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Screening for Visual Impairment in Older Adults: Systematic Review to Update the 1996 U.S. Preventive Services Task Force Recommendation

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Structured Abstract

Background: Impaired visual acuity is common in older adults. Screening for impaired visual acuity in primary care settings could identify older adults who are unaware of or do not report vision problems, and lead to interventions to improve vision, function and quality of life.

Purpose: To assess the effects of screening for impaired visual acuity in primary care settings in older (age > 65 years) adults.

Data Sources: We searched the Cochrane Controlled Trials Registry and Cochrane Database of Systematic Reviews (through 3rd Quarter 2008) and MEDLINE database (1996 – July 2008) for relevant studies and meta-analyses. We supplemented electronic searches with reviews of reference lists of relevant articles and solicited additional citations from experts.

Study Selection: We selected randomized trials and controlled observational studies that directly evaluated screening for impaired visual acuity in older adults. To evaluate indirect evidence on screening, we also included studies evaluating the diagnostic accuracy of screening tests for impaired visual acuity used in primary care settings, and randomized trials and controlled observational studies of treatments for impaired visual acuity due to refractive errors, cataracts, and age-related macular degeneration that reported clinical outcomes (visual acuity, quality of life, functional capacity, adverse events, or mortality).

Data Extraction: One investigator abstracted data and a second investigator checked data abstraction for accuracy. Two investigators independently assessed study quality using methods developed by the United States Preventive Services Task Force.

Data Synthesis (Results): Direct evidence from three fair-quality cluster randomized trials (N=4,728) found vision screening as part of multi-component primary care intervention associated with no benefits compared to usual care, delayed screening, or no screening on visual acuity or other clinical outcomes. One randomized controlled trial found vision screening by an ophthalmologist in frail older adults associated with an increased risk of falls (relative risk 1.57, 95% CI 1.20 to 2.05) and a trend towards increased risk of fractures (relative risk 1.74, 95% CI 0.97 to 3.11). No other trial evaluated harms associated with screening, and no studies evaluated optimal screening intervals.

Four studies found screening questions associated with low accuracy compared to visual acuity testing or an ophthalmologic examination for identification of vision impairment and four studies found visual acuity testing associated with low accuracy compared to an ophthalmologic examination for identification of any visual condition. Evidence on the diagnostic accuracy of the Amsler grid is limited to one study, and no studies evaluated diagnostic accuracy or utility of fundoscopic examination in primary care settings.

A large population-based study found that about 60% of older adults with vision impairment could achieve visual acuity of 20/40 or better with refractive correction. Based on numerous observational studies, over 90% of patients undergoing cataract surgery achieve visual acuity of 20/40 or better. Antioxidant vitamins and minerals are more effective than placebo for reducing

progression of dry age-related macular degeneration (adjusted odds ratio 0.68, 99% CI 0.49 to 0.93), though conclusions are largely influenced by results of a single, large, good-quality trial. For wet age-related macular degeneration, laser photocoagulation (relative risk 0.67 for 6+ lines visual acuity loss; 95% CI 0.53 to 0.83, five trials), photodynamic therapy (relative risk 0.22 for 3+ lines visual acuity loss, 95% CI 0.13 to 0.30, three trials), and vascular endothelin growth factor inhibitors (for 3+ lines visual acuity loss: pegaptanib [two trials] relative risk 0.71, 95% CI 0.61 to 0.84; ranibizumab [two trials] relative risk 0.21, 95% CI 0.16 to 0.27) are superior to placebo for prevention of visual acuity loss, though evidence on laser photocoagulation is limited by methodological shortcomings. Harms of commonly used interventions for uncorrected refractive error, cataract, and age-related macular degeneration appear to be substantially outweighed by benefits, though data on long-term benefits and harms of photodynamic therapy and vascular endothelin growth factor inhibitors are limited.

Limitations: We excluded non-English language studies, could not evaluate for publication bias because of small numbers of trials, included previously published systematic reviews on treatments that met quality threshold criteria, and did not construct outcomes tables.

Conclusions: Direct evidence is relatively limited, but shows that screening for impaired visual acuity in older adults in primary care settings is not associated with improved visual or other clinical outcomes and may be associated with unintended harms such as increased risk of falls. Effective treatments (benefits outweigh harms) are available for uncorrected refractive error, cataracts, and age-related macular degeneration. The Snellen chart is the standard for screening for impaired visual acuity in primary care, but its diagnostic accuracy is difficult to assess because a clinically relevant reference standard is not established. There remains no evidence on accuracy of fundoscopic examination by primary care providers. More research is needed to understand why the direct evidence on vision screening in older adults shows no benefit, despite the availability of effective treatments for common conditions associated with impaired visual acuity.

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CHAPTER 1. INTRODUCTION

Scope and Purpose

Impaired visual acuity is common in older adults.[1] In addition to a higher incidence and prevalence of primary ocular disease and systemic diseases associated with ocular disease in older compared to younger adults, older adults also experience normal age-related changes in vision. Because symptoms may be relatively mild or progress slowly, older adults may be unaware of or underreport impaired visual acuity. Older adults may also have difficulty recognizing or reporting impaired visual acuity due to the presence of co-morbidities such as cognitive impairment. Screening for vision disorders could help identify impaired visual acuity in older adults and lead to treatments that improve quality of life or functional capacity, or prevent or slow down progression of vision loss.

In 2008, the United States Preventive Services Task Force (USPSTF; see Appendix A for a comprehensive list of abbreviations) commissioned an evidence review on screening for impaired visual acuity in older adults, in order to inform an updated USPSTF guideline. The main purpose of the evidence review is to evaluate new evidence published since 1996 on screening for impaired visual acuity in older adults.[2]

Condition Definition

Impaired visual acuity refers to decreased clarity or sharpness of vision. In addition to decreased visual acuity, vision impairment can also be associated with decreases in low light vision, color vision, binocularity, contrast sensitivity, or stereopsis, as well as visual field loss (areas in the field of view in which objects cannot be seen). Visual acuity is most commonly assessed using the Snellen eye chart, which assesses the ability of patients to recognize letters of different sizes arranged in rows from a pre-specified distance (typically 20 feet). Roughly speaking, a person with 20/100 vision according to the Snellen chart would need to be 20 feet away to read the smallest letters that someone with "normal" (20/20) vision could read at 100 feet. Visual acuity can also be described in meters (6/6 in meters is equivalent to 20/20 in feet) or using the decimal or the logarithm of the minimum angle of resolution (logMAR) scale (Table 1).

The severity of decreased visual acuity varies. Vision impairment has been defined as visual acuity of worse than 20/40[3] or 20/50[4] but better than 20/200 (the threshold for legal blindness). In this report, we use the term "impaired visual acuity" rather than "vision impairment" because the latter term implies functional limitations. In addition, vision impairment could occur for reasons other than visual acuity loss. Visual acuity worse than 20/20 but better than 20/40 or 20/50 is thought to have minimal effects on reading ability, functional capacity, or quality of life. Although no standardized definition for "mild" impairment in visual acuity exists, some studies have used a definition of visual acuity between roughly 20/40 and 20/80.[3, 4] This degree of impaired visual

acuity is less likely to cause major functional limitations than more severe impairment in visual acuity, and may be more apt to be identified through screening.

This report focuses on impaired visual acuity associated with the following conditions: uncorrected refractive errors, cataracts, and age-related macular degeneration (ARMD). Diabetic retinopathy and glaucoma are addressed elsewhere by the USPSTF.[5, 6] Screening approaches for glaucoma (visual field assessment, fundoscopic examination, and intraocular pressure measurement) differ from the screening tests (visual acuity and central vision testing) typically used in primary care settings for the conditions included in this report. Screening for diabetic retinopathy typically occurs in the context of care for patients with known diabetes.

Prevalence and Burden of Disease

In 2000, approximately 1.8 million US adults older than 65 years were estimated to have impaired visual acuity (best-corrected vision worse than 20/40 but better than 20/200).[1] Based on mobile vision exams performed between 1999 and 2002, the National Health and Nutrition Examination Survey estimated an 8.8% prevalence of presenting impaired visual acuity in US adults greater than 60 years of age.[4] Impaired visual acuity rates in US adults were stable from 1986 through 1995.[7] Prevalence of impaired visual acuity rises with age in older adults, from 1.1% in persons 65 to 69 years of age to 16.7% in persons older than 80 years of age.[1] Impaired visual acuity is more prevalent in nursing home patients compared to community-dwelling older adults.[8, 9] In one survey of Baltimore area nursing home residents, the rate of impaired visual acuity was 18.8%.[9]

Impaired visual acuity is consistently associated with decreased functional capacity and quality of life in older persons, including the ability to live independently, with more severe impaired visual acuity associated with greater negative impacts.[10-13] Impaired visual acuity can affect ability to perform both basic and instrumental activities of daily living, work, drive safely or obtain a driver's license, and increase risk of falls and other accidental injuries.[14-18]

The link between visual impairment or specific causes of impaired visual acuity and mortality in older adults has been evaluated in a number of epidemiologic studies. Some data suggest an association between risk of mortality and impaired visual acuity (any cause), cataracts, or (to a lesser extent) ARMD, possibly because such conditions may be independent markers for increased cardiovascular risk.[19-25] However, other studies found any association largely attenuated or no longer present after adjustment for cardiovascular risk factors and other confounders.[26, 27]

Uncorrected refractive errors, cataracts, and ARMD are common causes of impaired visual acuity in older adults. In 2000, refractive errors were estimated to affect 6.7 million US adults over 65 years of age.[28] In older adults with impaired visual acuity (including those currently using corrective lenses), approximately 60% have correctable (to better than 20/40) refractive errors.[4] In general, the prevalence of hyperopia increases sharply with age, with a prevalence 4.2 to 7.4 times higher in the persons $\geq$ 80 years of age compared to those 40 to 49 years of age.[28] Among white men, the prevalence of hyperopia $\geq$ +3.0 diopters (D) is 3.6% among those 40 to 49 years of age, 14.1% among those 65 to 69 years of age, and 23.5% among those greater than 80 years of age. An exception to increasing prevalence of hyperopia with age is adult black men, in whom the

prevalence of hyperopia remains fairly constant across age groups, ranging from 1.5% to 3.9%.[28] Among adults over 65 years of age, the prevalence of myopia is relatively stable with increasing age, though prevalence varies among different ethnic/racial groups. For example, the prevalence of myopia < -1.0 D in black men aged 65 to 69 years is 8.1%, compared to 13.1% in Hispanic men and 17.7% in white men.[28]

In persons with low vision (defined as best-corrected visual acuity < 20/40), cataracts are the cause in approximately half of cases.[1] The prevalence of cataracts increases sharply with age. Over 5 million US adults over 65 years of age were estimated to have cataracts (not necessarily associated with vision impairment) in 2000.[29] In white women, prevalence increases from 27.7% in persons 65 to 69 years to 76.6% in persons $\geq$ 80 years. Respective figures in black women are 28.5% and 60.9%, in white men 22.4% and 71.3%, and in black men 17.5% and 46.2%. Cataracts are the most common cause of blindness (best-corrected visual acuity < 20/200) in black US adults over 40 years of age (37%), but are a relatively less frequent cause of blindness in white (8.7%) and Hispanic (14.3%) persons.[1]

In 2000, approximately 1.5 million US adults over 65 years of age were estimated to have ARMD and another 4.8 million were estimated to have drusen (a sign of early ARMD or increased risk for developing ARMD).[30] ARMD is not necessarily associated with impaired visual acuity, particularly in early stages. The proportion of patients with low vision attributable to ARMD ranges from 3% in black persons to 23% in white persons.[28] The prevalence of ARMD increases with age, rising from 1.1% among white men 65 to 69 years of age to 11.9% among those $\geq$ 80 years of age; a similar pattern is observed among white women (0.7% and 16.4%, respectively).[30] Prevalence is substantially lower among black men and women, even among older age groups (1.6% and 2.4% in persons older than 80 years of age, respectively). Advanced ARMD is more likely to be due to the neovascular or "wet" type of ARMD than to "dry" ARMD (geographic atrophy). ARMD is the most common cause of blindness among white persons (54% of cases) and accounts for a significant proportion of blindness among Hispanics (14.3%), but is a relatively infrequent cause of blindness among black persons (4.4%).[1]

Etiology and Natural History

Refractive errors are a general term to describe conditions associated with the inability of cornea and lens of the eye to bring parallel rays of light into sharp focus on the fovea, resulting in blurry vision. In adults, common types of refractive errors are myopia, hyperopia, and astigmatism. Myopia occurs when images are focused in front of the fovea, affecting ability to clearly view more distant objects.[31] Hyperopia occurs when images are focused behind the fovea, which affects the ability to sharply view closer objects. Hyperopia often presents or worsens with older age because of presbyopia, which refers to age-related changes in the eye including decreased elasticity of the lens, reducing near-focusing ability. Astigmatism is a condition in which there are two or more focal points in the eye, resulting in distortion of images at various distances. Progression of myopia in older adults can be associated with development and progression of cataracts.

Cataracts are opacities in the lens of the eye, which result in decreased visual acuity and glare.[32] The main subtypes of cataracts are defined by their anatomic location within the lens and are classified as nuclear, cortical, and subcapsular, or some combination of these subtypes. Cataracts often occur bilaterally, though their presence and severity is frequently asymmetrical. Cataract opacities and severity of impaired visual acuity progress over time, with a variable rate of progression.

ARMD affects the macula, or area of the retina responsible for central vision.[33] Drusen, which are white to yellow retinal lesions, are an early sign of ARMD when they occur in the macula. Although their presence is not clearly associated with vision loss, presence of more or larger drusen is associated with a greater risk of developing advanced ARMD. Advanced ARMD is usually classified into "wet" or "dry" forms. The "dry" form of advanced ARMD (also referred to as 'geographic atrophy') is associated with atrophy of the retinal layers and retinal pigmented epithelial cells. The "wet" form of ARMD is associated with the development of abnormal blood vessels in the choroid layer underneath the retina (choroidal neovascularization). Both types of advanced ARMD can cause blurred central vision, distorted vision, and decreased low light vision. In severe cases, advanced ARMD results in central scotomas (complete loss of central vision).

Risk Factors

Rates of impaired visual acuity are higher among Hispanics, persons of lower socioeconomic or educational status, and those without private health insurance.[1, 4] Risk factors for specific conditions causing impaired visual acuity vary depending on the condition. A positive family history is a major risk factor for both myopia and hyperopia.[31] In both sexes and in various ethnic/racial groups, latent hyperopia tends to become manifest with older age due to a loss in accommodation, with the exception of black men, in whom the prevalence of hyperopia remains relatively low.[28] Risk factors for cataracts include older age, smoking, alcohol use, exposure to ultraviolet light, diabetes, and exposure to corticosteroids.[34, 35] Lower socioeconomic status and black race are associated with higher rates of unoperated cataracts.[36] Risk factors for ARMD are not completely understood, but are thought to include older age, smoking, and family history.[37] ARMD is substantially more common in white persons compared to other races/ethnicities.[1]

Rationale for Screening/Screening Strategies

Impaired visual acuity due to uncorrected refractive error, cataracts, and age-related macular degeneration is common in adults and the prevalence increases with age.[1, 28-30] Impaired visual acuity in older adults may not be recognized or may remain unreported because vision changes can be relatively subtle, progress slowly over time, or occur in persons with cognitive dysfunction or other co-morbidities. However, even mildly impaired visual acuity can be associated with decreased quality of life and functional capacity and increase the likelihood of accidents and related injuries.[10-13] Screening for impaired visual acuity in the primary care setting is non-invasive and could potentially identify persons likely to benefit from referral for interventions to improve visual acuity or slow progression of ocular disease.[2, 38]

Interventions/Treatment

A number of interventions are available to treat common causes of impaired visual acuity. Although impaired visual acuity may be identified in the primary care setting, most interventions require the involvement of an eye care provider. For uncorrected refractive error, the most common treatment is corrective lenses (eyeglasses and contact lenses). Photorefractive surgery including laser in-situ keratomileusis (LASIK), photorefractive keratectomy (PRK) or laser epithelial keratomileusis (LASEK) is associated with more up-front costs compared to corrective lenses and more commonly selected as a treatment option by younger adults. For patients with impaired visual acuity that is not sufficiently improved by correcting refractive error, reading aids (such as magnifiers) are a treatment option.[39] For cataracts causing significant impairment in visual acuity, the most common treatment is surgical cataract extraction and intraocular lens implantation.[40] Antioxidants and vitamins have been found to slow the progression of some types of ARMD, but have no proven benefit in slowing cataract progression.[41-44] No treatment is known to reverse the retinal damage associated with dry ARMD.

The wet form of ARMD accounts for most of the vision loss and blindness associated with advanced ARMD. Treatments for wet ARMD are aimed at the abnormal retinal vascular growth (choroidal neovascularization) associated with this condition and responsible for vision loss. Laser photocoagulation is an established treatment for wet ARMD, but causes blind spots due to retinal damage in areas of treatment.[45] It is generally considered a treatment option only in patients with extrafoveal (outside of the foveal area) neovascularization, in order to avoid causing central visual field defects.[45-47] Photodynamic therapy (PDT) with verteporfin, a photoreactive agent, is associated with less retinal scarring as compared to laser photocoagulation and is an option for subfoveal (under the fovea) neovascularization. Patients are intravenously injected with verteporfin, which preferentially adheres to newly-formed neovascular blood vessels. The verteporfin is then activated by exposure to low-intensity laser, with resulting thrombosis and destruction of abnormal blood vessels. Another treatment for wet ARMD is intravitreal injection of a vascular endothelial growth factor (VEGF) inhibitor such as ranibizumab or pegaptanib in order to suppress growth of abnormal blood vessels. Other treatments that have been studied for wet ARMD include surgical implantation of corticosteroids,[48] intravitreal interferon alfa,[49] radiation,[50] and surgical procedures (submacular surgery and macular translocation). However, these therapies have either not been proven to be effective or have limited indications for use.

Current Clinical Practice

The clinical standard for identifying presence of impaired visual acuity is by evaluation of distance visual acuity using the Snellen eye chart or another standardized test of visual acuity. Pinhole visual acuity testing can be used to estimate whether impaired visual acuity is due to correctable refractive error (vision corrects or improves upon pinhole testing).[51] Reading distance testing can also be assessed using a handheld card or other screening tool.

Clinically significant cataracts can be visualized via physical examination as opacities in the lens. Impaired visual acuity due to cataracts should not completely correct with pinhole testing, though

partial correction may occur due to decreased light-scattering, particularly if myopia related to the cataract is present.[52]

The Amsler grid consists of evenly spaced horizontal and vertical lines (making squares) on a sheet.[53] It is used to detect retinal defects affecting central vision including ARMD, which can be associated with distortion in the boxes on the grid or blank areas in the grid (scotomas). The Amsler grid can also be used by patients as a self-monitoring tool for early signs or progression of macular disease.[54, 55]

Screening questions may be used to elicit self-perceived problems with vision.[56] Fundoscopic examination can also be performed in order to detect asymptomatic or early ARMD or other retinal disease. The frequency with which non-Snellen visual acuity tests, the Amsler grid, vision screening questionnaires, or fundoscopic examination is used in primary care is not known. [2, 38] Older adults with vision impairment are typically referred to an optometrist or ophthalmologist for further evaluation, correction of refractive error, and other treatments. About half of US adults over the age of 65 years report an eye exam within the last 12 months.[57]

Recommendations of Other Groups

Several North American organizations recommend vision screening in older adults (Table 2). In general, the American Academy of Family Physicians[58, 59] and the Canadian Task Force on Preventive Health Care,[38] which issue guidelines for primary care physicians, recommend Snellen visual acuity testing at unspecified intervals. Both groups either do not recommend fundoscopy due to insufficient evidence or do not comment on the role of fundoscopic examination. The American Academy of Ophthalmology[60] and the American Optometric Association[61] both recommend a full eye examination in older adults, including fundoscopic exam, at an interval of one to two years.

Previous USPSTF Recommendation

In 1996, the USPSTF recommended routine vision screening with Snellen acuity testing for older persons ("B" recommendation).[2] The USPSTF made no recommendation regarding optimal frequency of screening or use of screening questions to identify persons at higher risk for impaired visual acuity. The USPSTF found insufficient evidence to recommend for or against routine fundoscopic examination by the primary care physician in asymptomatic older adults.

CHAPTER 2. METHODS

Using the methods of the USPSTF that are fully detailed in Appendix B and with the input of members of the USPSTF, we developed an analytic framework (Figure 1) and key questions (KQs) to guide our literature search and review. The target population is adults older than 65 years evaluated in primary care settings and not known to have impaired visual acuity, including those with impaired visual acuity despite current use of corrective lenses. We also included studies of vision screening in eye specialty settings, but evaluated their applicability to primary care settings. We defined impaired visual acuity as visual acuity worse than 20/40 but better than 20/200. For treatments, which are typically provided in eye specialty settings, we focused on corrective lenses and photorefractive surgery for uncorrected refractive errors; cataract surgery and antioxidants or vitamins for cataracts; antioxidants or vitamins for dry ARMD; and laser photocoagulation, photodynamic therapy, and VEGF inhibitors for wet ARMD. Outcomes of interest were visual acuity, vision-related function or quality of life, general function or quality of life, falls, accidents, mortality, and adverse events related to treatment (such as surgical complications, keratitis, visual field deficits, loss of vision, and others). We excluded persons with glaucoma or diabetes.[5, 6]

The KQs are:

KQ1: Does vision screening in asymptomatic older adults result in improved morbidity or mortality or improved quality of life?

KQ2: Are there harms of vision screening in asymptomatic older adults?

KQ3: What is the accuracy of screening for early impairment in visual acuity due to uncorrected refractive error, cataracts or age-related macular degeneration?

KQ4: Does treatment of early impairment in visual acuity due to uncorrected refractive error, cataracts or age-related macular degeneration lead to improved morbidity/mortality, or quality of life?

KQ5: Are there harms of treating early impairment in visual acuity due to uncorrected refractive error, cataracts or age-related macular degeneration?

Search Strategies

We searched the Cochrane Controlled Trials Registry and Cochrane Database of Systematic Reviews (through 3rd Quarter 2008) and MEDLINE database (1996 – July 2008) for relevant studies and meta-analyses (search strategies described in Appendix B1). We also reviewed reference lists of relevant articles and queried experts in the field for additional citations.

Study Selection

Studies pertaining to screening, diagnosis, and treatment of impaired visual acuity were selected based on pre-defined inclusion and exclusion criteria developed for each KQ (Appendix B2). Two reviewers evaluated each study at the title/abstract and full-text article stages to determine eligibility for inclusion. The flow of studies from initial identification of titles and abstracts to final inclusion or exclusion is diagrammed in Appendix B3. We focused on studies reporting results in persons 65 years of age or older, but included studies of younger adults if sufficient data in the older age group were not available. We included systematic reviews of randomized trials if they met criteria for a good-quality study,[62] and fair- or good-quality systematic reviews of observational studies when no randomized trials were available. Studies that were excluded after review of the full-text articles and reasons for exclusion are listed in Appendix B4.

Data Abstraction and Quality Rating

We abstracted details about the patient population, study design, data analysis, follow-up, and results. One author abstracted data and another author verified data abstraction for accuracy. We used predefined criteria developed by the USPSTF to assess the internal validity of studies.[63] Two authors independently rated the internal validity of each study as "good," "fair," or "poor". For cluster randomized trials, in addition to standard USPSTF methods for assessing quality of randomized trials (described in Appendix B5), we also evaluated whether the statistical analyses adjusted for the cluster correlation.[64] For diagnostic accuracy studies, we used the *diagti* procedure (confidence intervals based on the exact method) in Stata (Stat version 10, StataCorp, College Station, TX) to calculate sensitivities and specificities and the *cci* procedure (confidence intervals based on the normal approximation) to calculate positive likelihood ratios (PLRs), negative likelihood ratios (NLRs), and diagnostic odds ratios (DORs). For all studies we evaluated applicability to populations likely to be encountered in primary care screening settings (e.g., whether patients were recruited from primary care settings, and the inclusion of patients with mild to moderate vision impairment). Discrepancies in quality ratings were resolved by discussion and consensus. We rated quality of systematic reviews using criteria described in Appendix B6 and verified the accuracy of data abstraction by systematic reviews by independently abstracting and rating the quality of all trials comparing a treatment to no treatment, placebo, or sham treatment.

Data synthesis

We assessed overall strength for each body of evidence addressing a particular KQ or part of a KQ (for example, different treatments) using methods developed by the USPSTF.[63] To assign an overall strength of evidence ("good," "fair," or "poor") we considered the number, quality and size of studies, consistency of results between studies, and directness of evidence.

For efficacy of treatments, we reported quantitative estimates for treatment effects from previously published systematic reviews meeting inclusion criteria after verifying data abstraction and

analyses.[62] For treatments with new, placebo-controlled trials not included in systematic reviews, we calculated updated relative risks with the new trials and corresponding confidence intervals using a random effects model (Review Manager Version 4.2.8, Copenhagen: The Nordic Cochrane Center, 2003).

For diagnostic tests, we classified PLRs > 10 and NLRs $\leq$ 0.1 as "large," PLRs > 5 and $\leq$ 10 and NLRs > 0.1 and $\leq$ 0.2 as "moderate," and PLRs > 2 and $\leq$ 5 and NLRs > 0.2 and $\leq$ 0.5 as "small."[65]

External review

We distributed a draft of the report for review by external experts not affiliated with the USPSTF (Appendix B7). Revisions have been made based on their comments.

CHAPTER 3. RESULTS

Key Question 1. Does vision screening in asymptomatic older adults result in improved morbidity or mortality or improved quality of life?

Summary

Three fair-quality cluster randomized trials (N=4,728) found vision screening in older adults as part of a multi-component screening intervention in primary care settings to be no more effective than no vision screening, delayed screening, or usual care for improving vision or functional outcomes. One fair-quality randomized trial (N=309) found vision screening by an optometrist in frail older adults associated with an increased risk of falls (rate ratio 1.57, 95% confidence interval [CI] 1.20 to 2.05) and a trend towards increased risk of fractures (rate ratio 1.74, 95% CI 0.97 to 3.11) compared to usual care. One prospective cohort study found an increased number of eye examinations over a five-year period associated with decreased risk of becoming unable to read newsprint and new functional limitations, but results do not appear to be directly applicable to vision screening in primary care settings. No study evaluates optimal vision screening intervals.

Evidence

There is no direct evidence from randomized trials that screening for impaired visual acuity in asymptomatic older adults is associated with improved visual outcomes, function, or other clinical outcomes. Three fair- or fair-to-good quality cluster randomized trials (N=4,728) evaluated vision screening as part of a multi-component screening intervention (Table 3, Appendices C1 and C2).[66-68] Methodological shortcomings in all trials include lack of intention-to-treat analysis and unclear blinding status of outcomes assessors. Only one trial[68] applied a cluster correlation correction when analyzing results.[64] The screening intervention varied in the three trials: one trial compared visual acuity testing (Glasgow acuity chart followed by pinhole testing for persons with visual acuity worse than 6/18) to targeted screening;[68] one compared immediate vision screening to delayed vision screening (screening methods not described well, but appeared to include Snellen acuity chart, test of ability to read newspaper letters at 25 cm, and assessment of difficulty in recognizing a face at 4 m or reading a newspaper);[66] and the third compared use of a screening question followed by visual acuity testing if positive to usual care.[67] None of the trials found vision screening associated with improvements (or lower likelihood of deterioration) in vision, likelihood of vision disorders, or functional impairment related to vision at 6 months to up to 5 years after the intervention (Table 3).

In the highest quality (rated fair-to-good) trial, universal vision screening identified about 10 times as many patients with impaired visual acuity and correctable impairment in visual acuity compared to targeted screening, yet found no difference in the rate of visual acuity worse than 20/60 after 3 to 5 years of follow-up.[68] Reasons for the negative findings are not entirely clear. However, only half of the patients advised to see an eye care provider after vision screening actually received new glasses. In addition, short-term improvements in vision may have been missed because outcomes were assessed after a median of 3.9 years, though no difference in visual outcomes was seen in a subgroup with shorter time to assessment (1.6 to 3 years). Other reasons for lack of benefit in the screening trials may include high loss to follow-up (in part related to advanced age and mortality in enrollees), similar frequency of vision disorder detection and treatment in the screening and control groups in one trial,[67] and low uptake of recommended interventions in one trial.[66]

One fair-quality trial found that vision screening by an optometrist in frail older adults (N=309) did not reduce risk of falls and fractures compared to usual care.[69] Screening included visual acuity testing using the Early Treatment Diabetic Retinopathy Study Chart, contrast sensitivity testing, visual field testing, assessment of intraocular pressure, slit lamp examination, and direct ophthalmoscopy. Screening led to new eyeglasses or referral for further treatment in about half (146/309; 47%) of the study's participants. After one year of follow-up, vision screening was associated with an increased risk of falls (rate ratio 1.57, 95% CI 1.20 to 2.05, p=0.01) and a trend towards increased risk of fractures (rate ratio 1.74, 95% CI 0.97 to 3.11, p=0.06) compared to usual care. Possible explanations for these results could be the need for a prolonged period of readjustment in frail older adults after receiving new eyeglasses, or increased activity or other behaviors following treatment for vision impairment that could place subjects at increased risk for falls.

One fair-quality prospective cohort study of Medicare beneficiaries aged 65 years or older found an association between the number of eye examinations over a 5 year period and the probability of

experiencing vision decline and functional limitations.[70] However, the study did not meet inclusion criteria as its applicability to screening is unclear and may be limited. The study did not distinguish between eye examinations for the purpose of screening versus monitoring of known eye diseases or systemic conditions associated with eye diseases, or describe whether screening was performed in primary care settings or in eye clinics. Among persons enrolled in the study that developed blindness or low vision or became unable to read newsprint, approximately one-quarter carried diagnoses of diabetes or glaucoma. The study also did not compare results of subjects who underwent at least one eye examination versus those who underwent no eye examinations. Methodological limitations of the study include high loss to follow-up, unclear reporting of attrition, and failure to report baseline characteristics stratified by the number of eye examinations, making it difficult to assess comparability between groups or likelihood for residual confounding. The study found each additional year with an eye examination associated with a 12% decrease in the probability of becoming unable to read newsprint (p=0.03), a 5% decrease in the probability of an increased number of activities of daily living limitations (p=0.003), and 13% decrease in the probability of an increased number of instrumental activities of daily living limitations (p=0.002). The association between each additional year of eye examinations and decreased probability of onset of low vision or blindness was not statistically significant (0.9% decrease, p=0.06).

No study directly evaluated effects of screening for impaired visual acuity in asymptomatic older adults at different intervals. One cohort study found that following a normal baseline eye examination, the likelihood of experiencing no significant visual field or visual acuity loss after 5 years was 97% in persons aged 60 to 69 years old, and 93% in persons aged 70 to 79 years old.[71]

We excluded a systematic review of community screening for impaired visual acuity in older adults because five of the six included trials evaluated multi-component screening interventions performed in the home (the sixth trial[68] is discussed above).[72] It found no benefit associated with community screening for impaired visual acuity. In addition, a trial of vision screening versus usual care was excluded because it only enrolled adults aged 40 to 64 years old.[73] Like the trials of screening in older adults, it found no significant differences between groups in vision outcomes.

Key Question 2. Are there harms of vision screening in asymptomatic older adults?

Summary

Data on harms from vision screening in older adults are sparse. None of the screening studies in primary care settings evaluated potential harms such as anxiety, complications of treatment, or exposure to unnecessary interventions due to false-positive screening tests. One trial reported an increased risk of falls following vision screening by an optometrist in frail older adults compared to usual care, and is described in more detail in KQ 1.

Evidence

Potential harms associated with vision screening include anxiety, complications of treatment, or exposure to unnecessary interventions due to false-positive screening tests. However, none of the screening studies in primary care settings evaluated harms associated with vision screening.[66-68, 70] One study, described in KQ 1, reported an increased risk of falls following screening by an optometrist.[69]

Key Question 3. What is the accuracy of screening for early impairment in visual acuity due to uncorrected refractive error, cataracts or age-related macular degeneration?

Summary

Studies of diagnostic accuracy for various vision screening questions have methodological shortcomings, but four studies are consistent in showing that no screening question is accurate compared to visual acuity testing or a detailed ophthalmologic examination for identifying impaired visual acuity. Visual acuity tests (four studies) and the Amsler grid (one study) are associated with low diagnostic accuracy compared to a detailed ophthalmologic examination for identifying the presence of any underlying visual condition, including conditions not necessarily associated with impaired visual acuity. No study directly compared the diagnostic accuracy of the Snellen test to an established, clinical relevant reference standard for impaired visual acuity. No studies evaluated the accuracy of pinhole testing for differentiating impaired visual acuity due to correctable refractive error from impaired visual acuity due to other causes. One very small study found non-ophthalmologists able to identify cataracts on physical examination as accurately as ophthalmologists. No studies evaluated the accuracy of fundoscopic examination by primary care clinicians for identifying ARMD or other conditions.

Evidence

Eight cross-sectional studies evaluated the accuracy of various diagnostic tests or screening questions for impaired visual acuity in older adults compared to a reference standard (Table 4, Appendices C3 and C4).[74-81] All of the studies had at least two methodological shortcomings. Only one study clearly reported independent interpretation of the reference standard,[78] only two studies clearly applied the reference standard to all patients,[75, 78] and only one study reported sufficient data to determine that an appropriately broad spectrum of patients was evaluated.[76] Four of the eight studies (three[75, 76, 79] evaluated screening questions and one[78] compared geriatrician to

ophthalmologic examination) reported diagnostic accuracy specifically in older adults; the remainder enrolled mixed populations of older and younger adults. One additional study did not meet inclusion criteria because it only enrolled patients aged 64 years and younger, but is discussed here contextually.[73]

Screening questions or questionnaires. Four studies found various screening questions or questionnaires to have low accuracy for identifying impaired visual acuity compared to visual acuity testing[75, 76, 79] or a detailed ophthalmologic examination[80] (Table 5). No screening question or questionnaire was associated with both high sensitivity and specificity, resulting in weak PLRs and NLRs. PLRs for various screening questions or screening questionnaires ranged from 1.19 to 3.23, and NLRs ranged from 0.23 to 0.78. The DORs (PLR divided by NLR), a measure of the discriminating power of a diagnostic test, were also weak and ranged from 1.60[79] to 9.45.[75] A study that did not meet inclusion criteria because it enrolled adults aged 40 to 64 years reported similar findings on accuracy of a screening question (PLR 3.99 [95% CI 3.09 to 5.15], NLR 0.77 [95% CI 0.71 to 0.84]).[73]

Visual acuity tests. Four studies found various visual acuity screening tests to have low accuracy compared to a full ophthalmologic examination for identifying the presence of any visual condition (Table 5).[74, 77, 80, 81] Interpretation of diagnostic accuracy based on this reference standard is a challenge because the clinical significance of visual conditions not necessarily associated with impaired visual acuity is unclear. No visual acuity test was associated with both high sensitivity and specificity, resulting in generally weak PLRs and NLRs. PLRs ranged from 1.00 to 8.07 and NLRs from 0.32 to 1.00, with DORs less than 10. The exception was one study that found presenting distance acuity $\leq$ 20/40 associated with a DOR of 18.9 (95% CI 13.64 to 26.26) for identifying any visual condition.[81] However, three other studies[74, 77, 80] found the same distance acuity threshold associated with DORs of 2.47 (95% CI 2.08 to 2.94)[77] to 4.40 (95% CI 2.69 to 7.18).[74] Two studies reported areas under the receiver operating curve that ranged from 0.66 to 0.83 for various tests of visual acuity.[74, 77] One study reported diagnostic accuracy of visual acuity testing specifically for identifying cataracts or early ARMD, with results similar to those for identifying any visual condition.[77] No studies compared the Snellen test to an established, clinically relevant reference standard for impaired visual acuity, possibly because the Snellen is often considered the clinical standard for evaluating visual acuity.

Amsler grid. One study found the Amsler grid associated with poor accuracy for identifying any visual condition (Table 5).[74] The PLR was 1.65 (95% CI 0.90 to 3.06) and the NLR was 0.91 (95% CI 0.82 to1.01). We found no other studies that evaluated diagnostic accuracy of the Amsler grid in persons without known ARMD or other retinal disease.

Clinical examination. One small (N=50) study found that among patients aged 64 to 97 and not known to have eye disease, 100% (9/9) patients with cataracts and 75% (3/4) patients with ARMD were correctly identified by a geriatrician compared to an ophthalmologist.[78] No false-positives were reported.

Pinhole testing. We identified no study that evaluated the accuracy of primary care clinic-based pinhole testing for differentiating impaired visual acuity due to correctible refractive error from impaired visual acuity due to other causes. One excluded study estimated a sensitivity of 79% and specificity of 98% for home pinhole testing (administered by a Census Bureau worker) compared to complete ophthalmologic exam (including refraction) for identifying uncorrectable refractive error, but did not perform an ophthalmologic exam in all patients and imputed data to calculate measures of diagnostic accuracy.[51] In addition, it was not designed to assess accuracy of pinhole testing for differentiating impaired visual acuity due to correctible refraction error from other causes, as it did not enroll a population of patients with impaired visual acuity on non-pinhole visual acuity testing.

Fundus examination. No studies evaluated accuracy or yield of dilated fundus examination by primary care providers. One retrospective study (N=1094) found that fundoscopic examination by an ophthalmologist identified clinically significant abnormalities in 2.7% of asymptomatic patients.[82]

Key Question 4. Does treatment of early impairment in visual acuity due to uncorrected refractive error, cataracts or age-related macular degeneration lead to improved morbidity/mortality or quality of life?

Summary

A number of treatments are effective at improving visual outcomes in patients with uncorrected refractive error, cataracts, or, in the case of ARMD, slowing disease progression. For uncorrected refractive error and cataracts, there is good evidence from a large body of observational data and accumulated clinical experience that the most common treatments (refractive lenses and cataract surgery) are highly effective at restoring normal or near-normal visual acuity. A large population-based study found that about 60% of older adults with impaired visual acuity could achieve visual acuity of 20/40 or better with refractive correction. Based on numerous observational studies, over 90% of patients undergoing cataract surgery achieve visual acuity of 20/40 or better. One randomized trial found immediate cataract surgery associated with decreased risk of second (though not first) fall compared to delayed surgery, resulting in a lower overall rate of falls (rate ratio 0.66, 95% CI 0.40 to 0.96, p=0.03). For wet ARMD, there is evidence from randomized trials that laser photocoagulation (relative risk 0.67 to 6+ lines visual acuity loss; 95% CI 0.53 to 0.83, five trials), PDT (relative risk 0.22 for 3+ lines visual acuity loss, 95% CI 0.53 to 0.83, five trials) and intravitreal injection with VEGF inhibitors (for 3+ lines visual acuity loss: pegaptanib [two trials] relative risk 0.71, 95% CI 0.61 to 0.84; ranibizumab [two trials] relative risk 0.21, 95% CI 0.16 to

0.27) are effective at slowing loss of visual acuity, though serious methodological shortcomings were present in trials of laser photocoagulation. Conclusions regarding effectiveness of vitamin and mineral supplements for treating dry ARMD are largely based on a single large, good-quality trial that found a decreased risk for disease progression (adjusted OR [odds ratio] 0.68, 99% CI 0.49 to 0.93). Evidence showing that treatment of early vision impairment is associated with improvement in vision-related function is relatively sparse and not always consistent with evidence showing improvements in visual acuity. (See Appendices C5-8 for full data abstraction and quality ratings on randomized controlled trials (RCTs) and systematic reviews on efficacy and harms of treatment).

