

Chapter 1:
General introduction

The work presented in this thesis focuses on depression and anxiety in visually impaired older adults (aged 50 years or older) from outpatient low vision rehabilitation organisations in the Netherlands and Belgium. To this end, the prevalence of depression and anxiety, a prediction model of having depression, and the utilisation of and perceived need for mental health services in this population are evaluated. In addition, the cost-effectiveness of a stepped care programme, implemented in low vision rehabilitation care, to address depression and anxiety in this population is investigated in a two-armed multicentre randomised controlled trial (RCT). Presented below is general information on the healthcare problem, main concepts and theoretical assumptions that motivated the aims and design of this thesis.

Vision, identity and environment

People give meaning to their life by interacting with their environment. From birth (and even before), people make contact with their environment through their senses. By seeing the effect of their actions, observing others and copying their behaviour, people learn to express themselves, and learn what is and is not accepted.^{1,2} Through their senses people gradually come to know themselves and their relation to the physical and social environment. Vision can be considered the most effective and efficient sense.^{1,2} When entering an unknown environment, within seconds people receive a wealth of information through their visual system. By combining this information with existing knowledge, people know, for instance, if there is danger, what objects and what kind of people are present, what the atmosphere and context is, and where and how they can sit down. No other sense equals this speed and accuracy.^{1,2} Over the last decades visual expectations have even been increasing due to the advancing visual culture and a digital world that demand an accelerated pace of life, in which good vision is more than helpful.² Therefore, partial or complete vision loss can have a major impact on people's lives.

Visual impairment in an ageing society

The definitions of low vision and blindness proposed by the World Health Organisation (WHO) are often used to describe visual impairment. The WHO defines low vision as the best corrected visual acuity in the better eye of <0.3 but ≥ 0.05 (Snellen notations) and/or a visual field of $<20^\circ$ around the central point of fixation, and blindness as a visual acuity of <0.05 and/or a visual field of $<10^\circ$ of fixation.³ Worldwide, various definitions of visual impairment are used for different purposes, such as criteria for health insurance, scientific research, or referral to low vision rehabilitation. In this thesis, the definition of the Dutch guideline for low vision rehabilitation is used, stating that all patients should have a visual acuity of ≤ 0.3 and/or a visual field of $\leq 30^\circ$ of fixation (or other severe visual field defects, such as hemianopia) and/or an evident help request for which options in regular ophthalmic practice are not adequate.⁴

According to the WHO, 285 million people worldwide are visually impaired, of whom 246 million have low vision and 39 million are blind.³ The burden of visual impairment is not equally distributed throughout the world: the least developed or low-income countries carry the largest burden (about 80%), where vision loss is mainly caused by treatable or preventable conditions. In more developed or high-income countries visual impairment is primarily a problem of the elderly, who may also have other functional or psychological limitations.³ In the Netherlands, 315,900 people were visually impaired in 2009 of whom 89% were aged 50 years or older.⁵ Because of an ageing society, the number of people with visual impairment of 50 years and older is expected to increase with 23% by the year 2020.^{5,6}

The most common causes of visual impairment in older adults are age-related macular degeneration (AMD), glaucoma, diabetic retinopathy, and cataract. AMD causes damage to the macula (the central part of the retina) reducing central vision, which can make it difficult or impossible to read, recognise faces, or drive a car.⁷ In glaucoma the optic nerve is gradually destroyed, which is mostly caused by an increased intraocular pressure. This may lead to gradual visual field loss (peripheral vision is usually affected) and decreased contrast and light sensitivity.⁸ Diabetic retinopathy is a

complication of diabetes mellitus in which prolonged periods of disturbed blood glucose levels damage the small blood vessels in the retina, which may lead to large 'blind spots' and eventually to severe vision loss.⁹ Cataract causes a gradual opacification of the lens leading to blurred vision, glare and haloes. Fortunately, surgery aimed at cataract extraction and implantation of an intraocular lens is very successful in restoring vision.¹⁰ However, this is not always the case for patients with additional eye conditions. Although developments in the treatment of these diseases are progressing, for AMD, glaucoma and diabetic retinopathy there is currently no cure.

