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Cost-effectiveness of basic vision rehabilitation (The basic VRS-effect study): study protocol for a randomised controlled trial

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Abstract

Purpose: To investigate the cost-effectiveness of a basic vision rehabilitation service (basic-VRS) in Portugal. We designed a parallel group, randomised controlled trial whose aim is to compare the effects and costs of 'usual low vision care' with a 'basic-VRS intervention' on self-reported visual ability and other psychosocial and health-related quality-of-life outcomes.

Methods: The trial will recruit participants that meet the following inclusion criteria: (1) visual acuity between 0.4–1.0 logMAR in the better-seeing eye, (2) cause of vision loss is diabetic retinopathy or age-related macular degeneration, (3) 18 years or older and iv) live in the community (not in nursing homes or other type of institution). Participants will be randomised to one of the study arms consisting of immediate intervention and delayed intervention. The delayed intervention group will receive 'usual care' or no intervention in the first 12 weeks. Visual acuity, contrast sensitivity and retinal structure will be assessed during the study.

Results: The primary outcome measure is visual ability, which will be evaluated with the Massof Activity Inventory, we expect that the intervention will raise the overall person measure or visual ability. Reading, health-related quality-of-life, anxiety and depression and social support will be also assessed. The analysis will be undertaken on an intention-to-treat basis. A cost-effectiveness analysis will be performed to provide information about the cost per unit of utility. To evaluate the cost-effectiveness of the intervention we will adopt the perspective of the healthcare system.

Conclusion: This study will provide additional evidence about the effects of basic-VRS on self-reported visual ability. Findings from this study should also contribute to better planning of low vision provision and, consequently, may contribute to reduce barriers to basic-VRS.

Introduction

Vision loss is an important cause of disability due to direct implications on physical, psychological and social aspects.[1] The World Health Organization International Statistical Classification of Diseases and Related Health Problems, 10th Revision (ICD-10) designates visual (or vision) impairment (VI), which includes blindness and low vision, based on presenting distance visual acuity. In the ICD-10, Chapter VII, H54, low vision is defined as visual acuity of less than 0.3 decimal Snellen (6/18, 0.5 logMAR) but equal to or better than 0.05 decimal Snellen (3/60, 1.3 logMAR),

or a corresponding visual field loss to less than 20 degrees. Blindness is defined as visual acuity of less than 0.05 decimal Snellen (3/60, 1.3 logMAR), or a corresponding visual field loss to less than 10 degrees in the better eye.[2] Vision impairment can lead to reduction of mobility,[3] well-being and an increased risk of depression and anxiety.[4–6] It can also lead to increased risk of family distress, social isolation, and reduced social participation.[4,7,8]

Vision rehabilitation (VR) can be defined as a mixture of health, educational and social interventions whose ultimate goal is to reduce the negative impact of VI. Visual ability, defined as the overall ability to perform activities that depends on vision, is normally reduced in people with VI.[9,10] The main goal of VR is to maximise an individual's visual function. Enhancing visual function in people with low vision includes, for example, the use of assistive devices or improving lighting. VR often requires also the acquisition of new skills such as handling assistive devices (e.g. haptic devices such as BrainPort[11]), adaptive mobility strategies, modifying the environment, or some other activity-specific intervention.[12–14] For instance, reading is a highly-valued activity in society and individuals who are unable to read face barriers in their daily activities.[15,16] In many cases the ability to read can be restored through the use of magnifiers and little training with the devices prescribed.[15,17] There is evidence that VR can improve the quality-of-life and independence to perform activities of daily living in people with VI.[5,18–20]

It is known that VI can increase expenditure at personal and societal levels, but information about the 'value for money' (benefits vs costs) of VR is still limited. VI leads to a significant economic burden due to direct costs such as inpatient and outpatient care and indirect costs such as informal care or productivity losses.[21–25] Informal care and productivity losses are likely to be consequences of vision disability (barriers faced by people with VI to live and develop skills) caused by reduced independence to perform activities of daily living and less job opportunities due to reduced ability to work.[26–28] These are the type of problems that can be tackled with effective VR. However, there is still a lack of knowledge regarding what impact VR can have on those economic issues.[14,19,29–31] Cost-effectiveness analysis (CEA) and health economic analysis will reveal the impact of VR.

Cost-effectiveness analysis consist of an economic analysis that compares the cost and effects of health interventions in order to evaluate which alternative presents the most favourable cost/benefit ratio. The results can be expressed in terms of incremental cost per unit of effect or in terms of the effect per unit cost.[32,33] The current lack of CEA addressing the economic impact of VR services is contributing to the poor development of integrated vision care that people with VI receive in several countries.[34,35] Additionally, the lack of CEA in this field is also contributing to the limited knowledge on the benefits of VR amongst patients, families and professionals, as well as to sub-standards of the services provided.[36–38] Eventually, CEA will also characterise the value for money of VR in terms of an optimisation of resources and reduction of the burden entailed by VI.

In this manuscript we present the study protocol for a parallel group, randomised controlled trial (RCT) addressing the cost-effectiveness of a basic vision rehabilitation service (basic-VRS) in Portugal ('The basic VRS-effect Study'). We define basic-VRS as: dispensing new glasses and magnifiers with little training and instructions to use the devices and help with activities of daily living. All provided in clinical settings with emphasis on reading tasks.

