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Screening for Impaired Visual Acuity in Older Adults: A Systematic Review to Update the 2009 U.S. Preventive Services Task Force Recommendation

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Structured Abstract

Background: Impaired visual acuity is common in older adults. In 2009, the U.S. Preventive Services Task Force (USPSTF) found insufficient evidence to assess the balance of benefits and harms of screening for visual acuity in older adults (I statement).

Purpose: This review updates the prior USPSTF review and will be used by the USPSTF to update its 2009 recommendation. It focuses on screening for impaired visual acuity and treatment of the following conditions: uncorrected refractive errors, cataracts, and age-related macular degeneration (AMD).

Data Sources: We searched the Cochrane Central Register of Controlled Trials, the Cochrane Database of Systematic Reviews, and MEDLINE (2008 to January 2016) and manually reviewed reference lists.

Study Selection: At least two reviewers independently evaluated each study to determine inclusion eligibility. We selected studies on screening versus no screening, delayed screening, or usual care; the diagnostic accuracy of screening tests in primary care settings; and treatment versus sham therapy, placebo, or no treatment for uncorrected refractive errors, cataracts, and AMD.

Data Extraction: We abstracted details about the study design, patient population, setting, screening method, interventions, analysis, followup, and results. Two investigators independently applied criteria developed by the USPSTF to rate the quality of each study as good, fair, or poor using a consensus process.

Data Synthesis (Results): Three cluster-randomized trials (all previously included in the 2009 USPSTF review) found no difference between vision screening versus no vision screening, usual care, or delayed screening on vision and other clinical outcomes. New evidence on the effectiveness of treatments versus placebo, sham, or no treatment was limited and did not change prior conclusions that effective treatments are available for uncorrected refractive error, cataracts, and AMD. New evidence on the diagnostic accuracy of screening tests for impaired visual acuity was also limited and did not change conclusions that screening questions or a questionnaire are inaccurate compared to a visual acuity test (e.g., the Snellen eye chart) or that a visual acuity test has suboptimal accuracy compared to a comprehensive ophthalmological examination; however, the clinical relevance of visual conditions identified on a comprehensive ophthalmological examination but not associated with impaired visual acuity is uncertain.

Limitations: We included previously published systematic reviews, only included English-language studies, and could not assess for publication bias due to small numbers of studies.

Conclusions: Impaired visual acuity is common in older adults, effective treatments are available for common causes of impaired visual acuity, and vision impairment can be identified noninvasively using the Snellen or other visual acuity chart. However, direct evidence found that vision screening in older adults in primary care settings is not effective for improving visual acuity or other clinical outcomes.

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Chapter 1. Introduction

Purpose and Previous U.S. Preventive Services Task Force Recommendation

This review updates a 2009 review for the U.S. Preventive Services Task Force (USPSTF)[1,2] on screening for impaired visual acuity in older adults. It will be used by the USPSTF to update its 2009 recommendation.[3] This review focuses on screening for and treatment of impaired visual acuity associated with the following conditions: uncorrected refractive errors, cataracts, and age-related macular degeneration (AMD). Diabetic retinopathy and screening for glaucoma are not addressed in this update because they are addressed elsewhere by the USPSTF[4,5] and involve different screening approaches (e.g., visual field assessment, funduscopic examination, and intraocular pressure measurement) or are considered part of diabetes followup and management. For this review, we use the term "impaired visual acuity" rather than "vision impairment" because the latter term implies functional limitations, which may or may not be present. In addition, vision impairment can occur for reasons other than visual acuity loss. For the purposes of this review, "asymptomatic" individuals are defined as those without known impaired visual acuity (based on current corrected vision) and who have not sought care for evaluation of vision problems.

In 2009, the USPSTF concluded that the current evidence was insufficient to assess the balance of benefits and harms of screening for visual acuity for the improvement of outcomes in older adults (I statement).[3] Although the USPSTF found that impaired visual acuity is common and that effective treatments are available for uncorrected refractive error, cataracts, and AMD, direct evidence showed that screening for vision impairment in older adults in primary care settings is not associated with improved functional outcomes and may be associated with unintended harms, such as increased risk of falls.

Condition Definition

Impaired visual acuity refers to decreased clarity or sharpness of vision. In addition to decreased or substandard visual acuity, uncorrected impaired visual acuity can also be associated with decreases in lowlight vision, color vision, binocularity, contrast sensitivity, accommodation, 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 determined in primary care settings using the Snellen eye chart, which assesses high contrast visual acuity based on the ability of patients to recognize letters of different sizes arranged in rows from a prespecified 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. Impaired visual acuity has been defined as visual acuity of worse than 20/40[6] or 20/50[7] but better than 20/200 (the threshold for legal

blindness). Visual acuity can be measured with or without refractive correction; for the purposes of this review, impaired visual acuity refers to current corrected visual acuity.

High contrast visual acuity worse than 20/20 but better than 20/40 is generally thought to have minimal effects on reading ability, functional capacity, or quality of life. In the United States, the visual acuity standard for driving is 20/40 or better. Although the International Council of Ophthalmology defined mild impaired visual acuity in 2002 as worse than 20/25 and better than 20/80,[8] some studies have used a definition for mild impaired visual acuity of between roughly 20/40 and 20/80.[6,7] This degree of impaired visual acuity is less likely to cause major functional limitations than more severe impairment, and may be more apt to be unidentified without screening. Although these criteria focus on findings for high contrast visual acuity, even normal high contrast visual acuity can be associated with decreased low contrast visual acuity and contrast sensitivity.[9]

AMD, cataracts, refractive errors, and presbyopia are common causes of impaired visual acuity in older adults. AMD leads to blurred vision and development of scotomas that obscure central vision. AMD is the leading cause of legal blindness for persons older than age 65 years. Atrophic or "dry" macular degeneration accounts for 85 to 90 percent of AMD cases. Cataracts lead to blurring of vision, increased sensitivity to glare, and loss of sensitivity to differences in contrast. Refractive errors, such as myopia (nearsightedness) or hyperopia (farsightedness), occur when the eye is unable to bring parallel rays of light into focus on the fovea.[10] Presbyopia, which occurs as part of the natural aging process of the eye, is the loss of the eye's ability to change its focus to see objects that are near (farsightedness). This occurs as the eyes' lenses begin to lose flexibility around age 45 years, and affects most people at some point in life.

Prevalence and Burden of Disease

In 2011, approximately 12.2 percent of Americans ages 65 to 74 years, and 15.2 percent of those age 75 years or older reported having vision loss.[11] Prevalence of impaired visual acuity rises significantly with age in older adults, from 1.1 percent in persons ages 65 to 69 years to 16.7 percent in persons older than age 80 years,[12] and the prevalence of both blindness and impaired visual acuity increases with age, especially among people age 75 years and older.[13] Prevalence of specific causes of impaired visual acuity (i.e., AMD, cataracts, refractive errors, and presbyopia) varies, as described below.

AMD

The prevalence of AMD in the 2005 to 2008 National Health and Nutrition Examination Survey was 6.5 percent in persons older than age 40 years and increased with age (2.8% in ages 40 to 59 years and 11.1% in age ≥60 years).[14] AMD is more common among whites and Hispanics compared to blacks, especially among the very old (≥75 years).[14,15]

Cataracts

In persons with low vision (defined as best-corrected visual acuity <20/40), cataracts are the cause in approximately half of cases.[16] The prevalence of cataracts increases sharply with age. Approximately 22 million U.S. adults age 40 years and older were estimated to have cataracts (not necessarily associated with vision impairment) in 2011,[17] and 50 percent of those age 80 years and older are estimated to have cataracts. In white women, prevalence increases from 27.7 percent in ages 65 to 69 years to 76.6 percent in those age 80 years or older. In black women, respective prevalence rates are 28.5 and 60.9 percent, in white men they are 22.4 and 71.3 percent, and in black men they are 17.5 and 46.2 percent.

Refractive Errors

In older adults with impaired visual acuity due to hyperopia or myopia (including those currently using corrective lenses), approximately 60 percent have correctable (to better than 20/40) refractive errors.[7] In general, the prevalence of hyperopia increases sharply with age, with a prevalence that is 4.2 to 7.4 times higher in persons age 80 years or older compared to those ages 40 to 49 years.[10,15] The prevalence of hyperopia requiring a correction of +3.0 diopters (D) or more ranges from about 5.9 percent in U.S. adults ages 50 to 54 years, to 15.2 percent in adults ages 65 to 69 years, to 20.4 percent in adults age 80 years and older. At any age, hyperopia is more common in whites than blacks or Hispanics, and is also more prevalent in women than men. For example, among white men, the prevalence of hyperopia of +3.0 D or more is 3.6 percent among those ages 40 to 49 years, 14.1 percent among those ages 65 to 69 years, and 23.5 percent among those older than 80 years. Respective rates for white women are 3.7, 17.8, and 27.2 percent, and for black women they are 3.1, 10.6, and 13.5 percent. 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 percent.[10]

Among adults older than age 65 years, the prevalence of myopia is relatively stable with increasing age, though prevalence varies among different ethnic/racial groups. For example, the prevalence of myopia of less than -1.0 D in black men ages 65 to 69 years is 8.1 percent compared with 13.1 percent in Hispanic men and 17.7 percent in white men.[10] The prevalence of myopia requiring a correction of less than -1.0 D also tends to decrease with age and ranges from about 27.1 percent in U.S. adults ages 50 to 54 years, to 14.7 percent in adults ages 65 to 69 years, to 16.8 percent in adults age 80 years and older. At any age, myopia is also more prevalent in whites than blacks or Hispanics.

Presbyopia

The prevalence of presbyopia, or age-related hyperopia, increases with age and affects most people at some point in life. The onset of presbyopia generally occurs around age 45 years, though onset tends to be somewhat earlier in people who live in areas with higher ambient temperatures.[18]

Regardless of its cause, impaired visual acuity is consistently associated with decreased

functional capacity and quality of life in older people, including the ability to live independently, with more severe impaired visual acuity associated with greater negative effects.[19-23] 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, as well as increase risk of falls and other accidental injuries.[24-28] However, there is interindividual variability in the degree of functional impairment in persons with the same degree of impaired visual acuity. Vision loss is also associated with higher prevalence of depression and social isolation.[20,29] Of older adults experiencing impaired visual acuity, 57.2 percent are at risk for mild or moderate depression compared to 43.5 percent of those without vision loss.[30] When combined with other chronic health conditions, vision loss is associated with overall poorer health among people age 65 years and older.[13]

According to the Centers for Disease Control and Prevention, an estimated 61 million U.S. adults are at high risk for serious vision loss, which can cause a substantial social and economic toll, including disability, loss of productivity, and reduced quality of life.[31] Experts predict that by 2030, rates of severe vision loss will double or triple as the aging population increases[30-32] and the number of older adults (age ≥65 years) increases.[13,20,30,33] Direct medical expenses for older adults with impaired visual acuity in the United States are $8.3 billion annually,[13] including an estimated annual $6.8 billion for cataract treatment.[34]

Etiology and Natural History

Refractive errors are a general term to describe conditions associated with the inability of the 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.[35] 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 due to 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 that generally progress over time.[36]

AMD affects the macula, the area of the retina responsible for central vision.[37] Drusen, which are white to yellow retinal lesions, are an early sign of AMD when they occur in the macula. Advanced AMD is usually classified into "wet" or "dry" forms. The dry form of advanced AMD (also referred to as "geographic atrophy") is more common and associated with atrophy of the retinal layers and retinal pigmented epithelial cells. The wet form of AMD is associated with the development of abnormal blood vessels in the choroid layer underneath the retina (choroidal neovascularization). Both types of advanced AMD can cause blurred central vision, distorted vision, and decreased lowlight vision. In severe cases, advanced AMD results in central scotomas (complete loss of central vision).

Risk Factors

Prevalence of impaired visual acuity is higher among people of lower socioeconomic or educational status and those without private health insurance.[7,10] 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.[35] In both sexes and in various ethnic/racial groups, latent hyperopia tends to 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.[10] Risk factors for cataracts include older age, smoking, alcohol use, exposure to ultraviolet light, eye trauma, ocular inflammatory diseases, diabetes, and exposure to corticosteroids.[38,39] Lower socioeconomic status and black race are associated with higher rates of unoperated cataracts.[40] Risk factors for AMD are not completely understood, but are thought to include older age, smoking, white race, obesity, diet, elevated cholesterol, cardiovascular disease, and family history.[41,42] AMD is more common in whites compared to other races/ethnicities.[10]

The Behavioral Risk Factor Surveillance System Vision Impairment Expert Panel concluded that the most substantial barriers to vision preventive care, treatment, and rehabilitation appear to be behavioral issues, followed by cost and geographic access. Behavioral and cultural issues of concern included patient belief systems, trust issues, education and language barriers, health literacy issues, immigration status, and concordance between doctor and patient.[43]

Rationale for Screening/Screening Strategies

Impaired visual acuity due to uncorrected refractive error, cataracts, and AMD is common in adults and the prevalence increases with age.[10,16,44] 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 comorbid conditions. However, mildly impaired visual acuity may be associated with decreased quality of life and functional capacity and increased likelihood of accidents and related injuries.[19,21-23] Disparities exist among racial/ethnic groups, with higher age-specific prevalence of diabetic retinopathy, open-angle glaucoma, and impaired visual acuity. Screening for impaired visual acuity in the primary care setting is noninvasive and could potentially identify persons likely to benefit from referral for interventions to improve visual acuity or slow progression of ocular disease.[1]

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. Presbyopia is often corrected with prescription glasses, contact lenses, reading glasses, progressive addition lenses, or bifocals. Refractive errors may be remedied with corrective lenses, contact lenses, or refractive surgery. Photorefractive surgery, including laser in situ keratomileusis (LASIK), photorefractive keratectomy, or laser

epithelial keratomileusis (LASEK), is associated with more upfront costs compared to corrective lenses and more commonly selected as a treatment option by younger adults. The risks and benefits of laser eye surgeries shift at and after midlife. Older patients undergoing photorefractive surgery may be slightly less likely to experience optimal results and slightly more likely to need repeat treatment or enhancement.[45]

For patients with impaired visual acuity that is not sufficiently improved by correcting refractive error, reading aids (such as magnifiers) are a treatment option.[46] For cataracts causing significant impairment in visual acuity, the most common treatment is surgical cataract extraction and intraocular lens implantation.[47] Cataract surgery is effective in improving vision in 90 percent of patients, has a low complication rate, generally can be performed as an outpatient procedure, and can restore vision even in patients with advanced cataracts.[48]

Antioxidants and vitamins have been found to slow the progression of some types of AMD, but have no proven benefit in slowing cataract progression.[49-52] No treatment is known to reverse the retinal damage associated with dry AMD. The wet form of AMD accounts for most of the vision loss and blindness associated with advanced AMD. For both dry and wet AMD, early identification and treatment may help to prevent permanent effects on vision. Treatments for wet AMD 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 AMD, but causes blind spots due to retinal damage in areas of treatment.[46] It is generally considered a treatment option only in patients with extrafoveal neovascularization, in order to avoid causing central visual field defects.[46,53,54] Photodynamic therapy (PDT) with verteporfin, a photoreactive agent, is associated with less retinal scarring compared with laser photocoagulation and is an option for subfoveal neovascularization. Another treatment for wet AMD is intravitreal injection of a vascular endothelial growth factor (VEGF) inhibitor, such as bevacizumab, ranibizumab, or pegaptanib, in order to suppress growth of abnormal blood vessels. Other treatments that have been studied for wet AMD include surgical implantation of corticosteroids,[55] intravitreal interferon alfa,[56] radiation,[57] and other surgical procedures (submacular surgery and macular translocation). However, these therapies have either not been proven to be effective or have limited indications for use because the effects of dry or wet AMD may be irreversible.

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 (i.e., vision corrects or improves upon pinhole testing).[58] 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 change of color or 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.[59]

The Amsler grid consists of evenly spaced horizontal and vertical lines (making squares) on a sheet.[60] It is used to detect retinal defects affecting central vision, including AMD, 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.[61,62]

Screening questions may be used to elicit self-perceived problems with vision.[63] Funduscopic examination can also be performed in order to detect asymptomatic or early AMD or other retinal disease. The frequency with which nonSnellen visual acuity tests, the Amsler grid, vision screening questionnaires, or funduscopic examination is used in primary care is not known.[1] Older adults with impaired visual acuity are typically referred to an optometrist or ophthalmologist for further evaluation, correction of refractive error, and other treatments. In a study estimating the level of self-reported access to eye care services, approximately half of U.S. adults older than age 65 years reported receiving an eye examination within the last 12 months.[64]

Commonplace use of electronic devices, such as smartphones and computers, to view small type for many hours presents a variety of visual demands significantly different from those of printed materials. Therefore, examination procedures and treatment regimens might need to be reconsidered, since an inability to address the effects of these demands could affect individuals' quality of life.[65]

Recommendations of Other Groups

The American Optometric Association recommends an annual eye examination conducted by an optometrist for all adults older than age 60 years, and the American Academy of Ophthalmology recommends a comprehensive examination conducted by an ophthalmologist every 1 to 2 years in patients age 65 years or older (**Table 2**).[34,66] The American Academy of Family Physicians' recommendation on screening for visual acuity in older adults is in agreement with the 2009 USPSTF recommendation (insufficient evidence).[67]

Chapter 2. Methods

Key Questions and Analytic Framework

Using the methods developed by the USPSTF,[68] the USPSTF determined the scope and Key Questions for this review. In conjunction with the USPSTF, investigators created an analytic framework with the Key Questions and the patient populations, interventions, and outcomes reviewed (**Figure**). One Contextual Question was also requested by the USPSTF to help inform the review. Contextual Questions are not reviewed using systematic review methodology.

Key Questions

1. Does vision screening in asymptomatic older adults result in improved vision, morbidity or mortality, quality of life, functional status, or cognition?
2. Are there harms of vision screening in asymptomatic older adults?
3. What is the accuracy of screening for early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD?
4. Does treatment of early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD lead to improved visual acuity, morbidity, mortality, vision-related quality of life, functional status, or cognition?
5. Are there harms of treating early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD?

Contextual Question

1. What is a clinically meaningful difference in visual acuity?

Search Strategies

We used the National Library of Medicine's Medical Subject Headings (MeSH®) and keyword nomenclature to search Ovid MEDLINE®, Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews (2008 to February 2015) for relevant English-language studies, systematic reviews, and meta-analyses published since the prior USPSTF review. MEDLINE search strategies are listed in **Appendix A1**. An update search conducted on January 6, 2016 using the same databases identified no new studies that would affect the conclusions or understanding of the evidence, and therefore the related USPSTF recommendation. We also reviewed reference lists of relevant articles for additional citations.

Study Selection

At least two reviewers independently evaluated each study to determine inclusion eligibility. We selected studies on the basis of inclusion and exclusion criteria developed for each Key Question

(**Appendix A2**). For studies on screening and diagnostic accuracy, we included studies of asymptomatic adults age 65 years or older without known impaired visual acuity (based on current corrected vision) and who have not sought care for evaluation of vision problems. For screening, we included randomized, controlled trials and controlled observational studies (cohort and case-control studies) that evaluated vision screening performed in primary care or community-based settings versus no screening, delayed screening, or usual care (e.g., targeted screening) and evaluated visual acuity, vision-related quality of life, functional capacity (including ability to drive and driving outcomes), mortality, cognition, or harms (including falls and fractures). For diagnostic accuracy, we included studies on diagnostic accuracy of vision screening tests, questions, or questionnaires performed in primary care or community settings. For treatment, we included studies of asymptomatic adults with mild to moderate vision impairment (defined as best visual acuity worse than 20/40 but better than 20/200) due to uncorrected refractive errors, AMD, or cataracts that evaluated effects of corrective lenses, reading aids, or photorefractive surgery (for refractive errors); cataract surgery; or vitamins and antioxidants, laser therapy, PDT, and VEGF (for AMD) on the outcomes described above for screening. We focused on randomized, controlled trials of treatment versus no treatment, but included controlled observational studies if evidence from randomized trials was insufficient. We excluded studies of screening and diagnostic testing performed in specialty settings and excluded trials of treatment in patients with visual acuity worse than 20/200 or who had other causes of vision loss. The selection of literature is summarized in the literature flow diagram (**Appendix A3**). **Appendix A4** lists excluded studies with reasons for exclusion.

Data Abstraction and Quality Rating

We abstracted details about the study design, patient population, setting, screening method, interventions, analysis, followup, and results. Two investigators independently applied criteria developed by the USPSTF[68] to rate the quality of each study as good, fair, or poor (**Appendix A5**). Discrepancies were resolved through a consensus process.

Data Synthesis

We assessed the aggregate internal validity (quality) of the body of evidence for each Key Question (good, fair, or poor) using methods developed by the USPSTF, based on quality of studies, precision of estimates, consistency of results between studies, and directness of evidence.[68] Data synthesis was based on evidence from the prior review as well as new evidence.

External Review

The draft report was reviewed by content experts (**Appendix A6**), USPSTF members, AHRQ Project Officers, and collaborative partners and was posted for public comment.

Response to Public Comments

The draft report was posted for public comment from July 21, 2015 to August 17, 2015 and few comments were received. No comments identified missing studies that met inclusion criteria or errors in the evidence reviewed, resulting in no changes to the findings or the conclusion of the report.

Chapter 3. Results

Key Question 1. Does Vision Screening in Asymptomatic Older Adults Result in Improved Vision, Morbidity or Mortality, Quality of Life, Functional Status, or Cognition?

Summary

Three cluster-randomized trials included in the prior USPSTF review found no difference between vision screening versus no vision screening, usual care, or delayed screening on vision and other clinical outcomes. One trial included in the prior USPSTF review found that vision screening by an optometrist in frail elderly persons was associated with an increased risk for falls (rate ratio, 1.57 [95% CI, 1.20 to 2.05]) and a trend toward increased risk for fractures (relative risk [RR], 1.74 [95% CI, 0.97 to 3.11]). No study published since the prior review evaluated the effects of vision screening in asymptomatic older adults versus no vision screening, usual care, or delayed screening.

Evidence

We identified no study published since the prior USPSTF review that evaluated the effects of vision screening in asymptomatic older adults versus no screening, delayed screening, or usual care on visual acuity, morbidity, mortality, quality of life, functional status, or cognition. The prior USPSTF review included three fair- to good-quality cluster-randomized trials (n=4,728) performed in primary care–applicable settings of vision screening in older adults as part of a multicomponent screening intervention (**Appendix B1**).[69-71] One trial compared universal visual acuity testing (Glasgow acuity chart followed by pinhole testing for persons with visual acuity worse than 20/60) versus targeted screening based on a brief screening questionnaire,[71] one compared immediate versus delayed vision screening,[69] and one compared use of a screening question followed by visual acuity testing, if positive, versus usual care.[70] Three trials were conducted in community or general practice settings,[69-71] while one study that did not meet inclusion criteria for the present review was conducted in an optometry clinic.[72] Duration of followup ranged from 6 months to 5 years. None of the trials found beneficial effects on visual acuity, likelihood of vision disorders, or functional impairment related to vision with vision screening. In the highest-quality and largest (n=3,346) trial, universal vision screening identified about 10 times as many patients with impaired visual acuity and correctable impairment as did targeted screening, yet there was no difference in likelihood of visual acuity worse than 20/60 after 3- to 5-year followup (RR, 1.07 [95% CI, 0.84 to 1.36]).[71] In this trial, only half of the patients advised to see an eye care provider after vision screening actually received new glasses, which could have attenuated potential benefits. Other reasons for lack of benefit in the screening trials may include the high loss to followup in all trials, similar frequency of vision disorder detection and treatment in the screening and control groups in one trial,[70] use of a screening question to identify persons for further testing in one trial,[70] and low uptake of recommended interventions in one trial.[69]

A fourth, fair-quality trial included in the prior USPSTF review did not meet inclusion criteria for this update because it involved vision screening by an optometrist (visual acuity, contrast sensitivity, and visual field testing; slit lamp examination; and direct ophthalmoscopy).[72] It found that in frail older adults (n=309), vision screening was not associated with reduced risk of falls (rate ratio, 1.57 [95% CI, 1.20 to 2.05]) or fractures (RR, 1.74 [95% CI, 0.97 to 3.11]) after 1 year compared with usual care. Rather, an opposite effect was observed: screening led to new eyeglasses or referral for further treatment in about half (146 of 309 [47%]) of study participants. A subsequent report of this same study also found no difference between groups in improvement in vision or vision-related quality of life after 1 year.[73]

Key Question 2. Are There Harms Associated With Vision Screening in Asymptomatic Older Adults?

Summary

No study published since the prior USPSTF review addressed harms of vision screening in asymptomatic older adults. See Key Question 1 for evidence on falls.

Evidence

No study published since the prior USPSTF review addressed harms of vision screening in asymptomatic older adults. As described above in Key Question 1, the prior review included one trial that reported an increased risk of falls and a trend toward increased risk of fractures among frail older adults who underwent vision screening by an optometrist versus usual care.[72] No study included in the prior USPSTF review evaluated other harms such as anxiety, complications of treatment, or unnecessary interventions resulting from false-positive screening tests.

Key Question 3. What Is the Accuracy of Screening for Early Impairment in Visual Acuity Due to Uncorrected Refractive Error, Cataracts, or AMD?

Summary

The prior USPSTF review included four studies that found that screening questions or questionnaires are not accurate for identifying persons with impaired visual acuity compared with the Snellen eye chart, and four studies that found that visual acuity testing is not accurate for identifying the presence of vision conditions compared with a detailed ophthalmologic examination. Two studies published subsequent to the prior USPSTF review found that a computerized vision screening tool or a flipchart version were not accurate compared with a detailed eye examination (sensitivity, 0.80; specificity, 0.68) and one study found that the Minimum Data Set 2.0 (MDS) Vision Patterns section was associated with poor diagnostic accuracy compared with an eye chart examination.

Evidence

The prior review identified eight cross-sectional studies that evaluated the diagnostic accuracy of screening for impaired visual acuity in older adults (**Appendix B2, B3**).[74-81] Four studies assessed the diagnostic accuracy of screening questions or questionnaires, with none reporting both high sensitivity and specificity compared to a standard (Snellen) eye chart as the reference standard.[75,76,79,80] Positive likelihood ratios (PLRs) ranged from 1.19 to 3.23 and negative likelihood ratios (NLRs) ranged from 0.23 to 0.78; diagnostic odds ratios (DORs), the ratio of the odds of testing positive if the subject has the target condition to the odds of testing positive if the subject does not have the target condition ([true positives/false negatives]/[false positives/true negatives]), were similarly weak, ranging from 1.60 to 9.45. Four studies reported low diagnostic accuracy of visual acuity tests compared to complete examination by an ophthalmologist for identifying visual conditions.[74,77,80,81] However, 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 was unclear. No visual acuity test was associated with both high sensitivity and specificity; resulting PLRs ranged from 1.00 to 8.07 and NLRs ranged from 0.32 to 1.00, resulting in DORs of less than 10. The exception was one study, which found that presenting distance acuity of 20/40 or worse was 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 was associated with weaker 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 characteristic curve of 0.66 and 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 AMD, with results similar to those for identifying any visual condition.[77] No study compared the Snellen test to an established, clinically relevant reference standard for impaired visual acuity, possibly because the Snellen test is often considered the clinical standard for evaluating visual acuity. One study assessed the Amsler grid and reported poor accuracy for identifying visual conditions (PLR, 1.65; NLR, 0.91).[74] One study reported that 100 percent of cataract patients and 75 percent of AMD patients were correctly identified by a geriatrician compared to an ophthalmologist, with no false positives.[78]

Three fair-quality, cross-sectional studies (reported in two publications) published subsequent to the prior review evaluated the diagnostic accuracy of screening tests in primary care settings for impaired visual acuity in older adults (**Table 3**, **Appendix C1**, **C2**).[82,83] Sample sizes ranged from 189 to 371 patients. A methodological shortcoming in all of these studies was uncertainty whether the reference standard was interpreted independently from the target test. In addition, the studies did not use predefined thresholds for positive results.

