

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository:<https://orca.cardiff.ac.uk/id/eprint/107412/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

van der Aa, HPA, Margrain, Thomas , van Rens, GHMB, Heymans, MW and van Nispen, RMA 2016. Psychosocial interventions to improve mental health in adults with vision impairment: systematic review and meta-analysis. *Ophthalmic And Physiological Optics* 36 (5) , pp. 584-606. 10.1111/opo.12313

Publishers page: <http://dx.doi.org/10.1111/opo.12313>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See <http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



Psychosocial interventions to improve mental health in adults with vision impairment: systematic review and meta-analysis

Hilde PA van der Aa (corresponding author) (h.vanderaa@vumc.nl)¹

Tom H Margrain (margrainth@cardiff.ac.uk)²

Ger HMB van Rens (rens@vumc.nl)^{1,3}

Martijn W Heymans (mw.heymans@vumc.nl)⁴

Ruth MA van Nispen (r.vannispen@vumc.nl)¹

¹ Department of Ophthalmology and the EMGO institute for Health and Care Research, VU University Medical Centre, De Boelelaan 1117, 1081 HV, Amsterdam, the Netherlands.

² School of Optometry and Vision Sciences, Cardiff University, CF24 4 LU, Cardiff, United Kingdom.

³ Department of Ophthalmology, Elkerliek Hospital, Wesselmanlaan 25, 5707 HA Helmond, the Netherlands.

⁴ Department of Epidemiology and Biostatistics, VU University Medical Centre, De Boelelaan 1117, 1081 HV, Amsterdam, the Netherlands.

Running head: Psychosocial interventions in low vision

Keywords: vision impairment, mental health, depression, anxiety, systematic review, meta-analysis

Conflict of interest

The authors report no conflicts of interest and have no proprietary interest in any of the materials mentioned in this article.

Acknowledgement

This work was supported by ‘ZonMw InZicht’, the Dutch Organisation for Health Research and Development – InSight Society [grant number 60-0063598108]. The sponsor had no role in the design and conduct of the present study or in the writing of the manuscript.

ABSTRACT

Purpose: To systematically assess the literature on psychosocial interventions to improve mental health (i.e. depression, anxiety, mental fatigue, loneliness, psychological stress and psychological well-being) in visually impaired adults (≥ 18 years).

Methods: The databases Medline, Embase and Psychinfo were searched for relevant studies, which were categorized into randomised controlled trials (RCTs), non-RCTs and before and after comparisons (BA). The Cochrane Collaboration Risk of Bias Tool was used to assess study quality. Standardized mean differences (SMD) were calculated to quantitatively summarize the outcomes of the RCTs and non-RCTs in a meta-analysis. Meta-regression was used to explore sources of heterogeneity in the data.

Results: The search identified 27 papers (published between 1981 and 2015), describing the outcomes of 22 different studies (14 RCTs, 4 non-RCTs, and 4 BAs). Pooled analyses showed that interventions significantly reduced depressive symptoms (SMD -0.30, 95% confidence interval (CI) -0.60 to -0.01), while effects on anxiety symptoms, mental fatigue, psychological stress and psychological well-being were non-significant. Meta-regression analyses showed homogeneity in effect sizes across a range of intervention, population, and study characteristics. Only a higher age of participants was associated with less effective results on depressive symptoms ($b=0.03$, 95% CI 0.01 to 0.05), psychological stress ($b=0.07$, 95% CI 0.01 to 0.13) and psychological well-being ($b=-0.03$, 95% CI -0.05 to 0.01). However, after removing a clear outlier the overall effect on depressive symptoms and the influence of age on depressive symptoms and psychological stress were no longer significant, while the influence of age on psychological well-being remained.

Conclusions: There is currently only limited evidence for the effectiveness of psychosocial interventions in the field of low vision. More well-designed trials are needed with specific attention for interventions tailored to the needs of elderly patients.

INTRODUCTION

Irreversible vision loss may prevent individuals from their primary means to engage in the world and perform valued activities.^{1,2} This requires significant adaptation, a process characterised by mental health problems.³ About one-third of people with visual impairment experience subthreshold depression and/or anxiety (indicating subclinical symptoms),⁴⁻⁶ 5-7% are diagnosed with a major depressive disorder⁴⁻⁶ and 7% with an anxiety disorder.⁴ These percentages are significantly higher than the prevalence in normally sighted peers.⁴ Vision loss is also associated with mental fatigue,^{1,7} less social contact,^{2,8} and can induce feelings of loneliness and social isolation.^{2,8}

The importance of targeted interventions to address mental health problems in people with visual impairment is increasingly becoming recognised.⁹⁻¹¹ However, compared to the large body of research in the general population,¹² research on psychosocial interventions to improve mental health in people with visual impairment is still in its infancy.⁹⁻¹¹ Rees et al. (2010)⁹ and Binns et al. (2012)¹⁰ performed a systematic review on the effects of multidisciplinary low vision rehabilitation services. They concluded that these services may improve aspects of clinical and functional ability, however, the effects on mood are less clear, and the number of well-designed and adequately reported studies is small. In addition, Holloway et al. (2015)¹¹ performed a systematic review and meta-analysis on problem solving interventions to improve psychosocial outcomes in people with visual impairment. Based on 8 trials, they showed that problem solving interventions can improve vision-related functioning and emotional distress. However, no evidence was found to support improvements in depressive symptoms.

These systematic reviews indicate that the effects of interventions to improve mental health in the field of low vision are unclear. However, these reviews have several

important drawbacks: 1) they do not include all types of psychosocial interventions, offered in different settings, aimed at increasing mental health in people with visual impairment, 2) they do not perform meta-regression analyses to identify sources of heterogeneity between the studies, and 3) the systematic reviews of Rees et al. (2010)⁹ and Binns et al. (2012)¹⁰ need an update on new and current studies in this upcoming field.

Therefore, we believe that it is important to provide a broad up-to-date systematic review, based on liberal inclusion criteria, to provide an overall view of the studies that are performed in this field. The aim of this study is to systematically review quantitative evidence on psychosocial interventions that address mental health problems in adults (≥ 18 years) with visual impairment and perform a meta-analysis with meta-regression. Since multiple studies indicate that visual impairment is associated with increased levels of depression,^{2,4-6} anxiety,^{2,4} mental fatigue,^{1,7} loneliness,^{2,8} psychological stress,⁷ and lower psychological well-being,^{1,7,8} these mental health problems were investigated in this study. The information of this review is essential to allow a targeted approach to reduce or prevent mental health problems in people with visual impairment.

METHODS

Search method

Potential articles were identified through searches in Medline, Embase and Psychinfo from their date of inception until June 3rd 2015, and the reference lists of retrieved articles. Other databases were also considered but, as the findings from the three initial databases were similar, additional searches were deemed unnecessary. Search syntaxes were developed in consultation with an experienced university librarian. A broad range of terms were used in the definitions of intervention studies, visual impairment, adults and mental health (Appendix 1 presents the full electronic search strategy). Reference lists of the retrieved articles were searched by hand to identify additional relevant studies. The selection procedure was performed by three researchers (HA, TM and RN) and included four stages: 1) reviewing title, 2) reviewing title and abstract, 3) reading the full text of the articles, and 4) quality assessment. Discrepancies were resolved by discussion.

Study criteria

The following inclusion criteria were used: 1) original research reported in English, 2) longitudinal design with a minimum of two measurement time-points, 3) participants were diagnosed with an eye disease as a cause of severe visual impairment, or had low vision (visual acuity ≤ 0.3 or visual field $\leq 30^\circ$), or blindness (visual acuity ≤ 0.05 or visual field $\leq 10^\circ$), 4) participants had a minimum age of 18 years, 5) sample size of ≥ 10 participants, 6) a psychosocial intervention designed to bring about modification of feelings, cognitions, attitudes, and behaviours was investigated, 7) the intervention was aimed at reducing mental health problems, 8) outcome measures on depression, anxiety, mental fatigue, loneliness, psychological stress, psychological well-being were reported.

Data extraction

The following general characteristics of the studies were extracted: 1) country and year of publication, 2) study design and measurement time-points, 4) sample information (i.e. mean age, proportion of women, visual impairment, sample size at baseline and drop-out rate), 5) outcome measures, 6) setting, 7) intervention, and 8) control condition.

Quality assessment

Randomised controlled trials (RCT), non-RCTs and before and after comparisons (BA) were distinguished. For quality assessment of these studies the Cochrane Collaboration Risk of Bias Tool (CCRB) was used by two of the three researchers who also performed the selection procedure (HA and TM). This tool considers seven parameters: 1) random sequence generation (selection bias), 2) allocation concealment (selection bias), 3) blinding of participants and staff (performance bias), 4) blinding of outcome assessment (detection bias), 5) incomplete outcome data addressed (attrition bias), 6) selective outcome reporting (reporting bias), and 7) other bias.¹³ Each parameter was rated as low risk, high risk or unclear risk (Appendix 2). For non-RCTs and BAs, parameters 1 to 3 were not rated because those study designs do not allow to meet these requirements. Discrepancies were resolved by discussion or by consulting another review author.

Synthesis of evidence

Because BAs preclude comparison of groups, a narrative method was used to synthesize evidence from these studies, taking study quality into account. For the RCTs and non-RCTs both a narrative and quantitative pooling method was used. Standardised mean

differences (SMD) for the total follow-up were determined to facilitate comparisons between different continuous scales that were used to determine mental health outcomes. Cohen's categories for classifying effect sizes were used: 0.2 represents a small effect, 0.5 a medium effect, and ≥ 0.8 a large effect.¹⁴ For each outcome the number of participants, mean change from baseline to follow-up and the standard deviation (SD) of these mean changes were extracted for the intervention and control group separately. In some cases the SD was derived from the standard error (SE), p-value, 95% confidence interval or other methods that are recommended by the Cochrane collaboration. If these parameters were not available, the authors were contacted by e-mail and asked to provide these data. Differences in change scores between the groups were divided by the SD of change, leading to an effect size (SMD) that allowed different studies to be pooled and compared. SMDs and 95% confidence intervals (CI) were reported. Before combining the data, statistical heterogeneity was assessed, using the I^2 test describing the percentage of variation between studies based on heterogeneity rather than on chance. Substantial heterogeneity ($I^2 > 50\%$) was detected, therefore, the results were combined in a meta-analysis using the random-effects model. Forest plots were provided to graphically display the estimated results, in which squares were provided that are proportional to the study's weight in the meta-analysis. In addition, meta-regression analyses were performed to explore sources of heterogeneity in the data in terms of study characteristics (i.e. year of publication, drop-out rates, risk of bias, study design: RCT vs. non-RCT), population characteristics (i.e. mean age of participants, percentage of females, people with specific eye diseases versus people with low vision or blindness in a range of eye conditions with different causes), characteristics of the intervention (i.e. individually or group-based interventions, setting: within low vision rehabilitation, at home or within a clinic/hospital), and characteristics

of the control condition (no intervention versus usual care/comparable intervention). To visualise the relationship between factors used in the meta-regression and the study outcomes, SMD bubble plots were used. Funnel plots (scatterplots of treatment effects against a measure of study size) were used to assess publication bias if enough studies were found to use this analysis. In the absence of publication bias points were symmetrical about the vertical line of this plot.

