	Kan et al.[83] reported significant difference between interventions: MD relative to placebo: 0.52 units lower (0.74 lower to 0.30 higher). Kawabata and Tsuji[60] reported no significant difference between interventions: MD relative to placebo: 0.58 units lower (1.80 lower to 0.64 higher). Kizawa et al.[82] reported no significant difference between interventions: MD relative to placebo: -1.00 units lower (1.81 lower to 0.19 higher).	All studies quantified dry eye symptoms using a Likert scale.
	Amplitude of accommodation, measured in D, at 12wk of follow-up.	110 (1 RCT)	⊕⊖⊖⊖[q] Very low	One study[61] reported a significant difference between the intervention arms: MD relative to placebo: 0.29 D lower (0.94 lower to 0.36 higher).	None.
	Blink rate, measured as the number of blinks per minute, at 2wk follow-up.	13 (1 RCT)	⊕⊖⊖⊖[r] Very low	Yagi et al.[75] reported no difference between the study intervention arms, but did not provide quantitative data.	None.
	Adverse event rate, measured at follow-up ranging from 6 to 12wk.	453 (3 RCTs)	⊕⊖⊖⊖[s] Very low	Two studies[82, 83] reported no adverse events. Kondo and Sawano[61], reported 15 adverse events in the combination supplement group and 19 in the placebo group; all were deemed unrelated to the interventions.	None.
Other oral interventions (Green tea, probiotic, and	Visual fatigue score measured using a questionnaire or rating	173 (2 RCTs)	⊕⊕⊖⊖[t] Low	Morita et al.[64] reported no difference with oral probiotics relative to placebo: MD	Both studies quantified visual fatigue using a VAS.

taurine supplements) vs placebo	scale, with follow-up ranging from 8 to 12wk.			relative to placebo: 3 units lower (13.06 lower to 7.06 higher). Maeda-Yamamoto et al.[63] reported no difference between Sunrouge, Yabukita and placebo green tea extracts.	
	CFF, measured in Hz, with follow-up ranging from 12d to 8wk.	84 (2 RCTs)	⊕⊖⊖⊖[u] Very low	Morita et al.[64] reported no difference with oral probiotics relative to placebo: MD relative to placebo: 0.03 Hz higher (1.60 lower to 1.66 higher). Zhang et al.[77] reported no difference with a taurine supplement relative to placebo: MD relative to placebo: 4 Hz lower (10.65 lower to 2.65 higher).	None.
	Dry eye symptom score, measured using a Likert scale or VAS, at 8wk of follow-up.	59 (1 RCT)	⊕⊖⊖⊖[v] Very low	Morita et al.[64] reported no difference with oral probiotics relative to placebo: MD relative to placebo: 2.20 units higher (7.11 lower to 11.51 higher).	Morita et al.[64] measured dry eye symptoms using a Likert scale.
	Amplitude of accommodation, measured in D, with follow-up ranging from 8 to 12wk.	173 (2 RCTs)	⊕⊖⊖⊖[w] Very low	Morita et al.[64] reported no difference with oral probiotics relative to placebo: MD relative to placebo: 0.27 D higher (1.17 lower to 1.71 higher). Maeda-Yamamoto et al.[63] reported an increase in amplitude of accommodation with Sunrouge green tea extract, relative to a placebo, but did not provide quantitative data.	None.
	Adverse events	114 (1 RCT)	⊕⊕⊕⊖[x] Moderate	Maeda-Yamamoto et al.[63] reported no adverse events.	

Abbreviations: CFF, critical flicker-fusion frequency; CI, confidence interval; D, dioptres; d, days; GRADE, Grading of Recommendations, Assessment, Development and Evaluation; mg, milligrams; m, months; MD, mean difference; NA, not applicable; RCT, randomized controlled trial; RR, relative risk; SMD, standardized mean difference; VAS, visual analogue scale; wk, weeks. *Only outcome measures evaluated by at least one study are listed in this table.

