Psychological and Psychosocial Interventions for Depression and Anxiety in Patients With Age-Related Macular Degeneration

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Title: Psychological and Psychosocial Interventions for Depression and Anxiety in Patients with Age-Related Macular Degeneration – A Systematic Review

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27 **Abstract**

28 Purpose: To review the current literature on psychosocial and psychological
29 interventions to prevent and treat depression and anxiety in patients with age-related
30 macular degeneration (AMD).

31 Methods: We conducted a systematic review of literature evaluating psychosocial and
32 psychological interventions for depression and anxiety in AMD patients. Primary
33 searches of PubMed, Cochrane library, EMBASE, Global Health, Web of Science,
34 EBSCO, and Science Direct were conducted to include all papers published until April
35 21st, 2018.

36 Results: Of a total of 398 citations retrieved, we selected 12 eligible studies published
37 between 2002 and 2016. We found 9 randomized controlled trials (RCT), and 3 non-
38 randomised intervention (NRI) studies. RCT studies suggested that interventions using
39 group self-management techniques, and individual behavioural activation plus low
40 vision rehabilitation can be effective to treat and prevent depression in AMD patients,
41 and one study suggested that a stepped-care intervention using cognitive-behavioural
42 techniques can be effective to manage anxiety and depression over time. NRI studies
43 highlighted a positive effect of self-help and emotion-focused interventions to reduce
44 depression.

45 Conclusions: Clinical practice with AMD patients can rely on some tailored cognitive-
46 behavioural therapeutic protocols to improve patients' mental health, but further clinical
47 trials will generate the necessary evidence-based knowledge to improve those
48 therapeutic techniques and offer additional tailored interventions for AMD patients.

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Key Words: Psychosocial Intervention; Psychological Intervention; Age-Related Macular Degeneration; Depression; Anxiety; Vision Disorders; Systematic Review.

Introduction

Age-related macular degeneration (AMD) is an ophthalmic condition commonly affecting adults aged 50 and older, and is regarded as a leading cause of vision loss, particularly in the developed world (1,2). The estimated global prevalence of AMD is 8.69%, being higher in Europe and North America than in Asia or Africa (2). AMD involves a deterioration of the eye's macula function leading to a variety of symptoms such as blurriness, and dark areas or distortion in central vision (1). In advanced stages, AMD entails a permanent loss of central vision, although the peripheral vision is usually preserved (1). There are two types of AMD: dry and wet AMD. Dry AMD presents with a spectrum of severity from mild, with minimal impact on vision, to advanced (also called Geographic Atrophy) that is associated with severe vision impairment. Wet AMD is an aggressive and potentially blinding condition, yet effective treatments exist in the form of vascular endothelial growth factor inhibitors (anti-VEGF), that can halt disease progression and preserve vision if initiated early in the course of the disease (3,4).

AMD is a potentially distressing medical condition as result of limitations imposed by vision loss (5-8). Previous studies on the experience of living with AMD (5,6,9,10) highlighted the potential importance of factors such as the acceptance of the disease and its consequences for vision, fears regarding disease progression and medical treatment, the way medical treatment and prognosis are communicated to patient, the communication between patient and health care-professionals, pre-conceptions on AMD, and quality of social support. A recent study conducted with wet AMD patients

(11) revealed key patient dimensions related to treatments and living with the disease, such as receive treatment to preserve vision, waiting time at the clinic, information about the diagnosis and treatment, trust in healthcare professionals, preserving vision, early access to treatment, pain relief, and visual aids. An ethnographic study exploring patients' perspectives of geographic atrophy (12), an advanced form of AMD, highlighted the negative impact of the disease on people's daily functioning, particularly in basic and essential activities such as reading, driving, watching movies, and negative interference with hobbies. Other implications revealed in this study included feeling frustration, fear of blindness, diminished social activities, financial limitations. Finally, another study (13) highlighted more optimistic experiences of illness in patients with the wet type of AMD, as patients appreciated the promising outcomes offered by anti-VEGF treatment.

The psychosocial implications of AMD have been highlighted by the co-occurrence of depression and anxiety in this patient group (15-20). Epidemiological research shows a wide prevalence range from 15.7% to 44% for depression, and 9.6% to 30.1% for anxiety among AMD patients (17). The prevalence of anxiety and depression among people with AMD is higher than in older adults without AMD. According to the World Health Organization (21), the prevalence of depression in older adults aged 60 to 79 is about 7.5% among females and above 5.5% among males. Within the same age range, the prevalence of anxiety is about 5% among females, and about 2.5% among males. In people age 80 and older the prevalence of depression and anxiety seem to be lower than in younger age groups, ranging from 4% to 5% for depression and 1% to 3% for anxiety (21). Finally, in a recent prospective longitudinal study examining the incidence and predictors of depressive and anxiety symptoms in older adults with vision impairment, having AMD was found to be a risk factor for developing depressive symptoms (22).

The factors underlying depression in AMD patients have not been widely studied (9,16,18), but the available literature has suggested that depression in these patients is mainly linked to vision loss and its negative consequences for patients' general functioning (23-27). Other studies have also suggested that depression in AMD patients can be negatively influenced by the lack of effective social support (27,28). The mental health problems in AMD might also be influenced by patients' age as depression has been found considerably prevalent in the elderly (21).

