

**Chapter 10:**  
**Summary and general discussion**

## Background and aims

In the Netherlands and Belgium visual impairment is primarily a problem of the elderly with common causes such as age-related macular degeneration (AMD), glaucoma, diabetic retinopathy, cataract, and brain injury. When people lose their sight in later life a profound sense of loss can be experienced. Many capabilities and activities to which people were strongly attached and which provided identity, security and meaning can be lost. Possibilities for participation, communication and autonomy may be reduced, which may affect a person's social status and their relationships with loved ones. Many people may start feeling depressed or anxious in such situations. In most cases this is a normal reaction to personal loss and would not be considered a mental illness. However, if depression and anxiety interfere with normal functioning and persist for a longer period of time, clinical support may be necessary.

Different levels of depression and anxiety can be distinguished: i) actual disorders according to the diagnostic and statistical manual of mental disorders (DSM) criteria, and ii) subthreshold symptoms (i.e. clinically relevant symptoms but no actual disorder). From a clinical perspective subthreshold depression and anxiety are important, because these are disabling conditions that need treatment, and these are the most important risk factors for developing actual major depressive or anxiety disorders, which may be averted by treatment. About one in three visually impaired older adults experience subthreshold depression and/or anxiety, which is about twice as high as the prevalence in the general older population. However, depression and anxiety are under-detected and under-treated in visually impaired older adults, and, until now, evidence on psychological interventions to address these problems in this population is scarce.

Studies in various populations have shown that offering low intensity treatments by means of a stepped care programme may reduce symptoms of depression and anxiety and prevent the onset of disorders in people who show subthreshold symptoms (indicated prevention). These low-intensity interventions could be incorporated in low vision rehabilitation care, which may increase the accessibility of mental health services for visually impaired older adults and allow staff to combine expertise on mental health and visual impairment. The main principle of stepped care is that patients start with lower intensity treatments and only move on to higher-intensity treatments when sufficient response is lacking, i.e. relatively few patients need to step up, leading to similar or better patient outcomes and lower costs than other (high-intensity) interventions. Therefore, a population-specific stepped care programme was developed and investigated in this thesis.

The overall aim of the work presented in this thesis is to gain knowledge on depression and anxiety in visually impaired older adults and cost-effective treatment possibilities to address these problems in low vision rehabilitation care. To this end, firstly, prevalence estimates of threshold and subthreshold depression and anxiety in visually impaired older adults compared with normally sighted peers were determined. Secondly, a prediction model of having subthreshold depression (the most important predictor of developing actual major depressive disorder) in visually impaired older adults was internally and externally validated. Thirdly, the utilisation of and perceived needs for mental health services in older adults with visual impairment were investigated. Fourthly, evidence of interventions to reduce mental health problems in visually impaired older adults was evaluated in a systematic review and meta-analysis. Finally, the cost-effectiveness of a stepped care intervention with evidence-based treatment components, implemented in low vision rehabilitation care to address depression and anxiety in visually impaired older adults was investigated. Presented below is a summary of the results, a discussion and conclusions, implications for clinical practice, and directions for future research.

## Prevalence of depression and anxiety

Studies aimed at determining the prevalence of subthreshold depression and anxiety in visually impaired older adults using screening questionnaires showed that approximately one third of older adults with visual impairment experience subthreshold depression and/or anxiety.<sup>1-5</sup> In this thesis, these findings are confirmed in a large sample of visually impaired older adults ( $n=615$ ) and are compared with normally sighted peers ( $n=1,232$ , **Chapter 2**). It was found that visually impaired older adults significantly more often experience subthreshold depression and anxiety. In addition, the most common mental health disorders were determined with a short diagnostic interview based on the DSM-IV criteria. It was found that approximately 5% of visually impaired older adults have a major depressive disorder, 1% has a dysthymic disorder, and 7% are diagnosed with an anxiety disorder (i.e. panic disorder (with and without agoraphobia), agoraphobia (without history of panic disorder), social phobia and/or generalized anxiety disorder). These numbers are also significantly higher than the prevalence estimates found in normally sighted peers. Agoraphobia (without a history of panic disorder) was found to be the most prevalent anxiety disorder in visually impaired older adults, indicating that people with visual impairment are especially vulnerable to develop anxiety related to specific places or situations, such as being in a crowd or using public transportation. These situations and places can be terrifying for persons with an inability to see other people's faces or read signs; moreover, these feelings may be amplified in a society that fails to design public spaces and facilities to match the needs of people with visual impairment.<sup>6,7</sup> In addition, social phobia is significantly more prevalent in visually impaired older adults compared with their normally sighted peers, indicating that visually impaired people are also more vulnerable and likely to develop anxiety in social situations, such as speaking in public or eating in the company of others. These situations may be especially difficult or shameful for people who, for instance, cannot see what they are eating and have to deal with a community that has limited understanding of their impairment and may have negative attitudes towards their disability.<sup>6,7</sup> Therefore, when diagnosing these disorders in visually impaired older adults, special attention should be paid to whether the experienced anxiety is realistic or not. Overall, the findings indicate that both threshold and subthreshold depression and anxiety are major problems in visually impaired older adults and that targeted interventions to address these conditions in this population are warranted.