RESULTS

Database search

The initial search identified 3,512 articles (Figure 1). After screening the titles and abstracts, 73 articles remained for which the inclusion and exclusion criteria were screened; this resulted in 27 articles describing 22 different studies (14 RCTs, 4 non-RCTs and 4 BAs) that were included in this review. Multiple articles describing different outcomes of the same study were jointly reviewed (Table 1).¹⁵⁻²³

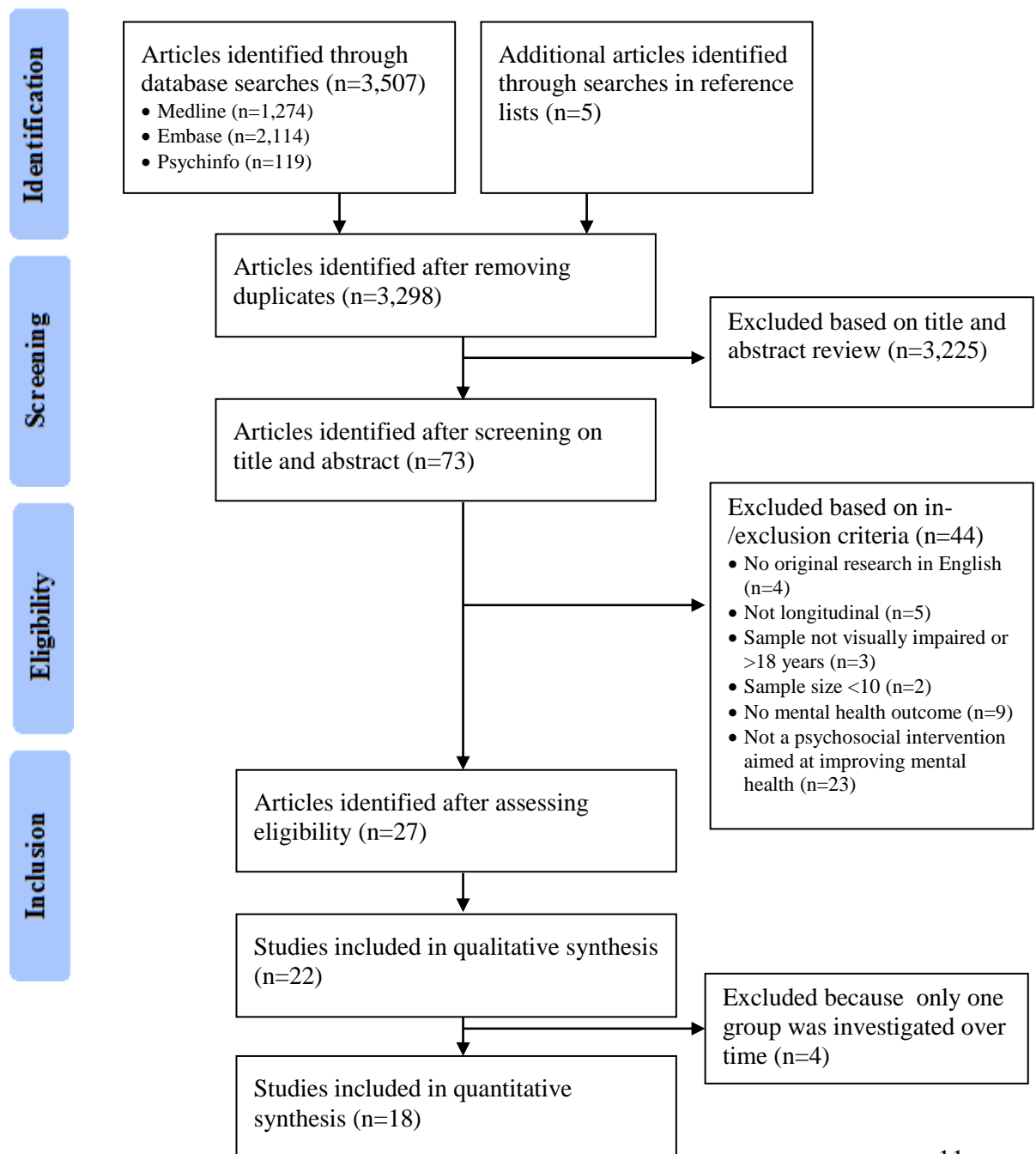


Figure 1. Flow-diagram of study inclusion process

Study characteristics

The 22 included studies included 2,092 participants, with sample sizes ranging from 12 participants²⁵ to 252 participants.¹⁸ The total period of follow-up ranged from 1 month²⁶ to 11 months,²⁴ drop-out ranged from 0%^{20,21,25-28} to 57%,²⁹ mean age ranged from 38 years^{22,23} to 84 years³⁰ and 10%^{20,21} to 79%³³ were female (Table 1). In almost half of the studies^{15-19,25,30-35} the participants were diagnosed with age-related macular degeneration (AMD), in 6 studies^{24,36-40} patients had vision impairment (indicating that participants had different eye conditions), in two studies^{20,21,26} patients were blind, in two studies^{27,41} patients were diagnosed with glaucoma, in two studies^{22,23,28} patients had diabetic retinopathy, and in one study²⁹ patients were diagnosed with Stargardt's disease. Half of the studies were performed in the United States of America,^{15-23,28-32,34,37} one in Australia,³⁶ seven in Europe (i.e. United Kingdom,^{25,39,40} Germany^{33,35,41} and the Netherlands²⁴) and three in Asian countries (i.e. Iran,²⁶ China²⁷ and Japan³⁸). Eighteen out of the 22 included studies were conducted in the last decade.^{15,16,18,19,24-27,29-33,36-40}

Patient reported outcomes

Table 1 provides an overview of the questionnaires that were used to measure mental health. The Profile of Mood States (POMS) was used in two studies^{34,38} to measure depressive symptoms, tension/anxiety symptoms, and mental fatigue. The Depression Anxiety Stress Scale (DASS) was used in two studies^{26,36} to measure depressive symptoms, anxiety symptoms and psychological stress. The subscales of the POMS and DASS show high reliability and internal validity in adults in general.⁴²⁻⁴⁴ The Geriatric

Depression Scale (GDS) was used in three studies,^{32,33,35} the Patient Health Questionnaire (PHQ)-9 was used in two studies,^{30,31} the Centre for Epidemiologic Studies Depression scale (CES-D) was used in one study,²⁹ the Beck Depression Inventory (BDI) was used in one study,²⁸ and the Hamilton rating scale for Depression (HAMD) was used in one study¹⁵ to measure symptoms of depression. These questionnaires all show good reliability and internal validity in adults in general,⁴⁵⁻⁵⁰ however, only the PHQ-9 was validated in a visually impaired sample.⁴⁹ Based on cut-off scores, the PHQ-9 was used in one study³⁰ and the HAMD in another^{15,16} to determine DSM-IV major and minor depressive disorder. These dichotomous outcomes could not be incorporated in the meta-analysis, instead, we only used the continuous scales of these outcome measures that were also provided by the authors.

The Self-rating Depression Scale (SDS) was used in two studies,^{22,23,27} and the Self rating Anxiety Scale (SAS) was used in one study²⁷ to determine depressive and anxiety symptomatology. The Wakefield self-rating depression scale and the University of California Los Angeles (UCLA) Loneliness scale was used in one study²⁰ to determine depressive symptomatology and loneliness, respectively. The reliability and validity of these scales are less well established, i.e. outdated methods were used to determine psychometric properties.⁵¹⁻⁵³

For psychological stress, the Perceived Stress Scale (PSS)-14 was used in one study.²⁹ This scale shows good reliability and internal validity,⁵⁴ however, the 10-item PSS was found to be superior to the 14-item PSS.⁵¹ In addition, the Problem Areas in Diabetes survey (PAID) was used in one study²⁸ to determine diabetes-related stress which is a reliable and valid instrument.⁵⁵

Psychological well-being was mostly determined with a mental health subscale of vision-related quality of life questionnaires: four studies^{15,29-31} used the 'mental

health' subscale of the National Eye Institute Visual Functioning Questionnaire (NEI-VFQ), one study³⁶ used the 'emotional well-being' subscale of the Impact of Visual Impairment scale (IVI), and one study⁴⁰ used the 'mental health' subscale of the Vision Quality of Life Core Measure (VCM1). These subscales show good reliability and validity in a visually impaired sample.⁵⁶⁻⁵⁸ In addition, several mental health subscales of health-related quality of life questionnaires were used: two studies^{24,32} used the 'mental health' subscale of the Short Form Health Survey (SF-36) and the Research and Development scale (RAND-36), which are well-established and reliable tools in adults in general,⁵⁹ one study²⁵ used the 'negative well-being' subscale of the Well-Being Questionnaire (WB-Q), which shows good reliability and validity in people with macular disease,⁶⁰ and another study³⁹ used the 'psychosocial well-being' subscale of the CORE outcome measure, which shows good reliability and internal validity in the general population.⁶¹ The Symptom Checklist (SCL) was used by one study²⁷ and the Kurzfragebogen zur Aktuellen Beanspruchung (KAB) by another study⁴¹ to determine psychological problems/strain. For these two questionnaires psychometric properties are unclear.

Interventions and their effectiveness

Eight studies^{15,16,22,23,27,29-31,37,39} were aimed at investigating the effectiveness of individually offered interventions, and twelve studies^{17-21,24-26,28,32-36,38,40,41} investigated group-based interventions (Table 1). Several group-based self-management programmes were tested, with core elements of teaching problem solving skills to help patients deal with limitations brought on by vision loss. In two RCTs in AMD patients conducted by Brody et al. (1999)³⁴ (n=92) and Brody et al.(2002, 2005)^{17,18} (n=252) showed that this type of intervention is effective in reducing psychological distress compared with

controls, and that effects on depressive symptoms were strongest for a subgroup of patients (n=32) who were clinically depressed at baseline.¹⁹ In two pilot studies in AMD patients conducted by Birk et al. (2004)³⁵ (n=22) and Wahl et al. (2006)³³ (n=24) these outcomes were confirmed but the beneficial effects deteriorated over time. In addition, in nine studies^{24,26,28,30-32,36,38,39} interventions were offered at low vision rehabilitation organisations. Of these, two RCTs investigated the effectiveness of a group-based self-management programme showing different results: Girdler et al. (2010)³² found a significant reduction in symptoms of depression in AMD patients (n=77) in favour of the intervention group, while Rees et al. (2015)³⁶ found no effective results in favour of the intervention group in increasing emotional well-being in patients with multiple eye conditions (n=153). In addition, in an RCT by Rovner et al. (2014)³⁰ beneficial results in AMD patients (n=188) for individually offered behavioural activation embedded in low vision rehabilitation care was found. Two other RCTs by Rovner et al. (2007, 2008)^{15,16} and Rovner et al. (2013)³¹ (n=206 and n=241, respectively) showed mixed results on the effectiveness of problem solving treatment (PST) on reducing depressive symptoms in AMD patients. Mixed results were also found by two smaller RCTs conducted by Bradley et al. (2005)²⁵ (n=12) and Evans et al. (1981, 1982)^{20,21} (n=84) and one BA conducted by Latham et al. (2013)⁴⁰ (n=29) on the effectiveness of peer support to increase psychological well-being in visually impaired persons. Favourable results were found in single RCTs for group-based rational emotive therapy for patients with late blindness (n=60),²⁶ and an expressive writing intervention for patients with Stargardt's disease (n=81).²⁹

Table 1. Characteristics of reviewed studies in order of publication year, divided into: 1) randomised controlled trials, 2) non-randomised controlled trials, and 3) before and after comparisons

| Author (year, country) | Study design (follow-up) | Sample: mean age, % female, vision impairment, sample size, % drop-out | Primary and secondary outcome measures | Setting | Intervention‡ | Control |
|---|--------------------------|--|--|-----------------|--|--|
| 1. Randomised controlled trials: | | | | | | |
| Rees et al. (2015, Australia) ³⁶ | 2-Arm RCT (6 months) | 80 years, 60% female, visual impairment, n=153, 16% drop-out | <i>Of interest:</i> depressive symptoms, anxiety symptoms, and stress (DASS), emotional wellbeing (subscale IVI). <i>Other outcomes:</i> self-efficacy (GSES), adaptation to vision loss (AVL), vision-related quality of life (IVI) | LVR | Group-based self-management programme: coping with illness and disability, techniques from adult learning, group processes, and cognitive-behavioural approaches (weekly 3-hour sessions, during 8 weeks, offered by two low vision rehabilitation counsellors and guest speakers) | Usual care |
| Bryan et al. (2014, USA) ²⁹ | 2-Arm RCT (7 weeks) | 42 years, 69% female, Stargardt's disease (juvenile form of AMD), | <i>Of interest:</i> depressive symptoms (CES-D), perceived stress (PSS), mental health (subscale NEI-VFQ). <i>Other outcomes:</i> social support, | Patients' homes | Expressive writing intervention: expressing emotions through written disclosure of a post traumatic experience (for 20 minutes on three separate days, during a 1-week period, | Neutral writing intervention (similar in dose and intensity) |

| | | | | | | |
|--|----------------------|--|--|-----|---|--|
| | | n=81, 57% drop-out | physical symptoms, vision-related quality of life (NEI-VFQ) | | participants were instructed by the researchers) | |
| Jalali et al. (2014, Iran) ²⁶ | 2-Arm RCT (1 month) | 20-40 years, gender not reported, blind, n=60, no drop-out | <i>Of interest:</i> depressive symptoms, anxiety symptoms, stress (DASS). <i>Other outcomes:</i> beliefs (Jones irrational beliefs questionnaire), self-esteem (Eysenck's self-esteem inventory) | LVR | Group-based rational emotive behavioural therapy: a comprehensive, active-directive psychotherapy which focuses on resolving emotional and behavioural problems (number of sessions and duration is unclear, offered by therapists of whom background is unclear) | No training |
| Rovner et al. (2014, USA) ³⁰ | 2-Arm RCT (4 months) | 84 years, 70% female, AMD, n=188, 10% drop-out | <i>Of interest:</i> depressive disorder (PHQ), mental health (subscale NEI-VFQ). <i>Other outcomes:</i> vision status, functional vision, physical health status, personality, behavioural activation, device use, vision-related quality of life (NEI-VFQ), | LVR | Behavioural activation: functional analytic psychotherapy which focusses on targeting behaviours that might maintain/worsen depression (6 in home 1-hour sessions, offered by 1 of 5 occupational therapists) + LVR | Supportive therapy (similar in dose and intensity) + LVR |
| Rovner et al. (2013, USA) ³¹ | 2-Arm RCT (6 months) | 82 years, 64% female, AMD, n=241, 11% drop-out | <i>Of interest:</i> depressive disorder (PHQ), mental health (subscale NEI-VFQ). <i>Other outcomes:</i> targeted vision function, control | LVR | Problem Solving Treatment: cognitive-behavioural intervention with a positive goal-oriented approach (mean of 6 sessions, 45-60 minutes per session, offered by trained bachelor | Supportive therapy (similar in dose and intensity) |