[a]Downgraded two levels due to risk of bias, as one study[62] had incomplete outcome data and selective reporting bias, and six studies[23, 62, 66, 67, 76, 79] had industry sponsorship.
[b]Downgraded two levels due to risk of bias, as all three studies[23, 66, 76] had industry sponsorship.
[c]Downgraded one level for risk of bias and two levels for imprecision, as one study[76] had industry sponsorship and a small sample size.
[d]Downgraded two levels, due to risk of bias; as one study[62] had incomplete outcome data and selective reporting bias, and four studies[23, 62, 76, 79] had industry sponsorship.
[e]Downgraded one level for each of risk of bias and imprecision, as two studies[23, 66] had industry sponsorship, and relatively wide CIs.
[f]Downgraded three levels due to risk of bias, as six studies had selective reporting bias,[23, 62, 67, 68, 76, 81] and seven studies had industry sponsorship. [23, 62, 66, 67, 76, 79, 81]
[g]Downgraded two levels, due to inconsistency due to the high inter-study heterogeneity, and one study[50] had baseline differences.
[h]Downgraded two levels, due to indirectness, as two studies[24, 50] did not explicitly report adverse events.
[i]Downgraded three levels due to imprecision, as one study[65] had a small sample size.
[j]Downgraded one level for each of risk of bias, inconsistency, and imprecision; one study[71] had industry sponsorship, one study[65] showed no inter-group differences with wide CIs, while the other[71] reported a positive effect with the carotenoid intervention, and both studies[65, 71] had a small sample size.
[k]Downgraded three levels for imprecision, as one study[65] had a small sample size.
[l]Downgraded two levels for imprecision, as one study[64] had a small sample size.
[m]Downgraded two levels for risk of bias and one level for imprecision, as in one study[59] the method of allocation concealment was not reported, the participants and outcome assessors were not masked, and it had a small sample size.
[n]Downgraded one level for each of risk of bias and imprecision, as in one study[53] the participants and outcome assessors were not masked, and this study had a small sample size.
[o]Downgraded three levels for risk of bias, as one study[61] had selective reporting bias, and three studies[61, 82, 83] had industry sponsorship.
[p]Downgraded two levels for risk of bias, as two studies[82, 83] had industry sponsorship.
[q]Downgraded two levels for risk of bias and one level for imprecision, as this study[61] had selective reporting bias, industry sponsorship, and small sample size.
[r]Downgraded three levels, due to imprecision, as one study[75] had a small sample size.
[s]Downgraded three levels for risk of bias, as one study[61] had selective reporting bias, and three studies[61, 82, 83] had industry sponsorship.
[t]Downgraded one level for each of risk of bias and imprecision, as one study[64] had industry sponsorship and wide CIs.
[u]Downgraded one level for risk of bias and two levels for imprecision, as one study[64] had industry sponsorship, and wide CIs, and this and another study[77] had small sample sizes.
[v]Downgraded one level for risk of bias and two levels for imprecision, as one study[64] had industry sponsorship, wide CIs, and a small sample size.
[w]Downgraded one level for risk of bias and two levels for imprecision, as one study[64] had industry sponsorship and wide CIs, and another study[63] had a small sample size.
[x]Downgraded one level due to imprecision, as results were obtained from a single study.[63]

Table 3. Key characteristics of randomised trials evaluating optical aids

Study	Intervention sub-category	Participant population	Intervention(s) (Frequency)	Comparator (Frequency)	Recruited sample size	Intervention duration
Clinical trial ID, NCT02921087 (2016)[88]	CLs	Symptomatic electronic device users	MF (F: Daily wear, daily disposable schedule).	SV (F: Daily wear, daily disposable schedule)	23	1 week
Clinical trial ID, NCT03585790 (2018)[87]	CLs	Symptomatic electronic device users	MF (F: NR)	SV (F: NR)	45	1 week
Dabrowiecki et al. (2020)[85]	Spectacles	Radiology residents	Blue light-blocking SVL (F: 8:00am to 5:00pm/day)	Non blue light-blocking SVL (F: 8:00am to 5:00pm/day)	10	1 week
Del Mar Segui-Crespo M et al. (2021)[84]	Spectacles	Pre-presbyopic, symptomatic computer users	PALs with low near add (F: when using electronic displays)	SVLs (F: when using electronic displays)	90	6 months
Horgen et al. (2004)[58]	Spectacles	Experienced VDT users	**#1:** Essilor Interview™ lenses (F: NR) **#2:** Zeiss Gradal™ room distance lenses (F: NR) **#3:** Technica™ American Optical lenses (F: NR)	SVLs (F: NR)	158	1 year
Kee et al. (2018)[22]	Spectacles	Computer users >2 hours/day	Zeiss PALs (F: NR)	Zeiss SVLs (F: NR)	64	1 month
Lin et al. (2017)[19]	Spectacles	Adults who did not perform VDT work for ≥ 1 hour beforehand	**#1:** High blue light-blocking SVLs (F: 1 x 2 hour session). **#2:** Low blue light-blocking SVLs (F: 1 x 2 hour session).	Non blue light-blocking SVLs (F: 1 x 2 hour session)	36	2 hours
Singh et al. (2021)[20]	Spectacles	Symptomatic computer users	**#1:** Blue light blocking SVLs with positive deception (F: 1 x 2 hour session)	**#1:** Non blue light-blocking SVLs with positive deception (F: 1 x 2 hour session)	120	2 hours