Two studies evaluated a computerized vision screening tool (Computer Vision Screen), and one of the studies also evaluated a flipchart version of the tool.[82] The original version of the screening tool included questions on history and symptoms as well as six tests of vision function (near visual acuity, visual field, fixation disparity, stereoacuity, high contrast distance visual acuity, and low contrast distance visual acuity); two items (fixation disparity and stereoacuity) were subsequently dropped due to poor performance. The studies (n=180 and n=200) were conducted in the United Kingdom among community-recruited participants

age 65 years or older (mean age, 77 to 80 years), of which about 30 percent had cataracts, 30 to 39 percent had significant refractive error, 51 to 58 percent had correctable visual loss, and 22 to 29 percent had significant macular degeneration. Results for the computerized screening tool were combined across the two studies. Individual component items and various combinations were assessed for optimal sensitivity and specificity against a "gold standard eye exam" that included detailed history and symptoms, slit lamp and dilated funduscopic examination, tests of visual acuity, visual field, orthoptic tests, and others. Optimal sensitivity (0.80) and specificity (0.68) were observed with the combination of abnormal high contrast visual acuity (threshold >0.19 logMAR) or abnormal near visual acuity, resulting in a PLR of 2.5 and a NLR of 0.29 (DOR, 8.6). The flipchart instrument performed similarly, based on the low contrast visual acuity test alone (sensitivity, 0.75; specificity, 0.77; PLR, 3.26; NLR, 0.32; DOR, 10.2).

A third study (n=371) compared the scores on the MDS Vision Patterns section against a standard visual acuity (Early Treatment Diabetic Retinopathy Study [ETDRS] chart) test for detecting impaired visual acuity.[83] Participants age 55 years or older (mean age, 80.7 years) were recruited from nursing homes and assessed by trained research staff (not further described). The prevalence of impaired visual acuity was about 40 percent, mean near visual acuity was 0.56 in the better eye and 0.81 in the worse eye, and mean distance visual acuity was 0.43 in the better eye and 0.64 in the worse eye. The MDS Visual Patterns section is scored from 0 to 4, with 0 indicating adequate vision and 4 severely impaired vision. Diagnostic accuracy was poor using any cutoff score on the MDS Visual Patterns. Using a cutoff score of 1 or greater (0 indicating adequate vision and scores of 1 to 3 indicating various degrees of impairment), sensitivity of the MDS Visual Patterns section for detecting visual acuity worse than 20/40 was 0.52 and specificity was 0.75, resulting in a PLR of 2.11 and a NLR of 0.64.

Key Question 4. Does Treatment of Early Impairment in Visual Acuity Due to Uncorrected Refractive Error, Cataracts, or AMD Lead to Improved Morbidity or Mortality or Quality of Life?

Summary

For uncorrected refractive error and cataracts, the prior USPSTF review found evidence from a large body of observational data and accumulated clinical experience that refractive lenses and refractive surgery are highly effective at restoring normal or near-normal visual acuity. For mild uncorrected refractive errors, the prior USPSTF review included two randomized trials of corrective lenses that reported beneficial effects on vision-related quality of life but not functional status. We identified no new randomized trial or controlled observational study on treatment versus no treatment for mild uncorrected refractive errors.

For cataracts, the prior USPSTF review found evidence from observational studies that more than 90 percent of patients undergoing cataract surgery achieve visual acuity of 20/40 or better,

and one trial found that immediate cataract surgery was associated with decreased risk of falls (rate ratio, 0.66 [95% CI, 0.40 to 0.96]). Two cohort studies of cataract surgery versus no cataract surgery that were not included in the prior USPSTF review found no effects on cognitive function or quality of life, though visual acuity was improved following cataract surgery in both studies.

For dry AMD, the prior USPSTF review included one large randomized trial, the Age-Related Eye Disease Study (AREDS), which found that an antioxidant and zinc combination was effective for lower likelihood of AMD progression (adjusted odds ratio [OR], 0.66 [95% CI, 0.47 to 0.93]), although the difference in the likelihood of losing 15 letters or more of visual acuity was not statistically significant (adjusted OR, 0.75 [95% CI, 0.55 to 1.02]) after 6 years of followup. Ten-year followup results from AREDS are consistent with prior results, with antioxidant supplements alone (OR, 0.70 [95% CI, 0.56 to 0.88]) or with added zinc (OR, 0.66 [95% CI, 0.53 to 0.83]) associated with decreased risk of AMD progression and the combination associated with decreased risk of visual acuity loss (OR, 0.71 [95% CI, 0.57 to 0.88]). Evidence on the effects of other vitamins and mineral treatments remains limited, with no clear effects on AMD progression or visual acuity.

For wet AMD, the prior USPSTF review included systematic reviews that found laser photocoagulation to be associated with lower likelihood of losing 6 lines or more of visual acuity versus placebo (five trials; RR, 0.67 [95% CI, 0.53 to 0.83]) and PDT was associated with lower likelihood of losing 3 lines or more of visual acuity versus placebo (four trials; RR, 0.80 [95% CI, 0.73 to 0.88]). We identified no trials of laser photocoagulation or PDT published since the prior USPSTF review.

The prior USPSTF review included four trials of intravitreal injection with VEGF inhibitors versus sham therapy; an updated meta-analysis based on these trials found that VEGF inhibitors were associated with greater likelihood of gaining 15 letters or more of visual acuity (RR, 2.92 [95% CI, 1.20 to 7.12]) and greater likelihood of having vision of 20/200 or better versus sham injection (RR, 1.47 [95% CI, 1.30 to 1.66]); beneficial effects were also observed in one trial with 2 years of followup. One trial each found that intravitreal injection with VEGF inhibitors was associated with small improvements in vision-related function and likelihood of driving among participants driving at baseline.

Evidence

Uncorrected Refractive Error

We identified no new randomized trial or controlled observational study on effects of treatment versus no treatment for mild impaired visual acuity on vision, vision-related quality of life, or function. The prior USPSTF review found good evidence from a large body of observational data and accumulated clinical experience that corrective lenses are highly effective at restoring normal or near-normal visual acuity. For mild uncorrected refractive errors, the prior USPSTF review included two randomized trials on the effects of immediate versus delayed corrective lenses (**Appendix B4**).[84,85] One trial provided a prescription and voucher for free eyeglasses,[84] while the other trial directly provided prescription glasses.[85] In one trial of community-dwelling

adults age 65 years or older,[84] mean baseline visual acuity was 20/63; in the other trial,[85] which evaluated nursing home patients age 55 years or older, about 30 percent were moderately myopic (-0.50 to -2.00 D), 30 percent were moderately hyperopic (+0.50 to +2.00 D), and about 25 percent had minimum impaired visual acuity (-0.50 to +0.50 D). Both trials reported improvements in vision-related quality of life in patients with immediate eyeglasses versus delayed treatment, and one of the trials[85] reported improvements in depressive symptoms. However, few differences in measures of general functional status or quality of life were found. A report from one of these studies[85] published subsequent to the USPSTF review also found no effects on function or cognitive status as measured by the Functional Independence Measure, Survey of Activities and Fear of Falling, Nursing Home Life-Space Diameter, and the Mini-Mental State Examination (**Appendix C3**).[86]

The prior review also included a large systematic review[87] of 27 randomized trials and 130 observational studies that found refractive surgery to be highly effective at improving refractive error (92% to 94% of persons with myopia and 86% to 96% with hyperopia achieved visual acuity of 20/40 or better) (**Appendix B5**), and three observational studies that found refractive surgery to be associated with improved quality of life.[88-90]

Cataracts

The prior USPSTF review identified no trials of cataract surgery versus no surgery, but included one systematic review of observational studies that found cataract surgery to be associated with improved visual acuity of 20/40 or better in more than 90 percent of patients and in 89 percent of all eyes (n=17,390) (**Appendix B6**).[91] One trial found that immediate cataract surgery was associated with a decreased risk of a second (but not first) fall, resulting in a lower overall risk of falls (rate ratio, 0.66 [95% CI, 0.40 to 0.96]).[92] Another trial found no effect of immediate second-eye surgery on risk of falls or fracture risk.[93] One trial of antioxidant vitamins versus placebo found no difference in risk of progression of cataract opacities (**Appendix B7**).[94]

Two fair-quality prospective cohort studies published since the prior USPSTF review assessed the effects of cataract surgery versus no surgery on measures of function or quality of life (**Appendix C3**, **C4**).[86,95] One study (n=45) conducted in U.S. nursing home patients age 55 years or older found no differences between cataract surgery and no surgery in measures of function and cognition after 4 months of followup, based on the Functional Independence Measure, Survey of Activities and Fear of Falling, Nursing Home Life-Space Diameter, and the Mini-Mental State Examination, despite improvement in visual acuity (distance acuity of 0.74 logMAR at baseline vs. 0.25 logMAR after surgery).[86] An earlier report from this study reported no differences on the Short Form-36, the Geriatric Depression Scale, or the Cataract Symptom Score, though cataract surgery was associated with improvements in vision-targeted health-related quality of life as measured by the Nursing Home Vision-Targeted Health-Related Questionnaire and the VF-14 (improvement on the VF-14 of 24.9 points following cataract surgery vs. 1.5 points without cataract surgery; p=0.004 after adjustment for age).[96] Another study (n=301) conducted in U.S. ophthalmology clinics among cataract patients age 55 years or older found no differences between cataract surgery versus no surgery in cognitive function (based on the Mattis Organic Mental Syndrome Screening Examination), though both groups improved from baseline.[95] There was also no effect of cataract surgery on depression (based on

the Center for Epidemiological Studies Depression Scale). Visual acuity improved following cataract surgery (visual acuity in worse eye of 0.55 logMAR at baseline vs. 0.28 logMAR after surgery), with no change in the no surgery group. Methodological shortcomings in the studies included lack of blinding of outcomes assessors and baseline differences in age, sex, comorbid conditions, and visual acuity. One study did not attempt to adjust for potential confounders.[86]

Dry (Nonexudative) AMD

Antioxidant Vitamins and Minerals and Other Supplements

The prior USPSTF review[1] included results from the large, good-quality AREDS[97] trial and a good-quality systematic review of nine trials (total n=5,769) of antioxidant supplements (**Appendix B8, B9**).[98] Since publication of the prior review, longer followup from the AREDS trial[99] and an updated version of the antioxidant systematic review,[100] with four additional trials (total n=6,510),[101-104] has been published. We also identified three other recently published, placebo-controlled trials[105-107] not included in the systematic review.

The sample sizes of trials included in the updated systematic review of antioxidant supplements versus placebo or no intervention ranged from 20 to 400 in 11 trials; two other trials (AREDS and the Vitamin E, Cataract, and Age-related Maculopathy[VECAT] Study) enrolled larger samples (n=2,556 and 1,204) (**Appendix C5**, **C6**). The interventions evaluated were zinc (five trials), lutein (two trials), vitamin E (one trial), antioxidant combination (four trials), or multiple interventions (one trial). Mean age ranged from 65 to 75 years (in 11 trials; two trials did not report mean age) and the proportion of females from 4 to 80 percent. Best-corrected visual acuity at baseline ranged from near-normal ,20/23 (0.073 logMAR), to 20/80 (0.60 logMAR). Mean duration of followup ranged from 6 months to 7 years. Quality of studies included in the systematic review was assessed using Cochrane Collaboration risk of bias criteria,[108] which included assessment of method of randomization, allocation concealment, blinding, and attrition. Most studies were judged to have low risk of bias (i.e., good quality), including the two largest studies, AREDS and VECAT.[100] In AREDS, the largest trial, participants were randomized to a daily antioxidant supplement containing vitamin C, E, and beta carotene, zinc, a combination of antioxidant supplement, and zinc or placebo. Nearly half of AREDS participants were age 70 years or older at baseline, 56 percent were women, and 96 percent were white. More than half were either current (8%) or former (48%) smokers. Participants were categorized according to baseline AMD severity, ranging from Category 1 (no existing AMD and <5 drusen) to Category 4 (advanced AMD with central geographic atrophy or neovascular AMD). Patients were required to have baseline best-corrected visual acuity of 20/32 (0.20 logMAR) or better. Followup from AREDS is now available through 10 years (**Appendix C7**).[99]

The three new trials not included in the systematic review[105-107] enrolled smaller samples than AREDS (n=84 to 300) and had shorter duration of followup (48 weeks to 3 years) (**Appendix C7**). Two studies evaluated lutein, either alone[105] or in combination with zeaxanthin,[106] while the third evaluated fish oil supplementation (containing 840 mg docosahexaenoic acid, 270 mg eicosapentaenoic acid, and 2 mg vitamin E).[107] Mean age of participants ranged from 69 to 74 years, and more than half were female (56% to 69%). The studies were conducted in China,[106] the United Kingdom,[105] and France.[107] Mean best-corrected visual acuity at baseline ranged from

20/22 to 20/40 (0.05 to 0.30 logMAR). All three trials were rated good quality (**Appendix C8**).

Mortality. Two trials reported effects of vitamins and minerals on mortality (**Table 4**).[99,107] Mortality outcomes were reported for AREDS severity categories 2, 3, and 4. After 10-years followup, AREDS found no significant difference between antioxidant use versus nonuse in risk of all-cause mortality (hazard ratio [HR], 1.06 [95% CI, 0.93 to 1.21]), cardiovascular mortality (RR, 1.20 [95% CI, 0.97 to 1.49]), or cancer mortality (RR, 0.94 [95% CI, 0.74 to 1.20]) after adjustment for age, sex, race, education, smoking status, body mass index, diabetes, angina, cancer, and hypertension.[99] However, for zinc use versus nonuse, there was a significant reduction in risk of all-cause (adjusted HR, 0.83 [95% CI, 0.73 to 0.95]) and cardiovascular mortality (adjusted RR, 0.80 [95% CI, 0.64 to 0.99]), though effects on cancer mortality were not statistically significant (adjusted RR, 0.84 [95% CI, 0.65 to 1.08]). In the second trial (n=300), daily fish oil was not associated with a statistically significant decrease in mortality risk versus placebo, though the estimate was imprecise and favored the intervention (2.2% [3/134] vs. 4.7% [6/129]; RR, 0.48 [95% CI, 0.12 to 1.88]).[107]

AMD progression and changes in visual acuity. The prior USPSTF review[1] included 6-year results from AREDS, which found a daily combined antioxidant supplement to be associated with reduced risk of AMD progression versus placebo (adjusted OR, 0.66 [99% CI, 0.47 to 0.93]).[97] Visual acuity outcomes were reported for the subgroup of patients in whom treatment is currently recommended (AREDS severity categories 3 and 4). Ten-year followup from AREDS reported similar results for antioxidant supplements alone (OR, 0.70 [95% CI, 0.56 to 0.88]) or with added zinc (OR, 0.66 [95% CI, 0.53 to 0.83]) (**Table 4**).[99] For zinc alone, results favored treatment, but the difference was not statistically significant (OR, 0.82 [95% CI, 0.66 to 1.02]).

Although the systematic review[100] included three other trials that reported effects of antioxidants or vitamins on risk of AMD progression, results were not pooled because of high statistical heterogeneity and none of the trials were new since publication of the prior USPSTF review (**Appendix C5, C6**). No statistically significant effects were observed in any of the trials; two small trials (n=58 and 78) evaluated zinc alone (OR, 0.50 [95% CI, 0.05 to 4.79][109] and 2.31 [95% CI, 0.58 to 9.26]),[110] and one larger trial (n=1,179) evaluated vitamin E alone (OR, 1.11 [95% CI, 0.80 to 1.55]).[111]

The prior USPSTF review included 6-year results from AREDS, which found that use of an antioxidant supplement was associated with a nonstatistically significant reduction in risk of loss of 15 letters or more of visual acuity versus placebo (adjusted OR, 0.75 [95% CI, 0.55 to 1.02]).[97] At 10-year followup, the combination of antioxidants plus zinc was associated with decreased risk of visual acuity loss (OR, 0.71 [95% CI, 0.57 to 0.88]) (**Table 4**); effects of an antioxidant alone or zinc alone were similar but remained statistically nonsignificant.[99] One trial (n=300) published subsequent to the prior USPSTF review found no difference between supplementation with fish oil capsules versus placebo in risk of visual acuity loss of 15 letters or more after 3 years (RR, 1.25 [95% CI, 0.69 to 2.26]).[107]

Two trials published since the prior USPSTF review evaluated effects of lutein with and without zeaxanthin on visual acuity.[105,106] In one trial (n=108), there was no difference between daily use of lutein or lutein plus zeaxanthin versus placebo in mean change in visual acuity from baseline

after 48 weeks of followup (**Table 4**).[106] In the second trial (n=84), daily use of lutein was associated with very small effects on visual acuity, with no clear difference versus placebo (0.01 logMAR improvement vs. -0.04 logMAR decline).[105]

Other outcomes. Long-term followup of AREDS participants at risk of developing advanced AMD found no significant difference in need for cataract surgery in participants taking any active AREDS intervention compared with placebo (RR, 1.01 [95% CI, 0.91 to 1.12]) (**Table 4**).[112] Another trial found that a daily fish oil supplement was associated with a marginally significant decrease in risk of developing cataracts, worsening cataract, or need for cataract surgery (RR, 0.80 [95% CI, 0.64 to 0.99]).[107]

Wet (Exudative) AMD

Laser Photocoagulation

The prior USPSTF review[1] included a good-quality Cochrane systematic review on the effects of laser photocoagulation versus no photocoagulation (12 trials; n=1,932) (**Appendix B8**).[113] We identified no new studies published since the prior USPSTF review comparing laser photocoagulation with no treatment.

The trials included in the systematic review compared either direct or grid laser photocoagulation versus no treatment. Enrollees were age 50 years and older, with a mean age of 70 to 74 years in three trials. In nine studies that reported sex, 50 to 77 percent were female. Mean baseline visual acuity ranged from 20/40 to 20/200 or better (0.03 to 1.00 logMAR), and the location of choroidal neovascularization associated with AMD (foveal, juxtafoveal, or extrafoveal) varied. Duration of followup ranged from 2 months to 5 years. The trials had methodological shortcomings, including use of open-label design, incomplete followup, lack of intention-to-treat analysis, and others.[1]

AMD progression and changes in visual acuity. Pooled estimates from the Cochrane review[113] found that laser photocoagulation was more effective than no treatment at preventing loss of 6 lines or more of visual acuity at 2-year followup (five trials; RR, 0.67 [95% CI, 0.53 to 0.83]; I^2=58%) (**Appendix B8**).[1] After 3- and 5-year followup, participants receiving laser photocoagulation were more likely to have visual acuity of 20/200 or better versus those who received no treatment (three trials; RR, 0.73 [95% CI, 0.61 to 0.86]; I^2=43%; and two trials; RR, 0.77 [95% CI, 0.66 to 0.90]; I^2=21%).

Other outcomes, including mortality, were not reported.

PDT

The prior USPSTF review[1] included a good-quality Cochrane systematic review of PDT for wet AMD (**Appendix B8**).[114] Though the Cochrane review was updated in 2009, no new trials were identified. We also identified no additional trials published since the prior USPSTF review.

The 2007 Cochrane systematic review included four trials (n=117 to 609; total n=1,210) of PDT

with verteporfin versus placebo. This included the large Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) trial,[115] which accounted for slightly less than half (n=609) of the total population included in the systematic review. TAP and two other trials, the Visudyne in Minimally Classic (VIM)[116] and Visudyne in Occult (VIO)[117] Choroidal Neovascularization trials, enrolled similar populations; mean age ranged from 75 to 79 years, 56 to 64 percent were female, and baseline visual acuity was about 20/80. The fourth trial, the Verteporfin in Photodynamic Therapy (VIP) trial,[118] enrolled a younger population (mean age, 49 years; 67% female) with slightly better visual acuity at baseline (20/64). Study duration in all trials was 2 years.

Mortality. The prior review found no difference between PDT with verteporfin versus placebo in risk of all-cause mortality, based on the TAP (3% vs. 4%; RR, 0.84 [95% CI, 0.35 to 1.99]) and VIP (2% vs. 3%; RR, 0.68 [95% CI, 0.15 to 2.97]) trials.[115,118] The VIM trial[119] reported no deaths in either the PDT or placebo group after 2-year followup.

AMD progression and changes in visual acuity. The systematic review found that PDT with verteporfin was associated with lower likelihood of losing 3 lines or more of visual acuity at 12-month (four trials; RR, 0.80 [95% CI, 0.69 to 0.93]; I^2=30%) and 24-month (four trials; RR, 0.80 [95% CI, 0.73 to 0.88]; I^2=0%) followup versus placebo (**Appendix B8**).[114] Patients undergoing PDT were also more likely to gain 3 lines or more of visual acuity at 12-month (three trials; RR, 2.19 [95% CI, 0.99 to 4.82]; I^2=0%) and 24-month followup (three trials; RR, 2.55 [95% CI, 1.31 to 4.99]; I^2=0%).

VEGF Inhibitors

The prior USPSTF review included a good-quality Cochrane systematic review[120] on the effectiveness of intravitreal injection with VEGF inhibitors, though only three trials (the Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular Age-Related Macular Degeneration [MARINA] trial[121] and two VEGF Inhibition Study in Ocular Neovascularization [VISION] trials, reported in one publication[122]; total n=1,906) compared VEGF inhibitors versus sham (**Appendix B8**). The prior USPSTF review included one additional trial (the Phase IIIB, multicenter, randomized double-masked sham Injection-controlled study of the Efficacy and safety of Ranibizumab [PIER] trial) (**Appendix B9**).[123] The systematic review was updated in 2014 to include results from the PIER trial; no other new trials of VEGF inhibitors versus sham or placebo were added.[124] Pooled estimates from the 2014 Cochrane review are of limited utility for our review, as many analyses included results from a trial[125] comparing VEGF inhibitors to PDT. Our literature search identified additional long-term followup from the MARINA trial (n=716) (**Appendix C9**).[126]

The four trials[121-123] of VEGF inhibitors versus sham injection (MARINA, PIER, and the VISION trials) enrolled 184 to 716 participants; 50 to 65 percent were female (**Table 5**). Mean age was 77 and 79 years in two studies, while in the other two studies, 62 percent of the population was older than age 75 years. Baseline visual acuity was about 20/80 in three studies, while in the fourth study, 72 percent of the population had baseline visual acuity between 20/40 and 20/200. The MARINA and PIER trials evaluated ranibizumab 0.3 to 0.5 mg every 1 to 3 months or sham injection,[121,123] and the VISION trials evaluated pegaptanib (0.3 to 3.0 mg).[122]

For the PIER trial, we only included 1-year results, as the sham group was discontinued during the second year due to a study protocol change. All trials were rated good quality (**Appendix C10**).

Mortality and other nonocular health outcomes. The MARINA trial previously found no difference between ranibizumab versus placebo in all-cause (2% vs. 3%; RR, 0.91 [95% CI, 0.34 to 2.44]) or vascular (1% vs. 2%; RR, 0.74 [95% CI, 0.21 to 2.60]) mortality after 2-year followup (**Table 5**).[121] There were no deaths in either group in the PIER trial,[123] and the VISION trials did not report mortality.[122] In MARINA, there was also no difference between ranibizumab and sham in risk of myocardial infarction (2% vs. 2%; RR, 1.12 [95% CI, 0.35 to 3.60]) or cerebrovascular accident (RR, 2.24 [95% CI, 0.49 to 10]) (**Table 5**).[121] The PIER trial reported no myocardial infarctions or cerebrovascular accidents in either group after 1 year.[123]

AMD progression and changes in visual acuity. Based on pooled estimates from a good-quality Cochrane systematic review,[120] the prior USPSTF review found that intravitreal injection of the VEGF inhibitors pegaptanib (two trials; RR, 0.71 [95% CI, 0.60 to 0.84]) and ranibizumab (one trial; RR, 0.14 [95% CI, 0.08 to 0.25]) were more effective at preventing visual acuity loss than no or sham treatment (**Appendix B8**).[1] Pooling data from all four trials,[121-123] VEGF inhibitor treatment was associated with greater likelihood of gaining more than 15 letters of visual acuity (RR, 2.92 [95% CI, 1.20 to 7.12]; absolute risk difference, 10% [95% CI, -7% to 27%]) (**Appendix D1**) and losing less than 15 letters of visual acuity (RR, 1.46 [95% CI, 1.22 to 1.75]; absolute risk difference, 27% [95% CI, 12% to 42%]) (**Appendix D2**) after 1-year followup compared with sham injection, though heterogeneity was high for both estimates (I^2=76% and 80%.) Use of VEGF inhibitors also resulted in greater proportions of patients with vision of 20/200 or better after 1-year followup versus sham injection (RR, 1.47 [95% CI, 1.30 to 1.66]; I^2=42%; absolute risk difference, 24% [95% CI, 12% to 37%]) (**Appendix D3**; **Table 5**). Only the MARINA trial[121] reported effects of VEGF inhibitors versus sham at 2-year followup; ranibizumab was associated with greater likelihood of gaining 15 letters or more of visual acuity (RR, 7.86 [95% CI, 4.08 to 15]), losing less than 15 letters of visual acuity (RR, 1.72 [95% CI, 1.52 to 1.94]), and having 20/200 vision or better (RR, 1.63 [95% CI, 1.44 to 1.86]) (**Table 5**).[121]

In posthoc subgroup analyses, the MARINA trial also found that in patients with visual acuity worse than 20/40 at baseline, ranibizumab was associated with greater likelihood of improvement to 20/40 or better after 1-year (27.9% vs. 10.6%; RR, 2.64 [95% CI, 1.41 to 4.92]) or 2-year (31.9% vs. 7.7%; RR, 4.13 [95% CI, 2.03 to 8.42]) followup (**Appendix C9**).[126] Patients with visual acuity better than 20/40 (0.3 logMAR) in at least one eye at baseline were also more likely to maintain good visual acuity (77.2% vs. 56.4% at 2 years; RR, 1.37 [95% CI, 1.14 to 1.64]).

Vision-related function. The prior USPSTF review found that ranibizumab was associated with better vision-related function scores at both 1- and 2-year followup compared with sham.[127] Changes from baseline in composite National Eye Institute Visual Function Questionnaire (NEI-VFQ) 25 scores favored ranibizumab, as did subscale scores for general vision, mental health, social functioning, and driving (**Appendix B9**). However, mean differences (<10 points on a 0 to 100 scale) were below criteria for clinically important differences.[127]

MARINA results on driving status published since the prior USPSTF review found that ranibizumab 0.3 and 0.5 mg was associated with increased likelihood of driving at 24 months in patients who were driving at baseline versus sham (81% vs. 78% vs. 67%, respectively; $p<0.05$ for both doses versus sham), though there was no difference in the proportion of drivers at 24 months among those who were not driving at baseline (9% for 0.5 mg dose vs. 7% for sham; p=0.65) (**Appendix C9**).[126]

Key Question 5. Are There Harms Associated With Treating Early Impairment in Visual Acuity Due to Uncorrected Refractive Error, Cataracts, or AMD?