| | | | | | | |
|--|----------------------|---|---|---------------------------|--|--|
| | | | strategies, activity inventory, physical health status, vision-related quality of life (NEI-VFQ) | | or master-level therapists) | |
| Sun et al. (2012, China) ²⁷ | 2-Arm RCT (6 months) | 62 years, gender not reported, glaucoma, n=100, no drop-out | <i>Of interest:</i> depressive symptoms (SDS), anxiety symptoms (SAS), psychological problems (SCL) | Clinical setting/hospital | Psychological therapy: specific content unclear (during 6 months, number of sessions unclear, provided by psychiatrists and specialist nurses) + physical therapy | Physical therapy; specific content unclear (during six months) |
| Girdler et al. (2010, USA) ³² | 2-Arm RCT (12 weeks) | 79 years, 65% female, AMD, n=77, 3% drop-out | <i>Of interest:</i> depressive symptoms (GDS), mental health (subscale SF36). <i>Other outcomes:</i> participation (ACS), adaptation to vision loss (AVL), self-efficacy (GSES, AMD-SEQ) | LVR | Group-based vision self-management programme: problem solving based on self-efficacy and group model of service delivery principles (weekly structured programme, during 8 weeks, led by an occupational therapist and a social worker) + usual care | Usual care |
| Rovner et al. (2007, 2008, USA) ^{15,16} † | 2-Arm RCT (6 months) | 81 years, 70% female, AMD, n=206, 8% drop-out | <i>Of interest:</i> depressive symptoms (HAMD), DSM-IV major and minor depressive disorder (Schedule for Affective Disorders and Schizophrenia and the HAMD), mental health (subscale NEI-VFQ). <i>Other outcomes:</i> visual acuity, | Patients' homes | Problem Solving Treatment: cognitive-behavioural intervention with a positive goal-oriented approach (6 in-home sessions, 45-60 minutes per session, during 8 weeks, provided by 2 nurses and 1 master's-level counsellor) + usual care | Usual care |

| | | | | | | |
|--|--------------------------------|--|---|---------------------------|---|--|
| | | | contrast sensitivity, vision-related quality of life (NEI-VFQ). | | | |
| Goldstein et al. (2007, USA) ³⁷ | 2-Arm RCT (3 months) | 78 years, 64% female, visual impairment, n=154, 3% drop-out | <i>Of interest:</i> emotional well-being/response (5 questions on a 4-point Likert scale on experiencing fear, sadness, frustration, hopefulness and peacefulness). <i>Other outcomes:</i> knowledge, adaptive behaviour, self-efficacy (AMD-SEQ). | Patients' homes | Educational video: incorporating cognitive restructuring to change emotional response with a focus on increasing knowledge and awareness (participants watched the video at home within 2 weeks, no additional support was provided). | Waiting list |
| Wahl et al. (2006, Germany) ³³ | 3-Arm pilot non-RCT (3 months) | 77 years, 79% female, AMD, n=45 (randomised in two intervention arms), n=24 (self-selected comparison group), 22% drop-out | <i>Of interest:</i> depressive symptoms (GDS). <i>Other outcomes:</i> coping, adaptation to vision loss (AVL) | Clinical setting/hospital | Group-based psychological intervention with an emphasis on cognitive behavioural therapy, investigated in two separate arms: 1. emotion focused to increase coping strategies 2. problem focused to develop solutions for behavioural consequences of AMD (3 sessions of 2 to 3 hours, over a three week period, offered as part of an eye clinic's treatment programme) | No intervention (control group not randomised) |
| Brody et al. | 3-Arm RCT (6 months) | 81 years, 67% | <i>Of interest:</i> psychological distress | Clinical setting/hospital | Group-based self-management programme: | Educational tape |

| | | | | | | |
|---|---------------------------|---|--|----------------------------|---|---|
| (2002, 2005, 2006, USA) ¹⁷⁻¹⁹ | months | female, AMD, n=252 (subgroup analysis 2006 n=32), 15% drop-out (2005) | (POMS total score), depressive symptoms (GDS). <i>Other outcomes:</i> self-efficacy (AMD-SEQ) | hospital | didactic presentation and group problem solving with guidance (weekly 2-hour sessions for 6 weeks, led by an experienced professional in public health and behavioural medicine) | intervention (2002) and waiting list (2005, 2006) |
| † | | | | | | |
| Bradley et al. (2005, UK) ²⁵ | 2-Arm pilot RCT (6 weeks) | 76 years, 50% female, MD, n=12, no drop-out | <i>Of interest:</i> negative well-being (W-BQ). <i>Other outcomes:</i> MD-related quality of life (MacDQol) | Clinical setting/ hospital | Group-based peer support and information provision: discussion groups were organised and 6 leaflets with information were distributed (6 weekly sessions of 1.5-hour, led by people experienced in living with MD) | Treatment delayed for 6 weeks |
| Brody et al. (1999, USA) ³⁴ | 2-Arm RCT (6 weeks) | 79 years, 50% female, AMD, n=92, 41% drop-out | <i>Of interest:</i> depressive symptoms, anxiety symptoms and mental fatigue (POMS). <i>Other outcomes:</i> self-efficacy (AMD-SEQ). | Clinical setting/ hospital | Group-based self-management programme: guided through a hierarchy of behavioural challenges to improve problem-solving techniques (weekly 2-hour sessions for 6 weeks, guided by peers and professionals whose background was not reported) | Waiting list |
| Kaluza et al. (1996, Germany) ⁴¹ | 2-Arm RCT (8 weeks) | 52 years, 78% female, open angle glaucoma, n=23, 13% drop-out | <i>Of interest:</i> psychological strain (KAB). <i>Other outcomes:</i> intraocular pressure, heartbeat. | Clinical setting/ hospital | Group-based relaxation training: performing autogenic relaxation exercises with peers and at home (weekly 1.5-hour session, during 8 weeks, provided by an experienced clinical | Waiting list |

psychologist)

2. Non-randomised controlled trials

| | | | | | | |
|--|-------------------------------|--|---|---------------------------|---|---|
| Ueda et al. (2013, Japan) ³⁸ | 3-Arm non-RCT(6 months) | 46 years, 32% female, visual impairment, n=79, drop-out not reported | <i>Of interest:</i> depressive symptoms, anxiety symptoms and mental fatigue (POMS). <i>Other outcomes:</i> psychological adjustment to vision loss, self-efficacy (Nottingham adjustment to vision loss scale) | LVR | 1. First arm received skills training, aimed at improving skills on orientation, mobility, activities of daily living), and group counselling, aimed at sharing experiences, psycho-education, and stress reduction techniques (weekly 1.5-hour sessions, during 10 weeks, guided by a clinical psychologist) 2. Second arm received the same skills training, and group counselling and additionally received individual counselling based on cognitive behavioural therapy (weekly for 45 minutes, during 10 weeks, provided by a clinical psychologist) | Skills training (similar in dose and intensity) |
| Birk et al. (2004, Germany) ³⁵ | 2-Arm pilot non-RCT (8 weeks) | 73 years, 64% female, AMD, n=22, 36% drop-out. | <i>Of interest:</i> depressive symptoms (GDS). <i>Other outcomes:</i> positive and negative affect, coping style. | Clinical setting/hospital | Group-based psychological intervention: exchange of information and experiences, muscle relaxation, increasing problem-solving skills, and an emphasis on cognitive behavioural therapy (weekly 1-hour sessions, | Usual care |

| | | | | | | |
|---|--------------------------|---|--|-----------------|---|--|
| Trozzolino et al. (2003, USA) ²⁸ | 2-Arm non-RCT (12 weeks) | 63 years, 65% female, diabetes retinopathy, n=48, no drop-out | <i>Of interest:</i> depressive symptoms (BDI), diabetes related psychological stress (PAID). <i>Other outcomes:</i> diabetes knowledge, serum glycosylated haemoglobin (HbA _{1c}). | LVR | during 5 weeks, offered by two group trainers with a background in clinical psychology) Group-based psycho-educational therapy: based on cognitive behavioural therapy aimed at increasing adherence to a diabetes regime and decreasing mental health problems (weekly sessions, during 12 weeks, offered by LVR professional) + optometric and rehabilitation training | Optometric and rehabilitation training (i.e. device use) |
| Evans et al. (1981, 1982, USA) ^{20,21} † | 2-Arm non-RCT (8 weeks) | 62 years, 10% female, blind veterans, n=84, no drop-out | <i>Of interest:</i> depressive symptoms (Wakefield self-rating depression scale), loneliness (UCLA loneliness scale) | Patients' homes | Group by telephone programme: telephone meetings with a group of peers using cognitive behavioural techniques (weekly 1-hour telephone meeting, during 8 weeks, guided by a counsellor) | No intervention |

3. Before and after comparisons

| | | | | | | |
|--------------------------------------|--------------------------------|---|--|-----|--|------------------|
| Barr et al. (2014, UK) ³⁹ | 1-Arm pilot BA (1 to 46 week) | 59 years, 66% female, visual impairment, n=64, 45% drop-out | <i>Of interest:</i> psychosocial well-being (CORE outcome measure) | LVR | Counselling and emotional support (no specific model) aimed at exploring thoughts and feelings about the impact of visual impairment, reflecting on beliefs, and identifying personal strengths (a maximum of 12 sessions for 50 | No control group |
|--------------------------------------|--------------------------------|---|--|-----|--|------------------|

| | | | | | | |
|---|----------------------|--|---|---------------------------|--|------------------|
| | | | | | minutes each, offered by experienced counsellors) | |
| Latham et al. (2013, UK) ⁴⁰ | 1-Arm BA (6 months) | 54 years, 45% female, visual impairment, n=29, drop-out not reported | <i>Of interest:</i> mental health (subscale VCM). <i>Other outcomes:</i> vision-related quality of life (VCM) | Clinical setting/hospital | Group-based emotional peer support service and telephone support: share fears and experiences that encourage a problem-solving approach (6 to 8 weekly sessions of 3 hours each, and telephone support once a month for 6 months after completion of the sessions, offered by trained and experienced staff) | No control group |
| Alma et al. (2013, The Netherlands) ²⁴ | 1-Arm BA (11 months) | 73 years, 69% female, visual impairment, n=29, 10% drop-out | <i>Of interest:</i> emotional well-being (subscale of the RAND-36). <i>Other outcomes:</i> adaptation to vision loss (AVL), helplessness (subscale ICQ), generic and vision-specific fear of falling. | LVR | Group-based rehabilitation programme: promote adaptation and psychosocial functioning by training practical skills, social interacting, problem solving, goal setting, and home-based exercises (20 weekly 2-hour sessions, and a booster session, offered by two trained occupational therapists) | No control group |
| Bernbaum et al. (1988, 1989 USA) ^{22,23} † | 1-Arm BA (12 weeks) | 38 years, 62% female, diabetic retinopathy, divided in two group: stable | <i>Of interest:</i> depressive symptoms (SDS), mental health (Rand Mental Health Index). <i>Other outcomes:</i> glucose control, body weight, | Fitness Centre | Rehabilitation programme: diabetes education, exercise programme, individually and group-based counselling (three times a week for 12 weeks, offered by a trained multidisciplinary | No control group |

| | | |
|-------------------|---------------------------------|--|
| or transitional | diabetes knowledge, self-esteem | team of specialists and psychologists) |
| vision (1988) and | (Rosenberg self-esteem scale) | |
| insulin-dependent | | |
| and independent | | |
| (1989), n=29, 10% | | |
| drop-out | | |

† Articles were jointly reviewed, because they were based on the same study.

‡ Individually offered unless stated otherwise.