## Validated prediction model of subthreshold depression

For early diagnosis and treatment it is important to identify patients who are at high risk of having subthreshold depression, which is the most important predictor of developing an actual major depressive disorder.<sup>8</sup> Although studies have shown that various factors are associated with depression in older adults with visual impairment, the results are inconsistent and prediction models have not been externally validated.<sup>9-16</sup> Therefore, it remains unclear which factors contribute to depression in visually impaired older adults and whether the findings are stable across different populations. In this thesis, a prediction model for subthreshold depression was internally validated in a large sample of visually impaired older adults in the Netherlands and Belgium ( $n=873$ ) and externally validated in a comparable Australian sample ( $n=124$ , **Chapter 3**). The following factors were found to contribute to having subthreshold depression in visually impaired older adults: female gender, a relatively younger age, a history of psychiatric disorder, having received mental health services in the past, a lower perceived health status, lower acceptance of vision loss, and living alone. People with these characteristics should be more carefully monitored and screened for depression. The outcomes were based on large sample sizes which are expected to provide robust estimates and Rasch analysis was used to ensure the psychometric properties of the outcome measures. This resulted in satisfactory model (fit) indices, suggesting that the prediction model is accurate and, therefore, promising for use in clinical practice. Most of the found predictors are comparable to those established in community subjects and in persons with other chronic disabilities,<sup>17-20</sup> an exception is the predictor younger age, which may be due to the disruptive influence of visual impairment at a relatively younger age when people are still working or, for instance, have to take care of their children. In addition, it was not the severity of the impairment

or the disability caused by it that proved to be critical for mental health in visually impaired older adults, but rather the individual's psychological response to this situation (acceptance of loss). This indicates that interventions need to focus on the acceptance of vision loss as an initial strategy to address depression. However, the influence of functional limitations on depression, which has been reported by others,<sup>21-24</sup> may have been overlooked in the present thesis because questions on visual functioning were combined in an overall vision-related quality of life score. In addition, although social support was not found to be a predictor, other studies found that this factor mediates the effect of vision loss on depression.<sup>23,24</sup> Moreover, environmental influences (e.g. accessibility of public spaces and facilities, sociocultural limitations) were not taken into account. Future studies should aim to investigate the influence of additional factors, with more emphasis on functional limitations (e.g. mobility, activities of daily living) and environmental influences, to further strengthen the knowledge on predictors of subthreshold depression in visually impaired older adults. In addition, it would be interesting to investigate if predictors of subthreshold anxiety differ from predictors of subthreshold depression in this population.

### Utilisation of and perceived need for mental health services

It is reported that depression and anxiety are under-detected and under-treated in visually impaired older adults.<sup>25-27</sup> However, evidence on mental healthcare utilisation and perceived need for these services in older adults with visual impairment is limited. This thesis shows that approximately 53% of older patients from low vision rehabilitation organisations with subthreshold depression and/or anxiety and 34% with an actual disorder do not receive any form of mental health services (Chapter 4). This may partly be due to the fact that especially non-mental healthcare staff (i.e. occupational therapists, physicians) underestimate the negative effects of vision loss on mental health, and standard procedures on screening and treating these symptoms are missing.<sup>26,27</sup> In practice, patients are only referred to a social worker or psychologist from the low vision rehabilitation organisation when symptoms of depression and/or anxiety are apparent and/or when patients ask for help themselves. Secondly, we found that especially older patients often do not perceive a need for professional mental health services or have difficulty in acknowledging and discussing this need. Patients are more likely to express a need for professional mental health services only when symptoms of depression and anxiety increase. About 29% of patients with subthreshold symptoms and 57% of patients with a disorder report to be in need of mental health services. The main reasons why patients do not receive treatment include lack of knowledge on mental illness and treatment possibilities, and self-reliance (i.e. the preference to solve one's emotional problems oneself).