Summary

The prior USPSTF review included one study reporting a higher risk of falls in older adults using multifocal lenses compared to unifocal lenses (OR, 2.09 [95% CI, 1.06 to 4.92]); three studies that reported an incidence of infectious keratitis that ranged from 0.3 to 3.6 cases per 10,000 contact lens wearers; and rates of corneal ectasia of 0 to 0.87 percent, based on five studies of LASIK, and rates of keratitis of 0 to 3.4 percent, based on six studies of LASIK and four studies of LASEK. No study published since the prior USPSTF review assessed harms of treatment of uncorrected refractive error compared to no treatment.

The prior USPSTF review included three systematic reviews on harms of cataract surgery, which reported pooled rates of posterior lens opacification of 28 percent after 5 years and 0.13 percent for endophthalmitis. No study published since the prior USPSTF review assessed the harms of cataract surgery versus no surgery.

The prior USPSTF review included a systematic review that found laser photocoagulation to be associated with greater risk of acute loss of 6 lines or more of visual acuity versus no treatment (3 months; RR, 1.41 [95% CI, 1.08 to 1.82]), and PDT was associated with increased risk of loss of 20 letters or more of visual acuity within 7 days of treatment versus placebo (three trials; RR, 3.75 [95% CI, 0.87 to 16]). One of two trials found that intravitreal VEGF inhibitor therapy was associated with greater likelihood of withdrawal versus sham; there were no differences in serious or other adverse events, but estimates were imprecise.

Evidence

Refractive Error

One small (n=156) prospective study[128] included in the prior USPSTF review found multifocal lenses to be associated with a higher risk of falls in older adults versus unifocal lenses (OR, 2.09 [95% CI, 1.06 to 4.92]). Three studies[129-131] found incidence of infectious keratitis ranging from 0.3 to 3.6 cases per 10,000 contact lens wearers; one study found incidence to be higher in persons older than age 50 years.[132] A meta-analysis reported corneal ectasia rates ranging from 0 to 0.87 percent in five studies of LASIK and keratitis rates ranging from 0 to 3.4 percent in six

studies of LASIK and four studies of LASEK.[87]

No study published since the prior USPSTF review assessed harms of treatment of uncorrected refractive error versus no treatment or usual care.

Cataracts

The prior USPSTF review included three systematic reviews[91,133,134] of numerous observational studies of cataract surgery, which found a pooled rate of posterior capsule opacification (clouding of the implanted lens, which leads to impairment of high- and low-contrast visual acuity and glare sensitivity) of 28 percent after 5 years and a pooled rate of 0.13 percent for endophthalmitis.

No study published since the prior USPSTF review assessed harms of cataract surgery versus no treatment or usual care.

AMD

Antioxidant Vitamins and Minerals and Other Supplements

The prior USPSTF review[1] found that use of antioxidant vitamins and mineral supplements was not associated with increased risk of most adverse events, based on evidence from a good-quality systematic review (**Appendix B8**).[98] Previous AREDS trial evidence found that use of zinc was associated with increased risk for hospitalization due to genitourinary causes versus nonuse (RR, 1.47 [95% CI, 1.19 to 1.80])[135] and use of an antioxidant supplement was associated with increased risk of skin yellowing compared to nonuse (RR, 1.38 [95% CI, 1.09 to 1.75]).[97]

Two trials published subsequent to the prior USPSTF review reported harms associated with use of vitamin and mineral supplements (**Table 4**; **Appendix C8**).[105,107] Neither study found a difference between supplement use versus placebo in risk of any adverse event (RR, 1.05 [95% CI, 0.97 to 1.13]), serious adverse events (RR, 1.05 [95% CI, 0.72 to 1.49]), serious ocular adverse events (RR, 1.18 [95% CI, 0.50 to 2.75]), or withdrawals due to adverse events (RR, 3.00 [95% CI, 0.33 to 28]).

Laser Photocoagulation

The prior USPSTF review[1] found that laser photocoagulation was associated with an increased risk for acute loss of 6 lines or more of visual acuity versus no treatment, despite protective effects on vision (RR, 1.41 [95% CI, 1.08 to 1.82]) (**Appendix B8**).[113] We identified no new studies on harms of laser photocoagulation versus no treatment.

PDT

Based on a good-quality systematic review[114] included in the prior USPSTF review,[1] PDT was associated with an increased risk of severe acute loss of visual acuity (defined as loss of ≥20 letters within 7 days of treatment) versus placebo, though the difference was not statistically

significant (three trials; RR, 3.75 [95% CI, 0.87 to 16]; I^2=28%.) Other adverse events, including visual disturbance (three trials; RR, 1.56 [95% CI, 1.21 to 2.01]; I^2=7%), injection site reactions (three trials; RR, 2.09 [95% CI, 1.29 to 3.39]; I^2=73%), photosensitivity (two trials; RR, 5.37 [95% CI, 1.01 to 29]; I^2=70%) and infusion-related back pain (four trials; RR, 9.93 [95% CI, 2.82 to 35]; I^2=0%), were all more likely to occur with PDT versus placebo, though some estimates were imprecise (**Appendix B8**). We identified no new studies on harms of PDT versus no treatment.

VEGF Inhibitors

Based on evidence included in the prior USPSTF review,[1] there were no significant differences between VEGF inhibitors and sham in incidence of withdrawals due to adverse events in the MARINA (RR, 0.88 [95% CI, 0.45 to 1.70][121]) and VISION (RR, 1.00 [95% CI, 0.27 to 3.66][122]) trials, though the MARINA trial reported a lower likelihood of any withdrawal in patients randomized to ranibizumab (RR, 0.46 [95% CI, 0.34 to 0.63]) (**Table 5**). Other adverse events occurred infrequently and point estimates were imprecise. For example, there were no significant differences between VEGF inhibitors and sham in incidence of serious ocular harms, including ocular hemorrhage (one trial; RR, 0.52 [95% CI, 0.08 to 3.62]), retinal detachment (two trials; RR, 0.17 [95% CI, 0.01 to 4.07] and 3.67 [95% CI, 0.20 to 65]) or endophthalmitis (two trials; RR, 5.49 [95% CI, 0.30 to 99] and 8.33 [95% CI, 0.50 to 140]) (**Table 5**).[121-123]

Contextual Question. What Is a Clinically Meaningful Difference in Visual Acuity?

Evidence to determine a clinically meaningful difference in visual acuity is limited, though standards for visual acuity classification are available. According to World Health Organization classification, visual acuity of 20/70 or better is classified as mild or no impairment.[136] The International Council of Ophthalmology uses a slightly lower (20/63 or better) threshold for mildly impaired visual acuity.[137] However, effects of even mildly impaired visual acuity are variable and can have a significant impact on quality of life; for example, the best-corrected visual acuity acceptable for driving in most U.S. states is 20/40.[138] Therefore, even relatively small changes in even "mild" impaired visual acuity could theoretically have a clinically important impact, depending on baseline visual acuity and type of work and other activities in which an individual is engaged.

Although definitions for a clinically important change in visual acuity vary across studies, a difference of at least 15 letters (equivalent to three lines on the ETDRS), representative of a doubling of the visual angle, is a commonly reported outcome in studies assessing visual acuity,[100,114,120] and has been used to represent a clinically meaningful difference.[127,139,140] This assumption is based primarily on studies that evaluate effects of changes in visual acuity on vision-related function. Studies using the NEI-VFQ to assess vision-related function, including AREDS, MARINA, and other trials, have found a difference of 10 points to be clinically meaningful to patients, corresponding to an approximately 15-letter change in visual acuity.[127,140] Other studies have questioned the appropriateness of using a 15-letter cutoff as indicative of a clinically meaningful difference.[141] For example, in people undergoing cataract surgery with

mild (acuity of 20/63 or better) to moderate (acuity of 20/80 to 20/160)[137] impaired visual acuity, evidence suggests that clinically meaningful changes in visual acuity following surgery can range from about 40 to 10 letters, depending on baseline acuity.[142,143] Another study conducted in people with AMD and moderate to severe (20/200 or worse) impaired visual acuity at baseline found that a 15-letter change in visual acuity was associated with NEI-VFQ score differences that ranged from 3.6 to 16.2 points.[144]

A factor that complicates determinations of clinically important differences in visual acuity is test-retest variability. Test-retest variability can range from 2 to 9 letters (0.04 to 0.19 logMAR), depending on the test setting and patient population.[145-147] For example, a 5-letter change in a person with baseline visual acuity of 20/100 has a 90 percent or greater probability of representing a true difference in visual acuity, while for someone with baseline acuity worse that 20/100, a 10-letter change would be required to have a similarly high probability of difference.[141] Therefore, a minimum difference of 10 letters (0.2 logMAR; two lines on the ETDRS)[147,148] may be required to indicate a true change in visual acuity (i.e., not a change due to test variability).

Chapter 4. Discussion

Summary of Review Findings

Table 6 summarizes the evidence reviewed for this update. We identified no new trials of vision screening versus no screening, delayed screening, or usual care. Three fair- to good-quality cluster-randomized trials included in the prior USPSTF review[1] that enrolled more than 4,700 patients found vision screening in older adults as part of a multicomponent screening intervention in primary care settings to be no more effective than no vision screening, delayed screening, or usual care.[69-71] A fourth trial found that optometrist screening was associated with an increased risk of falls in frail elderly.[72] The reason for an increased risk of falls in this trial was unclear, but could be related to difficulty adapting to large corrections in visual acuity or use of multifocal lenses. There remains no evidence to determine optimal screening intervals in older adults.

Conclusions regarding the suboptimal diagnostic accuracy of vision screening tests in primary care settings are also unchanged from the prior USPSTF review. Two new studies found that the accuracy of a computer-based screening tool was limited, and one study found that the MDS 2.0 Vision Patterns section questions performed poorly as a screening test.[82,83] The prior USPSTF review found that no screening question is comparable in accuracy to tests of visual acuity for identifying impaired visual acuity[75,76,79,80,149] and that the Snellen test is inaccurate compared to a detailed eye examination for identifying visual conditions identified on a comprehensive ophthalmological examination. However, the latter studies remain difficult to interpret, as the conditions identified on examination were not necessarily associated with impaired visual acuity. For example, it is not known whether identification of AMD 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. Although the Snellen test 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 test is often considered the standard for assessing visual acuity in clinical practice. There remains insufficient evidence to assess the accuracy or utility of pinhole testing, the Amsler grid, visual acuity tests other than the Snellen test, physical examination, or funduscopic examination performed in primary care settings.

Conclusions from the prior USPSTF review of strong evidence showing the effectiveness of treatments versus no treatment for common causes of impaired visual acuity also remain unchanged. As noted in the prior review, a very high proportion of patients experience favorable vision-related outcomes following treatment for impaired visual acuity due to refractive error and cataracts.[1] More than half of all older adults with impaired visual acuity achieve vision better than 20/40 with refractive correction,[7] which can be done noninvasively in most cases with corrective lenses. 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 more than 90 percent of patients, and is associated with improvements in vision-related quality of life.[91] Correction of refractive error and cataract removal are also associated with improvement in vision-related quality of life, although randomized trials and cohort studies have

not shown clear effects on measures of function, cognition, or depression.[84-86,95,96] For dry AMD, evidence showing the effectiveness of antioxidant vitamins and minerals for slowing progression of disease or improving visual acuity remains largely restricted to the large AREDS trials.[97,98] Extended (10-year) followup from AREDS is now available, showing continued benefits.[99] Antioxidants included in the AREDS formulation have been found to be associated with congestive heart failure (vitamin E[150]) and lung cancer in smokers (beta-carotene[151,152]) when prescribed for prevention of cancer or cardiovascular disease, although these harms were not observed in AREDS. For wet AMD, evidence reviewed in the prior USPSTF review found intravitreal injection with VEGF inhibitors and PDT with verteporfin to be effective treatment options with a relatively low incidence of serious harms, although they may be associated with an increased risk of acute decline in visual acuity.[114,120] 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. VEGF inhibitors have largely supplanted PDT and laser photocoagulation as treatment for wet AMD. We did not identify new sham-controlled trials of laser photocoagulation, PDT, or VEGF inhibitors.

Limitations

Our evidence review has some limitations. We included previously published systematic reviews. 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 predefined criteria.[153] In addition, we previously 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. Conclusions were based on the totality of evidence (i.e., evidence reviewed in the prior USPSTF review plus new evidence). 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, and some research has found that exclusion of non-English–language studies has little effect on conclusions of review of noncomplementary and alternative therapies.[154] Third, when randomized trials were available, they were too few in number to perform assessments for publication bias.

Emerging Issues/Next Steps

New therapies are being investigated for their effectiveness in the treatment of AMD. The small (n=114) Age-related Maculopathy Statin Study (ARMSS) trial of simvastatin 40 mg/day versus placebo found that simvastatin was associated with lower risk of AMD progression after 3 years of followup, although the difference was not statistically significant (54.4% vs. 70.2%; RR, 0.78 [95% CI, 0.58 to 1.04]).[155] Complement inhibitors (e.g., protease inhibitors) are also being investigated for their potential effects on AMD.[156]

Relevance for Priority Populations

The focus of this review was on screening in older adults, a priority population at particular risk for impaired visual acuity as well as sequelae from impaired visual acuity. Although black men are at higher risk of unoperated cataracts, there is no evidence to suggest that cataract surgery is less successful in this patient group. Low socioeconomic status is associated with poorer access to vision services.

Future Research

Important gaps remain 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 in primary care settings are needed to identify optimal methods for vision screening, identify potential subgroups within older populations for targeted screening, define appropriate screening intervals, and develop effective strategies for linking older adults with vision impairment to appropriate care. Screening strategies targeted at identification of AMD may be particularly suitable for future studies, given the potential for irreversible effects with delayed diagnosis. Studies are needed on diagnostic accuracy and utility of funduscopic examination, pinhole testing, the Amsler grid, and nonSnellen visual acuity charts in primary care settings for supplementing or replacing the Snellen visual eye chart. Research would also be helpful for determining the feasibility and accuracy of alternative screening modalities to supplement standard visual acuity testing in primary care settings, such as tests for dark adaptation, visual contrast, or useful field of view. Evidence on effectiveness of antioxidants and vitamins for the treatment of dry AMD remains largely dependent on a single large trial reporting a posthoc subgroup analysis[97] and would be strengthened by similar findings from other, well-designed trials that are also designed to adequately evaluate potential harms associated with components of the supplements, such as congestive heart failure and lung cancer risk. Trials to determine the comparative effectiveness of treatments for wet AMD, and the effectiveness of combinations of treatments, would help clarify optimal therapy. More studies are needed to understand the potential association between correction of refractive errors and risk of falls,[72] and, if an association is present, to identify methods for mitigating these risks (e.g., avoid large corrections in visual acuity, education or training with multifocal lens), and to better understand the association between improved visual acuity and vision-related quality of life with improved function.

Conclusions

Impaired visual acuity is common in older adults, effective treatments are available for common causes of impaired visual acuity, and vision impairment can be identified noninvasively using the Snellen or other visual acuity chart. However, direct evidence found no significant difference between vision screening in older adults in primary care settings versus no screening for improving visual acuity or other clinical outcomes.

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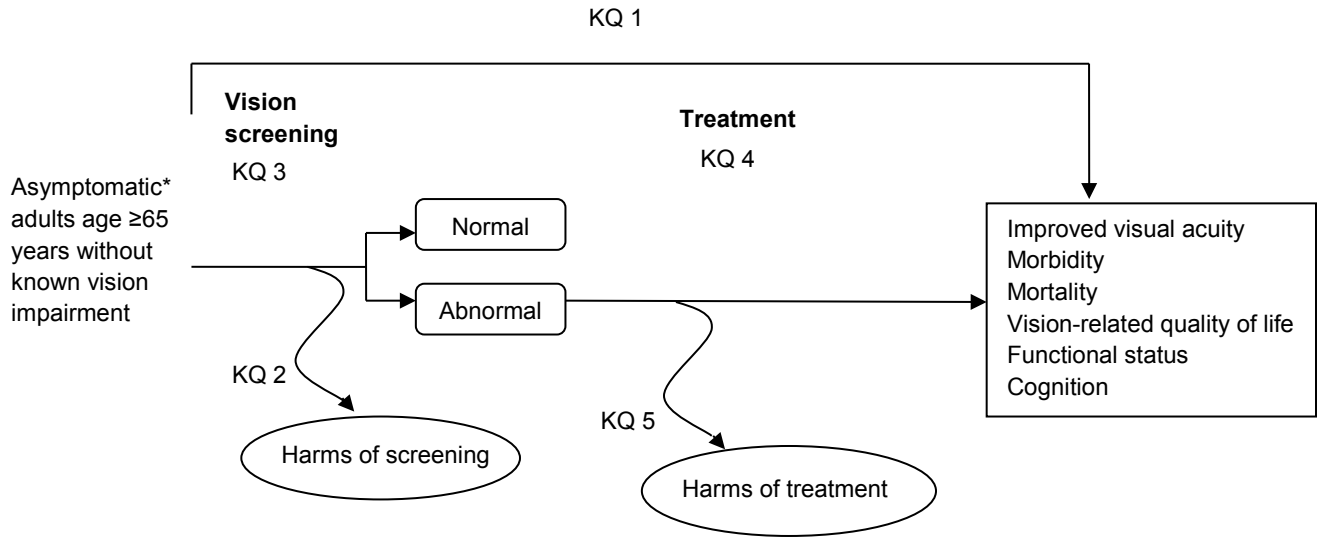
Figure 1. Analytic Framework



***** "Asymptomatic" individuals are defined as those without known impaired visual acuity (based on current corrected vision) who have not sought care for evaluation of vision problems.

Abbreviation: KQ = key question.

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 2004.[157]
Note: Visual impairment is 20/50 or worse; legal blindness is 20/200 or worse.

Abbreviation: LogMAR = logarithmic minimum angle of resolution.

Table 2. Recommendations of Other Groups

Organization	Recommendation/Clinical Guidance
American Academy of Ophthalmology[34]	Patients age 65 years or older without risk factors for eye disease (e.g. diabetes, glaucoma) should have comprehensive medical eye evaluations every 1 to 2 years.
American Optometric Association[66]	Annual eye examination for all adults older than age 60 years.
American Academy of Family Physicians[158]	Current evidence is insufficient to assess the balance of benefit and harms of screening for visual acuity for the improvement of outcomes in older adults.

Table 3. Studies of Diagnostic Accuracy Published Since the Prior USPSTF Review

Study, Year	Study design	Sample size	Reference standard	Target vision condition	Screening test	Sensitivity (95% CI)	Specificity (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)	Diagnostic odds ratio
Jessa, 2012[82] Study 1	Cross-sectional	180	"Gold standard eye exam," including computerized high-contrast visual acuity and low-contrast visual acuity tests	Any ocular disease	High contrast visual acuity >0.19 logMAR or abnormal near visual acuity	0.80 (0.72 to 0.86)	0.68 (0.57 to 0.77)	2.48 (1.76 to 3.49)	0.29 (0.20 to 0.45)	8.55
Jessa, 2012[82] Study 2	Cross-sectional	200	"Gold standard eye exam," including computerized high-contrast visual acuity and low-contrast visual acuity tests	Any ocular disease	A: High contrast visual acuity >0.9 logMAR or abnormal near visual acuity B: Low contrast visual acuity >0.49 logMAR	A: 0.75 (0.67 to 0.82) B: 0.75 (0.67 to 0.82)	A: 0.69 (0.58 to 0.78) B: 0.77 (0.66 to 0.85)	A: 2.45 (1.78 to 3.36) B: 3.26 (2.24 to 4.76)	A: 0.36 (0.25 to 0.51) B: 0.32 (0.22 to 0.46)	A: 6.81 B: 10.3
Swanson, 2009[83]	Cross-sectional	371	ETDRS chart	Any ocular disease	MDS Vision Patterns section score >0 (adequate)	0.52 (0.45 to 0.59)	0.75 (0.68 to 0.82)	2.11 (1.56 to 2.86)	0.64 (0.54 to 0.75)	3.30

Abbreviations: CI = confidence interval; ETDRS = Early Treatment Diabetic Retinopathy Study; logMAR = logarithm of the minimum angle of resolution; MDS = Minimum Data Set.

Table 4. Studies of Antioxidant Vitamins, Minerals, and Other Supplements Published Since the Prior USPSTF Review

Author, year Study n Duration of followup Quality	Interventions	Population	Vision-Related Outcomes	Other Outcomes	Adverse Events
Chew, 2013[99] AREDS (Report #35) n=2,459, focusing on AREDS categories 3 and 4 for vision-related outcomes; 3,476 for categories 2, 3, and 4; total sample 4,753 10 years Good	A. Antioxidant supplement (vitamin C 500 mg + vitamin E 400 IU + beta-carotene, 15 mg/day) B. Zinc 80 mg/day C. Antioxidant supplement + zinc D. Placebo	**A vs. B vs. C vs. D*** Median age: 69 vs. 70 vs. 69 vs. 69 years Sex: 55% vs. 57% vs. 56% vs. 56% female Race: 97% vs. 96% vs. 97% vs. 96% white 2% vs. 3% vs. 3% vs. 4% black 1% vs. 1% vs. <1% vs. <1% other AMD category: 2: 28% vs. 30% vs. 28% vs. 30% 3: 40% vs. 41% vs. 42% vs. 40% 4: 24% vs. 22% vs. 22% vs. 22%	**A vs. D†** Loss of visual acuity of ≥15 letters: ETDRS: OR, 0.83 (95% CI, 0.67 to 1.02) Visual acuity of <20/100: OR, 0.82 (95% CI, 0.64 to 1.07) Progression to advanced AMD: OR, 0.70 (95% CI, 0.56 to 0.88) **B vs. D†** Loss of visual acuity of ≥15 letters: ETDRS: OR, 0.86 (95% CI, 0.70 to 1.07) Visual acuity of <20/100: OR, 0.88 (95% CI, 0.69 to 1.14) Progression to advanced AMD: OR, 0.82 (95% CI, 0.66 to 1.02) **C vs D†** Loss of visual acuity of ≥15 letters: ETDRS: OR, 0.71 (95% CI, 0.57 to 0.88) Visual acuity of <20/100: OR, 0.72 (95% CI, 0.56 to 0.94) Progression to advanced AMD: OR, 0.66 (95% CI, 0.53 to 0.83)	**A + C (antioxidant) vs. B + D (no antioxidant)‡** All-cause mortality: 24.0% (439/1831) vs. 23.6% (427/1806); aHR§, 1.06 (95% CI, 0.93 to 1.21) CV mortality: aRR§, 1.20 (95% CI, 0.97 to 1.49) Cancer mortality: aRR, 1.07 (95% CI, 0.83 to 1.38) NonCV, noncancer mortality: aRR, 0.94 (95% CI, 0.74 to 1.20) **B + C (zinc) vs. A + D (no zinc)** All-cause mortality: 22.4% (401/1790) vs. 25.2% (465/1847); aHR, 0.83 (95% CI, 0.73 to 0.95) CV mortality: aRR, 0.80 (95% CI, 0.64 to 0.99) Cancer mortality: aRR, 0.84 (95% CI, 0.65 to 1.08) NonCV, noncancer mortality: aRR, 0.93 (95% CI, 0.73 to 1.18)	NR by treatment group; narrative report of no significant increase in incidence of hospitalization after adjustment for age, sex, smoking, and treatment group
Chew, 2009[112] AREDS (Report #25) n=4,757 total Up to 11 years (mean duration NR) Good	A. Any AREDS active treatment B. Placebo	Same as above	**A vs. B** Incident cataract surgery: 25.4% (798/3137) vs. 25.2% (369/1440); RR, 1.01 (95% CI, 0.91 to 1.12)	NR	NR

Table 4. Studies of Antioxidant Vitamins, Minerals, and Other Supplements Published Since the Prior USPSTF Review

Author, year Study n Duration of followup Quality	Interventions	Population	Vision-Related Outcomes	Other Outcomes	Adverse Events
Ma, 2012[106] n=108 48 weeks Good	A. Lutein 10 mg/day B. Lutein 20 mg/day C. Lutein 10 mg/day + zeaxanthin 10 mg/day D. Placebo	**A vs. B vs. C vs. D** Mean age: 70 vs. 69 vs. 69 vs. 69 years Sex: 62% vs. 56% vs. 56% vs. 60% female Race: NR BCVA: 0.30 vs. 0.28 vs. 0.28 vs. 0.31 logMAR Smoking history: 89% vs. 89% vs. 85% vs. 89% nonsmoker	**A vs. D** BCVA, mean change from baseline: -0.04 (95% CI, -0.11 to 0.03) vs. 0.00 (95% CI, -0.06 to 0.05); p=NS **B vs. D** BCVA, mean change from baseline: -0.02 (95% CI, -0.11 to 0.06) vs. 0.00 (95% CI, -0.06 to 0.05); p=NS **C vs. D** BCVA, mean change from baseline: -0.04 (95% CI, -0.10 to 0.01) vs. 0.00 (95% CI, -0.06 to 0.05); p=NS	NR	NR by treatment group; narrative report of no adverse events related to interventions
Murray, 2013[105] CLEAR n=84 1 year Good	A. Lutein 10 mg/day B. Placebo	**A vs. B** Mean age: 71.9 vs. 69.1 years Sex: 56% vs. 65% female Race: NR Visual acuity: 0.10 vs. 0.05 logMAR	**A vs. B** Visual acuity, mean change from baseline: 0.01 vs. -0.04; p<0.05	NR	**A vs. B** Withdrawals due to adverse events: 7.1% (3/42) vs. 2.3% (1/42); RR, 3.00 (95% CI, 0.33 to 28)
Souied, 2013[107] NAT2 n=300 3 years Good	A. Fish oil capsules (DHA 280 mg + EPA 90 mg + vitamin E 2 mg) 3x/day B. Placebo (olive oil 602 mg)	**A vs. B** Mean age: 74 vs. 73 years Sex: 69% vs. 61% female Race: NR Mean visual acuity in study eye: 0.14 vs. 0.12 logMAR Drusen: Absent: 0.7% vs. 0% <5: 0.7% vs. 2% 5–20: 17% vs. 22% >20: 81% vs. 76% Smoking history: Current: 7% vs. 9% Former: 14% vs. 17% Nonsmoker: 79% vs. 74%	**A vs. BII** Visual acuity, mean change from baseline: 0.155 (SD, 0.297) vs. 0.116 (SD, 0.258); p=0.311 Loss of visual acuity, proportion of subjects with loss of >15 letters ETDRS: 17.8% (21/118) vs. 14.3% (16/112); RR, 1.25 (95% CI, 0.69 to 2.26)	**A vs. B** All-cause mortality: 2.2% (3/134) vs. 4.7% (6/129); RR, 0.48 (95% CI, 0.12 to 1.88) Any adverse event: 93.3% (125/134) vs. 89.1% (115/129); RR, 1.05 (95% CI, 0.97 to 1.13) Any serious adverse event: 31.3% (42/134) vs. 30.2% (39/129); RR, 1.04 (95% CI, 0.72 to 1.49) Serious ocular adverse event: 8.2% (11/134) vs. 7.0% (9/129); RR, 1.18 (95% CI, 0.50 to 2.75) Cataract development, worsening or need for cataract surgery: 50% (67/134) vs. 62.5% (81/129); RR, 0.80 (95% CI, 0.64 to 0.99)	**A vs. B** Any adverse event: 93.3% (125/134) vs. 89.1% (115/129); RR, 1.05 (95% CI, 0.97 to 1.13) Any serious adverse event: 31.3% (42/134) vs. 30.2% (39/129); RR, 1.04 (95% CI, 0.72 to 1.49) Treatment-related adverse event (investigator-determined): 3.7% (5/134) vs. 1.6% (2/129); RR, 2.41 (95% CI, 0.48 to 12) Serious ocular adverse event: 8.2% (11/134) vs.