Methods/Design

Study design

To investigate the CEA of basic-VRS we designed a parallel group RCT whose aim is to compare the effects and costs of 'usual low vision care', which is currently 'no intervention' in Portugal, with a 'basic-VRS intervention' on self-reported visual ability. Participants' flow during the study is shown in *Figure* 1, the information included in this protocol is summarised in *Appendix* S2, *Consolidated Standards of Reporting Trials (CONSORT) Checklist*. Participants will be allocated to an immediate intervention group (IMI), or to a delayed intervention group (DEI). The schedule for the intervention, as well as the procedures and instruments used in the trial are summarised in *Table* 1. The delayed intervention group was included, despite previous evidence that the intervention is likely to be superior to 'usual care' (or no intervention), to control for a possible effect of 'attention to the problem'. In other words, we suspected that people with low vision may feel more optimistic and give more positive responses during interviews only because they start a process of 'solving their vision problems'. Therefore, the delayed intervention group is tested and receives attention from the research optometrist also at baseline, but only a real intervention at week 12. If attention is to have an effect on the main outcome measure without a real intervention, the effects are captured during the first 12 weeks in the delayed intervention group and can then be taken into consideration when assessing and discussing the impact of the intervention.

Inclusion and exclusion criteria

Participants (IMI and DEI) need to meet the following inclusion criteria: (1) visual acuity between 0.4–1.0 logMAR in the better-seeing eye; (2) primary diagnosis and cause of vision loss diabetic retinopathy or age-related

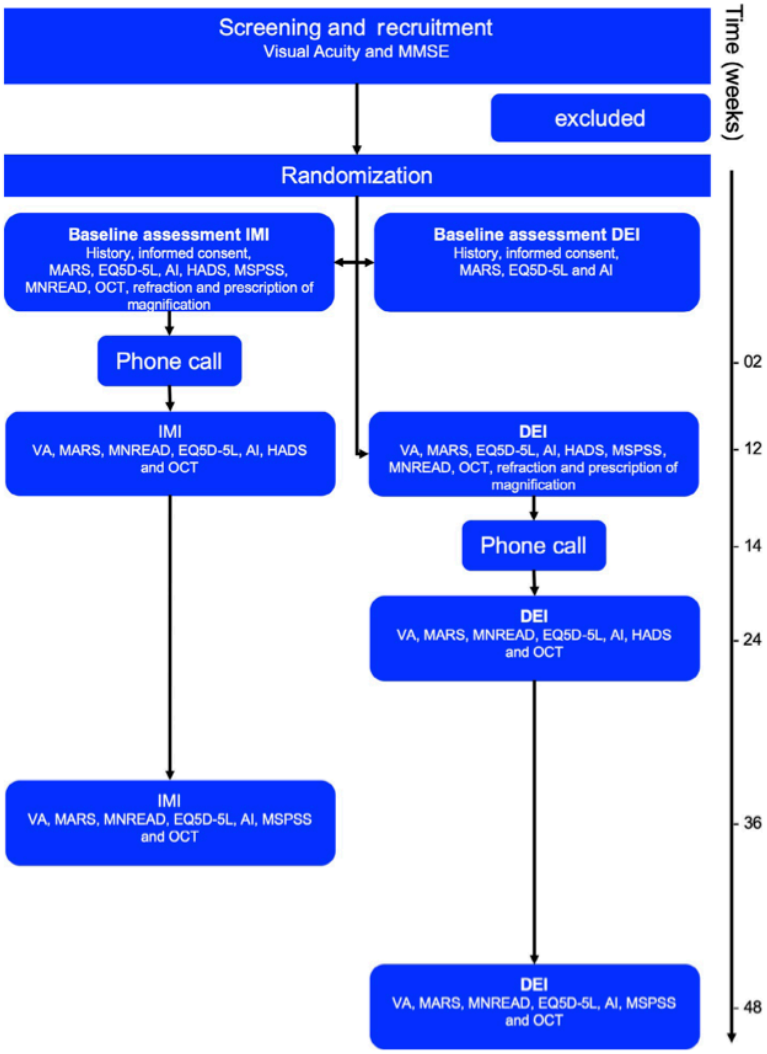

Figure 1. Diagram showing planned participant flow. Note: DEI, delayed intervention group; IMI, immediate intervention group; MMSE, mini-mental state examination. EQ5D and AI are defined in section 'Measures'.

macular degeneration; (3) 18 years or older and (4) live in the community (not in nursing homes or any type of institution). Recruited people that meet one or more of the following criteria will be excluded: (1) cognitive impairment based on scores on mini-mental state examination, (2) communication problems due to, for example, hearing impairment, or inability to speak Portuguese; (3) unable to read due to low level of education; (4) unable to attend the requested appointments at the study setting.