Despite the epidemiological importance of depression in AMD patients, previous studies have suggested that depression is a problem that tends to be neglected by health services, and consequently many AMD patients remain untreated for their mental health and well-being needs (9,29-32). To tackle depression in AMD patients is of particular importance considering that depression is a potential source of disability itself (33,34), most AMD patients are elderly who are a particular vulnerable group (26), and it is currently established that poor mental health is associated with greater resource use within the health system and an increase risk for comorbid physical health problems (35-37).

A range of psychological and psychosocial interventions have been regarded as evidence-based treatment options for depression and anxiety in general population (38-42). However, recent studies highlighted the need to develop tailored psychosocial interventions to address specific mental health needs of adults with AMD (9,43). Mental health needs in AMD patients are commonly associated with the impact of losing sight and losing independence (10,44,45), fears of uncertainty with regard to prognosis (10,44), anxiety associated with the diagnosis and medical treatments (9), coping with a chronic medical condition (10), burden related to regular hospital visits (9,11,12), and lack of social support (28). Additionally, in some AMD patients, particularly in patients

with wet AMD, their mental health needs might not be exclusively linked to visual impairment, as these patients can have their vision preserved by medical treatments (e.g. anti-VEGF) (46). In two studies examining anxiety related to receiving regular anti-VEGF treatment for wet AMD (9,47), patients reported being distressed by anticipatory anxiety of going blind in the future due to disease progression, and fear of going blind because of the intravitreal injections they regularly receive (anti-VEGF treatment). Finally, AMD is an age-related disease which means that part of patients' mental health needs is potentially triggered by ageing problems such as loneliness (48), fears of becoming a burden for carers (6), and management of health (11). It is therefore crucial to understand what specific psychosocial and psychological interventions we currently have available to treat depression and anxiety in patients with AMD. With this review we want to systematically analyse current literature on psychosocial intervention programmes specifically designed to treat or prevent depression and anxiety in AMD patients.

Methods

Search strategy and selection criteria

We conducted a systematic literature review of all relevant studies that investigated psychological and psychosocial treatments for depression and anxiety in adult patients with any type of AMD. We selected all studies that fulfilled the following inclusion criteria: original research reported in English; studies addressing adult participants aged 18 or older with the diagnosis of AMD; studies that have included a minimum of two repeated measurements of the outcome measure(s); studies that have had anxiety and / or depression as outcome measures; studies testing psychological or psychosocial intervention programmes designed to specifically prevent and/or reduce depression

and/or anxiety in people with AMD, and to cover psychological dimensions such as emotions, feelings, perceptions, attitudes, appraisals, cognitions, and behaviours. Studies testing other types of interventions such as vision rehabilitation, rehabilitative assistive devices (e.g. optical devices, CCTV, orientation and mobility) were only eligible for this review if the study clearly tested a particular psychological or psychosocial intervention as described in the inclusion criteria. We included studies addressing both types of AMD (wet and dry). All types of articles and study designs were considered, except for non-systematic reviews, case studies, and conference proceedings. We excluded articles lacking sufficient detail to determine whether all inclusion criteria were met.

Two authors (N.N. and H.S.) systematically conducted a search of electronic databases (PubMed, Cochrane library, EMBASE, Global Health, Web of Science, EBSCO, and Science Direct) to retrieve all articles published up to April 21st. 2018. We searched these databases using terms that are often used in literature to address psychological treatments for depression in AMD patients, including “Macular Degeneration” OR “Age-Related Macular Degeneration” OR “AMD” OR “Age-related eye disease” OR “vision loss” OR “visual impairment” OR “Low vision” AND “Depression” OR “Depressive” OR “Depressed” OR “Affective disorder” OR “mental health” AND “Anxiety” OR “Anxious” AND “Psychological treatment” OR “Psychological Intervention” OR “Psychosocial treatment” OR “Psychological intervention” OR “Rehabilitation” OR “Intervention” OR “Psychotherapy” OR “Therapy” OR “Cognitive-behavioural therapy” OR “CBT” OR “Psychodynamic Therapy” OR “Counselling” OR “Self-help” OR “Problem-solving therapy” OR “Transpersonal Therapy” OR “Stepped care” OR “Therapy”.

We followed the Cochrane handbook's guidelines for systematic review of interventions to select studies to be reviewed (49). Two authors (H.S. and N.N.) independently reviewed titles and abstracts and then the full-text articles to identify the eligible studies. Results of both researchers were compared, and non-eligible studies and duplicates were excluded. Next, the same researchers read the abstracts of the remaining article titles to determine whether they met inclusion criteria. Abstracts providing sufficient detail for exclusion were removed, and the remaining full-text articles were retrieved to be fully analysed. Full-text articles were read to determine inclusion, and disagreements were resolved via consensus. Data were analysed and summarized using a specific table (Table 1).

Risk of Bias Assessment

We assessed risk of bias for all included studies in this review. Randomized controlled trials (RCT) were independently assessed by two researchers (AM and HS) using the Cochrane Tool to Assess Risk of Bias of RCT Studies (49). The Cochrane tool was designed to address several sources of bias including selection bias, performance bias, detection bias, attrition bias, reporting bias, and other bias. The tool allow us to appraise whether the risk of bias for each source of bias is low, high or unknown.

Non-randomised intervention studies were independently assessed using ROBINS-I tool (50). The tool comprises the assessment of three bias domains: pre-intervention, including bias due to confounding and bias in selection of participants; at intervention, including bias in classification of interventions; and post-intervention, including bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes and bias in selection of the reported result.