LVR low vision rehabilitation, RCT randomised Controlled Trial, DASS Inventory Depression Anxiety Stress, GSES Generalised Self-Efficacy Scale, AVL Adaptation to Vision Loss scale, IVI Impact of Visual Impairment, USA United States of America, AMD Age-related Macular Degeneration, NEI-VFQ National Eye Institute Visual Functioning Questionnaire, PSS Perceived Stress Scale, CES-D Center for Epidemiologic Studies Depression scale, PHQ Patient Health Questionnaire, GDS Geriatric Depression Scale, SWL Satisfaction with Life scale, SCL Symptom Checklist, SDS self-rating depression scale, SAS self-rating anxiety scale, HAMD Hamilton rating scale for depression, HAM-A Hamilton rating scale for anxiety, ACS Activity Card Sort, SF36 Short Form Health Survey, AMD-SEQ Age-related Macular Degeneration Self-Efficacy Questionnaire, POMS Profile of Mood States, UK United Kingdom, MD Macular Degeneration, W-BQ Well-Being Questionnaire, MacDQoL Macular disease Dependent Quality of Life, KAB Kurzfragebogen zur Aktuellen Beanspruchung, BDI Beck Depression Inventory, PAID Problem Areas in Diabetes survey, UCLA University of California Los Angeles, VCM Vision Quality of Life Core Measure, ICQ Illness Cognition Questionnaire, RAND Research and Development

Quality assessment

Most RCTs^{15-19,29-32,36,37} had a low risk of selection bias because proper randomisation methods were used, however, in several studies^{25-27,34,41} this was not reported adequately and in one study³³ this was rated as a high risk because sequence generation was unclear and one of the comparison groups was not randomised (Table 2). Due to the nature of the interventions all RCTs used a pragmatic design in which blinding of participants and staff was not possible. The risk of detection bias in the RCTs was mostly rated as low because assessors were masked.^{15-19,29-33,36} One RCT³⁷ was assessed as having a high risk of detection bias because interviewers were not blinded. In addition, the non-RCTs and BAs were mostly rated as having a high risk of detection bias, because the chosen design complicated the possibility of blinding interviewers.^{22-24,35,39,40} The risk of attrition bias for most RCTs^{15-19,25-27,30-32,36,37} was rated as low (i.e. drop-out was low, intention-to-treat analyses were performed, missing data were not related to the outcome or significantly different between treatment arms). Three RCTs^{29,34,41} were assessed as having a high risk of attrition bias because of high drop-out rates or per protocol analyses. For the non-RCTs and BAs the assessments on attrition bias were mixed: five studies were rated as having a low risk,^{20-23,24,28,40} whereas three were rated as having a high risk of attrition bias.^{35,38,39} Risk of reporting bias was often unclear because trial registrations and/or study protocols were not available. Only Rovner et al. (2014)³⁰ and Rovner et al. (2013)³¹ provided sufficient information to assess a low risk of reporting bias (i.e. they performed their study as described in the study protocol). Risk of other types of bias was rated as high for all BAs for various reasons, mostly related to the chosen design (e.g. possible confounding).^{22-24,39,40} For the RCTs and non-RCTs these assessments were mixed. Fidelity to the treatment protocol was often not reported.

Table 2. Quality assessment based on the Cochrane Collaboration Risk of Bias Tool (low, high or unclear risk)

| Author (year, country) | Random sequence generation: Selection bias | Allocation concealment: Selection bias | Blinding of participants and professionals: Performance bias | Blinding of outcome assessment: Detection bias | Incomplete outcome data: Attrition bias | Selective reporting : Reporting bias | Other bias |
|---|---|---|---|--|--|--|---|
| 1. Randomised controlled trials: | | | | | | | |
| Rees et al. (2015, Australia) ³⁶ | Low: computer generated random allocation | Low: sealed envelopes | High: blinding impossible due to the nature of the intervention | Low: independent research assistants were masked | Low: intention-to-treat analysis, low drop-out (16%) | Unclear: trial was registered retrospectively, timing of reported outcomes does not match protocol | Unclear: no difference between responders and non-responders, adjusted for (few) baseline differences, only 17.9% of those eligible volunteered (possible selection bias), lack of objective fidelity checks. |
| Bryan et al. (2014, USA) ²⁹ | Low: random number generator | Unclear: not reported | High: blinding impossible due to the nature of the intervention | Low: outcomes obtained electronically directly from patients | High: high drop-out (57%), no sample size calculation, low power | Unclear: protocol not available | Unclear: no baseline imbalances, those who dropped-out were more depressed and stressed at baseline, no information on |

| | | | | | | | |
|--|--|--|---|--|--|---|--|
| Jalali et al. (2014, Iran) ²⁶ | Unclear: not reported | Unclear: not reported | High: blinding impossible due to the nature of the intervention | Unclear: outcomes obtained in groups, masking of interviewers not reported | Low: 100% of those enrolled completed the final outcome | Unclear: protocol not available | treatment fidelity is provided High: possible selection bias, baseline characteristics not reported, pre-test and follow-up not directly compared, no information on treatment fidelity |
| Rovner et al. (2014, USA) ³⁰ | Low: random numbers table | Low: sealed envelopes | High: blinding impossible due to the nature of the intervention | Low: research assistants were masked | Low: low drop-out (10%), high power | Low: trial registration and protocol available | Low: small baseline imbalances, no differences found between responders and non-responders, treatment fidelity maintained |
| Rovner et al. (2013, USA) ³¹ | Low: random number table with block design | Low: serially numbered, sealed envelopes | High: blinding impossible due to the nature of the intervention | Low: independent nurse was masked, only a small number of participants revealed allocation | Low: low drop-out (11%), enough power, intention-to-treat analysis | Low: protocol available, some outcomes not (yet) reported | Low: no baseline imbalances, treatment fidelity maintained |
| Sun et al. (2012, | Unclear: not | Unclear: not | High: blinding | Unclear: not | Low: 100% of | Unclear: | Unclear: no information on |

| | | | | | | | |
|--|---|-----------------------|---|--|---|--|---|
| China) ²⁷ | reported | reported | impossible due to the nature of the intervention | reported | those enrolled provided outcome data | protocol not available | baseline imbalances and treatment fidelity is provided |
| Girdler et al. (2010, USA) ³² | Low: computer generated random allocation | Unclear: not reported | High: blinding impossible due to the nature of the intervention | Low: assessor was masked, authors reported possible allocation disclosure | Low: intention-to-treat analysis, no drop-out | Unclear: no protocol available, only pilot study | Unclear: no baseline imbalances, however, probable selection bias and unclear if mixed-method analyses were used, treatment fidelity maintained |
| Rovner et al. (2007, 2008, USA) ^{15,16 †} | Low: fixed table, block design | Low: sealed envelopes | High: blinding impossible due to the nature of the intervention | Low: assessors were masked, 18% of participants revealed allocation, however, no difference in depression found indicating no significant bias | Low: low drop-out (8%), intention-to-treat analysis, sample size calculation not reported | Unclear: trial registration, however, 12 months follow-up not reported | Low: no baseline imbalances, treatment fidelity maintained |

| | | | | | | | |
|---|---|--|---|---|---|--|---|
| Goldstein et al. (2007, USA) ³⁷ | Low: randomized block design | Low: software assigned participants | High: blinding impossible due to the nature of the intervention | High: survey staff was not blinded | Low: enough power, low drop-out | Unclear: trial registration and protocol not available | Unclear: no baseline imbalances, however, drop-out analyses not performed and no information on treatment fidelity |
| Wahl et al. (2006, Germany) ³³ | High: unclear sequence generation, control group not randomised | Unclear: not reported | High: blinding impossible due to the nature of the intervention | Low: interviewers were masked | Unclear: no differences in responders and non-responders, however, low sample size, low power | Unclear: trial registration and protocol not available | Unclear: unclear when post-assessment took place, if baseline differences were statistically significant, and no information on treatment fidelity |
| Brody et al. (2002, 2005, 2006, USA) ¹⁷⁻¹⁹ † | Low: computer generated random allocation | Low: sequentially numbered, sealed envelopes | High: blinding impossible due to the nature of the intervention | Low: procedures to keep treatment allocation unknown to the interviewers (psychologists, researchers) | Low: no missing data, drop out only 15% and not related to treatment allocation (2002, 2005). | Unclear: trial registration and protocol not available | Unclear: no baseline imbalances, however, it is unclear if controls (taken together) crossed over to treatment before 6 month evaluation (2005 and 2006) and if treatment fidelity was maintained |

| | | | | | Subgroup analyses not enough power (2006) | | |
|--|---|---|--|------------------------------------|--|---|--|
| Bradley et al. (2005, UK) ²⁵ | Unclear: not reported | Unclear: not reported | High: blinding impossible due to the nature of the intervention | Unclear: not reported | Low: no drop- out | Unclear: trial registration and protocol not available | Unclear: no baseline imbalances, however, small sample size and treatment fidelity not reported |
| Brody et al. (1999, USA) ³⁴ | Unclear: insufficient information, not clear how randomization was performed | Unclear: insufficient information | High: blinding impossible due to the nature of the intervention | Unclear: assessor not reported. | High: per protocol analyses, intention-to- treat not reported, inadequate power with n=54 instead of n=102. | Unclear: some outcomes not reported | High: differences in follow up for intervention and control, baseline imbalance on vision, treatment fidelity unclear |
| Kaluza et al. (1996, Germany) ⁴¹ | Unclear: not reported | Unclear: not reported | High: blinding of participants | Unclear: not reported who | High: small sample size, low | Unclear: protocol not | High: baseline imbalances, possible contamination effect, |

impossible due to measures power, available treatment fidelity unclear
the nature of the psychological intention-to-
intervention strain treat analysis
unclear

2. Non-randomised controlled trials

| | | | | | | | |
|---|----|----|----|--|---|---------------------------------|--|
| Ueda et al. (2013, Japan) ³⁸ | NA | NA | NA | Unclear: unclear if assessors were blinded | High: small sample size, drop-out was not reported, per protocol analysis, no comparison of the original groups | Unclear: protocol not available | High: self-selected participants, groups matched on baseline characteristics, possible selection bias, treatment fidelity unclear |
| Birk et al. (2004, Germany) ³⁵ | NA | NA | NA | High: assessment performed by unmasked group trainer | High: small sample size, low power, high drop-out (36%), no intention-to-treat analysis | Unclear: protocol not available | Unclear: few baseline differences, however, analysis was on available cases rather than intention to treat, no specific information on treatment fidelity. |

| | | | | | | | |
|--|----|----|----|--|------------------|---------------------------------|---|
| Trozzolino et al. (2003, USA) ²⁸ | NA | NA | NA | Unclear: masking of investigator who obtained outcome not reported | Low: no drop-out | Unclear: protocol not available | Unclear: corrected for baseline differences on outcomes, however, treatment fidelity is unclear |
| Evans et al. (1981,1982, USA) ^{20,21} † | NA | NA | NA | Unclear: masking not reported | Low: no drop-out | Unclear: protocol not available | Low: the groups were well matched at baseline, treatment fidelity is partly discussed and maintained. |

3. Before and after comparisons

| | | | | | | | |
|--|----|----|----|---|---|---------------------------------|--|
| Barr et al. (2014, UK) ³⁹ | NA | NA | NA | High: therapists who offered intervention also assessed the outcome | High: high drop-out (45%) | Unclear: protocol not available | High: intervention varied strongly between participants (no specific model was used), possible selective reporting and confounding |
| Latham et al. (2013, UK) ⁴⁰ | NA | NA | NA | High: assessors knew participants followed the intervention. | Low: low drop-out, 25 of 29 starters provided data at | Unclear: protocol not available | High: Rasch analysis in small sample, possible confounding, different data collection methods used, treatment |

| | | | | | | | |
|--|----|----|----|---|--|---------------------------------|--|
| Alma et al. (2013, The Netherlands) ²⁴ | NA | NA | NA | High: assessors knew participants followed the intervention | 6 months. Low: low drop out, 26 of 29 starters finished the study | Unclear: protocol not available | fidelity unclear High: missing values imputed by average scores, only 6 (23%) participants attended all steps of the program, seasonal effects may have had an impact |
| Bernbaum et al. (1988, 1989, USA) ^{22,23} † | NA | NA | NA | High: research assistant were aware of treatment allocation | Low: low drop-out | Unclear: no protocol available | High: no baseline correction (1988), unclear why groups were not compared (insulin-dependent and independent, 1989), treatment fidelity unclear. |

† Articles were jointly reviewed, since they were based on the same study.

USA United States of America, UK United Kingdom

Meta-analysis

Random effect models were chosen because of high heterogeneity between the studies ($I^2 > 50\%$). Meta-regression was used to identify sources of heterogeneity in terms of study, intervention, control, and population characteristics.

Depression

A total of 16 trials (12 RCTs and 4 non-RCTs, of which two trials^{33,38} with two intervention arms that were included separately) assessed depressive symptoms. The forest plot demonstrated a small significant overall effect in reducing depressive symptoms in favour of the intervention group (SMD -0.30, 95% confidence interval (CI) -0.60 to -0.01, Figure 2A). The funnel plot showed one outlier,²⁶ indicating possible publication bias (Figure 2B). Meta-regression analysis showed that the mean age of participants partially explained heterogeneity across outcomes ($b=0.03$, 95% CI 0.01 to 0.05). Higher age of participants indicated less effective results (Figure 2C).

Anxiety

Five trials (4 RCTs and 1 non-RCT, of which one trial³⁸ with two intervention arms that were included separately) assessed anxiety symptoms. The forest plot demonstrated a medium overall effect in favour of the intervention group, however, this was not statistically significant (SMD -0.77, 95% CI -1.62 to 0.08, Figure 3A). The funnel plot indicated possible publication bias (Figure 3B). Meta-regression showed homogeneity in the effect size across the range of study, population and intervention characteristics that were investigated.

Psychological stress

Four studies (3 RCTs and 1 non-RCT) assessed psychological stress. A large overall effect size was found in favour of the intervention group, however, this was non-significant (SMD -1.26, 95% CI -2.78 to 0.25, Figure 4A). Meta-regression showed that the mean age of participants partially explained heterogeneity across outcomes ($b=0.07$, 95% CI 0.01 to 0.13).

Higher age of participants indicated less effective results (Figure 4B). An insufficient number of studies on this outcome were performed to produce a funnel plot.