The spectrum of acuities for the inclusion criteria corresponds to moderate vision impairment and they have been chosen because reading ability is expected to improve with strong reading glasses and moderate power magnifiers.[2,39] The rationale to include patients diagnosed with diabetic retinopathy and age-related macular degeneration is that these diagnoses represent the leading causes of low vision in the adult population in developed countries. These diseases typically affect people within different age groups which might be challenging when computing, for example, productivity losses or gains due to the intervention. Nevertheless, productivity will be excluded from our CEA because we will adopt the perspective of the healthcare system, productivity needs to be considered when adopting the societal perspective.

Cognitive status will be assessed using the Portuguese version of The Mini-Mental State Examination

Table 1. Summary of the measurements and schedule of the measurements that will be performed during the study

		Study phase				
Procedures	**Instruments**	**Base**	**12 weeks**	**24 weeks**	**36 weeks**	**48 weeks**
Demographic information	Electronic form	IMI,DEI	–	–	–	–
Visual acuity at far and near	ETDRS charts	IMI,DEI	IMI,DEI	DEI	IMI	DEI
Contrast sensitivity	MARS test	IMI,DEI	IMI,DEI	DEI	IMI	DEI
Refraction	Objective and subjective refraction at distance and near	IMI	DEI	–	–	–
Best magnifier for reading and near tasks	Magnifier or spectacles that will enable reading font N8 (0.4 logMAR)	IMI	DEI	–	–	–
Training with the magnifier	See *Table* 2 for a complete list	IMI	DEI	–	–	–
Reading assessment	MNread test	IMI	IMI,DEI	DEI	IMI	DEI
Cognitive status	Mini Mental State Examination (MMSE)	IMI,DEI	–	–	–	
Health utilities	EQ-5D	IMI,DEI	IMI,DEI	DEI	IMI	DEI
Visual ability	Massof Activity Inventory (MAI)	IMI,DEI	IMI,DEI	DEI	IMI	DEI
Depression and anxiety	Hospital Anxiety and Depression Scale (HADS)	IMI	IMI,DEI	DEI		
Social support	Multidimensional Scale of Perceived Social Support (MSPSS)	IMI	DEI	–	IMI	DEI
Analysis of structural stability of the macula	Optical coherence tomography (OCT)	IMI	IMI,DEI	DEI	IMI	DEI
General instructions	See *Appendix* S4 *Table* with Instructions	IMI	DEI	–	–	

'Study phase' define the measurements that will be performed in each group at the given timepoint. Base, baseline visit; DEI, delayed intervention group; IMI, immediate intervention group; W, weeks.

(MMSE).[40,41] MMSE scores 25–30 suggest a questionably significant degree of cognitive impairment, scores 21–24 mild cognitive impairment, 10–20 moderate cognitive impairment; and below 10 severe impairment.[42] We adjusted some vision-related tasks to make them suitable for people with VI: (1) for the task 'reading a sentence' we provide large print, and for (2) 'identifying a pen and a watch' we allow adjustment of the seeing distance to compensate for poor acuity. We exclude the last tasks, one consisting in 'writing a sentence' and the other asking to copy a pair of intersecting pentagons. Final scores will, therefore, be adjusted from 0 (minimum) to 28 (maximum).[43,44] These measures should be enough to use the instrument as a screening tool because previous studies have shown that a 6-item subset derived from the MMSE can be used to screen for cognitive impairment [45]

Recruitment and randomisation

Potential participants will be identified on a consecutive basis from the outpatient bookings at the department of ophthalmology, Hospital Santa Maria Maior E.P.E, Barcelos, Portugal. After selection, the first author will invite candidates by telephone to participate in this study. Candidates willing to participate will receive, by post or at the hospital, a 'participant information booklet' with complete information about the study. After agreeing with the terms of participation, participants are screened and, if they pass the screening, they will sign the consent form. Recruited participants will be included in the trial if they fulfil conditions imposed by the inclusion/ exclusion criteria. Participants will be allocated to the IMI or DEI to create the best possible match between the groups according to age and visual acuity. A blocked randomisation list with four participants per block was generated online using the platform Sealed Envelope Ltd. (https://www.sealedenvelope.com/simple-randomiser/v1/lists) by the last author (AFM). Blocks were stratified by age (64-or-less vs 65-or-more) and acuity (0.4–0.68 vs 0.70–1.00) categories leading to a total of 4 strata. The platform also generated a unique randomisation code. For each block, randomisation codes were placed in envelopes and divided according to strata, each participant takes the randomisation code from a sealed envelope. The randomisation code is sent by the accessor to the last author (AFM) that decodifies de code using the block randomisation list and gives information about the participant's group. In the clinical setting the first (LHM, Optometrist) and the fourth author (NM, Ophthalmologist) have training in low vision assessment and rehabilitation at clinical and research levels.

Experimental intervention and usual care

Usual care

Patients with low vision who receive medical eye care at the hospital where this study will be conducted do not receive any low vision magnifiers or special attention regarding

strategies to deal with low vision. There are general guidelines from the Portuguese government to help people with impairments, but none specifies interventions to be delivered to people with low vision.[46,47] Therefore, 'usual care' in Portugal is commonly defined as treatment of eye diseases and standard refraction.