Results

Figure 1 describes the process of study selection. We identified 398 articles from the databases, of which 361 were excluded on the basis of title and abstract review, including exclusion of duplicated articles, leaving 37 articles. After checking the full-text of these 37 articles, we excluded 26 for not meeting our eligibility criteria, with 11 articles remaining for review. Reference lists were reviewed using the same process, and 1 additional article was identified for inclusion, leaving a final list of 12 articles to be reviewed (Table 1). The main reasons for not meeting the eligibility criteria of this review were: studies which sample did not include patients with AMD; studies that did not test any psychosocial or psychological intervention for depression and/or anxiety in a sample composed of (at least partially) AMD patients; articles addressing study protocols; studies in which the outcome measures did not include depression and/or anxiety.

Table 1 summarized all articles included in the current review. The 12 articles selected for our review included studies published between 2002 and 2016. 9 articles comprised randomized controlled trial (RCT) studies. However, 3 articles (51-53) were part of the same original RCT study and reported different findings from the same source of data. The remaining 3 articles comprised non-randomized intervention studies (NRI), all of them using a pretest-posttest research design. 8 articles analysed in this review exclusively tested psychosocial / psychological interventions on AMD patients (51-58). The other 4 articles included in this review tested psychosocial / psychological interventions in clinical samples composed of a mixture of patients with different ophthalmological conditions, including AMD (59-62).

In all articles included in this review standardized questionnaires (e.g. Hospital Anxiety and Depression Scale; Beck's Depression Inventory; Geriatric Depressive Scale) were

used to assess patients' intensity and severity of symptoms of anxiety and depression (see Table 1).

Synthesis of RCT studies

Three articles examined different aspects of the effectiveness of a 6-week self-management programme from the same original RCT study (51-53). The self-management programme comprised a set of 6 group intervention sessions administered over 6 weeks. The overall intervention was composed of cognitive and behavioural components which included information on AMD, suggestions of ways to maintain and increase activity levels, re-evaluation of perceived barriers to independence, skills training in communicating with others about visual disability, handling challenges related to AMD, and requesting assistance when needed. One article (51) addressed the effect of the self-management programme on patients' quality of life and emotional distress. The intervention was associated with better mood, better functioning and lower emotional distress, particularly in depressed patients. The other article (52) assessed the effectiveness of the same self-management programme at 6-month follow-up, after the intervention has been completed. Results showed that at 6-month follow-up depressed patients had a reduction in emotional distress compared with the non-depressed and the depressed patients in the control group. Self-efficacy and functioning also improved. Finally, in the third article (53) authors examined a sub-set of participants who were clinically depressed at baseline of the original RCT study with the aim of assessing the effectiveness of the intervention programme to reduce depression symptoms at 6-month follow-up. Results suggested that at 6-month follow-up patients who had received the self-management intervention had a significantly greater reduction in depressive

symptoms than the controls. Additionally the reduction in depressive symptoms was also associated with greater self-efficacy.

Rovner et al. (56) tested the effectiveness of problem-solving treatment (PST) to prevent depressive disorders in AMD patients. PST comprised a manual-driven individual psychological treatment delivered in 6 individual in-home sessions during 8 weeks. The intervention was designed to address patients' negative perceptions that may interfere with finding practical solutions to problems. It was focussed on teaching problem-solving skills such as: defining problems; establishing realistic goals; generating, choosing, and implementing solutions; and evaluating outcomes. The main aim was to encourage patients to use these skills on a routine basis in order to develop compensatory strategies to achieve valued goals and to prevent depression. Results suggested that PST was effective in preventing depression at 2-month follow-up. However, after 6 months the intervention showed no positive effect in preventing depressive disorders in AMD patients.

A RCT conducted by Girdler et al. (55) tested the effectiveness of an 8-week structured vision self-management programme on AMD patients. The programme comprised a group-based intervention and relied on self-management and self-efficacy theories and principles. Programme activities included welcome and warm-up exercises, revision of homework, learning and practice activities, and homework assignments. Patients who received the intervention showed better participation in everyday activities and better outcomes in general health measures such as depression, quality of life and generalised self-efficacy, than the control group. During the treatment patients also showed improvements in participation, general health and depression. Gains on general health and participation were made regardless of whether patients were, or were not, depressed at baseline.

Rovner et al. (57) tested the efficacy of two interventions to prevent depressive disorders in AMD patients. One group received behaviour activation (BA) plus low vision rehabilitation (LVR), whereas other group received supportive therapy (SP) plus LVR. BA plus LVR was delivered in 6 individual in-home sessions during 8 weeks. This intervention was focussed on the link between action, mood and mastery. The main aim is to promote self-efficacy, social connection, mood and function. The SP plus LVR intervention was delivered in 6 individual in-home sessions during 8 weeks and was designed to facilitate discussion of illness, disability, and vision loss. Strategies in this treatment include facilitating personal expression about vision loss and disability. Results showed that at 4 months patients who received BA plus LVR were significantly less likely to develop a depressive disorder than those patients who received SP plus LVR. The treatment effect was more pronounced in patients with worse vision than in patients with better vision.

Rees et al. (60) tested the effectiveness of a low vision self-management programme in older adults with low vision (70% with AMD). The intervention programme comprised an 8-week (once a week) low vision self-management programme (Group Intervention). Each session lasted 3 hours and addressed problem-solving skills training and goal planning. Throughout the programme patients were invited to draw on and share their life experiences, coping mechanisms and stimulated to develop new skills and strategies based on problem-solving. At 1 and 6 month follow-up assessments, no significant between-group differences were found on depression and anxiety levels between patients who received the intervention and patients who only received usual care.