In addition, visual impairment can be caused by brain damage (e.g. by stroke, brain tumour or head injury). Vision is the product of a complex system of which the eyes are only one part. Visual stimuli are received through the eyes, interpreted by various brain centres, and finally translated into visual images. When the visual systems of the brain do not consistently understand or interpret what the eyes see, this will lead to (cerebral) visual impairment.¹¹

Disability caused by visual loss

The WHO defines disability as any limitation or function loss, deriving from an impairment that prevents the performance of activities considered normal for human beings.¹² The International Classification of Functioning, Disability and Health is used to define disability as a broad term for activity limitations, impairments and participation restrictions. It is defined as the interaction between: i) individuals with a health condition and personal factors (originating from the medical model of disability), and ii) environmental influences, such as negative social attitudes, inaccessible buildings and public spaces (originating from the social model of disability).¹²

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 security, identity and meaning can be lost.¹³⁻¹⁹ People derive their social identity from comparison with and expectations from others. Reduced possibilities for participation, communication and autonomy may affect people's social status, identity and relationships with others.^{1,2} The disability may be difficult to understand for partners, family members and friends, who may be overwhelmed by the consequences of having to take care of their loved one.^{1,2} In addition, visually impaired people are a minority within our society. Most other people have limited understanding of the nature and consequences of their impairment and may have negative attitudes towards their disability. This may isolate visually impaired persons and induce feelings of shame, which may restrain them from using low vision aids, such as an identification cane.^{1,2} The design of public spaces, buildings and facilities (e.g. supermarkets, ATMs, medical facilities) and the limited opportunities for attractive and adaptable work are also a great challenge for visually impaired persons and may reduce their participation in society.^{1,2}

Depression and anxiety in visually impaired older adults

Vision loss requires significant adaptation; not only on a practical and social level, but first and foremost on a psychological level. People need to integrate everything that is lost, including their self-image. This is even more difficult with the anticipation of further vision loss (eye diseases are often degenerative) and may also occur in a later stage of the disease/impairment, for instance when people lose their sight completely or lose their partner or caregiver. Many people may start feeling depressed or anxious in such situations.¹³⁻¹⁹ In most cases this is a normal reaction to an experience of loss and would not be considered a mental illness. Depressed mood may be part of the grieving process and anxiety or fear may be necessary emotions, for instance when it stops people from independently participating in traffic when the threat of getting harmed is very real. However, if depression and anxiety interfere with normal functioning and prolong for a longer period of time, clinical interference may be necessary.^{20,21}

Different clinical levels of depression and anxiety can be distinguished. There is general consensus on the definition of major depressive disorder, dysthymic disorder and the most prevalent anxiety

disorders: panic disorder, agoraphobia, social phobia and generalized anxiety disorder.²⁰ In this thesis the fourth edition of the diagnostic and statistical manual of mental disorders (DSM-IV-TR) with standard classifications of these mental disorders was used (Box 1).²⁰ In 2013, when the studies described in this thesis were already being conducted, the fifth edition of the DSM was published.²¹ However, these new criteria could not be incorporated in the studies conducted in this thesis. The most important changes are described in Box 1.

BOX 1. Criteria for mental disorders based on the diagnostic statistical manual (DSM)

DSM-IV criteria*	Changes in DSM-V
<p>Major Depressive Disorder: Depressed mood or a loss of interest or pleasure in daily life activities for at least 2 weeks and at least 5 of the following 9 symptoms that cause significant impairment in social, occupational or other important areas of functioning:</p> <ol style="list-style-type: none"> 1. Depressed mood most of the day, nearly every day 2. Diminished interest or pleasure in most activities, most of each day 3. Significant unintentional weight change or change in appetite 4. Change in sleep: insomnia or hypersomnia 5. Change in activity: psychomotor agitation or retardation 6. Fatigue or loss of energy 7. Guilt or feelings of worthlessness 8. Concentration: diminished ability to think or concentrate, or indecisiveness 9. Suicidality: recurrent thoughts of death <p>Symptoms are not better accounted for by bereavement (i.e. after the loss of a loved one) within the first two months.</p>	<p>The bereavement exclusion has been removed.</p>
<p>Dysthymic Disorder: Depressed mood most of the day for more days than not, for at least 2 years, and the presence of two or more of the following symptoms that cause significant impairment in social, occupational or other important areas of functioning:</p> <ol style="list-style-type: none"> 1. Poor appetite or overeating 2. Insomnia or sleeping too much 3. Low energy or fatigue 4. Low self-esteem 5. Poor concentration or difficulty making decisions 6. Feelings of hopelessness 	<p>What was referred to as dysthymia in DSM-IV now falls under the category of persistent depressive disorder, which includes both chronic major depressive disorder and the previous dysthymic disorder.</p>
<p>Panic disorder (with or without agoraphobia): Recurrent unexpected panic attacks and at least one of the attacks have been followed by 1 month (or more) of one (or more) of the following symptoms:</p> <ol style="list-style-type: none"> 1. Persistent concern about having additional attacks 2. Worry about the implications of the attack or its consequences (e.g., losing control, "going crazy") 3. A significant change in behaviour related to the attacks 4. The presences or absence of agoraphobia 	<p>Panic disorder with agoraphobia, panic disorder without agoraphobia, and agoraphobia without history of panic disorder are replaced by two diagnoses: panic disorder and agoraphobia, each with separate criteria.</p>