Intervention: 3 components

Best refractive correction for far and near. New glasses will be prescribed when the difference between refractions (the current glasses and the new refraction) is 2D or more, or if visual acuity improves at least five letters with the new refraction.[48] These are reference values and the patient will be involved in the decision, all prescribed glasses and the changes in acuity will be recorded. All further visual tests will be performed based on the 'normal' near addition with a starting add of 2.5 D. After that and according to the participant's preference, the near add for reading glasses will be adjusted to its maximum possible value (shortest working distance defined subjectively). For more details see *Appendix* S3, *Detailed Procedures*.

Prescription of magnification for reading. To find the required magnification we will use a method based on equivalent viewing distance (EVD).[49] The formula that will be used to determine the EVD and the power of the magnifier has been suggested by others[49] and is given by the expression below in which TPS stands for 'threshold print size':

$$\text{Required EVD} = (\text{Required TPS}/\text{Current TPS}) \times (\text{Current viewing distance}).$$

We want our participants to be able to read N8 (0.4 logMAR). We will assume that an acuity reserve of 2:1 (0.3 log units) is necessary for fluent reading (approximately 80 words-per-minute);[49] therefore, the required TPS is set at N4. The final power of the magnifier will be discussed with each participant to take into consideration individual preferences. For example, some people will choose to have lower magnification if it provides a wider field of view, while others might like the higher magnification. In some cases, only spectacles with high addition lenses including prisms to support convergence may be sufficient, lenses are supplied by Essilor (https://www.essilor.pt/). Other magnifiers are selected from a Schweizer catalogue (https://www.schweizer-optik.de/unternehmensbereich/improvision/). LED illuminated hand magnifiers are the first choice of prescribing devices and are available in powers ranging from 6 D to 56 D. LED illuminated stand magnifiers and special magnifiers (reading bars or bright field magnifiers) are also available These will be prescribed if participants show difficulties using LED Illuminated magnifiers (for example if they have a hand tremor) or when this type of device is considered inadequate for the participant's preferred near or reading task(s).

Instructions and training. We will provide a list of instructions on how to minimise the effect of reduced vision during activities of daily living, see *Appendix* S4, *Table* with instructions.[50–54] During the in-office training, participants will receive a supervised training session with their devices as given in *Table* 2, a large print version of the list is provided to take home.[48,55,56]

The intervention will be followed by a telephone call to ensure that participants are using their devices. If participants stop using the devices, the reasons for abandonment will be documented and the use will be encouraged. The phone call should take place within 2–3 weeks after participants have received their devices.

Measures

We included different types of measures because VR is likely to influence and be influenced by many factors. The key measurement is given by the Massof Activity Inventory (AI). AI gives a comprehensive summary of the ability to perform vision related activities and is expected to capture improvements in self-efficacy given by or developed during rehabilitation. The EQ-5D will be used to compute QALYs (defined in section Health-Related Quality of Life) and forms the basis of the CEA. Emotional status and social support are variables that can influence the effects of rehabilitation, or the attitude towards it.[57,58] Therefore, the inclusion of such metrics will provide key information to understand whether our intervention has been influenced by changes in these aspects.

Visual measures such as reading speed provide information about a very demanding visual task. Improvements in reading speed are also expected to reflect improvements in other vision related tasks. This information can therefore be interpreted in combination with patient-reported measures to characterise the impact of the intervention. Because we rely on patient-reported measures, it is important to ensure that participants have good judgement of their abilities/difficulties. We included the MMSE as a screening test for cognitive impairment to perform self-reported measures and, consequently, to participate in the study.

Baseline and control measures

Clinical and demographic information. Demographic information will include date of birth, marital status, occupation and years of education. Clinical information will include the disease that is the primary cause of VI, associated eye diseases, number of years with VI and comorbidities.

Visual acuity. Visual acuity (VA) is going to be used as reference for prescribing new glasses. Distance VA will be

Table 2. Instructions about using and practice with low vision aids

Aid	Description
Spectacles	• To find the correct working distance slowly bring the print closer to your eyes until the print comes into focus; using strong lenses may require a closer than usual working distance; • Move the print from right to left in front of your eye or move your head, be aware that moving your head may result in losing the focus; • Use good illumination during reading or other visually demanding tasks; • Use a reading stand if you find it difficult to maintain the correct distance or you feel fatigue due to postural demands imposed by your glasses;
Magnifiers	• Place the magnifier flat on the page and raise slowly away from the page until you get the clearest image. This procedure requires practice but after a while finding the lens-to-object distance should be almost automatic; • Be aware of the lens-to-eye distance, that changes the amount of information that you can see (field-of-view), shorter distances give a wider view; • To read move the page or move the magnifier and eye, depending on the task and the type of material;
• Use the aid every day starting with short training periods of 5–10 min each; • Be aware that initially reading may be slow because concentration is on the use of the device rather than the reading but that will get better with practice; • You may experience of headache and eyestrain, but this is harmless to your eyes and vision, take a break if you feel this way;	

assessed in a dim light room using an internally illuminated high contrast ETDRS chart, model 2425E, luminance 180 cd·square-meter^{-1} (https://www.precision-vision.com/) at 4 m or 2 m or 1 m, according with the severity of vision loss. The chart distance will be reduced to ensure that the participant can read at least 10 letters. A reduction of the distance to half of the calibrated chart size requires the addition of 0.3 logMAR units to the final acuity score.[59] Near VA will also be assessed with Early Treatment Diabetic Retinopathy Study (ETDRS) charts (https://www.precision-vision.com/) at 40 cm or at 20 cm or 10 cm. In both procedures, a letter by letter scoring will be employed.[60] VA will be measured monocularly at distance and binocularly at near.