Table 4. Studies of Antioxidant Vitamins, Minerals, and Other Supplements Published Since the Prior USPSTF Review

Author, year Study n Duration of followup Quality	Interventions	Population	Vision-Related Outcomes	Other Outcomes	Adverse Events
					7.0% (9/129); RR, 1.18 (95% CI, 0.50 to 2.75) Ocular adverse event: 65.7% (88/134) vs. 57.4% (74/129); RR, 1.14 (95% CI, 0.94 to 1.39) Cataract development, worsening or need for cataract surgery: 50% (67/134) vs. 62.5% (81/129); RR, 0.80 (95% CI, 0.64 to 0.99) Serious nonocular adverse event: 23.1% (31/134) vs. 23.2% (30/129); RR, 0.99 (95% CI, 0.64 to 1.54)

* Baseline characteristics for the original AREDS cohort.
† Results for participants with high risk of developing advanced AMD (AREDS Category 3 and 4).
‡ Results for participants with AMD (AREDS Category 2, 3, or 4).
§ Adjusted for age, sex, race, education, smoking status, body mass index, and presence of diabetes, angina, cancer, and hypertension.
ǁ 6-month, 1-year, and 2-year outcomes reported in Appendix.

Abbreviations: aHR = adjusted hazard ratio; AMD = age-related macular degeneration; AREDS = Age-Related Eye Disease Study; aRR = adjusted risk ratio; BCVA = best-corrected visual acuity; CI = confidence interval; CLEAR = Combination of Lutein Effects in the Aging Retina; CV = cardiovascular; EPA = eicosapentaenoic acid; ETDRS = Early Treatment Diabetic Retinopathy Study; logMAR = logarithm of the minimum angle of resolution; NAT2 = Nutritional AMD Treatment 2; NS = not significant; NR = not reported; OR = odds ratio; RR = relative risk; SD = standard deviation; USPSTF = U.S. Preventive Services Task Force.

Table 5. Studies of Vascular Endothelial Growth Factor Inhibitors for Age-Related Macular Degeneration

Trial name **Author, year** **N** **Duration of followup** ***Quality***	**Interventions**	**Population**	**Vision-Related Outcomes**	**Other Outcomes**	**Adverse Events**
MARINA Rosenfeld, 2006[159] n=716 2 years Good	A. Ranibizumab 0.3 to 0.5 mg every month (n=478) B. Sham injection (n=238)	**A vs. B** Mean age 77 vs. 77 years 64% vs. 67% female 96% vs. 97% white; 4% vs. 3% other Mean visual acuity 53.4 vs. 53.6 letters (approximately 20/80)	**A vs. B†** Visual acuity, gain ≥15 letters: 29.2% (140/478) vs. 5.0% (12/238); RR, 5.81 (95% CI, 3.29 to 10.26) Visual acuity, loss <15 letters: 94.6% (452/478) vs. 62.2% (148/238); RR, 1.52 (95% CI, 1.37 to 1.68) Visual acuity, 20/200 or better: 88.1% (421/478) vs. 57.1% (136/238); RR, 1.54 (95% CI, 1.37 to 1.73)	**A vs. B** All-cause mortality: 2.3% (11/478) vs. 2.5% (6/238); RR, 0.91 (95% CI, 0.34 to 2.44) Vascular mortality: 1.3% (6/478) vs. 1.7% (4/236); RR, 0.74 (95% CI, 0.21 to 2.60) MI: 1.9% (9/478) vs. 1.7% (4/238); RR, 1.12 (95% CI, 0.35 to 3.60) CVA: 1.9% (9/478) vs. 0.8% (2/238); RR, 2.24 (95% CI, 0.49 to 10)	**A vs. B** Withdrawals: 13.2% (63/478) vs. 28.6% (68/238); RR, 0.46 (95% CI, 0.34 to 0.63) Withdrawals due to adverse events: 4.8% (23/478) vs. 5.5% (13/238); RR, 0.88 (95% CI, 0.45 to 1.70) Serious, nonocular hemorrhage: 1.7% (8/478) vs. 0.8% (2/236); RR, 1.97 (95% CI, 0.42 to 9.23) Endophthalmitis: 5/478 vs. 0/238; RR, 5.49 (95% CI, 0.30 to 99) Uveitis: 1.3% (6/478) vs. 0% (0/238); RR, 6.49 (95% CI, 0.37 to 115) Retinal detachment: 0% (0/478) vs. 0.4% (1/238); RR, 0.17 (95% CI, 0.01 to 4.07)
PIER Regillo, 2008[123] n=184 1 year* Good	A. Ranibizumab 0.3 to 0.5 mg every month for 3 months, followed by every 3 months up to 12 months (n=121) B. Sham injection (n=63)	**A vs. B** Mean age 79 vs. 78 years 55% vs. 68% female 93% vs. 94% white; 7% vs. 6% other Mean visual acuity 54.8 vs. 55.1 letters (approximately 20/80)	**A vs. B** Visual acuity, gain ≥15 letters: 12.4% (15/121) vs. 9.5% (6/63); RR, 1.30 (95% CI, 0.53 to 3.19) Visual acuity, loss <15 letters: 86.8% (105/121) vs. 49.2% (31/63); RR, 1.76 (95% CI, 1.36 to 2.29) Visual acuity, 20/200 or better: 73.6% (89/121) vs. 44.4% (28/63); RR, 1.65 (95% CI, 1.23 to 2.23)	**A vs. B** Mortality and CV events: No deaths, MI, or CVA in either group	**A vs. B** Withdrawals: 0.8% (1/121) vs. 0% (0/63); RR, 1.57 (95% CI, 0.07 to 38) Ocular hemorrhage: 1.6% (2/121) vs. 3.2% (2/63); RR, 0.52 (95% CI, 0.08 to 3.61) Macular edema: 0.8% (1/121) vs. 3.2% (2/63); RR, 0.26 (95% CI, 0.02 to 2.82)

Table 5. Studies of Vascular Endothelial Growth Factor Inhibitors for Age-Related Macular Degeneration

Trial name Author, year N Duration of followup *Quality*	Interventions	Population	Vision-Related Outcomes	Other Outcomes	Adverse Events
VISION (2 trials; 1 publication) Gragoudas, 2004[122] n=1,186 (Ns for individual trials were 586 and 622 prior to exclusions) 1 year Good	A. Pegaptanib 0.3 to 3.0 mg every 6 weeks (n=890) B Sham injection (n=296)	**A vs. B** Mean age not reported; 62% vs. 61% age ≥75 years 58% vs. 60% female 97% vs. 95% white; 3% vs. 5% other Mean visual acuity 51.5 vs. 52.7 letters	**A vs. B** Visual acuity, gain ≥15 letters: 5.7% (51/890) vs. 2.0% (6/296); RR, 2.83 (95% CI, 1.23 to 6.52) Visual acuity, loss <15 letters: 68.8% (612/890) vs. 55.4% (164/296); RR, 1.24 (95% CI, 1.11 to 1.39) Visual acuity, 20/200 or better: 58.7% (522/890) vs. 44.3% (131/296); RR, 1.33 (95% CI, 1.15 to 1.52)	Not reported	**A vs. B** Withdrawals due to adverse events: 1% (9/890) vs. 1% (3/296); RR, 1.00 (95% CI, 0.27 to 3.66) Endophthalmitis: 1.3% (12/890) vs. 0% (0/296); RR, 8.33 (95% CI, 0.50 to 140) Traumatic lens injury: 0.6% (5/890) vs. 0% (0/296); RR, 3.67 (95% CI, 0.20 to 66) Retinal detachment: 0.6% (5/890) vs. 0% (0/296); RR, 3.67 (95% CI, 0.20 to 66) Severe (>30 letters) vision loss: 0.1% (1/890) vs. 0% (0/296); RR, 1.00 (95% CI, 0.04 to 24)

* 2-year results available, but sham group was maintained during the second year.
† 1-year results; 2-year results for visual outcomes appear in Appendix.

Abbreviations: CI = confidence interval; CV = cardiovascular; CVA = cerebrovascular accident; MARINA = Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular AMD; MI = myocardial infarction; PIER = Phase IIIb, Multicenter, Randomized, Double-Masked, Sham Injection–Controlled Study of the Efficacy and Safety of Ranibizumab; RR = risk ratio; USPSTF = U.S. Preventive Services Task Force; VISION = VEGF Inhibition Study in Ocular Neovascularization.

Table 6. Summary of Evidence

Key Question Topic	Main findings from 2009 USPSTF review	Number of studies identified for update	Number of participants identified for update	Study design identified for update	Summary of findings (including consistency and precision)	Applicability	Limitations (including reporting bias)	Overall study quality*
Key Question 1. Benefits of screening	3 cluster RCTs found no difference between vision screening and usual care, no vision screening, or delayed screening on vision and other clinical outcomes. 1 RCT found that vision screening by an optometrist in frail elderly persons was associated with an increased risk of falls (rate ratio, 1.57 [95% CI, 1.20 to 2.05]) and a trend toward increased risk of fractures (RR, 1.74 [95% CI, 0.97 to 3.11]).	None	-	-	Unchanged from the 2009 review; no new studies. Evidence was consistent and imprecise.	Good (mainly primary care-applicable settings, as part of multicomponent screening intervention)	All studies had different types of comparators. Reporting bias was not detected.	Fair
Key Question 2. Harms of screening	See Key Question 1 for evidence on falls.	None	-	-	Unchanged from the 2009 review; no new studies. Evidence was precise; unable to assess consistency (1 study)	Moderate (screening was done by an optometrist)	1 study only. Reporting bias was possible since most screening studies did not report harms.	Poor
Key Question 3. Accuracy of screening	4 studies found that screening questions are not accurate for identifying persons with vision impairment compared to the Snellen chart. 4 studies found that visual acuity testing is not accurate for identifying the presence of vision conditions compared to a detailed ophthalmologic exam. 1 study found that the Amsler grid is not accurate for identifying the presence of vision conditions compared to a detailed ophthalmologic exam. 1 very small (n=50) study found that non-ophthalmologists are as accurate as ophthalmologists for identifying presence of cataracts. All studies were cross-sectional.	3	751	Cross-sectional	2 new studies found that a computerized vision screening tool or a flipchart version were not accurate compared with a detailed eye exam and a third study found the Minimum Data Set 2.0 Vision Patterns section was associated with poor diagnostic accuracy compared with an eye chart exam; overall conclusions were unchanged from the 2009 review. Evidence was consistent and precise.	Moderate (tests are practical for primary care but were sometimes performed by optometrists)	Sometimes unclear if the reference standards were interpreted independently of the target test, lack of predefined thresholds for positive results. Reporting bias was possible as some studies reported accuracy based on optimal criteria for a positive test.	Fair

Table 6. Summary of Evidence

Key Question Topic	Main findings from 2009 USPSTF review	Number of studies identified for update	Number of participants identified for update	Study design identified for update	Summary of findings (including consistency and precision)	Applicability	Limitations (including reporting bias)	Overall study quality*
Key Question 4. Benefits of treatment *Uncorrected Refractive Error*	In 1 large population-based study, 60% of older adults with vision impairment achieved visual acuity of 20/40 or better with refractive correction. 2 RCTs found use of corrective lenses was associated with improvements in vision-related function, but effects on overall function were inconsistent. Numerous observational studies showed that >85% of patients achieved visual acuity of 20/40 or better following photorefractive surgery for myopia or hyperopia.	None	-	-	Unchanged from the 2009 review; no new studies. Evidence was consistent and precise.	Moderate	Mainly observational data and accumulated clinical experience Reporting bias was not detected.	Fair
Cataract	Numerous observational studies found that >90% of patients achieved visual acuity of 20/40 or better following cataract extraction and intraocular lens implantation. 3 observational studies found cataract surgery was associated with improved vision-related function. 1 trial found immediate first-eye cataract surgery was 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.	2	346	Prospective cohort	2 new studies reported improved visual acuity with surgery, with no differences between groups on cognitive function or quality of life; overall conclusions were unchanged from the 2009 review. Evidence was consistent for visual acuity and inconsistent for falls and precise.	Moderate	Mainly observational data. Reporting bias was not detected.	Fair

Table 6. Summary of Evidence

Key Question Topic	Main findings from 2009 USPSTF review	Number of studies identified for update	Number of participants identified for update	Study design identified for update	Summary of findings (including consistency and precision)	Applicability	Limitations (including reporting bias)	Overall study quality*
Dry AMD– Vitamin and Mineral Supplements	A large, good-quality (n=2,556) randomized trial, the Age-Related Eye Disease Study (AREDS), reported results stratified according to the severity of AMD at baseline. Among the subgroup of patients in whom treatment was currently recommended (AREDS categories 3 and 4), AREDS found that an antioxidant + zinc combination was effective for lower likelihood of AMD progression after 6 years of followup (adjusted OR, 0.66 [95% CI, 0.47 to 0.93]), although the difference in the likelihood of ≥15 letters of visual acuity loss was not statistically significant (adjusted OR, 0.75 [95% CI, 0.55 to 1.02]). A systematic review of 9 trials (including AREDS) found insufficient evidence to determine efficacy of vitamins and minerals other than the AREDs combination.	1 systematic review (updated version of the previously included systematic review, with 4 new RCTs) 3 RCTs + 2 additional reports from AREDS with 10-year followup	10,010	Systematic review and RCTs	10-year followup from AREDS is consistent with prior results, with antioxidant supplements alone (OR, 0.70 [95% CI, 0.56 to 0.88]) or with added zinc (OR, 0.66 [95% CI, 0.53 to 0.83]) associated with decreased risk of AMD progression and the combination associated with decreased risk of visual acuity loss (OR, 0.71 [95% CI, 0.57 to 0.88]). Evidence on the effects of other vitamins and mineral treatments remains limited, with no clear effects on AMD progression or visual acuity; overall conclusions were unchanged from the 2009 review. Evidence was consistent and precise.	Good (participants in AREDS and other studies in general had mild visual impairment at baseline)	Substantial heterogeneity in interventions assessed and outcomes reported. Reporting bias was not detected.	Good

Table 6. Summary of Evidence

Key Question Topic	Main findings from 2009 USPSTF review	Number of studies identified for update	Number of participants identified for update	Study design identified for update	Summary of findings (including consistency and precision)	Applicability	Limitations (including reporting bias)	Overall study quality*
Wet AMD–Laser Photo-coagulation	Laser photocoagulation was superior to no treatment for progression of vision loss (loss of ≥6 lines of visual acuity) at 2-year followup (RR, 0.67 [95% CI, 0.53 to 0.83]; 5 trials).	None	-	-	Unchanged from the prior review; no new studies. Evidence was consistent and precise.	Moderate	No new trials published since the prior review; older trials have relatively short duration of followup and methodological limitations, including use of open-label design, incomplete followup, lack of intention-to-treat analysis, and others. Reporting bias was not detected.	Fair
Wet AMD–Photodynamic Therapy	1 systematic review found that patients undergoing PDT with verteporfin were more likely to gain ≥3 lines of visual acuity at 12 months (3 trials; RR, 2.19 [95% CI, 0.99 to 4.82]; I^2=0%) and 24 months (3 trials; RR, 2.55 [95% CI, 1.31 to 4.99]; I^2=0%).	None	-	-	Unchanged from the prior review; no new studies. Evidence was consistent and precise.	Moderate	No new trials published since the prior review; evidence limited to 4 older trials, 1 of which enrolled a younger population than the others (mean age 49 vs. 75–79 years). Reporting bias was not detected.	Fair

Table 6. Summary of Evidence

Key Question Topic	Main findings from 2009 USPSTF review	Number of studies identified for update	Number of participants identified for update	Study design identified for update	Summary of findings (including consistency and precision)	Applicability	Limitations (including reporting bias)	Overall study quality*
Wet AMD–VEGF Inhibitors	RR, 0.71 (95% CI, 0.61 to 0.84), 2 RCTs for pegaptanib (1 trial) and RR, 0.21 (95% CI, 0.16 to 0.27), 2 RCTs for ranibizumab (2 trials)	Additional publication from previously included trial	-	Trial	Unchanged from the 2009 review; no new studies. Evidence was consistent and precise.	Moderate	No new trials published since the prior review; study population in the 4 included trials was older (>75 years) with moderate to severe impaired visual acuity at baseline. Reporting bias was not detected.	Fair
Key Question 5. Harms of treatment *Uncorrected Refractive Error*	1 small prospective study found that multifocal lenses were associated with a higher risk of falls in older adults compared to unifocal lenses (OR, 2.09 [95% CI, 1.06 to 4.92]). 3 studies found incidence of infectious keratitis ranging from 0.3 to 3.6 cases per 10,000 contact lens wearers; 1 study found incidence to be higher in persons age >50 years. Corneal ectasia rates ranged from 0% to 0.87% in 5 studies of LASIK, and keratitis rates ranged from 0% to 3.4% in 6 studies of LASIK and 4 studies of LASEK.	None	-	-	Unchanged from the 2009 review; no new studies. Evidence was consistent for contact lenses and refractive surgery (only 1 study for corrective lenses) and imprecise.	Moderate	Only 1 study on corrective lenses. Reporting bias was not detected.	Corrective lenses: Poor Contact lenses; refractive surgery: Fair
Cataract	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.	None	-	-	Unchanged from the 2009 review; no new studies. Evidence was consistent and precise.	Moderate	Mainly observational studies. Reporting bias was not detected.	Fair

Table 6. Summary of Evidence

Key Question Topic	Main findings from 2009 USPSTF review	Number of studies identified for update	Number of participants identified for update	Study design identified for update	Summary of findings (including consistency and precision)	Applicability	Limitations (including reporting bias)	Overall study quality*
Dry AMD–Vitamin and Mineral Supplements	The large AREDS trial found that zinc was associated with significantly increased risk of hospitalization for genitourinary causes compared to nonuse of zinc (RR, 1.47 [95% CI, 1.19 to 1.80]) and antioxidants were associated with increased risk of yellow skin compared to nonuse of antioxidants (RR, 1.38 [95% CI, 1.09 to 1.75]).	2	384	RCT	2 new trials found no difference between supplement use vs. placebo in risk of any adverse event (RR, 1.05 [95% CI, 0.97 to 1.13]), serious adverse events (RR, 1.05 [95% CI, 0.72 to 1.49]), serious ocular adverse events (RR, 1.18 [95% CI, 0.50 to 2.75]), or withdrawals due to adverse events (RR, 3.00 [95% CI, 0.33 to 28]). No new evidence on adverse events was associated with zinc or antioxidants; overall conclusions were unchanged from the 2009 review. Evidence was consistent. Evidence was precise for any adverse events but imprecise for other adverse events.	Good (participants in both studies had relatively mild visual impairment at baseline)	Neither trial was designed to assess harms and sample sizes were relatively small (n=94 and 300). Reporting bias was possible due to inconsistent reporting of harms.	Good
Wet AMD–Laser Photo-coagulation	Visual acuity loss of ≥6 lines compared to observation 3 months after treatment (absolute rate, 16.6%; RR, 1.41 [95% CI, 1.08 to 1.82]; 5 trials).	None	-	-	Unchanged from the prior review; no new studies. Evidence was consistent and precise.	Moderate	Included studies were not designed to assess harms and duration of followup was short in some studies. Reporting bias was possible due to inconsistent reporting of harms.	Fair

Table 6. Summary of Evidence

Key Question Topic	Main findings from 2009 USPSTF review	Number of studies identified for update	Number of participants identified for update	Study design identified for update	Summary of findings (including consistency and precision)	Applicability	Limitations (including reporting bias)	Overall study quality*
Wet AMD–Photodynamic Therapy	Increased risk of acute severe visual acuity loss (20 letters within 7 days of treatment) compared to placebo (2% vs. 0.2%; RR, 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%; RR, 6.50 [95% CI, 1.52 to 27.78]).	None	-	-	Unchanged from the prior review; no new studies. Evidence was consistent. Evidence was precise for risk of severe visual acuity loss and imprecise for infusion-related back pain.	Moderate	Evidence limited to 4 older trials; few adverse events reported. Reporting bias was possible due to inconsistent reporting of harms.	Fair
Wet AMD–VEGF 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.	None	-	-	Unchanged from the 2009 review; no new studies. Evidence was consistent and imprecise.	Moderate	Evidence limited to 4 older trials; few adverse events reported. Reporting bias was possible due to inconsistent reporting of harms.	Fair

* "Overall quality" is based on new evidence plus previously reviewed evidence.

Abbreviations: AREDS = Age-Related Eye Disease Study; AMD = age-related macular degeneration; CI = confidence interval; KQ = key question; LASEK = laser assisted sub-epithelial keratomileusis; LASIK = laser assisted in situ keratomileusis; NA = not applicable; OR = odds ratio; PTD = photodynamic therapy; RCT = randomized, controlled trial; RR = relative risk; VEGF = vascular endothelin growth factor.

Appendix A1. Search Strategies

Key Questions 1-2

Database: Ovid MEDLINE(R) without Revisions
1 Mass Screening/
2 exp Vision Tests/
3 exp Refractive Errors/
4 exp Macular Degeneration/
5 exp Vision Disorders/
6 exp Vision, Ocular/
7 exp Eye Diseases/
8 Cataract/
9 (presbyop$ or myop$ or astigmati$ or hyperop$ or cataract$ or "macular degeneration" or armd).mp.
10 or/2-9
11 1 and 10
12 11 not (adolescen$ or child$ or pediatric$ or toddler or infant$ or newborn or neonat$ or prematur$).mp.
13 limit 12 to humans
14 limit 13 to english language
15 limit 13 to abstracts
16 14 or 15

Database: EBM Reviews - Cochrane Central Register of Controlled Trials
1 Mass Screening/
2 exp Vision Tests/
3 exp Refractive Errors/
4 exp Macular Degeneration/
5 exp Vision Disorders/
6 exp Vision, Ocular/
7 exp Eye Diseases/
8 Cataract/
9 (presbyop$ or myop$ or astigmati$ or hyperop$ or cataract$ or "macular degeneration" or armd).mp.
10 or/2-9
11 1 and 10
12 11 not (adolescen$ or child$ or pediatric$ or toddler or infant$ or newborn or neonat$ or prematur$).mp.

Database: EBM Reviews - Cochrane Database of Systematic Reviews
1 ((vision or visual) adj5 screen$).mp.
2 (presbyop$ or myop$ or astigmati$ or hyperop$).mp.
3 (macula$ adj3 degenerat$).mp.
4 cataract$.mp.
5 1 and (or/2-4)
6 5 not (child$ or pediatr$ or neonat$ or prematur$).mp.

Key Question 3

Database: Ovid MEDLINE(R) without Revisions
1 Vision, Ocular/
2 Vision Disorders/
3 Vision Tests/
4 Refractive Errors/
5 Macular Degeneration/
6 Cataract/
7 Eye Diseases/
8 (presbyop$ or myop$ or astigmati$ or hyperop$ or cataract$ or "macular degeneration" or armd).mp.
9 vision.mp.
10 or/1-9

11 screen$.mp.
12 10 and 11
13 "Sensitivity and Specificity"/
14 (specificity or accurac$ or "predictive value").tw.
15 (sensitiv$ or diagnostic).mp.
16 or/13-15
17 12 and 16
18 17 not (adolescen$ or child$ or pediatric$ or toddler or infant or neonat$ or prematur$).mp.
19 limit 18 to humans
20 limit 19 to english language
21 limit 19 to abstracts
22 20 or 21

Database: EBM Reviews - Cochrane Central Register of Controlled Trials
1 Vision, Ocular/
2 Vision Disorders/
3 Vision Tests/
4 Refractive Errors/
5 Macular Degeneration/
6 Cataract/
7 Eye Diseases/
8 (presbyop$ or myop$ or astigmati$ or hyperop$ or cataract$ or "macular degeneration" or armd).mp.
10 or/1-9
11 screen$.mp.
12 10 and 11
13 "Sensitivity and Specificity"/
14 (specificity or accurac$ or "predictive value").tw.
15 (sensitiv$ or diagnostic).mp.
16 or/13-15
17 12 and 16
18 17 not (adolescen$ or child$ or pediatric$ or toddler or infant or neonat$ or prematur$).mp.

Database: EBM Reviews - Cochrane Database of Systematic Reviews
1 (presbyop$ or myop$ or astigmati$ or hyperop$).mp.
2 (macula$ adj3 degenerat$).mp.
3 cataract$.mp.
4 visual acuity.mp.
6 (diagno$ adj2 accur$).mp.
7 5 and 6

Key Questions 4-5

Database: Ovid MEDLINE(R) without Revisions
1 exp Refractive Errors/dt, pc, rt, th
2 exp Cataract/dh, dt, pc, rt, th
3 Cataract Extraction/
4 exp Macular Degeneration/dh, dt, pc, rt, su, th
5 exp Vision Disorders/dh, dt, pc, rt, su, th
6 or/1-5
7 6 not (adolescen$ or child$ or pediatric$ or toddler or infant$ or newborn or neonat$ or prematur$).mp.
8 limit 7 to humans
9 limit 8 to english language
10 limit 8 to abstracts
11 limit 10 to "all aged (65 and over)"
12 limit 11 to yr="2008 - 2014"

Appendix A1. Search Strategies

Database: EBM Reviews - Cochrane Central Register of Controlled Trials
1 exp Refractive Errors/dt, pc, rt, th
2 exp Cataract/dh, dt, pc, rt, th
3 Cataract Extraction/
4 exp Macular Degeneration/dh, dt, pc, rt, su, th
5 exp Vision Disorders/dh, dt, pc, rt, su, th
6 or/1-5
7 6 not (adolescen$ or child$ or pediatric$ or toddler or infant$ or newborn or neonat$ or prematur$).mp.