A RCT study conducted by Van der Aa et al. (61) tested the effectiveness of a stepped-care programme designed to prevent the onset of major depressive, dysthymic, and anxiety disorders in older people with visual impairment caused by age related eye

diseases (47% with AMD). The programme comprised 4 steps: 3 months of watchful waiting, with no intervention and only follow-up; 3 months of guided self-help including a self-help course based on cognitive-behavioural therapy to increase the awareness of depression and anxiety in relation to visual impairment; 3 months of problem solving treatment comprising a maximum of 7 face-to-face sessions; and referral to a GP, when increased symptoms of depression and anxiety still persisted after step 3. After 24-months follow-up, the intervention programme was associated with a significantly reduced incidence of depressive and anxiety disorders and less risk of having depression and anxiety in comparison with control group who received usual care.

Kamga et al. (59) investigated the efficacy of depression self-care tools in reducing depressive symptoms in patients with age-related eye disease (54% AMD). The intervention comprised large print written and audio tools incorporating cognitive-behavioural principles plus three 10-minute telephone calls from a lay coach, over 8-week follow-up. Control group received usual care. After adjusting for visual acuity, the intervention group showed that a significant reduction in depressive symptoms in comparison with the control group. However the intervention did not show any significant difference for anxiety symptoms.

Risk of Bias of RCT Studies

Table 2 synthesizes the assessment of risk of bias of RCT studies included in this review. Seven out of ten studies (table 3) showed an unclear or risk of bias in at least one domain of bias. The most common causes of unclear risk of bias were: the procedure for blinding the intervention to personnel had not been reported (51-53;55) – performance bias; the procedure for concealing the allocation sequence had not been

reported (55) – selection bias; the procedure for blinding outcome assessors had not been reported (55) – detection bias; attrition reported but with lack of details on the reasons for its occurrence (59) – attrition bias. High risk of bias was detected in several studies and the common causes were as follows: unmasking occurred in 26 intervention participants and in 11 controls and in all instances subjects inadvertently revealed their treatment assignment (56) – detection bias; both low vision staff and patients were unmasked (61) – detection bias; lack of data on non-significant differences between groups (55) – reporting bias; patients who volunteered and were selected for this study might have differed from other eligible individuals (61) – selection bias.

Synthesis of Non-Randomized Intervention Studies

Birk et al. (54) examined the effect of a psychosocial intervention to improve emotional and behavioural functioning in AMD patients. The intervention included 5 group sessions over 5 weeks addressing the following aspects of patients' functioning: progressive muscle relaxation; exchange of experiences related to living with AMD; thought, emotion, behaviour, to increase awareness on how both three interact; resources, to increase awareness on the available resources; problem solving, including description of problems and formulation of goals and alternative means of approaching these goals; and information, to exchange information and role of self-help groups and other specialized aids. Results showed a decrease in depressive symptoms in the intervention group in comparison with the non-intervention group. The study also showed that the negative affect increased in the non-intervention group and a decreased in the group who received intervention.

Wahl et al. (58) conducted a pretest-posttest study to evaluate the efficacy of short psychosocial group intervention to improve well-being in AMD patients. The authors

tested two interventions and compared them with the non-intervention group (control group). One intervention was based on an emotional-focused approach and aimed to help patients to learn how to deal with negative emotions related to living with AMD and vision loss. It included stimulation of emotional expression by a pair of group trainers. The other intervention was a problem-focused intervention and aimed to help patients to deal with all kinds of daily problems caused by AMD. It included discussing common problems and encouraging patients to analyse their problems and achieve realistic goals that can lead to better adaptation. Both interventions comprised 5 group sessions over 5 weeks. Patients who received emotion-focused intervention showed a limited decrease in depression symptoms, but no significant improvements in symptoms of depression were found in patients who received problem-focused intervention.

Van der Aa et al. (62) carried out a pretest-posttest study to mainly investigate the remission rates of subthreshold depression and anxiety, incidence rates of major depressive and anxiety disorders, and predictors of remission and incidence rates in older adults with visual impairment (46% AMD) after 3-months of “watchful waiting”. Watchful waiting didn’t include any type of intervention and the authors wanted to see the proportion of patients who managed to cope effectively with vision loss without intervention (resilient patients). After the watchful waiting period (3 months) patients showed a significant decrease in depression and anxiety. 34 % of patients recovered from subthreshold depression and/or anxiety and 18 % developed a depressive and/or anxiety disorder. Female gender, problems with adjustment to vision loss at baseline, more symptoms of depression and anxiety at baseline, and history of major depressive, dysthymic, and/or panic disorder were associated with poorer outcomes in depression and anxiety after the watchful waiting period.

Risk of Bias of Non-Randomized Intervention Studies

Table 3 synthesizes the assessment of risk of bias of NRI studies included in this review. The three studies assessed showed low risk of bias for the majority of bias domains. However, in one study (54) serious risk of bias was identified for measurement of outcomes. In that study it was not clear whether the outcomes were influenced by prior knowledge of the intervention, as the outcome assessors were not blind to treatment assignment.