Psychological well-being

A total of 10 RCTs investigated the effect of interventions on psychological well-being; of these, two RCTs were excluded from the analyses because of lack of information on the outcomes.^{25,37} A non-significant overall effect in favour of the intervention group was found (SMD 0.30, 95% CI -0.03 to 0.63, Figure 5A) and the funnel plot indicated possible publication bias (Figure 5B). Again, the meta-regression analyses showed that the mean age of participants helped partially explain heterogeneity across outcomes ($b=-0.03$, 95% CI -0.05 to -0.01), indicating that a higher age of participants resulted in less effective results (Figure 5C).

Fatigue

In two studies (1 RCT and 1 non-RCT³⁹ with two intervention arms that were included separately) mental fatigue was assessed. A non-significant overall effect was found (SMD -0.30, 95% CI -1.01 to 0.40, Figure 6), and not enough studies were found to produce a funnel plot. Meta-regression analyses showed homogeneity in the effect size across the range of study, population and intervention characteristics that were investigated.

Loneliness

Since loneliness was investigated in only one study,^{19,20} no meta-analysis was performed on this outcome measure. Outcomes of this study showed a large significant effect in favour of the intervention group (SMD -1.36, 95% CI -1.83 to -0.88).

Sensitivity analysis

A clear outlier²⁶ was found for the effects of interventions on depressive symptoms, anxiety symptoms, and psychological stress causing funnel plot asymmetry (see Figure 2B and 3B).

This outlier had a high effect size compared to the other studies and a high standard error based on a small study population ($n=60$). Therefore, the effect sizes on depressive symptoms, anxiety symptoms and psychological stress were determined without this clear outlier. After removal, the overall effects on depressive symptoms (SMD -0.15, 95% CI -0.31 to 0.02), anxiety symptoms (SMD -0.35, 95% CI -1.01 to 0.30) and psychological stress (SMD -0.16, 95% CI -0.46 to 0.15) decreased and the effect on depressive symptoms was no longer significant. In addition, the mean age of participants no longer significantly explained heterogeneity in the outcomes on depressive symptoms ($b=0.00$, 95% CI -0.01 to 0.01), and psychological stress ($b=0.01$, 95% CI -0.01 to 0.03).

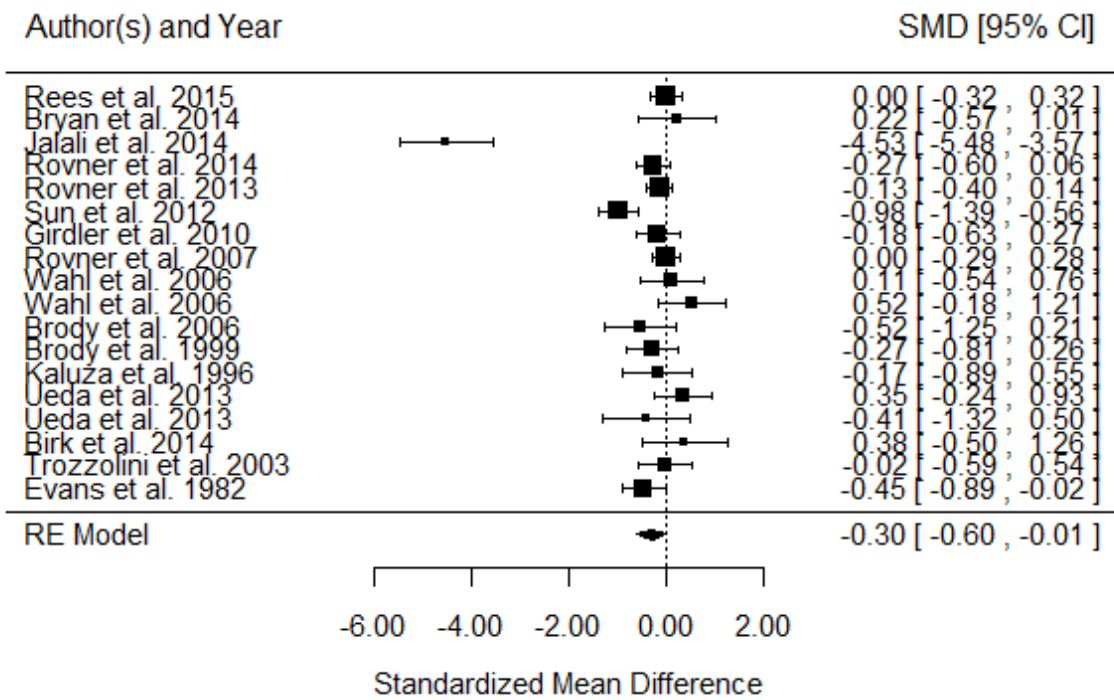


Figure 2A. Forest plot of the effects of interventions on depressive symptoms (n=18). In Wahl et al. (2006) and Ueda et al. (2013) two different intervention arms were compared with one control condition.

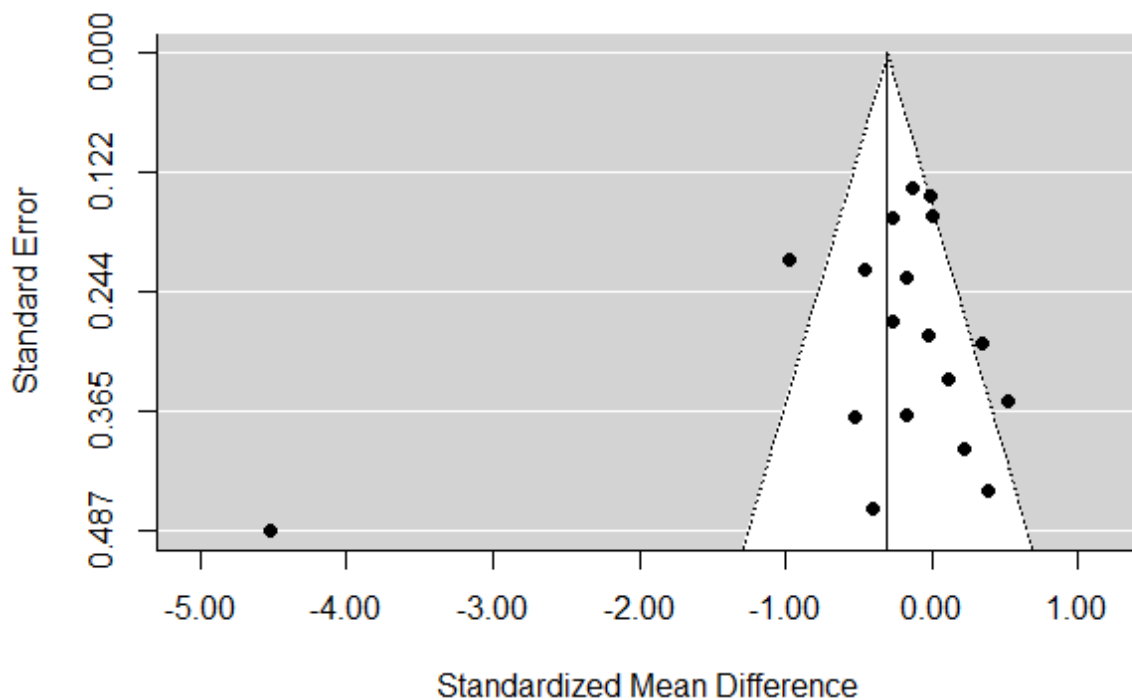


Figure 2B. Funnel plot of the effects of interventions on depressive symptoms (n=18)

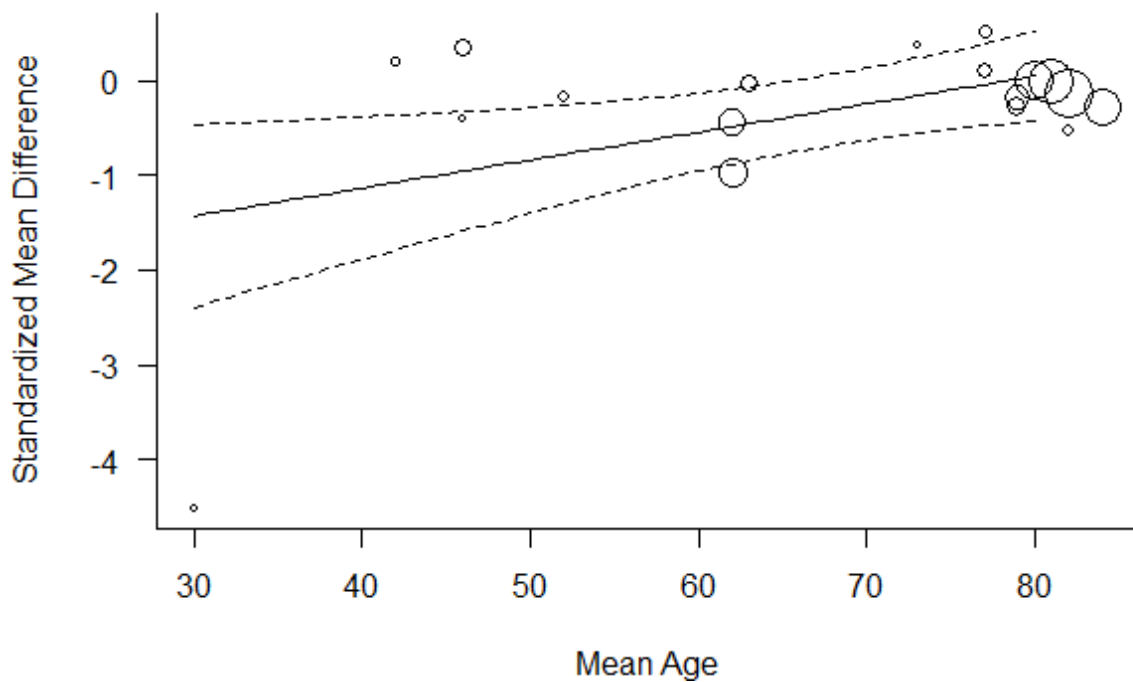


Figure 2C. Bubble plot of the effects of interventions on depressive symptoms versus mean age in years (n=18)

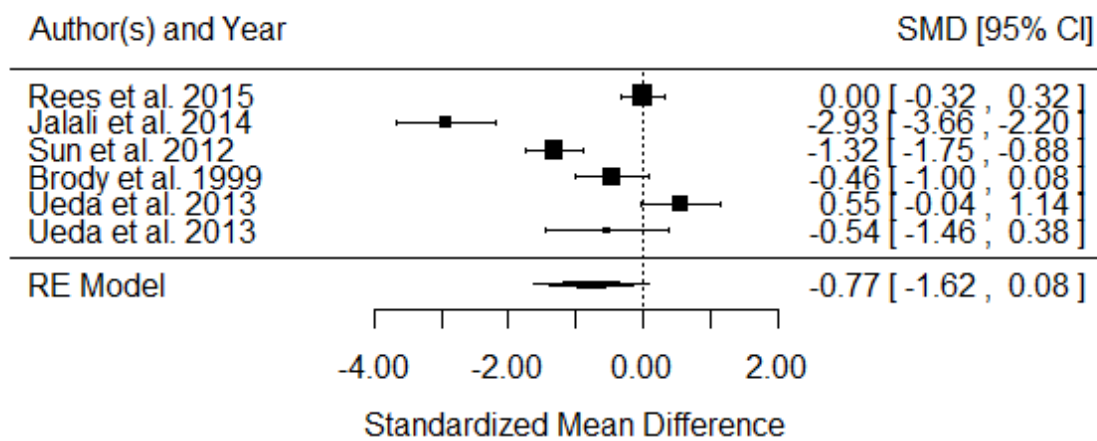


Figure 3A. Forest plot of the effects of interventions on anxiety symptoms (n=6). In Ueda et al. (2013) two different intervention arms were compared with one control condition.