Evidence

Uncorrected refractive error

Corrective lenses. In the National Health and Nutrition Examination Survey (NHANES) study, over 60% of persons over the age of 60 with presenting visual acuity worse than 20/50 could achieve visual acuity better than 20/40 with refractive correction.[4] We identified two fair-quality randomized trials (N=131 and 151) that found immediate correction of refractive error with eyeglasses in older (mean age 80 years) adults associated with improved short-term (2-3 month follow-up) vision-related quality of life or function compared to delayed treatment (Table 6).[83, 84] One trial[83] recruited patients during community health screening, while the other[84] recruited nursing home patients. In both trials, patients randomized to immediate eyeglasses experienced improvements in vision-related quality of life or function relative to the delayed-treatment groups on a variety of measures. For example, General Vision subscale scores of the National Eye Institute Visual Functioning Questionnaire (NEI-VFQ) were improved by a mean of about 10 (of 100) points in the immediate-treatment group in both trials, representing a moderate clinical improvement. However, there were few between-group differences on measures of general functional status.

Refractive surgery. A systematic review of 27 RCTs and 130 observational studies found LASIK, LASEK, and PRK to be similarly and highly effective at improving refractive errors, with 92-94% of persons with myopia and 86-96% of persons with hyperopia achieving visual acuity 20/40 or better (Table 7).[85] Several observational studies also found refractive surgery associated with improved quality of life.[86-88] Preliminary results from a meta-analysis conducted for a joint task force formed by the U. S. Food and Drug Administration (FDA) found that > 95% of patients are satisfied following LASIK, though final results of this study are not yet available [http://www.ascrs.org/index.cfm]. Data on incidence of glare, visual haloes, or worsened night vision following refractive surgery are sparse and inconsistent, with rates ranging from 0% to over 50%.[85]

Low vision aids. A systematic review of nine trials compared the effect of various low vision aids, including magnifiers, prism spectacles, telescopes and electronic devices, on improving reading speed (Table 7).[39] Secondary outcomes of this review were change in visual acuity and improvement in quality of life, but only one of the included trials reported any of these outcomes.[89] It found no difference between prism eyeglasses and conventional eyeglasses in logMAR acuity or

NEI-VFQ score. A non-randomized study of consecutively enrolled patients in a low vision clinic, not included in the review above, assessed quality of life outcomes 3 months following use of a variety of visual aids (including eyeglasses, magnifiers, and telescopes).[90] 21% of participants had visual acuity better than 20/60 at baseline. Following treatment, quality of life was improved on a number of measures, though there was no change from baseline in Medical Outcomes Study – Short Form Health Survey 36 (SF-36) scores.

Cataract

Surgery. We identified no randomized trials that evaluated visual outcomes associated with cataract surgery versus no surgery. A good-quality systematic review of 57 observational studies published between 1979 and 1991 (of 90 total included studies) found cataract surgery associated with post-operative visual acuity of 20/40 or better in 88.9% (95% CI 88.1% to 89.8%) of all eyes (N=17,390) and 95.2% (95% CI 94.7% to 95.7%) of eyes without preoperative ocular comorbidity (N=10,003) after weighting results by sample size and quality score (Table 8).[91] Only four of the studies were controlled cohort studies; the remainder were uncontrolled observational studies. The mean quality score of included studies averaged 43 out of a maximum possible 100 points.[92]

Benefits of cataract surgery on visual acuity may be lower at very advanced ages (e.g., older than 85 years). Some studies found very advanced age associated with a three- to four-fold difference in likelihood of achieving good visual outcomes after adjusting for potential confounders.[93-95] However, cataract surgery still appears to be associated with positive effects in the great majority of patients in this age group. One of the few studies specifically evaluating outcomes in this population found 85% of persons 85 years or older experienced improved visual acuity.[96]

Three good-quality, prospective observational studies found cataract surgery associated with clinically significant improvement in vision-related quality of life and function assessed using validated measures.[97-99] Two studies (N=464 and 772)[98, 99] prospectively enrolled and assessed quality of life in patients prior to cataract surgery and again following surgery. The other study was a controlled cohort study,[97] but enrolled a much smaller patient population (N=45). Four months following cataract surgery, two studies found mean Visual Function 14 (VF-14) scores increased by 17 to 25 points;[97, 98] one of these studies also found Nursing Home Vision-Targeted Health-Related Quality of Life Questionnaire (NHVQoL) scores increased an average of 22.1 points;[97] and a third study found Activities of Daily Vision Scale (ADVS) scores increased from 14.7 to 22.4 points (of 100).[99] Studies that reported patients' subjective assessment of vision-related function following surgery[100-102] are consistent with studies reporting improvements in formal vision-related quality of life measures, as are studies that assessed vision-related quality of life in the subgroup of persons over 80 years of age.[96, 103, 104]

The effect of cataract surgery on functional status or quality of life not directly related to vision is less clear. Results from a 4-month study found no significant difference in SF-36 scores from baseline following surgery, while a 12-month study found a worsening in SF-36 score compared to baseline.[97, 99] Another study found small or no statistically significant changes in domains of the functional assessment inventory,[101] and one study found no changes in depression scores (Center for Epidemiologic Studies Depression Scale [CES-D]) following cataract surgery.[105]

Two good-quality trials (N=545) compared effects of immediate (within 4 weeks) versus delayed (12 month waiting list) cataract surgery on falls in high-risk women[106, 107] (Table 9). Baseline fall rates in enrollees ranged from 45-51% during the 12 months preceding study entry. One trial evaluated initial (first-eye) cataract surgery[106] while the other evaluated second-eye cataract surgery.[107] Both trials adjusted for activity level following surgery. Immediate first-eye cataract surgery was associated with no significant difference compared to delayed surgery in risk of first fall (hazards ratio 0.95, 95% CI 0.69 to 1.35; p=0.77), though the risk of second fall was reduced (hazards ratio 0.60, 95% CI 0.36 to 0.98; p=0.04), resulting in a lower overall rate of falls per 1000 patient days (relative risk 0.66, 95% CI 0.40 to 0.96, p=0.03).[106] Immediate second-eye surgery was not associated with a reduction in incidence of first or second fall or overall falls per 1,000 patient days (relative risk 0.68, CI 0.39 to 1.19; p=0.18).[107] However, statistical power was limited because this trial was unable to enroll the prespecified number of patients.

Both trials reported fracture incidence as a secondary outcome. Results were mixed and had limited statistical power due to small numbers of events. Relative to the delayed-treatment group, the first-eye trial found an immediate surgery associated with a lower risk of fracture (relative risk 0.33, 95% CI 0.1 to 1.0; p=0.04).[106] The second-eye trial found no difference between immediate and delayed surgery in fracture risk, but the estimate was imprecise (relative risk 2.5, 95% CI 0.5 to 12.5; p=0.45).[107]

Incidence of motor vehicle crashes was assessed in one well-designed cohort study that prospectively followed 277 older drivers with cataracts who did or did not undergo cataract surgery.[108] The no-surgery group included more men and fewer whites than the surgery group, and the surgery group had worse visual acuity in both eyes at baseline relative to the surgery group. After 4 to 6 years, patients in the cataract surgery group had a lower risk of motor vehicle accidents compared to the no-surgery group (adjusted rate ratio of 0.47 [CI 0.23 to 0.94], absolute rate reduction 4.74 crashes per million miles driven).

One prospective cohort study (N=384) found that patients with cataracts who did not have surgery have increased mortality risk through up to 6 years of follow-up.[23] There were statistically significant baseline differences among the three enrolled groups (cataract surgery versus no surgery versus no cataract). Persons with cataracts who did not undergo surgery experienced 6.8 deaths per 100 patient-years, compared to 3.6 deaths per 100 patient-years in persons with cataracts who underwent surgery, and 0.9 deaths per 100 patient-years in those without cataracts (adjusted risk ratio 3.2 [CI 1.2 to 9.0] for cataract/no-surgery versus no-cataract).

Vitamins. One fair-quality trial found no clear difference between antioxidant vitamins versus placebo for progression of opacities in patients with cataracts[109] (Table 9). Although epidemiologic and other observational studies suggest that diets high in antioxidants or use of antioxidants is associated with a lower risk of cataract development,[110] randomized trials in patients without cataracts at baseline or in mixed populations of persons with and without cataracts failed to demonstrate positive effects of antioxidant supplements on cataract development or progression.[41, 42, 44, 111-113]

Dry (nonexudative) Age-related Macular Degeneration

Antioxidant vitamins and minerals. The large, good-quality Age-Related Eye Disease Study (AREDS; n=3640) found a multivitamin (vitamins C and E and beta carotene) plus zinc associated with reduced likelihood of progression to advanced ARMD (adjusted OR 0.68 [CI, 0.49 to 0.93]), though the difference in the likelihood of losing 15 or more letters of visual acuity did not reach statistical significance (adjusted OR 0.77 [CI, 0.58 to 1.03]).[114] A good-quality systematic review included nine randomized controlled trials (n=5569), but results were heavily influenced by AREDS (Table 10).[43] All trials enrolled patients with mild to advanced dry ARMD, with the exception of the Vitamin E, Cataract and Age-Related Maculopathy (VECAT) study (N=1204), which included some patients with no ARMD.[115] VECAT found no difference between vitamin E and placebo in likelihood of visual acuity loss of 15 or more letters, though results remain unpublished.[43] The systematic review also included a small (n=58) trial of zinc supplementation published only as a conference abstract[116] and a Chinese-language trial of zinc, vitamin C, and vitamin E that reported results poorly.[117] We rated the other trials included in the systematic review fair-[118-122] or poor-quality[123] (Appendix C6). The composition and doses of the antioxidant or mineral regimens varied in these trials. The systematic review found insufficient evidence to determine efficacy of vitamins and minerals other than the AREDs combination.[118, 120-123] A small (n=101), fair-quality trial that was not included in the systematic review found the combination of acetyl-*L*-carnitine, n-3 fatty acids, and coenzyme Q10 more effective than placebo for experiencing no deterioration in Snellen visual acuity (23% vs. 45%, p=0.015), but the proportion of patients experiencing clinically significant visual acuity loss was not reported.[124]

A review of four trials and eight observational studies conducted by the FDA found insufficient evidence to show use of lutein and zeaxanthin is associated with reduced risk of ARMD.[125] AREDS 2, an ongoing Phase III trial, is studying the effect of these and other antioxidants.

Other treatments. A systematic review of two small trials found gingko biloba associated with no beneficial effects on the rate of ARMD progression and no differences in visual acuity compared to placebo after 6 months of treatment.[126] Quality of life or mortality outcomes were not reported in either of the included trials. Rheopheresis was evaluated in one trial, but results were inconclusive and the trial had methodological shortcomings.[127] Further research on rheopheresis by this study's funder was halted in November 2007 (http://www.occulogix.com/pressreleases.htm).

Wet (exudative) Age-related Macular Degeneration

Laser photocoagulation. A good-quality systematic review found laser photocoagulation superior to no treatment for progression of vision loss (loss of 6+ lines of visual acuity) after 3 months (relative risk 1.41, 95% CI 1.08 to 1.82, five trials, N=1413) and 2 years (relative risk 0.67; 95% CI 0.53 to 0.83, five trials, N=1258) (Table 10).[45] We rated all trials poor-quality[128-132] due to methodological shortcomings, including use of an open-label design, incomplete follow-up, and lack of intention-to-treat analysis (Table 11 and Appendix C6). In addition, clinical and statistical heterogeneity (I^2=58%) were present in the pooled analysis. The trials enrolled subjects with visual acuity ranging from normal to worse than 20/200; and the proportion of patients with baseline vision worse than 20/200 ranged from 0% to 34%. The location of choroidal neovascularization

(foveal, juxtafoveal, or extrafoveal) also varied. Nonetheless, all trials found a benefit in favor of laser photocoagulation. No trial compared laser photocoagulation to PDT or VEGF inhibitors.

Photodynamic therapy with verteporfin. Two good-quality systematic reviews of PDT found verteporfin superior to placebo for preventing loss of visual acuity (Table 10).[133, 134] Both reviews included the Treatment of Age-Related Macular Degeneration With Photodynamic Therapy (TAP) Investigation[135] and the Verteporfin in Photodynamic Therapy (VIP) Trial.[136] The more recent of the two reviews[134] also included a third trial, the Visudyne in Minimally Classic Choroidal Neovascularisation (VIM) Trial.[137] We rated VIM fair-quality[137] and TAP and VIP good-quality (Table 11 and Appendix C6).[135, 136] Pooling all three trials (N=1065), one systematic review found verteprofin associated with a risk ratio reduction in loss of 3 or more lines of visual acuity of 0.22 after 2 years (CI 0.13 to 0.30), with a number-needed-to-treat of seven.[134] Three and 5-year results of open-label extension of the TAP study were similar to 2-year results.[138, 139]

None of the verteporfin trials reported quality of life outcomes. Two small, prospective observational studies that enrolled a total of 130 patients, most with classic choroidal neovascularization, found VF-14 scores decreased (indicating worse vision-related quality of life) following treatment, but the decrease was not statistically significant. [140, 141] Neither the TAP nor VIP trials found significant differences between verteporfin and placebo in risk of deaths two years after treatment,[133] and no deaths were reported during the 2-year VIM trial.[137]

Intravitreal injection of VEGF inhibitors. A good-quality systematic review found intravitreal injection with the VEGF inhibitors pegaptanib or ranibizumab effective for preventing visual acuity loss (defined as > 15 letters or 3 lines loss) and reducing the risk of blindness (defined as visual acuity worse than 20/200), based on three fair-quality, placebo-controlled trials (Tables 10 and 11).[142] A good-quality trial of ranibizumab that was not included in the systematic review also found it to be effective for outcomes related to visual acuity.[143] For pegaptanib at doses of 0.3, 1, or 3 mg, the systematic review found a pooled relative risk versus placebo of 0.71 for visual acuity loss (CI 0.60 to 0.84, two trials,[144] N=1186) at 12 month follow-up; the number-needed-to-treat to prevent one case of visual acuity loss ranged from 7 to 14 depending on the dose evaluated.[142] Pegaptanib also reduced the risk of blindness (visual acuity worse than 20/200) compared to placebo (relative risk 0.69; 95% CI 0.59 to 0.82, two trials). In two trials (N=900), ranibizumab at 0.3 or 0.5 mg was also associated with decreased risk of visual acuity loss (relative risk 0.21, 95% CI 0.16 to 0.27, Figure 2) and blindness (relative risk 0.35, 95% CI 0.21 to 0.57, Figure 3) compared to placebo at 12 months, with a number-needed-to-treat of about 2.5.[143, 145] Results at 24 months were similar to those at 12 months in one of the trials.[145]

Vision-associated function was assessed in three good-quality trials of VEGF inhibitors, though they were not primary outcomes in any study.[143, 146, 147] One trial found ranibizumab associated with a 5.2 to 5.6 point increases in composite NEI-VFQ scores at 1-year, compared to a decrease of 2.8 points with placebo ($p<0.01$ for difference).[146] Benefits were largely sustained through two years. A second trial found no difference between ranibizumab and placebo in mean scores on the near activities, distance activities, or vision-specific dependency subscales on the NEI-VFQ at one year.[143] One trial of pegaptanib reported outcomes on four (of 12) NEI-VFQ domains, including near vision, distance vision, role limitations and dependency.[147] While there was a trend towards

improvement in the near and distance vision domains, differences were not statistically or clinically significant. Composite NEI-VFQ scores were not reported.

One fair-quality, head-to-head trial (N=423) found ranibizumab superior to verteprofin PDT after 12 months for likelihood of losing < 15 letters (94-96% vs 64%) or gaining > 15 letters (36-40% vs 6%) of visual acuity.[148] Quality of life outcomes were not evaluated.

Combination therapy. The efficacy of PDT in combination with an intravitreal injection (ranibuzumab or corticosteroid) was studied in two trials (reported in three publications).[149-151] Based on the proportion of patients losing < 15 letters of visual acuity, one study (N=162) found combination therapy with ranibizumab superior to PDT alone (90.5% vs 67.9%; p<0.001) after 1-year of follow-up.[151] These results were attenuated but remained statistically significant at 2-years (87.6% vs 75.0%; p=0.04).[149] In the other trial, there was no significant difference between combination therapy with triamcinolone plus PDT versus PDT alone on this outcome (74.1% vs. 61.5%; p=0.78, N= 61).[150] Neither trial evaluated quality of life.

Other therapies. Good-quality Cochrane reviews found insufficient evidence to conclude that radiotherapy (11 trials),[50] intravitreal corticosteroids (three trials),[48] or intravitreal injection of interferon alfa (one trial)[49] are effective for treatment of wet ARMD. Macular translocation surgery was effective but associated with high rates of adverse events in a pilot trial and is not recommended as first-line therapy.[152, 153] Submacular surgery was no more effective than observation.[154]

Key Question 5. Are there harms of treating early impairment in visual acuity due to uncorrected refractive error, cataracts or age-related macular degeneration?

Summary

Data on harms associated with eyeglasses are limited to a small observational study showing an association between multifocal lens use and increased risk of falls in older adults (adjusted OR 2.09, 95% CI 1.06 to 4.92). Harms associated with other treatments for uncorrected refractive errors have also not been well-studied, but available data suggest a low incidence of serious harms such as infectious keratitis (contact lenses 0.3 to 0.9 cases per 10,000 wearers and photorefractive surgery 0% to 3.4%) and corneal ectasia (photorefractive surgery median rate 0.2%). The most common long-term complication of cataract extraction and intraocular lens implantation is posterior capsule opacification, which is present in over one-quarter of patients after 5 years. Serious complications

such as endophthalmitis are rare (0.13%). For dry ARMD, data from the large AREDS trials found antioxidant vitamins and minerals associated with increased risk of hospitalization for genitourinary causes (zinc) and yellow skin (antioxidants). In patients with wet ARMD, laser photocoagulation and PDT are associated with acute vision loss, including severe loss with the latter treatment (2% with PDT vs. 0.2% with placebo). However, long-term visual outcomes favor both of these treatments (see KQ 4). Serious harms appear to be uncommon following intravitreal injection with the VEGF inhibitors pegaptanib and ranibizumab, but evidence on long-term harms is not yet available.

Evidence

Uncorrected refractive error

Corrective lens. We identified no studies that evaluated harms associated with monofocal eyeglasses. One prospective study (N=87) found multifocal lens (bifocals, trifocals or progressive lens) associated with higher risk of falls in older adults (adjusted OR 2.09, 95% CI 1.06 to 4.92).[155]

Contact lens use, particularly the extended-wear type, is associated with keratitis, or inflammation (infectious or non-infectious) of the cornea.[156, 157] Two large (each enrolling > 10,000 subjects) prospective observational studies found incidence of vision loss due to infectious keratitis ranged from 0.3 to 0.9 cases per 10,000 wearers, regardless of age.[158, 159] Risk of keratitis increased substantially in a prospective study of extended-wear contact lens to 3.6 (CI 0.4 to 12.9) cases per 10,000 wearers;[160] and age > 50 years was found to increase risk of developing keratitis compared to age ≤ 25 years (OR 2.04; CI 1.40 to 2.98) in another prospective study.[161]

Photorefractive surgery. Photorefractive surgery is associated with subsequent corneal ectasia (bulging forward of the cornea due to weakening of supporting structures following surgery) and infectious keratitis, although their incidence has not been well reported. A good-quality systematic review of 27 trials and 130 observational studies only identified five studies reporting rates of corneal ectasia, with a median rate of 0.2% (range 0% to 0.87%) following LASIK surgery.[85] No studies reported rates of ectasia in PRK or LASEK-treated patients. It also found rates of infectious keratitis ranged from 0% to 0.16% following LASIK and 0% to 3.4% following LASEK, but this outcome was only reported in six LASIK (including four studies reporting no cases) and four LASEK studies.[85]

Cataract

Posterior capsule opacification of surgically implanted lens is the most common long-term complication following cataract surgery,[162] though it is usually readily treated with a brief external laser procedure. In one good-quality systematic review, 41 primarily uncontrolled studies published between 1979 and 1991 reported rates of posterior capsule opacification which ranged from 0.7% to 47.6% after 60 days to 5 years (pooled rate 19.7%; CI 19.1 to 20.3).[91, 92] A more recent systematic review of 49 studies found a pooled incidence of posterior capsule opacification of 11.8% (range

9.3 to 14.3%) at 1-year, 20.7% (range 16.6 to 24.9%) at 3-years and 28.4% (range 16.6 to 24.9%) at 5-years.[163]

A fair-quality systematic review of 215 observational studies (quality of included studies was not assessed) found a 0.13% rate of endophthalmitis, a serious inflammation of the intraocular cavities potentially associated with permanent vision loss, following cataract surgery.[164] Additional analyses suggested that the rate of endophthalmitis may be increasing, with a relative risk of 2.44 (CI 2.27 to 2.61) for surgeries completed since the year 2000 compared to surgeries in earlier decades, a finding that temporally coincides with increased use of sutureless clear corneal incisions.[164]

Other major complications associated with cataract surgery include bullous keratopathy (0.13%, 95% CI 0.2 to 0.4), dislocation of intraocular lens (0.3%, 95% CI 0.9 to 1.2), clinical cystoid macular edema (95% 1.4%, CI 1.2 to 1.6), and retinal detachment (0.7%, 95% CI 0.6 to 0.8%).[91]

Dry (nonexudative) Age-related Macular Degeneration

Antioxidant vitamins and minerals. A good-quality systematic review of nine trials found no clear association between zinc supplementation for treatment of dry ARMD and withdrawal due to gastrointestinal symptoms, but the number of events was small (5/146 in zinc-treated patients versus 2/140 in controls).[43] The large AREDS trial found treatment with zinc associated with significantly increased risk of hospitalization for genitourinary causes compared to non-use of zinc (11.1% versus 7.6%; p=0.0003) and treatment with antioxidants associated with increased risk of yellow skin compared to non-use of antioxidants (8.3% vs. 6.0%, p=0.008).[113, 165] There was no association between antioxidant supplementation and increased hospitalizations, mortality, or lung cancer. Risk of congestive heart failure was not specifically reported. Other trials of antioxidants for dry ARMD found no clear association with adverse events at the doses evaluated,[121, 123] though assessment and reporting of harms was generally suboptimal.

Wet (exudative) Age-related Macular Degeneration

Laser photocoagulation. A good-quality systematic review of 15 trials found laser photocoagulation associated with increased risk of visual acuity loss ≥ 6 lines compared to observation 3 months after treatment (absolute rate 16.6%; relative risk 1.41, 95% CI 1.08 to 1.82, five trials).[45] However, laser photocoagulation was superior to observation on visual acuity outcomes by 2 years (see KQ 4).

Photodynamic therapy with verteporfin. A good-quality systematic review of three trials found verteporfin associated with greater risk of acute severe visual acuity loss (20 letter loss within 7 days of treatment) compared to placebo (2% vs. 0.2%, relative risk 0.02, 95% CI 0.01 to 0.03, number needed to harm 50).[134] The systematic review also found verteporfin associated with a greater risk of infusion-related back pain compared to placebo (3.4% vs. 0.3%, relative risk 6.50, 95% CI 1.52 to 27.78).

Intravitreal injection of vascular endothelin growth factor inhibitors. A good-quality trial found 5 cases of presumed endophthalmitis, 6 cases of uveitis, and 11 cases of post injection intraocular pressure greater than 40 mm Hg among 477 patients treated with ranibizumab, compared to 0 cases for any of these adverse events among 236 patients treated with sham injections.[145] There were no clear differences in rates of hypertension or thromboembolic events. A second, smaller trial reported no cases of endophthalmitis or uveitis following ranibizumab intraveitreal injection, and did not report post injection intraocular pressure.[143]

A study that pooled data from two similarly designed trials of pegaptanib (N=892 pegaptanib-treated patients) found a rate of endophthalmitis of 1.3% (0.16% per injection, with 1 of 12 cases associated with 6+ lines of vision loss), 0.6% for traumatic cataract (0.07% per injection, 1 of 5 cases associated with severe vision loss), and 0.7% for retinal detachment (0.08% per injection, no cases associated with severe vision loss) following 1 year of treatment.[166] There were no differences between pegaptanib and placebo in rates of hypertensive or thromboembolic events.

A head-to-head trial reported 2 cases of endophthalmitis and 1 case of uveitis among 277 patients treated with ranibizumab, compared to no cases among 143 patients treated with verteporfin, with no differences in rates of hypertension or arterial thromboembolic events.[148] A second trial found 18 serious ocular adverse events among 105 patients treated with ranibizumab plus verteporfin, compared to 8 cases among 56 patients treated with photodynamic therapy alone.[149] Among the serious adverse events in the combination therapy group were 3 cases of endophthalmitis and 4 cases of uveitis (none reported in the PDT alone arm).

The manufacturer of ranibizumab sent a letter to clinicians in January 2007 regarding preliminary results of an ongoing trial that found increased stroke rates in patients treated with higher doses of intravitreal ranibizumab. Results of that trial have not yet been published, although 1-year data reported at a conference in February 2008 showed no difference in stroke rates regardless of dose (http://www.retinatoday.com/issues/0308/0308_01.php).

CHAPTER 4. DISCUSSION

Results of this evidence synthesis organized by KQ are summarized in Table 12.

Impaired visual acuity is common in older adults, and effective treatments are available for common causes of impaired visual acuity. Nonetheless, direct evidence found that vision screening in asymptomatic older adults in primary care settings was not effective for improving visual acuity or other clinical outcomes. Additional studies are needed to determine why trials of vision screening have shown no benefit. For any vision screening program to be effective, optimal screening approaches and intervals need to be defined, and older adults with impaired visual acuity effectively linked to appropriate follow-up care.

Compared to the 1996 USPSTF evidence synthesis,[2] there is now more direct evidence on vision screening in older adults. Three fair- to good-quality cluster randomized trials that enrolled over 4700 patients found vision screening in older adults as part of a multi-component screening intervention in primary care settings to be no more effective than no vision screening, delayed screening, or usual care. [66-68] A fourth trial found optometrist screening associated with an increased risk of falls in frail elderly.[69] Although one prospective cohort study found more eye examinations over a 5-year period associated with superior visual and functional outcomes, its applicability to vision screening in primary care settings is unclear because reasons for the eye examinations and eye examination settings were not described.[70] There remains no evidence to evaluate optimal screening intervals in older adults.

Despite the lack of direct evidence to support vision screening, there is strong evidence on effectiveness of treatments for common causes of impaired visual acuity. As concluded by the 1996 USPSTF review, a very high proportion of patients experience favorable vision-related outcomes following treatment for impaired visual acuity due to refractive error and cataracts.[2] Over half of older adults with impaired visual acuity could achieve vision better than 20/40 with refractive correction,[4] which can be done noninvasively in most cases with corrective lenses. Correction of refractive error is also associated with improvement in vision-related quality of life.[83, 84] In patients with cataracts, a large body of observational studies indicates that surgical extraction and intraocular lens implantation results in visual acuity of 20/40 or better in over 90% of patients, and is associated with improvements in vision-related quality of life.[91] For dry ARMD, there is evidence that antioxidant vitamins and minerals are effective for slowing progression of disease,[43] though conclusions are largely based on a single large trial (AREDS).[114] Antioxidants included in the AREDS formulation have been found to be associated with congestive heart failure (vitamin E[167]) and lung cancer in smokers (beta-carotene[168, 169]) when prescribed for prevention of cancer or cardiovascular disease, though these harms were not observed in AREDS. For wet ARMD, VEGF inhibitors and PDT with verteporfin appear to be effective treatment options with a relatively low incidence of serious harms.[134, 142] An important advantage of these treatments is that they are associated with less retinal scarring compared to laser photocoagulation, which is a particularly important consideration for patients with subfoveal (central) neovascularization.

Evidence on accuracy of screening tests for impaired visual acuity (or conditions associated with impaired visual acuity) is difficult to interpret. Although the Snellen remains the most widely used tool to measure visual acuity in primary care settings, no clinically relevant reference standard exists to determine its diagnostic accuracy, in part because the Snellen is often considered the standard for assessing visual acuity in clinical practice. Although some studies found Snellen testing inaccurate compared to a detailed ophthalmologic examination, the conditions identified on examination were not necessarily associated with impaired visual acuity. It is now known whether identification of ARMD or cataracts prior to the development of impaired visual acuity is associated with improved clinical outcomes compared to identification of these conditions after the development of early impaired visual acuity. As in the 1996 USPSTF evidence review,[2] evidence is consistent that no screening question is comparable in accuracy to tests of visual acuity.[73, 75, 76, 79, 80] There remains insufficient evidence to assess the accuracy or utility of pinhole testing, the Amsler grid, visual acuity tests other than the Snellen, physical examination, or fundoscopic examination.

Limitations

Our evidence review has some potential limitations. First, we included relevant systematic reviews, and the reliability of systematic reviews depends on how well they are designed and conducted. We therefore only included systematic reviews meeting a quality threshold based on pre-defined criteria.[62] In addition, we verified data abstraction of the systematic reviews by independently abstracting and rating the quality of trials comparing an intervention to placebo, sham treatment, or no treatment. Second, we excluded non-English language studies, which could introduce language bias. However, we identified no relevant non-English language studies in literature searches or when searching reference lists. Third, when randomized trials were available, they were too few in number to perform assessments for publication bias. Finally, we did not attempt to construct outcomes tables, because the direct trials of screening found no benefits.

Emerging Issues

A number of trials comparing different individual treatments and combination therapies for wet ARMD are currently in progress.[142] In October 2006, the National Eye Institute announced recruitment for the AREDS-2 trial, which will evaluate the benefits and harms of an antioxidant combination with reduced zinc and/or beta-carotene (http://areds-2.com/).

Future Research

We identified several important gaps in the evidence on screening for impaired visual acuity in older adults. There is no direct evidence showing that vision screening in older adults is effective for improving visual outcomes or other clinical outcomes. Well-designed studies are needed to identify optimal methods for vision screening, define appropriate screening intervals, and develop effective strategies for linking older adults with vision impairment to appropriate care. Studies are needed on diagnostic accuracy and utility of fundoscopic examination, pinhole testing, the Amsler grid, and non-Snellen visual acuity charts in primary care settings for supplementing or replacing the Snellen visual eye chart. More studies are needed on potential harms (particularly long-term harms) of VEGF inhibitors and PDT for wet ARMD. Evidence on effectiveness of antioxidants and vitamins for dry ARMD is largely dependent on a single large trial reporting a post-hoc subgroup analysis,[113] and would be strengthened by similar findings from other, well-designed trials that are also designed to adequately evaluate potential harms such as congestive heart failure and lung cancer risk. More studies are needed to understand the potential association between correction of refractive errors and risk of falls,[69] and, if an association is present, to identify methods for falls prevention.

Conclusions

Impaired visual acuity is common in older adults. There remains no direct evidence that vision screening in older adults in primary care settings is effective for improving visual acuity or other clinical outcomes, though evidence is limited to a relatively small number of trials in which vision screening was typically conducted as part of a multi-component assessment.[66-68] On the other hand, effective treatments are available for common causes of impaired visual acuity, and vision impairment can be identified non-invasively using the Snellen chart, though its diagnostic accuracy is difficult to estimate. Additional studies are needed to determine why direct studies of screening have been unable to demonstrate benefits despite the availability of effective treatments, to clarify the risk of potential unintended harms from screening (such as increased risk of falls),[69] and to define optimal intervals of screening. For any vision screening program to be effective, patients with impaired visual acuity must be linked to appropriate eye care and follow-up.

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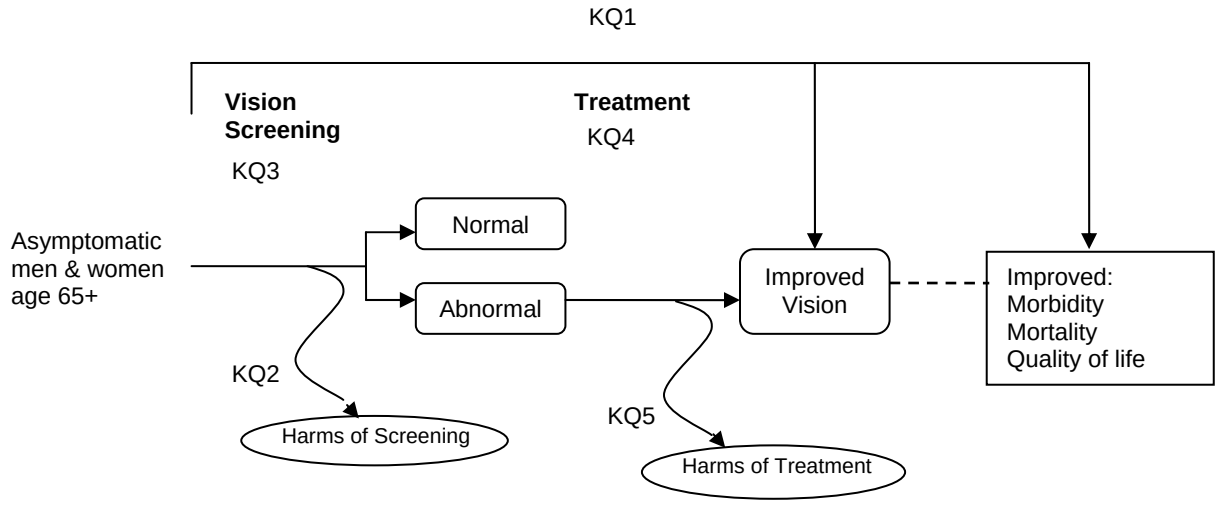
FIGURE 1. ANALYTIC FRAMEWORK AND KEY QUESTIONS



KQ 1. Does vision screening in asymptomatic older adults result in improved morbidity or mortality or improved quality of life?

KQ 2. Are there harms of vision screening in asymptomatic older adults?

KQ 3. What is the accuracy of screening for early visual impairment due to uncorrected refractive error, cataracts or age-related macular degeneration?

KQ 4. Does treatment of early visual impairment due to uncorrected refractive error, cataracts or age-related macular degeneration lead to improved morbidity/mortality, or quality of life?

KQ 5. Are there harms of treating early visual impairment due to uncorrected refractive error, cataracts or age-related macular degeneration?

Abbreviation: KQ = key question.

FIGURE 2. VISUAL ACUITY LOSS >15 LETTERS, RANIBIZUMAB VS. PLACEBO

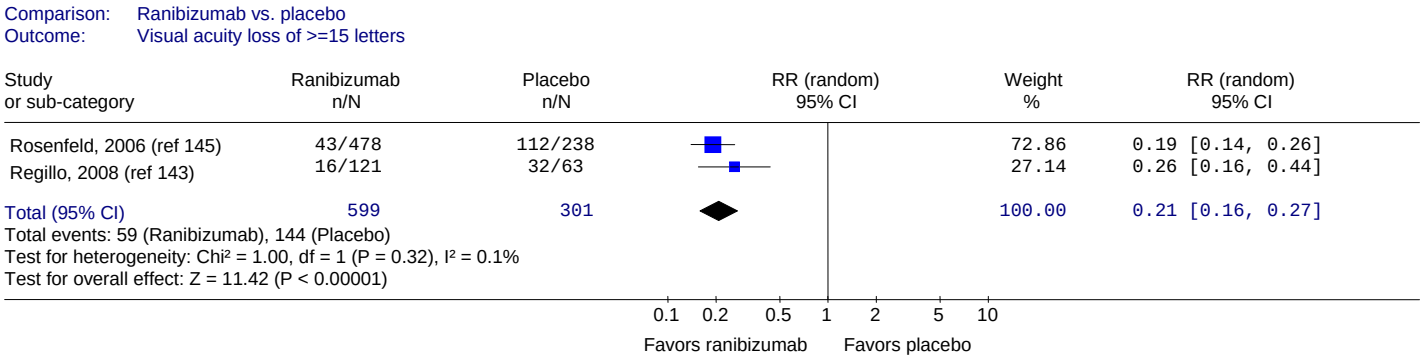


FIGURE 3. VISUAL ACUITY WORSE THAN 20/200, RANIBIZUMAB VS. PLACEBO

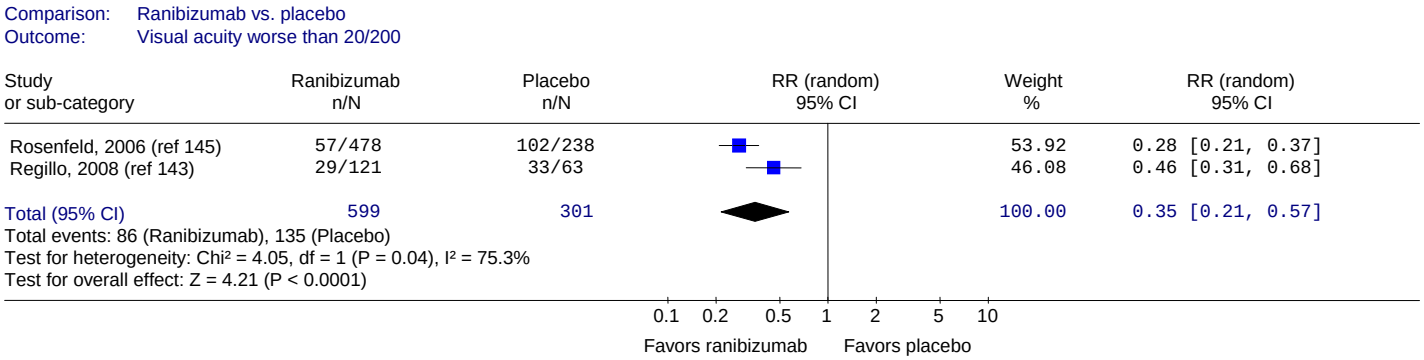


TABLE 1. MEASUREMENTS OF VISUAL ACUITY

Snellen		Decimal	LogMAR
Feet	Meters		
20/20	6/6	1.00	0.00
20/30	6/9	0.67	-0.18
20/40	6/12	0.50	-0.30
20/60	6/18	0.33	-0.48
20/80	6/24	0.25	-0.60
20/100	6/30	0.20	-0.70
20/160	6/48	0.13	-0.90
20/200	6/60	0.10	-1.00

Source: Holladay JT. *Visual acuity measurements. J Cataract Refract Surg.* 2004. **30**(2): p. 287-290.

Notes: Visual Impairment is 20/50 or worse; Legal Blindness is 20/200 or worse.

Abbreviation: LogMAR = logarithmic minimum angle of resolution.