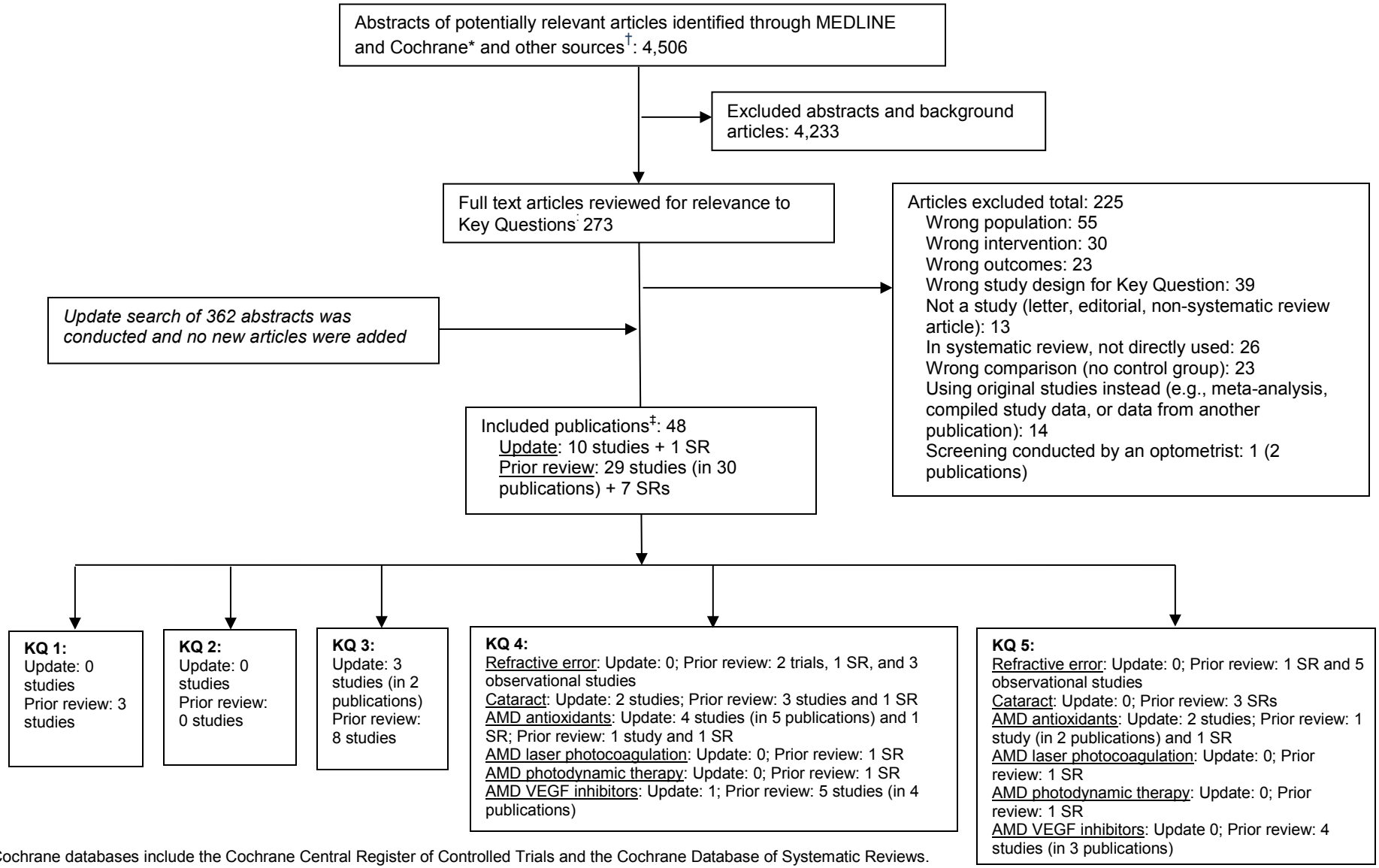
Database: EBM Reviews - Cochrane Database of Systematic Reviews
1 ("age-related macular degeneration" or "age related macular degeneration" or "AMD" or “ARMD”).ti,ab.
2 ("impaired visual acuity" or "impaired vision" or "visual acuity").ti,ab.
3 cataract$.ti,ab.
4 (presbyop$ or myop$ or astigmati$ or hyperop$).ti,ab.
5 treatment.ti,ab.
6 (or/1-4) and 5
7 6 not (child$ or pediatr$ or neonat$ or prematur$).mp.
8 limit 7 to new reviews
9 limit 8 to full systematic reviews
10 9 not diabet$.mp.

Appendix A2. Inclusion and Exclusion Criteria

	Include	Exclude
Key Questions 1 & 2. Screening Effectiveness and Harms		
Populations	Asymptomatic adults 65 years of age and older without known impaired visual acuity (based on current corrected vision) and who have not sought care for evaluation of vision problems	Known impaired visual acuity based on current corrected vision or who have sought care for evaluation of vision problems
Interventions	Vision screening performed in primary care or community-based settings, including multi-component screening with a distinct vision screening component	Vision screening performed in eye specialty settings
Outcomes	Visual acuity; vision-related quality of life; functional capacity. including ability to drive and driving outcomes; other measures of morbidity; mortality; cognition; harms, including falls and fractures	Reading speed and other tests of vision function
Study designs	Randomized controlled trials and controlled observational studies comparing vision screening to no screening, delayed screening or usual care (i.e. targeted screening.)	
Key Question 3. Diagnostic Accuracy		
Populations	Asymptomatic adults 65 years of age and older without known impaired visual acuity (based on current corrected vision) and who have not sought care for evaluation of vision problems	Known impaired visual acuity based on current corrected vision or who have sought care for evaluation of vision problems
Interventions	Vision screening tests performed in primary care or community-based settings; questions or questionnaires for impaired visual acuity	Diagnostic tests for vision screening performed in eye specialty settings (including fundoscopic examination performed by an eye professional and specialized diagnostic testing)
Outcomes	Sensitivity, specificity, positive and negative predictive values, areas under the receiver operating curve, other measures of diagnostic test accuracy	
Study designs	Studies evaluating diagnostic accuracy of a screening question or diagnostic test compared to a reference standard.	
Key Questions 4 & 5. Treatment Effectiveness and Harms		
Populations	Asymptomatic adults with vision impairment (current corrected visual acuity worse than 20/40 but better than 20/200) due to uncorrected refractive errors (myopia, hyperopia, astigmatism, or presbyopia), age-related macular degeneration, or cataracts.	Visual acuity worse than 20/200, other causes of vision loss
Interventions	Corrective lenses (eyeglasses and contact lenses), reading aids, photorefractive surgery (LASIK, LASEK, PRK), cataract surgery, vitamins and antioxidants, laser therapy, photodynamic therapy, vascular endothelin growth factor inhibitors	
Outcomes	Visual acuity; vision –related quality of life, functional capacity (including ability to drive and driving outcomes), other measures of morbidity; mortality; falls; fractures; other treatment-related harms.	Reading speed and other tests of vision function
Study designs	Randomized controlled trials comparing treatment to no treatment (including sham injection). Controlled observational studies will be included if evidence on harms from randomized trials is insufficient.	
All Key Questions		
Language	English language	
Settings	United States applicable, primary care relevant	

Abbreviations: LASEK = laser assisted sub-epithelial keratomileusis; LASIK = laser assisted in situ keratomileusis; PRK = photorefractive keratectomy.

Appendix A3. Literature Flow Diagram



*Cochrane databases include the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews.
†Other sources include prior reports, references lists, and referrals from experts.
‡Studies may be included for more than one Key Question.
Abbreviations: AMD = age-related macular degeneration; KQ = key question; SR = systematic review; VEGF = vascular endothelial growth factor.

Appendix A4. Excluded Studies

Epidemiological feasibility of cardiovascular primary prevention in general practice: a trial of vitamin E and aspirin. Collaborative group of the Primary Prevention Project. J Cardiovasc Risk. 1995;2(2):137-42. Excluded: wrong outcomes.

A screening update for smokers and ex-smokers. Johns Hopkins Med Lett Health After 50. 2012;24(11):4. Excluded: not a study (letter, editorial, non-systematic review article).

Abraham P, Yue H, Wilson L. Randomized, double-masked, sham-controlled trial of ranibizumab for neovascular age-related macular degeneration: PIER study year 2. Am J Ophthalmol. 2010;150(3):315-24.e1. Excluded: wrong population.

Adams AJ. Visionaries are often out of sight. Optom Vis Sci. 2010;87(5):299. Excluded: not a study (letter, editorial, non-systematic review article).

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Funk M, Karl D, Georgopoulos M, et al. Neovascular age-related macular degeneration: intraocular cytokines and growth factors and the influence of therapy with ranibizumab. Ophthalmology. 2009;116(12):2393-9. Excluded: wrong outcomes.

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Gehlbach P, Li T, Hatef E. Statins for age-related macular degeneration. Cochrane Database Syst Rev. 2012(3). Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

Geltzer A, Turalba A, Vedula SS. Surgical implantation of steroids with antiangiogenic characteristics for treating neovascular age-related macular degeneration. Cochrane Database Syst Rev. 2013(1). Excluded: wrong intervention.

Gilles MC, Walton R, Arnold J, et al. Comparison of outcomes from a phase 3 study of age-related macular degeneration with a matched, observational cohort. Ophthalmology. 2014;121(3):676-81. Excluded: wrong comparison (no control group).

Gillies MC, Islam FMA, Larsson J, et al. Triamcinolone-induced cataract in eyes with diabetic macular oedema: 3-year prospective data from a randomized clinical trial.[Erratum appears in Clin Experiment Ophthalmol. 2010 Oct; 38(7):741 Clin Experiment Ophthalmol. 2010;38(6):605-12. Excluded: wrong population.

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Gritz DC, Srinivasan M, Smith SD, et al. The Antioxidants in Prevention of Cataracts Study: effects of antioxidant supplements on cataract progression in South India. Br J Ophthalmol. 2006;90(7):847-51. Excluded: wrong population.

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Haller JA, Bandello F, Belfort R, Jr., et al. Randomized, sham-controlled trial of dexamethasone intravitreal implant in patients with macular edema due to retinal vein occlusion. Ophthalmology. 2010;117(6):1134-46.e3. Excluded: wrong population.

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Haritoglou C, Gerss J, Hammes HP, et al. Alpha-lipoic acid for the prevention of diabetic macular edema. Ophthalmologica. 2011;226(3):127-37. Excluded: wrong population.

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Hudson HL, Lane SS, Heier JS, et al. Implantable miniature telescope for the treatment of visual acuity loss resulting from end-stage age-related macular degeneration: 1-year results. Ophthalmology. 2006;113(11):1987-2001. Excluded: wrong population.

Huna-Baron R, Glovinsky Y, Habot-Wilner Z. Comparison between Hardy-Rand-Rittler 4th edition and Ishihara color plate tests for detection of dyschromatopsia in optic neuropathy. Graefes Arch Clin Exp Ophthalmol. 2013;251(2):585-9. Excluded: wrong population.

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Appendix A4. Excluded Studies

Ip MS, Oden NL, Scott IU, et al. SCORE Study report 3: study design and baseline characteristics. Ophthalmology. 2009;116(9):1770-7.e1. Excluded: wrong population.

Johnson EJ, Chung H-Y, Caldarella SM, et al. The influence of supplemental lutein and docosahexaenoic acid on serum, lipoproteins, and macular pigmentation. Am J Clin Nutr. 2008;87(5):1521-9. Excluded: wrong outcomes.

Joussen AM, Wong D, Walter P, et al. Surgical management of subfoveal choroidal neovascular membranes in age-related macular degeneration by macular relocation: experiences of an early-stopped randomised clinical trial (MARAN Study). Eye. 2010;24(2):284-9. Excluded: wrong intervention.

Kaiser PK, VIO Study Group. Verteporfin PDT for subfoveal occult CNV in AMD: two-year results of a randomized trial. Curr Med Res Opin. 2009;25(8):1853-60. Excluded: in systematic review, not directly used.

Kamdeu Fansi AA, Li G, Harasymowycz PJ. The validity of screening for open-angle glaucoma in high-risk populations with single-test screening mode frequency doubling technology perimetry (FDT). J Glaucoma. 2011;20(3):167-71. Excluded: wrong comparison (no control group).

Kemp A, Preen DB, Morlet N, et al. Myocardial infarction after intravitreal vascular endothelial growth factor inhibitors: a whole population study. Retina. 2013;33(5):920-7. Excluded: wrong comparison (no control group).

Kerr NM, Chew SSL, Eady EK, et al. Diagnostic accuracy of confrontation visual field tests. Neurology. 2010;74(15):1184-90. Excluded: wrong intervention.

Khandekar R, Al Raisi A. Oman Eye Study 2005: validity of screening tests used in the glaucoma survey. East Mediterr Health J. 2008;14(6):1360-4. Excluded: wrong population.

Khandekar R, Zutshi R, Ali M, et al. Influence of diabetes on the validity glaucoma screening by frequency doubling perimetry: a hospital-based study in Oman. Diabetes Technol Ther. 2008;10(4):278-82. Excluded: wrong intervention.

Kinge B, Stordahl PB, Forsaa V, et al. Efficacy of ranibizumab in patients with macular edema secondary to central retinal vein occlusion: results from the sham-controlled ROCC study. Am J Ophthalmol. 2010;150(3):310-4. Excluded: wrong population.

Klein R, Klein BE, Jensen SC, et al. Age-related maculopathy in a multiracial United States population: the National Health and Nutrition Examination Survey III. Ophthalmology. 1999;106(6):1056-65. Excluded: in systematic review, not directly used.

Koo E, Chang JR, Agron E, et al. Ten-year incidence rates of age-related cataract in the Age-Related Eye Disease Study (AREDS): AREDS report no. 33. Ophthalmic Epidemiol. 2013;20(2):71-81. Excluded: wrong outcomes.

Koss MJ, Kurz P, Tsobanelis T, et al. Prospective, randomized, controlled clinical study evaluating the efficacy of Rheopheresis for dry age-related macular degeneration. Dry AMD treatment with Rheopheresis Trial-ART. Graefes Arch Clin Exp Ophthalmol. 2009;247(10):1297-306. Excluded: wrong intervention.

Kurita N, Mayama C, Tomidokoro A, et al. Potential of the pentacam in screening for primary angle closure and primary angle closure suspect. J Glaucoma. 2009;18(7):506-12. Excluded: wrong intervention.

Kwon SI, Baek SU, Park IW. Comparison of natural course, intravitreal triamcinolone and macular laser photocoagulation for treatment of mild diabetic macular edema. Int J Med Sci. 2013;10(3):243-9. Excluded: wrong population.

Kwon SI, Kim YW, Bang YW, et al. Comparison of natural course, intravitreal triamcinolone, and intravitreal bevacizumab for treatment of macular edema secondary to branch retinal vein occlusion. J Ocul Pharmacol Ther. 2013;29(1):5-9. Excluded: wrong population.

Landa G, Butovsky O, Shoshani J, et al. Weekly vaccination with Copaxone (glatiramer acetate) as a potential therapy for dry age-related macular degeneration. Curr Eye Res. 2008;33(11):1011-3. Excluded: wrong outcomes.

Appendix A4. Excluded Studies

Lawrenson JG, Evans JR. Omega 3 fatty acids for preventing or slowing the progression of age-related macular degeneration. Cochrane Database Syst Rev. 2012(11). Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

Lebuisson DA, Leroy L, Rigal G. Treatment of senile macular degeneration with ginkgo biloba extract. A preliminary double-blind drug vs. placebo study. La Press Medicale. 1986;15(31):1556-8. Excluded: in systematic review, not directly used.

Lee BS, Munoz BE, West SK, et al. Functional improvement after one- and two-eye cataract surgery in the Salisbury Eye Evaluation. Ophthalmology. 2013;120(5):949-55. Excluded: wrong population.

Leffler CT, Davenport B, Rentz J, et al. Clinical predictors of the optimal spectacle correction for comfort performing desktop tasks. Clin Exp Optom. 2008;91(6):530-7. Excluded: wrong study design for Key Question.

Lim LS, Mitchell P, Seddon JM, et al. Age-related macular degeneration. Lancet. 2012;379(9827):1728-38. Excluded: not a study (letter, editorial, non-systematic review article).

Loewenstein JI, Palmberg PF, Connett JE, et al. Effectiveness of a pinhole method for visual acuity screening. Arch Ophthamol. 1985;103:222-3. Excluded: wrong population.

Loftus JV, Sultan MB, Pleil AM, et al. Changes in vision- and health-related quality of life in patients with diabetic macular edema treated with pegaptanib sodium or sham. Invest Ophthalmol Vis Sci. 2011;52(10):7498-505. Excluded: wrong population.

Lois N, McBain V, Abdelkader E, et al. Retinal pigment epithelial atrophy in patients with exudative age-related macular degeneration undergoing anti-vascular endothelial growth factor therapy. Retina. 2013;33(1):13-22. Excluded: wrong study design for Key Question.

Lord SR, Smith ST, Menant JC. Vision and falls in older people: risk factors and intervention strategies. Clin Geriatr Med. 2010;26(4):569-81. Excluded: not a study (letter, editorial, non-systematic review article).

Lubinski W, Podboraczynska-Jodko K, Gronkowska-Serafin J, et al. Visual outcomes three and six months after implantation of diffractive and refractive multifocal IOL combinations. Klin Oczna. 2011;113(7-9):209-15. Excluded: wrong study design for Key Question.

Lubinski W, Podboraczynska-Jodko K, Gronkowska-Serafin J, et al. Visual outcome three and six months after implantation of Acri.LISA 366D lenses. Klin Oczna. 2012;114(4):249-54. Excluded: wrong study design for Key Question.

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):1831-6. Excluded: wrong intervention.

Lundstrom M, Stenevi U, Thorburn W. Cataract surgery in the very elderly. J Cataract Refract Surg. 2000;26(3):408-14. Excluded: wrong study design for Key Question.

Ma L, Dou H-L, Huang Y-M, et al. Improvement of retinal function in early age-related macular degeneration after lutein and zeaxanthin supplementation: a randomized, double-masked, placebo-controlled trial. Am J Ophthalmol. 2012;154(4):625-34.e1. Excluded: wrong outcomes.

Macular Photocoagulation Study Group. Argon laser photocoagulation for senile macular degeneration. Results of a randomized clinical trial. Arch Ophthalmol. 1982;100(6):912-8. Excluded: in systematic review, not directly used.

Macular Photocoagulation Study Group. Krypton laser photocoagulation for neovascular lesions of age-related macular degeneration. Results of a randomized clinical trial. . Arch Ophthalmol. 1990;108(6):816-24. Excluded: in systematic review, not directly used.

Macular Photocoagulation Study Group. Laser photocoagulation of subfoveal recurrent neovascular lesions in age-related macular degeneration. Results of a randomized clinical trial. Arch Ophthalmol. 1991;109(9):1232-41. Excluded: in systematic review, not directly used.

Appendix A4. Excluded Studies

Macular Photocoagulation Study Group. Laser photocoagulation of subfoveal neovascular lesions in age-related macular degeneration. Results of a randomized clinical trial. . Arch Ophthalmol. 1991;109(9):1220-31. Excluded: in systematic review, not directly used.

Mangione CM, Phillips RS, Lawrence MG, et al. Improved visual function and attenuation of declines in health-related quality of life after cataract extraction. Arch Opthalmol. 1994;112:1419-25. Excluded: wrong study design for Key Question.

Mares-Perlman JA, Klein R, Klein BE, et al. Association of zinc and antioxidant nutrients with age-related maculopathy. Arch Ophthalmol. 1996;114(8):991-7. Excluded: wrong study design for Key Question.

Mataix J, Desco MC, Palacios E, et al. Photodynamic therapy for age-related macular degeneration treatment: epidemiological and clinical analysis of a long-term study. Ophthalmic Surg Lasers Imaging. 2009;40(3):277-84. Excluded: wrong study design for Key Question.

Mathew MC, Ervin A-M, Tao J, et al. Antioxidant vitamin supplementation for preventing and slowing the progression of age-related cataract. Cochrane Database Syst Rev. 2012;6:CD004567. Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

McGwin G, Jr., Owsley C, Gauthreaux S. The association between cataract and mortality among older adults. Ophthalmic Epidemiol. 2003;10(2):107-19. Excluded: in systematic review, not directly used.

McGwin G, Jr., Scilley K, Brown J, et al. Impact of cataract surgery on self-reported visual difficulties: comparison with a no-surgery reference group. J Cataract Refract Surg. 2003;29(5):941-8. Excluded: in systematic review, not directly used.

McNeil JJ, Robman L, Tikellis G, et al. Vitamin E supplementation and cataract: randomized controlled trial. Ophthalmology. 2004;111(1):75-84. Excluded: in systematic review, not directly used.

Mekjavic PJ, Kraut A, Urbancic M, et al. Efficacy of 12-month treatment of neovascular age-related macular degeneration with intravitreal bevacizumab based on individually determined injection strategies after three consecutive monthly injections. Acta Ophthalmol (Oxf). 2011;89(7):647-53. Excluded: wrong study design for Key Question.

Melki SA, Safar A, Martin J, et al. Potential acuity pinhole: a simple method to measure potential visual acuity in patients with cataracts, comparison to potential acuity meter. Ophthalmology. 1999;106(7):1262-7. Excluded: wrong outcomes.

Meuleners LB, Hendrie D, Lee AH, et al. The effectiveness of cataract surgery in reducing motor vehicle crashes: a whole population study using linked data. Ophthalmic Epidemiol. 2012;19(1):23-8. Excluded: wrong study design for Key Question.

Meuleners LB, Lee AH, Ng JQ, et al. First eye cataract surgery and hospitalization from injuries due to a fall: a population-based study. J Am Geriatr Soc. 2012;60(9):1730-3. Excluded: wrong study design for Key Question.

Meuleners LB, Ng JQ, Fraser M, et al. Impact of gender on first eye cataract surgery and motor vehicle crash risk for older drivers. Clin Experiment Ophthalmol. 2012;40(6):591-6. Excluded: wrong comparison (no control group).

Michael Y, Lin J, Gold R, et al. Interventions to Prevent Falls in Older Adults: Systematic Evidence Review for the U.S. Preventative Services Task Force. 2009. Excluded: wrong intervention.

Mitchell P, Korobelnik JF, Lanzetta P, et al. Ranibizumab (Lucentis) in neovascular age-related macular degeneration: evidence from clinical trials. Br J Ophthalmol. 2010;94(1):2-13. Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

Moradian S, Faghihi H, Sadeghi B, et al. Intravitreal bevacizumab vs. sham treatment in acute branch retinal vein occlusion with macular edema: results at 3months (Report 1). Graefes Arch Clin Exp Ophthalmol. 2011;249(2):193-200. Excluded: wrong population.

Morris MS, Jacques PF, Chylack LT, et al. Intake of zinc and antioxidant micronutrients and early age-related maculopathy lesions. Ophthalmic Epidemiol. 2007;14(5):288-98. Excluded: wrong outcomes.

Muether PS, Hermann MM, Koch K, et al. Delay between medical indication to anti-VEGF treatment in age-related macular degeneration can result in a loss of visual acuity. Graefes Arch Clin Exp Ophthalmol. 2011;249(5):633-7. Excluded: wrong study design for Key Question.

Appendix A4. Excluded Studies

National Eye Institute. Age-Related Eye Disease Study 2 (AREDS2): A Multi-center, randomized Trial of Lutein, Zeaxanthin, and Omega 3 Long-Chain Polyunsaturated Fatty Acids (Docosahexaenoic Acid [DHA] and Eicosapentaenoic Acid [EPA]) in Age-Related Macular Degeneration. 2009. Excluded: wrong comparison (no control group).

Newsome D, M. S, N. L, et al. Oral zinc in macular degeneration. Arch Ophthalmol. 1988;106(2):192-8. Excluded: in systematic review, not directly used.

Newsome DA. A randomized, prospective, placebo-controlled clinical trial of a novel zinc-monocysteine compound in age-related macular degeneration. Curr Eye Res. 2008;33(7):591-8. Excluded: in systematic review, not directly used.

Nongpiur ME, Sharma P. Horizontal Lang two-pencil test as a screening test for stereopsis and binocularity. Indian J Ophthalmol. 2010;58(4):287-90. Excluded: wrong outcomes.

Nuriyah Y, Ren X-T, Jiang L, et al. Comparison between ophthalmologists and community health workers in screening of shallow anterior chamber with oblique flashlight test. Chin Med Sci J. 2010;25(1):50-2. Excluded: wrong outcomes.

O'Dell BL. Role of zinc in plasma membrane function. J Nutr. 2000;130(5S Suppl):1432S-6S. Excluded: wrong outcomes.

Oliveira CM, Cristovao LM, Ribeiro ML, et al. Improved automated screening of diabetic retinopathy. Ophthalmologica. 2011;226(4):191-7. Excluded: wrong intervention.

Owsley C, McGwin G, Jr., Stalvey BT, et al. Educating older African Americans about the preventive importance of routine comprehensive eye care. J Natl Med Assoc. 2008;100(9):1089-95. Excluded: wrong intervention.

Patino CM, Varma R, Azen SP, et al. The impact of change in visual field on health-related quality of life the los angeles latino eye study. Ophthalmology. 2011;118(7):1310-7. Excluded: wrong study design for Key Question.

Piermarocchi S, Saviano S, Parisi V, et al. Carotenoids in Age-related Maculopathy Italian Study (CARMIS): two-year results of a randomized study. Eur J Ophthalmol. 2012;22(2):216-25. Excluded: in systematic review, not directly used.

Prasad AS. Zinc deficiency in humans: a neglected problem. J Am Coll Nutr. 1998;17(6):542-3. Excluded: not a study (letter, editorial, non-systematic review article).

Pulido JS, Winters JL, Boyer D. Preliminary analysis of the final multicenter investigation of rheopheresis for age related macular degeneration (AMD) trial (MIRA-1) results. Transactions of the American Ophthalmological Society Vol. 2006;104:221-31. Excluded: in systematic review, not directly used.

Reddy U, Krzystolik M. Antiangiogenic therapy with interferon alfa for neovascular age-related macular degeneration. Cochrane Database Syst Rev. 2008;1. Excluded: wrong intervention.

Rein DB, Wittenborn JS, Zhang X, et al. The cost-effectiveness of three screening alternatives for people with diabetes with no or early diabetic retinopathy. Health Serv Res. 2011;46(5):1534-61. Excluded: wrong study design for Key Question.

Renaud J, Levasseur M, Gresset J, et al. Health-related and subjective quality of life of older adults with visual impairment. Disabil Rehabil. 2010;32(11):899-907. Excluded: wrong study design for Key Question.

Renfro MO, Fehrer S. Multifactorial screening for fall risk in community-dwelling older adults in the primary care office: development of the fall risk assessment & screening tool. J Geriatr Phys Ther. 2011;34(4):174-83. Excluded: wrong study design for Key Question.

Richer S, Stiles W, Statkute L, et al. 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). Optometry 2004;75(4):216-30. Excluded: in systematic review, not directly used.

Richer SP, Stiles W, Graham-Hoffman K, et al. Randomized, double-blind, placebo-controlled study of zeaxanthin and visual function in patients with atrophic age-related macular degeneration: the Zeaxanthin and Visual Function Study (ZVF) FDA IND #78, 973. Optometry. 2011;82(11):667-80.e6. Excluded: wrong comparison (no control group).

Rine RM, Roberts D, Corbin BA, et al. New portable tool to screen vestibular and visual function--National Institutes of Health Toolbox initiative. J Rehabil Res Dev. 2012;49(2):209-20. Excluded: wrong population.

Appendix A4. Excluded Studies

Rogers DL, Neely DE, Chapman JB, et al. Comparison of the MTI Photoscreener and the Welch-Allyn SureSight autorefractor in a tertiary care center. J Aapos. 2008;12(1):77-82. Excluded: wrong population.

Sacu S, Michels S, Prager F, et al. Randomised clinical trial of intravitreal Avastin vs photodynamic therapy and intravitreal triamcinolone: long-term results. Eye. 2009;23(12):2223-7. Excluded: wrong comparison (no control group).

Schmidt-Erfurth U, Kaiser PK, Korobelnik JF, et al. Intravitreal aflibercept injection for neovascular age-related macular degeneration: ninety-six-week results of the VIEW studies. Ophthalmology. 2014;121(1):193-201. Excluded: wrong study design for Key Question.

Skelton DA, Howe TE, Ballinger C, et al. Environmental and behavioural interventions for reducing physical activity limitation in community-dwelling visually impaired older people. Cochrane Database Syst Rev. 2013;6:CD009233. Excluded: wrong intervention.

