Summary

Background, aims and methods

According to the World Health Organisation (WHO), in 2002 the number of people with visual impairment was estimated to be in excess of 161 million: 37 million people were blind and 124 had low vision. For the Netherlands, in 2000 the best estimation was that between 33,300 and 45,000 people (0.21% - 0.28% of the total Dutch population) were blind and between 115,000 and 175,000 (0.72% - 1.09%) had low vision according to the WHO criteria. The main causes of blindness and low vision in those aged 20 to 65 years are optic neuropathy, tapetoretinal dystrophies, myopia-related retinal disorders, diabetic retinopathy, age-related macular degeneration, other retinal disorders, glaucoma, and cataract. For the main causes of visual impairment (surgical) treatment options are limited. Most treatments are aimed at slowing down the progression of the eye disease, or the underlying disease must be found and treated (if possible) to prevent further vision loss. Although the prevalence of visual impairment in working-age adults is low, the impact is extremely high and affects all aspects of life. Therefore, many visually impaired persons have to rely on low vision rehabilitation.

The Netherlands has several rehabilitation services for visually impaired adults, including optometric services and multidisciplinary rehabilitation centres. For example, *Visio Het Loo Erf* (in Apeldoorn) provides comprehensive rehabilitation programs for visually impaired adults; their rehabilitation programs are only available for persons with complex problems or multiple rehabilitation demands, and include vision training, occupational therapy, mobility training, and coping with vision loss. Evidence regarding the efficacy of the rehabilitation programs has become increasingly important. Up to about 15 years ago the outcome of rehabilitation was calculated by objective measures at the disability level, such as reading speed, walking distance, and performance of daily activities. Recently, however, clinicians and researchers have become aware of the need for more subjective outcome measures, such as quality of life.

The main objective of the work presented in this thesis is to assess prognostic factors for quality of life after rehabilitation among visually impaired adults.

The specific aims of this thesis are:

- to assess the properties of the Functional Field Score;
- to review the literature on quality of life as an outcome of rehabilitation for visually impaired adults;
- to compare quality of life of visually impaired adults with quality of life in a healthy Dutch population and patients with other chronic diseases;
- to further validate one of the most widely used vision-related quality of life questionnaires;
- to assess the outcome of rehabilitation on the short term and long term;
- to provide guidelines for the referral of visually impaired persons to rehabilitation services in the Netherlands.

Chapters 2 and 3 address the Functional Field Score; these studies are based on data from a retrospective chart review of all low vision patients who entered an observational program prior to rehabilitation. We selected data of 58 patients aged 18 years or older, who had valid results from a Goldmann III−4e and V−4e visual field test for at least one eye. In these studies one eye could be blind.

Most of the studies with original data described in this thesis (Chapters 5, 6, and 7) were based on a prospective cohort study on the quality of life of visually impaired adults. We included patients aged 18 years or older who had sufficient understanding of the Dutch language and adequate cognitive abilities to understand the questions (as assessed by a research assistant in psychology). Participants were asked to complete a generic and a vision-related quality of life instrument on three occasions: i.e. at baseline (when the participants visited the rehabilitation centre for an observational week prior to rehabilitation), at 3 months after finishing rehabilitation, and at 12 months after finishing rehabilitation. The questionnaire was completed by 129 participants at baseline, by 87 at 3-months follow-up, and by 77 participants at 12-months follow-up.

The studies described in Chapters 4 and 8 were based on systematic reviews of the relevant literature.

Functional Field Score (FFS)

In 2001, the American Medical Association adopted the Functional Vision Score; this score is built on the Functional Acuity Scores and Functional Field Scores (FFS). In this thesis, we focused on the scoring method (grid method) and calculation of the FFS. Despite the

fact that grid scores are frequently used to assess visual field, the reliability of this method has not yet been investigated. The size of the visual field depends to a large extent on the stimulus intensity and stimulus size. Although the visual field is generally evaluated using the Goldmann isopter III−4e, it has the disadvantage that not all low-vision patients are able to see the stimulus corresponding to this isopter.

In Chapter 2 we evaluated the intra- and interrater reproducibility of the FFS. The FFSs of isopters III−4e and V−4e were analysed. Two raters independently scored the plots; the smallest detectable difference (SDD) and the weighted kappa were used to quantify agreement. The SDD expresses the smallest difference between two scores that can be interpreted as 'real' and cannot be attributed to measurement error. The SDDs were smaller than the minimally clinically important difference (MCID) of ten points; thus, the MCID can be distinguished from measurement error. The intraclass correlation coefficient (ICC) was used to quantify reliability. The intra- and inter ICCs were high (ICCs >0.98). It was concluded that both intra- and interrater reliability of the FFS were excellent.