BOX 1. Continued

<p>Agoraphobia (without history of panic disorder):</p> <ol style="list-style-type: none"> 1. Anxiety about being in places or situations from which escape might be difficult (or embarrassing) or in which help may not be available in the event of having an unexpected or situationally predisposed panic attack. Typically involving situations that include being outside the home alone; being in a crowd, or standing in a line; being on a bridge; or traveling in a train, bus, or automobile. 2. The situations are avoided (e.g., travel is restricted) or else are endured with marked distress or with anxiety about having a panic attack, or require the presence of a companion. 3. Criteria for panic disorder have never been met. 	<p>Endorsement of fears from two or more agoraphobic situations is now required, to distinguish this from specific phobias.</p>
<p>Social phobia or social anxiety disorder:</p> <ol style="list-style-type: none"> 1. A marked and persistent fear of one or more social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others. The individual fears that he/she will act in a way (or show anxiety symptoms) that will be humiliating or embarrassing. 2. Exposure to the feared social situation almost invariably provokes anxiety, which may take the form of a situationally bound or situationally predisposed panic attack. 3. The person recognises that the fear is excessive or unreasonable. 4. The feared social or performance situations are avoided or else are endured with intense distress or anxiety. 5. The avoidance, anxious anticipation, or distress in the feared social or performance situation(s) interferes significantly with the person's normal routine, occupational (academic) functioning, or social activities or relationships, or there is marked distress about having the phobia. 6. The duration is at least 6 months. 	<p>The requirement that adults recognise that their anxiety is excessive or unreasonable is deleted and the duration criterion is slightly changed and now required for all ages.</p>
<p>Generalized anxiety disorder:</p> <ol style="list-style-type: none"> 1. Excessive anxiety and worry (apprehensive expectation), occurring more days than not for at least 6 months, about a number of events or activities. 2. Difficulty to control the worry. 3. The anxiety and worry are associated with three (or more) of the following six symptoms (with at least some symptoms having been present for more days than not for the past 6 months): <ol style="list-style-type: none"> 1. Restlessness or feeling keyed up or on edge 2. Being easily fatigued 3. Difficulty concentrating or mind going blank 4. Irritability 5. Muscle tension 6. Sleep disturbance 4. The anxiety, worry, or physical symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. 	<p>No changes have been made.</p>

* For all diagnoses applies that symptoms are not due to the direct physiological effects of a substance (e.g., a drug, medication) or a general medical condition, and are not better accounted for by another mental disorder.

In addition, subthreshold depression and anxiety (indicating clinically relevant symptoms but no actual disorder according to the diagnostic criteria) are increasingly being recognised as significant clinical entities,²² since they are associated with decreased levels of health-related quality of life,²³ generate a substantial economic burden due to increased healthcare utilisation and productivity losses,^{24,25} and are associated with higher mortality rates.²⁶ In addition, they are the most important

predictors of developing actual disorders.²⁷ There is a wide range of definitions of subthreshold depression and anxiety, and not all of them share the same criteria related to the number of symptoms or the influence on individual functioning.²² In this thesis, two widely used and validated questionnaires were used to determine subthreshold depression and anxiety: the Centre for Epidemiologic Studies Depression scale (CES-D, with a score of ≥ 16 indicating subthreshold depression and/or anxiety),^{28,29} and the Hospital Anxiety and Depression Scale - Anxiety (HADS-A, with a score of ≥ 8 indicating subthreshold anxiety).³⁰ About one-third of visually impaired older adults experience subthreshold depression and/or anxiety,¹⁵⁻¹⁹ which is about twice as high as the prevalence estimated in the general older population (about 16%).³¹⁻³³ Depression and anxiety can have a detrimental impact on visually impaired older adults, leading to decreased health-related and vision-related quality of life.³⁴⁻³⁶

Multidisciplinary low vision rehabilitation

Although vision loss has a major impact, there are ways to help people deal with this loss by offering them practical and psychological support. In the Netherlands and Belgium, multidisciplinary services are provided by regional low vision rehabilitation organisations to support people in dealing with their visual impairment. These services include all measures aimed at reducing the impact of the disabling condition and improving quality of life. Although people can contact these organisations independently, a referral by a general practitioner (GP), ophthalmologist or by another physician is required. Mostly outpatient rehabilitation services are provided, i.e. assessing visual functioning, prescribing low vision aids, training in activities of daily living for example by occupational therapists (such as mobility training or computer training), and individual and group counselling by psychologists or social workers.⁴

In the Netherlands, low vision rehabilitation is operated by two large organisations: 'Royal Dutch Visio', 'Bartiméus', and the smaller 'Robert Coppes foundation'. In Belgium several organisations provide these services, of which 'Blindenzorg Licht & Liefde' is one. At present, these organisations have no structural policies to identify and treat depression and anxiety in visually impaired older adults, especially in a subthreshold state of the conditions. Therefore, symptoms are often not recognised and these visually impaired older adults may not receive mental health services.