Therefore, both patients and staff from low vision rehabilitation organisations need to be made aware of the high prevalence and recurrent nature of depression and anxiety, and of the evidence-based treatment possibilities to reduce these symptoms, even in a subclinical state of the conditions (i.e. low-intensity treatment). Professionals need to be made aware of the possibility that especially elderly patients may have difficulty in acknowledging and discussing a need for support and stimulate patients in overcoming this difficulty. In addition, feasible screening and monitoring procedures should become a routine part of low vision rehabilitation care. In this thesis, the Centre for Epidemiologic Studies Depression scale (CES-D) and the Hospital Anxiety and Depression Scale – Anxiety (HADS-A) were used to screen for symptoms of depression and anxiety.<sup>28-30</sup> Although these questionnaires provide a reliable outcome, for implementation the brief and validated Patient Health Questionnaire for depression and anxiety with four questions (PHQ-4) may be a suitable alternative.<sup>31</sup> This latter questionnaire, which can also be used by non-mental health staff, may easily be implemented in low vision rehabilitation care to screen for depression and anxiety, and to monitor these symptoms over a longer period of time.<sup>31</sup> When elevated symptoms of depression and/or anxiety are determined with this short screener, a more extensive questionnaire can be used to determine symptom severity. In addition, low-intensity psychological treatment options should be incorporated into low vision rehabilitation care to increase accessibility for patients and enable staff (even non-mental health staff) to help patients address these problems.

### Systematic review and meta-analysis on psychological treatment

In the past decades about 400 randomised controlled trials (RCTs) have examined the effects of psychological interventions for depression in adults; these showed that especially cognitive behavioural therapy (CBT), problem solving treatment (PST), behavioural activation, non-directive counselling, and interpersonal psychotherapy are effective in treating depression.<sup>32</sup> These interventions proved to be equally effective, and about equally effective as anti-depressants on the short term.<sup>33,34</sup> In addition, these interventions are equally acceptable in older adults,<sup>35</sup> and have a beneficial effect on reducing symptoms of depression and preventing the onset of disorders in patients with subthreshold symptoms.<sup>36</sup> Moreover, CBT seems to be beneficial in treating depression in people with comorbid somatic disorders (i.e. cancer, HIV infection, multiple sclerosis, rheumatoid arthritis, vascular disease, diabetes mellitus).<sup>37</sup> And, although fewer studies have investigated the effects of psychological interventions on anxiety, systematic reviews have shown that PST and CBT are also effective in reducing anxiety.<sup>38</sup>

Compared to the large body of research in the general population, research on treating depression and anxiety in people with visual impairment is still in its infancy. In this thesis, quantitative evidence on treating mental health problems in visually impaired adults in which (besides depression and anxiety) also loneliness, fatigue, psychological stress and psychological well-being were taken into account, was systematically reviewed and a meta-analysis with meta-regression was performed (Chapter 5). A total of 24 different trials were found, of which most aimed at investigating the effects of interventions on depression ( $n=18$ ), and only a few trials investigated the effects on anxiety ( $n=6$ ), psychological stress ( $n=4$ ), fatigue ( $n=2$ ) and loneliness ( $n=1$ ). It was found that psychological interventions in comparison with a control condition have a small significant overall effect on reducing depression and a medium significant overall effect on reducing anxiety in visually impaired adults. However, after removing a clear outlier these effects were no longer significant. Especially self-management programmes,<sup>39,40</sup> behavioural activation,<sup>41</sup> and PST<sup>42,43</sup> seem promising in reducing depression and anxiety in this population. However, evidence is scarce and long-term outcomes are either not available or were not reported. Mean age moderates the overall effects of interventions on depression, psychological stress and psychological well-being, indicating that interventions are less effective in the elderly and more attention needs to be paid to this age group in the future. In addition, few long-term outcomes were assessed to study maintenance effects of interventions and no information on the cost-effectiveness of treatments was found. Moreover, few high-quality studies were found and possible publication bias (based on funnels plots) was present, limiting the conclusions that can be drawn. Therefore, more high-quality studies with longer follow-up measurements, including outcome measures on anxiety, stress, fatigue and loneliness, and with specific focus on elderly populations are needed to enable to draw valid conclusions.