Discussion

The current systematic review summarized relevant evidence regarding RCT and NRI studies testing psychological and psychosocial interventions specifically designed to treat or prevent depression and anxiety in AMD patients. This review uncovered 12 papers, most of them published since 2006, which suggests that the psychological interventions for AMD is a relatively recent topic of research. The study of psychological implications of vision loss has not been widely explored and remains a niche topic within the fields of psychology and medicine. In 2015, a systematic review addressing the psychological adjustment to vision loss in adults found 52 papers, 35 of which had been published between 2000 and 2012 (63). The lack of research investment in these topics might also be one of the reasons for why depression related to age-related eye diseases has not been tackled by many healthcare and low vision services (9, 29-32). Vision loss in older adults is a growing problem, particularly in western countries, and entails complex psychosocial needs, high risk for social vulnerability and for long-term mental health problems (2,5,9,17).

The studies included in this review examined the effectiveness of psychosocial and psychological interventions which were mainly composed of cognitive-behavioural

techniques such as self-management, self-help, problem solving, behavioural activation, and emotion-focused intervention. Although all studies have tested the effectiveness of the intervention programme to reduce symptoms of depression, only four studies included anxiety as an outcome measure (59-62). Five out of seven RCT studies suggested effective interventions to prevent and treat depression in AMD patients (53,55,57,59,61), and one of these studies also showed positive outcomes for anxiety (61). However, only 4 studies in our review had included an outcome measure for anxiety (60-63), which suggests the need for additional research investigating the effect of psychological and psychosocial interventions on anxiety related to AMD.

The successfully tested interventions included group self-management techniques, self-help techniques, an integrated psychosocial intervention comprising individual in-home sessions of behavioural activation plus low vision rehabilitation, and stepped type of intervention using cognitive behavioural techniques such as self-help and problem solving. Additionally, the most effective interventions had also a strong tailoring strand as they were designed to address patients' specific needs related to functional and psychosocial implications of AMD, vision loss and ageing, which is consistent with other studies conducted with adults with visual impairment (9,43). However, the evidence generated by available RCT studies is still limited and in some cases unclear due to the potential risk of bias and small sample sizes found in some studies. Finally, the majority of studies reviewed did not investigate the longevity of intervention effects which is crucial to understand the actual effectiveness of the intervention for preventing or reducing depression and anxiety in this particular clinical group.

Non-randomised intervention studies are regarded to have less potential for generating robust evidence due to the possible existence and magnitude of selection bias (64). However, the three studies reviewed here (54,58,62) showed good quality in terms of

risk of bias and suggested the potential usefulness of psychosocial interventions using techniques such as muscle relaxation, exchanging living experiences (living with AMD and/or vision loss), increasing awareness of available resources and specialised aids, problem solving, and emotional focused techniques to help patients dealing with negative emotions. Finally, a period of 3 months of watchful waiting was also suggested as potentially useful to understand which patients can recover from subthreshold depression and/or anxiety without specialised intervention (62).

Factors related to ageing might also be taken into account when addressing depression and anxiety in AMD patients. Older adults can be particularly susceptible to mental health problems, particularly depression and anxiety which tend to appear together in the elderly (65,66). Factors of different nature have been associated with depression and anxiety in older adults. The main biological factors are chronic health conditions (65,67), hearing and vision loss (63,68,69), disability and functional limitations (67,70), high blood pressure (71), and vascular problems (72). Psychological and cognitive factors associated with depression and anxiety in the elderly are self-perceived health (73), personality traits (neuroticism) (74,75), dysfunctional coping (75), negative self-image (74), and other psychopathological problems (76). Experience of loneliness and perceived social isolation can also play an important role as factors of depression and anxiety in the elderly. A recent study conducted with older adults found a longitudinal and bidirectional association between experiencing loneliness and higher risk for major depression disorder (MDD) and generalized anxiety disorder (GAD) two years later (77). In the same study, perceived social isolation was also found independently associated with MDD and GAD. Another study conducted with adults aged 55 and older found a significant association between clinical anxiety and an almost threefold increased risk of subsequent dementia (78). Finally, a longitudinal prospective study

conducted with people aged 50 and older highlighted that depression and anxiety symptoms fluctuate overtime (22). According to the same study, the main risk factors for depression and anxiety include living alone, having just enough money to cover expenses, having macular degeneration, difficulties with adaptation to vision loss, reduced health related quality of life, and experiencing symptoms of anxiety / depression. The findings suggest the need to tackle those risk factors as part of the psychological and psychosocial intervention for people with vision loss, in order to prevent relapse of depression and anxiety, which can also occur in people with AMD.

It is therefore paramount to take into account factors underlying mental health problems in the elderly when developing psychological and psychosocial interventions for people with AMD. The intervention might benefit from an interdisciplinary approach covering different patient needs, such as physical health, mental health, and social support. Current evidence-based interventions for depression and anxiety in the elderly might also be considered for AMD, such as modular CBT (79,80), Interpersonal Psychotherapy (81-83), Mindfulness (84), and Psychopharmacological treatments (80).

Study Limitations and Conclusions

We made several attempts to minimize bias in this review, including a sensitive and systematic search strategy spanning several electronic databases, and the use of a standardized form to extract the data from articles – both were made by 2 independent reviewers. However, we acknowledge 3 main limitations to this review. First, only articles in English were included in this review, which can be considered a limitation because there is literature on the topic in other languages. Second, the terminology we used to perform the search for articles reflects both the state of the art and our previous experience, and possibly bias, as researchers and clinicians. Finally, we did not include any grey literature which might limit the scope of this review. However, all grey

literature found in this topic was composed of works showing lack of details on how the study was conducted and how data were analysed, which compromised our article selection and risks of bias checking. Examples of this literature are conference proceedings, newsletters, and working papers.