TABLE 2. VISION SCREENING RECOMMENDATIONS

Organization	Recommended ages for vision screening (in years)	Frequency (in years)	Test	Last year updated
American Academy of Family Physicians (AAFP)[58, 59]	Adults >65	Not specified	Snellen visual acuity test	2007
American Academy of Ophthalmology (AAO)[60]	Adults <40	Every 5-10	Comprehensive medical eye evaluation	2005
	Adults 40-54	Every 2-4		
	Adults 55-64	Every 1-3		
	Adults >65	Every 1-2		
American Optometric Association (AOA)[61]	Adults 18-60	Every 2	Comprehensive eye and vision exam*	2005
	Adults ≥61	Every 1		
Canadian Task Force on Preventive Health Care (CTFPHC)[38]	Adults ≥65	During Periodic Health Exam (PHE)	Snellen visual acuity test	1995
U.S. Preventive Services Task Force (USPSTF)[2]	Adults ≥65	Frequency at the discretion of clinician	Snellen visual acuity test	1996

**May include any/all of the following: patient history; visual acuity; preliminary testing; refraction; ocular motility, binocular vision and accommodation; ocular health assessment and systemic health screening; supplemental testing if indicated.*

TABLE 3. RANDOMIZED CONTROLLED TRIALS OF VISION SCREENING IN OLDER ADULTS

Study, Year, Title	Screening intervention	Study design	Setting	Patient population	Results	Loss to follow-up	Quality score
Cumming et al, 2007[69] *Improving vision to prevent falls in frail older people*	Visual acuity assessed with Early Treatment Diabetic Retinopathy Study Chart at 2.4 m; contrast sensitivity with the CSV-1000E Chart 1 at 2.4 m; visual fields with Humphrey automated visual field unit; Perkins applanation tonometer; intraocular pressure with slit lamp exam and direct ophthalmoscopy	Random-ized controlled trial	Community based - patients received in-home care and/or at study clinic	70 years or older n=616 Australia	Vision screening vs. no vision screening Falls: Rate ratio 1.57 (95% CI 1.20 to 2.05; p=0.001) Fractures: Relative risk 1.74 (95% CI 0.97 to 3.11)	84/616 (14%)	Fair
Eekhof et al, 2000[66] *Effects of screening for disorders among the elderly: an intervention study in general practice*	Assessment of difficulty in recognizing a face at 4 meters and/or reading normal letters in a newspaper, and/or impaired vision with both by Snellen eye chart or not being able to read normal newspaper letters at 25 cm distance	Cluster random-ized controlled trial	Primary care clinic	75 years or older n=1121 The Netherlands	Immediate versus delayed vision screening Visual disorder in 2nd year: 51% vs. 47% (p=0.68)	16% (93/576) patients who underwent immediate screening did not participate in second year; otherwise unclear	Fair
Moore et al, 1997[67] *A randomized trial of office-based screening for common problems in older persons*	Vision screening: Question to assess difficulty performing everyday activities, followed by Snellen eye chart if positive	Cluster random-ized controlled trial	Primary care clinic	70 years or older n=261 United States	Vision screening versus usual care Improvement in vision at 6 months: 20% (20/99) vs. 24% (31/131), p=0.45	12% (31/261) at 6 months	Fair
Smeeth et al, 2003[68] *Screening older people for impaired vision in primary care: a cluster randomized trial*	Detailed health assessment by a trained nurse, including Glasgow eye chart and pinhole testing if visual acuity less than 6/18 in either eye (targeted screening only consisted of a brief health assessment)	Cluster random-ized controlled trial	Primary care clinic	75 years or older n=3249 United Kingdom	Universal vs. targeted vision screening: Visual acuity less than 6/18 in either eye at median 3.9 years: RR 1.07 (95% CI 0.84 to 1.36, p=0.58) National Eye Institute visual function questionnaire at median 3.9 years (mean score, 0 to 100 scale): 86.0 vs. 85.6 (p=0.69)	(1807/3249) did not complete outcome assessment (1465 deaths)	Good-Fair

Abbreviations: CI = confidence interval, RR = relative risk, .

TABLE 4. STUDIES OF DIAGNOSTIC TEST ACCURACY

Study, Year, Title	Type of study	Age of enrollees and sample size	Proportion with visual conditions	Reference standard	Index text	Quality score
Ariyasu et al, 1996[74] *Sensitivity, specificity, and predictive values of screening tests for eye conditions in a clinic-based population*	Cross-sectional	"Most patients" 20 to 59 years old n=317	43% refractive error, 16% cataract, 4% macular degeneration, 4% strabismus, 2% amblyopia	Detailed ophthalmologic assessment	Amsler grid Near visual acuity Distance visual acuity	Poor-Fair
Eekhof et al, 2000[75] *Screening for hearing and visual loss among elderly with questionnaires and tests: which method is the most convincing for action?*	Cross-sectional	75 years or older n=1121	Snellen chart <0.3: 10.8%	Snellen chart and low vision chart (testing vision at reading distance)	Screening questions	Fair
Hiller et al, 1983[76] *Validity of a survey question as a measure of visual acuity impairment*	Cross-sectional	25 to 74 years n=1466 for subgroup 65 to 74 years old	Snellen 20/25 or worse: 69%	Snellen chart	Screening question	Fair
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Cross-sectional	49 years or older n=3654	Posterior subcapsular cataract: 3.9%, cortical cataract: 19.1%, nuclear cataract: 47.0%; early ARMD 4.50%; refractive error 4.50%; any vision condition 34.50%	Detailed ophthalmologic assessment	Presenting distance visual acuity (logMAR chart) Pinhole distance visual acuity Presenting reading acuity (with current reading glasses)	Poor-Fair
McMurdo et al, 1988[78] *The detection of visual disability in the elderly*	Cross-sectional	64 to 97 years n=50	18% previously undiagnosed cataract; 8% previously undiagnosed ARMD	Ophthalmologist examination	Geriatrician examination	Fair
Teh et al, 2006[79] *Utility of a patient-response screening question for visual impairment*	Cross-sectional	60 years or older n=112	Snellen 6/12 or worse: 81%	Snellen chart	Screening question	Poor-fair

TABLE 4. STUDIES OF DIAGNOSTIC TEST ACCURACY

Study, Year, Title	Type of study	Age of enrollees and sample size	Proportion with visual conditions	Reference standard	Index text	Quality score
Wang et al, 1998[80] *Evaluation of screening schemes for eye disease in a primary care setting*	Cross-sectional	40 years or older n=405	50.7% (13% cataract, ARMD and refractive error not reported)	Detailed ophthalmologic assessment	Screening questionnaire Presenting distance visual acuity, followed by pinhole visual acuity if worse than 20/30	Poor-Fair
Woods et al, 1998[81] *Screening for ophthalmic disease in older subjects using visual acuity and contrast sensitivity*	Cross-sectional	50 years or older n=2522	12% (50 to 64 years) and 23% (>64 years) macular degeneration, 4.9% and 27.2% cataract	Detailed ophthalmologic assessment	Distance visual acuity (Snellen) Near visual acuity (Snellen)	Fair

Abbreviations: ARMD = age-related acular degeneration, CI = confidence interval, LogMAR = logarithmic minimum angle of resolution.

TABLE 5. STUDIES OF DIAGNOSTIC TEST ACCURACY, RESULTS

Study, Year, Title	Reference standard	Target vision condition	Screening test	Sensitivity	Specificity
Amsler grid					
Ariyasu et al, 1996[74] *Sensitivity, specificity, and predictive values of screening tests for eye conditions in a clinic-based population*	Ophthalmologic examination	Any ocular disease, excluding refractive error	Amsler grid	0.20 (0.14-0.27)	0.88 (0.80-0.94)
Physical examination					
McMurdo et al, 1988[78] *The detection of visual disability in the elderly*	Ophthalmologist examination	A: Cataract B: ARMD	Positive finding on physical examination	A: 1.0 (9/9) B: 0.75 (3/4)	A: 1.0 (41/41) B: 1.0 (46/46)
Screening questions					
Eekhof et al, 2000[75] *Screening for hearing and visual loss among elderly with questionnaires and tests: which method is the most convincing for action?*	Snellen chart	Visual acuity ≤ 0.3 (about 20/60 on Snellen)	Trouble recognizing face by questionnaire	0.60 (0.51-0.69)	0.82 (0.79-0.84)
		Difficulty with low vision chart at reading distance	Trouble reading newspaper by question-naire	0.83 (0.76-0.88)	0.67 (0.64-0.70)
Hiller et al, 1983[76] *Validity of a survey question as a measure of visual acuity impairment*	Snellen chart	A: Visual acuity ≤ 20/50 B: Visual acuity ≤ 20/100	Trouble seeing by questionnaire	A: 0.34 (0.28-0.41) B: 0.48 (0.32-0.63)	A: 0.84 (0.82-0.86) B: 0.82 (0.80-0.84)
Teh et al, 2006[79] *Utility of a patient-response screening question for visual impairment*	Snellen chart	Visual acuity ≤ 20/40	Problem with vision by questionnaire	0.68 (0.58-0.78)	0.43 (0.22-0.66)

TABLE 5. STUDIES OF DIAGNOSTIC TEST ACCURACY, RESULTS

Study, Year, Title	Positive likelihood ratio	Negative likelihood ratio	Diagnostic odds ratio
Amsler grid			
Ariyasu et al, 1996[74] *Sensitivity, specificity, and predictive values of screening tests for eye conditions in a clinic-based population*	1.65 (0.90-3.06)	0.91 (0.82-1.01)	1.82 (0.90-3.69)
Physical examination			
McMurdo et al, 1988[78] *The detection of visual disability in the elderly*	Not calculated	Not calculated	Not calculated
Screening questions			
Eekhof et al, 2000[75] *Screening for hearing and visual loss among elderly with questionnaires and tests: which method is the most convincing for action?*	3.23 (2.66-3.93)	0.49 (0.40-0.61)	6.56 (4.42-9.72)
	2.47 (2.20-2.78)	0.26 (0.18-0.37)	9.45 (6.08-14.7)
Hiller et al, 1983[76] *Validity of a survey question as a measure of visual acuity impairment*	A: 2.15 (1.72-2.69) B: 2.69 (1.94-3.74)	A: 0.78 (0.71-0.86) B: 0.64 (0.48-0.84)	A: 2.75 (2.00-3.78) B: 4.24 (2.33-7.72)
Teh et al, 2006[79] *Utility of a patient-response screening question for visual impairment*	1.19 (0.80-1.77)	0.74 (0.42-1.33)	1.60 (0.62-4.16)

TABLE 5. STUDIES OF DIAGNOSTIC TEST ACCURACY, RESULTS

Study, Year, Title	Reference standard	Target vision condition	Screening test	Sensitivity	Specificity
Wang et al, 1998[80] *Evaluation of screening schemes for eye disease in a primary care setting*	Ophthalmologic examination	Any ocular disease	A: Problem with vision by questionnaire B: Problem with vision by question-naire followed by visual acuity ≤ 20/40	A: 0.90 (0.85-0.94) B: 0.57 (0.50-0.64)	A: 0.44 (0.37-0.51) B: 0.79 (0.73-0.84)
Visual acuity testing					
Ariyasu et al, 1996[74] *Sensitivity, specificity, and predictive values of screening tests for eye conditions in a clinic-based population*	Ophthalmologic examination	Any ocular disease, excluding refractive error	Near visual acuity ≤ 20/30	0.83 (0.75-0.89)	0.32 (0.23-0.44)
			≤ 20/40	0.76 (0.68-0.83)	0.49 (0.38-0.61)
			≤ 20/60	0.60 (0.52-0.69)	0.64 (0.53-0.74)
Ariyasu et al, 1996[74] *Sensitivity, specificity, and predictive values of screening tests for eye conditions in a clinic-based population*	Ophthalmologic examination	Any ocular disease, excluding refractive error	Presenting distance visual acuity ≤ 20/30	0.75 (0.69-0.81)	0.51 (0.42-0.61)
			≤ 20/40	0.68 (0.61-0.74)	0.67 (0.58-0.76)
			≤ 20/60	0.53 (0.46-0.60)	0.86 (0.78-0.92)
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Ophthalmologic examination	A: Nuclear cataract B: Early ARMD C: Any eye disease	Pinhole distance acuity ≤ 20/30	A: 0.31 (0.28-0.34) B: 0.45 (0.37-0.53) C: 0.34 (0.31-0.37)	A: 0.89 (0.87-0.91) B: 0.79 (0.78-0.80) C: 0.86 (0.84-0.87)
			≤ 20/40	A: 0.13 (0.11-0.15) B: 0.21 (0.15-0.28) C: 0.15 (0.13-0.17)	A: 0.98 (0.97-0.99) B: 0.92 (0.91-0.93) C: 0.96 (0.95-0.97)
			≤ 20/60	A: 0.08 (0.06-0.10) B: 0.10 (0.06-0.16) C: 0.09 (0.07-0.11)	A: 0.99 (0.98-1.00) B: 0.95 (0.94-0.96) C: 0.97 (0.96-0.98)

TABLE 5. STUDIES OF DIAGNOSTIC TEST ACCURACY, RESULTS

Study, Year, Title	Positive likelihood ratio	Negative likelihood ratio	Diagnostic odds ratio
Wang et al, 1998[80] *Evaluation of screening schemes for eye disease in a primary care setting*	A: 1.60 (1.41-1.83) B: 2.72 (2.03-3.65)	A: 0.23 (0.15-0.36) B: 0.54 (0.46-0.65)	A: 6.88 (4.06-11.7) B: 5.00 (3.23-7.74)
Visual acuity testing			
Ariyasu et al, 1996[74] *Sensitivity, specificity, and predictive values of screening tests for eye conditions in a clinic-based population*	1.23 (1.04-1.46)	0.52 (0.32-0.86)	2.34 (1.23-4.47)
Ariyasu et al, 1996[74] *Sensitivity, specificity, and predictive values of screening tests for eye conditions in a clinic-based population*	1.50 (1.19-1.90) 1.67 (1.22-2.30) 1.54 (1.26-1.90)	0.49 (0.33-0.71) 0.62 (0.47-0.81) 0.48 (0.36-0.65)	3.09 (1.71-5.55) 2.70 (1.53-4.77) 3.18 (1.96-5.18)
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	2.08 (1.57-2.76) 3.76 (2.34-6.03) A: 2.83 (2.35-3.40) B: 2.16 (1.80-2.59) C: 2.43 (2.14-2.76)	0.47 (0.37-0.60) 0.54 (0.46-0.64) A: 0.78 (0.74-0.81) B: 0.69 (0.60-0.80) C: 0.77 (0.74-0.80)	4.40 (2.69-7.18) 6.90 (3.82-12.5) A: 3.65 (2.93-4.55) B: 3.11 (2.26-4.30) C: 3.17 (2.69-3.73)
	A 6.57 (4.29-10.1) B: 2.59 (1.87-3.58) C: 3.74 (2.95-4.73) A: 8.07 (4.44-14.7) B: 2.01 (1.24-3.28) C: 2.98 (2.23-3.97)	A: 0.89 (0.87-0.91) B: 0.86 (0.80-0.93) C: 0.89 (0.86-0.91) A: 0.93 (0.91-0.95) B: 0.95 (0.90-1.00) C: 0.94 (0.92-0.96)	A: 7.40 (4.78-11.5) B: 3.01 (2.01-4.49) C: 4.22 (3.27-5.45) A: 8.69 (4.76-15.8) B: 2.13 (1.25-3.63) C: 3.17 (2.34-4.30)

TABLE 5. STUDIES OF DIAGNOSTIC TEST ACCURACY, RESULTS

Study, Year, Title	Reference standard	Target vision condition	Screening test	Sensitivity	Specificity
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Ophthalmologic examination	A: Nuclear cataract B: Early ARMD C: Any eye disease	Presenting distance visual acuity ≤ 20/30	A: 0.44 (0.41-0.47) B: 0.56 (0.48-0.64) C: 0.47 (0.44-0.50)	A: 0.77 (0.74-0.79) B: 0.66 (0.64-0.68) C: 0.74 (0.72-0.76)
			≤ 20/40	A: 0.25 (0.22-0.28) B: 0.34 (0.27-0.42) C: 0.27 (0.24-0.29)	A: 0.90 (0.88-0.92) B: 0.82 (0.81-0.83) C: 0.87 (0.86-0.88)
			≤ 20/60	A: 0.13 (0.11-0.15) B: 0.13 (0.08-0.20) C: 0.14 (0.12-0.16)	A: 0.96 (0.95-0.97) B: 0.92 (0.91-0.93) C: 0.94 (0.93-0.95)
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Ophthalmologic examination	A: Nuclear cataract B: Early ARMD C: Any eye disease	Reading acuity ≤ 20/30	A: 0.97 (0.96-0.98) B: 0.99 (0.96-1.00) C: 0.98 (0.97-0.99)	A: 0.03 (0.02-0.04) B: 0.03 (0.02-0.04) C: 0.03 (0.02-0.04)
			≤ 20/40	A: 0.88 (0.86-0.90) B: 0.95 (0.90-0.98) C: 0.89 (0.87-0.91)	A: 0.20 (0.18-0.22) B: 0.16 (0.15-0.17) C: 0.19 (0.18-0.21)
			≤ 20/60	A: 0.57 (0.54-0.60) B: 0.70 (0.62-0.77) C: 0.59 (0.56-0.62)	A: 0.59 (0.56-0.62) B: 0.53 (0.51-0.55) C: 0.59 (0.57-0.61)
Wang et al, 1998[80] *Evaluation of screening schemes for eye disease in a primary care setting*	Ophthalmologic examination	Any ocular disease	Presenting distance visual acuity ≤ 20/40	0.61 (0.54-0.68)	0.72 (0.65-0.78)
Woods et al, 1998[81] *Screening for ophthalmic disease in older subjects using visual acuity and contrast sensitivity*	Ophthalmologic examination	Any ocular disease, excluding refractive error	Near visual acuity ≤ 20/30	0.77 (0.74-0.80)	0.68 (0.63-0.73)
Woods et al, 1998[81] *Screening for ophthalmic disease in older subjects using visual acuity and contrast sensitivity*	Ophthalmologic examination	Any ocular disease, excluding refractive error	Presenting distance visual acuity ≤ 20/30	0.74 (0.71-0.77)	0.87 (0.83-0.90)

TABLE 5. STUDIES OF DIAGNOSTIC TEST ACCURACY, RESULTS

Study, Year, Title	Positive likelihood ratio	Negative likelihood ratio	Diagnostic odds ratio
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	A: 1.91 (1.69-2.16) B: 1.65 (1.42-1.90) C: 1.81 (1.65-1.98)	A: 0.73 (0.68-0.77) B: 0.67 (0.56-0.80) C: 0.72 (0.68-0.76)	A: 2.63 (2.20-3.15) B: 2.47 (1.79-3.40) C: 2.53 (2.19-2.92)
	A: 2.50 (2.05-3.05) B: 1.89 (1.50-2.37) C: 2.07 (1.81-2.38)	A: 0.83 (0.80-0.87) B: 0.80 (0.72-0.90) C: 0.84 (0.81-0.87)	A: 3.00 (2.38-3.79) B: 2.34 (1.67-3.28) C: 2.47 (2.08-2.94)
	A: 3.22 (2.35-4.41) B: 1.65 (1.09-2.49) C: 2.33 (1.89-2.88)	A: 0.91 (0.88-0.93) B: 0.94 (0.89-1.00) C: 0.92 (0.89-0.94)	A: 3.55 (2.54-4.96) B: 1.75 (1.09-2.80) C: 2.55 (2.02-3.21)
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	A: 1.00 (0.99-1.01) B: 1.02 (1.00-1.04) C: 1.01 (1.00-1.02)	A: 1.00 (0.63-1.60) B: 0.42 (0.10-1.69) C: 0.66 (0.42-1.03)	A: 1.00 (0.62-1.61) B: 2.42 (0.65-8.98) C: 1.53 (0.97-2.42)
	A: 1.10 (1.06-1.14) B: 1.13 (1.09-1.18) C: 1.10 (1.07-1.13)	A: 0.60 (0.49-0.73) B: 0.32 (0.16-0.62) C: 0.58 (0.49-0.68)	A: 1.84 (1.46-2.32) B: 3.59 (1.78-7.26) C: 1.90 (1.55-2.32)
	A: 1.39 (1.28-1.52) B: 1.48 (1.33-1.65) C: 1.44 (1.35-1.54)	A: 0.73 (0.67-0.79) B: 0.57 (0.45-0.72) C: 0.70 (0.64-0.75)	A: 1.91 (1.62-2.26) B: 2.61 (1.85-3.68) C: 2.07 (1.80-2.38)
Wang et al, 1998[80] *Evaluation of screening schemes for eye disease in a primary care setting*	2.18 (1.70-2.79)	0.54 (0.45-0.66)	4.02 (2.65-6.09)
Woods et al, 1998[81] *Screening for ophthalmic disease in older subjects using visual acuity and contrast sensitivity*	2.41 (2.08-2.80)	0.34 (0.30-0.38)	7.15 (5.52-9.26)
Woods et al, 1998[81] *Screening for ophthalmic disease in older subjects using visual acuity and contrast sensitivity*	5.66 (4.36-7.34)	0.30 (0.27-0.33)	18.9 (13.6-26.3)

TABLE 5. STUDIES OF DIAGNOSTIC TEST ACCURACY, RESULTS

Study, Year, Title	Reference standard	Target vision condition	Screening test	Sensitivity	Specificity

Abbreviations: ARMD = age-related macular degeneration.

TABLE 5. STUDIES OF DIAGNOSTIC TEST ACCURACY, RESULTS

Study, Year, Title	Positive likelihood ratio	Negative likelihood ratio	Diagnostic odds ratio

TABLE 6. UNCORRECTED REFRACTIVE ERROR - RANDOMIZED CONTROLLED TRIALS

Study, Year Title	Study design Purpose of study Country	Patients	Intervention Duration of follow-up	Results	Quality score
Coleman et al, 2006[83] *Treatment of uncorrected refractive error improves vision-specific quality of life*	RCT To evaluate the benefits of eyeglasses and magnifiers in elderly patients with uncorrected refractive error U.S.	N=131 Mean age 80.4 years (SD 8.2) 72% female 63% White; 18% Black; 8% Asian; 3% Hispanic; 8% Other Mean baseline visual acuity 20/63	Intervention group: Received vision correction aids immediately (glasses, magnifier or both) Control group: Received a voucher and prescription to obtain vision correction aids at the conclusion of the trial (3 months later) 3-month follow-up	Mean change from baseline at 3 months, with glasses vs without glasses National Eye Institute Visual Functioning Questionnaire: Composite score: 6.5 (SD 9.3) vs -0.8 (SD 10.8); p<0.01 Selected individual components: -General health: 4.2 (SD 18.0) vs -0.4 (SD 17.4); p=.17 -General vision: 10.4 (SD 18.2) vs -2.1 (SD 14.0); p<0.01 -Near vision: 7.6 (SD 19.1) vs 0.4 (SD 17.4); p=0.04 -Distance vision: 3.3 (SD 23.2) vs -6.3 (SD 22.7); p=0.03 -Social functioning: 4.5 (SD 21.0) vs -0.9 (SD 19.6); p=0.17 -Mental health: 11.2 (SD 25.3) vs 0.4 (SD 24.2); p=0.02 GDS score -0.3 (SD 1.9) vs -0.1 (SD 2.1); p=0.58 Rosow-Breslau functioning scale: 0.07 (SD 1.3) vs -0.4 (SD 1.4); p=0.07 Distance visual acuity: 5.5 (SD 10.0) vs 3.9 (10.4); p=0.41 Near visual acuity: 6.1 (SD 13.3) vs 2.2 (SD 11.4); p=0.10	Fair
Owsley et al, 2007[84] *Effect of refractive error correction on health-related quality of life and depression in older nursing home residents*	RCT To examine the effect of treating uncorrected refractive error through spectacle correction on vision-targeted health-related quality of life and depressive symptoms in nursing home residents U.S.	N=151 Mean age 78.7 years (SD 8.3) 76% female	Immediate (within 1 week) refractive error correction with glasses vs delayed correction (glasses dispensed 2 months later) 2-month follow-up	Immediate vs delayed correction at 2 months: NHVQoL subscale score - range 0-100 ·General vision: 77.3 vs 65.0; p<0.001 ·Reading: 92.9 vs 84.7; p<0.001 ·Ocular symptoms: 81.4 vs 78.3; p=0.23 ·mobility: 91.5 vs 90.0; p=0.24 ·Psychological distress: 76.0 vs 70.7; p=0.02 ·Activities of daily living: 99.7 vs 99.1; p=0.17 ·Activities and hobbies: 98.0 vs 94.0; p=0.04 ·Adaptation and coping: 92.4 vs 90.0; p=0.11 ·Social interaction: 97.3 vs 94.1; p=0.03 VF-14 total score - range 0-100 95.7 vs 83.1; p<0.001 SF-36 score - range 0-100 ·Mental component summary 81.9 vs 80.8; p=0.96 ·Physical component summary 47.6 vs 46.1; p=0.24 GDS score 3.6 vs 4.9; p=0.003	Fair

Abbreviations: GDS = geriatric depression scale, SD = standard deviation, SF-36 = Medical Outcomes Study - Short Form Health Survey 36 , VF-14 = Health survey questionnaire designed specifically for ophthalmology. "VF" stands for Visual Function, and "14" refers to the 14 questions in the main section of the questionnaire.

TABLE 7. UNCORRECTED REFRACTIVE ERROR - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Literature searches	Patients/trials	Interventions
Murray et al, 2005[85] *A systematic review of the safety and efficacy of elective photorefract-ive surgery for the correction of refractive error*	To systematic-ally review the evidence for safety and efficacy of PRK, LASEK and LASIK for the correction of myopia, hyperopia and astigmatism	MEDLINE, MEDLINE Extra, EMBASE, BIOSIS, Science Citation Index, Cochrane Controlled Trials Register, National Research Register Clinical Trials, Current Controlled Trials, FDA Premarket Approval (PMA) Database Web of Science Proceedings, Conference Papers Index, Zetoc, Association for Research in Vision and Ophthalmology (ARVO) Abstracts Database, American Society of Cataract and Refractive Surgery-American Society of Ophthalmic Administrators (ASCRS-ASOA) Abstracts Database; 2000-2005	LASIK: 64 studies (73 publications; 4 RCTs); LASEK: 26 studies (40 publications; 14 RCTs); PRK: 40 (9 RCTs) case series	Primary treatment with any type of excimer laser used to perform PRK, LASEK, and LASIK for refractive correction of myopia, hyperopia or astigmatism.
Virgili et al, 2008[39] *Reading aids for adults with low vision*	To assess the effects of reading aids for adults with low vision	CCRCT (Cochrane Central Register of Controlled Trials), MEDLINE, EMBASE, SIGLE, LILACS (Latin American and Caribbean Health Science Literature Database) and IndMed through July 2006; Science Citation Index; hand search British Journal of Visual Impairment 1983-1999 and Journal of Visual Impairment and Blindness1976-1991	9 trials: Culham 2004 (n=20); Eperjesi 2004 (n=12); Goodrich 2001 (n=22); Kleweno 2001 (n=13); Ortiz 1999 (n=10); Peterson 2003 (n=70); Smith 2005 (n=243); Spitzberg 1995 (n=39); Stelmack 1991 (n=37)	Magnifiers, CCTV (stand-mounted and hand-held); prism spectacles

Abbreviations: BSCVA = Best Spectacle-Corrected Visual Acuity, CCTV = closed-circuit television, LASEK = Laser Assisted Sub-Epithelial Keratomileusis , LASIK = Laser Assisted in Situ Keratomileusis, PRK = Photorefractive Keratectomy.

TABLE 7. UNCORRECTED REFRACTIVE ERROR - SYSTEMATIC REVIEWS

Study, Year, Title	Results	Conclusion	Quality score
Murray et al, 2005[85] *A systematic review of the safety and efficacy of elective photorefract-ive surgery for the correction of refractive error*	Uncorrected visual acuity of 20/20 or better in myopia: PRK 70%, LASEK 62%, LASIK 64% 20/40 or better: PRK 92%, LASEK 92% and <u>Efficacy</u> LASIK 94% Highly myopic eyes achieved High myopia at baseline, 20/20: PRK14% and LASIK 44% compared with Low myopia at baseline: PRK 76% and LASIK 81% Correction of myopia/myopic astigmatism, median across all 3 treatments: 68% to 75% of eyes achieving within 0.5 D of their intended correction; 86% to 92% of eyes achieved within 1.0 D. Correction of hyperopia: 61% of eyes achieved within 0.5 D of intended correction after PRK and LASIK; 79% and 88% for PRK and LASIK respectively within 1.0 D. <u>Harms</u> Ectasia (5 LASIK studies): median rate 0.2% (range 0% to 0.87%) Loss of ≥2 lines of BSCVA in myopia: PRK 0.5%, LASEK 0% and LASIK 0.6% Loss of ≥2 lines of BSCVA in hyperopia: PRK 7.0%, LASIK 3.5%	The safety and efficacy of photorefractive surgery should be considered against the alternative methods of correction; adverse events occur rarely from a statistical standpoint.	Good
Virgili et al, 2008[39] *Reading aids for adults with low vision*	Reading speed: prism spectacles were no better than conventional spectacles in the single study comparing them; for other interventions, there was no difference in reading speed among the treatments although this could have been due to problematic design and reporting among the included studies	No evidence supports any particular low vision reading aid over another; the studies included in the SR were of questionable quality and potentially biased	Good

TABLE 8. CATARACT - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Literature searches	Patients/trials	Interventions	Results	Conclusion	Quality score
Powe et al,1994[91] *Synthesis of the literature on visual acuity and complications following cataract extraction with intraocular lens implantation*	To define the effectiveness and risks of cataract surgery	MEDLINE 1975-April 1991; reference lists	83 single-arm observational studies and 7 cohort studies Median n=231 (17 to 22,791)	22 studies: phacoemulsification; 58 studies: extracapsular extraction; 1 study: intracapsular extraction; 18 studies: mixed phaco-emulsification and extracapsular extraction	Pooled % of eyes with 20/40 acuity or better: 95.5% (CI 95.1% to 95.9%) in pts with no ocular comorbidities and 87% (CI 89.3% to 90.2%) for all eyes Harms - pooled rates - % (CI): Endophtalmitis 0.13 (0.09 to 0.17) Bullous keratopathy 0.3 (0.2 to 0.4) Malposition/dislocation of IOL 1.1 (0.9 to 1.2) Clinical cystoid macular edema 1.4 (1.2 to 1.6) Angiographic cystoid macula edema 3.5 (2.9 to 4.0) Retinal detachment 0.7 (0.6 to 0.8) Posterior capsular opacification 19.7 (19.1 to 20.3)	Cataract surgery yields excellent visual acuity and is relatively safe regardless of method of surgical extraction	Good
Schaumberg et al, 1998[163] *A systematic overview of the incidence of posterior capsule opacification*	To obtain an estimate of the incidence of posterior capsule opacification (PCO) and to explore factors that may influence its development	MEDLINE 1979-1996; reference lists	49 studies (design NR); total n=NR	27 studies: extracapsular extraction; 9 studies: phaco-emulsification; 13 studies: mixed extracapsular extraction and phaco-emulsification	Pooled rate, incidence of posterior capsule opacification: 1 year: 11.8% (9.3%-14.3%) 3 years: 20.7% (16.6%-24.9%) 5 years: 28.4% (18.4%-38.4%)	Visually significant PCO develops in more than 25% of patients undergoing extracap-sular extraction or phacoemulsifi cation with IOL within 5 years of surgery	Fair

TABLE 8. CATARACT - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Literature searches	Patients/trials	Interventions	Results	Conclusion	Quality score
Taban et al, 2005[164] *Acute endophthal-mitis following cataract surgery*	To determine the reported incidence of acute endophthalmitis following cataract extraction and to explore possible contributing factors	Cochrane (database not specified); MEDLINE 1963-March 2003; reference lists; textbook hand search; conference proceed-ings and abstracts	215 studies (design NR); total n=NR	NR	Pooled rate, incidence of endophthalmitis: 0.128% Rate 1963-1999: 0.109% Rate 2000-2003: 0.265% (RR 2.44. CI 2.27 to 2.61)	Incidence of endophthalmi tis associated with cataract extraction has increased over the last decade and may be linked to the increasing use of sutureless clear corneal incisions.	Fair

Abbreviations: CI = confidence interval, IOL = intraocular lenses, NR = not relevant, PCO = posterior capsule opacification, RR = relative risk.

TABLE 9. CATARACT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Study design Purpose of study	Patients	Intervention Duration of follow-up	Results	Quality score
Chylack et al, 2002[109] *The Roche European American Cataract Trial (REACT): a randomized clinical trial to investigate the efficacy of an oral antioxidant micronutrient to slow progression of age-related cataract*	To determine if a mixture of oral antioxidants would modify progression of cataract Double-blind PCT of consecutively enrolled patients	Able to provide written informed consent; able to attend for all visits; ≥ 40 years old; at least one eye met the following ocular criteria: cataract extraction unlikely within two years, immature idiopathic 'senile' cataract present in one or both eyes, U.S. patients: presence of minimal cataract by Lens Opacities Classification System [LOCS II]14 criteria, U.K. patients: presence of cataract of minimal Oxford grade; logMAR acuity ≤0.5; ocular media clear enough to capture good images of the lens; remote risk of angle closure glaucoma; pupil dilatable to 6mm; oscillatory movement displacement threshold ≤50S; no visually significant fundus pathology; no clinical signs of glaucoma and intraocular pressure; no history of amblyopia, eye surgery, argon or YAG laser eye treatment, or major eye trauma; no history of iritis, retinal crystalline deposits, or optic nerve disease; no extended (daily for >3 months) use of ocular corticosteroid or glaucoma therapy; no participation in another clinical trial investigating an anticataract formulation within the last year.	Antioxidant multivitamin (250mg vitamin C + 200mg vitamin E + 6mg beta carotene) tid vs placebo 3 years follow-up	Multiple methods used to evaluate changes in lens opacities; following 3 years of treatment there was a marginally significant between group difference in cataract progression (p=0.048) based on the primary outcome measure only (% pixels opaque) and not for other measure of cataract progression (e.g. LOCS)	Fair
Foss et al, 2006[107] *Falls and health status in elderly women following second eye cataract surgery: a randomized controlled trial*	RCT To determine if second eye cataract surgery reduces the risk of falling and to measure associated health gain	Women in the UK age ≥70 yrs with a previous, successful cataract operation who had a second, operable cataract	Cataract surgery vs no/delayed treatment 1 year follow-up	Proportion of patients with falls: 48/120 (40%) immediate surgery group vs 41/119 (34%) delayed treatment group; HR 1.06 (CI 0.69 to 1.61; p=0.80) Proportion of patients with second falls: 22/120 (18%) immediate surgery group vs 22/119 (18%) delayed treatment group; HR 0.85 (CI 0.49 to 1.56; p=0.61) Rate of falling per 1,000 patient days: 2.9 immediate treatment group vs 4.3 delayed treatment group; Rate ratio 0.68 (CI 0.39 to 1.19; p=0.18)	Good

TABLE 9. CATARACT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Study design Purpose of study	Patients	Intervention Duration of follow-up	Results	Quality score
Harwood et al, 2004[106] *Falls and health status in elderly women following first eye cataract surgery: a randomized controlled trial*	RCT To determine if first eye cataract surgery reduces the risk of falling and to measure associated health gain	Women in the UK age ≥70 yrs with cataract who were suitable for surgery and had not had previous ocular surgery	Cataract surgery (phaco-emulsification) vs no/delayed treatment 1 year follow-up	Proportion of patients with falls: 76/154 (49%) immediate surgery group vs 69/152 (45%) delayed treatment group; HR 0.95 (CI 0.69 to 1.35; p=0.77) Proportion of patients with second falls: 28/154 (18%) immediate surgery group vs 38/152 (25%) delayed treatment group; HR 0.60 (CI 0.36 to 0.98; p=0.04) Rate of falling per 1,000 patient days: 1.0 immediate treatment group vs 1.52 delayed treatment group; Rate ratio 0.66 (CI 0.45 to 0.96; p=0.03) Fracture incidence: 4/154 (3%) immediate treatment group vs 12/152 (8%) delayed treatment group; Risk ratio 0.33 (CI 0.1 to 1.0; p=0.04)	Good

Abbreviations: CI = confidence interval, PCT = placebo controlled trial, RCT = randomized controlled trial.