Based on the extensive research on interventions in reducing depression and anxiety in the general population (i.e. CBT, PST, behavioural activation), we expect that these interventions may also be effective in visually impaired older adults. The particular challenge lies in making these interventions accessible (regarding both content and design) for people with visual impairment. Different formats to present these interventions to increase accessibility and reduce healthcare costs should be explored. This implies that the RCT we conducted on the cost-effectiveness of a stepped care programme (with components of CBT and PST) investigated in this thesis, with a 24-month follow-up addressing both depression and anxiety in older adults with visual impairment, is particularly relevant.

### Effectiveness of the stepped care programme

To the best of our knowledge, the RCT presented in this thesis is the first to investigate a stepped care programme to address depression and anxiety in visually impaired older adults. Evidence-based treatment components were tailored to the needs of visually impaired older adults with

subthreshold depression and anxiety, based on focus group meetings with professionals and patients from low vision rehabilitation organisations. A two-armed single-masked multicentre RCT was performed, exactly as described in the original protocol (**Chapter 6**), to compare the effectiveness of this stepped care programme with usual care. Results show that the intervention is effective in preventing the incidence of major depressive, dysthymic and anxiety disorders in comparison with usual care (**Chapter 8**). After 24 months, 38 participants from the stepped care group (29%) compared with 62 participants from the usual care group (46%) developed a disorder (absolute difference 17%; 95% confidence interval (CI) 13 to 22). Compared to usual care the intervention significantly reduced the incidence of the disorders (relative risk 0.63; 95% CI 0.57 to 0.69), even if time to the event was taken into account (adjusted hazard ratio 0.57; 95% CI 0.35 to 0.93). The number needed to treat was 5.8. In both groups, most people developed a major depressive disorder (21% of the total study population), followed by dysthymia (11%), generalized anxiety disorder (11%), agoraphobia without history of panic disorder (9%), panic disorder (8%; 3% with agoraphobia and 5% without agoraphobia), and social phobia (7%). In addition, a significant improvement in symptoms of depression and anxiety and vision-related quality of life in favour of stepped care in comparison with usual care was found. These favourable results were achieved by investigating different protocol-driven treatment components, based on successful randomisation and single masking. Drop-out rates were high but acceptable (i.e. enough power was maintained and drop-out was not related to treatment allocation) and treatment fidelity was largely maintained. In contrast to previous trials in the field of low vision, this study addressed both depression and anxiety, which is relevant considering the high comorbidity of these conditions.<sup>44</sup> Moreover, the pragmatic design greatly enhanced the generalisability of the results.

Especially after the first two steps of the programme (i.e. watchful waiting and the self-help course) a difference in the incidence of depressive and anxiety disorders in favour of stepped care compared with usual care was found. Although it is not possible to assess the specific contributions of each individual step of the programme (based on the chosen design), these outcomes suggest that especially these steps are crucial. On the other hand, the latter steps may also be essential in maintaining the effects. Future studies might choose a dismantling approach to determine redundant treatment components. In addition, for some patients the 3-month watchful waiting period may not be appropriate (**Chapter 7**). Although watchful waiting is a relevant first step, i.e. overall symptoms of depression and anxiety are significantly reduced, many patients (18% of the total study population) still develop a disorder during this period, which might be prevented by offering treatment earlier. Although they were given the opportunity to do so, almost none of these patients contacted the research team or clinical staff when symptom severity increased. This may confirm our previous findings that elderly patients often do not perceive a need for treatment or have difficulty in acknowledging and discussing this need. Especially female patients, with difficulty adjusting to their vision loss, higher depression and anxiety symptoms at the start of watchful waiting, and a history of depressive or anxiety disorder, are more likely to develop a disorder during this period. Screening tools may be used to identify patients with these characteristics, who may benefit more from direct treatment or a shorter period of watchful waiting. In addition, offering a passive psychoeducational intervention (e.g. materials such as leaflets, emails or information websites), which are also very brief and inexpensive and prove to be effective in reducing symptoms of depression and anxiety in the general population,<sup>45</sup> may be an important addition to watchful waiting. It may help people deal with their symptoms of depression and anxiety and may help them to contact healthcare providers when symptoms increase.