Snodderly DM. Evidence for protection against age-related macular degeneration by carotenoids and antioxidant vitamins. Am J Clin Nutr. 1995;62(6 Suppl):1448S-61S. Excluded: not a study (letter, editorial, non-systematic review article).

Solomon SD, Lindsley K, Vedula SS, et al. Anti-vascular endothelial growth factor for neovascular age-related macular degeneration. Cochrane Database Syst Rev. 2014;8:CD005139. Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

Souayah N, Khella SL. A prospective double-blind, placebo-controlled study of thalidomide sensory symptoms in an elderly population with age-related macular degeneration. J Clin Neurosci. 2010;17(5):571-3. Excluded: wrong intervention.

Stur M, Tittl M, Reitner A, et al. Oral zinc and the second eye in age-related macular degeneration. Invest Ophthalmol Vis Sci. 1996;37(7):1225-35. Excluded: in systematic review, not directly used.

Swamy B, Cumming RG, Ivers R, et al. Vision screening for frail older people: a randomised trial. Br J Ophthalmol. 2009;93(6):736-41. Excluded: screening conducted by an optometrist.

Swanson MW, Bodner E, Sawyer P, et al. Visual acuity's association with levels of leisure-time physical activity in community-dwelling older adults. J Aging Phys Act. 2012;20(1):1-14. Excluded: wrong study design for Key Question.

Tan JS, Wang JJ, Flood V, et al. Dietary antioxidants and the long-term incidence of age-related macular degeneration: the Blue Mountains Eye Study. Ophthalmology. 2008;115(2):334-41. Excluded: wrong study design for Key Question.

Teikari JM, Rautalahti M, Haukka J, et al. Incidence of cataract operations in Finnish male smokers unaffected by alpha tocopherol or beta carotene supplements. J Epidemiol Community Health. 1998;52(7):468-72. Excluded: wrong population.

Thatch AB, Yau L, Hoang C, et al. Time to clinically significant visual acuity gains after ranibizumab treatment for retinal vein occlusion: BRAVO and CRUISE trials. Ophthalmology. 2014;121(5):1059-66. Excluded: wrong population.

Tielsch JM, Sommer A, Witt K, et al. Blindness and visual impairment in an American urban population. The Baltimore Eye Survey. Arch Ophthalmol. 1990;108(2):286-90. Excluded: wrong outcomes.

Tseng VL, Yu F, Lum F, et al. Risk of fractures following cataract surgery in Medicare beneficiaries. JAMA. 2012;308(5):493-501. Excluded: wrong population.

Tufail A, Patel PJ, Egan C, et al. Bevacizumab for neovascular age related macular degeneration (ABC Trial): multicentre randomised double masked study. Bmj. 2010;340. Excluded: wrong comparison (no control group).

Vallance JH, Johnson B, Majid MA, et al. A randomised prospective double-masked exploratory study comparing combination photodynamic treatment and intravitreal ranibizumab vs intravitreal ranibizumab monotherapy in the treatment of neovascular age-related macular degeneration. Eye (London, England). 2010;24(10):1561-7. Excluded: wrong comparison (no control group).

van der Made S, Kelly ER, Berendschot TT, et al. Consuming a buttermilk drink containing lutein-enriched egg yolk daily for 1 year increased plasma lutein but did not affect serum lipid or lipoprotein concentrations in adults with early signs of age-related macular degeneration. J Nutr. 2014;144(9):1370-7. Excluded: wrong outcomes.

van Leeuwen R, Boekhoorn S, Vingerling JR, et al. Dietary intake of antioxidants and risk of age-related macular degeneration. JAMA. 2005;294(24):3101-7. Excluded: wrong study design for Key Question.

VandenLangenberg GM, Mares-Perlman JA, Klein R, et al. Associations between antioxidant and zinc intake and the 5-year incidence of early age-related maculopathy in the Beaver Dam Eye Study. Am J Epidemiol. 1998;148(2):204-14. Excluded: wrong study design for Key Question.

Vedula SS, Krzystolik MG. Antiangiogenic therapy with anti-vascular endothelial growth factor modalities for neovascular age-related macular degeneration. Cochrane Database Syst Rev. 2008(2). Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

VIM Study Group. Verteporfin therapy in subfoveal minimally classis choroidal neovascularization in age-related macular degeneration. Arch Ophthalmol. 2005;123:448-57. Excluded: in systematic review, not directly used.

VIP Study Group. Photodynamic therapy of subfoveal choroidal neovascularization in pathologic myopia with verteporfin. Ophthalmology. 2001;108:841-52. Excluded: in systematic review, not directly used.

Vishwanathan R, Chung M, Johnson EJ. A systematic review on zinc for the prevention and treatment of age-related macular degeneration. Invest Ophthalmol Vis Sci. 2013;54(6):3985-98. Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

Weigert G, Kaya S, Pemp B, et al. Effects of lutein supplementation on macular pigment optical density and visual acuity in patients with age-related macular degeneration. Invest Ophthalmol Vis Sci. 2011;52(11):8174-8. Excluded: in systematic review, not directly used.

West SK, Rubin GS, Broman AT, et al. How does visual impairment affect performance on tasks of everyday life? The SEE Project. Salisbury Eye Evaluation. Arch Ophthalmol. 2002;120(6):774-80. Excluded: wrong study design for Key Question.

Wolf S, Holz FG, Korobelnik J-F, et al. Outcomes following three-line vision loss during treatment of neovascular age-related macular degeneration: subgroup analyses from MARINA and ANCHOR. Br J Ophthalmol. 2011;95(12):1713-8. Excluded: wrong outcomes.

Writing Committee for the UKA-RMDEMRUG. The neovascular age-related macular degeneration database: multicenter study of 92976 ranibizumab injections: report 1: visual acuity. Ophthalmology. 2014;121(5):1092-101. Excluded: wrong comparison (no control group).

Writing Group for the ARG. Effect of long-chain -3 fatty acids and lutein + zeaxanthin supplements on cardiovascular outcomes: results of the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. JAMA Intern Med. 2014;174(5):763-71. Excluded: wrong comparison (no control group).

Yehoshua Z, de Amorim Garcia Filho CA, Nunes RP, et al. Systemic complement inhibition with eculizumab for geographic atrophy in age-related macular degeneration: the COMPLETE study. Ophthalmology. 2014;121(3):693-701. Excluded: wrong outcomes.

Criteria for Assessing Internal Validity of Individual Studies

The Methods Work Group for the US Preventive Services Task Force (USPSTF) developed a set of criteria by which the internal validity of individual studies could be evaluated. The USPSTF accepted the criteria, and the associated definitions of quality categories, that relate to internal validity at its September 1999 meeting.

This appendix describes the criteria relating to internal validity and the procedures that topic teams follow for all updates and new assessments in making these judgments.

All topic teams use initial "filters" to select studies for review that deal most directly with the question at issue and that are applicable to the population at issue. Thus, studies of any design that use outdated technology or that use technology that is not feasible for primary care practice may be filtered out before the abstraction stage, depending on the topic and the decisions of the topic team. The teams justify such exclusion decisions if there could be reasonable disagreement about this step. The criteria below are meant for those studies that pass this initial filter. Presented below are a set of minimal criteria for each study design and then a general definition of three categories: "good," "fair," and "poor," based on those criteria. These specifications are not meant to be rigid rules but rather are intended to be general guidelines, and individual exceptions, when explicitly explained and justified, can be made. In general, a "good" study is one that meets all criteria well. A "fair" study is one that does not meet (or it is not clear that it meets) at least one criterion but has no known "fatal flaw." "Poor" studies have at least one fatal flaw.

Systematic Reviews

Criteria:

- Comprehensiveness of sources considered/search strategy used.
- Standard appraisal of included studies.
- Validity of conclusions.
- Recency and relevance are especially important for systematic reviews.

Definition of ratings from above criteria:

Good: Recent, relevant review with comprehensive sources and search strategies; explicit and relevant selection criteria; standard appraisal of included studies; and valid conclusions.

Fair: Recent, relevant review that is not clearly biased but lacks comprehensive sources and search strategies.

Poor: Outdated, irrelevant, or biased review without systematic search for studies, explicit selection criteria, or standard appraisal of studies.

Randomized Controlled Trials and Cohort Studies

Criteria:

- Initial assembly of comparable groups:
  - For RCTs: adequate randomization, including first concealment and whether potential confounders were distributed equally among groups.

  - For 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.
- All important outcomes considered.
- Analysis: adjustment for potential confounders for cohort studies, or intention to treat analysis for RCTs.

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; all important outcomes are considered; and appropriate attention to confounders in analysis. In addition, for RCTs, intention to treat analysis is used.

Fair: Studies will be graded "fair" if any or all of the following problems occur, without the fatal flaws noted in the "poor" category below: Generally comparable groups are assembled initially but some question remains whether some (although not major) differences occurred with 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. Intention to treat analysis is done for RCTs.

Poor: Studies will be graded "poor" if any of the following fatal flaws 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. For RCTs, intention to treat analysis is lacking.

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 variables.

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.

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 fatal flaw such as: Uses inappropriate reference standard; screening test improperly administered; biased ascertainment of reference standard; very small sample size or very narrow selected spectrum of patients.

Source: Procedure Manual. *U.S. Preventive Services Task Force Procedure Manual.* Available at: http://www.uspreventiveservicestaskforce.org/Page/Name/procedure-manual.

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Federal Partners

Food and Drug Administration/Center for Drug Evaluation and Research

National Institute on Aging/National Institutes of Health

Veteran's Health Administration

Appendix B1. Studies of Screening for Impaired Visual Acuity Included in the Prior USPSTF Review

Author, Year Study Design Country Setting Duration of Followup Quality	Population	Sample size	Intervention	Results
Eekhof, 2000[69] Cluster RCT The Netherlands General practice 2 years Fair	Mean age 81 years 64% female Race not reported Baseline visual acuity: Not reported	1,121	A. Screening: assessment of difficulty in recognizing a face at 4 m 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 B. Delayed screening	A vs. B Proportion with visual disorder in 2nd year: 51% (95% CI 45% to 58%) vs. 47% (95% CI 42% to 52%); p=0.68 Vision problem detected: 49% vs. NR
Moore, 1997[70] Cluster RCT United States Community-based office practice 6 months Fair	Mean age 76 years 62% female Race: Not reported Baseline visual acuity: Not reported	261	A. Screening: question to assess difficulty performing everyday activities, followed by Snellen eye chart if positive B. Usual care	A vs. B Improvement in vision at 6 months: 20% (20/99) vs. 24% (31/131); RR 0.85 (95% CI 0.52 to 1.40) Vision problem detected: 20% vs. 19%
Smeeth, 2003[71] Cluster RCT United Kingdom General practice 3-5 years Good	Mean age 80 years 62% female Race not reported Reported difficulty seeing newsprint: 8% vs. 10%	3,346	A. Universal screening: detailed health assessment by a trained nurse, including Glasgow eye chart and pinhole testing if visual acuity less than 6/18 in either eye B. Targeted screening: brief health assessment	A vs. B Visual acuity less than 6/18 (20/60): RR 1.07 (95% CI 0.84 to 1.36) NEI-VFQ mean composite score (scale 0 to 100; higher score = better quality of life): 86.0 vs. 85.6; mean difference 0.4 (95% CI -1.7 to 2.5) Found to have visual acuity <6/18 in either eye: 27% (451/1662) vs. 3.1% (53/1684)

Abbreviations: CI = confidence interval; NEI-VFQ = National Eye Institute Vision Function Questionnaire; NR = not reported; RCT = randomized controlled trial.

Appendix B2. Characteristics of Diagnostic Accuracy Studies Included in the Prior USPSTF Review

Study, Year	Type of Study	Age of Enrollees and Sample Size	Proportion With Visual Conditions	Reference Standard	Screening Text	Quality
Ariyasu, 1996[74]	Cross-sectional	"Most patients" 20 to 59 years old n=317	43% refractive error, 16% cataract, 4% macular degeneration, 4% strabismus, 2% amblyopia	Ophthalmologic examination	Amsler grid abnormal	Poor-Fair
Eekhof, 2000[75]	Cross-sectional	75 years or older n=1121	Snellen chart <0.3: 10.8%	Snellen chart	Screening questions	Fair
Hiller, 1983[76]	Cross-sectional	25 to 74 years n=3997 (1466 for subgroup) 65 to 74 years old	Snellen 20/25 or worse: 69%	Snellen chart	Screening question	Fair
Ivers, 2001[77]	Cross-sectional	49 years or older n=3654	3.9% posterior subcapsular cataract, 19.1% cortical cataract, 47.0% nuclear cataract, 4.5% early AMD, 4.5% refractive error, 34.50% any vision condition	Ophthalmologic examination	Presenting distance visual acuity (logMAR chart) Pinhole distance visual acuity Presenting reading acuity (with current reading glasses)	Poor-Fair
McMurdo, 1988[78]	Cross-sectional	64 to 97 years n=50	18% previously undiagnosed cataract, 8% previously undiagnosed AMD	Ophthalmologist examination	Positive finding on physical examination	Fair
Teh, 2006[79]	Cross-sectional	60 years or older n=124	Snellen 6/12 or worse: 81%	Snellen chart	Screening question	Poor-Fair
Wang, 1998[80]	Cross-sectional	40 years or older n=405	50.7% (13% cataract, AMD and refractive error not reported)	Ophthalmologic examination	Screening questionnaire Presenting distance visual acuity, followed by pinhole visual acuity if worse than 20/30	Poor-Fair
Woods, 1998[81]	Cross-sectional	50 years or older n=3283	12% (50 to 64 years) and 23% (>64 years) macular degeneration, 4.9% and 27.2% cataract	Ophthalmologic examination	Presenting distance visual acuity Near visual acuity	Fair

Abbreviations: AMD = age-related macular degeneration; CI = confidence interval; LogMAR = logarithmic minimum angle of resolution.

Appendix B3. Studies of Diagnostic Accuracy Included in the Prior USPSTF Review

Study, Year	Reference Standard	Target Vision Condition	Screening Test	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Diagnostic Odds Ratio (95% CI)
Amsler grid								
Ariyasu, 1996[74]	Ophthalmologic examination	Any ocular disease, excluding refractive error	Amsler grid	0.20 (0.14-0.27)	0.88 (0.80-0.94)	1.65 (0.90-3.06)	0.91 (0.82-1.01)	1.82 (0.90-3.69)
Physical examination								
McMurdo, 1988[78]	Ophthalmologic examination	A: Cataract B: AMD	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)	Not calculated	Not calculated	Not calculated
Screening questions								
Eekhof, 2000[75]	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)	3.23 (2.66-3.93)	0.49 (0.40-0.61)	6.56 (4.42-9.72)
		Difficulty with low vision chart at reading distance	Trouble reading newspaper by questionnaire	0.83 (0.76-0.88)	0.67 (0.64-0.70)	2.47 (2.20-2.78)	0.26 (0.18-0.37)	9.45 (6.08-14.7)
Hiller, 1983[76]	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)	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, 2006[79]	Snellen chart	Visual acuity ≤20/40	Problem with vision by questionnaire	0.68 (0.58-0.78)	0.43 (0.22-0.66	1.19 (0.80-1.77)	0.74 (0.42-1.33)	1.60 (0.62-4.16)
Wang, 1998[80]	Ophthalmologic examination	Any ocular disease	A: Problem with vision by questionnaire B: Problem with vision by questionnaire 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)	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, 1996[74]	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	1.23 (1.04-1.46)	0.52 (0.32-0.86)	2.34 (1.23-4.47)
			≤20/40	0.76 (0.68-0.83)	0.49 (0.38-0.61	1.50 (1.19-1.90)	0.49 (0.33-0.71)	3.09 (1.71-5.55)
			≤20/60	0.60 (0.52-0.69)	0.64 (0.53-0.74	1.67 (1.22-2.30)	0.62 (0.47-0.81)	2.70 (1.53-4.77)

Appendix B3. Studies of Diagnostic Accuracy Included in the Prior USPSTF Review

Study, Year	Reference Standard	Target Vision Condition	Screening Test	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Diagnostic Odds Ratio (95% CI)
Ariyasu, 1996[74]	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	1.54 (1.26-1.90)	0.48 (0.36-0.65)	3.18 (1.96-5.18)
			≤20/40	0.68 (0.61-0.74)	0.67 (0.58-0.76	2.08 (1.57-2.76)	0.47 (0.37-0.60)	4.40 (2.69-7.18)
			≤20/60	0.53 (0.46-0.60)	0.86 (0.78-0.92	3.76 (2.34-6.03)	0.54 (0.46-0.64)	6.90 (3.82-12.5)
Ivers, 2001[77]	Ophthalmologic examination	A: Nuclear cataract B: Early AMD 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)	A: 2.83 (2.35-3.40) B: 2.16 (1.80-2.59) C: 2.43 (2.14-2.76)	A: 0.78 (0.74-0.81) B: 0.69 (0.60-0.80) C: 0.77 (0.74-0.80)	A: 3.65 (2.93-4.55) B: 3.11 (2.26-4.30) C: 3.17 (2.69-3.73)
			≤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)	A 6.57 (4.29-10.1) B: 2.59 (1.87-3.58) C: 3.74 (2.95-4.73)	A: 0.89 (0.87-0.91) B: 0.86 (0.80-0.93) C: 0.89 (0.86-0.91)	A: 7.40 (4.78-11.5) B: 3.01 (2.01-4.49) C: 4.22 (3.27-5.45)
			≤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)	A: 8.07 (4.44-14.7) B: 2.01 (1.24-3.28) C: 2.98 (2.23-3.97)	A: 0.93 (0.91-0.95) B: 0.95 (0.90-1.00) C: 0.94 (0.92-0.96)	A: 8.69 (4.76-15.8) B: 2.13 (1.25-3.63) C: 3.17 (2.34-4.30)
Ivers, 2001[77]	Ophthalmologic examination	A: Nuclear cataract B: Early AMD 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)	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)
			≤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)	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)
			≤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)	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)

Appendix B3. Studies of Diagnostic Accuracy Included in the Prior USPSTF Review

Study, Year	Reference Standard	Target Vision Condition	Screening Test	Sensitivity (95% CI)	Specificity (95% CI)	Positive Likelihood Ratio (95% CI)	Negative Likelihood Ratio (95% CI)	Diagnostic Odds Ratio (95% CI)
Ivers, 2001[77]	Ophthalmologic examination	A: Nuclear cataract B: Early AMD 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)	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)
			≤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)	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)
			≤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)	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, 1998[80]	Ophthalmologic examination	Any ocular disease	Presenting distance visual acuity ≤20/40	0.61 (0.54-0.68)	0.72 (0.65-0.78	2.18 (1.70-2.79)	0.54 (0.45-0.66)	4.02 (2.65-6.09)
Woods, 1998[81]	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	2.41 (2.08-2.80)	0.34 (0.30-0.38)	7.15 (5.52-9.26)
Woods, 1998[81]	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	5.66 (4.36-7.34)	0.30 (0.27-0.33)	18.9 (13.6-26.3)

Abbreviation: AMD = age-related macular degeneration.

Appendix B4. Trials of Treatment of Uncorrected Refractive Error Included in the Prior USPSTF Review

Study, Year	Study Design Purpose of Study Country	Patients	Intervention Duration of Followup	Results	Quality
Coleman, 2006[84]	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 followup	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=0.17 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, 2007[85]	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 followup	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; NHVQoL = Nursing Home Vision-Targeted Health-Related Quality of Life Questionnaire; SD = standard deviation; RCT = randomized controlled trial; SF-36 = Short-Form Health Survey 36-item; VF-14 = Visual Function (14 Questions).

Appendix B5. Systematic Reviews of Treatment of Uncorrected Refractive Error Included in the Prior USPSTF Review

Study, Year	Aims	Literature Searches	Patients/Trials	Interventions	Results	Conclusion	Quality
Murray, 2005[87]	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	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.	Uncorrected visual acuity of 20/20 or better in myopia: PRK 70%, LASEK 62%, LASIK 64% 20/40 or better: PRK 92%, LASEK 92% <u>Efficacy</u> LASIK 94% highly myopic eyes achieved High myopia at baseline, 20/20: PRK 14%, LASIK 44% Low myopia at baseline: PRK 76%, 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%, 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

Abbreviations: BSCVA = best spectacle-corrected visual acuity; LASEK = laser assisted sub-epithelial keratomileusis; LASIK = laser assisted in situ keratomileusis; PRK = photorefractive keratectomy; RCT = randomized controlled trial.

Appendix B6. Systematic Reviews of Treatment of Cataracts Included in the Prior USPSTF Review

Study, Year	Aims	Literature Searches	Patients/Trials	Interventions	Results	Conclusion	Quality
Powe,1994[91]	To define the effectiveness and risks of cataract surgery	MEDLINE 1975 to 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 phacoemulsification and extracapsular extraction	Pooled % of eyes with 20/40 acuity or better: 95.5% (CI 95.1% to 95.9%) in patients 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, 1998[133]	To obtain an estimate of the incidence of PCO and to explore factors that may influence its development	MEDLINE 1979 to 1996; reference lists	49 studies (design NR); total n=NR	27 studies: extracapsular extraction; 9 studies: phacoemulsification; 13 studies: mixed extracapsular extraction and phacoemulsification	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%)	Visually significant PCO develops in more than 25% of patients undergoing extracapsular extraction or phacoemulsification with IOL within 5 years of surgery	Fair
Taban, 2005[134]	To determine the reported incidence of acute endophthalmitis following cataract extraction and to explore possible contributing factors	Cochrane (database not specified); MEDLINE 1963 to March 2003; reference lists; textbook hand search; conference proceedings 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 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

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

Appendix B7. Trials of Treatment of Cataracts Included in the Prior USPSTF Review

Study, Year	Study Design Purpose of Study	Patients	Intervention Duration of Followup	Results	Quality
Chylack, 2002[94]	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 all visits; age ≥40 years; ≥1 eyes met the following ocular criteria: cataract extraction unlikely within 2 years, immature idiopathic 'senile' cataract present in 1 or both eyes, U.S. patients: presence of minimal cataract by 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 6 mm; oscillatory movement displacement threshold ≤50 S; 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 (250 mg vitamin C + 200 mg vitamin E + 6 mg beta carotene) tid vs. placebo 3 years followup	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, 2006[93]	RCT To determine if second eye cataract surgery reduces the risk of falling and to measure associated health gain	Women in the U.K. age ≥70 years with a previous, successful cataract operation who had a second, operable cataract	Cataract surgery vs. no/delayed treatment 1 year followup	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
Harwood, 2005[92]	RCT to determine if first eye cataract surgery reduces the risk of falling and to measure associated health gain	Women in the U.K. age ≥70 years with cataract who were suitable for surgery and had not had previous ocular surgery	Cataract surgery (phacoemulsification) vs. no/delayed treatment 1 year followup	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 0.40 to 0.96; p=0.03)	Good

Appendix B7. Trials of Treatment of Cataracts Included in the Prior USPSTF Review

Study, Year	Study Design Purpose of Study	Patients	Intervention Duration of Followup	Results	Quality
				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)	

Abbreviations: CI = confidence interval; LOCS = Lens Opacities Classification System; HR = hazard ratio; PCT = placebo controlled trial; RCT = randomized controlled trial; YAG = yttrium aluminium garnet.

Appendix B8. Systematic Reviews of Age-Related Macular Degeneration Included in the Prior USPSTF Review

Study, Year	Aims	Literature Searches	Patients/Trials	Interventions
Evans, 2008[98] *Antioxidant vitamin and mineral supplements*	To assess the effects of antioxidant vitamin or mineral supplementation, alone or in combination, on the progression of AMD	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	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 vs. lutein + broad-spectrum antioxidant 1 trial: zinc oxide 80 mg QD, vitamin C, vitamin E vs. placebo
Evans, 2008[49] *Ginkgo biloba*	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	2 trials: Fies 2002 (n=99); Lebuisson 1986 (n=20); total n=119	Gingko biloba extract EGb 761, doses 60-160 mg QD; placebo
Vedula, 2008[120]	To investigate the effects of anti-VEGF modalities for treating neovascular AMD	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)	Pegaptanib 0.3, 1.0 or 3.0 mg Ranibizumab 0.3 or 0.5 mg Verteporfin PDT Sham injection/sham PDT
Virgili, 2007[113]	To examine the effect of laser photocoagulation on neovascular (wet) AMD	CCRCT, MEDLINE, EMBASE, LILACS, NRR, ZETOC through March 2007	15 trials; 12 of which compared laser photocoagulation to no treatment	Laser photocoagulation No treatment
Wormald, 2008[114]	To examine the effects of photodynamic therapy in the treatment of AMD	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	IV verteporfin (2 trials: 6 mg/m^2; 1 trial dose NR) + cold laser vs placebo + cold laser

Appendix B8. Systematic Reviews of Age-Related Macular Degeneration Included in the Prior USPSTF Review

Study, Year	Results	Conclusion	Quality
Evans, 2008[98] *Antioxidant vitamin and mineral supplements*	**All comparisons** *Any multivitamin or antioxidant vs placebo* Change in visual acuity, defined as a loss of ≥3 lines (≥15 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) AMD 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 AMD 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 lines (≥15 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) AMD progression as a dichotomous variable (AREDS): adjusted OR 0.68 (CI 0.53 or 0.87) AMD progression as a continuous variable (AMDSG): mean difference -0.06 (CI -0.62 to 0.50) *Vitamin E vs. placebo (VECAT)* Change in visual acuity, defined as a loss of ≥3 lines (≥15 letters) on a logMAR chart: OR 1.05 (CI 0.70 to 1.57) AMD progression: OR 0.11 (CI 0.80 to 1.55) *Zinc vs. placebo (AREDS, Holz 1993, Newsome 1988, Stur 1996)* Change in visual acuity, defined as a loss of ≥3 lines (≥15 letters) on a logMAR chart (AREDS, Newsome 1988; I^2=0%): OR 0.81 (CI 0.66 to 0.99) Mean difference visual acuity (Newsome 1988, Stur 1996; I^2=56.6%): results somewhat inconsistent but no statistically significant difference found between treatment and control groups in both trials AMD progression as a dichotomous variable (AREDS, Holz 1993, Stur 1996; I^2=29.0%): pooled OR 0.73 (0.58-0.93) *Lutein vs. placebo (LAST)* Mean difference visual acuity: 0.04 (-0.15 to 0.23)	Limited evidence, based primarily on AREDS, suggests a benefit in the use of antioxidant vitamins and minerals in slowing AMD 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, 2008[49] *Ginkgo biloba*	*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 AMD progression. There may be harms associated with gingko biloba use, but they have been too inadequately reported.	Good

Appendix B8. Systematic Reviews of Age-Related Macular Degeneration Included in the Prior USPSTF Review

Study, Year	Results	Conclusion	Quality
Vedula, 2008[120]	*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 3.0 mg dose vs sham; NNT 6.67 0.3 mg dose, 6.25 1.0 mg dose, 14.28 3.0 mg 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 score at 2-year followup* ANCHOR Trial: 5.9 ranibizumab 0.3 mg vs. 8.1 ranibizumab 0.5 mg vs 2.2 verteprofin MARINA Trial: 4.8 ranibizumab 0.3 mg vs. 4.5 0.5 mg 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 0.5 mg dose relative to 0.3 mg 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, 2007[113]	*Photocoagulation vs no treatment* Visual acuity, loss of ≥6 lines at 3 months (5 trials): RR 1.41 (95% CI 1.08 to 1.82; I^2=0%) Visual acuity, loss of ≥6 lines at 2 years (5 trials): RR 0.67 (95% CI 0.53 to 0.83; I^2=58%) Visual acuity 20/200 or better at 1-3 years (3 trials): RR 0.73 (95% CI 0.61 to 0.86; I^2=43%) Visual acuity 20/200 or better at 5 years followup (2 trials): RR 0.77 (95% CI 0.66 to 0.90; I^2=21%)	Photocoagulation is effective for certain types of AMD (extrafoveal CNV). For juxta- or sub-foveal CNV patients, the benefit of laser photocoagulation is less clear.	Good
Wormald, 2008[114]	*Laser photocoagulation vs sham* Loss of >3 lines of visual acuity at 12 months (4 trials): RR 0.80 (95% CI 0.69 to 0.93; I^2=30%) Loss of >3 lines of visual acuity at 24 months (4 trials): RR 0.80 (95% CI 0.73 to 0.83; I^2=0%) Loss of ≥6 lines of visual acuity at 12 months (4 trials): RR 0.70 (95% CI 0.56 to 0.88; I^2=0%) Loss of ≥6 lines of visual acuity at 24 months (4 trials): RR 0.66 (95% CI 0.53 to 0.83; I^2=31%) Gain of ≥3 lines of visual acuity at 12 months (3 trials): RR 2.19 (95% CI 0.99 to 4.82; I^2=0%) Gain of ≥3 lines of visual acuity at 24 months (3 trials): RR 2.55 (95% CI 1.31 to 4.99; I^2=0%) *Harms* Severe acute loss of visual acuity (3 trials): RR 3.75 (95% CI 0.87 to 16; I^2=28%) Visual disturbance (3 trials): RR 1.56 (95% CI 1.21 to 2.01; I^2=7%) Injection site reaction (3 trials): RR 2.09 (95% CI 1.29 to 3.39; I^2=73%) Infusion-related back pain (4 trials): RR 9.93 (95% CI 2.82 to 35; I^2=0% Allergic reaction (2 trials): RR 0.94 (95% CI 0.34 to 2.56; I^2=0%) Photosensitivity (2 trials): RR 5.37 (95% CI 1.01 to 29; I^2=70%)	Photodynamic therapy is effective in preventing further visual loss due to AMRD, although the effect size is unclear.	Good

Abbreviations: AE = adverse event; AMD = age-related macular degeneration; CI = confidence interval; IV = intravenous; logMAR = logarithmic minimum angle of resolution; NEI -VFQ = National Eye Institute Visual Functioning Questionnaire; NNH = number needed to harm; NNT = number needed to treat; NR = not reported; NRR = National Research Register; OR = odds ratio; PDT = photodynamic therapy; pts = patients; QD = daily; QoL = quality of life; RR = relative risk; VECAT = Vitamin E, Cataract and Age-Related Maculopathy Study; VEGF = vascular endothelial growth factor; WMD = weighted mean difference.