In Chapter 3 we investigated underestimation of field loss in FFS between the Goldmann isopters III−4e and V−4e in visually impaired patients, in order to develop a predictive model for the FFS_{III-4e} based on the FFS_{V-4e} that adjusts for possible confounders. Linear regression was used to develop the model, setting FFS_{III-4e} as the dependent variable and FFS_{V-4e} as the independent variable. The FFS_{V-4e} was larger than FFS_{III-4e} - the mean difference being 14.6 points. Multiple linear regression analysis showed that age, Functional Acuity Score, primary eye disease and central/peripheral loss were not confounders for the prediction of FFS_{III-4e}. The FFS_{III-4e} was estimated using the following equation: $FFS_{III-4e} = -19.25 + 1.063*FFS_{V-4e}$. In practice, just subtracting 19.25 points of the value of FFS_{V-4e} will be sufficient to estimate the value of FFS_{III-4e}. This model should give confidence about using the larger isopter to determine the visual impairment of a person by means of the FFS.

Review of quality of life in visually impaired adults

Increased attention to the concept of vision-related quality of life has resulted in several studies exploring the effect of different rehabilitation programs on quality of life. However, because these studies used different vision-related quality of life questionnaires to compare different rehabilitation programs for different populations, it is difficult to discuss and assess the effectiveness of these programs. Therefore, we conducted a systematic review of the evidence for the effectiveness of the various rehabilitation programs in improving the

quality of life of visually impaired adults (Chapter 4). First, we systematically searched and selected literature from different sources. We included (quasi-) randomised trials of studies on quality of life of persons aged 18 years or older, of either sex, with irreversible visual impairment. Also included were trials that compared multidisciplinary rehabilitation with monodisciplinary rehabilitation and with no rehabilitation. Two reviewers independently extracted data and assessed trial quality. Considering the diversity of vision rehabilitation interventions, 10 studies (11 articles) were categorized into three groups of related intervention types: the educational group programs, methods of enhancing vision, and vision rehabilitation programs. Educational group programs tended to be preferable to individual programs, or to no treatment. Some enhancing vision methods are effective in improving quality of life, including adaptation of lighting, and conventional rehabilitation. Prescription of prism spectacles is effective in improving reading skills, but not necessarily in improving quality of life. Participants receiving a comprehensive rehabilitation program experienced a better psychological well-being and performed more independently on living skills after treatment compared with a no-treatment group. However, this program was not effective in improving independence regarding orientation and mobility skills.

The evidence from randomised controlled trials supports the positive effect of rehabilitation on vision-related quality of life. However, this evidence is based on single studies, and the results need to be confirmed in additional studies. The complexity and diversity of patients' needs implies the necessity to adapt any rehabilitation program to the individual patient profile. Studies on prognostic factors are needed in order to develop such patient profiles for specific rehabilitation programs. In general, not all improvements remained stable on the long term, which might indicate the need for (better) aftercare programs or clinical follow-up of the patients.

Quality of life compared to other chronic conditions

Generic health-related quality of life (HRQoL) questionnaires are useful to compare the quality of life of visually impaired persons with that of persons with chronic conditions that are not vision related. Chapter 5 describes the generic HRQoL and health status of visually impaired patients, and compares the HRQoL of visually impaired patients with that of both the general Dutch population and of patients with other chronic conditions. The chronic conditions selected for their hypothetical influence on (aspects of) vision-related quality of life were: acute coronary syndrome, chronic fatigue syndrome, pulmonary disease, diabetes mellitus type 1 and type 2, hearing impairment, major depressive disorder, multiple

sclerosis, severe mental illness, stroke and major trauma. Generic HRQoL was assessed using the EuroQol (EQ-5D), which is one of the most commonly used instruments. It consists of five questions covering the dimensions mobility, self-care, usual activities, pain or discomfort, and anxiety or depression. The EQ-5D scores of visually impaired adults were compared with EQ-5D norms of the Dutch population and of patients with other chronic conditions; both sets of data were taken from the literature. We found that visual impairment has a substantial impact on the quality of life when compared with other chronic conditions. The average $EQ\text{-}5D_{index}$ score of the total study population was 0.73. The values of the $EQ\text{-}5D_{index}$ are set on a scale in which 0 corresponds to death and 1 to a state of perfect health. Visually impaired patients reported more problems on every dimension of the EQ-5D than the general Dutch population. Only patients with chronic fatigue syndrome and stroke patients reported more problems on every dimension of the EQ-5D than visually impaired patients. Visual impairment disturbs quality of life more than diabetes mellitus type 2, coronary syndrome and hearing impairments, but less than stroke, multiple sclerosis, chronic fatigue syndrome, major depressive disorder and severe mental illness.