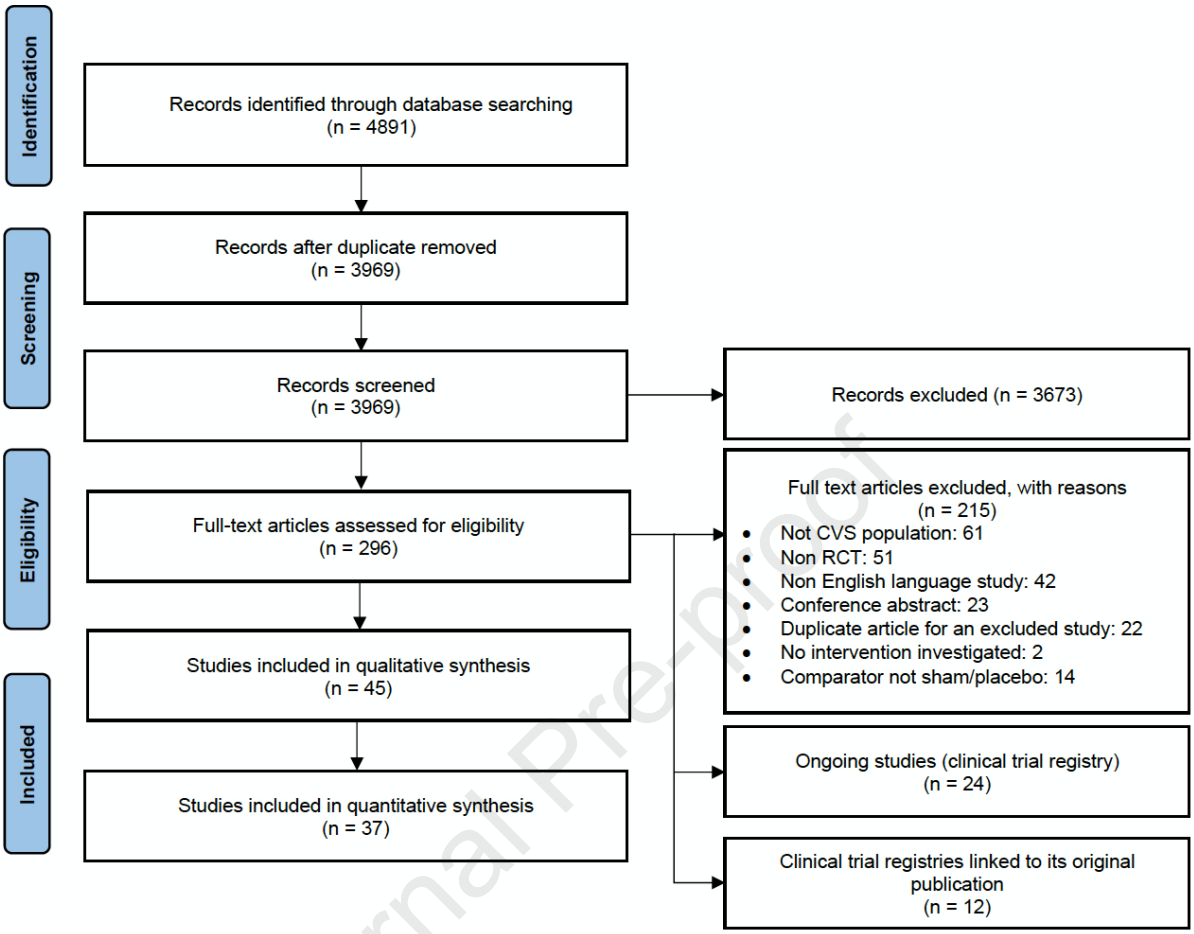
			#2: Blue light blocking SVLs with negative deception (F: 1 x 2 hour session)	**#2:** No blue light-blocking SVLs with negative deception (1 x 2 h session)		
Wiggins et al. (1992)[74]	Spectacles	Soft CL users	Subjective residual astigmatism corrected with trial lenses (F: 1 x 25 minute session)	SVLs with +0.12 D (F: 1 x 25 minute session)	12	25 minutes
Yammouni and Evans et al. (2020)[80]	Spectacles	Symptomatic computer users	**#1:** Low add +0.50 SVLs (F: NR) **#2:** Low add +0.75 SVLs (F: NR) **#3:** Low add +1.25 SVLs (F: NR).	Plano lenses (F: NR)	107	<1 day