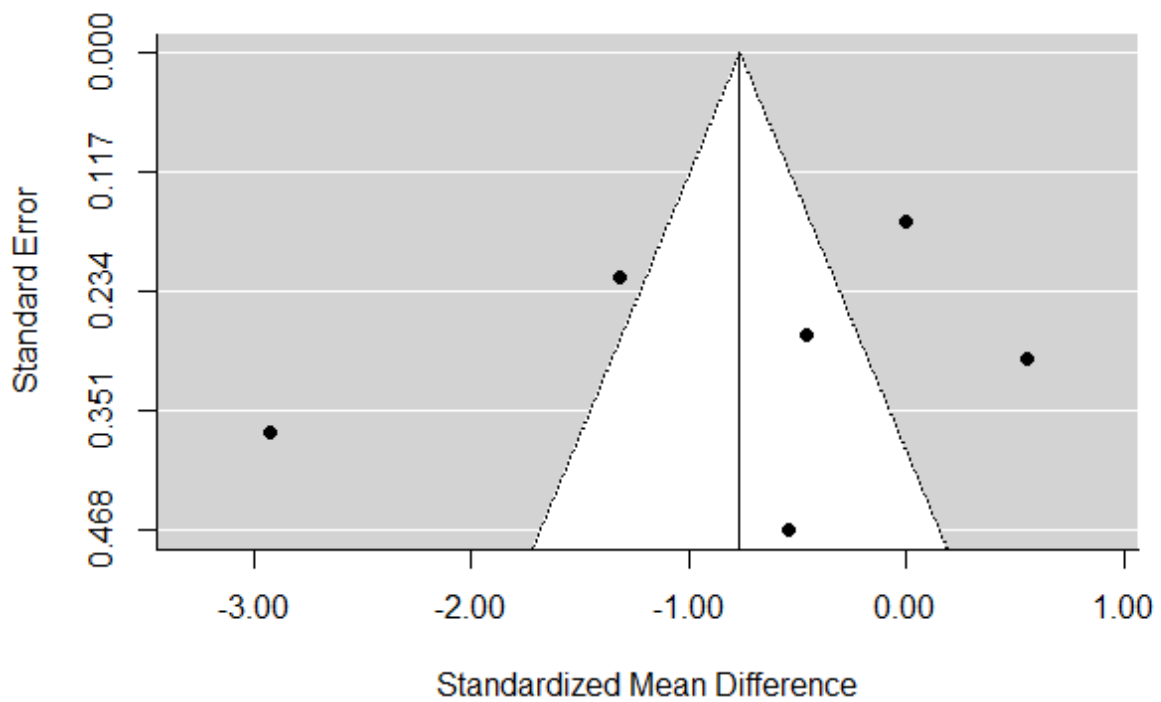


Figure 3B. Funnel plot of the effects of interventions on anxiety symptoms (n=6)

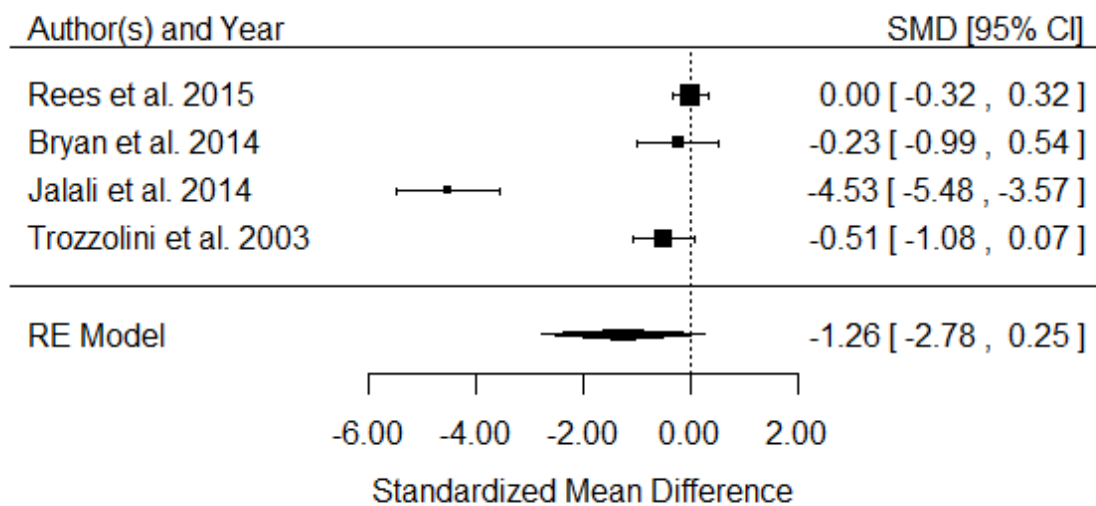


Figure 4A. Forest plot of the effects of interventions on psychological stress (n=4)

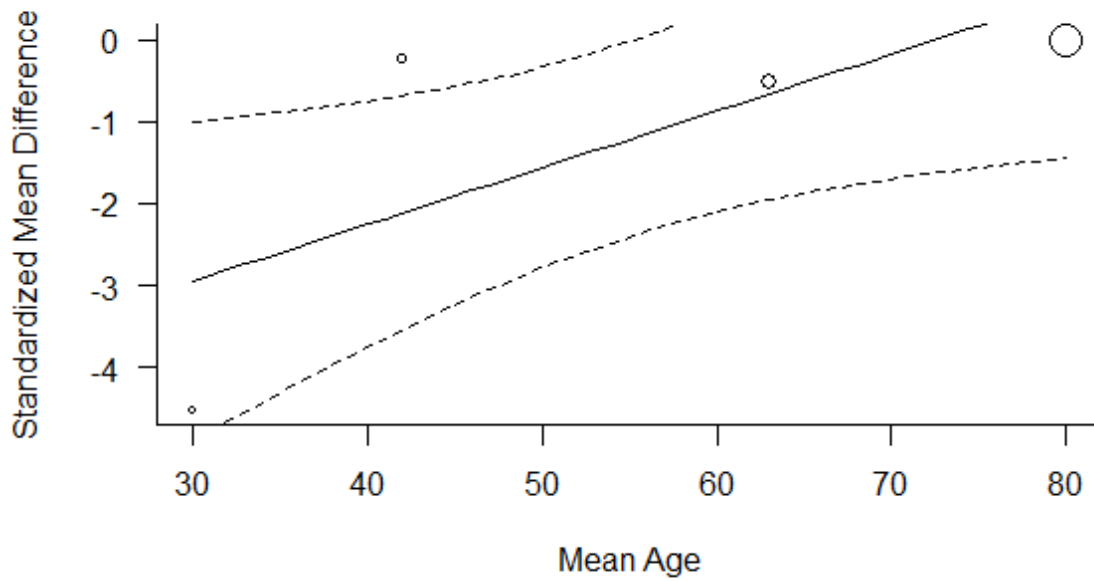


Figure 4B. Bubble plot of the effects of interventions on psychological stress versus mean age in years (n=4)

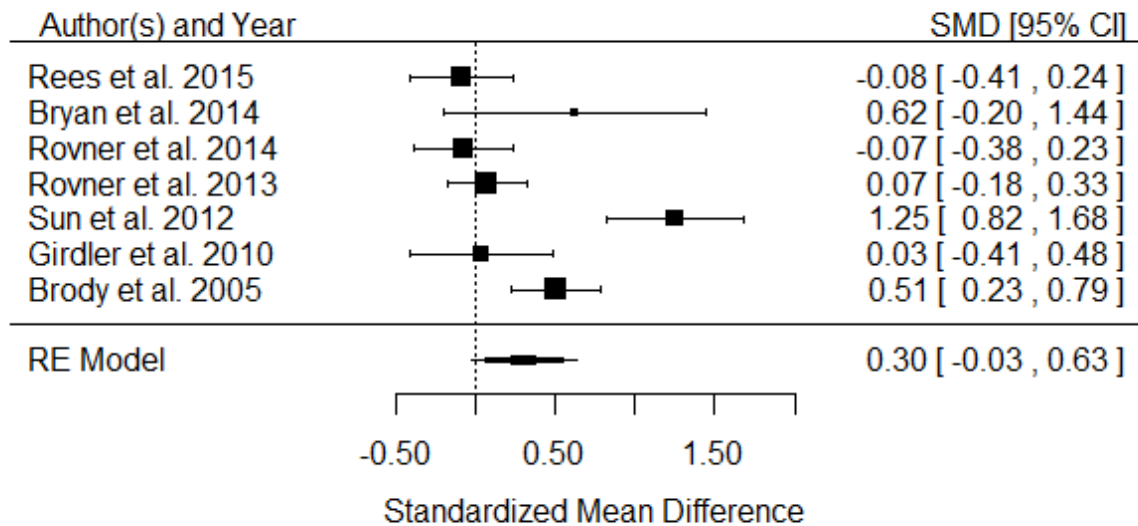


Figure 5A. Forest plot of the effects of interventions on psychological well-being (n=7)

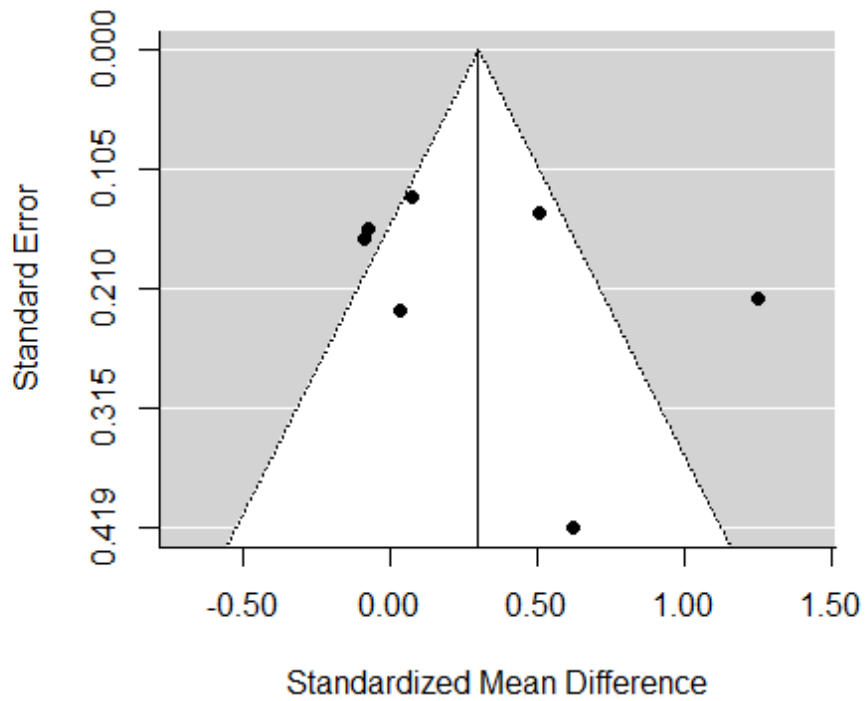


Figure 5B. Funnel plot of the effects of interventions on psychological well-being (n=7)

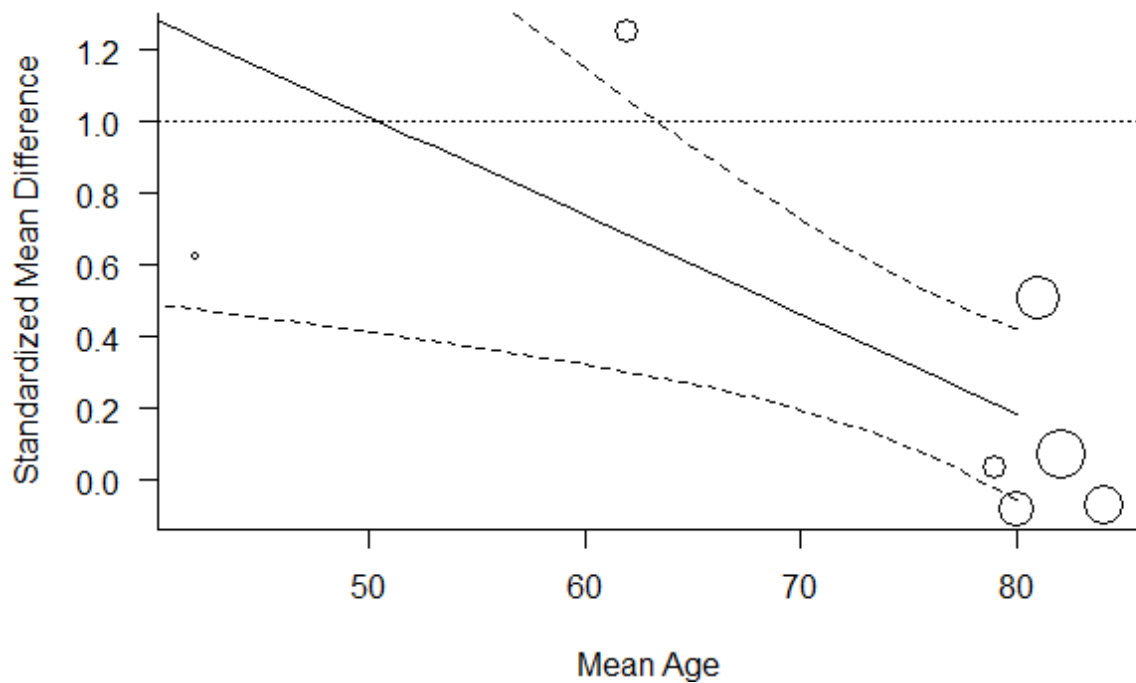


Figure 5C. Bubble plot of the effects of interventions on psychological well-being versus mean age in years (n=7)

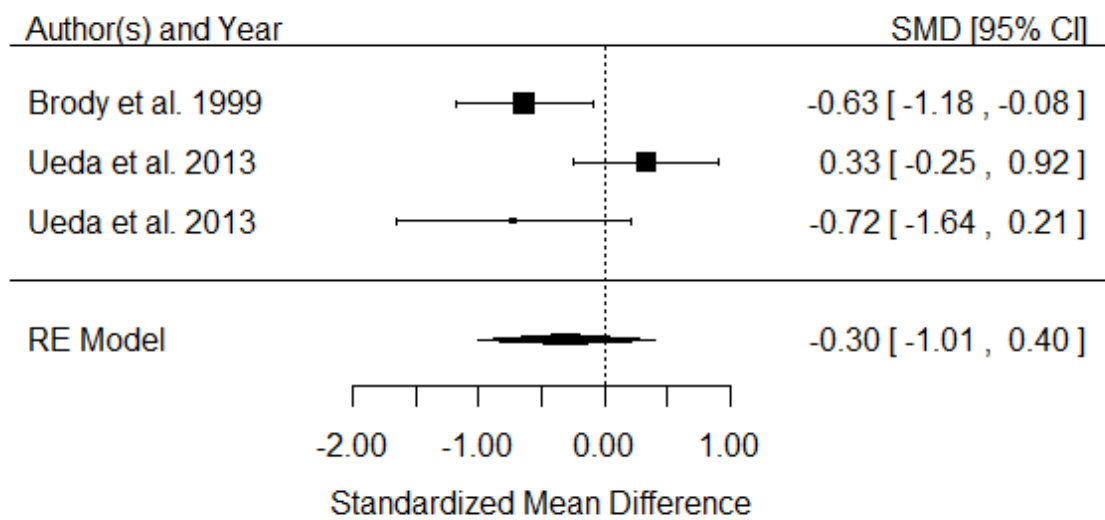


Figure 6. Forest plot of the effects of interventions on mental fatigue (n=3). In Ueda et al. (2013) two different intervention arms were compared with one control condition.