Mental healthcare

The first step in offering mental healthcare for people with visual impairment is to screen for and monitor depression and anxiety, as these symptoms are notoriously under-detected and under-treated in this population.^{35,37} Care providers tend to underestimate the negative effects of vision loss on mental health and standard procedures are missing.^{37,38} Secondly, evidence-based interventions should be offered to help people deal with depression and anxiety. There is increasing research on interventions to address depression in people with visual impairment.^{35,39,40} It is recognised that targeted interventions are necessary to address depression in this high-risk group, in which functional ability and mental health are closely related.³⁵ There is some evidence for the effectiveness of problem solving treatment and self-management programmes to address depression in this population.^{35,39,40} However, so far, evidence is scarce and long-term effective results are often lacking. Moreover, evidence for interventions to address anxiety is especially scarce. Although anxiety is also a prevalent problem in older adults with visual impairment and often overlaps with symptoms of depression (many risk factors are shared and similar treatments have shown to be effective)⁴¹ it is remarkably understudied. Therefore, this thesis addresses both these disabling conditions in visually impaired older adults.

Prevention

Three types of interventions to prevent mental disorders are distinguished by Mrazek & Haggerty.⁴² Firstly, universal preventive interventions that are aimed at the total population regardless of any risk status (e.g. media campaigns). Secondly, selective preventive interventions that are aimed at people who have been exposed to risk factors and, therefore, have an increased risk

of developing a mental disorder, but have not yet developed symptoms (e.g. support groups). Thirdly, indicated preventive interventions that are aimed at people who show subthreshold symptoms, but do not yet meet the diagnostic criteria of a disorder. This type of prevention aims to delay or prevent the onset of new cases and reduce the severity of subthreshold symptoms. These symptoms are the most important predictors of developing actual disorders.²⁷ Indicated prevention mostly resembles conventional treatment and well-designed interventions based on indicated prevention are promising in reducing mental disorders.⁴³ In the Netherlands, indicated prevention is incorporated in mental healthcare. Regional mental healthcare institutes often have a specialised department that provides this type of prevention, in which they closely collaborate with primary healthcare professionals. Because this type of prevention is promising, the stepped care intervention investigated in this thesis is aimed at indicated prevention.

Stepped care

Both Dutch and British mental health guidelines (i.e. the National Institute for Health and Clinical Excellence) recommend using a stepped care service delivery model in patients with symptoms of depression.^{44,45} In stepped care, patients receive subsequent treatment components by order of intensity, i.e. patients start with low-intensity interventions and only move on to higher-intensity interventions when a sufficient response is lacking. Symptoms are monitored systematically throughout the entire process. With this care model, the aim is to maximise the effectiveness of an intervention and make the best use of available resources.⁴⁵

Studies in various populations show favourable results for stepped care in reducing depression.⁴⁶ One study by van 't Veer and colleagues, showed that a stepped care programme with four consecutive steps for older people with subthreshold depression and/or anxiety from primary care practices was effective in preventing major depressive and anxiety disorders (relative risk 0.49).⁴⁷ This programme is used as an example to develop the stepped care programme for people with visual impairment that is described in this thesis. The programme is tailored to the needs of people with visual impairment based on multiple focus groups with social workers and psychologists from low vision rehabilitation organisations and patient representatives. Exercises and examples are altered and specific attention is paid to the physical and psychological consequences of vision loss and the difficulty of adapting to this impairment. In addition, specific attention is paid to the manner in which the programme is offered (e.g. Braille and audio version of written documents).