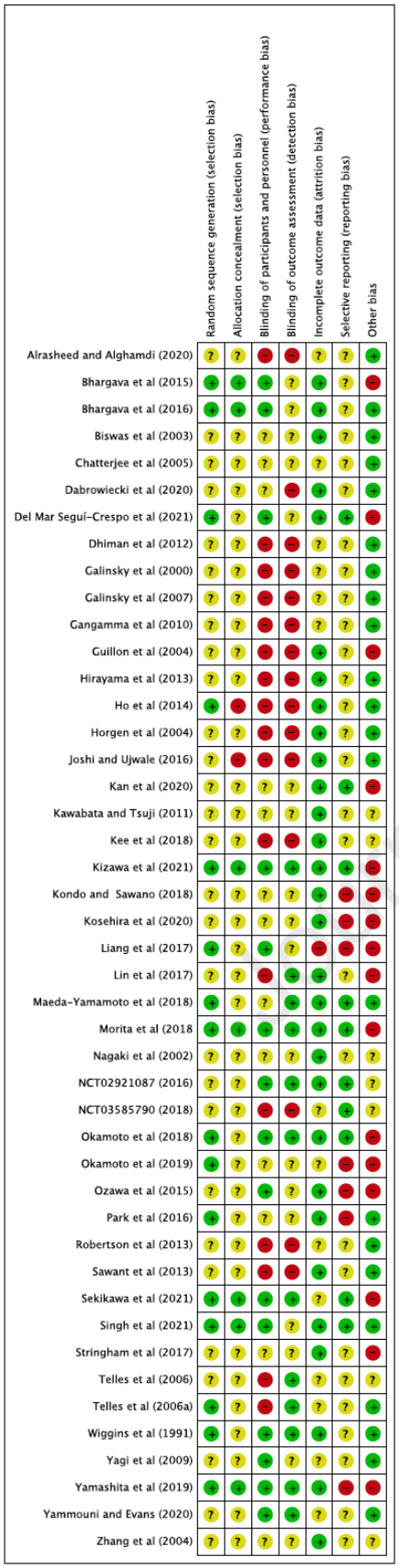
Abbreviations: CL, contact lens; CLs, contact lenses; D, dioptres; F, frequency; MF, multifocal; NR, not reported; PALs, progressive addition lenses; SV, single vision; SVLs, single vision lenses; VDT, visual display terminal.

Table 4. Key characteristics of randomised trials evaluating formulations of oral berry extract