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Literature searches	Patients/trials
Evans et al, 2008[43] *Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration*	To assess the effects of antioxidant vitamin or mineral supplementation, alone or in combination, on the progression of ARMD	CCRCT, MEDLINE, EMBASE, National Research Register through 2007, PubMed in process through 24 January 2006, AMED 1985-January 2006, SIGLE 1980-March 2005	9 trials (18 publications) Primary publications: Richer 1996 - AMDSG (n=71); Age-Related Eye Disease Study Research Group 2001 - AREDS (n=3640); Holz 1993 (n=58); Kaiser 1995 (n=20); Newsome 1988 (n=174); Stur 1996 (n=112); Garrett 1999 - VECAT study (n=1204); Richer 2004 - LAST study (n=90); Wang 2004 (n=400); total n=5769

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Interventions
Evans et al, 2008[43] *Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration*	3 trials: zinc 200 mg QD vs placebo 2 trials: broad-spectrum antioxidant compound vs placebo 1 trial: vitamin E 500 mg QD vs placebo 1 trial: zinc 80 mg QD vs antioxidant combination vs zinc + antioxidants vs placebo 1 trial: lutein 10 mg QD v lutein + broad-spectrum antioxidant 1 trial: zinc oxide 80 mg QD, vitamin C, vitamin E vs placebo

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Results	Conclusion	Quality score
Evans et al, 2008[43] *Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration*	All comparisons Any multivitamin or antioxidant vs placebo: Change in visual acuity - defined as a loss of 3 or more lines (15 or more letters) on a logMAR chart (AREDS, Newsome 1988, VECAT; I^2=27.7%) Random effects model: pooled OR 0.83 (CI 0.63 to 1.09; p=0.18); Fixed effects model: pooled OR 0.81 (CI 0.67 to 0.98; p=0.03) Mean difference visual acuity (AMDSG, Kaiser 1995, Newsome 1988, Stur 1996, LAST; I^2=0%): pooled SMD 0.02 (CI -0.21 to 0.26) ARMD progression as a dichotomous variable: (AREDS, Holz 1993, Stur 1996. VECAT; I^2=64.2%) OR range: 0.50 to 2.31; no pooled analysis due to heterogeneity of studies ARMD progression as a continuous variable (AMDSG): mean difference -0.06 (CI -0.62 to 0.50) Individual comparisons Multivitamin supplements vs placebo (AREDS, Kaiser 1995, Richer 1996, Richer 2004) Change in visual acuity - defined as a loss of 3 or more lines (15 or more letters) on a logMAR chart (AREDS): OR 0.77 (CI 0.62 to 0.96) vs placebo Mean difference visual acuity (Kaiser 1995, AMDSG, LAST; I^2=0%): pooled SMD 0.16 (CI -0.19 to 0.51) ARMD progression as a dichotomous variable (AREDS): adjusted OR 0.68 (CI 0.53 or 0.87)A ARMD progression: OR 0.11 (CI 0.80 to 1.55) Zinc vs placebo (AREDS, Holz 1993, Newsome 198	Limited evidence, based primarily on AREDS, suggests a benefit in the use of antioxidant vitamins and minerals in slowing ARMD progression (risk reduction ~20-25%.) The AREDS population was relatively well-nourished at the trial's initiation and this may have had some effect on the trial results. Prolonged antioxidant use had been found to be harmful in some other populations (e.g. smokers)	Good

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Literature searches	Patients/trials
Evans et al, 2008[126] *Ginkgo biloba extract for age-related macular degeneration*	To determine the effect of ginkgo biloba extract on the progression of ARMD	CCRCT (Quarter 4, 2005), MEDLINE (1966-January 2006, week 3), EMBASE (1980-January 2006), SIGLE (1980-2005/03), AMED (1985-January 2006), NRR (2005, Issue 4); reference lists, Science Citation Index; expert recommendation	2 trials: Fies 2002 (n=99); Lebuisson 1986 (n=20); total n=119 pts
Meads et al, 2003[133] *Clinical effectiveness and cost-utility of photodynamic therapy for wet age-related macular degeneration: a systematic review and economic evaluation*	To establish the clinical and cost-effectiveness of photodynamic therapy for neovascular ARMD	Cochrane Library (2001, Issue 3), MEDLINE (1993-Aug 2001), EMBASE (1993-Aug 2001), Science Citation Index (1993-2001); health technology assessment web sites; internet sites of verteporfin manufacturers; reference lists; industry submissions	2 trials: Treatment of Age-related Macular Degeneration with Photodynamic Therapy Study Group - TAP 1999 (n=609); Verteporfin in Photodynamic Therapy Study Group - VIP 2001 (n=2001); total n=2610 pts

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Interventions
Evans et al, 2008[126] *Ginkgo biloba extract for age-related macular degeneration*	Gingko biloba extract EGb 761, doses 60-160 mg QD; placebo
Meads et al, 2003[133] *Clinical effectiveness and cost-utility of photodynamic therapy for wet age-related macular degeneration: a systematic review and economic evaluation*	IV verteporfin 6 mg/m2 + cold laser vs placebo + cold laser

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Results	Conclusion	Quality score
Evans et al, 2008[126] *Ginkgo biloba extract for age-related macular degeneration*	Gingko biloba 160 mg QD vs placebo (1 trial; n=20): Change in visual acuity: WMD 1.70 (CI 1.21 to 2.19) Clinical improvement: OR 36.00 (2.72 to 476.28) Gingko biloba 60 mg QD vs 240 mg QD (1 trial; n=99): Mean visual acuity: WMD 0.05 (CI -0.03 to 0.13) >0.2 improvement in visual acuity score: OR 2.29 (CI 0.90 to 5.80) No serious AEs reported in either trial (headache, blood in stool and abdominal pain reported in 3/99 patients)	There is inadequate evidence from 2 small, short-term trials to draw conclusions regarding the effect of gingko biloba on ARMD progression. There may be harms associated with gingko biloba use, but they too have been inadequately reported.	Good
Meads et al, 2003[133] *Clinical effectiveness and cost-utility of photodynamic therapy for wet age-related macular degeneration: a systematic review and economic evaluation*	Results not pooled TAP Loss of >15 letters (3 lines) at 24 months: 47.0% verteporfin vs 62.3% placebo; RR 0.75 (CI 0.65 to 0.88) Loss of >30 letters (6 lines) at 24 months: 18.2% verteporfin vs 30.0% placebo; RR 0.61 (CI 0.45 to 0.81) Proportion of pts with visual acuity of <34 letters at 24 months: 41.0% verteporfin vs 55.1% placebo; RR 0.75 (CI 0.63-0.88) VIP Loss of >15 letters (3 lines) at 24 months: 54.0% verteporfin vs 67% placebo; RR 0.81 (CI 0.68 to 0.96) Loss of >30 letters (6 lines) at 24 months: 30% verteporfin vs 47% placebo; RR 0.63 (CI 0.48 to 0.83) Proportion of pts with visual acuity of <34 letters at 24 months: this outcome not reported Harms: TAP mortality at 24 months: 3.2% verteporfin vs 3.9% placebo; RR 0.84 (0.35-1.99) VIP mortality at 24 months: 1.8% verteporfin vs 2.6% placebo; RR 0.68 (CI 0.15 to 2.97)	Photodynamic therapy is effective at preventing further visual loss due to AMD, although this conclusion is based largely on the results of the TAP trial. With the addition of a cost effectiveness analysis included in this review, the authors concluded that there is a need for further research on this topic.	Good

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Literature searches	Patients/trials
Vedula et al, 2008[142] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	To investigate the effects of anti-vascular endothelial growth factor (anti-VEGF) modalities for treating neovacular ARMD	CCRCT, MEDLINE, EMBASE, LILACs through February 2008; hand search of Association for Research in Vision & Ophthalmology meeting abstracts	5 trials (15 publications) Primary publications: Brown 2006 - ANCHOR Trial (n=423); Macugen 2007 - EOP 1003 Trial (n=578); Leys 2007 - EOP 1004 Trial (n=612); Heier 2006 - FOCUS Trial (n=162); Rosenfeld 2006 - MARINA Trial (n=716)
Virgili et al, 2008[45] *Laser photocoagulation for age-related macular degeneration*	To examine the effect of laser photocoagulation on neovascular (wet) ARMD	CCRCT, MEDLINE, EMBASE, LILACS, National Research Register (NRR), ZETOC through March 2007	15 trials (34 publications) Primary publications: Arnold 1997; Canadian Ophthalmology Study Group 1993 (n=55); Bressler 1996 (n=100); Canadian Ophthalmology Study Group 1993 (n=191); Cardillo 1993 (n=23); Coscas 1983 (n=60); Coscas 1991 (n=160); Duch Mestres 1993 (n-41); Moorfields 1982 (n=128); Macular Photocoagulation Study Group - MPS Argon Extra 1982 (n=224); Macular Photocoagulation Study Group - MPS Krypton Juxta 1990 (n=496); Macular Photocoagulation Study Group - MPS Subf. New 1991 (n=371); Macular Photocoagulation Study Group - MPS Subf. Recurrent 1991 (n=206); Bressler 2000 & Submacular Surgery Trials Research Group 2000 - SST 2000 (n=70); Versteeg-Tijmes 1982 (n=13, excluding 13 non-ARMD eyes); Yassur 1982 (n=96)

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Interventions
Vedula et al, 2008[142] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	Pegaptanib 0.3, 1.0 or 3.0mg Ranibizumab 0.3 or 0.5mg Verteporfin PDT sham injection/sham PDT
Virgili et al, 2008[45] *Laser photocoagulation for age-related macular degeneration*	12 studies: Photocoagulation vs no treatment 1 study: photocoagulation vs surgery 1 study: argon vs krypton laser wavelength 1 study: argon vs dye red laser wavelength

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Results	Conclusion	Quality score
Vedula et al, 2008[142] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	Change in visual acuity (% of patients losing ≥3 lines of acuity at 1 year) Pegaptanib (all doses) vs sham: RR 0.71 (CI 0.60 to 0.84); NSD for 3.0mg dose vs sham; NNT 6.67 0.3mg dose, 6.25 1.0mg dose, 14.28 3.0mg dose Ranibizumab (both doses) vs sham: RR 0.14 (CI 0.08 to 0.25); NNT 3.13 (both doses) Blindness Pegaptanib RR 0.69 (CI 0.59 to 0.82) Ranibizumab RR 0.28 (CI 0.21 to 0.37) Quality of life - Mean change in NEI-VFQ scores at 2 years follow-up ANCHOR Trial: 5.9 ranibizumab 0.3mg vs 8.1 ranibizumab 0.5mg vs 2.2 verteprofin MARINA Trial: 4.8 ranibizumab 0.3mg vs 4.5 0.5mg ranibizumab vs -6.4 sham injection Ranibizumab: similar rates of serious AEs including mortality Unpublished data from SAILOR Trial reported by the drug's manufacturer showed a significantly higher stroke risk with 0.5mg dose relative to 0.3mg dose(p=0.02; no sham control in this trial) Pegaptanib: Serious ocular AEs (endophthalmitis, retinal detachment, traumatic cataract) in tx groups, none in sham group	Both interventions effective a reducing visual acuity loss and progression to blindness with improved QoL outcomes	Good
Virgili et al, 2008[45] *Laser photocoagulation for age-related macular degeneration*	Direct photocoagulation vs no treatment Visual acuity at 3 months: NNH 20 (CI 13 to 100) Reading ability at 3 years: NNT 6 (CI 3 to 33); at 5 years: NNT 7 (CI 4 to 33) Perifoveal photocoagulation of subfoveal CNV Visual acuity, loss of 6 lines or more at 2 years*: NNT 3 (CI 2 to 8) *only timepoint with SS difference b/t treatment and control, although photocoagulation was favored for other timepoints Grid photocoagulation of subfoveal CNV Visual acuity, loss of 2 or more lines: RR 1.83 (CI 1.10 to 3.05); NNT 5 (CI 3 to 20) Photocoagulation vs surgery No SS difference between treatments, although surgery was favored for visual acuity and QOL outcomes Argon vs krypton lasers No difference between argon and krypton at 2 years in visual acuity changes	Photocoagulation is effective for certain types of ARMD (extrafoveal CNV). For juxta- or sub- foveal CNV patients, the benefit of laser photocoagulation is less clear,	Good

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Literature searches	Patients/trials
Wormald et al, 2008[134] *Photodynamic therapy for neovascular age-related macular degeneration*	To examine the effects of photodynamic therapy in the treatment of ARMD	CCRCT, MEDLINE EMBASE through March 2007; Science Citation Index (no date specified); expert recommendation	3 trials (7 publications) Primary publications: Treatment of Age-related Macular Degeneration with Photodynamic Therapy Study Group - TAP 1999 (n=609); Visudyne in minimally classic choroidal neovascularization study - VIM 2005 (n=117); Verteporfin in Photodynamic Therapy Study Group - VIP 2001 (n=2001); total n=1065 pts

Abbreviations: ARMD = age-related macular degeneration, CI = confidence interval, logMAR = logarithm
institute visual functioning questionnaire, NNH = number needed to harm, NNT = number needed to treat,
quality of life, RR = relative risk, VECAT = vitamin E, cataract and age-related maculopathy study, VEGF =

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Interventions
Wormald et al, 2008[134] *Photodynamic therapy for neovascular age-related macular degeneration*	IV verteporfin (2 trials: 6 mg/m2; 1 trial dose NR) + cold laser vs placebo + cold laser

nic minimum angle of resolution, NEI -VFQ = national eye
NR = not relevant, PDT = photodynamic therapy, QoL =
= vascular endothelial growth factor.

TABLE 10. ARMD - SYSTEMATIC REVIEWS

Study, Year, Title	Results	Conclusion	Quality score
Wormald et al, 2008[134] *Photodynamic therapy for neovascular age-related macular degeneration*	Loss of >3 lines of visual acuity at 24 months: pooled RR (2 trials: TAP, VIP) 0.78 (CI 0.7-0.87); risk ratio reduction 0.22 (CI 0.13 to 0.30); NNT: 7 (population: patients with subfoveal choroidal neovascularization with baseline visual acuity 20/40-20/200) Loss of >6 lines of visual acuity at 24 months: pooled RR (2 trials: TAP, VIM) 0.60 (CI 0.49-0.73); risk ratio reduction 0.40 (CI 0.27-0.51); NNT: 7 (population: patients with subfoveal choroidal neovascularization with baseline visual acuity 20/40-20/200) Mean number of lines of vision lost at 24 months (1 trial: TAP): 2.7 lines verteporfin vs 1.2 control; mean difference 1.2 (p<0.001) No QoL outcomes reported Acute severe visual acuity decrease (within 13 days of tx): Absolute risk difference 0.01 (CI 0.01 to 0.03); NNH 30 (range 30-100)	Photodynamic therapy is effective in preventing further visual loss due to AMD although the effect size is unclear.	Good

TABLE 11. ARMD - RANDOMIZED, PLACEBO-CONTROLLED TRIALS

Study, Year, Title	Study design Purpose of study	Patients	Intervention Duration of follow-up	Results	Quality Score
ARMD (Dry)					
AREDS Research Group, 2001[114] *A randomized, placebo-controlled clinical trial of high-dose supplementation with vitamins C and E, beta carotene and zinc for age-related macular degeneration and vision loss: AREDS Report No. 8*	To evaluate the effect of high-dose vitamins C and E, beta carotene and zic supplements on AMD progression and visual acuity PCT	n=3640 Median age 56 yrs 56% female 96% White; 3% Black; <1% other Mean BCVA at baseline better than 20/32 for all participants	Antioxidant multivitamin - 500 mg vitamin C+400 IU vitamin E+5 mg beta carotene/day zinc 80mg/day antioxidant multivitamin + zinc placebo 7 years	Progession to advanced ARMD: antioxidants vs placebo: OR 0.77 (0.56 to 1.05; p=0.03) zinc vs placebo: OR 0.71 (0.51 to 0.98; p=0.005) antioxidants + zinc vs placebo: OR 0.68 (0.49 to 0.93; p=0.002) Loss of ≥15 letters of VA: antioxidants vs placebo: OR 0.87 (0.67 to 1.15; p=0.20) zinc vs placebo: OR 0.82 (0.63 to 1.08; p=0.07)antioxidants + zinc vs placebo: OR 0.77 (0.58 to 1.03; p=0.02) ORs adjusted for age, sex, race, baseline ARMD category amd smoking status	Good
Feher et al, 2005[124] *Improvement of visual functions and fundus alterations in early age-related macular degeneration treated with a combination of acetyl-L-carnitine, n-3 fatty acids and coenzyme Q10*	To determine how a combination of acetyl-L-carnitine, n-3 fatty acids and coenzyme Q10 influenced visual function in patients with early ARMD PCT	n=106 Age 55-70 years; diagnosis of early bilateral ARMD; visual acuity between 8/10 and 4/10 (Snellen decimal scale); agree to discontinue current vitamin regimen; be highly motivated, alert, oriented, mentally competent and able to understand and comply w the requirements of the study	100mg ALC + 530mg n-3 fatty acids + 10mg CoQ10 2x/day placebo (soy oil) 2x/day 12 month follow-up	Visual acuity in months affected eye (secondary outcome): mean change from baseline at 12 months (Snellen chart) patients 'improved or unchanged': 77% (37/48) treatment vs 55% (29/53) placebo patients 'deteriorated': 23% (11/48) vs 44% (24/53) NSD in less affected eyes AEs not reported; 3 withdrawals dues to AEs (2 treated group; 1 placebo group)	Fair

TABLE 11. ARMD - RANDOMIZED, PLACEBO-CONTROLLED TRIALS

Study, Year, Title	Study design Purpose of study	Patients	Intervention Duration of follow-up	Results	Quality Score
Kaiser et al, 1995[123] *Visaline in the treatment of age-related macular degeneration*	To assess the effect of a multivitamin supplement on ARMD progression	n=20 Mean age 72 yrs 65% female Mean far VA 0.57	1.5mg buphenine HCl, 10mg beta carotene, 10mg tocopherol acetate, 50mg ascorbic acid 2 tablets, 2x/day placebo 6 months	Change in mean far VA: multivitamin 0.07 (SD 0.05) vs placebo 0.05 (SD 0.07); p=NS	Fair
Newsome et al, 1988[118] *Oral zinc in macular degeneration*	To assess the effect of zinc on ARMD progression	n=174 Mean age 67.9 yrs 65% female 32% VA >20/25	zinc 100mg bid placebo 24 months	Proportion of patients with loss of 3 lines (15 letters) or more: zinc 6/80 (7.5%) vs placebo 11/71 (15.5%) Change in VA (letters lost): zinc -4.1 vs placebo -7.1	Fair
Richer et al, 1996[120] ARMD Study Group, *Multicenter ophthalmic and nutritional age-related macular degeneration study - part 2: antioxidant intervention and conclusions*	To assess the effect of a broad-spectrum antioxidant supplement on ARMD PCT	n=71 Mean age 72 yrs 7% female Mean far VA (LogMAR, right eyes) 0.26	Antioxidant multivitamin (beta carotene 20,000 IU, vitamin E 200 IU, vitamin C 750 mg, citrus bioflavonoid complex 125 mg, quercitin (bioflavonoid) 50 mg, bilberry extract (bioflavonoid) 5 mg, rutin (bioflavonoid) 50 mg, zinc picolinate 12.5 mg, selenium 50 mcg, taurine 100 mg, n-acetyl cysteine 100mg, l-glutathione 5 mg, vitamin B2 25 mg, chromium 100 mcg) qd placebo 18 months	Mean visual acuity at 18 months (Log MAR): antioxidant 0.33 (SE 0.07) vs placebo 0.29 (SE 0.05)	Fair
Richer et al, 2004[121] *Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study*	To determine whether nutritional supplementation with lutein or lutein together with antioxidants, vitamins and minerals improves visual function and symptoms in atrophic ARMD	n=90 Mean age 73 yrs 4% female Mean VA (right eye, LogMAR) 0.377	10mg lutein, with or without additional multivitamin 12 months	Change in Snellen letter equivalent: lutein alone +5.4 letters vs lutein/multivitamin +3.5 letters vs placebo -2.1 letters Change in visual acuity: lutein alone -0.10 vs lutein+multivitamin -0.03 vs placebo -0.14	Fair

TABLE 11. ARMD - RANDOMIZED, PLACEBO-CONTROLLED TRIALS

Study, Year, Title	Study design Purpose of study	Patients	Intervention Duration of follow-up	Results	Quality Score
Stur et al, 1996[122] *Oral zinc and the second eye in age-related macular degeneration*	To investigate the short-term effect of oral zinc substitution on the development of age-related macular degeneration in the second eye with exudative ARMD in the first eye	n=112 Mean age 71.5 yrs 57% female Mean VA (LogMAR) 0.0745	200mg zinc sulfate placebo 2 years	Change in VA at 24 months: zinc -0.013 (SD 0.01) vs placebo -0.024 (SD 0.01); p=0.52	Fair
ARMD (Wet)					
Laser photocoagulation					
Macular Photocoagulation Study Group, 1982[128] *Argon laser photocoagulation for senile macular degeneration*	To determine if argon laser photocoagulation is useful in preventing severe vision loss in eyes with evidence of macular degeneration	n=224 Mean age not reported: 52/224 age 50-64; 104/224 (46%) age 65-75; 68/224 (30%) age >75 yrs 51% female BCVA 20/32 or better: 105/224	laser photocoagulation vs no treatment	Increase in lines of VA or no change from baseline at 18 months: treatment group 61/100 (61.0%) vs no-treatment group 30/98 (30.6%) Loss of 2-5 lines of VA at 18 months: treatment group 23/100 (23.0%) vs no-treatment group 16/98 (16.3%) Loss of 6-9 lines of VA at 18 months: treatment group 8/100 (8.0%) vs no-treatment group 24/98 (24.5%) Loss of 10 or more lines of VA at 18 months: treatment group 8/100 (8.0%) vs no-treatment group 16/98 (16.3%)	Poor

TABLE 11. ARMD - RANDOMIZED, PLACEBO-CONTROLLED TRIALS

Study, Year, Title	Study design Purpose of study	Patients	Intervention Duration of follow-up	Results	Quality Score
Macular Photocoagulation Study Group, 1990[129] *Krypton laser photocoagulation for neovascular lesions of age-related macular degeneration*	To determine whether krypton laser photocoagulation would be of benefit in preventing visual acuity loss in eyes with ARMD	n=496 Mean age not reported: 26/496 (5%) age 50-59 yrs; 147/496 (29%) age 60-69 yrs; 240/496 (48%) age 70-79 yrs; 83/497 (17%) age ≥80 yrs 53% female BCVA 20/40 or better: 157/496 (32%) Median length of follow-up: 48 months	laser photocoagulation vs no treatment	Increase in lines of VA or no change from baseline at 36 months: treatment group 47/174 (27.0%) vs no-treatment group 29/169 (17.2%) Loss of 2-5 lines of VA at 36 months: treatment group 41/174 (23.6%) vs no-treatment group 42/169 (24.9%) Loss of 6-9 lines of VA at 36 months: treatment group 55/174 (31.6%) vs no-treatment group 54/169 (32.0%) Loss of 10 or more lines of VA at 36 months: treatment group 31/174 (17.8%) vs no-treatment group 44/169(26.0%)	Poor
Macular Photocoagulation Study Group, 1991[130] *Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration*	To determine the effect of laser photocoagulation of subfoveal neovascularization in eyes with ARMD but without previous photocoagulation of the macula	n=373 Mean age not reported: 16/373 (4%) age 50-59 yrs; 80/373 (21%) age 60-69 yrs; 186/373 (50%) age 70-79 yrs; 91/373 (24%) age ≥80 yrs 56% female BCVA 20/20 or better: 106/373 (28%); 20/25-20/100: 190/373 (51%); 20/250 or worse: 76/373 (20%)	laser photocoagulation vs no treatment	Loss of <2 lines of VA at 24 months: treatment group 37/114 (32.5%) vs no-treatment group 20/112 (17.9%) Loss of 2-3 lines of VA at 24 months: treatment group 27/114 (23.7%) vs no-treament group 20/112 (17.9%) Loss of 4-5 lines of VA at 24 months: treatment group 27/114 (23.7%) vs no-treament group 31/112 (27.7%) Loss of ≥6 lines of VA at 24 months: treatment group 23/114 (20.2%) vs no-treament group 41/112 (36.6%)	Poor

TABLE 11. ARMD - RANDOMIZED, PLACEBO-CONTROLLED TRIALS

Study, Year, Title	Study design Purpose of study	Patients	Intervention Duration of follow-up	Results	Quality Score
Macular Photocoagulation Study Group, 1991[131] *Laser photocoagulation of subfoveal recurrent neovascular lesions in age-related macular degeneration*	To determine the effect on vision of laser treatment of subfoveal neovascular lesions compared with no treatment	n=206 Mean age not reported: 4/206 (2%) age 50-59 yrs; 57/206 (28%) age 60-69 yrs; 112/206 (54%) age 70-79 yrs; 33/206 (16%) age ≥80 yrs 52% female BCVA 20/20 or better: 70/206(34%); 20/25-20/100: 73/206 (35%); 20/250 or worse: 63/206 (31%)	laser photocoagulation vs no treatment	Loss of <2 lines of VA at 24 months: treatment group 10/35 (28.6%) vs no-treatment group 15/46 (32.6%) Loss of 2-3 lines of VA at 24 months: treatment group 10/35 (28.6%) vs no-treatment group 10/46 (21.7%) Loss of 4-5 lines of VA at 24 months: treatment group 12/35 (34.3%) vs no-treatment group 8/46 (17.4%) Loss of ≥6 lines of VA at 24 months: treatment group 3/35 (8.6%) vs no-treatment group 13/46 (28.3%)	Poor
Moorfields et al, 1982[132] *Treatment of senile disciform macular degeneration: a single-blind randomized trial by argon laser photocoagulation*	To determine the effects of argon laser photocoagulation in the treatment of neovascular disciform macular degeneration in the elderly	n=128 Baseline characteristics not reported Inclusion criteria required age 50-80 yrs; no description of BCVA at baseline	laser photocoagulation vs no treatment	Loss of <2 lines of VA at 24 months: treatment group 3/51 (5.9%) vs no-treatment group 3/50 (6.0%) Loss of 2-3 lines of VA at 24 months: treatment group 11/51(21.6%) vs no-treatment group 10/50 (20.0%) Loss of 4-5 lines of VA at 24 months: treatment group 14/51 (27.4%) vs no-treatment group 16/50 (32.0%) Loss of ≥6 or more lines of VA at 24 months: treatment group 9/51 (17.6%) vs no-treatment group 14/50 (28%)	Poor

TABLE 11. ARMD - RANDOMIZED, PLACEBO-CONTROLLED TRIALS

Study, Year, Title	Study design Purpose of study	Patients	Intervention Duration of follow-up	Results	Quality Score
Photodynamic therapy					
Azab et al, 2005[137] (VIM Study Group) *Verteporfin therapy of subfoveal minimally classic choroidal neovascularization in age-related macular degeneration*	To compare the treatment effect and safety of photodynamic therapy with verteporfin using a standard or reduced light fluence rate with that of placebo in patients with subfoveal minimally classic choroidal neovascularization with ARMD	n=117 Mean age 78 yrs Mean BCVA: 20/80 92% subfoveal lesion(s)	verteporfin or placebo IV + photodynamic therapy	Loss of 3 or more lines of VA at 12 months: verteporfin 15/72 (20.8%) vs placebo 18/38 (47.4%); RR 0.93 (ci 0.75 TO 1.15) Loss of 6 or more lines of VA at 12 months: verteporfin 3/72 (4.2%) vs placebo 6/38 (15.8%); RR	Good
TAP Study Group, 1999[135] *Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration: one-year results of 2 randomized clinical trials - TAP Report 1(TAP).* Other publications: Kaiser, 2006, TAP and VIP Report 3	To determine if photodynamic therapy with verteporfin can safely reduce the risk of vision loss in patients with subfoveal choroidal neovascularization	n=609 Mean age 75.3 yrs 56% female 98% White, 2% other Mean BCVA: 20/80-2 89% subfoveal lesion(s)	verteporfin or placebo IV + photodynamic therapy	Loss of 6 or more lines of VA at 12 months: verteporfin 59/402 (14.7%) vs placebo 49/207 (23.7%); RR 0.62 (CI 0.44 to 0.87) Loss of 3 or more lines of VA at 12 months: verteporfin 156/402 (38.8%) vs placebo 111/207 (53.6%); RR 0.72 (CI 0.61 to 0.86)	Good

TABLE 11. ARMD - RANDOMIZED, PLACEBO-CONTROLLED TRIALS

Study, Year, Title	Study design Purpose of study	Patients	Intervention Duration of follow-up	Results	Quality Score
VIP Study Group, 2001[136] *Verteporfin therapy of subfoveal choroidal neovascularization: two-year results of a randomized clinical trial including lesions with occult with no classic choroidal neovascularization - Verteporfin in Photodynamic Therapy Report 2 (VIP)*	To determine if photodynamic therapy with verteporfin can safely reduce the risk of vision loss compared with a placebo	n=339 Mean age 75 yrs 99% White; 1% other Mean BVCA: 20/50+1 83.4% subfoveal lesion(s)	verteporfin or placebo IV + photodynamic therapy	Loss of 3 or more lines of VA at 12 months: verteporfin 114/225 (50.7%) vs placebo 62/114 (54.3%); RR 0.44 (CI 0.25 to 0.77)	Good
VEGF inhibitors					
Gragoudas et al, 2004[144] *Pegaptanib for neovascular age-related macular degeneration* (VISION; 2 trials) also: VEGF Inhibitor Study Group, 2006; Leys, 2007	To test the short-term safety and effectiveness of pegaptanib	n=1208 Mean age NR; Age range 50-64 years: 6%; 65-74 years: 32%; 75-84 years: 52%; ≥85 years: 10% 58% female 96% White; 4% Other Mean visual acuity, study eye: 51.8 letters (SD 12.8)	0.3mg, 1.0mg or 3.0mg pegaptanib every 6 weeks up to 48 weeks (9 txs) vs sham injection	Patients with loss of <15 letters at 54 weeks: 0.3mg pegaptanib 206/294 (70%) vs. 1.0mg pegaptanib 213/300 (71%) vs. 3.0mg pegaptanib 193/296 (65%) vs. sham injection 164/296 (55%); p<0.05 for all active doses vs. sham injection; NSD between pegaptanib doses. Pooled RR all doses 0.71 (0.60 to 0.84). VA worse than 20/200 at 54 weeks: 0.3mg pegaptanib 111/294 (38%) vs. 1.0mg pegaptanib 128/300 (43%) vs. 3.0mg pegaptanib 129/296 (44%) vs. sham injection 165/296 (56%). Pooled RR all doses 0.69 (0.59 to 0.82).	Fair

TABLE 11. ARMD - RANDOMIZED, PLACEBO-CONTROLLED TRIALS

Study, Year, Title	Study design Purpose of study	Patients	Intervention Duration of follow-up	Results	Quality Score
Regillo et al, 2008[143] *Randomized, double-masked, sham-controlled trial of ranibizumab for neovascular age-related macular degeneration: PIER study year 1*	To evaluate the effectiveness and safety of ranibizumab for the treatment of minimally classic or occult with no classic choroidal neovasculatization associated with ARMD. Prospective, double-blind RCT	n=184 Mean age ~78 yrs 60% female neovascular ARMD	0.3mg or 0.5mg ranibizumab vs sham injection; dosing 1x/month for 3 months followed by 1x every 3 months 12 months	Mean change from baseline VA at 12 months: 0.3mg -1.6 letters vs 0.5mg -0.2 letters vs sham injection -16.3 letters. Proportion of patients losing ≤15 letters of VA at 12 months: 0.3mg 83.3% vs 0.5mg 90.2% vs sham injection 49.2%; p<0.001 for both doses vs sham Proportion of patients gaining ≥ letters of VA at 12 months: 0.3mg 11.7% vs 0.5mg 13.1% vs sham injection 9.5% Proportion of patients with VA worse than 20/200 at 12 months: 0.3mg 23.3% vs 0.5mg 24.6% v sham injection 52.4% (p=0.001 both doses vs sham) No statistically significant difference between groups in NEI-VFQ 25 subscale score (data not reported)	Good

TABLE 11. ARMD - RANDOMIZED, PLACEBO-CONTROLLED TRIALS

Study, Year, Title	Study design Purpose of study	Patients	Intervention Duration of follow-up	Results	Quality Score
Rosenfeld et al, 2006[145] *MARINA Trial Ranibizumab for neovascular age-related macular degeneration.* Other publications: Boyer et al, 2007	To evaluate the effectiveness and safety of ranibizumab for the treatment of minimally classic or occult with no classic choroidal neovasculatization associated with ARMD. Double-blind PCT	n=716 Mean age 77 years (SD 8) 65% female ARMD	0.3mg or 0.5mg ranibizumab 1x/month (range 23-37 days) for 2 years vs sham injection 2 years	Mean change in visual acuity at 12 months: ranibizumab 0.3mg 6.5 letters vs. ranibizumab 0.5mg 7.2 letters vs. placebo -10.4 letters; p<0.001 for both doses ranibizumab vs. placebo. Mean change in visual acuity at 24 months: ranibizumab 0.3mg 5.4 letters vs. ranibizumab 0.5mg 6.6 letters vs. placebo -14.9 letters; p<0.001 for both doses ranibizumab vs. placebo. % of patients with <15 letters lost at 12 months: ranibizumab 0.3mg 94.5% vs. ranibizumab 0.5mg 94.6% vs. placebo 62.2%; p<0.001 for both doses ranibizumab vs. placebo. % of patients with <15 letters lost at 24 months: ranibizumab 0.3mg 92.0% vs. ranibizumab 0.5mg 90.0% vs. placebo 52.9%; p<0.001 for both doses ranibizumab vs. placebo	Fair

Abbreviations: AE = adverse event, ARMD = age-related macular degeneration, CCT = center for clinical trials, CRVO = central retinal vein occlusion, ETDRS = early treatment diabetic retinopathy study, PCT = placebo controlled trial.

TABLE 12. SUMMARY OF EVIDENCE

Number of studies: Overall quality rating	Limitations	Consistency	Primary care applicability	Summary of findings
KQ1 Overall effect of screening on final outcomes				
4 RCTs: Fair quality	Vision screening assessed as part of a multicomponent intervention in most studies; methodological shortcomings in trials; fairly small numbers of trials	Consistent	High	Three cluster RCT's found no difference between vision screening and usual care, no vision screening, or delayed screening on vision and other clinical outcomes. One RCT found vision screening by an optometrist in frail elderly persons associated with an increased risk of falls (RR 1.57, 95% CI 1.20 to 2.05) and a trend towards increased risk of fractures (RR 1.74, 95% C I 0.97 to 3.11).
KQ2 Harms of screening				
1 RCT: Fair quality	Not applicable	Not applicable	Not applicable	See KQ 1 for evidence on falls.
KQ3 Accuracy of screening				
8 studies of diagnostic accuracy: Fair quality	Methodological shortcoming in trials; no studies assessing accuracy or utility of Amsler grid, fundoscopic examination, or pinhole testing in primary care settings	Consistent	Moderate (some studies conducted in mixed populations of younger and older adults or in non-primary care settings)	Four studies found that screening questions are not accurate for identifying persons with vision impairment compared to the Snellen chart. Four studies found that visual acuity testing is not accurate for identifying the presence of vision conditions compared to a detailed ophthalmologic examination. One study four that the Amsler grid is not accurate for identifying the presence of vision conditions compared to a detailed ophthalmologic examination. One very small (n=50) study found non-ophthalmologists are as accurate as ophthalmologists for identifying presence of cataracts.

TABLE 12. SUMMARY OF EVIDENCE

Number of studies: Overall quality rating	Limitations	Consistency	Primary care applicability	Summary of findings
KQ4 Treatment				
Age-related macular degeneration (DRY)				
7 RCTs: Fair quality	Conclusions are heavily influenced by results of one large trial	Some inconsist-ency	High	A large randomized trial found a multivitamin and zinc combination effective for slowing progression of ARMD (adjusted OR 0.68, 99% CI 0.49 to 0.93), though the difference in the likelihood of losing 15 or more letters of visual acuity was not statistically significant (adjusted OR 0.77, 95% CI 0.58 to 1.03).
Age-related macular degeneration (WET)				
11 RCTs: Fair - good quality	Relatively small numbers of trials	Consistent	High	Laser photocoagulation: RR 0.67 for 6+ lines visual acuity loss; 95% CI 0.53 to 0.83, 5 RCTs (poor quality, but consistent). Photodynamic therapy: RR 0.22 for 3+ lines visual acuity loss, 95% CI 0.13 to 0.30, 3 RCTs (fair to good quality). Vascular endothelin growth factor inhibitors: RR 0.71, 95% CI 0.61 to 0.84, 2 RCTs for pegaptanib and RR 0.21, 95% CI 0.16-0.27, 2 RCTs for ranibizumab for 3+ lines visual acuity loss (fair to good quality).
Cataracts				
3 RCTs, plus numerous observational studies: Fair quality	Two trials compared immediate to delayed cataract surgery for effects on falls; most observational studies have methodological shortcomings	Consistent	High	Numerous observational studies found that over 90% of patients achieve visual acuity 20/40 or better following cataract extraction and intraocular lens implantation. Three observational studies found cataract surgery associated with improved vision-related function. One trial found immediate first-eye cataract surgery associated with a decreased rate of second (but not first) fall compared to delayed surgery, resulting in a lower overall rate of falls (rate ratio 0.66, 95% CI 0.40 to 0.96, p=0.03), but a second trial found no effect of second-eye cataract surgery on falls.
Uncorrected refractive error				
2 RCTs, 2 systematic reviews, plus numerous observational studies: Fair - good quality	Few trials comparing treatments for uncorrected refractive error versus placebo or no therapy	Consistent	High	In 1 large population-based study, 60% of older adults with vision impairment can achieve visual acuity 20/40 or better with refractive correction. Two RCTs found use of corrective lenses associated with improvements in vision-related function, but effects on overall function inconsistent. Numerous observational studies show that over 85% of patients achieve visual acuity 20/40 or better following photorefractive surgery for myopia or hyperopia.

TABLE 12. SUMMARY OF EVIDENCE

Number of studies: Overall quality rating	Limitations	Consistency	Primary care applicability	Summary of findings
KQ5 Harms of treatment				
Age-related macular degeneration (DRY)				
3 RCTs, 1 systematic review: Fair quality	Data on harms poorly reported	Consistent	High	The large AREDS trial found zinc associated with significantly increased risk of hospitalization for genitourinary causes compared to non-use of zinc (11.1% versus 7.6%; p=0.0003) and antioxidants associated with increased risk of yellow skin compared to non-use of antioxidants (8.3% vs. 6.0%, p=0.008).
Age-related macular degeneration (WET)				
5 RCTs, 2 systematic reviews: Fair to good quality	Some data on harms are not yet published, data on long-term effects of photodynamic therapy and vascular endothelin growth factor inhibitors is limited	Consistent	High	Laser photocoagulation: Visual acuity loss ≥6 lines compared to observation 3 months after treatment (absolute rate 16.6%; relative risk 1.41 [95% CI 1.08 to 1.82], 5 trials). Photodynamic therapy: Increased risk of acute severe visual acuity loss (20 letter loss within 7 days of treatment) compared to placebo (2% vs. 0.2%, relative risk 0.02, 95% CI 0.01 to 0.03) and increased risk of infusion-related back pain compared to placebo (3.4% vs. 0.3%, relative risk 6.50, 95% CI 1.52 to 27.78). Vascular endothelin growth factor inhibitors: more cases of endophthalmitis and uveitis compared to placebo, but small numbers of events. No increase in risk of systemic hypertension or arterial thromboembolic events.
Cataracts				
3 systematic reviews of observational studies: Fair quality	No data on harms from placebo-controlled trials	Some inconsist-ency in reported rates	High	Systematic reviews of numerous observational studies of cataract surgery found a pooled rate of posterior capsule opacification of 28% after 5 years, and a pooled rate of 0.13% for endophthalmitis.
Uncorrected refractive error				
1 systematic review, 4 observational studies: Poor-fair quality	Little data on harms for corrective lenses; many observational studies did not report rates of harms associated with photorefractive surgery	Consistent	High	One small prospective study found multifocal lenses associated with a higher risk of falls in older adults compared to unifocal lenses (OR 2.09, 95% CI 1.06 to 4.92). Three studies found incidence of infectious keratitis ranges from 0.3 to 3.6 cases per 10,000 contact lens wearers; one study found incidence to be higher in persons over 50 years old. Corneal ectasia rates range from 0% to 0.87% in five studies of LASIK, keratitis rates range from 0% to 3.4% in 6 studies of LASIK and 4 studies of LASEK.

Abbreviations: AREDS = age-related eye disease study, CI = confidence interval, KQ = key question, LASEK = laser assisted sub-epithelial keratomileusis, LASIK = laser assisted in situ keratomileusis, RCT = randomized controlled study, RR = relative risk, SR = systematic review.

APPENDIX A. ABBREVIATIONS

Abbreviation	Meaning
ADVS	Activities of Daily Vision Scale, used to assess the impact of cataract surgery
AE	Adverse Event
AREDS	Age-related Eye Disease Study
ARMD, AMD	Age-related Macular Degeneration
BCVA	Best-Corrected Visual Acuity
BSCVA	Best Spectacle-Corrected Visual Acuity
CCT	Center for Clinical Trials
CES-D	Center for Epidemiologic Studies Depression Scale
CI	Confidence Interval
CNV	Choroidal Neovascularisation
CRVO	Central Retinal Vein Occlusion
CSS	Cataract Symptom Score
D	Diopters
DORS	Diagnostic Odds Ratio
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
GDS	Geriatric Depression Scale
IOL	Intraocular Lenses
KQ	Key Question
LASEK	Laser Assisted Sub-Epithelial Keratomileusis
LASIK	Laser Assisted in Situ Keratomileusis
LOCS	Lens Opacities Classification System
logMAR	Logarithmic Minimum Angle of Resolution
MI	Myocardial infarction
MMSE	Mini-Mental State Examination
NA	Not Applicable
NEI-VFQ	National Eye Institute Visual Functioning Questionnaire
NHANES	National Health and Nutrition Examination Survey
NHVQoL	Nursing Home Vision-Targeted Health-Related Quality of Life Questionnaire
NLR	Negative Likelihood Ratio
NNH	Number-Needed-to-Harm
NNT	Number-Needed-to-Treat
NR	Not Relevant
OR	Odds Ratio
PCO	Posterior Capsule Opacification
PCT	Placebo Controlled Trial
PDT	Photodynamic Therapy
PLR	Positive Likelihood Ratio
PRK	Photorefractive Keratectomy
QoL	Quality of Life
RCT	Randomized Controlled Trial
RR	Relative Risk
SD	Standard Deviation
SF-36	Medical Outcomes Study - Short Form Health Survey 36
TAP	Treatment of Age-Related Macular Degeneration With Photodynamic Therapy
UCVA	Uncorrected Visual Acuity
US	United States
USPSTF	United States Preventive Services Task Force
VECAT	Vitamin E, Cataract and Age-Related Maculopathy Study
VEGF	Vascular Endothelial Growth Factor
VF-14	Health survey questionnaire designed for ophthalmology. "VF" stands for Visual Function, and "14" refers to the 14 questions in the main section of the questionnaire.
VIM	Visudyne in Minimally Classic Choroidal Neovascularisation Trial
VIP	Verteporfin in Photodynamic Therapy

Diagnostic Accuracy Searches

Database: ***Ovid MEDLINE(R)***

1 exp Vision/
2 exp Vision Disorders/
3 exp Mass Screening/
4 exp Geriatric Assessment/
5 1 or 2
6 3 and 5
7 limit 6 to "all aged (65 and over)"
8 4 and 5
9 7 or 8
10 screen$.mp.
11 exp Vision Tests/
12 10 and 11
13 limit 12 to "all aged (65 and over)"
14 exp Refractive Errors/
15 (presbyop$ or myop$ or astigmati$ or hyperop$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
16 14 or 15
17 exp Macular Degeneration/
18 (degenerat$ adj3 macula$).mp.
19 armd.mp.
20 or/17-19
21 exp Cataract/
22 cataract.mp.
23 21 or 22
24 16 or 20 or 23
25 24 and (3 or 4 or 12)
26 limit 25 to "all aged (65 and over)"
27 7 or 13 or 26
28 limit 27 to english language
29 limit 27 to abstracts
30 28 or 29
31 exp "Sensitivity and Specificity"/
32 5 or 11 or 24
33 31 and 32
34 limit 33 to "all aged (65 and over)"
35 limit 34 to english language
36 limit 34 to abstracts
37 35 or 36
38 37 not 30
39 from 38 keep 1-579

Database: ***EBM Reviews - Cochrane Central Register of Controlled Trials***

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3 exp Mass Screening/
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5 exp Refractive Errors/
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7 exp Macular Degeneration/
8 (degenerat$ adj3 macula$).mp.
9 armd.mp.