Moreover, patients with a history of depressive or anxiety disorder do not respond well to the stepped care programme, i.e. they still frequently develop a disorder. For them the low-intensity treatments offered in our programme may not be sufficient; this is confirmed by another trial in which a similar stepped care programme was not effective in preventing relapse depression in older people.<sup>46</sup> People who experience recurrent disorders differ from those who experience first episodes, for instance a family history of depression and the number of previous episodes

play an important role in recurrent depressive disorder.<sup>47</sup> We believe these people would benefit more from a direct referral to their general practitioner (GP) to discuss further (higher-intensity) treatment options, and should not be treated with the low-intensity interventions of the stepped care programme offered in this thesis.

### Cost-effectiveness of the stepped care programme

To support the recommendation to implement the stepped care programme on a larger scale, the cost-effectiveness of the programme in comparison with usual care was evaluated (**Chapter 9**), which is highly relevant considering the increasing number of patients with visual disabilities due to an ageing society and the scarce resources available for healthcare. Moreover, an assumption of stepped care is that it reduces healthcare costs by offering lower-intensity treatment (with lower costs) first. We found that, in addition to the positive clinical outcomes, the stepped care programme is associated with modest (non-significant) cost savings, mainly due to decreased secondary mental healthcare utilisation and less hospitalisation, as compared to usual care. The probability that the intervention is cost-effective compared to usual care is 59%, 77%, 88% and 95% or more when society is willing to pay €0, €10,000, €20,000 and €33,000 per disorder prevented, respectively. Decision makers need to decide whether these are acceptable probabilities and amounts of money for society to pay to prevent one anxiety or depressive disorder in older adults with visual impairment.

Future studies should investigate how the cost-effectiveness of the stepped care programme in comparison with usual care can be improved. An option would be to tailor interventions to the need for treatment as expressed by patients and their symptom severity, i.e. the period of watchful waiting may differ based on symptom severity and personal needs, and patients with a history of depressive or anxiety disorder may benefit from receiving higher-intensity treatment options. In addition, other evidence-based treatment options could be added to the model (e.g. behavioural activation or exercise programmes), and the self-help course (step 2 of the programme) could be offered as an internet-based therapy, which has proven to be effective in the general population,<sup>48</sup> to increase the cost-effectiveness of the programme.

### Strengths and limitations

This thesis has several strengths. It provides a broad view on depression and anxiety in visually impaired older adults, i.e. prevalence estimates and related factors were determined, patients' perspectives on receiving mental health services were explored, and treatment possibilities were evaluated. In addition, evidence from previous studies was systematically reviewed and analysed to be able to determine a targeted approach for the work performed in this thesis. Therefore, this work offers important additional information to the growing body of research on depression and anxiety in people with visual impairment. In contrast to previous research, this thesis addressed both depression and anxiety in visually impaired older adults because of the high comorbidity of these conditions. Moreover, a high-quality RCT with a long follow-up (24 months) was performed to investigate both the effectiveness and cost-effectiveness of a stepped care intervention, whereas previous research on psychological interventions in the field of low vision failed to take the cost-effectiveness of interventions into account. The pragmatic design of the RCT supports the economic evaluation and increases the generalizability of the results. The stepped care intervention was adapted to the needs of visually impaired older adults and implemented in low vision rehabilitation care, which may increase the accessibility of psychological support for people with visual impairment and the continuation of the intervention after the trial. Both occupational therapists (who often have the first contact with patients), social workers, and psychologists were involved in offering the intervention, which contributes to broad support for the intervention and attention for symptoms of depression and anxiety within the low vision rehabilitation centres. In addition, large sample sizes were used to determine the outcomes, which increases the reliability of the results. Therefore, the outcomes of the work presented in this thesis may prove to be important for both research and clinical practice.