In conclusion, the available evidence of psychological and psychosocial interventions to prevent and treat depression in AMD patients suggest the potential usefulness of some cognitive-behavioural therapeutic techniques when incorporated in tailored intervention programmes designed to address patients' specific needs. This is a topic where more robust RCT studies are needed to provide further evidence-based guidance for clinical practice with older adults with vision loss, particularly patients with AMD. Future studies should confirm the effectiveness of the therapeutic techniques previously tested, as well as alternative high-tailored psychosocial interventions that will improve care delivery at multidisciplinary medical and rehabilitation settings.

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Figure 1. Flow Diagram of Articles Selection Process

Table 1 – Summary of Reviewed Studies

Ref.	Country	Intervention Sample	Control Group	Setting	Design	Intervention(s)	Outcome Measures for Depression and Anxiety	Main Outcomes
Brody et al. 2002 (51*)	US	SMG: 86 adults with AMD; MA=80.7; F=71%	WLG: 71 adults with AMD; MA=80.7; F=61% TRG: 74 AMD patients; MA=81.2; F=66%	Patients recruited from: ophthalmologists' offices; the media; AMD registry; Health fairs; and Senior centres.	RCT	6-week / 6 sessions, 12-hour self-management programme (Group Intervention). Each session comprised 2 elements: didactic presentations; and group problem-solving with guided practice. The overall intervention was composed of cognitive and behavioural components. Cognitive components mainly included information on AMD, suggestions of ways to maintain and increase activity levels, and re-evaluation of perceived barriers to independence. Behavioural components mainly included skills training in communicating with others about visual disability, handling challenges related to AMD, and requesting assistance when needed. Controls received 12-hour Tape-recorded health lecturers or were at waiting list for intervention.	POMS; SCID-IV.	3-way interaction ($P=.001$) showed that after self-management intervention, depressed patients had a reduction in emotional distress compared with the non-depressed and the depressed patients in the control group. Decreased emotional distress was associated with better self-efficacy after completing the intervention programme.

Birk et al. 2004 (54)	Germany	14 adults with AMD; MA: 73.1; F=64%	8 adults with AMD; MA: 72.6; F=62%	University Department of Ophthalmology	PPCG	Psychosocial intervention (5 groups session over 5 weeks) comprising: Progressive muscle relaxation; Exchange of experiences related to living with AMD; Thought, Emotion, Behaviour, to increase awareness on how both three interact; Resources, to increase awareness on the available resources; Problem solving, including description of problems and formulation of goals and alternative means of approaching these goals; and Information, to exchange information and role of self-help groups and other specialized aids.	GDS-15	Depressive symptoms decreased in the intervention group, and increased in the control group (T-test; $P=.06$); Negative affect increased in the control group and decreased in the intervention group (T-test; $P=.02$).
Brody et al. 2005 (52*)	US	SMG: 82 adults with AMD; MA=80.5; F=72%	WLG: 66 adults with AMD; MA=80.3; F=65% TRG 66 adults with AMD; MA=81.3; F=65%	Patients recruited from: ophthalmologists' offices; the media; AMD registry; Health fairs; and Senior centres.	RCT	6-week / 6 sessions, 12-hour self-management programme (Group Intervention). Each session comprised 2 elements: didactic presentations; and group problem-solving with guided practice. The overall intervention was composed of cognitive and behavioural components. Cognitive components mainly included information on AMD, suggestions of ways to maintain and increase activity levels, and re-evaluation of perceived barriers to independence.	POMS; SCID-IV.	At 6-months follow-up, 3-way interaction ($F_{1,209}=14.51$, $P=.001$) showed that after self-management intervention, depressed patients had a reduction in emotional distress compared with the non-depressed and the depressed patients in the control group.

						<p>Behavioural components mainly included skills training in communicating with others about visual disability, handling challenges related to AMD, and requesting assistance when needed.</p> <p>Controls received 12-hour Tape-recorded health lectures or were at waiting list for intervention.</p>		
Brody et al. 2006 (53*)	US	SMG: 12 adults with AMD; MA=81.2; F=58%	<p>WLG: 12 adults with AMD; MA=81; F=66.7%</p> <p>TRG: 8 adults with AMD; MA=81.9; F=75%</p>	University ophthalmology clinic	RCT	<p>12-hour Self-management programme comprising a 6-week AMD education program (Group Intervention). This programme consists of cognitive elements, information about AMD, services, re-evaluation of barriers, and positive challenges, communication about AMD, problem solving using vignettes, and modelling of adaptive behaviours.</p> <p>Controls received Tape recorded education conditions comprised a series of 12 hours of health lectures, or were at waiting list for intervention.</p>	GDS-15; SCID-IV	At 6-month follow-up of AMD patients who were clinically depressed at baseline, the self-management group had a significantly greater reduction in depressive symptoms than the controls ($z=-1.86$; $P=.03$). Reduction in depressive symptoms was associated with greater self-efficacy in the self-management group (Spearman $\rho=-0.72$, $P<.05$)
Wahl et al. 2006 (59)	Germany	45 adults with AMD	22 adults with AMD;	University Department of Ophthalmology	PPS	Intervention –five group sessions across five weeks.	GDS-15	After Emotion-focused intervention, patients showed a limited decreased in