10 exp Cataract/
11 cataract.mp.
12 (1 or 2) and (3 or 4)
13 or/5-11
14 13 and (3 or 4)
15 12 or 14
16 sensitivity.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
17 specificity.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
18 accura$.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
19 (16 and 17) or 18
20 15 and 19
21 (child$ or pediatri$ or infant$ or neonat$).ti.
22 20 not 21
23 from 22 keep 1-44

Database: ***EBM Reviews - Cochrane Database of Systematic Reviews***
1 cataract$.ab.
2 macular degeneration$.ab.
3 refractive error$.ab.
4 (presbyop$ or astigmati$ or myop$ or hyperop$).ab.
5 (vision or visual).ab.
6 or/1-4
7 screen$.mp. [mp=title, abstract, full text, keywords, caption text]
8 accura$.mp. [mp=title, abstract, full text, keywords, caption text]
9 sensitivity.mp. [mp=title, abstract, full text, keywords, caption text]
10 specificity.mp. [mp=title, abstract, full text, keywords, caption text]
11 (Cochrane Eyes and Vision Group).mp. [mp=title, abstract, full text, keywords, caption text]
12 5 and 6
13 7 and 12
14 or/8-10
15 13 and 14
16 11 and 15
17 (child$ or pediatri$ or infant$ or neonat$).ti.
18 16 not 17
19 (glaucoma or diabet$).ti.
20 18 not 19
21 from 20 keep 1-14

Screening Searches

Database: ***Ovid MEDLINE(R)***
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2 exp Vision Disorders/
3 exp Mass Screening/
4 exp Geriatric Assessment/
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6 3 and 5
7 limit 6 to "all aged (65 and over)"
8 4 and 5
9 7 or 8
10 screen$.mp.
11 exp Vision Tests/
12 10 and 11
13 limit 12 to "all aged (65 and over)"

14 exp Refractive Errors/
15 (presbyop$ or myop$ or astigmati$ or hyperop$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
16 14 or 15
17 exp Macular Degeneration/
18 (degenerat$ adj3 macula$).mp.
19 armd.mp.
20 or/17-19
21 exp Cataract/
22 cataract.mp.
23 21 or 22
24 16 or 20 or 23
25 24 and (3 or 4 or 12)
26 limit 25 to "all aged (65 and over)"
27 7 or 13 or 26
28 limit 27 to english language
29 limit 27 to abstracts
30 28 or 29
31 from 30 keep 1-498

Database: ***EBM Reviews - Cochrane Central Register of Controlled Trials***
1 ((vision or visual) adj5 screen$).mp.
2 (presbyop$ or myop$ or astigmati$ or hyperop$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
3 (macula$ adj3 degenerat$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
4 armd.mp.
5 cataract$.mp.
6 screen$.mp.
7 or/2-5
8 6 and 7
9 1 or 8
10 (elder$ or old or aged).mp.
11 9 and 10
12 (child$ or pediatri$ or infant or neonat$).mp.
13 11 not 12
14 from 13 keep 1-95

Database: ***EBM Reviews - Cochrane Database of Systematic Reviews***
1 ((vision or visual) adj5 screen$).mp.
2 (presbyop$ or myop$ or astigmati$ or hyperop$).mp. [mp=title, abstract, full text, keywords, caption text]
3 (macula$ adj3 degenerat$).mp. [mp=title, abstract, full text, keywords, caption text]
4 armd.mp.
5 cataract$.mp.
6 screen$.mp.
7 or/2-5
8 6 and 7
9 1 or 8
10 (elder$ or old or aged).mp.
11 9 and 10
12 (child$ or pediatri$ or infant or neonat$).mp.
13 11 not 12
14 from 13 keep 1-28

APPENDIX B1. VISION SEARCH STRATEGIES

Treatment Searches

Database: ***Ovid MEDLINE(R)***

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2 exp Cataract/nu, dh, pc, dt, rt, rh, th [Nursing, Diet Therapy, Prevention & Control, Drug Therapy, Radiotherapy, Rehabilitation, Therapy]
3 exp Macular Degeneration/nu, pc, dh, dt, rt, rh, su, th [Nursing, Prevention & Control, Diet Therapy, Drug Therapy, Radiotherapy, Rehabilitation, Surgery, Therapy]
4 exp Refractive Errors/nu, pc, dt, rt, rh, th [Nursing, Prevention & Control, Drug Therapy, Radiotherapy, Rehabilitation, Therapy]
5 Presbyopia/pc, dt, rt, rh, su, th [Prevention & Control, Drug Therapy, Radiotherapy, Rehabilitation, Surgery, Therapy]
6 or/1-5
7 exp Vital Statistics/
8 exp "Quality of Life"/
9 6 and (7 or 8)
10 exp Time Factors/
11 exp Prognosis/
12 10 and 11
13 6 and 12
14 9 or 13
15 limit 14 to "all aged (65 and over)"
16 limit 15 to english language
17 limit 15 to abstracts
18 16 or 17
19 from 18 keep 1-365

Database: ***EBM Reviews - Cochrane Central Register of Controlled Trials***

1 exp Vision/
2 exp Vision Disorders/
3 exp Refractive Errors/
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5 exp Macular Degeneration/
6 (degenerat$ adj3 macula$).mp.
7 armd.mp.
8 exp Cataract/
9 cataract.mp.
10 1 or 2
11 or/3-9
12 10 and 11
13 treatment$.ab.
14 12 and 13
15 (child$ or pediatri$ or infant$ or neonat$).ti.
16 14 not 15
17 (glaucoma or diabet$).ti.
18 16 not 17
19 (geriatri$ or aged or elderly or old).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
20 18 and 19
21 from 20 keep 1-306

APPENDIX B1. VISION SEARCH STRATEGIES

Database: ***EBM Reviews - Cochrane Database of Systematic Reviews***

1 cataract$.ab.
2 macular degeneration$.ab.
3 refractive error$.ab.
4 (presbyop$ or astigmati$ or myop$ or hyperop$).ab.
5 or/1-4
6 (Cochrane Eyes and Vision Group).mp. [mp=title, abstract, full text, keywords, caption text]
7 5 and 6
8 (child$ or pediatri$ or infant or neonat$).ab.
9 7 not 8
10 (glaucoma or diabet$).ti.
11 9 not 10
12 from 11 keep 1-22

APPENDIX B2. INCLUSION AND EXCLUSION CRITERIA

All Key Questions

Populations:

Include: Asymptomatic adults ages 65 years and older (if insufficient data for adults 65 years and older will include studies enrolling adults in general) with vision impairment (visual acuity worse than 20/40 but better than 20/200), uncorrected refractive errors (due to myopia, hyperopia, astigmatism, or presbyopia), age-related macular degeneration (ARMD), or cataracts

Exclude: Persons with known vision impairment, cataracts, ARMD, diabetes, or glaucoma

Languages:

Include: English language

Key Questions 1 & 2

Interventions:

Include: Vision screening performed in primary care or eye specialty settings, including multi-component screening with a distinct vision screening component

Exclude: Community-based or in-home interventions

Study designs:

Include: Randomized controlled trials and controlled observational studies

Outcomes:

Include: Visual acuity; quality of life, functional capacity (including ability to drive and driving outcomes), other measures of morbidity; mortality

Exclude: Falls, reading speed and other tests of vision function

Key Question 3

Interventions:

Include: Screening questions or diagnostic tests used for vision screening in primary care settings (e.g., Snellen eye chart, other visual acuity charts, physical examination, fundoscopic examination performed by a primary care clinician)

Exclude: Diagnostic tests used for vision screening in eye specialty settings (including fundoscopic examination performed by an eye professional and specialized diagnostic testing)

Study designs:

Include: Studies evaluating diagnostic accuracy of a screening question or diagnostic test compared to a reference standard

Outcomes:

Include: Sensitivity, specificity, positive and negative predictive values, areas under the receiver operating curve, other measures of diagnostic test accuracy

Key Questions 4 & 5

Interventions:

Include: Corrective lenses (eyeglasses and contact lenses), reading aids, photorefractive surgery (LASIK, LASEK, PRK), vitamins and antioxidants, laser therapy, photodynamic therapy, vascular endothelin growth factor inhibitors

Study designs:

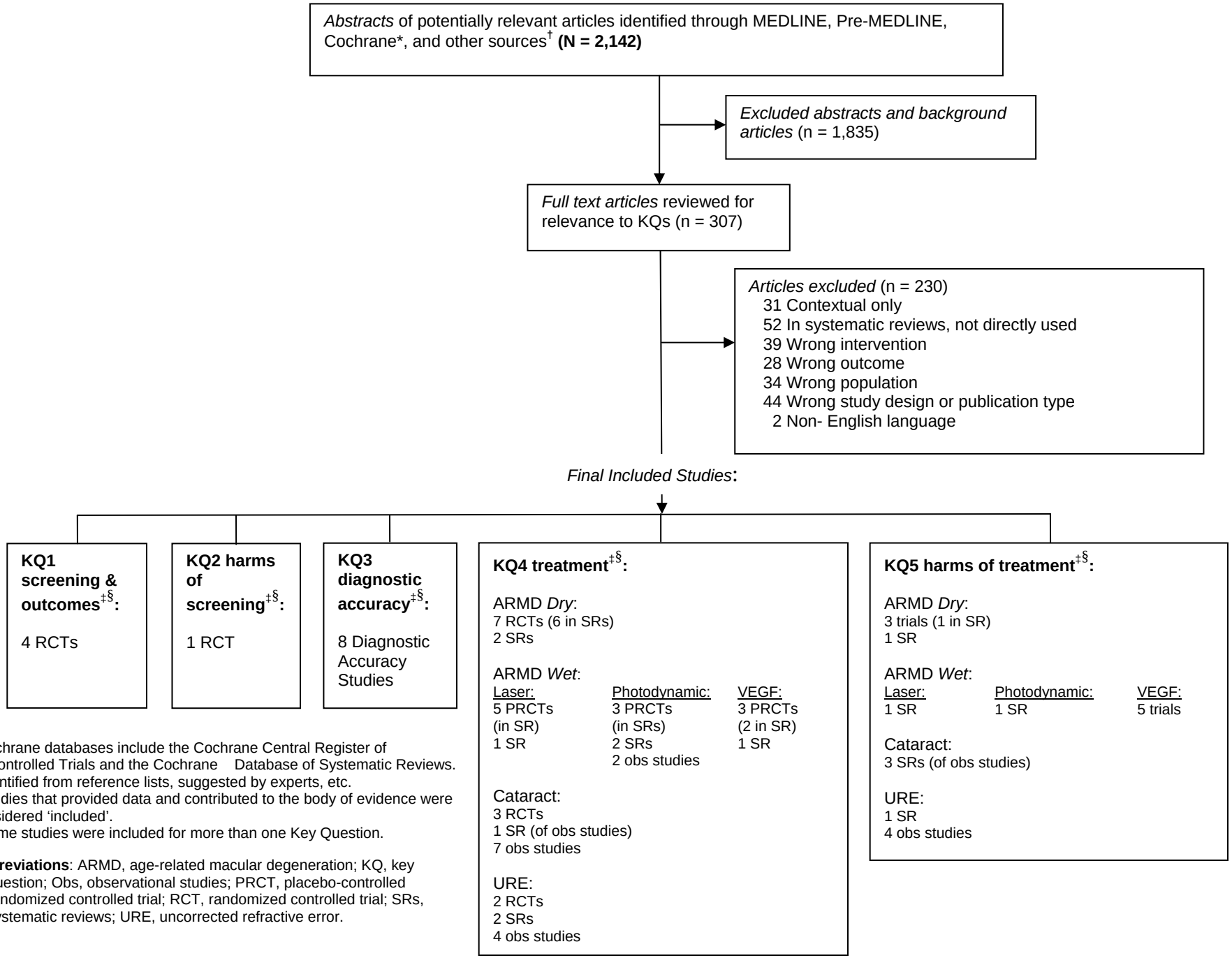
Include: Randomized controlled trials, controlled observational studies if insufficient evidence from randomized trials

Outcomes:

Include: Visual acuity; quality of life, functional capacity (including ability to drive and driving outcomes), other measures of morbidity; mortality

Exclude: Reading speed and other tests of vision function

APPENDIX B3. LITERATURE FLOW DIAGRAM



*Cochrane databases include the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.
†Identified from reference lists, suggested by experts, etc.
‡Studies that provided data and contributed to the body of evidence were considered 'included'.
§Some studies were included for more than one Key Question.

Abbreviations: ARMD, age-related macular degeneration; KQ, key question; Obs, observational studies; PRCT, placebo-controlled randomized controlled trial; RCT, randomized controlled trial; SRs, systematic reviews; URE, uncorrected refractive error.

APPENDIX B4. EXCLUDED STUDIES

Contextual Only:

Arias L, Garcia-Arumi J, Ramon JM, et al. Photodynamic therapy with intravitreal triamcinolone in predominantly classic choroidal neovascularization: one-year results of a randomized study. *Ophthalmology*. 2006;113(12):2243-2250.

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Brannan S, Dewar C, Sen J, et al. A prospective study of the rate of falls before and after cataract surgery. *Br J Ophthalmol*. 2003;87(5):560-562.

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Holladay JT. Visual acuity measurements. *J Cataract Refract Surg*. 2004;30(2):287-290.

Jung S, Coleman A, Weintraub NT. Vision screening in the elderly. *J Am Med Dir Assoc*. 2007;8(6):355-362.

Kaiser PK. Verteporfin therapy of subfoveal choroidal neovascularization in age-related macular degeneration: 5-year results of two randomized clinical trials with open-label extension. TAP Report No. 8. *Graefe's Arch Clin Exp Ophthalmology*. 2006;244:1132-1142.

Klein BE, Klein R, Kathryn LP, et al. Prevalence of Age-related Lens Opacities in a Population. *Ophthalmology*. 1992;99(4):546-552.

Klein R, Klein BEK, Lee KE, et al. Changes in Visual Acuity in a Population Over a 15-year Period: The Beaver Dam Eye Study. *Am J Ophthalmol*. 2006;142(4):539-549.e532.

Luke M, Ziemssen F, Bartz-Schmidt KU, et al. Quality of life in a prospective, randomised pilot-trial of photodynamic therapy versus full macular translocation in treatment of neovascular age-related macular degeneration--a report of 1 year results. *Graefes Arch Clin Exp Ophthalmol*. 2007;245(12):1831-1836.

APPENDIX B4. EXCLUDED STUDIES

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Mary ET. Where Is the Vision for Fall Prevention? *J Am Geriatr Soc*. 2001;49(5):676-677.

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APPENDIX B5. U.S. PREVENTIVE SERVICES TASK FORCE QUALITY RATING CRITERIA FOR RCTS AND OBSERVATIONAL STUDIES*

Diagnostic Accuracy Studies

Criteria:

- Screening test relevant, available for primary care, adequately described
- Study uses a credible reference standard, performed regardless of test results
- Reference standard interpreted independently of screening test
- Handles indeterminate results in a reasonable manner
- Spectrum of patients included in study
- Sample size
- Administration of reliable screening test

Definition of ratings based on above criteria:

Good: Evaluates relevant available screening test; uses a credible reference standard; interprets reference standard independently of screening test; reliability of test assessed; has few or handles indeterminate results in a reasonable manner; includes large number (more than 100) broad-spectrum patients with and without disease.

Fair: Evaluates relevant available screening test; uses reasonable although not best standard; interprets reference standard independent of screening test; moderate sample size (50 to 100 subjects) and a "medium" spectrum of patients.

Poor: Has important limitation such as: uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size of very narrow selected spectrum of patients.

Randomized Controlled Trials (RCTs) and Cohort Studies

Criteria:

- Initial assembly of comparable groups**:** RCTs—adequate randomization, including concealment and whether potential confounders were distributed equally among groups; cohort studies—consideration of potential confounders with either restriction or measurement for adjustment in the analysis; consideration of inception cohorts
- Maintenance of comparable groups (includes attrition, cross-overs, adherence, contamination)
- Important differential loss to follow-up or overall high loss to follow-up
- Measurements: equal, reliable, and valid (includes masking of outcome assessment)
- Clear definition of interventions
- Important outcomes considered
- Analysis: adjustment for potential confounders for cohort studies, or intention-to-treat analysis for RCTs; for cluster RCTs, correction for correlation coefficient

APPENDIX B5. U.S. PREVENTIVE SERVICES TASK FORCE QUALITY RATING CRITERIA FOR RCTS AND OBSERVATIONAL STUDIES*

Definition of ratings based on above criteria:

Good: Meets all criteria: Comparable groups are assembled initially and maintained throughout the study (follow-up at least 80 percent); reliable and valid measurement instruments are used and applied equally to the groups; interventions are spelled out clearly; important outcomes are considered; and appropriate attention to confounders in analysis.

Fair: Studies will be graded "fair" if any or all of the following problems occur, without the important limitations noted in the "poor" category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred in follow-up; measurement instruments are acceptable (although not the best) and generally applied equally; some but not all important outcomes are considered; and some but not all potential confounders are accounted for.

Poor: Studies will be graded "poor" if any of the following major limitations exists: Groups assembled initially are not close to being comparable or maintained throughout the study; unreliable or invalid measurement instruments are used or not applied at all equally among groups (including not masking outcome assessment); and key confounders are given little or no attention.

Case Control Studies

Criteria:

- Accurate ascertainment of cases
- Nonbiased selection of cases/controls with exclusion criteria applied equally to both
- Response rate
- Diagnostic testing procedures applied equally to each group
- Measurement of exposure accurate and applied equally to each group
- Appropriate attention to potential confounding variable

Definition of ratings based on criteria above:

Good: Appropriate ascertainment of cases and nonbiased selection of case and control participants; exclusion criteria applied equally to cases and controls; response rate equal to or greater than 80 percent; diagnostic procedures and measurements accurate and applied equally to cases and controls; and appropriate attention to confounding variables.

Fair: Recent, relevant, without major apparent selection or diagnostic work-up bias but with response rate less than 80 percent or attention to some but not all important confounding variables.

Poor: Major selection or diagnostic work-up biases, response rates less than 50 percent, or inattention to confounding variables.

***Reference:**

Harris RP, Helfand M, Woolf SH, et al. Current methods of the U.S. Preventive Services Task Force: a review of the process. *Am J Prev Med.* 2001:20(3S); 21-35.

APPENDIX B6. QUALITY RATING CRITERIA FOR SYSTEMATIC REVIEWS*

Overall quality rating for each systematic review is based on the below questions. Ratings are summarized as: *Good, Fair, or Poor*:

- Search dates reported? *Yes or No*
- Search methods reported? *Yes or No*
- Comprehensive search? *Yes or No*
- Inclusion criteria reported? *Yes or No*
- Selection bias avoided? *Yes or No*
- Validity criteria reported? *Yes or No*
- Validity assessed appropriately? *Yes or No*
- Methods used to combine studies reported? *Yes or No*
- Findings combined appropriately? *Yes or No*
- Conclusions supported by data? *Yes or No*

Definitions of ratings based on above criteria

Good: Meet all criteria: Reports comprehensive and reproducible search methods and results; reports pre-defined criteria to select studies and reports reasons for excluding potentially relevant studies; adequately evaluates quality of included studies and incorporates assessments of quality when synthesizing data; reports methods for synthesizing data and uses appropriate methods to combine data qualitatively or quantitatively; conclusions supported by the evidence reviewed.

Fair: Studies will be graded fair if they fail to meet one or more of the above criteria, but the limitations are not judged as being major.

Poor: Studies will be graded poor if they have a major limitation in one or more of the above criteria.

***Created from the following publications**:

Harris RP, Helfand M, Woolf SH, et al. Current methods of the U.S. Preventive Services Task Force: a review of the process. *Am J Prev Med.* 2001:20(3S); 21-35.

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APPENDIX B7. EXPERT REVIEWERS OF THE DRAFT REPORT

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APPENDIX C1. RANDOMIZED TRIALS OF VISION SCREENING IN OLDER ADULTS

Study, Year, Title	Screening intervention	Purpose of study	Study design	Setting	Inclusion criteria	Exclusion criteria
Cumming et al, 2007[69] *Improving vision to prevent falls in frail older people*	Visual acuity was measured using the Early Treatment Diabetic Retinopathy Study Chart at 2.4 m-test distance Contrast sensitivity was measured using the CSV-1000E Chart 1 at 2.4m-test distance Visual fields were measured using a Humphrey automated visual field unit with a frequency doubling technology visual field instrument Intraocular pressure was assessed using a Perkins applanation tonometer An eye exam was performed using slit lamp biomicroscopy and direct opthalmoscopy	To determine the efficacy of vision and eye exams with subsequent treatment of vision problems, for preventing falls and fractures	Random-ized controlled trial	Community based - patients received in-home care and/or at study clinic	Age >70 years; living independently in the community; no cataract surgery or new eyeglasses prescription in the 3 months preceding study entry; if cognitively impaired, a caregiver was needed to complete the monthly falls calendar	NR
Eekhof et al, 2000[66] *Effects of screening for disorders among the elderly: an intervention study in general practice*	Assessment of difficulty in recognizing a face at 4 meters and/or reading normal letters in a newspaper, and/or impaired vision with both by Snellen eye chart or not being able to read normal newspaper letters at 25 cm distance	Compare initial screening for four disorders versus no screening in persons 75 years or older	Cluster random-ized controlled trial	Primary care clinic	75 years or older	Too ill, suffering from dementia, or not able to participate for other reasons

APPENDIX C1. RANDOMIZED TRIALS OF VISION SCREENING IN OLDER ADULTS

Study, Year, Title	Number of treatment & control subjects (number approached, number eligible, number enrolled)	Subject age, gender, diagnosis	Country & setting	Sponsor	Measures	Interventions or exposures
Cumming et al, 2007[69] *Improving vision to prevent falls in frail older people*	NR/NR/616 enrolled	Mean age 80.6 years 68% female Mean baseline visual acuity (intervention group only) 20/30	Australia Study clinic and/or homes	National Health and Medical Research Council of Australia	Primary outcome: incidence of falls over 12 months of follow-up	A: Vision tests and eye exams, including treatment (e.g. glasses) and/or referrals to other health care providers B: Standard care (no vision testing or eye exams)
Eekhof et al, 2000[66] *Effects of screening for disorders among the elderly: an intervention study in general practice*	12 general practices enrolled 1470 patients screened 1368 eligible Number randomized unclear, 1121 evaluated (576 in initial screening, 545 no initial screening)	Mean age: 81 years Female: 64% vs. 68% Non-white: Not reported	The Netherlands General practice clinics	NR	Visual disorders, defined as having difficulty in recognizing a face at 4 m, and/or reading normal letters in a newspaper, and/or impaired vision with both eyes (Snellen <0.3), or not being able to read normal newspaper letters at 25 cm	A: Screening in first and second year for hearing disorder, visual disorder, urinary incontinence, and mobility disorder B: No screening in first year, screening in second year

APPENDIX C1. RANDOMIZED TRIALS OF VISION SCREENING IN OLDER ADULTS

Study, Year, Title	Results	Duration of follow-up	Loss to follow-up	Compliance to treatment	Adverse events & withdrawals due to AE's	Quality score
Cumming et al, 2007[69] *Improving vision to prevent falls in frail older people*	Primary outcome: Falls, treated vs. untreated group Rate ratio 1.57 (95% CI 1.20 to 2.05; p=0.001) Other outcomes: patients requiring treatment (intervention group only) new glasses - 92/309 (29.8%) referral to ophthalmologist - 64*/309 (20.7%) refused new glasses/referral - 11/309 (3.6%) *Some persons were referred for more than 1 type of treatment	12 months	84/616 (14%)	146/309 in control group needed treatment or referral (11 declined treatment or referral) All receiving new eyeglasses complied (n=92) Followed through with referrals (n=64*) 7/15 persons that were referred for cataract surgery had surgery by the end of the follow up period *Some persons were referred for more than 1 type of treatment	NR	Fair
Eekhof et al, 2000[66] *Effects of screening for disorders among the elderly: an intervention study in general practice*	Immediate versus delayed vision screening Visual disorder in 2nd year: 51% vs. 47% (p=0.68)	1 year	16% (93/576) patients who underwent immediate screening did not participate in second year; otherwise unclear	36/59 persons referred to ENT or ophthalmologist followed through with referral	NR	Fair

APPENDIX C1. RANDOMIZED TRIALS OF VISION SCREENING IN OLDER ADULTS

Study, Year, Title	Screening intervention	Purpose of study	Study design	Setting	Inclusion criteria	Exclusion criteria
Moore et al, 1997[67] *A randomized trial of office-based screening for common problems in older persons*	Vision screening: Question to assess difficulty performing everyday activities, followed by Snellen eye chart if positive	Compare a structured screening intervention to usual care in persons 70 years or older	Cluster randomized controlled trial	Primary care clinic	70 years or older, English speaking, not acutely or terminally ill, and able to answer questions	NR
Smeeth et al, 2003[68] *Screening older people for impaired vision in primary care: cluster randomized trial*	Detailed health assessment by a trained nurse, including Glasgow eye chart and pinhole testing if visual acuity less than 6/18 in either eye (targeted screening only consisted of a brief health assessment)	Compare universal screening (assessment and visual acuity) with targeting screening in persons 75 years or older	Cluster randomized controlled trial	Primary care clinic	75 years or older	Resident in a long stay hospital or nursing home or terminally ill

Abbreviations: CI = confidence interval, NR = not reported, RR = relative risk.

APPENDIX C1. RANDOMIZED TRIALS OF VISION SCREENING IN OLDER ADULTS

Study, Year, Title	Number of treatment & control subjects (number approached, number eligible, number enrolled)	Subject age, gender, diagnosis	Country & setting	Sponsor	Measures	Interventions or exposures
Moore et al, 1997[67] *A randomized trial of office-based screening for common problems in older persons*	26 internal medicine and family practice groups enrolled 316 patients screened 309 eligible 261 enrolled (112 to screening and 149 to usual care)	Mean age: 77 vs. 76 years Female: 65% vs. 59% Non-white: 21% vs. 19%	US Primary care clinics	Robert Wood Johnson Clinical Scholars Program and the National Institute on Aging Geriatric Academic Program	Self-reporting improvement in vision	A: Screening based on structured screening form (for vision a screening question followed by Snellen eye chart if positive response) B: Usual care
Smeeth et al, 2003[68] *Screening older people for impaired vision in primary care: cluster randomized trial*	106 general practices enrolled 4340 patients screened 3249 randomized (1565 to universal screening and 1684 to targeted screening)	Median age: 80 vs. 80 years Female: 60% vs. 63% Non-white: Not reported Proportion reporting difficulty seeing newsprint: 8% vs. 10%	UK Primary care clinics	Medical Research Council	Visual acuity less than 6/18	A: Universal screening: Brief and detailed health assessment including measurement of visual acuity w Glasgow acuity chart (reported as Snellen equivalent acuity), referral to an ophthal-mologist for pinhole vision <6/18, or referral to an optometrist if pinhole vision corrected to better than 6/18 B: Targeted screening: Brief screening assessment, with detailed assessment only for specified range / level of problems

APPENDIX C1. RANDOMIZED TRIALS OF VISION SCREENING IN OLDER ADULTS

Study, Year, Title	Results	Duration of follow-up	Loss to follow-up	Compliance to treatment	Adverse events & withdrawals due to AE's	Quality score
Moore et al, 1997[67] *A randomized trial of office-based screening for common problems in older persons*	Vision screening versus usual care Improvement in vision at 6 months: 20% (20/99) vs. 24% (31/131), p=0.45	6 months	12% (31/261) at 6 months	NR	NR	Fair
Smeeth et al, 2003[68] *Screening older people for impaired vision in primary care: cluster randomized trial*	Universal vs. targeted vision screening: Visual acuity less than 6/18 in either eye: RR 1.07 (95% CI 0.84 to 1.36, p=0.58) National Eye Institute visual function questionnaire (mean score, 0 to 100 scale): 86.0 vs. 85.6 (p=0.69)	3 to 5 years (median 3.9 years)	56% (1807/3249) did not complete outcome assessment (1465 deaths)	80% of those referred to an optician saw one at least once; 55% eligible for referral to ophthalmologist referred and uptake 88%	NR	Good-Fair

APPENDIX C2. QUALITY RATINGS OF RANDOMIZED CONTROLLED TRIALS ON VISION SCREENING IN OLDER ADULTS

Study, Year	Random assignment	Allocation concealed	Groups similar at baseline	Eligibility criteria specified	Blinding: outcome assessors or data analysts	Intention-to-treat analysis	Reporting of attrition, contamination, etc
Cumming et al, 2007[69] *Improving vision to prevent falls in frail older people*	Randomized but method not described	Yes	Yes	Yes	Can't tell	Yes	Yes
Eekhof et al, 2000[66] *Effects of screening for disorders among the elderly: an intervention study in general practice*	Yes	NA (cluster)	Yes	Yes	Can't tell	No	Yes
Moore et al, 1997[67] *A randomized trial of office-based screening for common problems in older persons*	Yes	NA (cluster)	Yes	Yes	Can't tell	No	Yes
Smeeth et al, 2003[68] *Screening older people for impaired vision in primary care: cluster randomized trial*	Yes	NA (cluster)	Yes	Yes	Can't tell	No	Yes

Abbreviations: NA = not available.

APPENDIX C2. QUALITY RATINGS OF RANDOMIZED CONTROLLED TRIALS ON VISION SCREENING IN OLDER ADULTS

Study, Year	Differential loss to follow-up or overall high loss to follow-up	Appropriate analysis including cluster correlation	Funding source	External validity	Quality score
Cumming et al, 2007[69] *Improving vision to prevent falls in frail older people*	No	NA	National Health and Medical Research Council of Australia	Number screened and eligible not reported Mean sever-ity of visual acuity im-pairment not reported	Fair
Eekhof et al, 2000[66] *Effects of screening for disorders among the elderly: an intervention study in general practice*	Yes	No	Can't tell	Appears highly applicable to screening settings in primary care	Fair
Moore et al, 1997[67] *A randomized trial of office-based screening for common problems in older persons*	Yes	No	Robert Wood Johnson Clinical Scholars Program; National Institute on Aging Geriatric Academic Program	Appears highly applicable to screening settings in primary care	Fair
Smeeth et al, 2003[68] *Screening older people for impaired vision in primary care: cluster randomized trial*	Yes	Yes	MRC/Dept of Health (UK)	Appears highly applicable to screening settings in primary care	Good-Fair

APPENDIX C3. STUDIES OF DIAGNOSTIC TEST ACCURACY

Study, Year	Type of study	Screening test	Reference standard	Setting	Screener	Age of enrollees	N	Proportion with condition	Subjects
Any eye disease									
Ariyasu et al, 1996[74] *Sensitivity, specificity, and predictive values of screening tests for eye conditions in a clinic-based population*	Cross-sectional	Near visual acuity Distance visual acuity Amsler grid	Detailed ophthal-mologic assess-ment	Eye clinic	Ophthal-mologist	"Most patients" 20 to 59 years old	317	43% refractive error, 16% cataract, 4% macular degeneration, 4% strabismus, 2% amblyopia	Patients attending for first time an eye clinic in Southern California
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Cross-sectional	Presenting distance visual acuity (with current distance glasses) Pinhole distance visual acuity Presenting reading acuity (with current reading glasses)	Detailed ophthal-mologic assess-ment	Unclear	Ophthal-mologist	49 years or older	3654	34.50%	Population based sample from the Blue mountains area west of Sydney, Australia
Wang et al, 1998[80] *Evaluation of screening schemes for eye disease in a primary care setting*	Cross-sectional	Questionnaire Pinhole visual acuity	Detailed ophthal-mologic assess-ment	Primary care clinic	Unclear	40 years or older	405	50.7% (13% cataract, ARMD and refractive error not reported)	Patients attending a primary care clinic in Maryland
Woods et al, 1998[81] *Screening for ophthalmic disease in older subjects using visual acuity and contrast sensitivity*	Cross-sectional	Distance visual acuity Near visual acuity	Detailed ophthal-mologic assess-ment	Eye clinic	Ophthal-mologist	50 years or older	2522	12% (50 to 64 years) and 23% (>64years) macular degeneration, 4.9% and 27.2% cataract	Population-based sample from residents at least 50 years old in New South Wales, Australia

APPENDIX C3. STUDIES OF DIAGNOSTIC TEST ACCURACY

Study, Year	Sensitivity	Specificity	Area under receiver operating curve	Index text	Quality score
Any eye disease					
Ariyasu et al, 1996[74] *Sensitivity, specificity, and predictive values of screening tests for eye conditions in a clinic-based population*	Amsler grid: 19% (40/206) Near visual acuity: 20/30 or worse: 83% (145/174); 20/40 or worse: 75% (130/174); 20/50 or worse: 67% (116/174); 20/60 or worse: 59% (102/174) Distance visual acuity: 20/30 or worse: 74% (191/258); 20/40 or worse: 65% (168/258); 20/50 or worse: 55% (143/258); 20/60 or worse: 59% (122/258)	Amsler grid: 92% (46/50) Near visual acuity: 20/30 or worse: 53% (20/38); 20/40 or worse: 74% (28/38); 20/50 or worse: 82% (31/38); 20/60 or worse: 84% (32/38) Distance visual acuity: 20/30 or worse: 73% (41/56); 20/40 or worse: 89% (50/56); 20/50 or worse: 96% (54/56); 20/60 or worse: 98%(55/56)	Near visual acuity: 0.74 +/- 0.04 Distance visual acuity: 0.83 +/- 0.04 (patients 40 years or older only)	Amsler grid Near visual acuity Distance visual acuity	Poor-Fair
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Presenting distance visual acuity: 20/30 or worse: 47%; 20/40 or worse: 27%; 20/60 or worse: 14% Pinhole distance visual acuity: 20/30 or worse: 34%; 20/40 or worse: 15%; 20/60 or worse: 9% Presenting reading acuity: 20/30 or worse: 98%; 20/40 or worse: 89%; 20/50 or worse: 59%	Presenting distance visual acuity: 20/30 or worse: 74%; 20/40 or worse: 87%; 20/60 or worse: 94% Pinhole distance visual acuity: 20/30 or worse: 86%; 20/40 or worse: 96%; 20/60 or worse: 97% Presenting reading acuity: 20/30 or worse: 3%; 20/40 or worse: 19%; 20/50 or worse: 59%	Presenting distance visual acuity: 0.72 Pinhole distance visual acuity: 0.66 Presenting reading acuity: 0.72	Presenting distance visual acuity (logMAR chart) Pinhole distance visual acuity Presenting reading acuity (with current reading glasses)	Poor-Fair
Wang et al, 1998[80] *Evaluation of screening schemes for eye disease in a primary care setting*	Questionnaire (questions weighted in logistic regression): 90% (95% CI 86-94%) Presenting visual acuity ≤ 20/40: 61%(95% CI 54-68%) Questionnaire with visual acuity as 2nd screening: 57% (95% CI 50-64%)	Questionnaire (questions weighted in logistic regression): 44% (95% CI 36 -50%) Presenting visual acuity ≤ 20/40: 72% (95% CI 66-78%) Question-naire with visual acuity as 2nd screening: 79% (95% CI 73-85%)	NR	Screening questionnaire Presenting distance visual acuity, followed by pinhole visual acuity if worse than 20/30	Poor-Fair
Woods et al, 1998[81] *Screening for ophthalmic disease in older subjects using visual acuity and contrast sensitivity*	Distance visual acuity <6/9: 74% Near visual acuity <6/9: 77%	Distance visual acuity <6/9: 87% Near visual acuity <6/9: 68%	NR	Distance visual acuity (Snellen) Near visual acuity (Snellen)	Fair

APPENDIX C3. STUDIES OF DIAGNOSTIC TEST ACCURACY

Study, Year	Type of study	Screening test	Reference standard	Setting	Screener	Age of enrollees	N	Proportion with condition	Subjects
Cataract									
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Cross-sectional	Presenting distance visual acuity (with current distance glasses) Pinhole distance visual acuity Presenting reading acuity (with current reading glasses)	Detailed ophthal-mologic assess-ment	Eye clinic	Ophthal-mologist	49 years or older	3654	Posterior subcapsular cataract: 3.9%, cortical cataract: 19.1%, nuclear cataract: 47.0%; any eye condition: 34.50%	Population based study from the Blue mountains area west of Sydney, Australia
McMurdo et al, 1988[78] *The detection of visual disability in the elderly*	Cross-sectional	Geriatrician examination	Ophthal-mologist examination	Primary care clinic	Geria-trician	64 to 97 years	50	18% (9/50) with previously undiagnosed cataract	Patients attending a day clinic
Early ARMD									
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Cross-sectional	Presenting distance visual acuity (with current distance glasses) Pinhole distance visual acuity Presenting reading acuity (with current reading glasses)	Detailed ophthal-mologic assess-ment	Eye clinic	Ophthal-mologist	49 years or older	3654	4.50%	Population based study from the Blue mountains area west of Sydney, Australia
McMurdo et al, 1988[78] *The detection of visual disability in the elderly*	Cross-sectional	Geriatrician examination	Ophthal-mologist examination	Primary care clinic	Geria-trician	64 to 97 years	50	8% (4/50) with previously undiagnosed macular degeneration	Patients attending a day clinic

APPENDIX C3. STUDIES OF DIAGNOSTIC TEST ACCURACY

Study, Year	Sensitivity	Specificity	Area under receiver operating curve	Index text	Quality score
Cataract					
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	(Results reported for posterior subcapsular cataract, cortical cataract, and nuclear cataract, respectively) Presenting distance visual acuity: 20/30 or worse: 61%, 57%, 44%; 20/40 or worse: 41%, 33%, 25%; 20/60 or worse: 28%, 17%, 13% Pinhole distance visual acuity: 20/30 or worse: 53%, 40%, 31%; 20/40 or worse: 26%, 15%, 13%; 20/60 or worse: 20%, 10%, 8% Presenting reading acuity: 20/30 or worse: 100%, 98%, 97%; 20/40 or worse: 89%, 90%, 88%; 20/50 or worse: 63%, 65%, 57%	(Results reported for posterior subcapsular cataract, cortical cataract, and nuclear cataract, respectively) Presenting distance visual acuity: 20/30 or worse: 67%, 72%, 77%; 20/40 or worse: 83%, 86%, 90%; 20/60 or worse: 92%, 94%, 96% Pinhole distance visual acuity: 20/30 or worse: 80%, 83%, 89%; 20/40 or worse: 93%, 94%, 98%; 20/60 or worse: 96%, 96%, 99% Presenting reading acuity: 20/30 or worse: 3%, 3%, 3%; 20/40 or worse: 16%, 18%, 20%; 20/50 or worse: 53%, 57%, 59%	(Results reported for posterior subcapsular cataract, cortical cataract, and nuclear cataract, respectively) Presenting distance visual acuity: 0.67, 0.69, 0.65 Pinhole distance visual acuity: 0.68, 0.69, 0.67 Present-ing reading acuity: 0.63, 0.64, 0.61	Presenting distance visual acuity (logMAR chart) Pinhole distance visual acuity Presenting reading acuity (with current reading glasses)	Poor-Fair
McMurdo et al, 1988[78] *The detection of visual disability in the elderly*	Geriatrician examination: 100% (9/9)	Geriatrician examination: 100% (0/41)	NR	Geriatrician examination	Poor-Fair
Early ARMD					
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Presenting distance visual acuity: 20/30 or worse: 56%; 20/40 or worse: 34%; 20/60 or worse: 13% Pinhole distance visual acuity: 20/30 or worse: 45%; 20/40 or worse: 21%; 20/60 or worse: 10% Presenting reading acuity: 20/30 or worse: 99%; 20/40 or worse: 95%; 20/50 or worse: 70%	Presenting distance visual acuity: 20/30 or worse: 66%; 20/40 or worse: 82%; 20/60 or worse: 92% Pinhole distance visual acuity: 20/30 or worse: 79%; 20/40 or worse: 92%; 20/60 or worse: 95% Presenting reading acuity: 20/30 or worse: 3%; 20/40 or worse: 16%; 20/50 or worse: 53%	Presenting distance visual acuity: 0.65 Pinhole distance visual acuity: 0.64 Presenting reading acuity: 0.67	Presenting distance visual acuity (logMAR chart) Pinhole distance visual acuity Presenting reading acuity (with current reading glasses)	Poor-Fair
McMurdo et al, 1988[78] *The detection of visual disability in the elderly*	Geriatrician examination: 75% (3/4)	Geriatrician examination: 100% (0/46)	NR	Geriatrician examination	Poor-Fair

APPENDIX C3. STUDIES OF DIAGNOSTIC TEST ACCURACY

Study, Year	Type of study	Screening test	Reference standard	Setting	Screener	Age of enrollees	N	Proportion with condition	Subjects
Refractive error									
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Cross-sectional	Presenting distance visual acuity (with current distance glasses)	Corrected visual acuity	Unclear	Ophthal-mologist	49 years or older	3654	4.50%	Population based study from the Blue mountains area west of Sydney, Australia
Visual loss or visual acuity impairment									
Eekhof et al, 2000[75] *Screening for hearing and visual loss among elderly with questionnaires and tests: which method is the most convincing for action?*	Cross-sectional	Screening questions ("Are you able to recognize a face from a distance of 4 m" and "Are you able to read normal newspaper letters")	Snellen chart and low vision chart (testing vision at reading distance)	Primary care clinics	Primary care provider	75 years or older	1121	Snellen chart <0.3: 10.8%	Patients 75 years and older at 12 general practice clinics in the Netherlands
Hiller et al, 1983[76] *Validity of a survey question as a measure of visual acuity impairment*	Cross-sectional	Screening question ("Do you have trouble with your vision even when wearing glasses or contact lenses?")	Snellen chart	mobile eye exam clinic	Ophthal-mologist	25 to 74 years (sub-group results for 65 to 74 years)	3997 (1,466 - 65 to 74 years old)	Snellen 20/25 or worse: 69%	Patients enrolled in population-based sample of community-dwelling adults in the U.S. who reported ever wearing glasses or contact lenses
Teh et al, 2006[79] *Utility of a patient-response screening question for visual impairment*	Cross-sectional	Screening question ("Do you have a problem with vision that affects your everyday life?")	Snellen chart	Geriatric assess-ment clinic	Unclear	60 years or older	112	Snellen 6/12 or worse: 81%	Patients 60 and older in a geriatric assessment clinic in Singapore

Abbreviations: ARMD = age-related macular degeneration; CI = confidence interval.