However, the work described here also has some limitations. First, we focus on patients from low vision rehabilitation organisations only. Therefore, the outcomes cannot be generalized to visually impaired older adults who do not receive these services. Second, our validated prediction model was based on cross-sectional data. Therefore, it is not possible to infer causality between the identified risk factors and subthreshold depression. Future studies are necessary to determine whether these factors lead to change in depression over time. Third, the performed RCT had a single-blinded study design in combination with patient reported outcomes. The fact that participants were not blinded may have exaggerated the treatment effects for the subjective outcomes. Fourth, it may be argued that the limited number of participants who had a history of depressive or anxiety disorder in our trial (i.e. 69 participants) limit conclusions that can be drawn on the effectiveness of stepped-care in comparison with usual care in people who have a history of these disorders compared to people who do not. Fifth, the self-reported cost questionnaires that were used for the economic evaluation are prone to recall bias and the results are only representative for the Dutch setting preventing generalizability to other countries. Finally, although our stepped care programme was compared with usual care, enabling us to compare the intervention with routine clinical practice, we could not investigate the actual gain of the stepped care service delivery model (containing different treatment components) compared to for instance one (high intensity) treatment component. Final conclusions on the cost-effectiveness of the stepped care model can only be drawn when it is compared with other (possibly less cost-effective) healthcare systems, such as matched care (the current standard approach) or high-intensity care.<sup>49</sup>

### Implications for practice and future research

Based on the outcomes of this thesis, it cannot be denied that both depression and anxiety are major problems in visually impaired older adults. Especially female patients with a relatively younger age, who have a history of mental health problems, live alone, have poorer health and lower acceptance of vision loss, should be carefully monitored and screened for depression. In addition, many patients do not receive treatment. This may be because standard screening and treating procedures are missing or because especially older patients with lower symptoms of depression and anxiety do not perceive a need for professional mental health services. Therefore, screening and monitoring procedures should become a routine part of low vision rehabilitation care. Both patients and staff need to become aware of the high prevalence and recurrent nature of these conditions, and (low intensity) evidence-based treatment options to address depression and anxiety should be implemented in low vision rehabilitation care to increase the accessibility of mental health services for people with visual impairment.

The stepped care programme investigated in this thesis is a promising intervention to treat depression and anxiety in visually impaired older adults, since it is clinically superior to usual care. The incidence of depressive and anxiety disorders was significantly reduced by offering this programme in low vision rehabilitation care. In addition, stepped care is associated with modest cost savings compared with usual care and the probability that the intervention is cost-effective compared with usual care is 95% or more at a willingness-to-pay of €33,000 per disorder prevented. This is a significant investment and decision makers need to decide whether this is an acceptable amount of money for society to pay. Future studies should investigate how the cost-effectiveness of stepped care in comparison with usual care can be optimised. Options that could

be explored are: 1) tailoring interventions to the need for treatment as expressed by patients and have them choose from different treatment options, 2) tailoring the watchful waiting period to symptom severity and adding passive psychoeducational interventions, 3) adding other evidence-based treatment options to the model (e.g. exercise programmes), 4) directly referring patients with a history of depressive or anxiety disorder to higher intensity treatment, and 5) exploring if offering (internet-based) e-mental health interventions would increase the cost-effectiveness of the programme and would be feasible in a visually impaired population.

Moreover, future studies may aim to investigate the cost-effectiveness of the different treatment components (based on a more explanatory trial design), and aim to investigate stepped care compared with other service delivery models (such as matched care or high-intensity treatment) to be able to determine the actual gain of the stepped care service delivery model in addressing depression and anxiety in visually impaired older adults. Finally, we expected stepped care to positively influence acceptance of vision loss, which is an important predictor of having subthreshold depression in visually impaired older adults, however, this was not the case. Future studies may investigate other possible mediating factors (e.g. illness cognitions, problem solving ability, quality of the therapeutic relationship) to gain knowledge on underlying mechanisms that actually cause the intervention to prevent depressive and anxiety disorders and reduce symptoms of depression and anxiety in older adults with visual impairment.