Study	Participant population	Intervention(s) (Dose; Frequency)	Comparator (Dose; Frequency)	Recruited sample size	Intervention duration
Kosehira et al. (2020)[81]	Symptomatic computer users	Bilberry extract (D: 240mg; F: 1 capsule/d)	Oral placebo (D: NR; F: 1x/d)	109	12 weeks
Liang et al. (2017)[62]	Symptomatic computer users	Bilberry extract (D: 160mg; F: 1 capsule/d)	Oral placebo (D: NR; F: 1x/d)	21	6 weeks
Ozawa et al. (2015)[23]	Symptomatic VDT users	Bilberry extract (D: 160mg; F: 3 capsules, 1x/d)	Oral placebo, containing starch, crystalline cellulose, and calcium stearate (D: NR; F: 3 capsules, 1x/d)	88	8 weeks
Okamoto et al. (2018)[66]	Symptomatic VDT users	Bilberry extract (D: 60mg; F: 1 capsule/d)	Oral placebo, consisting of edible oil and corn-starch (D: 555mg; F: 1 capsule/d)	47	12 weeks
Okamoto et al. (2019)[67]	Symptomatic VDT users	Bilberry extract (D: 60mg; F: 1 capsule/d)	Oral placebo, containing edible oil and corn-starch (D: 555mg; F: 1x/d)	44	12 weeks
Park et al. (2016)[68]	Computer users >2 hours/d	Vaccinium ulginosum extract (DA9301) tablet (D: 1000mg; F: 1x/d)	Oral placebo, containing lactose (D: NR; F: NR)	60	4 weeks
Sekikawa et al. (2021)[79]	Symptomatic VDT users	Bilberry extract capsule (D: 43.2mg; F: 1x/d).	Placebo capsule (D: NR; F: 1x/d).	32	6 weeks
Yamashita et al. (2019)[76]	Symptomatic computer user	MaquiBright™ capsule D: 120mg dextrin +60mg MaquiBright (21mg anthocyanins + 15mg delphinidins + 4mg delphinidin-3,5-O-diglucoside; F: 1x/d).	Oral placebo (D: 180mg; F: 1x/d).	74	4 weeks

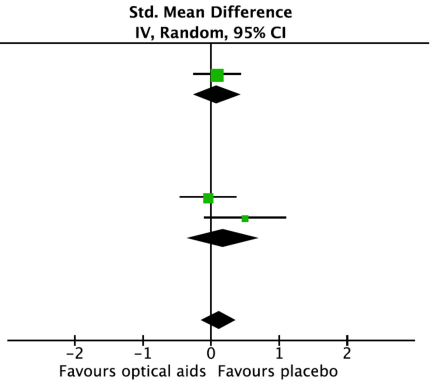
Abbreviations: d, day; D, dose; F, frequency; mg, milligrams; NR, not reported; VDT, visual display terminal; x, times.





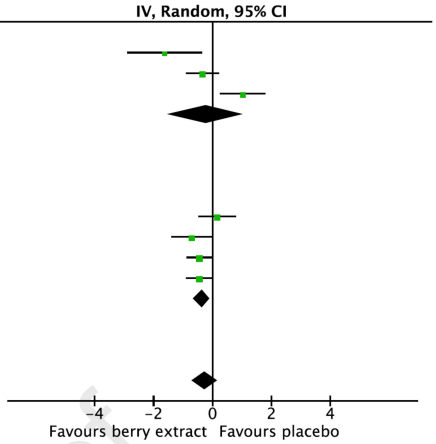
Optical aids – Visual fatigue or asthenopia score

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.1.1 Likert scale								
Kee et al (2018)	1.8	1	64	1.71	1.05	64	48.0%	0.09 [−0.26, 0.43]
Subtotal (95% CI)			**64**			**64**	**48.0%**	**0.09 [−0.26, 0.43]**
Test for overall effect: Z = 0.49 (P = 0.62)								
1.1.2 VAS								
NCT03585790 (2018)	20	22.2	45	21	25.19	45	34.9%	−0.04 [−0.46, 0.37]
NCT02921087 (2016)	153.9	124.9	22	100.7	79.2	22	17.2%	0.50 [−0.10, 1.10]
Subtotal (95% CI)			**67**			**67**	**52.0%**	**0.18 [−0.34, 0.71]**
Heterogeneity: $Tau^2 = 0.08$; $Chi^2 = 2.12$, df = 1 (P = 0.15); $I^2 = 53\%$								
Test for overall effect: Z = 0.69 (P = 0.49)								
Total (95% CI)			**131**			**131**	**100.0%**	**0.11 [−0.14, 0.37]**
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 2.15$, df = 2 (P = 0.34); $I^2 = 7\%$								
Test for overall effect: Z = 0.87 (P = 0.38)								
Test for subgroup differences: $Chi^2 = 0.09$, df = 1 (P = 0.76), $I^2 = 0\%$								