Appendix B9. Trials of Age-Related Macular Degeneration Included in the Prior USPSTF Review

Study, Year	Study Design Purpose of Study	Patients	Intervention Duration of Followup	Results
AMD (Dry)				
AREDS Research Group, 2001[97] and Johnson 2007[135] *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 PCT	n=3640 Median age 56 years 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 80 mg/day Antioxidant multivitamin + zinc Placebo 7 years	Progression to advanced AMD: 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: adjusted OR 0.66 (0.47 to 0.93) 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: adjusted OR 0.75 (0.55 to 1.02) ORs adjusted for age, sex, race, baseline AMD category and smoking status Increased risk for hospitalization due to genitourinary causes versus non-use (RR 1.47, 95% CI 1.19 to 1.80)
AMD (Wet)				
VEGF inhibitors				
Gragoudas, 2004[122] (VISION; 2 trials)	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)	0.3, 1.0, or 3.0 mg pegaptanib every 6 weeks up to 48 weeks (9 treatments) vs. sham injection	Pegaptanib (all doses) vs sham: Visual acuity, gain ≥15 letters: 5.7% (51/890) vs. 2.0% (6/296); RR 2.83 (95% CI 1.23 to 6.52) Visual acuity, loss <15 letters: 68.8% (612/890) vs. 55.4% (164/296) Visual acuity, 20/200 or better: 58.7% (522/890) vs. 44.3% (131/296) Withdrawals due to adverse events: 1% (9/890) vs. 1% (3/296); RR 1.00 (95% CI 0.27 to 3.66) Endophthalmitis: 1.3% (12/890) vs. 0% (0/296); RR 8.33 (95% CI 0.50 to 140) Traumatic lens injury: 0.6% (5/890) vs. 0% (0/296); RR 3.67 (95% CI 0.20 to 66) Retinal detachment 0.6% (5/890) vs. 0% (0/296); RR 3.67 (95% CI 0.20 to 66) Severe (>30 letters) vision loss: 0.1% (1/890) vs. 0% (0/296); RR 1.00 (95% CI 0.04 to 24)
Regillo, 2008[123] *PIER study year 1*	To evaluate the effectiveness and safety of ranibizumab for treatment of minimally classic or occult with no classic choroidal neovasculatization associated with AMD. Prospective, double-blind RCT.	n=184 Mean age ~78 years 60% female Neovascular AMD	0.3 or 0.5 mg ranibizumab vs sham injection; dosing 1x/month for 3 months followed by 1x every 3 months 12 months	Ranibizumab (all doses) vs. sham: Visual acuity, gain ≥15 letters: 12.4% (15/121) vs. 9.5% (6/63); RR 1.30 (95% CI 0.53 to 3.19) Visual acuity, loss <15 letters: 86.8% (105/121) vs. 49.2% (31/63) Visual acuity, 20/200 or better: 73.6% (89/121) vs. 44.4% (28/63) Mortality and CV events: No deaths, MI or CVA in either group Withdrawals: 0.8% (1/121) vs. 0% (0/63); RR 1.57 (95% CI 0.07 to 38) Ocular hemorrhage: 1.6% (2/121) vs. 3.2% (2/63); RR 0.52 (95% CI 0.08 to 3.61) Macular edema: 0.8% (1/121) vs. 3.2% (2/63); RR 0.26 (95% CI 0.02 to 2.82)

Appendix B9. Trials of Age-Related Macular Degeneration Included in the Prior USPSTF Review

Study, Year	Study Design Purpose of Study	Patients	Intervention Duration of Followup	Results
Rosenfeld et al, 2006[121] *MARINA Trial*	To evaluate the effectiveness and safety of ranibizumab for treatment of minimally classic or occult with no classic choroidal neovasculatization associated with AMD. Double-blind PCT.	n=716 Mean age 77 years (SD 8) 65% female AMD	0.3 or 0.5 mg ranibizumab 1x/month (range 23-37 days) for 2 years vs. sham injection 2 years	*Ranibizumab (all doses) vs. sham:* Visual acuity, gain ≥15 letters: 29.2% (140/478) vs. 5.0% (12/238); RR 5.81 (95% CI 3.29 to 10.26) Visual acuity, loss <15 letters: 94.6% (452/478) vs. 62.2% (148/238) Visual acuity, 20/200 or better: 88.1% (421/478) vs. 57.1% (136/238) All-cause mortality: 2.3% (11/478) vs. 2.5% (6/238); RR 0.91, 95% CI 0.34 to 2.44 Vascular mortality: 1.3% (6/478) vs. 1.7% (4/236); RR 0.74, 95% CI 0.21 to 2.60 MI: 1.9% (9/478) vs. 1.7% (4/238); RR 1.12, 95% CI 0.35 to 3.60 CVA: 1.9% (9/478) vs. 0.8% (2/238); RR 2.24, 95% CI 0.49 to 10 Withdrawals: 13.2% (63/478) vs. 28.6% (68/238); RR 0.46 (95% CI 0.34 to 0.63) Withdrawals due to adverse events: 4.8% (23/478) vs. 5.5% (13/238); RR 0.88 (95% CI 0.45 to 1.70) Serious, nonocular hemorrhage: 1.7% (8/478) vs. 0.8% (2/236); RR 1.97 (95% CI 0.42 to 9.23) Endophthalmitis: 5/478 vs 0/238; RR 5.49 (95% CI 0.30 to 99) Uveitis: 1.3% (6/478) vs. 0% (0/238); RR 6.49 (95% CI 0.37 to 115) Retinal detachment: 0% (0/478) vs. 0.4% (1/238); RR 0.17 (95% CI 0.01 to 4.07) *Ranizumab 0.3 mg vs. 0.5 mg vs. sham* Vision related quality of life (NEI-VFQ), mean change from baseline: 1-year followup, composite score (95% CI): 5.2 (3.5 to 6.9) vs. 5.6 (3.9 to 7.4) vs. −2.8 (−4.6 to −1.1); ranibizumab vs. sham p<0.01 General health score: −2.6 (−5.0 to 0.2) vs. −5.1 (−7.6 to −2.6) vs. −6.9 (−9.6 to −4.3); ranibizumab vs. sham p=NS Mental health score: 12.0 (9.4 to 14.6) vs. 13.1 (10.0 to 16.2) 3.3 (0.5 to 6.1); ranibizumab vs. sham p<0.01 Social functioning score: 3.1 (0.3 to 5.9) vs. 3.8 (1.2 to 6.3) vs. −5.1 (−7.7 to −2.5); ranibizumab vs. sham p<0.01 Driving score: −2.1 (−5.9 to 1.7) vs. −0.4 (− 3.8 to 3.0) vs. −12.4 (−16.0 to −8.7); ranibizumab vs. sham p<0.0 12-year followup, composite score: 4.8 (2.9 to 6.8) vs. 4.5 (2.5 to 6.5) vs. −6.5 (−8.4 to −4.6); ranibizumab vs. sham p<0.01 General health score: −5.7 (−8.6 to −2.8) vs. −6.7 (−9.6 to −3.8) vs −9.0 (−12.0 to −6.2); ranibizumab vs. sham p=NS Mental health score: 11.9 (8.9 to 14.9) v.s 12.6 (9.4 to 15.8) vs. −0.7 (−3.7 to 2.4); ranibizumab vs. sham p<0.01 Social functioning score: 1.9 (−1.1 to 4.9) vs. 1.4 (−1.6 to 4.3) vs. −9.5 (−12.0 to −6.5); ranibizumab vs. sham p<0.01 Driving score: −1.6 (−5.7 to 2.5) vs. −2.7 (−6.3 to 0.9) vs. −17.1 (−21.0 to −13.0); ranibizumab vs. sham p<0.01

Abbreviations: AMD = age-related macular degeneration; BCVA = best-corrected visual acuity; CI = confidence interval; NR = not reported; NS = not significant; OR = odds ratio; PCT = placebo controlled trial; RCT = randomized controlled trial; RR = risk ratio; SD = standard deviation; VEGF = vascular endothelial growth factor.

Appendix C1. Studies of Diagnostic Test Accuracy Published Since the Prior USPSTF Review

Study, Year	Type of Study	Screening Test	Reference Standard	Setting	Screener	Age of Enrollees	N	Proportion With Condition	Subjects
Jessa, 2012[82] Study 1	Cross-sectional	6-item Computer Vision screener (CVS)	"Gold standard eye exam," including computerized high-contrast visual acuity and low-contrast visual acuity tests	Community settings and optometrist offices, United Kingdom	Optometrist	≥65 years (mean 77 years)	180	Cataract: 31.7% Significant refractive error: 39.4% Correctable visual loss: 58.3% Significant macular degeneration: 28.9%	46% male 12% seen in community 10% no spectacles, 46.6% multifocal, 23.9% distance vision, 38.3% near vision
Jessa, 2012[82] Study 2	Cross-sectional	4-item Computer Vision screener (CVS) and Flip-chart Vision Screener (FVS)	"Gold standard eye exam," including computerized high-contrast visual acuity and low-contrast visual acuity tests	Community settings and optometrist offices, United Kingdom	Optometrist	≥65 years (mean 77 years)	200	Cataract: 30.7% Significant refractive error: 30% Correctable visual loss: 51% Significant macular degeneration: 22.5%	31% male 31.5% seen in community 15.5% no spectacles, 44.5% multifocal, 22.5% distance vision, 31.5% near vision
Swanson, 2009[83]	Cross-sectional	Minimum Data Set (MDS) Vision Patterns section	ETDRS chart	17 nursing homes United States	Trained research staff	>55 years 60-69 years: 10.4% 70-79 years: 32.9% 80-89 years: 41.8% >90 years: 16.0%	371	Impaired visual acuity: 40.6% (151/371)	Mean age: 80.7 years Female sex: 80.6% Race: 73.3% white, 26.4% black, 0.3% Hispanic Mean MMSE: 20.9 Near visual acuity, better eye: 0.56 Near visual acuity, worse eye: 0.81 Distance visual acuity, better eye: 0.43 Distance visual acuity, worse eye: 0.64

Appendix C1. Studies of Diagnostic Test Accuracy Published Since the Prior USPSTF Review

Study, Year	Sensitivity	Specificity
Jessa, 2012[82] Study 1	**High-contrast visual acuity (Va >0.19 LogMAR)** **CVS** Cataract: 86.0% (95% CI 74.2 to 93.7%) Refractive error: 76.1% (95% CI 64.5 to 85.4%) Correctable visual loss: 79.1% (95% CI 70.0 to 86.4%) AMD: 75.0% (95% CI 61.1 to 86.0%) **Low-contrast visual acuity (Va >0.39 LogMAR)** **CVS** Cataract: 79.0% (95% CI 66.1 to 88.6%) Refractive error: 69.0% (95% CI 56.9 to 79.5%) Correctable visual loss: 66.7% (95% CI 56.8 to 75.6%) AMD: 75.0% (95% CI 61.1 to 86.0%) **Optimal (high-contrast visual acuity >0.39 LogMAR or near visual acuity):** 79.5% (95% CI 71.5 to 85.7%)	**High-contrast visual acuity (Va >0.19 LogMAR)** **CVS** Cataract: 51.2% (95% CI 42.1 to 60.3%) Refractive error: 54.1% (95% CI 44.3 to 63.7%) Correctable visual loss: 60.0% (95% CI 48.0 to 71.2%) AMD: 50.0% (95% CI 41.0 to 59.0%) **Low-contrast visual acuity (Va >0.39 LogMAR)** **CVS** Cataract: 55.3% (95% CI 46.1 to 64.3%) Refractive error: 55.1% (95% CI 45.2 to 64.6%) Correctable visual loss: 58.7% (95% CI 46.7 to 69.9%) AMD: 56.3% (95% CI 47.2 to 65.0%) **Optimal (high-contrast visual acuity >0.39 LogMAR or near visual acuity):** 67.9% (95% CI 57 to 77.3%)
Jessa, 2012[82] Study 2	**High-contrast visual acuity (Va >0.19 LogMAR)** **CVS** Cataract: 65.6% (95% CI 52.3 to 77.3%) Refractive error: 73.3% (95% CI 60.3 to 83.9%) Correctable visual loss: 64.7% (95% CI 54.6 to 73.9%) AMD: 62.2% (95% CI 46.5 to 76.2%) **FVS** Cataract: 57.4% (95% CI 44.1 to 70.0%) Refractive error: 63.3% (95% CI 49.9 to 75.4%) Correctable visual loss: 55.9% (95% CI 45.7 to 65.7%) AMD: 51.1% (95% CI 35.8 to 66.3%) **Low-contrast visual acuity (Va >0.39 LogMAR)** **CVS** Cataract: 63.9% (95% CI 50.6 to 75.8%) Refractive error: 70.0% (95% CI 56.8 to 81.2%) Correctable visual loss: 63.7% (95% CI 53.6 to 73.0%) AMD: 66.7% (95% CI 51.1 to 80.0%) **FVS** Cataract: 68.9% (95% CI 55.7 to 80.1%) Refractive error: 70.0% (95% CI 56.8 to 81.2%) Correctable visual loss: 70.6% (95% CI 60.7 to 79.2%) AMD: 62.2% (95% CI 46.5 to 76.2%) **Optimal cut-off (high-contrast visual acuity >0.19 LogMAR or near visual acuity):** 75.4% (95% CI 67.1 to 82.2%)	**High-contrast visual acuity (Va >0.19 LogMAR)** **CVS** Cataract: 59.7% (95% CI 51.1 to 67.9%) Refractive error: 60.7% (95% CI 52.1 to 68.9%) Correctable visual loss: 34.7% (95% CI 25.4 to 45.0%) AMD: 58.1% (95% CI 49.9 to 65.9%) **FVS** Cataract: 67.6% (95% CI 59.2 to 75.3%) Refractive error: 67.9% (95% CI 59.5 to 75.5%) Correctable visual loss: 72.5% (95% CI 62.5 to 81.0%) AMD: 78.7% (95% CI 71.4 to 84.9%) **Low-contrast visual acuity (Va >0.39 LogMAR)** **CVS** Cataract: 64.8% (95% CI 56.2 to 72.7%) Refractive error: 65.0% (95% CI 56.5 to 72.9%) Correctable visual loss: 70.4% (95% CI 60.3 to 79.2%) AMD: 63.9% (95% CI 55.8 to 71.4%) **FVS** Cataract: 63.3% (95% CI 54.7 to 71.3%) Refractive error: 70.0% (95% CI 61.7 to 77.5%) Correctable visual loss: 71.4% (95% CI 61.4 to 80.1%) AMD: 67.7% (95% CI 59.8 to 75.0%) **Optimal cut-off (high-contrast visual acuity >0.19 LogMAR or near visual acuity):** 69.2% (95% CI 58.3 to 78.4%)
Swanson, 2009[83]	52% (95% CI 45% to 59%)	75% (95% CI 68% to 82%)

Abbreviations: AMD = age-related macular degeneration, CI = confidence interval, CVS = computer Vision screener, ETDRS = Early Treatment Diabetic Retinopathic Study, FVS = flip-chart vision screener, MDS = minimum data sets, MMSE = Mini-Metal State Examination.

Appendix C2. Quality Assessment of Studies of Diagnostic Test Accuracy Published Since the Prior USPSTF Review

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
Jessa, 2012[82]	Yes	No; n=380	Yes	Yes	Yes	Unclear	Fair
Swanson, 2009[83]	Yes	No; n=371	Yes	Yes	Yes	Unclear	Fair

Appendix C3. Studies of Treatment of Uncorrected Refractive Error or Cataracts Published Since the Prior USPSTF Review

Author, Year	Study Design	Country Number of Centers and Setting	Inclusion Criteria	Number Randomized, Analyzed Attrition	Intervention (n)	Study Participants	Outcome Measures
Refractive error							
Elliott, 2009[86] Also cataracts	Prospective cohort	United States 17 nursing homes	Age ≥55 years, with a MMSE score ≥13	Screened: NR Eligible: NR Enrolled: 187 Analyzed: 187 Attrition: NR Loss to followup: NR	A. Immediate treatment of refractive error with new bifocal glasses (n=78) B. Delayed treatment of refractive error by 2 months (n=64)	A vs. B Mean age: 79 vs. 78 years Female sex: 77% vs. 75% Race: 62% white, 37% black, 1% Hispanic vs. 75% white, 25% black, 0% Hispanic Comorbidities Glaucoma: 1.3% vs. 6.5% AMD: 16.7% vs. 14.5% Cataract: 68.0% vs. 60.3% Diabetic retinopathy: 3.9% vs. 9.7%	Physical function, cognitive status, fear of falling
Cataracts							
Elliott, 2009[86] See also Owsley, 2007[96]	Prospective cohort	United States 17 nursing homes	Age ≥55 years, with a MMSE score ≥13; cataract patients had to have cataract in one or both eyes that caused functional problems	Screened: NR Eligible: NR Enrolled: 187 Analyzed: 187 Attrition: NR Loss to followup: NR	A. Cataract surgery (n=30) B. No cataract treatment (n=15)	A vs. B Mean age: 81 vs. 87 years Female sex: 73% vs. 87% Race: 77% white, 23% black vs. 80% white, 20% black Visual acuity: NR Comorbidities Glaucoma: 0% vs. 6.7% AMD: 10% vs. 20% Cataract: 100% vs. 100% Diabetic retinopathy: 0% vs. 0%	Physical function, cognitive status, fear of falling
Hall, 2005[95] Impact of Cataract on Mobility Study (also included in prior review)	Prospective cohort	United States 10 ophthalmology practices and 2 optometry clinics	Age ≥55 years with cataract in one or both eyes (for those with cataract), visual acuity ≤20/40, no previous cataract surgery. Exclude: amblyopia, dementia, Parkinson disease, or psychosis	Screened: NR Eligible: NR Enrolled: 301 Analyzed: 301 Attrition: NR Loss to followup: NR	A. Cataract, treated with surgery (n=122) B. Cataract, no treatment (n=87) C. No cataract (n=92)	A vs. B vs. C Mean age: 70.9 vs. 71.1 vs. 66.8 years; p<0.001 Female sex: 58% vs. 40% vs. 51%; p=0.04 Race: 90.2% vs. 81.6% vs. 82.6% White (others NR) Mean visual acuity, better eye: 0.28 vs. 0.16 vs. -0.02 Mean visual acuity, worse eye: 0.55 vs. 0.35 vs. 0.09 Mean CES depression scale score: 6.9 vs. 8.2 vs. 5.4; p=0.03	Cognitive function, visual acuity

Appendix C3. Studies of Treatment of Uncorrected Refractive Error or Cataracts Published Since the Prior USPSTF Review

Author, Year	Duration of Followup	Results	Adverse Events	Sponsor	Quality
Refractive error					
Elliott, 2009[86] Also cataracts	2 months	A vs. B Functional Independence Measure*, baseline-followup Assessed by certified nursing assistant: 47.9-47.5 vs. 53.5-51.8; between-group p=0.16-0.37 Assessed by patient: 50.8-49.1 vs. 57.4-55.2; between-group p=0.08-0.75 Survey of Activities**, baseline-followup Activity: 8.6-8.6 vs. 9.1-8.9; between-group p=0.30-0.34 Restriction: 8.1-8.4 vs. 7.5-7.5; between-group p=0.29-0.32 Mini-Mental State Examination***, baseline-followup: 20.2-19.4 vs. 21.7-20.5; between-group p=0.06-0.72 * Range 0-91; higher scores indicate greater independence ** Activity subscale range 0-14, higher scores indicate greater activity; restriction subscale range 0-14, higher score indicates more activities performed less often than 5 years earlier *** Score <24 indicates cognitive impairment	NR	Retirement Research Foundation, EyeSight Foundation of Alabama, and National Institutes of Health	Fair
Cataracts					
Elliott, 2009[86] See also Owsley, 2007[96]	4 months	A vs. B Functional Independence Measure*, baseline-followup Assessed by certified nursing assistant: 49.9-50.9 vs. 47.7-41.5; between-group p=0.78-0.07 Assessed by patient: 48.5-50.5 vs. 51.5-51.9; between-group p=0.67-0.39 Survey of Activities**, baseline-followup Activity: 8.4-8.2 vs. 8.7-9.0; between-group p=0.37-0.31 Restriction: 7.8-6.5 vs. 7.0-6.4; between-group p=0.48-0.79 Mini-Mental State Examination***, baseline-followup: 21.3-20.4 vs. 19.7-17.0; between-group p=0.32-0.27 NHVQoL, baseline-followup General vision: 57.2-79.3 vs. 65.7-67.7; p=0.005 Reading: 69.4-93.6 vs. 78.3-78.3; p=0.001 Social interaction: 86.4-98.1 vs. 94.2-91.2; p=0.033 VF-14, baseline-followup: 68.7-93.6 vs. 80.5-82.0; p=0.004 * Range 0-91; higher scores indicate greater independence ** Activity subscale range 0-14, higher scores indicate greater activity; restriction subscale range 0-14, higher score indicates more activities performed less often than 5 years earlier *** Score <24 indicates cognitive impairment	NR	Retirement Research Foundation, EyeSight Foundation of Alabama, and National Institutes of Health	Fair
Hall, 2005[95] Impact of Cataract on Mobility Study (also included in prior review)	2 years (cognitive function assessed at 1 year)	A vs. B vs. C Mean visual acuity, better eye: 0.09 vs. 0.17 vs. -0.01; between-group p<0.001 Mean visual acuity, worse eye: 0.28 vs. 0.38 vs. 0.12; between-group p<0.001 Change in visual acuity significant only in surgery group (p=0.003 in better eye and p=0.03 in worse eye) Mean CES depression scale score: 6.0 vs. 8.7 vs. 4.5; between-group p=0.001	NR	National Institutes of Health, Research to Prevent Blindness, and Eyesight Foundation	Fair

Abbreviations: AMD = age-related macular degeneration, CES = Center for Epidmiologic Studies, MMSE = Mini-Mental State Examination, NHVQoL = Nursing Home Vision-Targeted Health-Related Quality of Life Questionairre, NR = not reported, VF-14 = Vision Function (14 Questions).

Appendix C4. Quality Assessment of Observational Studies of Treatment of Uncorrected Refractive Error or Cataracts Published Since the Prior USPSTF Review

Author, Year	Did the study attempt to enroll all (or a random sample of) patients meeting inclusion criteria, or a random sample (inception cohort)?	Were the groups comparable at baseline on key prognostic factors (e.g., by restriction or matching)?	Did the study use accurate methods for ascertaining exposures and potential confounders?	Were outcome assessors and/or data analysts blinded to the exposure being studied?	Did the article maintain comparable groups (report attrition, contamination, adherence, and cross-over)?	Did the study perform appropriate statistical analyses on potential confounders?	Is there important differential or overall high loss to followup?	Were outcomes pre-specified and defined and ascertained using accurate methods?	Quality
Elliott, 2009[86]	Unclear	Yes; except age	Yes	Unclear	Yes	Yes	No/No	Yes	Fair
Hall, 2005[95] Impact of Cataract on Mobility Study (also included in prior review)	Yes; consecutive	No; not age, sex, comorbidities, or visual acuity	Yes	No	No	Yes	No/No	Unclear; used unvalidated MOMSSE instrument	Fair

Abbreviation: MOMSSE = Mattis Organic Mental Syndrome Screening Examination.