Monitoring retinal changes. Retinal thickness in the macula will be monitored with Topcon 3D OCT-2000 optical coherence tomography (OCT) (https://www.topcon.co.jp/en/eyecare/products/product/diagnostic/oct/3DOCT-2000_E.html) during the duration of study (48 weeks). The programme selected for the capture is the 'Macula Radial' which measures a diameter of 6 mm centred at the fovea. This will allow us to determine if changes in VA are associated with changes in retinal structure and ultimately will be used to exclude participants, whose retinal structure deteriorates, from the study or from analysis.

Main outcome measures

Visual ability. Visual ability, as previously defined, will be measured before and after the intervention to quantify the effect of rehabilitation. We will use the Massof Activity Inventory (AI)[61,62] which is an adaptive instrument designed to provide an individualised assessment of difficulties caused by vision impairment. The AI consists of a hierarchal structure in which specific cognitive and motor visual tasks (e.g., pouring or mixing without spilling) underlie more global goals (e.g., preparing meals). Disabilities occur when an individual reports difficulty in achieving important goals. Difficulties achieving a goal are said to depend on the difficulty experienced in the tasks that underlie each goal. Goals are split between three objectives: social functioning, recreation and daily living. Respondents first rate the importance of each goal with four possible responses ranging from 'not important' to 'very important'. Goals rated 'not important' are skipped, and as such are not considered in the final visual ability score as these are not relevant to the person's daily life. For goals rated 'slightly important' or above, participants are asked to rate difficulty on a five-point scale ranging from 'not difficult' to 'impossible to do'.[61,62] As in previous studies we establish visual ability as the main outcome measure, to compute the sample size, we are assuming a change of 0.7 logit on visual ability measured 12 weeks after the intervention (details in section sample size).

Reading. Reading will be tested to determine vision related reading difficulties before and after the intervention. Reading parameters will also be used to estimate the magnification required for reading. Specifically, we will determine: (1) reading acuity (RA)—which is the smallest size of the font that the patient can read without making significant errors; (2) maximum reading speed (MRS)—which is the patient's reading speed when it is not limited by the font

size; and (3) critical print size (CPS)—which is the smallest size that the patient can read with the maximum read speed. After the intervention, reading will be assessed with the prescribed magnification. For measuring reading parameters we will use the Portuguese version of the Minnesota Low-Vision Reading Test (MNread test)[63–65] (https://www.precision-vision.com/). This instrument uses 28 sentences, each sentence fits into the 3-line without use of hyphenation or extra blank spaces. No punctuation is shown, and uppercase letters are used only for initial capitalisation of sentences and proper names. Reading speed will be measured binocularly at a distance of 40 cm or adjusted, according with the needs, to 20 or 10 cm.

Secondary outcome measures

Contrast sensitivity. Contrast sensitivity is a good predictor of print size for reading and helps to predict reading fluency.[43] For example, a patient with near VA between 0.85 and 1.00 logMAR is likely to achieve fluent reading only if contrast sensitivity is better than 1.05 logCS.[43] Contrast sensitivity will be assessed binocularly at 40 cm with near correction of 2.5 D using the Mars Contrast Sensitivity Test (https://www.marsperceptrix.com/), which has a gradual letter-by-letter contrast, illuminance on the surface of the test is approximately 330 lux. The patient will be encouraged to respond until two consecutive letters are read incorrectly. The log contrast sensitivity is given by the final correctly read letter, which is the letter prior to the two consecutive errors, minus the number of errors prior to the final correct letter.

Anxiety and depression. Anxiety and depression will be assessed with the Portuguese version of the Hospital Anxiety and Depression Scale (HADS).[66] HADS is a 14-item self-report scale, comprising 2 subscales evaluating levels of depression (HADS-Depression) and levels of anxiety (HADS-Anxiety). The HADS has been used extensively in the hospital setting as a standardised psychological screening tool for emotional disorders,[67] and has also been used in studies addressing vision loss.[44,68] Each subscale includes seven items, generating scores between 0 and 21, for anxiety (Cronbach's alpha of 0.89) and depression (Cronbach's alpha of 0.91). A score of 8 and above is widely used to indicate the presence of clinical levels of anxiety or depression that may warrant further psychological investigation.[44,67,69,70]

Social support. Previous research has suggested that people with vision impairment have increased risk of suffering from social isolation and reduced social support.[6,71] In our study we will measure patients' perceived social support using the Portuguese version of Multidimensional Scale of Perceived Social Support (MSPSS).[72] This scale has 12 questions that are divided into 3 subcategories (family, friends and significant others) of 4 questions each. The score for each question ranges 1–7, where 1 is 'strongly disagrees' and 7 is 'completely agree'. To assess individual sub-categories, the score for the questions of the category need to be summed and then divided by 4. To assess to the whole scale, the sum of rating for all questions is added up and then the total score is divided by 12. The lower the score the lower the perceived social support.