## References

- Brody BL, Gamst AC, Williams RA, et al. Depression, visual acuity, comorbidity, and disability associated with age-related macular degeneration. *Ophthalmol* 2001;108(10):1893-1900.
- Hayman KJ, Kerse NM, La Grow SJ, Woules T, Robertson MC, Campbell AJ. Depression in older people: visual impairment and subjective ratings of health. *OptomVis Sci* 2007;84:1024-30.
- Lotery A, Xu X, Zlatava G, Loftus J. Burden of illness, visual impairment and health resource utilisation of patients with neovascular age-related macular degeneration: results from the UK cohort of a five-country cross-sectional study. *Br J Ophthalmol* 2007;91:1303-7.
- Tsai SY, Cheng CY, Hsu WM, Su TP, Liu JH, Chou P. Association between visual impairment and depression in the elderly. *J Formos Med Assoc* 2003;102:86-90.
- Evans JR, Fletcher AE, Wormald RP. Depression and anxiety in visually impaired older people. *Ophthalmology* 2007;114:283-8.
- Diepeveen C, Teurlings L, Verstraten P. Ooit gezien maar nog niet uitgekeken. Houten/Diegem: Bohn Stafleu van Loghum; 2000. Dutch.
- Royal Dutch Visio. Visiedocument expertisegroep psychosociaal: Hulp bij psychosociale gevolgen van visuele beperking. Huizen: Royal Dutch Visio; 2014. Dutch.
- Smit F, Ederveen A, Cuijpers P, Deeg D, Beekman A. Opportunities for cost-effective prevention of late-life depression: an epidemiological approach. *Arch Gen Psychiatry* 2006; 63:290-296.
- Hayman KJ, Kerse NM, La Grow SJ, et al. Depression in older people: visual impairment and subjective ratings of health. *Optom Vis Sci* 2007;84:1024-30.
- Tsai SY, Cheng CY, Hsu WM, et al. Association between visual impairment and depression in the elderly. *J Formos Med Assoc* 2003;102:86-90.
- 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.
- Tolman J, Hill RD, Kleinschmidt JJ, Gregg CH. Psychosocial adaptation to visual impairment and its relationship to depressive affect in older adults with age-related macular degeneration. *Gerontologist* 2005;45:747-53.
- Rees G, Xie J, Holloway EE, et al. Identifying distinct risk factors for vision-specific distress and depressive symptoms in people with vision impairment. *Invest Ophthalmol Vis Sci* 2013;54:7431-8.
- Zheng DD, Bokman CL, Lam BL, et al. Longitudinal relationships between visual acuity and severe depressive symptoms in older adults: the Salisbury Eye Evaluation study. *Aging Ment Health* 2015;1-8.
- Brody BL, Gamst AC, Williams RA, et al. Depression, visual acuity, comorbidity, and disability associated with age-related macular degeneration. *Ophthalmol* 2001;108:1893-900.
- Rovner BW, Casten RJ, Tasman WS. Effect of depression on vision function in age-related macular degeneration. *Arch Ophthalmol* 2002;120:1041-4.
- Cole MG, Dendukuri N. Risk factors for depression among elderly community subjects: a systematic review and meta-analysis. *Am J Psychiatry* 2003;160:1147-56.
- Hackett ML, Anderson CS. Predictors of depression after stroke: a systematic review of observational studies. *Stroke* 2005;36:2296-301.
- Pizzi C, Manzoli L, Mancini S, Costa GM. Analysis of potential predictors of depression among coronary heart disease risk factors including heart rate variability, markers of inflammation, and endothelial function. *Eur Heart J* 2008;29:1110-7.
- Fisher L, Chesla CA, Mullan JT, Skaff MM, Kanter RA. Contributors to depression in Latino and European-American patients with type 2 diabetes. *Diabetes Care* 2001;24:1751-7.
- Casten R, Rovner B. Update on depression in age-related macular degeneration. *Curr Opin Ophthalmol* 2013;24:239-43.
- Rees G, Xie J, Holloway EE, et al. Identifying distinct risk factors for vision-specific distress and depressive symptoms in people with vision impairment. *Invest Ophthalmol Vis Sci* 2013;54:7431-8.
- van Nispen RM, Vreeken HL, Comijs HC, Deeg DJ, van Rens GH. Role of vision loss, functional limitations and the supporting network in depression in a general population. *Acta Ophthalmol* 2016;94:76-82.