Oral berry extract – Visual fatigue or asthenopia score

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
3.1.1 Likert scale								
Liang et al (2017)	3.9	1	8	5.5	0.8	6	7.4%	−1.62 [−2.90, −0.35]
Park et al (2016)	0.46	4.5	26	2.42	6.81	24	15.9%	−0.34 [−0.90, 0.22]
Sekikawa et al (2021)	5	1.11	15	4	0.74	15	12.8%	1.03 [0.26, 1.80]
Subtotal (95% CI)			**49**			**45**	**36.2%**	**−0.23 [−1.50, 1.04]**
Heterogeneity: $Tau^2 = 1.06$; $Chi^2 = 14.48$, df = 2 (P = 0.0007); $I^2 = 86\%$								
Test for overall effect: Z = 0.35 (P = 0.73)								
3.1.2 VAS								
Okamoto et al (2018)	42.1	27.8	21	38.2	19.6	18	14.8%	0.16 [−0.47, 0.79]
Okamoto et al (2019)	41.3	16.9	17	53.4	16.7	18	14.0%	−0.70 [−1.39, −0.02]
Ozawa et al (2015)	25.7	19.02	43	35.4	24.94	37	17.6%	−0.44 [−0.88, 0.01]
Yamashita et al (2019)	59	31.11	37	70	16.29	37	17.4%	−0.44 [−0.90, 0.02]
Subtotal (95% CI)			**118**			**110**	**63.8%**	**−0.37 [−0.67, −0.07]**
Heterogeneity: $Tau^2 = 0.02$; $Chi^2 = 3.76$, df = 3 (P = 0.29); $I^2 = 20\%$								
Test for overall effect: Z = 2.41 (P = 0.02)								
Total (95% CI)			**167**			**155**	**100.0%**	**−0.27 [−0.70, 0.16]**
Heterogeneity: $Tau^2 = 0.22$; $Chi^2 = 19.74$, df = 6 (P = 0.003); $I^2 = 70\%$								
Test for overall effect: Z = 1.24 (P = 0.22)								
Test for subgroup differences: $Chi^2 = 0.04$, df = 1 (P = 0.83), $I^2 = 0\%$								

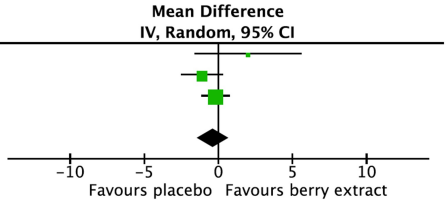


Oral berry extract – Critical flicker-fusion frequency (Hz)

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Okamoto et al (2018)	39.6	6.8	21	37.6	4.6	18	7.7%	2.00 [−1.60, 5.60]
Ozawa et al (2015)	35.2	2.62	43	36.3	3.65	37	36.0%	−1.10 [−2.51, 0.31]
Yamashita et al (2019)	31.3	2.1	37	31.5	2.1	37	56.2%	−0.20 [−1.16, 0.76]
Total (95% CI)			**101**			**92**	**100.0%**	**−0.35 [−1.39, 0.69]**

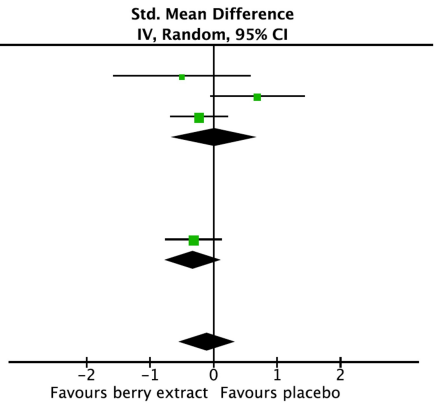
Heterogeneity: $Tau^2 = 0.26$; $Chi^2 = 2.81$, df = 2 (P = 0.25); $I^2 = 29\%$

Test for overall effect: Z = 0.67 (P = 0.51)