Sample size

To compute the minimum number of participants required to detect a significant difference in the activity inventory score (main outcome measure) at 12 weeks, we used information from previous studies and some preliminary data from our study.[73–75] From our pilot data we set a change in AI scores from −0.13 logits in week 1 to 0.93 logits in week 12 in the IMI. With type I error rate (alpha) set at 0.05 (two-tailed) and aiming to a power of 0.90, a minimum of 22 participants per arm are required. Sample size calculations were performed with SAS analytics software, Studio Release: 3.7 (www.sas.com), the code and the results of the simulation are given in *Appendix* S1, *Sample Size*. Based on the number of dropouts in the first 20 participants recruited, we expect a dropout ratio of 15% and because of that 52 patients will be recruited.

Health economic evaluation

Economic evaluation is important to help decision makers with resource allocation issues and setting priorities.[33] It requires a comparative analysis in terms of cost and consequences. Consequences in economic evaluation can be measure through changes in physical, social or functioning (effects) or through changes in quality of life of patients (utility).[76] To evaluate the cost-effectiveness of the intervention in our RCT we will adopt the perspective of the healthcare system.

Health-related quality of life. Health-Related Quality of Life (QoL) and well-being are two separate concepts; although, QoL is often used as a proxy for well-being in health-related interventions. The Centre for Disease Control and Prevention states in its website that 'there is general agreement that, at minimum, well-being includes the presence of positive emotions and moods (e.g., contentment, happiness), the absence of negative emotions (e.g., depression, anxiety), satisfaction with life, fulfilment and positive functioning. In simple terms, well-being can be described as judging life positively and feeling good. For public health purposes, physical well-being (e.g., feeling very healthy and full of energy) is also viewed as critical to overall well-being. QoL is more linked to patient outcomes and has generally focused on

deficits in functioning (e.g., pain, negative affect). In contrast, well-being focuses on assets in functioning, including positive emotions and psychological resources (e.g., positive affect, autonomy, mastery) as key components'.[77]A possible interpretation of these definitions is that the boundaries between well-being and QoL are often fuzzy, and some patient outcomes may be capturing both. In this trial we use a generic instrument to assess QoL but it is possible that we also capture aspects of well-being. Measuring QoL before and after the intervention will allow us to determine the impact of vision rehabilitation on this variable and the results will be expressed in quality-adjusted life-year. The quality-adjusted life year or quality-adjusted life-year (QALY) is a generic measure of disease burden, including both the quality and the quantity of life lived. One QALY equates to one year lived in perfect health and it assumes that health is a function of length of life and quality of life and combines these values into a single index number.[78] To determine QALYs, one multiplies the utility value associated with a given state of health by the years lived in that state. A year of life lived in perfect health is worth 1 QALY (1 year of life × 1 utility value). The gains (or losses) are determined by the differences between QALYs,[79,80] in our case, the difference between the QALYs obtained before and after the intervention.

We selected the EQ-5D-5L, which is a standardised instrument developed by the EuroQol Group (www.euroqol.org), to measure of health-related quality of life. The descriptive questionnaire compromises five dimensions, where three are related to function (Mobility, Self-Care and Usual Activities) and the other two describe feelings (Pain/Discomfort and Anxiety/Depression). All dimensions have five possible levels of response, these define a total of 55 possible combinations of items that correspond to 3125 unique health states.[81,82]

Costs of the intervention—estimates

A provisional and theoretical estimate of the costs of the intervention based on the healthcare perspective is given in *Table* 3. Costs are estimated considering the material and equipment (e.g., visual tests and visual aids set) needed to provide a basic rehabilitation service in a hospital. Allowing for an initial investment for the material and equipment of 3870€ and an equipment lifetime of 8 years, the value of annual depreciation is 483.75€, which means that per year, the material and equipment have a cost of 483.75€ for the hospital. Furthermore, we estimate the total time spent by the rehabilitation professional with each patient is one and a half hours. Overhead hospital costs include administrative and clerical support and were estimated using hospital annual reporting costs for the ophthalmology department. We calculated overheads costs per medical appointment dividing overheads annuals costs for the ophthalmology department by the number of ophthalmic medical appointments provided in that year.

Magnifiers and/or lenses for glasses will be also considered for the estimation. The final costs will be calculated in real data according with the devices dispensed to each patient. For cost-effectiveness analyses the incremental cost-effectiveness ratio (ICER) needs to be computed using the expression:

$$\text{ICER} = (\text{Cost intervention} - \text{Cost alternative})/(\text{Effect intervention} - \text{Effect alternative})$$

In our case the Cost-alternative will be zero, the Effect-intervention will be measured in both groups (IMI and DEI). Costs will be expressed in euro and effects in QALY. The effects (benefits) of a basic-VRS are expected to have limited duration as a result of factors such as changes in visual acuity or refraction; therefore, in our analysis we will estimate the number of years during which participants are expected to benefit from the intervention, using recommendations from the literature.[83] A 3% discount rate will be applied for each year passed since the intervention.[84–86] For example, if the benefit in the first year is 1 QALY we assume that will be 0.97 in the second year after intervention. In cost effectiveness evaluation some decisions are based on limited number of patients and for that reason various assumptions are made. However, these assumptions may not be accurate, which introduces uncertainty.[87] In order to measure and evaluate uncertainty, a sensitivity analysis will be also performed.