		<p>EFG: 23 adults with AMD; MA=76.5;F=90%;</p> <p>PFG: 22 adults with AMD; MA=76.6; F=68%</p>	MA=77.3; F=77%			<p>Emotion-focused intervention: aiming to help patients to learn how to deal with negative emotions related to living with AMD and vision loss. It included stimulation of emotional expression by a pair of group trainers.</p> <p>Problem-focused intervention: aiming to help patients to deal with all kinds of daily problems caused by AMD. It included discussing common problems and encouraging patients to analyse their problems and achieve realistic goals that can lead to better adaptation.</p>		depression scores (-0.55) (ANCOVA $P = .047$; Effect size: 2.7%). No decrease in depression was found after problem-focused intervention.
Rovner et al. 2007 (57)	US	105 adults with AMD; MA=81.3; F=65.7%	101 adults with AMD; MA=81; F=74.3%	In-home	RCT	<p>Problem-Solving treatment (PST) delivered in 6 individual in-home sessions during 8 weeks.</p> <p>PST comprised a manual-driven individual psychological treatment designed to address patients' negative perceptions that may interfere with finding practical solutions to problems. It is focussed on teaching problem-solving skills such as: defining problems; establishing realistic goals; generating, choosing, and implementing solutions; and</p>	HDRS	At 2-months follow-up patients who received PST had less than half the odds of developing depression as controls (odds ratio [OR], 0.39; 95% confidence interval [CI], 0.17-0.92; $P = .03$). Logistic regression showed that PST can also prevent loss of a valued activity and consequently prevent depression (OR, 2.55; 95% CI, 1.18-5.50; $P=.02$).

						evaluating outcomes. The main aim is to encourage patients to use these skills on a routine basis in order to develop compensatory strategies to achieve valued goals and to prevent depression.		At 6 months, no significant differences were found in the prevalence of depressive disorders between PST group and controls (OR, 0.65; 95% CI, 0.33-1.39; P=.29)
Girdler et al. 2010 (56)	Australia	36 adults with AMD; MA=79.4; F=72%	41 adults with AMD; MA=80.4; F=58.5%	Vision rehabilitation services	RCT	8-week (24 h) structured Vision Self-Management Programme comprising welcome and warm-up exercises, revision of homework, learning and practice activities), and homework assignments. It is a group-based intervention and relied on self-management and self-efficacy theories and principles. Controls: usual care	GDS-15	After intervention depression symptoms (GDS scores) dropped from 10.58 to 8.05 (ANCOVA, P=.001; effect size=0.17) (cut-off score for clinical depression is 11). GDS scores in control group increased from 10.58 to 11.28 05 (ANCOVA, P=.001; effect size=0.17).
Rovner et al. 2014 (58)	US	BA+LVR: 96 adults with AMD; MA=85.2; F=72.9%	ST+LVR: 92 adults with AMD	In-home	RCT	One group received Behavioural Activation + Low Vision Rehabilitation: delivered in 6 individual in-home sessions during 8 weeks. This intervention was focussed on the link between action, mood and mastery. The main aim is to promote self-efficacy, social connection, mood and function.	PHQ-9	Regression analysis showed that at 4 months, Behavioural activation + low vision rehabilitation subjects were significantly less likely to develop a depressive disorder than Supportive treatment + low vision rehabilitation subjects (RR, 0.51; P = 0.037). Treatment effect was more pronounced in patients with

						Another group received Supportive therapy + Low Vision Rehabilitation: delivered in 6 individual in-home sessions during 8 weeks. This intervention was designed to facilitate discussion of illness, disability, and vision loss. Strategies in this treatment include facilitating personal expression about vision loss and disability.		worse vision (RR, 0.37; 95% CI, 0.14-0.96) than in patients with better vision (RR, 0.80; 95% CI, 0.29-2.18).
Rees et al. 2015 (61)	Australia	93 adults with Low Vision: 70% with AMD; MA=80.1; F=58%	60 adults with Low Vision: 69.5% with AMD; MA=80.5; F=38%	Low Vision Rehabilitation setting	RCT	8-week (once a week) Low vision self-management programme (Group Intervention): Sessions of 3 h in duration addressing problem-solving skills training and goal planning. Patients were invited to draw and share their life experiences, coping mechanisms and stimulated to develop new skills and strategies based on problem-solving.	DASS	At 1 and 6 month follow-up assessments, no significant between-group differences were found on depression and anxiety measured by DASS ($P > 0.05$). Univariate and multivariate analyses revealed no impact of the intervention on outcome measures.
Van der Aa et al. 2015 (62)	Netherlands / Belgium	131 adults with VI: 47% with AMD; MA=72.4; F=70%	134 adults with VI: 45% with AMD; MA=74.9; F=70%.	Rehabilitation setting and in-home	RCT	Stepped-care programme protocol comprising 4 steps. Step 1 – Watchful Waiting (3 months): period of watchful waiting. All patients were contacted by telephone at baseline and after 3 months.	CES-D; HADS-A	After 24-months follow-up, the intervention programme was associated with a significantly reduced incidence of depressive (CES-D) and anxiety disorders (HADS-A), with a relative risk of 0.63 ($P = .01$).