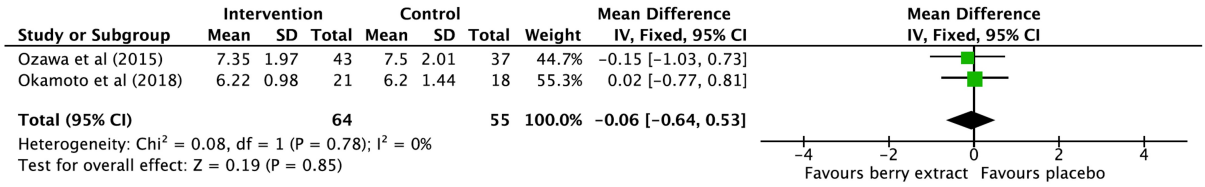


Oral berry extract – Dry eye symptom score

Study or Subgroup	Intervention Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
3.3.1 Likert scale								
Liang et al (2017)	3.5	1.1	8	4.3	1.9	6	12.3%	−0.50 [−1.58, 0.58]
Sekikawa et al (2021)	4	0.74	15	3	1.85	15	20.8%	0.69 [−0.05, 1.43]
Yamashita et al (2019)	11.7	14.81	37	15	13.63	37	33.1%	−0.23 [−0.69, 0.23]
Subtotal (95% CI)			**60**			**58**	**66.1%**	**0.01 [−0.66, 0.68]**
Heterogeneity: $Tau^2 = 0.21$; $Chi^2 = 5.11$, df = 2 (P = 0.08); $I^2 = 61\%$								
Test for overall effect: Z = 0.04 (P = 0.97)								
3.3.2 VAS								
Ozawa et al (2015)	21.2	22.95	43	29.1	26.76	37	33.9%	−0.32 [−0.76, 0.13]
Subtotal (95% CI)			**43**			**37**	**33.9%**	**−0.32 [−0.76, 0.13]**
Test for overall effect: Z = 1.40 (P = 0.16)								
Total (95% CI)			**103**			**95**	**100.0%**	**−0.10 [−0.54, 0.33]**
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 6.03$, df = 3 (P = 0.11); $I^2 = 50\%$								
Test for overall effect: Z = 0.46 (P = 0.65)								
Test for subgroup differences: $Chi^2 = 0.64$, df = 1 (P = 0.42), $I^2 = 0\%$								



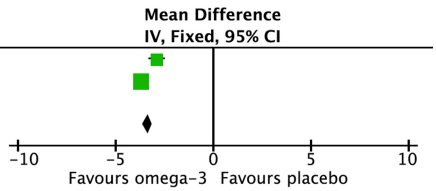
Oral berry extract – Amplitude of accommodation (D)



Oral omega-3 fatty acid – Dry eye symptom score

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Bhargava et al (2015)	3.9	2.2	220	6.8	2.2	236	41.9%	−2.90 [−3.30, −2.50]
Bhargava et al (2016)	3.9	2	256	7.6	2	266	58.1%	−3.70 [−4.04, −3.36]
Total (95% CI)			**476**			**502**	**100.0%**	**−3.36 [−3.63, −3.10]**

Heterogeneity: $Chi^2 = 8.75$, df = 1 (P = 0.003); $I^2 = 89\%$
Test for overall effect: Z = 25.21 (P < 0.00001)

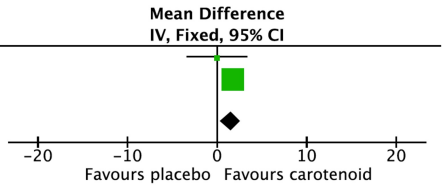


Oral carotenoid – Critical flicker-fusion frequency (Hz)

Study or Subgroup	Intervention Mean	SD	Total	Placebo Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Nagaki et al (2002)	38.4	4.8	13	38.4	3.9	13	11.2%	0.00 [-3.36, 3.36]
Stringham et al (2017)	27.12	1.96	35	25.38	1.84	13	88.8%	1.74 [0.55, 2.93]
Total (95% CI)			**48**			**26**	**100.0%**	**1.55 [0.42, 2.67]**

Heterogeneity: $Chi^2 = 0.91$, df = 1 (P = 0.34); $I^2 = 0\%$

Test for overall effect: Z = 2.70 (P = 0.007)



Précis

Spectacles (including multifocal and blue-blocking) and nutritional supplements are commonly proposed for treating eye strain from computer use, yet our systematic review finds no high certainty evidence to support these therapies.