DISCUSSION

To the best of our knowledge, this review is the first to systematically assess the effectiveness of all psychosocial interventions aimed at improving mental health in people with visual impairment. It shows a growing recognition of the need to address various psychological consequences of vision impairment. The number of studies conducted in recent years has increased, i.e. 18 out of 22 studies were conducted in the last decade.

Of the 22 studies that were found, most were aimed at investigating the effects of interventions on depressive symptoms (n=16) and the psychological well-being of patients (n=10). Only a few trials investigated the effects on anxiety symptoms (n=5), psychological stress (n=4), mental fatigue (n=2) and loneliness (n=1). In comparison with a control condition, no significant overall effects on anxiety symptoms, psychological stress, mental fatigue and psychological well-being were found. Interventions only appeared to have a small significant effect on depressive symptoms (SMD -0.30, 95% CI -0.60 to -0.01), however, after removing a clear outlier²⁶ this effect was also no longer significant. The outlier had a high risk of bias, a relatively short follow-up period (1 month), and a low age of participants (20 to 40 years), which may have caused the aberrant result.

Based on the meta-regression analyses, we found no significant sources of heterogeneity across a range of study, intervention, control, and population characteristics, such as sample size, drop-out rates, study design (RCT vs. non-RCT), or interventions designed for people with a specific eye condition compared to people with visual impairment in general (different causes). In contrast to what we may have expected, interventions that were offered within the setting of low vision rehabilitation care (which may increase accessibility for those with visual impairment) were not more effective than interventions offered in other settings (e.g. hospital/clinical setting). In addition, we found no significant difference in group-based and individually offered interventions. Only the mean age of

participants partially explained heterogeneity in outcomes on depressive symptoms, psychological stress, and psychological well-being. Higher age of participants indicated slightly less effective results. However, after removing the previously mentioned outlier,²⁶ the mean age of participants no longer significantly explained heterogeneity in the outcomes on depressive symptoms and psychological stress, but the influence of age on psychological well-being remained. Mental health problems in older adults differ from those earlier in the lifespan, considering presentation of the symptoms, etiology, risk and protective factors.⁶³ Tailoring interventions based on these differences may be essential for effective treatment of mental health problems in older adults with visual impairment.

A limited number of good-quality studies was found. In several RCTs randomisation methods were not reported adequately. In addition, design choices (i.e. performing non-RCTs and BAs) often complicated possibilities for blinding assessors and induced risks of selection bias and confounding. Reporting bias was often unclear (in 20 out of 22 studies) because study protocols were missing and fidelity to the treatment protocol was often not reported. In addition, sample sizes were often low and follow-up periods short. Future studies should aim to improve the standard on research on psychosocial interventions in the field of low vision by performing and adequately reporting on high quality trials.

Strengths and limitations

In contrast to previous systematic reviews,⁹⁻¹¹ all types of psychosocial interventions, offered in different settings, aimed at increasing mental health in people with visual impairment were included, and meta-regression analyses were performed to identify sources of heterogeneity between the studies. A large number of studies were found (i.e. 22) and current state-of-the-art meta-analytic techniques were used.

However, we also recognise a number of limitations. Due to the small number of high quality studies and possible publication bias (based on asymmetry in the funnel plots) it is not possible to draw solid conclusions regarding the benefits of psychosocial interventions on mental health in people with visual impairment. This is in line with the systematic review of Holloway et al. (2015)¹¹ in which 6 out of 8 trials were also included in the current review^{15-19, 31,32,34} (two were not specifically aimed at improving mental health). Their conclusions on the effects of problem solving interventions on mental health in people with visual impairment were also limited due to the small number of good quality trials. In addition, a variety of psychosocial intervention types (e.g. self-management programmes, behavioural activation, PST) and a lack of homogenous outcome measures complicate the interpretation of the results. Furthermore, we did not include outcomes on post-traumatic-stress, suicidal ideation or alcohol misuse, and did not perform searches in other databases (such as the Cochrane Library) which may have caused us to overlook some studies. Finally, most questionnaires that were used in the studies were not validated in a visually impaired sample.

Implications for practice and future research

There is currently only limited evidence for the effectiveness of psychosocial interventions in the field of low vision. Few high quality studies, lack of homogeneity in intervention types, study populations and outcome measures, and possible publication bias limit conclusions that can be drawn. The synthesis of available evidence support the need for well-designed high quality studies, i.e. choosing an RCT design, which is properly powered, using proper randomisation methods, with blinded outcome assessment, based on trial registration and published study protocols, with longer follow-up measurements to investigate maintenance effects of interventions. The cost-effectiveness of interventions is currently completely lacking and should also be addressed. In addition, although anxiety symptoms, stress, mental

fatigue and loneliness are prevalent in people with visual impairment,^{1,2,4,7,8} only a few studies have assessed these outcomes. Therefore, more studies on interventions that address these problems are warranted. Finally, interventions seem to be less effective on increasing psychological well-being in the elderly, indicating that more attention may be needed for this age group in future research.

REFERENCES

1. Mojon-Azzi SM, Sousa-Poza A & Mojon DS. Impact of low vision on well-being in 10 European countries. *Ophthalmologica* 2008;222:205-12.
2. Kempen GI, Ballemans J, Ranchor AV, van Rens GH & Zijlstra GA. The impact of low vision on activities of daily living, symptoms of depression, feelings of anxiety and social support in community-living older adults seeking vision rehabilitation services. *Qual Life Res* 2012;21:1405-11.
3. van der Aa HP, Xie J, Rees G, Fenwick E, Holloway EE, van Rens GH & van Nispen RM. Validated prediction model of depression in visually impaired older adults. *Ophthalmology* [Epub ahead of print]: 8 Jan 2016, DOI: 10.1016/j.ophtha.2015.11.028.
4. van der Aa HPA, HC Comijs, BWJH Penninx, GHMB van Rens & RMA van Nispen. Major depressive and anxiety disorders in visually impaired er adults. *Invest Opth Vis Sci* 2015;56:849–54.
5. Brody BL, Gamst AC, Williams RA, et al. Depression, visual acuity, comorbidity, and disability associated with age-related macular degeneration. *Ophthalmology* 2001;108:1893-1900.
6. Horowitz A, Reinhardt JP, Kennedy GJ. Major and subthreshold depression among older adults seeking vision rehabilitation services. *Am J Geriatr Psychiatry* 2005;13:180-7.
7. Chia EM, Wang JJ, Rochtchina E, Smith W, Cumming RR, Mitchell P. Impact of bilateral visual impairment on health-related quality of life: the Blue Mountains Eye Study. *Investigative ophthalmology & visual science* 2004;45(1):71-6.
8. Fenwick E, Rees G, Pesudovs K, et al. Social and emotional impact of diabetic retinopathy: a review. *Clin Experiment Ophthalmol* 2012;40:27-38.

9. Rees G, Ponczek E, Hassell J, Keeffe JE & Lamoureux EL. Psychological outcomes following interventions for people with low vision: a systematic review. *Expert Review of Ophthalmology* 2010;5: 385-403.
10. Binns AM, Bunce C, Dickinson C, et al. How Effective is Low Vision Service Provision? A Systematic Review. *Survey of Ophthalmology* 2012;51:34-65.
11. Holloway EE, Xie J, Sturrock BA, Lamoureux EL & Rees G. Do problem-solving interventions improve psychosocial outcomes in vision impaired adults: A systematic review and meta-analysis. *Patient Education and Counseling* 2015;98:553-64.
12. Cuijpers P. Psychotherapies for adult depression: recent developments. *Curr Opin Psychiatry* 2015; 28: 24-9.
13. Higgins JPT, Altman DG, Gotzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ* 2011;343:d5928.
14. Cohen J. Statistical power analysis for the behavioral sciences (2nd ed.). Lawrence Erlbaum Associates, Inc., Hillsdale, NJ, 1988.
15. Rovner BW, Casten RJ, Hegel MT, Leiby BE & Tasman WS. Preventing depression in age-related macular degeneration. *Archives of general psychiatry* 2007;64:886-92.
16. Rovner BW & Casten RJ. Preventing Late-life Depression in Age-Related Macular Degeneration. *Am J Geriatr Psychiatry* 2008;16:454-9.
17. Brody BL, Roch-Levecq AC, Gamst AC, Maclean K, Kaplan RM & Brown SI. Self-management of age-related macular degeneration and quality of life: a randomized controlled trial. *Arch Ophthalmol* 2002;120:1477-83.
18. Brody BL, Roch-Levecq AC, Thomas RG, Kaplan RM & Brown SI. Self-management of Age-related Macular Degeneration at the 6-Month Follow-up A Randomized Controlled Trial. *Arch Ophthalmol* 2005;123:46-53.

19. Brody BL, Roch-Levecq AC, Kaplan RM, Moutier CY & Brown SI. Age-Related Macular Degeneration: Self-Management and Reduction of Depressive Symptoms in a Randomized, Controlled Study. *JAGS* 2006;54:1557-62.
20. Evans RL & Jaureguy BM. Group therapy by phone: a cognitive behavioral program for visually impaired elderly. *Social work in Health Care* 1981;7:79-90.
21. Evans RL, Werkhoven W & Fox HR. Treatment of social isolation and loneliness in a sample of visually impaired elderly persons. *Psychological Reports* 1982;51:103-8.
22. Bernbaum M, Albert SG, & Duckro PN. Psychosocial profiles in patients with visual impairment due to diabetic retinopathy. *Diabetes Care* 1988;11:551-7.
23. Bernbaum M, Albert SG, Brusca SR et al. A model clinical program for patients with diabetes and vision impairment. *The Diabetes Educator* 1989;15:325-30.
24. Alma MA, Groothoff JW, Melis-Dankers BJM, Suurmeijer TPBM & van der Mei SF. The effectiveness of a multidisciplinary group rehabilitation program on the psychosocial functioning of elderly people who are visually impaired. *Journal of Visual Impairment & Blindness* 2013;5-16.
25. Bradley P, Mitchell J & Bradley C. Peer support for people newly diagnosed with macular degeneration: A pilot study. *International Congress Series* 2005;1282:211-5.
26. Jalali MDM, Moussavi MS, Yazdi SAA & Fadardi JS. Effectiveness of rational emotive behavior therapy on psychological well-being of people with late blindness. *J Rat-Emo Cognitive-Behav Ther* 2014;32:233-47.
27. Sun W, Wu F, Kong J, et al. Analysis on the psychological factors of glaucoma and the influence of the psychological therapy after the education on the glaucoma club. *Int Eye Sci* 2012;12:1619-22.

28. Trozzolino L, Thompson PS, Tansman MS & Azen SP. Effects of a psychoeducational group on mood and glycemic control in adults with diabetes and visual impairments. *JVIB* 2003;230-9.
29. Bryan JL & Lu Q. Vision for improvement: Expressive writing as an intervention for people with Stargardt's disease, a rare eye disease. *J Health Psychol* [Epub ahead of print, Jun 16 2014], DOI: 10.1177/1359105314536453.
30. Rovner BW, Casten RJ, Hegel MT, et al. Low vision depression prevention trial in age-related macular degeneration: a randomized clinical trial. *Ophthalmology* 2014;121:2204-11.
31. Rovner BW, Casten RJ, Hegel MT, et al. Improving function in age related macular degeneration- a randomized controlled trial. *American Academy of Ophthalmology* 2013;120(8):1649-55.
32. Girdler SJ, Boldy DP, Dhaliwal SS, Crowley M & Packer TL. Vision self-management for older adults: a randomised controlled trial. *The British journal of ophthalmology* 2010;94:223-8.
33. Wahl H, Kammerer A, Holz F, et al. Psychosocial intervention for age-related macular degeneration: a pilot project. *Journal of Visual Impairment & Blindness* 2006:533-43.
34. Brody BL, Williams RA, Thomas RG, Kaplan RM, Chu RM & Brown SI. Age-related macular degeneration: a randomized clinical trial of a self-management intervention. *Ann Behav Med* 1999;21:322-9.
35. Birk T, Hickl S, Wahl HW, et al. A psychosocial training program for elderly patients with age-related macular degeneration: findings of a pilot evaluation study. *Z Gerontol Geriatr* 2004;37:363-5.
36. Rees G, Xie J, Chiang PP, et al. A randomised controlled trial of a self-management programme for low vision implemented in low vision rehabilitation services. *Patient Education and Counseling* 2015;98:174-81.