APPENDIX C3. STUDIES OF DIAGNOSTIC TEST ACCURACY

Study, Year	Sensitivity	Specificity	Area under receiver operating curve	Index text	Quality score
Refractive error					
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Presenting distance visual acuity: 20/30 or worse: 82%; 20/40 or worse: 49%; 20/60 or worse: 22%	Presenting distance visual acuity: 20/30 or worse: 78%; 20/40 or worse: 89%; 20/60 or worse: 94%	Presenting distance visual acuity: 0.88 Pinhole visual acuity: 0.62 Presenting reading acuity: 0.60	Presenting distance visual acuity (logMAR chart) Pinhole distance visual acuity Presenting reading acuity (with current reading glasses)	Poor-Fair
Visual loss or visual acuity impairment					
Eekhof et al, 2000[75] *Screening for hearing and visual loss among elderly with questionnaires and tests: which method is the most convincing for action?*	"Are you able to recognize a face from a distance of 4 m": 60% (73/122) "Are you able to read normal newspaper letters": 83% (123/149)	"Are you able to recognize a face from a distance of 4 m": 81% (814/999) "Are you able to read normal newspaper letters": 67% (643/965)	NR	Screening questions	Fair
Hiller et al, 1983[76] *Validity of a survey question as a measure of visual acuity impairment*	"Trouble seeing": 22% (224/1012) for visual acuity 20/25 or worse, 34% (74/216) for 20/50 or worse, 48% (21/44) for 20/100 or worse	"Trouble seeing": 89% (409/454) for visual acuity 20/25 or worse, 84% (1051/1250) for 20/50 or worse, 82% (1170/1422) for 20/100 or worse	NR	Screening question	Fair
Teh et al, 2006[79] *Utility of a patient-response screening question for visual impairment*	"Do you have a problem with vision that affects your everyday life?": 68% (62/91)	"Do you have a problem with vision that affects your everyday life?": 43% (9/21)	NR	Screening question	Poor-fair

APPENDIX C4. QUALITY RATINGS, STUDIES OF DIAGNOSTIC TEST ACCURACY

Study, Year	Appropriate spectrum of patients	Adequate sample size (>500)	Credible reference standard used	Reference standard applied to all patients	Screening test adequately described	Reference standard interpreted independently	Quality score
Ariyasu et al, 1996[74] *Sensitivity, specificity, and predictive values of screening tests for eye conditions in a clinic-based population*	Can't tell	No	Yes	Can't tell	Yes	No	Poor-Fair
Eekhof et al, 2000[75] *Screening for hearing and visual loss among elderly with questionnaires and tests: which method is the most convincing for action?*	Can't tell	Yes	Yes	Yes	Yes	Can't tell	Fair
Hiller et al, 1983[76] *Validity of a survey question as a measure of visual acuity impairment*	Yes	Yes	Yes	Can't tell	Yes	Can't tell	Fair
Ivers et al, 2001[77] *Sensitivity and specificity of tests to detect eye disease in an older population*	Can't tell	Yes	Yes	Can't tell	Yes	Can't tell	Poor-Fair
McMurdo et al, 1988[78] *The detection of visual disability in the elderly*	Can't tell	No	Yes	Yes	Yes	Yes	Fair
Teh et al, 2006[79] *Utility of a patient-response screening question for visual impairment*	Can't tell	No	Yes	Can't tell	Yes	Can't tell	Poor-Fair
Wang et al, 1998[80] *Evaluation of screening schemes for eye disease in a primary care setting*	Can't tell	No	Yes	No	Yes	Can't tell	Poor
Woods et al, 1998[81] *Screening for ophthalmic disease in older subjects using visual acuity and contrast sensitivity*	Can't tell	Yes	Yes	No	Yes	Can't tell	Poor-Fair

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Purpose of study	Study design	Inclusion criteria
ARMD (Dry)			
AREDS Research Group, 2001[114] *A randomized, placebo-controlled clinical trial of high-dose supplementation with vitamins C and E, beta carotene and zinc for age-related macular degeneration and vision loss: AREDS Report No. 8*	To evaluate the effect of high-dose vitamins C and E, beta carotene and zinc supplements on AMD progression and visual acuity	Placebo-controlled trial	BCVA 20/32 or better in at least one eye; at least 1 eye free from eye disease that could complicate assessment of ARMD, lens opacity progression or VA
Feher et al, 2005[124] *Improvement of visual functions and fundus alterations in early age-related macular degeneration treated with a combination of acetyl-L-carnitine, n-3 fatty acids and coenzyme Q10*	To determine how a combination of acetyl-L-carnitine, n-3 fatty acids and coenzyme Q10 influenced visual function in patients with early ARMD	Placebo-controlled trial	Age 55-70 years; diagnosis of early bilateral ARMD; visual acuity between 8/10 and 4/10 (Snellen decimal scale); agree to discontinue current vitamin regimen; be highly motivated, alert, oriented, mentally competent and able to understand and comply with the requirements of the study
Kaiser et al, 1995[123] *Visaline in the treatment of age-related macular degeneration*	To assess the effect of a multivitamin supplement on ARMD progression	Double-blind, placebo-controlled RCT	Age >50years who had previously consulted an ophthalmologist for 'nonserous' ARMD; BCVA 20/100 to 20/25
Newsome et al, 1988[118] *Oral zinc in macular degeneration*	To assess the effect of zinc on ARMD progression	Double-blind, placebo-controlled RCT	Presence of ARMD evidence by ophthalmoscopically visible drusen with varying degrees of pigmentary change; VA in at least one eye 20/80 or better

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Exclusion criteria	Number screened/ eligible/ enrolled
ARMD (Dry)		
AREDS Research Group, 2001[114] *A randomized, placebo-controlled clinical trial of high-dose supplementation with vitamins C and E, beta carotene and zinc for age-related macular degeneration and vision loss: AREDS Report No. 8*	Previous ocular surgery on disease-free eye; illness or disorders that would make long-term follow-up or compliance with study protocol unlikely or difficult	NR/4754/3640
Feher et al, 2005[124] *Improvement of visual functions and fundus alterations in early age-related macular degeneration treated with a combination of acetyl-L-carnitine, n-3 fatty acids and coenzyme Q10*	Diagnosis of late ARMD; exudative retinal disease; clinically significant corneal opacity or cataracts; inherited retinal dystrophies or degenerative myopia; unstable glaucoma; PVR, rhegmatogenous retinal detachment; optic nerve disease; active intraocular inflammatory disease; refractive error >+4 diopters and -6 diopters; significant cardiovascular or cerebrovascular diseases; severe or uncontrolled hepatic, renal, pulmonary and thyearoid disease or diabetes; history of HIV infection, hepatitis B or C or other immunosuppressive disorders; history of alcoholism, drug abuse or severe mental disorders; Practicing vegetarian or had an abnormal diet (<1600 or >3500 kcal/day); poor general health or unstable diseases; known or suggested hypersensitivity to study compounds; use of corticosteroid, phenothiazine and antimalarial drugs within 1 month of study and during 12-month study period	NR/NR/106
Kaiser et al, 1995[123] *Visaline in the treatment of age-related macular degeneration*	Presence of 'serous' ARMD; diabetes mellitus; endocrine problems; cardiac dysrhythmia; status following cardiac infarction; uncontrolled hypotension; presence of other ocular diseases	NR/NR/20
Newsome et al, 1988[118] *Oral zinc in macular degeneration*	Presence of serious eye disease or cataract judged to be clinically sufficient to reduce vision more than one line; diabetes mellitus or other know systemic or metabolic disease; congenital condition that might interfere with the interpretation of results	NR/NR/174

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Subject age, gender, diagnosis	Country & setting	Sponsor	Measures
ARMD (Dry)				
AREDS Research Group, 2001[114] *A randomized, placebo-controlled clinical trial of high-dose supplementation with vitamins C and E, beta carotene and zinc for age-related macular degeneration and vision loss: AREDS Report No. 8*	Median age 56 years 56% female 96% White; 3% Black; <1% other Mean BCVA at baseline better than 20/32 for all participants	US; multicenter	National Eye Institute, National Institutes of Health, Bausch and Lomb	Primary outcome: progression to advanced ARMD Secondary outcomes: loss of VA, development of wet ARMD
Feher et al, 2005[124] *Improvement of visual functions and fundus alterations in early age-related macular degeneration treated with a combination of acetyl-L-carnitine, n-3 fatty acids and coenzyme Q10*	Mean age 63.2 years (SD 2.70) 67% female Diagnosis - inclusion criteria specified early ARMD	Hungary; single-center, ophthalmology clinic	NR	Primary outcome: visual field mean defect Secondary outcomes: visual acuity (Snellen and ETDRS charts; logMAR); foveal sensitivity; changes in fundus alteration
Kaiser et al, 1995[123] *Visaline in the treatment of age-related macular degeneration*	Mean age 72 years 65% female Mean far VA 0.57	Switzerland; single center, clinic	NR	Change in visual acuity
Newsome et al, 1988[118] *Oral zinc in macular degeneration*	Mean age 67.9 years 65% female 32% VA >20/25	United States; setting NR	Utah State University; Mary Katherine Peterson Foundation	Change in visual acuity

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Intervention	Results
ARMD (Dry)		
AREDS Research Group, 2001[114] *A randomized, placebo-controlled clinical trial of high-dose supplementation with vitamins C and E, beta carotene and zinc for age-related macular degeneration and vision loss: AREDS Report No. 8*	Antioxidant multivitamin - 500 mg vitamin C+400 IU vitamin E+5 mg beta carotene/day zinc 80mg/day antioxidant multivitamin + zinc placebo	Progression to advanced ARMD: antioxidants vs placebo: OR 0.77 (0.56 to 1.05; p=0.03) zinc vs placebo: OR 0.71 (0.51 to 0.98; p=0.005) antioxidants + zinc vs placebo: OR 0.68 (0.49 to 0.93; p=0.002) Loss of ≥3 lines of VA: antioxidants vs placebo: OR 0.87 (0.67 to 1.15; p=0.20) zinc vs placebo: OR 0.82 (0.63 to 1.08; p=0.07) antioxidants + zinc vs placebo: OR 0.77 (0.58 to 1.03; p=0.02) ORs adjusted for age, sex, race, baseline ARMD category and smoking status
Feher et al, 2005[124] *Improvement of visual functions and fundus alterations in early age-related macular degeneration treated with a combination of acetyl-L-carnitine, n-3 fatty acids and coenzyme Q10*	100mg ALC + 530mg n-3 fatty acids + 10mg CoQ10 2x/day placebo (soy oil) 2x/day	Visual acuity in most affected eye (secondary outcome): mean change from baseline at 12 months (Snellen chart) patients 'improved or unchanged': 77% (37/48) treatment vs. 55% (29/53) placebo patients 'deteriorated': 23% (11/48) vs. 44% (24/53) NSD in less affected eyes
Kaiser et al, 1995[123] *Visaline in the treatment of age-related macular degeneration*	1.5mg buphenine HCl, 10mg beta carotene, 10mg tocopherol acetate, 50mg ascorbic acid 2 tablets, 2x/day placebo	Change in mean far VA: multivitamin 0.07 (SD 0.05) vs placebo 0.05 (SD 0.07); p=NS
Newsome et al, 1988[118] *Oral zinc in macular degeneration*	zinc 100mg bid placebo	Proportion of patients with loss of 3 lines or more: zinc 6/80 (7.5%) vs placebo 11/71 (15.5%) Change in VA (letters lost): zinc -4.1 vs placebo -7.1

Study, Year, Title	Duration of follow-up	Loss to follow-up	Adverse events & withdrawals due to adverse effects	Quality score	Comments
ARMD (Dry)					
AREDS Research Group, 2001[114] *A randomized, placebo-controlled clinical trial of high-dose supplementation with vitamins C and E, beta carotene and zinc for age-related macular degeneration and vision loss: AREDS Report No. 8*	mean 6.3 years	692/3640 (6 year data): 19%	Hospitalizations (due to infection) antioxidants vs no antioxidants: 29/1823 (1.6%) vs 15/1798 (0.8%); p<0.05 Hospitalizations (due to genitourinary cause) zinc vs no zinc: 134.1783 (7.5%) vs 90/1838 (4.9%); p<0.01	Good	
Feher et al, 2005[124] *Improvement of visual functions and fundus alterations in early age-related macular degeneration treated with a combination of acetyl-L-carnitine, n-3 fatty acids and coenzyme Q10*	12 months	NR; withdrawals 5/101 (5%)	AEs not reported; 3 withdrawals dues to AEs (2 treated group; 1 placebo group)	Fair	
Kaiser et al, 1995[123] *Visaline in the treatment of age-related macular degeneration*	6 months	NR	NR	Fair	
Newsome et al, 1988[118] *Oral zinc in macular degeneration*	24 months	23/174 (13.2%)	NR	Fair	

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Purpose of study	Study design	Inclusion criteria
Richer, 1996[120] ARMD Study Group *Multicenter ophthalmic and nutritional age-related macular degeneration study - part 2: antioxidant intervention and conclusions*	To assess the effect of a broad-spectrum antioxidant supplement on ARMD	Double-blind PCT	Previous loss of at least 1 line of VA attributable to ARMD
Richer et al, 2004[121] *Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study*	To determine whether nutritional supplementation with lutein or lutein together with antioxidants, vitamins and minerals improves visual function and symptoms in atrophic ARMD	Double-blind, placebo-controlled RCT	Diagnosis of atrophic ARMD and at least one vision-degrading visual-psychosocial abnormality associated with ARMD in one or both eyes; clear non-lenticular ocular media, free of advanced glaucoma and diabetes or any other ocular or systemic disease that could affect central or parafoveal macular visual function
Stur et al, 1996[122] *Oral zinc and the second eye in age-related macular degeneration*	To investigate the short-term effect of oral zinc substitution on the development of age-related macular degeneration in the second eye with exudative ARMD in the first eye	Double-blind, placebo-controlled RCT	Age >50 years with exudative ARMD in one eye with no evidence on exudative ARMD and VA 20/40 or better in second eye

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Exclusion criteria	Number screened/ eligible/ enrolled
Richer, 1996[120] ARMD Study Group *Multicenter ophthalmic and nutritional age-related macular degeneration study - part 2: antioxidant intervention and conclusions*	Confounding ocular or systemic disease with ocular manifestations	NR/NR/71
Richer et al, 2004[121] *Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study*	Recent (within 6 months) cataract or retinal surgery, use of photosensitizing drugs or did not meet ophthalmic/visual entrance criteria; previous (within 6 months) use of lutein supplements	109/NR/90
Stur et al, 1996[122] *Oral zinc and the second eye in age-related macular degeneration*	Dense senile cataract and/or any other eye disease that could produce significant and permanent loss of VA during the follow up period; physical status preventive of required follow-up examinations; history of serious systemic or metabolic disease	NR/NR/112

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Subject age, gender, diagnosis	Country & setting	Sponsor	Measures
Richer, 1996[120] ARMD Study Group *Multicenter ophthalmic and nutritional age-related macular degeneration study - part 2: antioxidant intervention and conclusions*	Mean age 72 years 7% female Mean far VA (LogMAR, right eyes) 0.26	United States; multiple VA eye clinics	US Department of Veteran Affairs; Twin Laboratories; Stereo Optical; Eye Communications Inc; Illinois College of Optometry; Pacific University College of Optometry; Ezell Foundation	Change in visual acuity
Richer et al, 2004[121] *Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study*	Mean age 73 years 4% female Mean VA (right eye, LogMAR) 0.377	United States; vision clinic	Department of Veteran Affairs	Change in visual acuity
Stur et al, 1996[122] *Oral zinc and the second eye in age-related macular degeneration*	Mean age 71.5 years 57% female Mean VA (LogMAR) 0.0745	Austria; single outpatient clinic	NR	Change in visual acuity

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Intervention	Results
Richer, 1996[120] ARMD Study Group *Multicenter ophthalmic and nutritional age-related macular degeneration study - part 2: antioxidant intervention and conclusions*	Antioxidant multivitamin (beta carotene 20,000 IU, vitamin E 200 IU, vitamin C 750 mg, citrus bioflavonoid complex 125 mg, quercitin (bioflavonoid) 50 mg, bilberry extract (bioflavonoid) 5 mg, rutin (bioflavonoid) 50 mg, zinc picolinate 12.5 mg, selenium 50 mcg, taurine 100 mg, n-acetyl cysteine 100mg, l-glutathione 5 mg, vitamin B2 25 mg, chromium 100 mcg) qd placebo	Mean visual acuity at 18 months (Log MAR): antioxidant 0.33 (SE 0.07) vs placebo 0.29 (SE 0.05)
Richer et al, 2004[121] *Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study*	10mg lutein, with or without additional multivitamin	Change in Snellen letter equivalent: lutein alone +5.4 letters vs lutein/multivitamin +3.5 letters vs placebo -2.1 letters Change in visual acuity: lutein alone -0.10 vs lutein+multivitamin -0.03 vs placebo -0.14
Stur et al, 1996[122] *Oral zinc and the second eye in age-related macular degeneration*	200mg zinc sulfate placebo	Change in VA at 24 months: zinc -0.013 (SD 0.01) vs placebo -0.024 (SD 0.01); p=0.52

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Duration of follow-up	Loss to follow-up	Adverse events & withdrawals due to adverse effects	Quality score	Comments
Richer, 1996[120] ARMD Study Group *Multicenter ophthalmic and nutritional age-related macular degeneration study - part 2: antioxidant intervention and conclusions*	18 months	59/71 enrolled pts still in study at 18 months	Withdrawals due to AEs: antioxidant 1/35 (2.9%) vs placebo 0/24 (0%)	Fair	
Richer et al, 2004[121] *Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study*	12 months	4/90 (4%)	No significant between-group differences, no further data provided Cardiac AEs trended lower in the lutein+multivitamin group vs the other group combined	Fair	
Stur et al, 1996[122] *Oral zinc and the second eye in age-related macular degeneration*	2 years	14/112 (12.5%)	Withdrawals due to AEs: zinc 6/56 (10.7%) vs placebo 2/56 (3.8%) Neovascularization: zinc 9/56 (16.1%) vs placebo 5/56 (8.9%)	Fair	

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Purpose of study	Study design	Inclusion criteria
ARMD (Wet)			
Laser photocoagulation			
Macular Photocoagulation Study Group, 1982[128] *Argon laser photocoagulation for senile macular degeneration*	To determine if argon laser photocoagulation is useful in preventing severe vision loss in eyes with evidence of macular degeneration	RCT; blinding unclear	Age ≥50 years; presence of drusen; angiographic evidence of choroidal neovascular membrane; BCVA 20/100 or better; symptoms related to neovascular membrane; no prior photocoagulation in study eye; no other ocular disease that could affect VA; ability to provide informed consent
Macular Photocoagulation Study Group, 1990[129] *Krypton laser photocoagulation for neovascular lesions of age-related macular degeneration*	To determine whether krypton laser photocoagulation would be of benefit in preventing visual acuity loss in eyes with ARMD	RCT; blinding unclear	Age ≥50 years; presence of drusen in the macula of at least one eye; BCVA 20/4000
Macular Photocoagulation Study Group, 1991[130] *Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration*	To determine the effect of laser photocoagulation of subfoveal neovascularization in eyes with ARMD but without previous photocoagulation of the macula	RCT; blinding unclear	Age ≥50 years; documented presence of leaking choroidal neovascular lesion under geometric center of foveal avascular zone (FAZ) or within 150 µm of center contiguous w scar from earlier treatment of choroidal neo-vascularization; no prior laser treatment to FAZ center; size of neo-vascular lesion and old treatment scar such that portion of the retina within 1 disc diameter of FAZ center would remain untreated and old and new treated area would not exceed 6 disc areas; BCVA 20/40 to 20/320; no other ocular disease that could compromise VA; no current or past use of systemic steroids; ability to return for follow-up and provide informed consent

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Exclusion criteria	Number screened/ eligible/ enrolled
ARMD (Wet)		
Laser photocoagulation		
Macular Photocoagulation Study Group, 1982[128] *Argon laser photocoagulation for senile macular degeneration*	NR	NR/NR/224
Macular Photocoagulation Study Group, 1990[129] *Krypton laser photocoagulation for neovascular lesions of age-related macular degeneration*	NR	NR/NR/496
Macular Photocoagulation Study Group, 1991[130] *Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration*	NR	NR/NR/373

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Subject age, gender, diagnosis	Country & setting	Sponsor	Measures
ARMD (Wet)				
Laser photocoagulation				
Macular Photocoagulation Study Group, 1982[128] *Argon laser photocoagulation for senile macular degeneration*	Mean age not reported: 52/224 age 50-64; 104/224 (46%) age 65-75; 68/224 (30%) age >75 years 51% female BCVA 20/32 or better: 105/224	United States; 12 ophthalmology clinics	National Eye Institute; National Institutes of Health	Change in visual acuity
Macular Photocoagulation Study Group, 1990[129] *Krypton laser photocoagulation for neovascular lesions of age-related macular degeneration*	Mean age not reported: 26/496 (5%) age 50-59 years; 147/496 (29%) age 60-69 years; 240/496 (48%) age 70-79 years; 83/497 (17%) age ≥80 years 53% female BCVA 20/40 or better: 157/496 (32%) Median length of follow-up: 48 months	United States; 13 ophthalmology clinics	National Eye Institute; National Institutes of Health	Change in visual acuity
Macular Photocoagulation Study Group, 1991[130] *Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration*	Mean age not reported: 16/373 (4%) age 50-59 years; 80/373 (21%) age 60-69 years; 186/373 (50%) age 70-79 years; 91/373 (24%) age ≥80 years 56% female BCVA 20/20 or better: 106/373 (28%); 20/25-20/100: 190/373 (51%); 20/250 or worse: 76/373 (20%)	United States; 13 ophthalmology clinics	National Eye Institute; National Institutes of Health	Change in visual acuity

Study, Year, Title	Intervention	Results
ARMD (Wet)		
Laser photocoagulation		
Macular Photocoagulation Study Group, 1982[128] *Argon laser photocoagulation for senile macular degeneration*	laser photocoagulation vs no treatment	Increase in lines of VA or no change from baseline at 18 months: treatment group 61/100 (61.0%) vs no-treatment group 30/98 (30.6%) Loss of 2-5 lines of VA at 18 months: treatment group 23/100 (23.0%) vs no-treatment group 16/98 (16.3%) Loss of 6-9 lines of VA at 18 months: treatment group 8/100 (8.0%) vs no-treatment group 24/98 (24.5%) Loss of 10 or more lines of VA at 18 months: treatment group 8/100 (8.0%) vs no-treatment group 16/98 (16.3%)
Macular Photocoagulation Study Group, 1990[129] *Krypton laser photocoagulation for neovascular lesions of age-related macular degeneration*	laser photocoagulation vs no treatment	Increase in lines of VA or no change from baseline at 36 months: treatment group 47/174 (27.0%) vs no-treatment group 29/169 (17.2%) Loss of 2-5 lines of VA at 36 months: treatment group 41/174 (23.6%) vs no-treatment group 42/169 (24.9%) Loss of 6-9 lines of VA at 36 months: treatment group 55/174 (31.6%) vs no-treatment group 54/169 (32.0%) Loss of 10 or more lines of VA at 36 months: treatment group 31/174 (17.8%) vs no-treatment group 44/169(26.0%)
Macular Photocoagulation Study Group, 1991[130] *Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration*	laser photocoagulation vs no treatment	Loss of <2 lines of VA at 24 months: treatment group 37/114 (32.5%) vs no-treatment group 20/112 (17.9%) Loss of 2-3 lines of VA at 24 months: treatment group 27/114 (23.7%) vs no-treatment group 20/112 (17.9%) Loss of 4-5 lines of VA at 24 months: treatment group 27/114 (23.7%) vs no-treatment group 31/112 (27.7%) Loss of ≥6 lines of VA at 24 months: treatment group 23/114 (20.2%) vs no-treatment group 41/112 (36.6%)

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Duration of follow-up	Loss to follow-up	Adverse events & withdrawals due to adverse effects	Quality score	Comments
ARMD (Wet)					
Laser photocoagulation					
Macular Photocoagulation Study Group, 1982[128] *Argon laser photocoagulation for senile macular degeneration*	2 years	Authors state no pts lost to follow-up; however 20/224 were still being followed at 2 years (study endpoint)	Withdrawals: 119/224 (53%) at 1 year	Poor	
Macular Photocoagulation Study Group, 1990[129] *Krypton laser photocoagulation for neovascular lesions of age-related macular degeneration*	3 years; mean length of follow up 48 mos	150/494 were still being followed at 3 years (study endpoint)	Withdrawals: 259/496 (52%) at 2 years (median follow-up) AEs reported in treated group only Treatment beyond center of avascular zone: 46/247 (18.6%) Increased hemorrhage: 22/247 (8.9%) Perforation of Bruch's mem-brane: 9/247 (3.6%) Retrobulbar hemorrhage: 4/247 (1.6%) Retinal pigment epithelium rip: 3/247 (1.2%)	Poor	
Macular Photocoagulation Study Group, 1991[130] *Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration*	2 years	6/192 were still being followed at 2 years	AEs reported in treated group only New hemorrhage: 48/184 (26%) Retinal or vitreous hemorrhage identified during treatment: 6/184 (3.3%) Perforation of Bruch's membrane: 4/184 (2.2%) Retinal hole, retinal pigment epithelium rip, retrobulbar hemorrhage all <1%	Poor	

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Purpose of study	Study design	Inclusion criteria
Macular Photocoagulation Study Group, 1991[131] *Laser photocoagulation of subfoveal recurrent neovascular lesions in age-related macular degeneration*	To determine the effect on vision of laser treatment of subfoveal neovascular lesions compared with no treatment	RCT; blinding unclear	Age ≥50 years; documented presence of leaking choroidal neovascular lesion with well-demarcated boundaries no larger that 3.5 standard disc areas; new vessels under the geometric center of foveal avascular zone; BCVA 20/40 to 20/320; no prior photocoagulation in macula of study eye; no other eye disease that could compromise VA; no current or past use of systemic steroids; ability to return for 5 years of follow-up and provide informed consent
Moorfields et al, 1982[132] *Treatment of senile disciform macular degeneration: a single-blind randomized trial by argon laser photocoagulation*	To determine the effects of argon laser photo-coagulation in the treatment of neovascular disciform macular de-generation in the elderly	RCT	Age 50-80 years; presence of vascular disciform lesion with a well-defined neovascular membrane, with edges between 100 and 1500 µm from the center of the fovea; detachment of the sensory retina with associated visual symptoms; presence of drusen in the affected and fellow eye
Photodynamic therapy			
TAP Study Group, 1999[135] *Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration: one-year results of 2 randomized clinical trials - TAP Report 1 (TAP)* Other publications: Kaiser, 2006, TAP and VIP Report 3	To determine if photodynamic therapy with verteporfin can safely reduce the risk of vision loss in patients with subfoveal choroidal neo-vascularization	Double-blind, placebo-controlled RCT	Age ≥50 years; choroidal neovascularization secondary (CNV) to ARMD; CNV under the geometric center of the foveal avascular zone; evidence of classic CNV; area of CNV at least 50% of the area of the total neovascular lesion; greatest linear dimension of lesion ≤5400 µm; BC TAP protocol VA 73-34 letters; willing and able to provide informed consent

Study, Year, Title	Exclusion criteria		Number screened/ eligible/ enrolled
Macular Photocoagulation Study Group, 1991[131] *Laser photocoagulation of subfoveal recurrent neovascular lesions in age-related macular degeneration*		NR	NR/NR/206
Moorfields et al, 1982[132] *Treatment of senile disciform macular degeneration: a single-blind randomized trial by argon laser photocoagulation*	Presence of subretinal exudates or hemorrhages precluding an adequate view of the subretinal structures and new vessel membrane; disease preventing adequate fundus examination and laser photocoagulation; other diseases associated with visual loss; previous photocoagulation in the eye under consideration; myopia of greater than 3 diopters; inability or unwillingness to provide informed consent		NR/NR/128
Photodynamic therapy			
TAP Study Group, 1999[135] *Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration: one-year results of 2 randomized clinical trials - TAP Report 1 (TAP)* Other publications: Kaiser, 2006, TAP and VIP Report 3	Tear of retinal pigment epithelium; any significant ocular disease that has or could compromise vision in the study eye and confound analysis of the primary outcome; inability to obtain photographs to document CNV, including difficulty with venous access; history of treatment for CNV in study eye other than nonfoveal confluent laser photocoagulation; participation in another ophthalmic clinical trial or use of any other investigational drugs within 12 weeks prior to the start of study treatment; active hepatitis or clinically significant liver disease; porphyearia or porohyearin sensitivity; prior photodynamic therapy for CNV; intraocular surgery within 2 months of study entry or capsulotomy within 1 month in study eye		NR/NR/609

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Subject age, gender, diagnosis	Country & setting	Sponsor	Measures
Macular Photocoagulation Study Group, 1991[131] *Laser photocoagulation of subfoveal recurrent neovascular lesions in age-related macular degeneration*	Mean age not reported: 4/206 (2%) age 50-59 years; 57/206 (28%) age 60-69 years; 112/206 (54%) age 70-79 years; 33/206 (16%) age ≥80 years 52% female BCVA 20/20 or better: 70/206(34%); 20/25-20/100: 73/206 (35%); 20/250 or worse: 63/206 (31%)	United States; 13 ophthalmology clinics	National Eye Institute; National Institutes of Health	Change in visual acuity
Moorfields et al, 1982[132] *Treatment of senile disciform macular degeneration: a single-blind randomized trial by argon laser photocoagulation*	Baseline characteristics not reported Inclusion criteria required age 50-80 years; no description of BCVA at baseline	UK; setting NR	National Institutes of Health	Change in visual acuity
Photodynamic therapy				
TAP Study Group, 1999[135] *Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration: one-year results of 2 randomized clinical trials - TAP Report 1 (TAP)* Other publications: Kaiser, 2006, TAP and VIP Report 3	Mean age 75.3 years 56% female 98% White, 2% other Mean BCVA: 20/80-2 89% subfoveal lesion(s)	United States and Europe; 22 ophthalmology clinics	QLT PhotoTherapeutics Inc; CIBA Vision, Bulach Switzerland	Loss of letters of VA

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Intervention	Results
Macular Photocoagulation Study Group, 1991[131] *Laser photocoagulation of subfoveal recurrent neovascular lesions in age-related macular degeneration*	laser photocoagulation vs no treatment	Loss of <2 lines of VA at 24 months: treatment group 10/35 (28.6%) vs no-treatment group 15/46 (32.6%) Loss of 2-3 lines of VA at 24 months: treatment group 10/35 (28.6%) vs no-treatment group 10/46 (21.7%) Loss of 4-5 lines of VA at 24 months: treatment group 12/35 (34.3%) vs no-treatment group 8/46 (17.4%) Loss of ≥6 lines of VA at 24 months: treatment group 3/35 (8.6%) vs no-treatment group 13/46 (28.3%)
Moorfields et al, 1982[132] *Treatment of senile disciform macular degeneration: a single-blind randomized trial by argon laser photocoagulation*	laser photocoagulation vs no treatment	Loss of <2 lines of VA at 24 months: treatment group 3/51 (5.9%) vs no-treatment group 3/50 (6.0%) Loss of 2-3 lines of VA at 24 months: treatment group 11/51(21.6%) vs no-treatment group 10/50 (20.0%) Loss of 4-5 lines of VA at 24 months: treatment group 14/51 (27.4%) vs no-treatment group 16/50 (32.0%) Loss of ≥6 or more lines of VA at 24 months: treatment group 9/51 (17.6%) vs no-treatment group 14/50 (28%)
Photodynamic therapy		
TAP Study Group, 1999[135] *Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration: one-year results of 2 randomized clinical trials - TAP Report 1 (TAP)* Other publications: Kaiser, 2006, TAP and VIP Report 3	verteporfin or placebo IV + photodynamic therapy	Loss of ≥6 lines of VA at 12 months: verteporfin 59/402 (14.7%) vs placebo 49/207 (23.7%); RR 0.62 (CI 0.44 to 0.87) Loss of ≥3 lines of VA at 12 months: verteporfin 156/402 (38.8%) vs placebo 111/207 (53.6%); RR 0.72 (CI 0.61 to 0.86)

Study, Year, Title	Duration of follow-up	Loss to follow-up	Adverse events & withdrawals due to adverse effects	Quality score	Comments
Macular Photocoagulation Study Group, 1991[131] *Laser photocoagulation of subfoveal recurrent neovascular lesions in age-related macular degeneration*	2 years	35/370 were still being followed at 2 years	AEs reported in treated group only New hemorrhage: 30/97 (26%) Retinal or vitreous hemorrhage identified during treatment: 6/97 (3.3%) Perforation of Bruch's membrane: 2/97 (2.2%) Retinal pigment epithelium rip: 2/97 (2.1%)	Poor	
Moorfields et al, 1982[132] *Treatment of senile disciform macular degeneration: a single-blind randomized trial by argon laser photocoagulation*	2 years	27/128 (21%)	Withdrawals: 27/128 (21%)	Poor	
Photodynamic therapy					
TAP Study Group, 1999[135] *Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration: one-year results of 2 randomized clinical trials - TAP Report 1 (TAP)* Other publications: Kaiser, 2006, TAP and VIP Report 3	1 year	36/609 (5.9%)	Acute severe loss of VA: verteporfin 3/402 (0.7%) vs placebo 0/207 (0%) Infusion-related back pain: verteporfin 9/402 (2.2%) vs placebo 0/207 (0%)	Good	

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Purpose of study	Study design	Inclusion criteria
VIM Study Group, 2005[171] *Verteporfin therapy of subfoveal minimally classic choroidal neovascularization in age-related macular degeneration (VIM)*	To compare the treatment effect and safety of photodynamic therapy w verteporfin using a standard or re-duced light fluence rate to placebo in patients w subfoveal minimally classic choroidal neo-vascularization with ARMD	Double-blind, placebo-controlled RCT	BCVA of at least 30 (TAP protocol) for lesions of 4 MPS disc areas or less and of 30 to 65 for lesions 4-5 MPS disc areas; evidence of CNV due to ARMD in which at least 50% of the lesion was CNV; fluorescent pattern of some classic CNV that was less than 50% of the entire area of the lesion
VIP Study Group, 2001[170] *Verteporfin therapy of subfoveal choroidal neovascularization: two-year results of a randomized clinical trial including lesions with occult with no classic choroidal neovascularization - Verteporfin in Photodynamic Therapy Report 2 (VIP)*	To determine if photodynamic therapy with verteporfin can safely reduce the risk of vision loss compared with a placebo	Double-blind, placebo-controlled RCT	Age ≥50 years; choroidal neovascularization secondary (CNV) to ARMD; CNV under the geometric center of the foveal avascular zone; evidence of classic CNV; area of CNV at least 50% of the area of the total neovascular lesion; greatest linear dimension of lesion ≤5400 µm; BC TAP protocol VA 73-34 letters; willing and able to provide informed consent