						<p>Step 2: Guided Self-Help (3 months): written, digital, audio, and Braille version of a self-help course based on cognitive behavioural therapy. Main aims include: to increase awareness of depression and anxiety in relation to having visual impairment; to increase awareness of pleasurable activities; to set personal goals; to identify negative thought patterns and personal communication styles; and continuing to use learn skills.</p> <p>Step 3 Problem-Solving Treatment (3 months) comprising a maximum of 7 face-to-face sessions. During each session seven steps of problem solving treatment were completed.</p> <p>Step 4 Referral to a GP: When increased symptoms of depression and anxiety still persisted after step 3 the patients was contacted to be referred to her/his GP.</p> <p>Controls received usual care.</p>		Drop-out rates were not significantly different between the intervention group and controls.
Van der Aa et al. 2015 (63)	Netherlands /Belgium / 2015	265 adults with VI; 46% with AMD;	Adults with AMD (N not known)	Rehabilitation setting	PPS	Stepped-care programme comprising a 3-month period of watchful waiting. All patients were contacted by telephone at baseline and after 3 months. During this	CES-D; HADS-A	Depression and anxiety decreased significantly ($p < 0.001$) after a 3-month watchful waiting period: 3.8

		MA= 73.7; F=69.8%				period all participants received usual care of low-vision rehabilitation centres.		points on CES-D and 1.4 on HADS-A. 34 % of patients recovered from subthreshold depression and/or anxiety and 18 % developed a depressive and/or anxiety disorder. Female gender (OR 0.49), problems with adjustment to vision loss at baseline (OR 1.02), more symptoms of depression and anxiety at baseline (OR 1.06), and history of major depressive, dysthymic, and/or panic disorder (OR 2.28) were associated with poorer outcomes in depression and anxiety after the watchful waiting period.
Kamga et al. 2016 (60)	Canada	41 adults with VI: 54% with AMD; MA=75.1; F=66%	39 adults with VI: 56% with AMD; MA=73; F=59%	Retinal Clinics	RCT	Large print written and audio tools incorporating cognitive-behavioural principles plus three 10-minute telephone calls from a lay coach. (8-week follow-up); Control group received usual care, i.e., they received one coach call and the same intervention after the follow-up interview.	PHQ-9; GAD-7	Linear regression after adjusting for visual acuity showed that the intervention reduced depressive symptoms by 2.1 points more than in control group ($P=.04$). No significant changes were found for anxiety symptoms.

*** These three articles were part of the same RCT study, although reporting a different analysis of the same original data.**

¹No information available on sample mean age and percentage of female patients

AMD – Age-related macular disease; BA+LVR – Behavioural Activation + Low Vision Rehabilitation; BDI-II – Beck’s Depression Inventory; CES-D - The Centre for epidemiological studies depression revised;

CG- Control group; DASS - Depression, anxiety, stress scale; EFG – Emotion-focused group; F - % of Females; GAD-7 - Generalized Anxiety Disorder 7-item scale; GDS-15 – Geriatric depressive scale;

GP – General Practitioner; HADS-A - Hospital anxiety and depression scale – Anxiety sub-scale; HDRS - Hamilton depression rating scale; MA – Mean age; OR – Odds Ratio; PFG – Problem-focused group

PHQ-9 – The patient health questionnaire; POMS - The Profile of mood states; PPS- Pre-test–post-test study; PPCG – Preintervention–postintervention comparison-group; RCT – Randomized controlled trial;

SCID-IV - Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders; SMG – Self-Management group; ST+LVR – Supportive Therapy + Low Vision Rehabilitation;

TRG – Tape-recorded group; UCG – Usual Care Group; VI – Visual Impairment; WLG- Waiting List Group

Table 2– Assessment of Risk of Bias in RCT Studies – Cochrane Tool

[illegible]

Rees et al. 2015 (60)	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Van der Aa et al. 2015 (61)	Low risk	High risk (6)	Low risk	High risk (7)	Low risk	Low risk	Low risk
Kamga et al. 2016 (59)	Low risk	Low risk	Low risk	Low risk	Unclear risk (8)	Low risk	Low risk

(a) These three articles were part of the same RCT study, although reporting a different analysis of the same original data.

- (1) The procedure for blinding the intervention to personnel was not reported.
- (2) According to authors, unmasking occurred in 26 intervention participants and in 11 controls. In all instances, subjects inadvertently revealed their treatment assignment.
- (3) The procedure for concealing the allocation sequence was not reported.
- (4) The procedure for blinding outcome assessors was not reported.
- (5) Lack of data on non-significant differences between groups.
- (6) According to authors, selection bias might have occurred because patients who volunteered and were selected for this study might have differed from other eligible individuals.
- (7) According to authors, both low vision staff and patients were unmasked.
- (8) Attrition was reported but with lack of details on the reasons for its occurrence.

Table 3 – Risk of Bias Assessment for Non-Randomised Studies

STUDY AUTHOR	Study Design	TYPE OF BIAS						
		Bias due to Confounding	Bias in selection of participants	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result
Birk et al. 2004 (54)	Pretest- Posttest	Low risk	Low risk	Low risk	Low risk	Low risk	Serious risk (1)	Low risk
Wahl et al. 2006 (58)	Pretest- Posttest	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk
Van de Aa et al. 2015 (62)	Pretest- Posttest	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk	Low risk

(1) Not clear if the outcome measure have been influenced by knowledge of the intervention; The outcome assessors were not blind to treatment assignment.