Plan for data analysis

Data analysis will be performed with SPSS statistics software (https://www.ibm.com/SPSS/Modeler) and R (lme4 package) (https://cran.r-project.org/). For descriptive statistics means, median, standard deviation, interquartile range and frequency distribution will be calculated according to the type of variable (continuous/ discrete) and its distribution (normal or skewed). Kolmogorov-Smirnov tests or equivalent will be performed to assess normality. To detect changes in repeated (longitudinal) measurements we will consider the effect of group (IMI vs DEI) and time. Linear mixed models will be used to analyse repeated measurements. Longitudinal data analysis will be performed by fitting random coefficient models which will allow the regression coefficients (i intercepts and slopes) to be unique to each subject, i.e., the individual time trajectories can vary randomly.[88–92] For this analysis, individual outcome measures will be defined as 'dependent variable' or 'response variable of interest' (e.g., 'visual ability').

Table 3. Estimates of costs (healthcare system perspective) for a basic vision rehabilitation service (basic-VRS) per patient

	Resource use (units = hours)	Costs (units = euro)
Material and equipment	NA	4.84
Optometrist's preparation	0.25	2.09
Optometrist's examination	1	8.35
Device dispensing and training	0.5	4.175
Overhead hospital costs	NA	11.81
Magnifiers and lenses for the glasses	NA	100
Total	1.75	131.26

Participants will be defined as 'random factors' or 'group specific effects'. Explanatory factors or 'fixed factors' are: 'group' and 'time-point'.

Rasch analysis will be used to analyse results of the AI. The analysis will be conducted using the Andrich rate scale model[93] for polytomous data with Winsteps software,version 4.4.0, (https://www.winsteps.com/winsteps.htm to estimate person measures, item difficulties and threshold for each response category.[94] The unit of measure used by Rasch for calibrating items and measuring person is logits (log-odd units). Items with positive scores are harder to perform than the mean of the items; the higher the score the higher level of vision required. The opposite is expected for item with negative scores. Positive person measures indicate visual ability above the mean ability required for the items, while a negative person measure score means indicates the opposite.[95]

Ethics approval and trial registration

The trial started in 02/09/2016 with ethics application, the first participant has been assessed in March 2017. The study has been reviewed by the Ethics Committee for Life Sciences and Health of the University of Minho received approval number SECVS 147/2016 and also by the ethics committee at the hospital. The study was registered with the Portuguese data protection authority with the approval number 7012/ 2017. The basic VRS-effect study is registered in the ISRCTN at http://www.isrctn.com (Identifier: ISRCTN10894889), adheres to the CONSORT guidelines (http://www.consort-statement.org), and conforms to the tenets of the Declaration of Helsinki. The provisional date to stop the trial is 30/09/2020.

Data input, storage and quality control

Data from each of the study visits will be recorded manually by the researcher and stored on a secure server for subsequent data analysis. Members of the research team not involved in data collection will perform random checks to assess the quality of the recorded data. This step will require manually cross checking the entries in the spreadsheets with the original data collection forms.

Discussion

This study has been motivated by the lack of evidence about the 'value for money' of basic vision rehabilitation services (basic-VRS) in Portugal. Previous research has shown that vision impairment in Portugal is a common condition that leads to significant costs at personal and societal levels.[24,25,96] The general lack of cost-effectiveness analysis (CEA)[97] may delay decisions to implement more and better basic-VRS and creates barriers to the development of vision rehabilitation.[31,98–100] But, why do we need to perform a CEA now if magnifiers have been dispensed in many hospitals regularly since, at least, 1970?[101] Recent systematic reviews showed that better evidence on the cost-effectiveness of using magnifiers is necessary.[14] In addition, despite the widespread prescription of magnifiers, there still is insufficient evidence on the effect of different types of low-vision aids on reading performance.[17,102] In summary, there is sufficient evidence that more studies, in particular trials, are necessary to increase the knowledge about the 'value for money' of basic-VRS.

The expected impact of this study

Previous studies have shown that vision rehabilitation increases quality of life.[5,19,20] These studies presented a few limitations such as participants receiving more than one type of intervention simultaneously and the absence of control group.[12,19] The charcaterisation of cost-effectiveness of a basic-VRS will provide information about resource utilisation and their effects, such information can be used to improve service delivery and access. Research has identified three types of barriers when developing and referring patients to low vision services: (1) ophthalmologists often forget to refer their patients; (2) patients are not familiar with the concept of rehabilitation; and (3) patients think that rehabilitation is only for blind individuals.[36,99,103] We hope that our trial will help to reduce these barriers at a local level (Portugal) and at global level where the mentioned issues exist.