Study, Year, Title	Exclusion criteria		Number screened/ eligible/ enrolled
VIM Study Group, 2005[171] *Verteporfin therapy of subfoveal minimally classic choroidal neovascularization in age-related macular degeneration (VIM)*		NR	NR/NR/117
VIP Study Group, 2001[170] *Verteporfin therapy of subfoveal choroidal neovascularization: two-year results of a randomized clinical trial including lesions with occult with no classic choroidal neovascularization - Verteporfin in Photodynamic Therapy Report 2 (VIP)*	Features of any condition other than age-related macular degeneration associated with CNV in study eye; tear of retinal pigment epithelium; any significant ocular disease that has or could compromise vision in the study eye and confound analysis of the primary outcome; inability to obtain photographs to document CNV, including difficulty with venous access; history of treatment for CNV in study eye other than nonfoveal confluent laser photocoagulation; participation in another ophthalmic clinical trial or use of any other investigational drugs within 12 weeks prior to the start of study treatment; active hepatitis or clinically significant liver disease; porphyearia or porohyearin sensitivity; prior photodynamic therapy for CNV; intraocular surgery within 2 months of study entry or capsulotomy within 1 month in study eye		NR/NR/339

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Subject age, gender, diagnosis	Country & setting	Sponsor	Measures
VIM Study Group, 2005[171] *Verteporfin therapy of subfoveal minimally classic choroidal neovascularization in age-related macular degeneration (VIM)*	Mean age 78 years Mean BCVA: 20/80 92% subfoveal lesion(s)	United States and Europe; 19 ophthalmology clinics	QLT PhotoTherapeutics Inc; Novartis Ophthalmics AG, Bulach, Switzerland	Loss of at least 15 letters of VA at 12 months
VIP Study Group, 2001[170] *Verteporfin therapy of subfoveal choroidal neovascularization: two-year results of a randomized clinical trial including lesions with occult with no classic choroidal neovascularization - Verteporfin in Photodynamic Therapy Report 2 (VIP)*	Mean age 75 years 99% White; 1% other Mean BVCA: 20/50+1 83.4% subfoveal lesion(s)	United States and Europe; 28 ophthalmology clinics	QLT PhotoTherapeutics Inc; CIBA Vision, Bulach, Switzerland	Loss of fewer than 8 letters of VA

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Intervention	Results
VIM Study Group, 2005[171] *Verteporfin therapy of subfoveal minimally classic choroidal neovascularization in age-related macular degeneration (VIM)*	verteporfin or placebo IV + photodynamic therapy	Loss of ≥3 lines of VA at 12 months: verteporfin SF 10/36 (27.8%) vs. verteporfin RF 5/36 (13.9%) vs. placebo 18/38 (47%) Loss of ≥6 lines of VA at 12 months: verteporfin SF 3/36 (8%) vs verteporfin RF 0/36 (0%) vs. placebo 6/38 (16%) Loss of ≥3 lines of VA at 24 months: verteporfin SF 17/32 (8%) vs verteporfin RF 9/34 (26.4%) vs. placebo 18/37 (48.6%) Loss of ≥6 lines of VA at 24 months: verteporfin SF 4/32 (12.5%) vs. verteporfin RF 6/34 (17.6%) vs. placebo 13/37 (35.1%)
VIP Study Group, 2001[170] *Verteporfin therapy of subfoveal choroidal neovascularization: two-year results of a randomized clinical trial including lesions with occult with no classic choroidal neovascularization - Verteporfin in Photodynamic Therapy Report 2 (VIP)*	verteporfin or placebo IV + photodynamic therapy	Loss of ≥3 lines of VA at 12 months: verteporfin 114/225 (50.7%) vs placebo 62/114 (54.3%); RR 0.44 (CI 0.25 to 0.77)

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Duration of follow-up	Loss to follow-up	Adverse events & withdrawals due to adverse effects	Quality score	Comments
VIM Study Group, 2005[171] *Verteporfin therapy of subfoveal minimally classic choroidal neovascularization in age-related macular degeneration (VIM)*	2 years	14/117 (12.0%)	Acute severe loss of VA: verteporfin 1/77 (1.3%) vs placebo 1/40 (2.5%) Infusion-related back pain: verteporfin 9/77 (11.7%) vs placebo 1/40 (2.5%)	Good	
VIP Study Group, 2001[170] *Verteporfin therapy of subfoveal choroidal neovascularization: two-year results of a randomized clinical trial including lesions with occult with no classic choroidal neovascularization - Verteporfin in Photodynamic Therapy Report 2 (VIP)*	2 years	47/339 (13.9%)	Acute severe loss of VA: verteporfin 10/225 (4.4%) vs placebo 0/114 (0%) Infusion-related back pain: verteporfin 5/225 (2.2%) vs placebo 0/114 (0%)	Good	

Study, Year, Title	Purpose of study	Study design	Inclusion criteria
VEGF inhibitors			
Gragoudas et al, 2004[144] *Pegaptanib for neovascular age-related macular degeneration* (VISION; 2 trials) *Other publications* : VEGF Inhibitor Study Group, 2006; Leys, 2007	To test the short-term safety and effectiveness of pegaptanib	2 con-current, pro-spective double-blind RCTs	≥50 years with subfoveal sites of choroidal neovascularization secondary to ARMD and best corrected visual acuity of 20/40-20/320 in study eye and 20/800 or better in other eye
Regillo et al, 2008[143] *Randomized, double-masked, sham-controlled trial of ranibizumab for neovascular age-related macular degeneration: PIER study year 1*	To evaluate the efficacy and safety of ranibizumab	Double-blind RCT	Age≥50 years; primary or recurrent subfoveal CNV secondary to AMD, with the total CNV area (classic plus occult CNV) composing 50% of the total AMD lesion area; total AMD lesion size of 12 disk areas (DA); best-corrected VA of 20/40 to 20/320; minimally classic or occult with no classic CNV were eligible only if they met the criteria for presumed disease progression

Study, Year, Title	Exclusion criteria	Number screened/ eligible/ enrolled
VEGF inhibitors		
Gragoudas et al, 2004[144] *Pegaptanib for neovascular age-related macular degeneration* (VISION; 2 trials) *Other publications* : VEGF Inhibitor Study Group, 2006; Leys, 2007	Patients were ineligible to participate in the study if they had atrophy exceeding 25% of the total lesion area or subfoveal scarring in the study eye; history of previous subfoveal thermal laser therapy or previous or concomitant therapy with any investigational agent to treat AMD (except vitamins and minerals); other exclusion criteria were likelihood of requiring cataract surgery within 2 years; other potential causes of CNV, including myopia of 8 diopters or more or axial length of 25 mm or more, ocular histoplasmonthsis syndrome, angioid streaks, choroidal rupture, or multifocal choroiditis; any intraocular surgery within 3 months or extrafoveal/juxtafoveal laser within 2 weeks of study entry; previous posterior vitrectomy or scleral buckling surgery; and presence of retinal pigment epithelial tears or rips; diabetic retinopathy; history or evidence of severe cardiac disease; a myocardial infarction within 6 months; ventricular tachyarrhythmia requiring ongoing treatment or unstable angina; history or evidence of peripheral vascular disease; stroke within 12 months of study entry; acute ocular or periocular infection; previous therapeutic radiation to the eye, head, or neck; any treatment w	NR/NR/1208
Regillo et al, 2008[143] *Randomized, double-masked, sham-controlled trial of ranibizumab for neovascular age-related macular degeneration: PIER study year 1*	Prior treatment with PDT; external-beam radiation therapy, transpupillary thermotherapy, or subfoveal laser photocoagulation (or juxtafoveal or extrafoveal laser photocoagulation one month before day zero); permanent structural damage to the central fovea; subretinal hemorrhage involving the fovea if 1 DA or 50% of the total lesion area; prior treatment with an antiangiogenic drug or if the nonstudy eye received PDT seven days before day zero	NR/NR/184

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Subject age, gender, diagnosis	Country & setting	Sponsor	Measures
VEGF inhibitors				
Gragoudas et al, 2004[144] *Pegaptanib for neovascular age-related macular degeneration* (VISION; 2 trials) *Other publications* : VEGF Inhibitor Study Group, 2006; Leys, 2007	Mean age NR; Age range 50-64 years: 6%; 65-74 years: 32%; 75-84 years: 52%; ≥85 years: 10% 58% female 96% White; 4% Other Mean visual acuity, study eye: 51.8 letters (SD 12.8)	N. America, S. America, Europe, Israel, Australia 117 sites	Eyetech Pharmaceuticals and Pfizer	Change in visual acuity, measured by loss of <15 letters at week 54
Regillo et al, 2008[143] *Randomized, double-masked, sham-controlled trial of ranibizumab for neovascular age-related macular degeneration: PIER study year 1*	Mean age ~78 years 60% female neovascular ARMD	US 43 sites setting NR	Genentech and Novartis Pharma AG	Change in visual acuity from baseline (ETDRS)

Study, Year, Title	Intervention	Results
VEGF inhibitors		
Gragoudas et al, 2004[144] *Pegaptanib for neovascular age-related macular degeneration* (VISION; 2 trials) *Other publications* : VEGF Inhibitor Study Group, 2006; Leys, 2007	0.3mg, 1.0mg or 3.0mg pegaptanib every 6 weeks up to 48 weeks (9 txs) sham injection	Patients with loss of >3 lines of VA at 54 weeks: 0.3mg pegaptanib 88/294 (29.9%) vs. 1.0mg pegaptanib 87/300 (29.0%) vs. 3.0mg pegaptanib 103/296 (34.8%) vs. sham injection 132/296 (44.6%); All combined doses pegaptanib vs sham injection: RR 0.77 (CI 0.65 to 0.92; p=0.004)
Regillo et al, 2008[143] *Randomized, double-masked, sham-controlled trial of ranibizumab for neovascular age-related macular degeneration: PIER study year 1*	0.3mg or 0.5mg ranibizumab 1x/month for 3 months followed by every 3 months sham injection	Mean change from baseline VA at 12 months: 0.3mg -1.6 letters vs 0.5mg -0.2 letters vs sham injection -16.3 letters Loss of >3 lines of of VA at 12 months: 0.3mg 10/60 (16.7%) vs 0.5mg 6/61 (9.8%) vs sham injection 32/63 (50.8%) Gain of ≥3 lines of VA at 12 months: 0.3mg 7/60 (11.7%) vs 0.5mg 8/61 (13.1%) vs sham injection 6/63 (9.5%) Patients with VA worse than 20/200 at 12 months: 0.3mg 14/60 (23.3%) vs 0.5mg 15/61(24.6%) v sham injection 33/63 (52.4%) No statistically significant difference between groups in NEI-VFQ 25 subscale score (data not reported)

Study, Year, Title	Duration of follow-up	Loss to follow-up	Adverse events & withdrawals due to adverse effects	Quality score	Comments
VEGF inhibitors					
Gragoudas et al, 2004[144] *Pegaptanib for neovascular age-related macular degeneration* (VISION; 2 trials) *Other publications* : VEGF Inhibitor Study Group, 2006; Leys, 2007	54 weeks	NR	Withdrawals due to AEs: 1% in pegabtanib groups and 1% in sham injection groups Serious AEs: 19% in pegaptanib groups vs 15% in sham injection groups No systemic AEs; death rate 2% in all groups Endophthalmitis 0.16% pegaptanib Traumatic cataract 0.07% pegaptanib Retinal detachment 0.08% pegaptanib	Fair	1186/1208 randomized patients included in analyses; 4 post-randomization exclusions
Regillo et al, 2008[143] *Randomized, double-masked, sham-controlled trial of ranibizumab for neovascular age-related macular degeneration: PIER study year 1*	12 months	none reported; all patients accounted for	No cases of endophthalmitis, uveitis, retinal detachment or lens damage in any treatment group Ocular hemorrhage: 2/59 (3.4%) 0.3mg group vs 0/61 (0%) 0.5mg group vs 2/63 (3.2%) sham injection group Macular edema: 1/59 (1.7%) 0.3mg group vs 0/0 (0%) 0.5mg group vs 2/63 (3.2%) sham injection group Hypertension 4/59 (6.8%) 0.3mg group vs 6/61 (9.8%) 0.5mg group vs 5/63 (8.1%) sham injection group	Good	

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Purpose of study	Study design	Inclusion criteria
Rosenfeld et al, 2006[145] *MARINA Trial* *Ranibizumab for neovascular age-related macular degeneration* Other publications: Boyer 2007	To evaluate the effectiveness and safety of ranibizumab for the treatment of minimally classic or occult with no classic choroidal neovasculatization associated with ARMD	Pro-spective, double-blind RCT	Age ≥50 years; best corrected visual acuity 20/40 to 20/320 (Snellen equivalent determined with use of ETDRS chart); primary or recurrent choroidal neovascularization associated with ARMD, involving the foveal center; have a type of lesion that had been assessed with the use of fluorescein angiography and fundus photography as minimally classic or occult with no classic choroidal neovascularization; have a maximum lesion size of 12 optic-disk areas, with neovascularization composing ≥50% of the entire lesion; have presumed recent disease progression, as evidenced by observable blood, recent vision loss or a recent increase in a lesion's greatest linear diameter of >10% .
Cataract			
Chylack et al, 2002[109] *The Roche European American Cataract Trial (REACT): a randomized clinical trial to investigate the efficacy of an oral antioxidant micronutrient to slow progression of age-related cataract*	To determine if a mixture of oral antioxidants would modify progression of cataract	Double-blind placebo-controlled trial of consecutively enrolled patients	Able to provide written informed consent; able to attend for all visits; ≥ 40 years old; at least one eye met the following ocular criteria: cataract extraction unlikely within two years, immature idiopathic 'senile' cataract present in one or both eyes, U.S. patients: presence of minimal cataract by Lens Opacities Classification System [LOCS II]14 criteria, U.K. patients: presence of cataract of minimal Oxford grade; logMAR acuity ≤0.5; ocular media clear enough to capture good images of the lens; remote risk of angle closure glaucoma; pupil dilatable to 6mm; oscillatory movement displacement threshold ≤50S; no visually significant fundus pathology; no clinical signs of glaucoma and intraocular pressure; no history of amblyopia, eye surgery, argon or YAG laser eye treatment, or major eye trauma; no history of iritis, retinal crystalline deposits, or optic nerve disease; no extended (daily for >3 months) use of ocular corticosteroid or glaucoma therapy; no participation in another clinical trial investigating an anticataract formulation within the last year.

Study, Year, Title	Exclusion criteria	Number screened/ eligible/ enrolled
Rosenfeld et al, 2006[145] *MARINA Trial* *Ranibizumab for neovascular age-related macular degeneration* Other publications: Boyer 2007	Prior treatment with verteporfin photodynamic therapy, external-beam radiation therapy, or transpupillary thermotherapy in the study eye; treatment with verteporfin photodynamic therapy in the nonstudy eye less than 7 days preceding day 0; previous participation in a clinical trial (for either eye) involving antiangiogenic drugs (pegaptanib, ranibizumab, anecortave acetate, protein kinase C inhibitors, etc.); previous intravitreal drug delivery (e.g., intravitreal corticosteroid injection or device implantation) in the study eye; previous subfoveal focal laser photocoagulation in the study eye; laser photocoagulation (juxtafoveal or extrafoveal) in the study eye within 1 month preceding day 0; history of vitrectomy surgery in the study eye; history of submacular surgery or other surgical intervention for AMD in the study eye; previous participation in any studies of investigational drugs within 1 month preceding day 0 (excluding vitamins and minerals)... *continued below*	NR/NR/716
Cataract		
Chylack et al, 2002[109] *The Roche European American Cataract Trial (REACT): a randomized clinical trial to investigate the efficacy of an oral antioxidant micronutrient to slow progression of age-related cataract*	Pregnancy; insulin dependent diabetes mellitus; severe renal failure or kidney stones; fat malabsorption syndrome; history of major intestinal surgery; chronic diarrhea; alcoholism; extended use of systemic corticosteroid treatment; use of anticoagulants; regular use of any vitamin supplement.	NR/445/315

Study, Year, Title	Subject age, gender, diagnosis	Country & setting	Sponsor	Measures
Rosenfeld et al, 2006[145] *MARINA Trial* *Ranibizumab for neovascular age-related macular degeneration* Other publications: Boyer 2007	Mean age 77 years (SD 8) 65% female ARMD	US 96 sites - clinical setting NR	Genentech and Novartis Pharma	Change in visual acuity measured by loss of fewer than 15 letters from baseline (ETDRS)
Cataract				
Chylack et al, 2002[109] *The Roche European American Cataract Trial (REACT): a randomized clinical trial to investigate the efficacy of an oral antioxidant micronutrient to slow progression of age-related cataract*	Mean age 66.2 years 59% female UK cohort older and had poorer nutritional status at baseline (p<0.005)	US and UK; 3 outpatient ophthalmology clinics	F. Hoffmann-LaRoche Ltd; Roche Vitamins	Primary outcome: cataract progression

Study, Year, Title	Intervention	Results
Rosenfeld et al, 2006[145] *MARINA Trial* *Ranibizumab for neovascular age-related macular degeneration* Other publications: Boyer 2007	0.3mg or 0.5mg ranibizumab 1x/month (range 23-37 days) for 2 years sham injection	Mean change in visual acuity at 12 months: ranibizumab 0.3mg 6.5 letters vs. ranibizumab 0.5mg 7.2 letters vs. placebo -10.4 letters; p<0.001 for both doses ranibizumab vs. placebo Mean change in visual acuity at 24 months: ranibizumab 0.3mg 5.4 letters vs. ranibizumab 0.5mg 6.6 letters vs. placebo -14.9 letters; p<0.001 for both doses ranibizumab vs. placebo Loss of >3 lines of VA at 12 months: ranibizumab 0.3 mg 13/238 (5.5%) vs ranibizumab 0.5mg 13/240 (5.4%) vs sham injection 90/238 (37.8%); All combined doses ranibizumab vs sham injection RR 0.19 (CI 0.12 to 0.28; p<0.0001) Loss of >3 lines of VA at 24 months: ranibizumab 0.3 mg 19/238 (8.0%) vs ranibizumab 0.5mg 24/240 (10.0%) vs sham injection 112/238 (47.1%); All combined doses ranibizumab vs sham injection RR 0.26 (CI 0.19 to 0.36; p<0.0001)
Cataract		
Chylack et al, 2002[109] *The Roche European American Cataract Trial (REACT): a randomized clinical trial to investigate the efficacy of an oral antioxidant micronutrient to slow progression of age-related cataract*	Antioxidant multivitamin (250mg vitamin C + 200mg vitamin E + 6mg beta carotene) tid placebo	Multiple methods used to evaluate changes in lens opacities; following 3 years of treatment there was a marginally significant between group difference in cataract progression (p=0.048) based on the primary outcome measure only (% pixels opaque) and not for other measure of cataract progression (e.g. LOCS)

Study, Year, Title	Duration of follow-up	Loss to follow-up	Adverse events & withdrawals due to adverse effects	Quality score	Comments
Rosenfeld et al, 2006[145] *MARINA Trial* *Ranibizumab for neovascular age-related macular degeneration* Other publications: Boyer 2007	2 years	8/716 (1.1%)	Withdrawals due to AEs: 16/716 (2.2%) Serious AEs: ranibizumab 0.3mg 3/238 (1.3%) vs. ranibizumab 0.5mg 5/239 (2.0%) vs. placebo 2/236 (<1%) All-cause mortality: ranibizumab 0.3mg 5/238 (2.1%) vs. ranibizumab 0.5mg 6/239 (2.5%) vs. placebo 6/236 (2.5%)	Fair	
Cataract					
Chylack et al, 2002[109] *The Roche European American Cataract Trial (REACT): a randomized clinical trial to investigate the efficacy of an oral antioxidant micronutrient to slow progression of age-related cataract*	3 years	47%	NR	Fair	Only 'completers' included in 3-year analysis; authors acknowledge primary outcome measure of questionable clinical significance due to its ability to measure very small changes in lens opacities - modeling used to predict long-term effect on cataract progression

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Purpose of study	Study design	Inclusion criteria
Foss et al, 2006[107] *Falls and health status in elderly women following second eye cataract surgery: a randomised controlled trial*	To determine if second eye cataract surgery reduces the risk of falling and to measure associated health gain	RCT; immediate vs delayed treatment	Women age ≥70 years with a previous, successful cataract operation who had a second, operable cataract
Harwood et al, 2004[106] *Falls and health status in elderly women following first eye cataract surgery: a randomised controlled trial*	To determine if first eye cataract surgery reduces the risk of falling and to measure associated health gain	RCT; immediate vs delayed treatment	Women age ≥70 years with cataract who were suitable for surgery and had not had previous ocular surgery

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Exclusion criteria	Number screened/ eligible/ enrolled
Foss et al, 2006[107] *Falls and health status in elderly women following second eye cataract surgery: a randomised controlled trial*	Complex cataracts due to Fuch's corneal dystrophy, active intraocular inflammation, lens zonule dehiscence or lens instability; visual field defects; severe comorbid eye disease affecting visual acuity; memory problems preventing the completion of questionnaires or reliable recall of falls	1000/313/239
Harwood et al, 2004[106] *Falls and health status in elderly women following first eye cataract surgery: a randomised controlled trial*	Cataracts not eligible for surgery by phacoemulsification due to Fuch's corneal dystrophy, active intraocular inflammation, lens zonule dehiscence or lens instability; refractive error in second eye of > +4.00 or ≤ -6.00 DS; visual field defects; severe comorbid eye disease affecting visual acuity; partially sighted as a result of cataract; memory problems preventing the completion of questionnaires or reliable recall of falls	1600/482/306

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Subject age, gender, diagnosis	Country & setting	Sponsor	Measures
Foss et al, 2006[107] *Falls and health status in elderly women following second eye cataract surgery: a randomised controlled trial*	Mean age 79.5 years 100% female Cataract	UK; hospital ophthalmology clinic	Health Foundation Trent Regional Health Authority	Primary outcome: patient-recorded falls Secondary outcomes: change in health status
Harwood et al, 2004[106] *Falls and health status in elderly women following first eye cataract surgery: a randomised controlled trial*	Mean age 78.5 years 100% female Cataract	UK; multiple ophthalmologic/optometric clinics	Trent Regional NHS Research and Development scheme PPP (Health) Foundation	Primary outcome: patient-recorded falls following cataract surgery Secondary outcomes: change in various QOL measures

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Intervention	Results
Foss et al, 2006[107] *Falls and health status in elderly women following second eye cataract surgery: a randomised controlled trial*	Cataract surgery no/delayed treatment	Proportion of patients with falls: 48/120 (40%) immediate surgery group vs 41/119 (34%) delayed treatment group; HR 1.06 (CI 0.69 to 1.61; p=0.80) Proportion of patients with second falls: 22/120 (18%) immediate surgery group vs 22/119 (18%) delayed treatment group; HR 0.85 (CI 0.49 to 1.56; p=0.61) Rate of falling per 1,000 patient days: 2.9 immediate treatment group vs 4.3 delayed treatment group; Rate ratio 0.68 (CI 0.39 to 1.19; p=0.18)
Harwood et al, 2004[106] *Falls and health status in elderly women following first eye cataract surgery: a randomised controlled trial*	Cataract surgery (phacoemulsification) no/delayed treatment	Proportion of patients with falls: 76/154 (49%) immediate surgery group vs 69/152 (45%) delayed treatment group; HR 0.95 (CI 0.69 to 1.35; p=0.77) Proportion of patients with second falls: 28/154 (18%) immediate surgery group vs 38/152 (25%) delayed treatment group; HR 0.60(CI 0.36 to 0.98; p=0.04) Rate of falling per 1,000 patient days: 1.0 immediate treatment group vs 1.52 delayed treatment group; Rate ratio 0.66 (CI 0.45 to 0.96; p=0.03) Fracture incidence: 4/154 (3%) immediate treat-ment group vs 12/152 (8%) delayed treatment group; Risk ratio 0.33 (CI 0.1 to 1.0; p=0.04)

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Duration of follow-up	Loss to follow-up	Adverse events & withdrawals due to adverse effects	Quality score	Comments
Foss et al, 2006[107] *Falls and health status in elderly women following second eye cataract surgery: a randomised controlled trial*	12 months	16/239 (7%)	NR	Good	
Harwood et al, 2004[106] *Falls and health status in elderly women following first eye cataract surgery: a randomised controlled trial*	12 months	13/306 (4%)	NR	Good	

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS

Study, Year, Title	Purpose of study	Study design	Inclusion criteria
Uncorrected refractive error			
Coleman et al, 2006[83] *Treatment of uncorrected refractive error improves vision-specific quality of life*	To evaluate the benefits of eyeglasses and magnifiers in elderly patients with uncorrected refractive error	Prospective RCT	Age >65 years with habitual binocular visual acuity 20/32 or worse whose distance or near visual acuity could be improved by at least 2 lines of acuity; fixed residence for 3 months of study; speak and understand English; have a phone or other method of being contacted by research team; ambulatory with a cane or walker; MMSE score ≥23; capable of providing informed consent
Owsley et al, 2007[84] *Effect of refractive error correction on health-related quality of life and depression in older nursing home residents*	To examine the effect of treating uncorrected refractive error through spectacle correction on vision-targeted health-related quality of life and depressive symptoms in nursing home residents	RCT immediate vs. delayed treatment	Able to answer simple questions about vision and daily activities; age ≥55 years; English speaker; Mini-Mental State Examination (MMSE) score ≥13; uncorrected refractive error in 1 or both eyes for near or far test distances as determined by routine eye exam w/optometrist within 1 month of study entry; correction of uncorrected refractive error had to improve visual acuity by at least 1 mile on a distance visual acuity chart for at least 1 eye according to optometrist's records

Study, Year, Title	Exclusion criteria		Number screened/ eligible/ enrolled
Uncorrected refractive error			
Coleman et al, 2006[83] *Treatment of uncorrected refractive error improves vision-specific quality of life*		NR	1309/131/131
Owsley et al, 2007[84] *Effect of refractive error correction on health-related quality of life and depression in older nursing home residents*		NR	NR/NR/151

Study, Year, Title	Subject age, gender, diagnosis	Country & setting	Sponsor	Measures
Uncorrected refractive error				
Coleman et al, 2006[83] *Treatment of uncorrected refractive error improves vision-specific quality of life*	Mean age 80.4 years (SD 8.2) 72% female 63% White; 18% Black; 8% Asian; 3% Hispanic; 8% Other. Mean baseline visual acuity 20/63	US Community screening centers followed by home visit	UCLA Claude D. Pepper Older American Independence Center	Primary outcome: Change in National Eye Institute Visual Functioning Questionnaire Secondary outcomes: Change in visual acuity based on logMAR chart; Overall functioning based on the Rosow-Breslau function questionnaire
Owsley et al, 2007[84] *Effect of refractive error correction on health-related quality of life and depression in older nursing home residents*	Mean age 78.7 years (SD 8.3) 76% female Diagnosis - Uncorrected refractive error; concomitant cataract (64%), ARMD (16%), diabetic retinopathy (6%), glaucoma (4%)	US; 17 nursing homes	Retirement Research Foundation, the EyeSight Foundation of Alabama, The Pearle Vision Foundation, NIH grant r21-EY14071, Research to Prevent Blindness Inc	Primary outcomes: QOL based on Nursing Home Vision-Targeted Health-Related Quality of Life (NHVQoL) Questionnaire and the VF-14; depressive symptoms based on Geriatric Depression Scale

Study, Year, Title	Intervention	Results
Uncorrected refractive error		
Coleman et al, 2006[83] *Treatment of uncorrected refractive error improves vision-specific quality of life*	Intervention group: Received vision correction aids immediately (glasses, magnifier or both) Control group: Received a voucher and prescription to obtain vision correction aids at the conclusion of the trial (3 months later)	Mean change from baseline at 3 months, with glasses vs. without glasses National Eye Institute Visual Functioning Questionnaire: Composite score: 6.5 (SD 9.3) vs. -0.8 (SD 10.8); p<0.01 Selected individual components: -General health: 4.2 (SD 18.0) vs. -0.4 (SD 17.4); p=.17 -General vision: 10.4 (SD 18.2) vs. -2.1 (SD 14.0); p<0.01 -Near vision: 7.6 (SD 19.1) vs. 0.4 (SD 17.4); p=0.04 -Distance vision: 3.3 (SD 23.2) vs. -6.3 (SD 22.7); p=0.03 -Social functioning: 4.5 (SD 21.0) vs. -0.9 (SD 19.6); p=0.17 -Mental health: 11.2 (SD 25.3) vs. 0.4 (SD 24.2); p=0.02 Geriatric Depression Scale: -0.3 (SD 1.9) vs. -0.1 (SD 2.1); p=0.58 Rosow-Breslau functioning scale: 0.07 (SD 1.3) vs. -0.4 (SD 1.4); p=0.07 Distance visual acuity: 5.5 (SD 10.0) vs. 3.9 (10.4); p=0.41 Near visual acuity: 6.1 (SD 13.3) vs. 2.2 (SD 11.4); p=0.10
Owsley et al, 2007[84] *Effect of refractive error correction on health-related quality of life and depression in older nursing home residents*	Immediate (within 1 week) refractive error correction with glasses vs. delayed correction (glasses dispensed 2 months later)	Immediate vs. delayed correction at 2 months: NHVQoL subscale score - range 0-100 ·General vision: 77.3 vs. 65.0; p<0.001 ·Reading: 92.9 vs. 84.7; p<0.001 ·Ocular symptoms: 81.4 vs. 78.3; p=0.23 ·mobility: 91.5 vs. 90.0; p=0.24 ·Psychological distress: 76.0 vs. 70.7; p=0.02 ·Activities of daily living: 99.7 vs. 99.1; p=0.17 ·Activities and hobbies: 98.0 vs. 94.0; p=0.04 ·Adaptation and coping: 92.4 vs. 90.0; p=0.11 ·Social interaction: 97.3 vs. 94.1; p=0.03 VF-14 total score - range 0-100 95.7 vs. 83.1; p<0.001 SF-36 score - range 0-100 ·Mental component summary 81.9 vs. 80.8; p=0.96 ·Physical component summary 47.6 vs. 46.1; p=0..24 GDS score 3.6 vs. 4.9; p=0.003

Study, Year, Title	Duration of follow-up	Loss to follow-up	Adverse events & withdrawals due to adverse effects	Quality score	Comments
Uncorrected refractive error					
Coleman et al, 2006[83] *Treatment of uncorrected refractive error improves vision-specific quality of life*	3 months	20/131 (15%)	NR	Fair	
Owsley et al, 2007[84] *Effect of refractive error correction on health-related quality of life and depression in older nursing home residents*	2 months	9/151 (6%)	NR	Fair	p-values adjusted based on baseline value of outcome and baseline mental status

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS. Continued

Abbreviations: AE = adverse effect, AMD = age-related macular degeneration, ARMD = age-related macular degeneration, CI = confidence interval, CNV = choroidal neovascularisation, ETDRS = Early Treatment Diabetic Retinopathy Study , GDS = geriatric depression scale, LOCS = Lens Opacities Classification System, logMAR = logarithmic minimum angle of resolution, MI = myocardial infarction, MMSE = mini mental state examination, NHVQoL = nursing home vision-targeted health-related quality of life questionnaire, NR = not relevant, QOL = quality of life, RCT = randomized controlled study, RR = relative risk, SD = standard deviation.

**Rosenfeld et al, 2006 exclusion criteria continued..* subretinal hemorrhage in the study eye that involves the fovea, if the size of the hemorrhage is either 50% or more of the total lesion area or 1 or more disc areas in size; subfoveal fibrosis or atrophy in the study eye; CNV in either eye due to other causes, such as ocular histoplasmosis, trauma, or pathologic myopia; retinal pigment epithelial tear involving the macula in the study eye; any concurrent intraocular condition in the study eye (e.g., cataract or diabetic retinopathy) that, in the opinion of the investigator, could either (a) require medical or surgical intervention during the 24-month study period to prevent or treat visual loss that might result from that condition, or (b) if allowed to progress untreated, could likely contribute to loss of at least 2 Snellen equivalent lines of best corrected visual acuity over the 24-month study period; active intraocular inflammation (grade trace or above) in the study eye; urgent vitreous hemorrhage in the study eye; history of rhegmatogenous retinal detachment or macular hole (Stage 3 or 4) in the study eye; history of idiopathic or autoimmune-associated uveitis in either eye; infectious conjunctivitis, keratitis, scleritis, or endophthalmitis in either eye; aphakia

APPENDIX C5. TREATMENT - RANDOMIZED CONTROLLED TRIALS. Continued

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Random assignment	Allocation concealed	Groups similar at baseline	Eligibility criteria specified	Blinding: patients	Blinding: providers
AREDS Research Group, 2001[114] *A randomized, placebo-controlled clinical trial of high-dose supplementation with vitamins C and E, beta carotene and zinc for age-related macular degeneration and vision loss: AREDS Report No. 8*	Randomized but method not described	Yes	Yes	Yes	Yes	Yes
Coleman et al, 2006[83] *Treatment of uncorrected refractive error improves vision-specific quality of life*	Randomized but method not described	Yes	Yes	Yes	NA	NA
Cumming et al, 2007[69] *Improving vision to prevent falls in frail older people: a randomized trial*	Randomized but method not described	Yes	Yes	Yes	NA	NA
Foss et al, 2006[107] *Falls and health status in elderly women following second eye cataract surgery: a randomised controlled trial*	Yes	Yes	Yes	Yes	NA	NA
Harwood et al, 2005[106] *Falls and health status in elderly women following first eye cataract surgery: a randomised controlled trial*	Yes	Yes	Yes	Yes	NA	NA
Kaiser et al, 1995[123] *Visaline in the treatment of age-related macular degeneration: a pilot study*	Randomized but method not described	Can't tell	Yes	Yes	Yes	Yes
MPS Group 1982[128] *Argon laser photocoagulation for senile macular degeneration. Results of a randomized clinical trial*	Yes	Can't tell	No	Yes	No	No

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Blinding: outcome assessors or data analysts	Intention-to-treat analysis	Reporting of attrition, contamin-ation, etc	Differential loss to follow-up, overall high loss to follow-up, or incomplete follow-up
AREDS Research Group, 2001[114] *A randomized, placebo-controlled clinical trial of high-dose supplementation with vitamins C and E, beta carotene and zinc for age-related macular degeneration and vision loss: AREDS Report No. 8*	Can't tell	Yes	Yes	No
Coleman et al, 2006[83] *Treatment of uncorrected refractive error improves vision-specific quality of life*	Can't tell	No	Yes	Yes
Cumming et al, 2007[69] *Improving vision to prevent falls in frail older people: a randomized trial*	Can't tell	Yes	Yes	No
Foss et al, 2006[107] *Falls and health status in elderly women following second eye cataract surgery: a randomised controlled trial*	No	Yes	Yes	No
Harwood et al, 2005[106] *Falls and health status in elderly women following first eye cataract surgery: a randomised controlled trial*	No	Yes	Yes	No
Kaiser et al, 1995[123] *Visaline in the treatment of age-related macular degeneration: a pilot study*	Can't tell	Yes	No	Can't tell
MPS Group 1982[128] *Argon laser photocoagulation for senile macular degeneration. Results of a randomized clinical trial*	No	No	Yes	Yes

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Funding source	External validity	Quality score
AREDS Research Group, 2001[114] *A randomized, placebo-controlled clinical trial of high-dose supplementation with vitamins C and E, beta carotene and zinc for age-related macular degeneration and vision loss: AREDS Report No. 8*	National Eye Institute, National Institutes of Health, Bausch and Lomb Inc	Median age 56 yrs Mean BCVA at baseline better than 20/32 for all participants	Good
Coleman et al, 2006[83] *Treatment of uncorrected refractive error improves vision-specific quality of life*	UCLA Claude D. Pepper Older American Independence Center	Appears applicable to screening population; average visual acuity 20/63	Fair
Cumming et al, 2007[69] *Improving vision to prevent falls in frail older people: a randomized trial*	National Health and Medical Research Council of Australia	Number screened and eligible not reported. Mean severity of visual acuity impairment not reported	Fair
Foss et al, 2006[107] *Falls and health status in elderly women following second eye cataract surgery: a randomised controlled trial*	Health Foundation Trent Regional Health Authority	At baseline similar number of prior falls reported in both groups	Good
Harwood et al, 2005[106] *Falls and health status in elderly women following first eye cataract surgery: a randomised controlled trial*	Trent Regional NHS Research and Development Scheme; PPP (Health) Foundation	At baseline similar number of prior falls reported in both groups	Good
Kaiser et al, 1995[123] *Visaline in the treatment of age-related macular degeneration: a pilot study*	NR	Mean age 72 yrs 65% female Mean far VA 0.57	Fair
MPS Group 1982[128] *Argon laser photocoagulation for senile macular degeneration. Results of a randomized clinical trial*	National Eye Institute, National Institutes of Health	BCVA 20/32 or better: 105/224 (47%)	Poor

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Random assignment	Allocation concealed	Groups similar at baseline	Eligibility criteria specified	Blinding: patients	Blinding: providers
MPS Group 1991a[130] *Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration*	Randomized but method not described	Can't tell	Yes	Yes	No	No
MPS Group 1991b[131] *Laser photocoagulation of subfoveal recurrent neovascular lesions in age-related macular degeneration. Results of a randomized clinical trial*	Randomized but method not described	Can't tell	No	Yes	No	No
MPS Group 1990[129] *Krypton laser photocoagulation for neovascular lesions of age-related macular degeneration. Results of a randomized clinical trial*	Randomized but method not described	Can't tell	No	Yes	No	No
Moorfields, 1982[132] The Moorefields Macular Study Group *Treatment of senile disciform macular degeneration: a single-blind randomised trial by argon laser photocoagulation*	Randomized but method not described	Can't tell	Can't tell	Yes	Can't tell	Can't tell
Newsome, 1988[118] *Oral zinc in macular degeneration*	Yes	Yes	Yes	Yes	Yes	Yes
Owsley et al, 2007[84] *Effect of refractive error correction on health-related quality of life and depression in older nursing home residents*	Randomized but method not described	Can't tell	Yes	Yes	NA	NA

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Blinding: outcome assessors or data analysts	Intention-to-treat analysis	Reporting of attrition, contamin-ation, etc	Differential loss to follow-up, overall high loss to follow-up, or incomplete follow-up
MPS Group 1991a[130] *Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration*	No	No	Yes	Yes
MPS Group 1991b[131] *Laser photocoagulation of subfoveal recurrent neovascular lesions in age-related macular degeneration. Results of a randomized clinical trial*	No	No	Yes	Yes
MPS Group 1990[129] *Krypton laser photocoagulation for neovascular lesions of age-related macular degeneration. Results of a randomized clinical trial*	No	No	No	Yes
Moorfields, 1982[132] The Moorefields Macular Study Group *Treatment of senile disciform macular degeneration: a single-blind randomised trial by argon laser photocoagulation*	Can't tell	No	Yes	No
Newsome, 1988[118] *Oral zinc in macular degeneration*	Yes	No	Yes	No
Owsley et al, 2007[84] *Effect of refractive error correction on health-related quality of life and depression in older nursing home residents*	Can't tell	Yes	Yes	No

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Funding source	External validity	Quality score
MPS Group 1991a[130] *Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration*	National Eye Institute, National Institutes of Health	BCVA 20/20 or better: 106/373 (28%); 20/25-20/100: 190/373 (51%); 20/250 or worse: 76/373 (20%)	Poor
MPS Group 1991b[131] *Laser photocoagulation of subfoveal recurrent neovascular lesions in age-related macular degeneration. Results of a randomized clinical trial*	National Eye Institute, National Institutes of Health	BCVA 20/20 or better: 70/206(34%); 20/25-20/100: 73/206 (35%); 20/250 or worse: 63/206 (31%)	Poor
MPS Group 1990[129] *Krypton laser photocoagulation for neovascular lesions of age-related macular degeneration. Results of a randomized clinical trial*	National Eye Institute, National Institutes of Health	BCVA 20/40 or better: 157/496 (32%)	Poor
Moorfields, 1982[132] The Moorefields Macular Study Group *Treatment of senile disciform macular degeneration: a single-blind randomised trial by argon laser photocoagulation*	National Eye Institute, National Institutes of Health, Medical Research Council	Inclusion criteria required age 50-80 yrs; no description of BCVA at baseline	Poor
Newsome, 1988[118] *Oral zinc in macular degeneration*	Utah State University; Mary Katherine Peterson Foundation	Mean age 67.9 yrs 65% female 32% VA >20/25	Fair
Owsley et al, 2007[84] *Effect of refractive error correction on health-related quality of life and depression in older nursing home residents*	Retirement Research Foundation, the EyeSight Foundation of Alabama, The Pearle Vision Foundation, NIH grant r21-EY14071, Research to Prevent Blindness Inc	Number screened and eligible not reported. Mean refractive error +0.19 vs. -0.19 (spherical equivalents, SD)	Fair

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Random assignment	Allocation concealed	Groups similar at baseline	Eligibility criteria specified	Blinding: patients	Blinding: providers
Regillo et al, 2008[143] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	Yes	NA	Yes	Yes	Yes	No
Richer et al, 1996[120] ARMD Study Group *Multicenter ophthalmic and nutritional age-related macular degeneration study -- part 2:antioxidant intervention and conclusion*	Randomized but method not described	Can't tell	Yes	Yes	Yes	Yes
Richer et al, 2004[121] *Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study (Lutein Antioxidant Supplementation Trial)*	Yes	Yes	No	Yes	Yes	Yes
Rosenfeld et al, 2006[145] *Ranibizumab for neovascular age-related macular degeneration*	Randomized but method not described	Can't tell	Yes	Yes	Yes	No
Stur et al, 1996[122] *Oral zinc and the second eye in age-related macular degeneration*	Randomized, but method not described	Can't tell	Yes	Yes	Yes	Yes
TAP Study Group, 1999[135] *Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: one-year results of 2 randomized clinical trials--TAP report*	Yes	Yes	No	Yes	Yes	Yes

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Blinding: outcome assessors or data analysts	Intention-to-treat analysis	Reporting of attrition, contamin-ation, etc	Differential loss to follow-up, overall high loss to follow-up, or incomplete follow-up
Regillo et al, 2008[143] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	Yes	Yes	Yes	No
Richer et al, 1996[120] ARMD Study Group *Multicenter ophthalmic and nutritional age-related macular degeneration study -- part 2:antioxidant intervention and conclusion*	Yes	Can't tell	Yes	Yes
Richer et al, 2004[121] *Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study (Lutein Antioxidant Supplementation Trial)*	Yes	Can't tell	Yes	Yes
Rosenfeld et al, 2006[145] *Ranibizumab for neovascular age-related macular degeneration*	Yes	Yes	Yes	No
Stur et al, 1996[122] *Oral zinc and the second eye in age-related macular degeneration*	Can't tell	No	Yes	No
TAP Study Group, 1999[135] *Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: one-year results of 2 randomized clinical trials--TAP report*	Yes	Yes	Yes	No

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Funding source	External validity	Quality score
Regillo et al, 2008[143] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	Genentech; Novartis Pharma AG	Mean baseline VA 20/63 to 20/80; most patients newly diagnosed with ARMD (87% within one year of diagnosis)	Good
Richer et al, 1996[120] ARMD Study Group *Multicenter ophthalmic and nutritional age-related macular degeneration study -- part 2:antioxidant intervention and conclusion*	US Department of Veteran Affairs; Twin Laboratories; Stereo Optical; Eye Communications Inc; Illinois College of Optometry; Pacific University College of Optometry; Ezell Foundation	Mean age 72 yrs 7% female Mean far VA (LogMAR, right eyes) 0.26	Fair
Richer et al, 2004[121] *Double-masked, placebo-controlled, randomized trial of lutein and antioxidant supplementation in the intervention of atrophic age-related macular degeneration: the Veterans LAST study (Lutein Antioxidant Supplementation Trial)*	Department of Veterans Affairs	Mean age 73 yrs 4% female Mean VA (right eye, LogMAR) 0.377	Fair
Rosenfeld et al, 2006[145] *Ranibizumab for neovascular age-related macular degeneration*	Genentech and Novartis	>85% had visual acuity >20/200	Fair
Stur et al, 1996[122] *Oral zinc and the second eye in age-related macular degeneration*	Austrian Foundation for the Propogation of Scientific Research	Mean age 71.5 yrs 57% female Mean VA (LogMAR) 0.0745	Fair
TAP Study Group, 1999[135] *Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: one-year results of 2 randomized clinical trials--TAP report*	QLT PhotoTherapeutics, CIBA Vision AG	Mean BCVA: 20/80-2 89% subfoveal lesion(s)	Good

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Random assignment	Allocation concealed	Groups similar at baseline	Eligibility criteria specified	Blinding: patients	Blinding: providers
VIM Study Group, 2005[137] *Verteporfin therapy of subfoveal minimally classic choroidal neovascularization in age-related macular degeneration (VIM): 2-year results of a randomized clinical trial*	Randomized but method not described	Yes	Yes	Yes	Yes	Yes
VIP Study Group, 2001[136] *Photodynamic therapy of subfoveal choroidal neovascularization in pathologic myopia with verteporfin. 1-year results of a randomized clinical trial--VIP report no. 1*	Yes	Yes	Yes	Yes	Yes	Yes
VISION Clinical Trial Group, 2006[166] *Pegaptanib sodium for neovascular age-related macular degeneration: two-year safety results of the two prospective, multicenter, controlled clinical trials*	Randomized but method not described	Can't tell	Yes	Yes	Yes	No

Abbreviations: BCVA = best corrected visual acuity, MPS = Macular Photocoagulation Study Group, NA = not applicable, NR = not reported, SD = standard deviation.