Evaluation of a vision-related quality of life questionnaire

The Visual Functioning Questionnaire (VFQ-25) is one of the most widely used measures of vision-related quality of life. However, the questionnaire does not meet some psychometric quality criteria. In Chapter 6 we re-evaluated the psychometric properties of the VFQ-25 for a group of visually impaired working-age adults. Three items on automobile driving were excluded from further analyses because they showed a high ceiling effect or had too many missing values. First, the items of the VFQ-25 were subjected to an exploratory factor analysis. Next, a separate Rasch analysis was performed on each factor. We examined step thresholds and goodness of fit statistics of the items. Finally, we examined differential item functioning. The results indicated that modifications of the original VFQ-25 structure are necessary. Factor analysis indicated four domains: Near Activities, Distance Activities & Mobility, Mental Health & Dependency, and Pain & Discomfort; these accounted for 46.4% of the total variance. Most items showed some degree of threshold disordering. All disordered thresholds were recoded from the original 5-point scale by collapsing two or three categories to form a 4-point or a 3-point scale. After collapsing the item response categories, all items showed ordered thresholds. The Near Activities domain showed excellent fit, the Distance Activities & Mobility domain

good fit, the Mental Health & Dependency domain and the Pain & Discomfort domain an unsatisfactory fit. Two items showed uniform differential item functioning.

Prognostic factors for quality of life in visually impaired working-age adults

The overall aim of rehabilitation for visually impaired adults is to improve the quality of life and (societal) participation. The complexity and diversity of patients' needs makes it necessary to adapt the rehabilitation program to individual patient profiles. These patient profiles can be based on factors responsible for differences in quality of life outcome between certain groups of patients (prognostic factors). In Chapter 7 we obtained the short and long-term outcome of a comprehensive rehabilitation program on quality of life for visually impaired adults, and on prognostic baseline factors. The change between subsequent measurements of the four factors of the VFQ-25 was measured, and the longitudinal relationship between vision-related quality of life on the one hand and possible prognostic factors on the other was evaluated by means of random coefficient analyses. When the factor scores one year after rehabilitation were compared with baseline scores, the Mental Health & Dependency scale showed a significant improvement. For participants who received rehabilitation, age appeared to be a significant prediction variable for all factors. Additionally, the Functional Visual Score and time of onset of visual impairment were predictors for the factor Pain & Discomfort. Although additional studies are needed to confirm our results, these findings should lead to adjustments in the rehabilitation programs.

Guidelines on the referral of visually impaired persons to low vision services

Although there are several guidelines on the referral of visually impaired persons, only the one devised by the American Academy of Ophthalmology is evidence based. However, because this guideline is not applicable to the Dutch healthcare system, we decided to develop evidence-based guidelines for the referral of visually impaired persons to low vision services (Chapter 8). We systematically searched the literature for definitions of visual impairment, for physician-patient communication, and for outcome of interventions for visually impaired persons. Results of the selected articles were summarised and rated according to the level of evidence. Other considerations, such as the current organisation of rehabilitation for visually impaired persons in the Netherlands, were also taken into

account. In this study, we slightly adapted the WHO criteria in order to include all people who experience problems with reading and other daily life activities due to visual impairment. A large number of recommendations were devised. Among these is that the complete diagnosis should be communicated to the patient and that a second appointment should be offered in which the diagnosis and potential treatment options are discussed again. Another recommendation is that, in general, visually impaired adults eligible for referral should be referred for the provision of low vision aids, and that patients with complex problems or extensive rehabilitative demands should be referred to a rehabilitation centre.

Conclusions

One of the central themes in this thesis is the reliability and validity of the Functional Field Score (FFS) as a part of the Functional Visual Score; the reliability and the agreement of the FFS proved to be sufficient. The FFS corresponding to stimulus III−4e can be estimated from the FFS corresponding to stimulus V−4e by subtracting 19.25 points. It can be seen that an overestimation of the FFS by using a larger isopter leads to a remarkably higher Functional Visual Score. As this might have serious consequences for benefits, we recommend that the Functional Visual Score be adapted in the next edition of the American Medical Association guidelines.

A second important aim was to assess the generic and vision-related quality of life of visually impaired adults. We found that generic health-related quality of life is reduced in visually impaired patients compared to a healthy reference group. Compared with other chronic conditions, visual impairment has a stronger effect on quality of life than diabetes mellitus type 2, coronary syndrome and hearing impairment, but less than stroke, multiple sclerosis, chronic fatigue syndrome, major depressive disorder and severe mental illness. To assess vision-related quality of life, we re-evaluated one of the most popular vision-related quality of life questionnaires, the VFQ-25. Although our results regarding this evaluation require confirmation and some additional analyses, we were able to show that the new factor structure is a better alternative to evaluate the outcome of rehabilitation programs in visually impaired working-age adults compared to the original factor structure.

Finally, we have shown that evidence regarding the outcome of rehabilitation programs in improving quality of life of visually impaired adults is scarce. The systematic review presented in Chapter 4 provided some evidence for the effectiveness of the outcome of parts of rehabilitation programs. This thesis presents the first long-term outcomes on

quality of life of visually impaired working-age adults. Changes in quality of life after rehabilitation are generally small. Based on our findings, there is evidence that rehabilitation programs offered at the rehabilitation centre might need adaptations tailored to the individual needs of the visually impaired adult. Age, Functional Vision Score and time of onset of the visual impairment were predictors for changes in quality of life. This information may be helpful in assessing the best referral patterns for specific groups of patients. For now, the guidelines presented in this thesis provides recommendations based on 'best' available evidence on how to refer visually impaired persons to rehabilitation services.