37. Goldstein RB, Dugan E, Trachtenberg F & Peli E. The impact of a video intervention on the use of low vision assistive devices. *Optom Vis Sci* 2007;84:208-17.
38. Ueda Y & Tsuda A. Differential outcomes of skill training, group counseling, and individual cognitive therapy for persons with acquired visual impairment. *Japanese Psychological Research* 2013;55:229-40.
39. Barr W, Hodge S, Leeven M, Bowen L & Knox P. Emotional support and counselling for people with visual impairment: Quantitative findings from a mixed methods pilot study. *Counselling and Psychotherapy Research* 2012;12:294-302.
40. Latham K. Evaluation of an emotional support service for the visually impaired. *Optometry and Vision Science* 2013;90:836-42.
41. Kaluza G, Stempel I & Maurer H. Stress reactivity of intraocular pressure after relaxation training in open-angle glaucoma patients. *Journal of Behavioral Medicine* 1996;19:587-98.
42. Curran SL, Andrykowski MA, Studts JL. Short Form of the Profile of Mood States (POMS-SF): Psychometric information. *Psychological Assessment* 1995;7(1):80-83.
43. Kim HJ, Abraham I. Psychometric comparison of single-item, short, and comprehensive depression screening measures in Korean young adults. *Int J Nurs Stud* 2016;56:71-80.
44. Crawford JR, Henry JD. The Depression Anxiety Stress Scales (DASS): normative data and latent structure in a large non-clinical sample. *Br J Clin Psychol* 2003;42:111-31.
45. Smarr KL, Keefer AL. Measures of depression and depressive symptoms: Beck Depression Inventory-II (BDI-II), Center for Epidemiologic Studies Depression Scale (CES-D), Geriatric Depression Scale (GDS), Hospital Anxiety and Depression Scale (HADS), and Patient Health Questionnaire-9 (PHQ-9). *Arthritis Care Res (Hoboken)* 2011;63:S454-66.
46. Choi SW, Schalet B, Cook KF, Cella D. Establishing a common metric for

depressive symptoms: Linking the BDI-II, CES-D, and PHQ-9 to PROMIS Depression.

Psychological Assessment. 2014;26:513-27.

47. Beekman AT, Deeg DJ, van Limbeek J, et al. Criterion validity of the Centre for Epidemiologic Studies Depression scale (CES-D): results from a community-based sample of older subjects in The Netherlands. *Psychol Med*. 1997;27:231-5.

48. Kroenke K, Spitzer RL, Williams JB. The PHQ-9. *J Gen Intern Med*. 2001;16:606-13.

49. Lamoureux EL, Tee HW, Pesudovs K, et al. Can clinicians use the PHQ-9 to assess depression in people with low vision. *Optom Vis Sci*. 2009;86:139-145.

50. Williams JB. Standardizing the Hamilton Depression Rating Scale: past, present, and future. *Eur Arch Psychiatry Clin Neurosci* 2001;251:II6-12.

51. Zung WW, Richards CB, Short MJ. Self-rating depression scale in an outpatient clinic. Further validation of the SDS. *Arch Gen Psychiatry* 1965;13(6):508-15.

52. Snaith RP, Ahmed SN, Mehta S, Hamilton M. Assessment of the severity of primary depressive illness. Wakefield self-assessment depression inventory. *Psychol Med* 1971;1(2):143-9.

53. Russell D, Peplau LA, Cutrona CE. The revised UCLA Loneliness Scale: concurrent and discriminant validity evidence. *J Pers Soc Psycho* 1980;39(3):472-80.

54. Lee EH. Review of the psychometric evidence of the perceived stress scale. *Asian Nurs Res (Korean Soc Nurs Sci)* 2012;6(4):121-7.

55. Lee EH, Lee YW, Lee KW, Kim YS, Nam MS. Measurement of diabetes-related emotional distress using the Problem Areas in Diabetes scale: psychometric evaluations show that the short form is better than the full form. *Health Qual Life Outcomes* 2014;12:142.

56. Stelmack JA, Stelmack TR, Massof RW. Measuring low-vision rehabilitation outcomes with the NEI VFQ-25. *Invest Ophthalmol Vis Sci* 2002;43(9):2859-68.

57. Lamoureux EL, Pallant JF, Pesudovs K, Rees G, Hassell JB, Keeffe JE. The impact of vision impairment questionnaire: an assessment of its domain structure using confirmatory factor analysis and rasch analysis. *Invest Ophthalmol Vis Sci* 2007;48(3):1001-6.
58. Lamoureux EL, Pesudovs K, Pallant JF, et al. An evaluation of the 10-item vision core measure 1 (VCM1) scale (the CoreModule of the Vision-Related Quality of Life scale) using Rasch analysis. *Ophthalmic Epidemiol* 2008;15:224Y33.
59. Ware J, Kosinski M. SF-36 Health Survey: physical & mental health summary scales: a manual for users of Version 1. Lincoln (RI): QualityMetric Inc, 2001.
60. Mitchell J, Bradley C. Psychometric evaluation of the 12-item Well-being Questionnaire for use with people with macular disease. *Qual Life Res* 2001;10:465-473.
6. Connell J, Barkham M, Stiles, et al. Distribution of CORE-OMscores in a general population, clinical cut-off points and comparison with the CIS-R. *British Journal of Psychiatry* 2007;190:74.
62. Cuijpers P, van Straten A & Warmerdam L. Are individual and group treatments equally effective in the treatment of depression in adults? A meta-analysis. *Eur J Psychiat* 2008;22:1.
63. Zarit SH, Zarit JM. *Mental Disorders in Older Adults, Second Edition: Fundamentals of Assessment and Treatment*. New York, USA: The Guilford Press; 2011.

APPENDIX 1: Full search strategy for MEDLINE including limits

Visual impairment

("Visually Impaired Persons"[Mesh] OR "Vision Disorders"[Mesh] OR "Eye Diseases"[Mesh:NoExp] OR "Asthenopia"[Mesh] OR "Corneal Diseases"[Mesh] OR "Eye Diseases, Hereditary"[Mesh] OR "Eye Hemorrhage"[Mesh] OR "Eye Infections"[Mesh] OR "Cataract"[Mesh] OR "Ocular Hypertension"[Mesh] OR "Optic Nerve Diseases"[Mesh] OR "Retinal Diseases"[Mesh] OR ((vision disorder*[tiab] OR "visually impaired"[tiab] OR "visual impairment"[tiab] OR "low vision"[tiab] OR "visually disabled"[tiab] OR "reduced vision"[tiab] OR "subnormal vision"[tiab] OR blindness[tiab] OR "double vision"[tiab] OR diplopia*[tiab] OR "Hemianopsia"[tiab] OR "visual loss"[tiab] OR cataract[tiab] OR glaucoma[tiab] OR "macular degeneration"[tiab] OR retinopathy[tiab]) NOT medline[sb]))

Mental health

"Behavioral Symptoms"[Mesh:NoExp] OR "Depression"[Mesh] OR "Mental Fatigue"[Mesh] OR "Stress, Psychological"[Mesh] OR "Emotions"[Mesh] OR "Anxiety Disorders"[Mesh] OR "Mood Disorders"[Mesh] OR "Quality of Life"[Mesh] OR "Social Isolation"[Mesh] OR depress*[tiab] OR melancholia[tiab] OR dysthymi*[tiab] OR fatigue[tiab] OR tired*[tiab] OR burnout[tiab] OR stress[tiab] OR stressed[tiab] OR anxiety[tiab] OR fear[tiab] OR panic[tiab] OR nervous*[tiab] OR loneliness[tiab] OR lonely[tiab] OR lonesome[tiab] OR desolate[tiab] OR isolation[tiab] OR wellbeing[tiab] OR "psychological health"[tiab] OR trait[tiab] OR traits[tiab]

Treatment

"Rehabilitation"[Mesh] OR "Intervention Studies"[Mesh] OR "Psychotherapy"[Mesh] OR "Psychiatric Somatic Therapies"[Mesh] OR "prevention and control" [Subheading] OR "Self-Help Groups"[Mesh] OR "Self Care"[Mesh] OR "Antidepressive Agents"[Mesh] OR "Psychiatric Status Rating Scales"[Mesh] OR rehabilitation[tiab] OR "self-help"[tiab] OR "self help"[tiab] OR "self-management"[tiab] OR "self management"[tiab] OR "watchful waiting"[tiab] OR "problem solving treatment"[tiab] OR "problem solving therapy"[tiab] OR PST[tiab] OR CBT[tiab] OR "stepped-care"[tiab] OR (("cognitive behavioral"[tiab] OR "cognitive behavioural"[tiab] OR Psychotherapy[tiab] OR intervention[tiab] OR interventions[tiab] OR training[tiab]) NOT medline[sb])

Adults only

NOT (("Adolescent"[Mesh] OR "Child"[Mesh] OR "Infant"[Mesh] OR adolescen*[tiab] OR child*[tiab]

OR schoolchild*[tiab] OR infant*[tiab] OR girl*[tiab] OR boy*[tiab] OR teen[tiab] OR teens[tiab] OR teenager*[tiab] OR youth*[tiab] OR pediater*[tiab] OR paediatr*[tiab] OR puber*[tiab]) NOT ("Adult"[Mesh] OR adult*[tiab] OR man[tiab] OR men[tiab] OR woman[tiab] OR women[tiab] OR aged[tiab] OR elderly[tiab] OR senior[tiab] OR "er people"[tiab] OR "er adult"[tiab] OR "er adults"[tiab] OR geriatr*[tiab]))

Publication types filter:

NOT ("addresses"[Publication Type] OR "biography"[Publication Type] OR "comment"[Publication Type] OR "directory"[Publication Type] OR "editorial"[Publication Type] OR "festschrift"[Publication Type] OR "interview"[Publication Type] OR "lectures"[Publication Type] OR "legal cases"[Publication Type] OR "legislation"[Publication Type] OR "letter"[Publication Type] OR "news"[Publication Type] OR "newspaper article"[Publication Type] OR "patient education handout"[Publication Type] OR "popular works"[Publication Type] OR "congresses"[Publication Type] OR "consensus development conference"[Publication Type] OR "consensus development conference, nih"[Publication Type])

Limited to humans

NOT (animals[mh] NOT humans[mh])

APPENDIX 2: Cochrane Collaboration Risk of Bias Tool

| |
|--|
| <p>1. Random sequence generation (selection bias)*</p> <p><i>Low risk:</i> computer random number generator, random number table or other methods were used to randomise participants. <i>High risk:</i> quasi-random methods were used.</p> |
| <p>2. Allocation concealment (selection bias)*</p> <p><i>Low risk:</i> sequence of allocation was concealed, for example by using central allocation and sealed envelopes. <i>High risk:</i> sequence of allocation was known, for example by staff.</p> |
| <p>3. Blinding of participants and personnel (performance bias)*</p> <p><i>Low risk:</i> participants and staff were masked and it was unlikely that masking could have been broken. Or there was no masking or incomplete masking, but it would be unlikely that the outcomes were influenced. <i>High risk:</i> one or both criteria were not met.</p> |
| <p>4. Blinding of outcome assessment (detection bias)</p> <p><i>Low risk:</i> assessors were masked (e.g. participants were asked not to reveal their allocation). Or assessors were not masked (for example in non-RCTs), but the outcome was unlikely to be influenced. <i>High risk:</i> one or both criteria were not met.</p> |
| <p>5. Incomplete outcome data addressed (attrition bias)</p> <p><i>Low risk:</i> no or limited missing data, follow-up rates and compliance were similar in groups, reasons for missing data were not related to the outcome and intention-to-treat analysis was performed. <i>High risk:</i> imbalances in numbers or reasons for missings between groups, probable that missing data would change the outcome, or per-protocol analyses were performed.</p> |
| <p>6. Selective outcome reporting (reporting bias)</p> <p><i>Low risk:</i> trial registration or study protocol was available and all pre-specified outcomes (of interest to this review) were reported. <i>High risk:</i> pre-specified outcomes were not or incompletely reported.</p> |
| <p>7. Other bias</p> <p><i>Low risk:</i> the study appeared to be free of other sources of risk. <i>High risk:</i> issues specific to study design, such as cross-over designs or cluster randomization, or considerable baseline imbalances on the outcomes or important participant characteristics, or lack of fidelity to the treatment protocol</p> |

* Not assessed for non-randomised controlled trials (RCTs) and before and after comparisons (BAs), because the chosen designs do not allow meeting these requirements.