In the current manuscript we mentioned, at least, three published study protocols that, at first glance, seem to be similar to our work. Therefore, we briefly discuss what is different in the current design and motivation. The Low Vision Intervention Trial (LOVIT II) and the Portable Electronic Vision Enhancement System (p-EVES) are different from our study because they were designed to answer a

different question, that is, these studies compared two different types of low vision interventions. The LOVIT II compared impact of basic low vision intervention with low vision rehabilitation,[73,98] whereas the p-EVES compared the impact of electronic vision enhancement system devices with conventional optical low vision aids.[104] Both protocols include an economic evaluation comparing the two types of interventions, the LOVIT II uses a parallel arms design and the p-EVES uses a cross-over design. These two studies have also adopted different primary and secondary outcome measures. cross-over design has some advantages when compared with parallel arms (LOVIT II). For instance, a smaller sample is typically required when using cross-over.[105] In addition, all participants in our study will have access to the benefits of the intervention which increases the benefits of participation. A study conducted by Dunbar *et al.* (2012) was designed to find benefits of vision rehabilitation according to the level of visual acuity (participants' interquartile range for acuity was 0.06–0.30 logMAR).[73] Dunbar's study was expected to answer a different research question and also differs from ours in several of the secondary outcome measures. Although we learned some lessons from Dunbar's study, according to the author, Chapter 6 of the thesis,[58] it is important to address outcomes of emotional status and social support in order to explain the variability of the rehabilitation effects. Therefore, we decided to include some of these measures in our protocol.

Strengths of this trial

According to the available literature, our clinical trial is the first designed to perform a CEA of a basic-VRS despite that other trials have been conducted in recent years assessing the effects of vision rehabilitation.[73,104,106] We are using state-of-the-art instruments to perform a comprehensive characterisation of the outcomes of the intervention and the factors that can interfere with it, including instruments for characterisation of well-being (anxiety and depression scale and perception of social support) and QoL (EQ5D).

The AI is an adaptive visual function questionnaire designed to provide an individualised assessment of difficulties of a visually impaired respondent when performing valued activities. Because our intervention is likely to affect only 'near vision' or 'reading' tasks one can ask if it is sensitive enough to detect changes in visual ability after our intervention. To deal with this we plan to perform an analysis of the AI scores using all items (46 in the Portuguese version) and also using those only related to reading and/or near vision. However, we consider that the intervention is likely to bring extra levels of confidence to our participants to attend social events and to participate in activities in which reading is important but note the only requirement. In other words, the intervention is likely to affect several aspects beyond reading and the overall person measure obtained from the AI is likely to capture that. The preliminary results used to compute the sample size are already indicative of that (see *Appendix* S1, *Sample Size*). Previous studies have shown that there is a crosstalk between improving visual performance, being able to perform visual tasks, emotional and social factors.[107] Because of that we believe that assessing depression, anxiety and perceived social support before and after the intervention will help to understand if these aspects also influenced our intervention.

Other studies provided information about costs and effects of rehabilitation interventions in people with impaired vision. However, most studies involved other domains such as preventing depression.[108,109] Our study investigates the effect of a basic-VRS delivered in a public hospital focused in a single interaction with an optometrist that will provide a reading aid, basic training with the aid and instructions to reduce the effect of low vision in activities of daily living. This study is expected to provide for the first time the costs and consequences of a basic-VRS. In addition, our study design can be easily replicated in other countries to assess basic-VRS.

Challenges and limitations of the current study protocol

We have a few threats to our protocol and the first is the risk of being unable to capture the effects of basic-VRS with the EQ5D-5L. That is, it may be impossible to observe a significant change in QALY. Others have shown that this is a possibility, but meanwhile the instrument has been updated.[110] According to recent literature, condition-specific questionnaire scores (NEI VFQ-25) can be converted to EQ5D-based utility scores but the results are often inadequate.[111] An alternative to the EQ5D in future studies can be The Health Utilities Index which will be used in a subset of patients.[112] The main difference between the current and the previous version of the EQ5D is that it incorporates a 5-point scale, in contrast with a previous 3-point scale, which may produce 3125 unique health states. This allows better measurement properties in terms of distribution, ceiling, informativity, discriminatory power and patient preferences.[113,114] We have conducted a pilot analysis with 17 participants and the results were encouraging. The 5-point scales reduced significantly the ceiling effects when compared with the previous 3-points scale.[59,115]

A second limitation of our protocol is the follow-up period that cannot be more than 36 weeks due to funding limitations. We consider that this is not a major limitation because most of the previous studies have shown that the effects of rehabilitation should be perceived within

12 weeks (~3 months); although, that may depend on nature of the intervention (e.g. psychosocial vs provision of training with devices).[48,73,75,83]

Another possible problem for the final conclusions lies in the recruitment process. The number of patients attending the hospital where the study is conducted is limited; thus, preventing us from recruiting all participants at a single time point. Our researcher will not be blinded for the group allocation and we recognise that can increase the risk of bias. We specifically discuss this in work meetings and the researcher is alerted to this fact.

Trial status

At the time of submission of this protocol this trial is recruiting.

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Conflict of interest

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

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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Sample size.
Appendix S2. CONSORT checklist.
Appendix S3. Detailed procedures.
Appendix S4. Table with instructions.