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Blinding: outcome assessors or data analysts	Intention-to-treat analysis	Reporting of attrition, contamin-ation, etc	Differential loss to follow-up, overall high loss to follow-up, or incomplete follow-up
VIM Study Group, 2005[137] *Verteporfin therapy of subfoveal minimally classic choroidal neovascularization in age-related macular degeneration (VIM): 2-year results of a randomized clinical trial*	Yes	No	Yes	No
VIP Study Group, 2001[136] *Photodynamic therapy of subfoveal choroidal neovascularization in pathologic myopia with verteporfin. 1-year results of a randomized clinical trial--VIP report no. 1*	Yes	Yes	Yes	No
VISION Clinical Trial Group, 2006[166] *Pegaptanib sodium for neovascular age-related macular degeneration: two-year safety results of the two prospective, multicenter, controlled clinical trials*	Yes	Yes	No	No

APPENDIX C6. QUALITY RATINGS OF TREATMENT RANDOMIZED CONTROLLED TRIALS

Study, Year	Funding source	External validity	Quality score
VIM Study Group, 2005[137] *Verteporfin therapy of subfoveal minimally classic choroidal neovascularization in age-related macular degeneration (VIM): 2-year results of a randomized clinical trial*	Novartis Pharma AG, QLT Inc	Mean BCVA: 20/80 92% subfoveal lesion(s)	Good
VIP Study Group, 2001[136] *Photodynamic therapy of subfoveal choroidal neovascularization in pathologic myopia with verteporfin. 1-year results of a randomized clinical trial--VIP report no. 1*	Novartis Ophthalmics AG, QLT Inc	Mean BVCA: 20/50+1 83.4% subfoveal lesion(s)	Good
VISION Clinical Trial Group, 2006[166] *Pegaptanib sodium for neovascular age-related macular degeneration: two-year safety results of the two prospective, multicenter, controlled clinical trials*	Eyetech Pharmaceuticals and Pfizer	Mean visual acuity 51 to 53	Fair

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Patients/trials
ARMD (Dry)				
Evans et al, 2008[43] *Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration*	To assess the effects of antioxidant vitamin or mineral supplementation, alone or in combination, on the progression of ARMD	CCRCT, MEDLINE, EMBASE, National Research Register through 2007, PubMed in process through 24 January 2006, AMED 1985-January 2006, SIGLE 1980-March 2005	RCTs of antioxidant vitamins or mineral supplementation, alone or in combination, vs placebo or no treatment in ARMD patients	9 trials (18 publications) Primary publications: Richer 1996 - AMDSG (n=71); Age-Related Eye Disease Study Research Group 2001 - AREDS (n=3640); Holz 1993 (n=58); Kaiser 1995 (n=20); Newsome 1988 (n=174); Stur 1996 (n=112); Garrett 1999 - VECAT study (n=1204); Richer 2004 - LAST study (n=90); Wang 2004 (n=400); total n=5769
Evans et al, 2008[126] *Ginkgo biloba extract for age-related macular degeneration*	To determine the effect of ginkgo biloba extract on the progression of AMD	CCRCT (Quarter 4, 2005), MEDLINE (1966-January 2006, week 3), EMBASE (1980-January 2006), SIGLE (1980-2005/03), AMED (1985-January 2006), NRR (2005, Issue 4); reference lists, Science Citation Index; expert recommendation	RCTs of ginkgo biloba vs control in AMD patients	2 trials: Fies 2002 (n=99); Lebuisson 1986 (n=20); total n=119 pts

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Main efficacy outcome
ARMD (Dry)				
Evans et al, 2008[43] *Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration*	9 RCTs	Mean age: 70 years 55% female Varying degree of ARMD by trial (mild to advanced, including AREDS, the largest trial)	3 trials: zinc 200 mg QD vs placebo 2 trials: broad-spectrum antioxidant compound vs placebo 1 trial: vitamin E 500 mg QD vs placebo 1 trial: zinc 80 mg QD vs antioxidant combination vs zinc + antioxidants vs placebo 1 trial: lutein 10 mg QD v lutein + broad-spectrum antioxidant 1 trial: zinc oxide 80 mg QD, vitamin C, vitamin E vs placebo	Change in vision (Secondary outcome: disease progression)
Evans et al, 2008[126] *Ginkgo biloba extract for age-related macular degeneration*	2 RCTs: 160 mg QD gingko biloba vs placebo (1 trial); 240 mg QD gingko biloba v 60 mg QD gingko biloba (1 trial)	1 trial: eye clinic outpatients <55 years w/ARMD, mean age 67 years, gender NR; 1 trial: eye clinic outpatients >59 years, mean age 76 years, 27% male	Gingko biloba extract EGb 761, doses 60-160 mg QD; placebo	Primary outcomes: number of patients with disease progression and/or new visual loss due to AMD; QOL

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Main efficacy results	Harms results
ARMD (Dry)		
Evans et al, 2008[43] *Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration*	All comparisons Any multivitamin or antioxidant vs placebo: Change in visual acuity - defined as a loss of 3 or more lines (15 or more letters) on a logMAR chart (AREDS, Newsome 1988, VECAT; I^2=27.7%) Random effects model: pooled OR 0.83 (CI 0.63 to 1.09; p=0.18); Fixed effects model: pooled OR 0.81 (CI 0.67 to 0.98; p=0.03) Mean difference visual acuity (AMDSG, Kaiser 1995, Newsome 1988, Stur 1996, LAST; I^2=0%): pooled SMD 0.02 (CI -0.21 to 0.26) ARMD progression as a dichotomous variable: (AREDS, Holz 1993, Stur 1996. VECAT; I^2=64.2%) OR range: 0.50 to 2.31; no pooled analysis due to heterogeneity of studies ARMD progression as a continuous variable (AMDSG): mean difference -0.06 (CI -0.62 to 0.50) Individual comparisons Multivitamin supplements vs placebo (AREDS, Kaiser 1995, Richer 1996, Richer 2004) Change in visual acuity - defined as a loss of 3 or more lines (15 or more letters) on a logMAR chart (AREDS): OR 0.77 (CI 0.62 to 0.96) vs placebo Mean difference visual acuity (Kaiser 1995, AMDSG, LAST; I^2=0%): pooled SMD 0.16 (CI -0.19 to 0.51) ARMD progression as a dichotomous variable (AREDS): adjusted OR 0.6	None reported
Evans et al, 2008[126] *Ginkgo biloba extract for age-related macular degeneration*	Gingko biloba 160 mg QD vs placebo (1 trial; n=20): Change in visual acuity: WMD 1.70 (CI 1.21 to 2.19) Clinical improvement: OR 36.00 (2.72 to 476.28) Gingko biloba 60 mg QD vs 240 mg QD (1 trial; n=99): Mean visual acuity: WMD 0.05 (CI -0.03 to 0.13) >0.2 improvement in visual acuity score: OR 2.29 (CI 0.90 to 5.80)	No serious AEs reported in either trial (headache, blood in stool and abdominal pain reported in 3/99 patients)

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Conclusion	Quality score
ARMD (Dry)		
Evans et al, 2008[43] *Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration*	Limited evidence, based primarily on AREDS, suggests a benefit in the use of antioxidant vitamins and minerals in slowing ARMD progression (risk reduction ~20-25%.) The AREDS population was relatively well-nourished at the trial's initiation and this may have had some effect on the trial results. Prolonged antioxidant use had been found to be harmful in some other populations (e.g. smokers)	Good
Evans et al, 2008[126] *Ginkgo biloba extract for age-related macular degeneration*	There is inadequate evidence from 2 small, short-term trials to draw conclusions regarding the effect of gingko biloba on ARMD progression. There may be harms associated with gingko biloba use, but they too have been inadequately reported	Good

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Patients/trials
ARMD (Wet)				
Meads et al, 2003[133] *Clinical effectiveness and cost-utility of photodynamic therapy for met age-related macular degeneration: a systematic review and economic evaluation*	To establish the clinical and cost-effectiveness of photodynamic therapy for neovascular AMD	Cochrane Library (2001, Issue 3), MEDLINE (1993-Aug 2001), EMBASE (1993-Aug 2001), Science Citation Index (1993-2001); health technology assessment web sites; internet sites of verteporfin manufacturers; reference lists; industry submissions	RCTS of photodynamic therapy vs no treatment or laser treatment in patients with wet ARMD	2 trials: Treatment of Age-related Macular Degeneration with Photodynamic Therapy Study Group - TAP 1999 (n=609); Verteporfin in Photodynamic Therapy Study Group - VIP 2001 (n=2001); total n=2610 pts
Vedula et al, 2008[142] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	To investigate the effects of anti-vascular endothelial growth factor (anti-VEGF) modalities for treating endovascular ARMD	CCRCT, MEDLINE, EMBASE, LILACs through February 2008; hand search of Association for Research in Vision & Ophthalmology meeting abstracts	RCTs of anti-VEGF modalities in ARMD	5 trials (15 publications) Primary publications: Brown 2006 - ANCHOR Trial (n=423); Macugen 2007 - EOP 1003 Trial (n=578); Leys 2007 - EOP 1004 Trial (n=612); Heier 2006 - FOCUS Trial (n=162); Rosenfeld 2006 - MARINA Trial (n=716)

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Main efficacy outcome
ARMD (Wet)				
Meads et al, 2003[133] *Clinical effectiveness and cost-utility of photodynamic therapy for met age-related macular degeneration: a systematic review and economic evaluation*	2 RCTs: verteporfin IV + laser vs placebo IV + laser	ARMD patients 2 trials: mean age 75 years; 98% white 1 trial: NR Baseline visual acuity in treated eye: TAP - 53 letters; VIP - 46 letters	IV verteporfin 6 mg/m2 + cold laser vs placebo + cold laser	Visual acuity changes
Vedula et al, 2008[142] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	RCTs - 2 trials: pegaptanib 0.3, 1.0 or 3.0mg vs sham injection 1 trial: ranibizumab 0.3 or 0.5mg + sham verteporfin PDT therapy vs sham ranibizumab + active verteporfin PDT therapy 1 trial: 0.3 or 0.5mg ranibizumab vs sham injection 1 trial: 0.5mg ranibizumab + verteprofin PDT vs verteporfin PDT only	Mean age range 73-78 years 46-69% female Diagnosis of ARMD	Pegaptanib 0.3, 1.0 or 3.0mg Ranibizumab 0.3 or 0.5mg Verteporfin PDT sham injection/sham PDT	Visual acuity after at least 1 year follow up

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Main efficacy results	Harms results
ARMD (Wet)		
Meads et al, 2003[133] *Clinical effectiveness and cost-utility of photodynamic therapy for met age-related macular degeneration: a systematic review and economic evaluation*	Results not pooled. TAP Loss of >15 letters (3 lines) at 24 months: 47.0% verteporfin vs 62.3% placebo; RR 0.75 (CI 0.65 to 0.88) Loss of >30 letters (6 lines) at 24 months: 18.2% verteporfin vs 30.0% placebo; RR 0.61 (CI 0.45 to 0.81) Proportion of pts with visual acuity of <34 letters at 24 months: 41.0% verteporfin vs 55.1% placebo; RR 0.75 (CI 0.63-0.88) VIP Loss of >15 letters (3 lines) at 24 months: 54.0% verteporfin vs 67% placebo; RR 0.81 (CI 0.68 to 0.96) Loss of >30 letters (6 lines) at 24 months: 30% verteporfin vs 47% placebo; RR 0.63 (CI 0.48 to 0.83) Proportion of pts with visual acuity of <34 letters at 24 months: this outcome not reported.	Results not pooled TAP mortality at 24 months: 3.2% verteporfin vs 3.9% placebo; RR 0.84 (0.35-1.99) VIP mortality at 24 months: 1.8% verteporfin vs 2.6% placebo; RR 0.68 (CI 0.15 to 2.97)
Vedula et al, 2008[142] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	Change in visual acuity (% of patients losing ≥3 lines of acuity at 1 year) Pegaptanib (all doses) vs sham: RR 0.71 (CI 0.60 to 0.84); NSD for 3.0mg dose vs sham; NNT 6.67 0.3mg dose, 6.25 1.0mg dose, 14.28 3.0mg dose Ranibizumab (both doses) vs sham: RR 0.14 (CI 0.08 to 0.25); NNT 3.13 (both doses) Blindness Pegaptanib RR 0.69 (CI 0.59 to 0.82) Ranibizumab RR 0.28 (CI 0.21 to 0.37) Quality of life - Mean change in NEI-VFQ scores at 2 years follow-up ANCHOR Trial: 5.9 ranibizumab 0.3mg vs 8.1 ranibizumab 0.5mg vs 2.2 verteprofin MARINA Trial: 4.8 ranibizumab 0.3mg vs 4.5 0.5mg ranibizumab vs -6.4 sham injection	Ranibizumab: similar rates of serious AEs including mortality Unpublished data from SAILOR Trial reported by the drug's manufacturer showed significantly higher stroke risk w 0.5mg dose relative to 0.3mg dose(p=0.02; no sham control in this trial) Pegaptanib: Serious ocular AEs (endophthalmitis, retinal detachment, traumatic cataract) in tx groups, none in sham group

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Conclusion	Quality score
ARMD (Wet)		
Meads et al, 2003[133] *Clinical effectiveness and cost-utility of photodynamic therapy for met age-related macular degeneration: a systematic review and economic evaluation*	Photodynamic therapy is effective at preventing further visual loss due to AMD, although this conclusion is based largely on the results of the TAP trial. With the addition of a cost effectiveness analysis included in this review, the authors concluded that there is a need for further research on this topic.	Good
Vedula et al, 2008[142] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	Both interventions effective a reducing visual acuity loss and progression to blindness with improved QoL outcomes	Good

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Patients/trials
Virgili et al, 2008[45] *Laser photocoagulation for age-related macular degeneration*	To examine the effect of laser photocoagulation on neovascular (wet) ARMD	CCRCT, MEDLINE, EMBASE, LILACS, National Research Register (NRR), ZETOC through March 2007	RCTs of laser photocoagulation for neovascular ARMD	15 trials (34 publications) Primary publications: Arnold 1997; Canadian Ophthalmology Study Group 1993 (n=55); Bressler 1996 (n=100); Canadian Ophthalmology Study Group 1993 (n=191); Cardillo 1993 (n=23); Coscas 1983 (n=60); Coscas 1991 (n=160); Duch Mestres 1993 (n-41); Moorfields 1982 (n=128); Macular Photocoagulation Study Group - MPS Argon Extra 1982 (n=224); Macular Photocoagulation Study Group - MPS Krypton Juxta 1990 (n=496); Macular Photocoagulation Study Group - MPS Subf. New 1991 (n=371); Macular Photocoagulation Study Group - MPS Subf. Recurrent 1991 (n=206); Bressler 2000 & Submacular Surgery Trials Research Group 2000 - SST 2000 (n=70); Versteeg-Tijmes 1982 (n=13, excluding 13 non-ARMD eyes); Yassur 1982 (n=96)
Wormald et al, 2008[134] *Photodynamic therapy for neovascular age-related macular degeneration*	To examine the effects of photodynamic therapy in the treatment of ARMD	CCRCT, MEDLINE EMBASE through March 2007; Science Citation Index (no date specified); expert recommendation	RCTs of photodynamic therapy (vs another treatment, placebo or no treatment) in ARMD patients	3 trials (7 publications) Primary publications: Treatment of Age-related Macular Degeneration with Photodynamic Therapy Study Group - TAP 1999 (n=609); Visudyne in minimally classic choroidal neovascularisation study - VIM 2005 (n=117); Verteporfin in Photodynamic Therapy Study Group - VIP 2001 (n=2001); total n=1065 pts

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Main efficacy outcome
Virgili et al, 2008[45] *Laser photocoagulation for age-related macular degeneration*	RCTSs - various laser treatments vs no or sham treatment	Mean age: NR All participants had diagnosis of ARMD, although this was defined in only 5 studies; CNV location: subfoveal (7 studies); extrafoveal and/or juxtafoveal (8 studies)	12 studies: Photocoagulation vs no treatment 1 study: photocoagulation vs surgery 1 study: argon vs krypton laser wavelength 1 study: argon vs dye red laser wavelength	Changes in visual acuity and contrast sensitivity (Secondary outcomes: reading ability, performance in vision-related tasks, QOL)
Wormald et al, 2008[134] *Photodynamic therapy for neovascular age-related macular degeneration*	3 RCTs: verteporfin IV + laser vs placebo IV + laser	ARMD patients 2 trials: mean age 75 years; 98% white 1 trial: NR	IV verteporfin (2 trials: 6 mg/m2; 1 trial dose NR) + cold laser vs placebo + cold laser	Prevention of visual loss, based on visual acuity

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Main efficacy results	Harms results
Virgili et al, 2008[45] *Laser photocoagulation for age-related macular degeneration*	Direct photocoagulation vs no treatment Visual acuity at 3 months: NNH 20 (CI 13 to 100) Reading ability at 3 years: NNT 6 (CI 3 to 33); at 5 years: NNT 7 (CI 4 to 33) Perifoveal photocoagulation of subfoveal CNV Visual acuity, loss of 6 lines or more at 2 years*: NNT 3 (CI 2 to 8) *only timepoint with SS difference b/t treatment and control, although photocoagulation was favored for other timepoints Grid photocoagulation of subfoveal CNV Visual acuity, loss of 2 or more lines: RR 1.83 (CI 1.10 to 3.05); NNT 5 (CI 3 to 20) Photocoagulation vs surgery No SS difference between treatments, although surgery was favored for visual acuity and QOL outcomes Argon vs krypton lasers No difference between argon and krypton at 2 years in visual acuity changes	None reported
Wormald et al, 2008[134] *Photodynamic therapy for neovascular age-related macular degeneration*	Loss of >3 lines of visual acuity at 24 months: pooled RR (2 trials: TAP, VIP) 0.78 (CI 0.7-0.87); risk ratio reduction 0.22 (CI 0.13 to 0.30); NNT: 7 (population: patients with subfoveal choroidal neovascularization with baseline visual acuity 20/40-20/200) Loss of >6 lines of visual acuity at 24 months: pooled RR (2 trials: TAP, VIM) 0.60 (CI 0.49-0.73); risk ratio reduction 0.40 (CI 0.27-0.51); NNT: 7 (population: patients with subfoveal choroidal neovascularization with baseline visual acuity 20/40-20/200) Mean number of lines of vision lost at 24 months (1 trial: TAP): 2.7 lines verteporfin vs 1.2 control; mean difference 1.2 (p<0.001) No QOL outcomes reported	Acute severe visual acuity decrease (within 13 days of tx): Absolute risk difference 0.01 (CI 0.01 to 0.03); NNH 30 (range 30-100)

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Conclusion	Quality score
Virgili et al, 2008[45] *Laser photocoagulation for age-related macular degeneration*	Photocoagulation is effective for certain types of ARMD (extrafoveal CNV). For juxta-or sub- foveal CNV patients, the benefit of laser photocoagulation is less clear,	Good
Wormald et al, 2008[134] *Photodynamic therapy for neovascular age-related macular degeneration*	Photodynamic therapy is effective in preventing further visual loss due to AMD although the effect size is unclear.	Good

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Patients/trials
Cataracts				
Powe et al, 1994[91] *Synthesis of the literature on visual acuity and complications following cataract extraction with intraocular lens implantation*	To define the effectiveness and risks of cataract surgery	MEDLINE 1975-April 1991; reference lists	Original studies published between 1975 and April, 1991 with primary data on standard extracapsular extraction or phacoemulsification with posterior chamber IOL implantation or published between 1980 and April 1991 on intracapsular cataract extraction with flexible anterior chamber IOL implantation; visual acuity outcomes or complications were reported; English language	83 single-arm observational studies and 7 cohort studies Median n=231 (17 to 22,791)
Schaumberg et al, 1998[163] *A systematic overview of the incidence of posterior capsule opacification*	To obtain an estimate of the incidence of posterior capsule opaci-fication (PCO) and to explore factors that may influence its development	MEDLINE 1979-1996; reference lists	Studies of PCO published between 1979 and 1996 reporting total sample size, length of follow-up and postoperative rate of PCO; English language	49 studies (design NR); total n=NR

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Main efficacy outcome
Cataracts				
Powe et al, 1994[91] *Synthesis of the literature on visual acuity and complications following cataract extraction with intraocular lens implantation*	90 non-RCTs	Mean age: 71 years 58% female (reported in 23 studies)	22 studies: phacoemulsification; 58 studies: extracapsular extraction; 1 study: intracapsular extraction; 18 studies: mixed phacoemulsification and extracapsular extraction	Proportion of eyes with 20/40 or better visual acuity post-surgery
Schaumberg et al, 1998[163] *A systematic overview of the incidence of posterior capsule opacification*	49 studies	NR	27 studies: extracapsular extraction; 9 studies: phacoemulsification; 13 studies: mixed extracapsular extraction and phacoemulsification	Safety outcome: estimate of PCO occurrence 1, 3 and 5 years post-surgery (safety study, no efficacy outcomes)

Study, Year, Title	Main efficacy results	Harms results
Cataracts		
Powe et al, 1994[91] *Synthesis of the literature on visual acuity and complications following cataract extraction with intraocular lens implantation*	Pooled % of eyes with 20/40 acuity or better: 95.5% (CI 95.1% to 95.9%) in pts with no ocular comorbidities and 87% (CI 89.3% to 90.2%) for all eyes	Pooled rates - % (CI):Endophalmitis 0.13 (0.09 to 0.17) Bullous keratopathy 0.3 (0.2 to 0.4) Malposition/dislocation of IOL 1.1 (0.9 to 1.2) Clinical cystoid macular edema 1.4 (1.2 to 1.6)Angi-ographic cystoid macula edema 3.5 (2.9 to 4.0) Retinal detachment 0.7 (0.6 to 0.8) Posterior capsular opaci-fication 19.7 (19.1 to 20.3)
Schaumberg et al, 1998[163] *A systematic overview of the incidence of posterior capsule opacification*	NR	Pooled rate, incidence of PCO: 1 year: 11.8% (9.3%-14.3%) 3 years: 20.7% (16.6%-24.9%) 5 years: 28.4% (18.4%-38.4%)

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Conclusion	Quality score
Cataracts		
Powe et al, 1994[91] *Synthesis of the literature on visual acuity and complications following cataract extraction with intraocular lens implantation*	Cataract surgery yields excellent visual acuity and is relatively safe regardless of method of surgical extraction	Good
Schaumberg et al, 1998[163] *A systematic overview of the incidence of posterior capsule opacification*	Visually significant PC0 develops in more than 25% of patients undergoing extracapsular extraction or phacoemulsification with IOL within 5 years of surgery	Fair

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Patients/trials
Taban et al, 2005[164] *Acute endophthalmitis following cataract surgery*	To determine reported in-cidence of acute endo-phthalmitis following cat-aract extraction and to explore poss-ible contributing factors	Cochrane (database not specified); MEDLINE 1963-March 2003; reference lists; textbook hand search; conference proceedings and abstracts	Studies published in English of humans; primary or secondary cataract surgery with or without IOL; included post-surgery endophthalmitis outcomes	215 studies (design NR); total n=NR
Uncorrected refractive error				
Murray et al, 2005[85] *A systematic review of the safety and efficacy of elective photorefractive surgery for the correction of refractive error*	To systematically review the evidence for safety and efficacy of PRK, LASEK and LASIK for the correction of myopia, hyperopia and astigmatism	MEDLINE, MEDLINE Extra, EMBASE, BIOSIS, Science Citation Index, Cochrane Controlled Trials Register, National Research Register Clinical Trials, Current Controlled Trials, FDA Premarket Approval (PMA) Database Web of Science Proceedings, Conference Papers Index, Zetoc, Association for Research in Vision and Ophthalmology (ARVO) Abstracts Database, American Society of Cataract and Refractive Surgery-American Society of Ophthalmic Administrators (ASCRS-ASOA) Abstracts Database; 2000-2005	Studies published from 2000 onward; prospective studies with at least 300 eyes; retrospective case series with at least 500 eyes; RCTs comparing LASIK and PRK, LASIK and LASEK, and PRK and LASEK	LASIK: 4 trials, 64 case series (73 publications); LASEK: 14 RCTs (16 publications), 26 case series (40 publications); PRK: 9 RCTs, 40 case series

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Main efficacy outcome
Taban et al, 2005[164] *Acute endophthalmitis following cataract surgery*	215 studies	NR	NR	Incidence of acute endophthalmitis (safety study, no efficacy outcomes)
Uncorrected refractive error				
Murray et al, 2005[85] *A systematic review of the safety and efficacy of elective photorefractive surgery for the correction of refractive error*	27 RCTs; 130 case series	Adults undergoing photorefractive surgery for correction of myopia, hyperopia or astigmatism	Studies of primary treatment with any type of excimer laser used to perform PRK, LASEK, and LASIK for refractive correction of myopia, hyperopia or astigmatism	Achievement of the intended visual outcome, uncorrected visual acuity, stability of visual result and need for further refractive surgery Safety outcomes: incidence of serious complications and unintended consequence

Study, Year, Title	Main efficacy results		Harms results
Taban et al, 2005[164] *Acute endophthalmitis following cataract surgery*		NR	Pooled rate, incidence of endophthalmitis: 0.128% Rate 1963-1999: 0.109% Rate 2000-2003: 0.265% (RR 2.44. CI 2.27 to 2.61)
Uncorrected refractive error			
Murray et al, 2005[85] *A systematic review of the safety and efficacy of elective photorefractive surgery for the correction of refractive error*	Uncorrected visual acuity of 20/20 or better in myopia: PRK 70%, LASEK 62%, LASIK 64% 20/40 or better: PRK 92%, LASEK 92% and LASIK 94% Highly myopic eyes achieved High myopia at baseline, 20/20: PRK14% and LASIK 44% compared with Low myopia at baseline: PRK 76% and LASIK 81% Correction of myopia/myopic astigmatism, median across all 3 treatments: 68% to 75% of eyes achieving within 0.5 D of their intended correction; 86% to 92% of eyes achieved within 1.0 D. Correction of hyperopia: 61% of eyes achieved within 0.5 D of intended correction after PRK and LASIK; 79% and 88% for PRK and LASIK respectively within 1.0 D.		Ectasia (5 LASIK studies): median rate 0.2% (range 0% to 0.87%) Loss of ≥2 lines of BSCVA in myopia: PRK 0.5%, LASEK 0% and LASIK 0.6% Loss of ≥2 lines of BSCVA in hyperopia: PRK 7.0%, LASIK 3.5%

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Conclusion	Quality score
Taban et al, 2005[164] *Acute endophthalmitis following cataract surgery*	Incidence of endophthalmitis associated with cataract extraction has increased over the last decade and may be linked to the increasing use of sutureless clear corneal incisions	Fair
Uncorrected refractive error		
Murray et al, 2005[85] *A systematic review of the safety and efficacy of elective photorefractive surgery for the correction of refractive error*	The safety and efficacy of photorefractive surgery should be considered against the alternative methods of correction; adverse events occur rarely from a statistical standpoint.	Good

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Aims	Databases searched; Literature search dates; Other data sources	Eligibility criteria	Patients/trials
Virgili et al, 2008[39] *Reading aids for adults with low vision*	To assess the effects of reading aids for adults with low vision	CCRCT (Cochrane Central Register of Controlled Trials), MEDLINE, EMBASE, SIGLE, LILACS (Latin American and Caribbean Health Science Literature Database) and IndMed through July 2006; Science Citation Index; hand search British Journal of Visual Impairment 1983-1999 and Journal of Visual Impairment and Blindness1976-1991	RCTs or quasi-RCTs comparing any device to aid in low vision correction to another	9 trials: Culham 2004 (n=20); Eperjesi 2004 (n=12); Goodrich 2001 (n=22); Kleweno 2001 (n=13); Ortiz 1999 (n=10); Peterson 2003 (n=70); Smith 2005 (n=243); Spitzberg 1995 (n=39); Stelmack 1991 (n=37)

Abbreviations: AREDS = age-related eye disease study, ARMD = age-related macular degeneration, CI = confidence interval, CNV = choroidal neovascularisation, IOL = intraocular lenses, LASIK = laser assisted in situ keratomileusis, LASEK = laser assisted sub-epithelial keratomileusis, NEI-VFQ = national eye institute visual functioning questionnaire, NNH = number needed to harm, NR = not reported, PCO = posterior capsule opacification, PDT = photodynamic therapy, PRK = photorefractive keratectomy, RCT = randomized controlled trials, RR = relative risk, SR = systematic review, VECAT =vitamin E, cataract and age-related maculopathy study, VEGF = vascular endothelial growth factor.

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Characteristics of identified articles: study designs	Characteristics of identified articles: populations	Characteristics of identified articles: interventions	Main efficacy outcome
Virgili et al, 2008[39] *Reading aids for adults with low vision*	Within-subject design (8) and one parallel group RCT	Patients with low vision due to a variety of causes, including ARMD	Magnifiers, CCTV (stand-mounted and hand-held); prism spectacles	Increase in reading speed

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Main efficacy results	Harms results
Virgili et al, 2008[39] *Reading aids for adults with low vision*	Reading speed: prism spectacles were no better than conventional spectacles in the single study comparing them; for other interventions, there was no difference in reading speed among the treatments although this could have been due to problematic design and reporting among the included studies	None reported

APPENDIX C7. TREATMENT - SYSTEMATIC REVIEWS

Study, Year, Title	Conclusion	Quality score
Virgili et al, 2008[39] *Reading aids for adults with low vision*	No evidence supports any particular low vision reading aid over another; the studies included in the SR were of questionable quality and potential biased	Good

APPENDIX C8. QUALITY RATINGS OF TREATMENT SYSTEMATIC REVIEWS

Study, Year	Search dates	Search methods reported	Comprehensive search	Inclusion criteria reported	Selection bias avoided	Validity criteria reported
Evans et al, 2008[43] *Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration*	Up to August 2007	Yes	Yes	Yes	Yes	Yes
Evans et al, 2008[126] *Ginkgo biloba extract for age-related macular degeneration*	Up to January 2006	Yes	Yes	Yes	Yes	Yes
Meads et al, 2003[133] *Clinical effectiveness and cost-utility of photodynamic therapy for met age-related macular degeneration: a systematic review and economic evaluation*	Up to August 2001	Yes	Yes	Yes	Yes	Yes
Murray et al, 2005[85] *A systematic review of the safety and efficacy of elective photorefractive surgery for the correction of refractive error*	Up to 2006	Yes	Yes	Yes	Can't tell	Yes
Powe et al, 1994[91] *Synthesis of the literature on visual acuity and complications following cataract extraction with intraocular lens implantation*	Up to April 1991	Yes	Yes	Yes	Can't tell	Yes

APPENDIX C8. QUALITY RATINGS OF TREATMENT SYSTEMATIC REVIEWS

Study, Year	Validity assessed appropriately	Methods used to combine studies reported	Findings combined appropriately	Conclusions supported by data	Quality score
Evans et al, 2008[43] *Antioxidant vitamin and mineral supplements for slowing the progression of age-related macular degeneration*	Yes	Yes	Yes	Yes	Good
Evans et al, 2008[126] *Ginkgo biloba extract for age-related macular degeneration*	Yes	Yes	Yes	Yes	Good
Meads et al, 2003[133] *Clinical effectiveness and cost-utility of photodynamic therapy for met age-related macular degeneration: a systematic review and economic evaluation*	Yes	Yes	Yes	Yes	Good
Murray et al, 2005[85] *A systematic review of the safety and efficacy of elective photorefractive surgery for the correction of refractive error*	Yes	Yes	Yes	Yes	Good
Powe et al, 1994[91] *Synthesis of the literature on visual acuity and complications following cataract extraction with intraocular lens implantation*	Yes	Yes	Yes	Yes	Good

APPENDIX C8. QUALITY RATINGS OF TREATMENT SYSTEMATIC REVIEWS

Study, Year	Search dates	Search methods reported	Comprehensive search	Inclusion criteria reported	Selection bias avoided	Validity criteria reported
Schaumberg et al, 1998[163] *A systematic overview of the incidence of posterior capsule opacification*	Up to 1996	Partial	Can't tell	Yes	Can't tell	No
Taban et al, 2005[164] *Acute endophthalmitis following cataract surgery*	Up to March 2007	Yes	Yes	Yes	Yes	Yes
Vedula et al, 2008[142] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	Up to February 2008	Yes	Yes	Yes	Yes	Yes
Virgili et al, 2008[45] *Laser photocoagulation for age-related macular degeneration*	Up to March 2007	Yes	Yes	Yes	Yes	Yes
Virgili et al, 2008[39] *Reading aids for adults with low vision*	Up to July 2006	Yes	Yes	Yes	Yes	Yes
Wormald et al, 2008[134] *Photodynamic therapy for neovascular age-related macular degeneration*	Up to March 2007	Yes	Yes	Yes	Yes	Yes

APPENDIX C8. QUALITY RATINGS OF TREATMENT SYSTEMATIC REVIEWS

Study, Year	Validity assessed appropriately	Methods used to combine studies reported	Findings combined appropriately	Conclusions supported by data	Quality score
Schaumberg et al, 1998[163] *A systematic overview of the incidence of posterior capsule opacification*	No	Yes	Yes	Yes	Fair
Taban et al, 2005[164] *Acute endophthalmitis following cataract surgery*	Yes	Yes	Yes	Yes	Fair
Vedula et al, 2008[142] *Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration*	Yes	Yes	Yes	Yes	Good
Virgili et al, 2008[45] *Laser photocoagulation for age-related macular degeneration*	Yes	Yes	Yes	Yes	Good
Virgili et al, 2008[39] *Reading aids for adults with low vision*	Yes	Yes	Yes	Yes	Good
Wormald et al, 2008[134] *Photodynamic therapy for neovascular age-related macular degeneration*	Yes	Yes	Yes	Yes	Good