- Kempen GIJM, Ranchor AV, Ambergen T, Zijlstra GAR. The mediating role of disability and social support in the association between low vision and depressive symptoms in older adults. *Qual Life Res* 2014;23:1039-43.
- Casten R, Rovner B. Update on depression in age-related macular degeneration. *Curr Opin Ophthalmol* 2013;24:239-43.
- Rees G, Fenwick EK, Keeffe JE, Mellor D, Lamoureux EL. Detection of depression in patients with low vision. *Optom.Vis.Sci.* 2009;86(12):1328-1336.
- Fenwick EK, Lamoureux EL, Keeffe JE, Mellor D, Rees G. Detection and management of depression in patients with vision impairment. *Optom Vis Sci* 2009;86(8):948-954.
- Beekman AT, Deeg DJ, Van Limbeek J, Braam AW, De Vries MZ, Van Tilburg W. Criterion validity of the Center 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.
- Haringsma R, Engels GI, Beekman AT, Spinhoven P. The criterion validity of the Center for Epidemiological Studies Depression Scale (CES-D) in a sample of self-referred elders with depressive symptomatology. *Int J Geriatr Psychiatry* 2004;19:558-63.
- Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002;52:69-77.
- Kroenke K, Spitzer RL, Williams JB, Löwe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. *Psychosomatics* 2009;50:613-21.
- Cuijpers P. Psychotherapies for adult depression: recent developments. *Curr Opin Psychiatry* 2015; 28: 24-9.
- Barth J, Munder T, Gerger H, et al. Comparative efficacy of seven psychotherapeutic interventions for depressed patients: a network meta-analysis. *PLoS Med* 2013; 10: e1001454.
- Cuijpers P, Sijbrandij M, Koole SL, et al. The efficacy of psychotherapy and pharmacotherapy in treating depressive and anxiety disorders: a meta-analysis of direct comparisons. *World Psychiatry* 2013; 12:137-48.
- Cuijpers P, van Straten A, Smit F, Andersson G. Is psychotherapy for depression equally effective in younger and older adults? A meta-regression analysis. *Int Psychogeriatr* 2009; 21: 16-24.
- Cuijpers P, Koole SL, van Dijke A, et al. Psychotherapy for subclinical depression: a meta-analysis. *Br J Psychiatry* 2014; 205:268-74.
- Beltman MW, Voshaar RC, Speckens AE. Cognitive-behavioural therapy for depression in people with a somatic disease: meta-analysis of randomized controlled trials. *Br J Psychiatry* 2010; 197: 11-9.
- Seekles W, Cuijpers P, Kok R, Beekman A, van Marwijk H, van Straten A. Psychological treatment of anxiety in primary care: a meta-analysis. *Psychol Med* 2013; 43: 351-61.
- 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.
- 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.
- 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.
- 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.
- Rovner BW, Casten RJ. Preventing Late-life Depression in Age-Related Macular Degeneration. *Am J Geriatr Psychiatry* 2008;16:454-9.
- Cairney J, Corna LM, Veldhuizen S, Herrmann N, Streiner DL. Comorbid depression and anxiety in later life. patterns of association, subjective well-being, and impairment. *Am J Geriatr Psychiatry* 2008, 16(3):201-208.
- Donker T, Griffiths KM, Cuijpers P, Helen Christensen H. Psychoeducation for depression, anxiety and psychological distress: a meta-analysis. *BMC Med* 2009; 7:79.
- Apil SR, Hoencamp E, Judith Haffmans PM, Spinhoven P. A stepped care relapse prevention program for depression in older people: a randomized controlled trial. See comment in PubMed Commons below *Int J Geriatr Psychiatry* 2012;27:583-91.

47. Burcusa SL, Iacono WG. Risk for recurrence in depression. *Clin Psychol Rev* 2007;27:959-85.
48. Wagner B, Horn AB, Maercker A. Internet-based versus face-to-face cognitive-behavioral intervention for depression: a randomized controlled noninferiority trial. *J Affect Disord* 2014; 152: 113-21.
49. van Straten A, Hill J, Richards DA, Cuijpers P. Stepped care treatment delivery for depression: a systematic review and meta-analysis. *Psychological Medicine* 2015; 45: 231-46.