The final programme contains four steps that take approximately three months each. The first step is a period of watchful waiting, involving an active decision to not directly treat subthreshold depression and anxiety, but, instead, to intermittently reassess the symptoms after three months.⁴⁸ This may be an appropriate first step since many patients remit from subthreshold depression and anxiety without offering active treatment.^{49,50} Therefore, this approach may prevent overtreatment and reduce healthcare costs.⁴⁸ In the second step, an extended and altered version of the 'Coping with Depression' self-help course is offered, with elements of cognitive behavioural therapy (CBT). This course has been found effective in preventing major depressive and anxiety disorders in community subjects and is used in routine practice in several countries.⁵¹ The altered course (called 'Blik op je Dip' in Dutch) that is used in this thesis, is available in written, digital, audio and Braille formats and is supported by trained occupational therapists from low vision rehabilitation organisations. The course contains seven chapters on: 1) depression and anxiety in relation to having visual impairment, 2) fatigue and stress in relation to depression and anxiety in people with visual impairment, 3) pleasurable activities can still be carried out despite being visually impaired, 4) replacing self-defeating thoughts with healthier thoughts, 5) negative thought patterns and replace unhelpful with helpful thoughts, 6) personal communication styles, and 7) reflecting on everything that has been learned and setting goals for the future. If this intervention is insufficient in reducing subthreshold depression and anxiety, people move on to the third step, in which they receive problem solving treatment (PST). PST has been found effective in reducing depression in older adults and short-term effective results have been found on preventing depressive

disorder in older adults with AMD.^{52,53} In this thesis, PST is offered by trained social workers and psychologists from low vision rehabilitation organisations, based on a maximum of seven sessions. During each session seven steps of PST are completed: 1) clarify the problem, 2) establish realistic goals, 3) generate multiple alternative solutions by brainstorming, 4) explore pros and cons of the alternative solutions, 5) select the best solution, 6) conduct a plan to carry out the best solution, and 7) evaluate the process. If elevated symptoms of depression and anxiety still persist after this third step, patients move to the fourth and final step of the programme, in which they are referred to their GP to discuss further treatment and the use of medication. Participants who develop an actual depressive and/or anxiety disorder during the course of the intervention are directly referred to their GP.

A two-armed multicentre RCT with a pragmatic design is performed to investigate the effectiveness of the stepped care programme compared with usual care. This design is chosen to test the intervention in the full spectrum of everyday clinical practice in order to maximise generalisability. The programme is offered by trained and experienced low vision rehabilitation staff. Along with an economic evaluation, this trial can inform healthcare providers and decision makers of treatment effectiveness and costs in real-life situations.

Aim and outline of the thesis

The aim of the work presented in this thesis is to gain knowledge about depression and anxiety in visually impaired older adults. The first section is aimed at depression and anxiety in this population and has the following chapters:

- In *Chapter 2* prevalence estimates of subthreshold depression and anxiety, major depressive, dysthymic and anxiety disorders (i.e. panic disorder (with and without agoraphobia), agoraphobia (without history of panic disorder), social phobia and generalized anxiety disorder) in visually impaired older adults are determined and compared with normally sighted peers.
- In *Chapter 3* a multivariable prediction model for having subthreshold depression is internally validated in a Dutch/Belgian sample of visually impaired older adults and is externally validated in a comparable Australian sample.
- In *Chapter 4* the utilisation of, perceived need for, and barriers to use mental health services in older adults with visual impairment is investigated. Andersen's Behavioural Model is used as a framework to determine factors related to needs for mental health services from the patient's perspective.
- In *Chapter 5* a systematic review on treatment of mental health problems in visually impaired adults is presented. Literature is systematically searched and selected, and a meta-analysis with meta-regression is performed to analyse the effects of interventions on psychological outcome measures of relevant studies.

The second section is aimed at investigating a stepped care programme to address depression and anxiety in visually impaired older adults. This section has the following chapters:

- In *Chapter 6* the design and protocol development of the stepped care programme, incorporated in low vision rehabilitation care, is presented. A detailed description of the study design, setting, population and intervention is given.
- In *Chapter 7* the effect of watchful waiting, the first step of the stepped care programme, is described. Remission rates of subthreshold depression and anxiety, incidence rates of major depressive and anxiety disorders, and associated predictors are assessed.
- In *Chapter 8* the effectiveness of the stepped care programme in comparison with usual care in preventing the incidence of major depressive and anxiety disorders in visually impaired older adults with subthreshold depression and/or anxiety is investigated in an RCT. Secondary outcomes are: symptoms of depression and anxiety, adaptation to vision loss and vision- and health-related quality of life. In addition, a process evaluation is presented.
- In *Chapter 9* an economic evaluation of the stepped care programme in comparison with usual care is presented; both a cost-effectiveness and cost-utility analysis are performed.

The final part of this thesis consists of a summary and discussion of the outcomes of these nine chapters and the consequences for both daily practice and research. The thesis is completed with a summary in the Dutch language and a supplement describing actions taken by the investigator in a case of 'phishing' during the data collection.

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