Appendix C5. Systematic Reviews of Age-Related Macular Degeneration Published Since the Prior USPSTF Review

Author, Year	Comparison	Databases Searched, Date of Last Search	Number and Design of Studies	Interventions and Number of Patients	Methods for Rating Methodological Quality of Primary Studies	Methods for Synthesizing Results of Primary Studies	Results	Adverse Events	Quality
Evans, 2012[100]	Antioxidant vitamin or mineral supplement vs. placebo/no intervention	MEDLINE, EMBASE, CCRCT, AMED, OpenGrey, mRCT, ClinicalTrials.gov through August 2012	13 RCTs zinc (5 trials), lutein (2 trials), vitamin E (1 trial), antioxidant combination (4 trials); multiple interventions (1 trial)	A. Antioxidant vitamin or mineral supplement A1. Multivitamin or mineral supplement A2. Zinc B. Placebo/no intervention n/N by treatment group not reported; total n=6,150	Risk of bias assessment using criteria from Cochrane Handbook for Systematic Review Interventions (2011)	For dichotomous outcomes, calculated RRs and standard error and converted reported ORs to RRs when possible. Random effects model used to assess SMD for continuous outcomes. If ≤3 trials, fixed effects model was used.	**A vs. B (SMD)** Visual acuity, loss of ≥3 lines (3 trials): OR 0.81 (95% CI 0.67 to 0.98) Mean visual acuity (4 trials): no meta-analysis; SMD range -0.80 to 0.14; CI significant for 1 study (SMD -0.80, 95% CI -1.27 to -0.32) Mean change in visual acuity (3 trials): no meta-analysis; SMD range -0.34 to 0.42; CI not significant for any trial AMD progression, dichotomous: no meta analysis; OR ranged from 0.50 to 2.31; CI not significant for any trial **A1 vs. B** Mean visual acuity (2 trials): SMD 0.00 (95% CI -0.45 to 0.45) Mean change in visual acuity (2 trials): SMD 0.34 (95% CI -0.10 to 0.79) AMD progression, continuous (2 trials): no meta-analysis conducted; results from individual trials found no significant difference AMD progression, dichotomous (1 trial): adjusted OR (for ages, sex smoking and AMD category) 0.68 (95% CI 0.53 to 0.87) **A2 vs. B** Visual acuity, loss of ≥3 lines (2 trials): OR 0.81 (95% CI 0.66 to 0.99) Mean visual acuity (1 trial): SMD 0.15 (95 % CI -0.29 to 0.60) Mean change in visual acuity (1 trial): SMD -0.34 (95% CI -0.79 to 0.11) AMD progression, dichotomous (3 trials): OR 0.73 (95% CI 0.58 to 0.93)	No meta-analysis; narrative review suggested higher rates of withdrawals due to adverse events in participants taking zinc vs. placebo. Other harms not well reported.	Good

Abbreviations: AMD = age-related macular degeneration, CI = confidence interval, OR = odds ratio, RCT = randmized controlled trial, RR = risk ratio, SMD = standardized mean difference.

Appendix C6. Quality Assessment of Systematic Reviews of Age-Related Macular Degeneration Published Since the Prior USPSTF Review

Author, Year	"A priori" design provided?	Duplicate study selection and data abstraction?	Comprehensive literature search performed?	Non-English language studies considered for inclusion?	Conducted searches for unpublished (gray) literature?	List of included studies provided?	List of excluded studies provided with reasons?	Characteristics of the included studies provided?	Scientific quality of included studies assessed or documented?	Sensitivity analyses or stratified analyses conducted according to study quality?	Study conclusions supported by the evidence?	Conflict of interest stated for systematic review or individual studies?	Quality
Evans, 2012[100]	Yes	Yes Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes Yes	No	Yes	Yes No	Good

Appendix C7. Studies of Supplements for Age-Related Macular Degeneration Published Since the Prior USPSTF Review

Author, Year Study Name	Study Design	Country Setting	Inclusion criteria	Randomized Analyzed Attrition	Intervention
Chew, 2013[99] AREDS (Report #35)	RCT (long-term observational followup)	United States Multicenter	Age 55 to 80 years with AMD and BCVA ≥20/32 in at least one eye	n=2,459, focusing on AREDS categories 3 and 4 for vision-related outcomes; 3,476 for categories 2, 3, and 4; total sample 4,753 Attrition: NA	A. Antioxidant supplement (vitamin C 500 mg + vitamin E 400 IU + beta-carotene, 15 mg/day) B. Zinc 80 mg/day C. Antioxidant supplement + zinc D. Placebo
Chew, 2009[112] AREDS (Report #25)	RCT (long-term observational followup)	United States Multicenter	Age 55 to 80 years with AMD and BCVA ≥20/32 in at least one eye	Randomized: 4,757 Analyzed (post-trial followup): 4,577 Attrition: NA	A. Any AREDS active treatment B. Placebo
Ma, 2012[106]	RCT	China Single center	Age 50-79 years with early AMD used AREDS classification	Randomized: 108 Analyzed: 107 Attrition: 0.9% (1/108)	A. Lutein 10 mg/day B. Lutein 20 mg/day C. Lutein 10 mg/day + zeaxanthin 10 mg/day D. Placebo
Murray, 2013[105] CLEAR	RCT	United Kingdom Multicenter	Age 50-80 years with AMD grade 0 to 4 (Rotterdam criteria); BCVA logMAR ≥0.5, with minimal cataract	Randomized: 84 Analyzed: 73 Attrition: 13% (11/84)	A. Lutein 10 mg/day B. Placebo
Souied, 2013[107] NAT2	RCT	France Single hospital-based ophthalmology clinic	Age ≥55 to <85 years with visual acuity >0.4 logMAR in study eye with early age-related maculopathy (presence of drusen or reticular pseudodrusen) in study eye and AMD in the fellow eye	Randomized: 300 Analyzed: 263 for efficacy analysis, 300 for safety analysis Attrition: 21% (63/300)	A. Fish oil capsules (DHA 280 mg + EPA 90 mg + vitamin E 2 mg) 3x/day B. Placebo (olive oil 602 mg)

Appendix C7. Studies of Supplements for Age-Related Macular Degeneration Published Since the Prior USPSTF Review

Author, Year Study Name	Study Participants	Duration of Followup	Results
Chew, 2013[99] AREDS (Report #35)	A vs. B vs. C vs. D* Median age 69 vs. 70 vs. 69 vs. 69 years 55% vs. 57% vs. 56% vs. 56% female Race: 97% vs. 96% vs. 97% vs. 96% white 2% vs. 3% vs. 3% vs. 4% black 1% vs. 1% vs. <1% vs. <1% other AMD category: 2: 28% vs. 30% vs. 28% vs. 30% 3: 40% vs. 41% vs. 42% vs. 40% 4: 24% vs. 22% vs. 22% vs. 22%	10 years	**A + C (antioxidant) vs. B+D (no antioxidant)** *(Participants with AMD category 2, 3 or 4 at baseline)* All-cause mortality: 24.0% (439/1831) vs. 23.6% (427/1806); aHR* 1.06 (95% CI 0.93 to 1.21) CV mortality: aRR 1.20 (95% CI 0.97 to 1.49) Cancer mortality: aRR 1.07 (95% CI 0.83 to 1.38) Non-CV, non-cancer mortality: aRR 0.94 (95% CI 0.74 to 1.20) **B + C (zinc) vs. A + D (no zinc)** All-cause mortality: 22.4% (401/1790) vs. 25.2% (465/1847); aHR 0.83 (95% CI 0.73 to 0.95) CV mortality: aRR 0.80 (95% CI 0.64 to 0.99) Cancer mortality: aRR 0.84 (95% CI 0.65 to 1.08) Non-CV, non-cancer mortality: aRR 0.93 (95% CI 0.73 to 1.18) **A vs. D** Loss of visual acuity ≥15 letters ETDRS: OR 0.88 (95% CI 0.73 to 1.06) Visual acuity <20/100: OR 0.87 (95% CI 0.68 to 1.11) Progression to advanced AMD: OR 0.74 (95% CI 0.59 to 0.92) **B vs. D** Loss of visual acuity ≥15 letters ETDRS: OR 0.89 (95% CI 0.74 to 1.08) Visual acuity <20/100: OR 0.91 (95% CI 0.71 to 1.15) Progression to advanced AMD: OR 0.87 (95% CI 0.70 to 1.07) **C vs. D** Loss of visual acuity ≥15 letters ETDRS: OR 0.76 (95% CI 0.63 to 0.93) Visual acuity <20/100: OR 0.75 (95% CI 0.58 to 0.97) Progression to advanced AMD: C vs D: OR 0.69 (95% CI 0.56 to 0.86) *Participants with AMD category 3 or 4 at baseline* **A vs. D** Loss of visual acuity ≥15 letters ETDRS: OR 0.83 (95% CI 0.67 to 1.02) Visual acuity <20/100: OR 0.82 (95% CI 0.64 to 1.07) Progression to advanced AMD: OR 0.70 (95% CI 0.56 to 0.88) **B vs. D** Loss of visual acuity ≥15 letters ETDRS: OR 0.86 (95% CI 0.70 to 1.07) Visual acuity <20/100: OR 0.88(95% CI 0.69 to 1.14) Progression to advanced AMD: OR 0.82 (95% CI 0.66 to 1.02) **C vs. D** Loss of visual acuity ≥15 letters ETDRS: OR 0.71 (95% CI 0.57 to 0.88) Visual acuity <20/100: OR 0.72 (95% CI 0.56 to 0.94) Progression to advanced AMD: C vs D: OR 0.66 (95% CI 0.53 to 0.83) *Participants with AMD category 4 at baseline* **A vs. D** Loss of visual acuity ≥15 letters ETDRS: OR 0.75 (95% CI 0.53 to 1.06) Visual acuity <20/100: OR 0.76 (95% CI 0.52 to 1.12) Progression to advanced AMD: OR 0.64 (95% CI 0.46 to 0.91) **B vs. D**

Appendix C7. Studies of Supplements for Age-Related Macular Degeneration Published Since the Prior USPSTF Review

Author, Year Study Name	Study Participants	Duration of Followup	Results
			Loss of visual acuity ≥15 letters ETDRS: OR 0.68 (95% CI 0.48 to 0.96) Visual acuity <20/100: OR 0.66 (95% CI 0.45 to 0.98) Progression to advanced AMD: OR 0.68 (95% CI 0.49 to 0.96) **C vs. D** Loss of visual acuity ≥15 letters ETDRS: OR 0.54 (95% CI 0.38 to 0.78) Visual acuity <20/100: OR 0.58 (95% CI 0.38 to 0.86) Progression to advanced AMD: C vs D: OR 0.56 (95% CI 0.40 to 0.79)
Chew, 2009[112] AREDS (Report #25)	Not reported by treatment group for this analysis (see Chew 2013 for characteristics for the entire AREDS cohort)	Up to 11 years (mean followup not reported)	**A vs. B** Incident cataract surgery: 25.4% (798/3137) vs. 25.2% (369/1467); RR 1.01 (95% CI 0.01 to 1.13)
Ma, 2012[106]	A vs. B vs. C vs. D Mean age 70 vs. 69 vs. 69 vs. 69 years 62% vs. 56% vs. 56% vs. 60% female Race not reported BCVA 0.30 vs. 0.28 vs. 0.28 vs. 0.31 logMAR 89% vs. 89% vs. 85% vs. 89% non-smoker	48 weeks	**A vs. D** BCVA, mean change from baseline: -0.04 (95% CI -0.11 to 0.03) vs. -0.00 (95% CI -0.06 to 0.05); p=NS **B vs. D** BCVA, mean change from baseline: -0.02 (95% CI -0.11 to 0.06) vs. -0.00 (95% CI -0.06 to 0.05); p=NS **C vs. D** BCVA, mean change from baseline: -0.04 (95% CI -0.10 to 0.01) vs. -0.00 (95% CI -0.06 to 0.05); p=NS
Murray, 2013[105] CLEAR	A vs. B Mean age 71.9 vs. 69.1 years 56% vs. 65% female Race not reported Visual acuity 0.10 vs. 0.05 logMAR	1 year	**A vs. B** Visual acuity, mean change from baseline: 0.01 v.s -0.04; p<0.05
Souied, 2013[107] NAT2	A vs B Mean age 74 vs. 73 years 69% vs. 61% female Race not reported Mean visual acuity in study eye 0.14 vs. 0.12 logMAR Cataracts 61% vs. 62% Drusen: Absent: 0.7% vs. 0% <5: 0.7% vs. 2% 5-20: 17% vs. 22% >20: 81% vs. 76% Pigmentary changes: 23% vs. 22% Stage of maculopathy: Stage 1: 78% vs. 78% Stage 2: 22% vs. 22% Smoking history: Current: 7% vs. 9%	3 years	**A vs. B** All-cause mortality: 2.2% (3/134) vs. 4.7% (6/129); RR 3.00 (95% 0.33 to 28) Best-corrected visual acuity, mean change from baseline (logMAR): 6 months: 0.040 (SD 0.122) vs. 0.007 (SD 0.118) 1 year: 0.0037 (SD 0.173) vs. 0.0008 (SD 0.122) 2 years: 0.086 (SD 0.231) vs. 0.057 (SD 0.201) 3 years: 0.155 (SD 0.297) vs. 0.116 (SD 0.258); p=0.311 Loss of visual acuity, proportion of subjects with decrease >15 letters on ETDRS chart: 6 months: 3.1% (4/131) vs. 1.6% (2/126); RR 1.92 (95% CI 0.36 to 10) 1 year: 5.3% (7/131) vs. 0.8% (1/123); RR 6.57 (95% CI 0.82 to 53) 2 years: 10.8% (13/120) vs. 9.5% (11/116); RR 1.14 (95% CI 0.53 to 2.45) 3 years: 17.8% (21/118) vs. 14.3% (16/112); RR 1.25 (95% CI 0.69 to 2.26)

Appendix C7. Studies of Supplements for Age-Related Macular Degeneration Published Since the Prior USPSTF Review

Author, Year Study Name	Study Participants	Duration of Followup	Results
	Former: 14% vs. 17% Nonsmoker: 79% vs. 74% CVD: 93% vs. 80% Metabolic and nutrition disorders: 53% vs. 59% Musculoskeletal and connective tissue disorders: 45% vs. 49% GI disorder: 30% vs. 33% Concomitant medications: Lipid-lowering agents: 49% vs. 53% Renin-angiotensin system agents: 42% vs. 36% Anti-inflammatory and anti-rheumatic agents: 16% vs. 29% Diabetes: 12% vs. 10%		

Appendix C7. Studies of Supplements for Age-Related Macular Degeneration Published Since the Prior USPSTF Review

Author, Year Study Name	Adverse Events	Sponsor	Quality	Comments
Chew, 2013[99] AREDS (Report #35)	Not reported by treatment group; narrative report of no significant increase in incidence of hospitalization after adjustment for age, sex, smoking and treatment group	National Eye Institute/National Institutes of Health	Good	Hazard ratios for mortality outcomes adjusted for age, sex, race, education, smoking status, BMI, diabetes, angina, cancer, hypertension
Chew, 2009[112] AREDS (Report #25)	Not reported	National Eye Institute/National Institutes of Health	Good	None
Ma, 2012[106]	Not reported by treatment group; narrative report of no adverse events related to interventions	Not reported	Good	None
Murray, 2013[105] CLEAR	A vs. B Withdrawals due to adverse events: 7.1% (3/42) vs. 2.3% (1/42); RR 3.00 (95% 0.33 to 28)	BASF, UK Medical Research Council, Manchester Biomedical Research Center, Greater Manchester Comprehensive Local Research Network	Good	None
Souied, 2013[107] NAT2	A vs. B Any adverse event: 93.3% (125/134) vs. 89.1% (115/129); RR 1.05 (95% CI 0.97 to 1.13) Any serious AE: 31.3% (42/134) vs. 30.2% (39/129); RR 1.04 (95% CI 0.72 to 1.49) Treatment-related AE (investigator-determined): 3.7% (5/134) vs. 1.6% (2/129); RR 2.41 (95% CI 0.48 to 12) Serious ocular AE: 8.2% (11/134) vs 7.0% (9/129); RR 1.18 (95% CI 0.50 to 2.75) Ocular AE: 65.7% (88/134) vs 57.4% (74/129); RR 1.14 (95% CI 0.94 to 1.39) Cataract development, worsening or need for cataract surgery: 50% (67/134) vs. 62.5% (81/129); RR 0.80 (95 % CI 0.64 to 0.99) Serious non-ocular AE: 23.1% (31/134) v.s 23.2% (30/129); RR 0.99 (95% CI 0.64 to 1.54)	Bausch & Lomb	Good	None

Abbreviations: AMD = age-related macular degeneration, aHR = adjusted hazard ratio, aRR = adjusted risk ratio, BCVA = best corrected visual acuity, CV = cardiovascular, DHA = docosahexaenoic acid, EPA = eicosapentaenoic acid, ETDRS = Early Treatment Diabetic Retinopathy Study, IU = international units, mg = milligrams, NA = not applicable, OR = odds ratio, RCT = randomized controlled trial, RR = risk ratio, UK = United Kingdom.

Appendix C8. Quality Assessment of Studies of Supplements for Age-Related Macular Degeneration Published Since the Prior USPSTF Review

Author, year	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?	Patient masked?	Attrition and withdrawals reported?	Loss to followup differential/high?	People analyzed in the groups in which they were randomized?	Quality
Chew, 2013[99] and Chew, 2009[112] (AREDS)	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes	Yes	No	Yes	Good
Ma, 2012[106]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Good
Murray, 2013[105]	Yes	Unclear	Yes	Yes	Yes	Unclear	Yes	Yes	No	Yes	Good
Souied, 2013[107]	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Good

Appendix C9. Studies of Vascular Endothelial Growth Factor Inhibitors for Age-Related Macular Degeneration Published Since the Prior USPSTF Review

Author, year	Study Design	Number of Centers Country	Duration of Followup	Interventions	Patient Characteristics	Inclusion/Exclusion Criteria	Randomized Analyzed Attrition
Bressler, 2013[126] MARINA (post-hoc analysis)	RCT	Multicenter (96 sites) United States	2 years	A. Ranibizumab injection 0.5 mg/month (n=240) B. Ranibizumab injection 0.3 mg/month (n=238) C. Sham injection (n=238)	A vs. B vs. C (post-hoc analysis) Proportion of patients responding "yes" to NEI VFQ-25 question "are you currently driving at least once in while?": 68.1% vs. 68.2% vs. 69.6% B vs. C (group A not reported) VA better than 20/40 in one or both eyes: n=110 vs. 133 VA worse than 20/40 in both eyes: n= 129 vs. 104	Age ≥50 years with subfoveal CNV secondary to AMD and best corrected VA 20/40 to 20/320 with primary of recurrent CNV secondary to AMD with maximum lesion size 12 disk areas, presumed recent progression	Randomized: 716 Analyzed: 716 Attrition: 0%

Appendix C9. Studies of Vascular Endothelial Growth Factor Inhibitors for Age-Related Macular Degeneration Published Since the Prior USPSTF Review

Author, year	Clinical Health Outcomes	Adverse Events	Quality	Comment
Bressler, 2013[126] MARINA (post-hoc analysis)	**A vs. B vs. C (1 year followup)** Proportion of patients responding "yes" to NEI VFQ-25 question "are you currently driving at least once in while?": 65.5% vs. 64.3% vs. 52.1% (n/N not reported); change from baseline -2.6% vs. -3.9% vs. -17.5%; A vs. C p=0.0005; B vs. C p=0.010 Proportion of patients reporting driving at baseline and still driving at followup: 87.8% vs. 87.8% vs. 74.0% (n/N not reported); A vs. C p=0.002; B vs. C p=0.002 Mean change from baseline in NEI VFQ-25 driving function subscale (scale 0-100; higher score = better function): -2.1 vs. -0.4 vs. -12.5; A vs. C p=0.0004, mean treatment difference 12.1 (95% CI 7.1 to 17.1); B vs. C p<0.001, mean treatment difference 10.4 (95% CI 5.2 to 15.7) **A vs. B vs. C (2 year followup)** Proportion of patients responding "yes" to NEI VFQ-25 question "are you currently driving at least once in while?": 60.4% vs. 57.5% vs. 49.2% (n/N not reported); change from baseline -7.7% vs. -10.7% vs. -20.4% A vs. C p=0.026; B vs. C p=0.010 Proportion of patients reporting driving at baseline and still driving at followup (n/N not reported): 81.3% vs. 78.4% vs. 67.2%; A vs. C p=0.008; B vs. C p=0.090 Mean change from baseline in NEI VFQ-25 driving function subscale: -2.1 vs. -2.8 vs. -17.3; A vs. C p<0.001, mean treatment difference 14.5 (95% CI 8.9 to 20.1); B vs. C p<0.001, mean treatment difference 15.2 (95% CI 9.4 to 21.0) **A vs. C (1 year followup; results for group B not reported)** Proportion of patients with VA better than 20/40 in one or both eyes at baseline and at followup: 82.7% (91/110) vs. 62.4% (83/133); RR 1.33 (95% CI 1.13 to 1.55) Proportion of patients with VA worse than 20/40 in both eyes at baseline improved to VA better than 20/40 in one or both eyes at followup: 27.9% (36/129) vs 10.6% (11/104); RR 2.64 (95% CI 1.41 to 4.92) **A vs. C (2 year followup; results for group B not reported)** Proportion of patients with VA better than 20/40 in one or both eyes at baseline and at followup: 77.2% (85/110) vs. 56.4% (75/133); RR 1.37 (95% CI 1.14 to 1.64) Proportion of patients with VA worse than 20/40 in both eyes at baseline improved to VA better than 20/40 in one or both eyes at followup: 31.9% (41/129) vs. 7.7% (8/104); RR 4.13 (95% CI 2.03 to 8.42)	A vs B CVA: 3.3% (8/239) vs. 1.3% (3/236); RR 2.63 (95% CI 0.71 to 9.81) B vs. C CVA: 1.3% (3/238) vs. 1.3% (3/326); RR 0.99 (95% CI 0.20 to 4.86)	Good	ANCHOR results outside the scope of this report (ranibizumab vs. verteporfin)

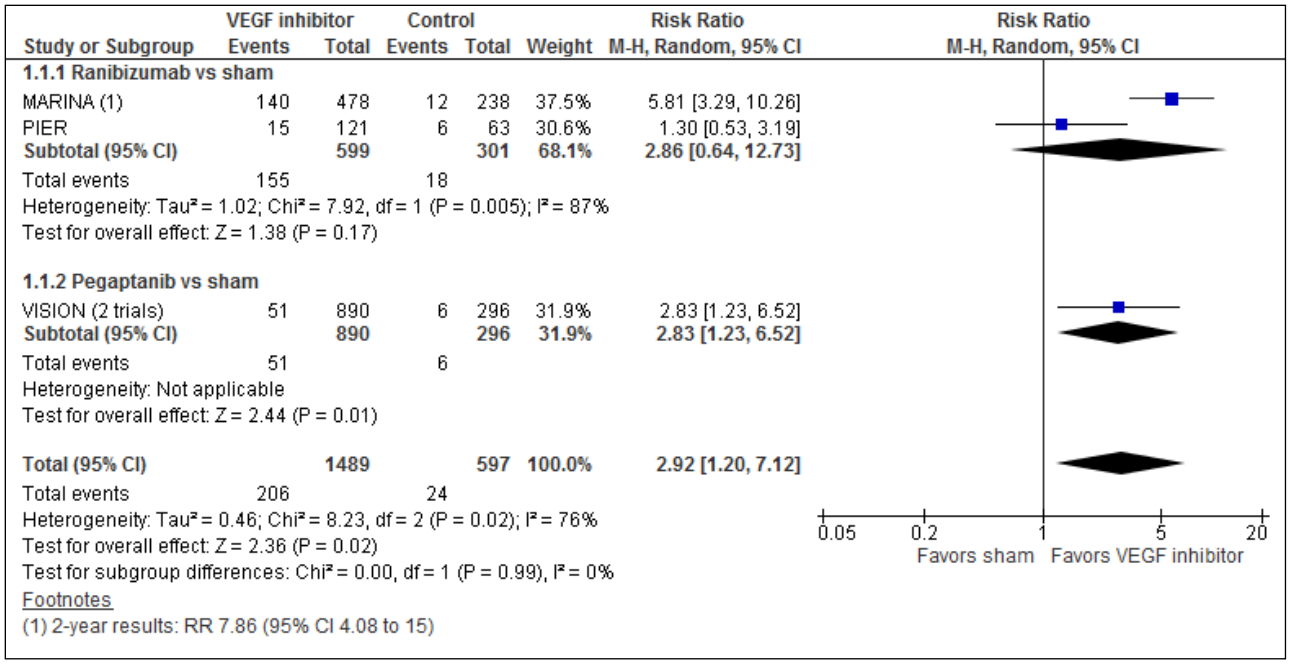
Abbreviations: AMD = age-related macular degeneration; CI = confidence interval, CNV = choroidal neovascularization; CVA = cerebrovascular accident; MI = myocardial infarction, NEI VFQ-25 = National Eye Institute Visual Function Questionairre 25, RCT = randmized controlled trial, RR = risk ratio, VA = visual acuity.
Note: Prior report studies abstracted in Appendix B.

Appendix C10. Quality Assessment of Trials of Vascular Endothelial Growth Factor Inhibitors for Age-Related Macular Degeneration

Author, year	Randomization adequate?	Allocation concealment adequate?	Groups similar at baseline?	Eligibility criteria specified?	Outcome assessors masked?	Care provider masked?	Patient masked?	Attrition and withdrawals reported?	Loss to followup differential/ high?	People analyzed in the groups in which they were randomized?	Quality
MARINA (Rosenfeld 2006 primary publication[121])	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Good
PIER (Regillo 2008 primary publication[123])	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes (1-year results only)	Good
VISION (Gragoudas 2004 primary publication[122])	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Good

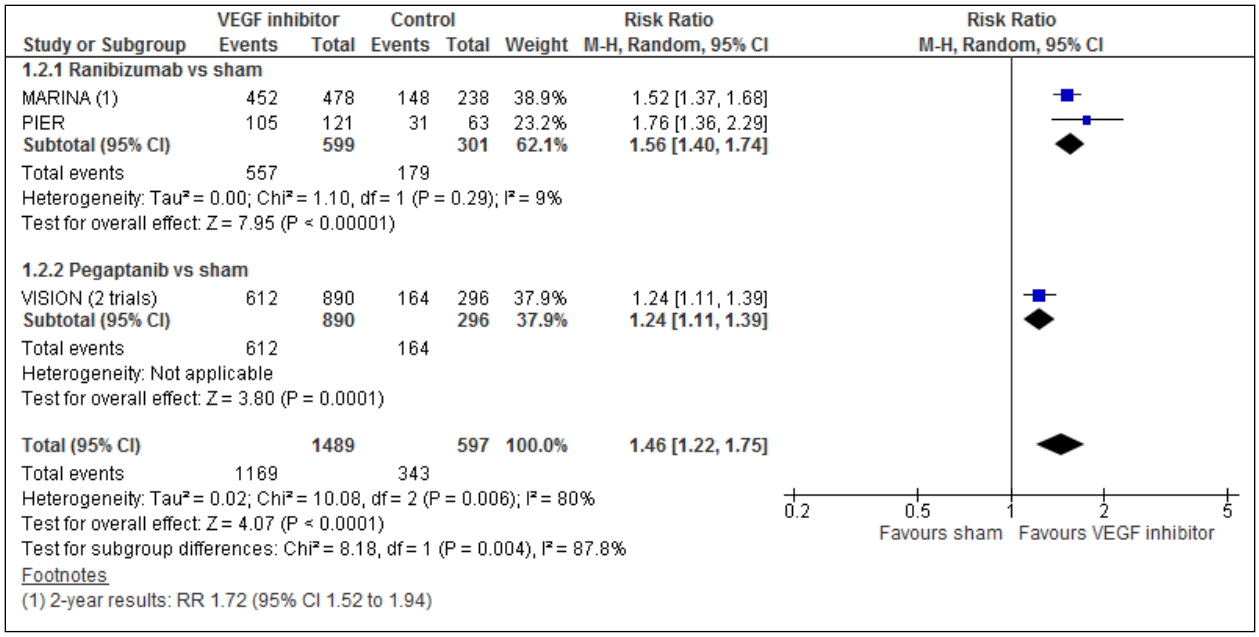
Note: Prior review studies abstracted in Appendix B.

Appendix D1. Gain of 15 Letters or More of Visual Acuity With Use of Vascular Endothelial Growth Factor Inhibitors at 1-Year Followup



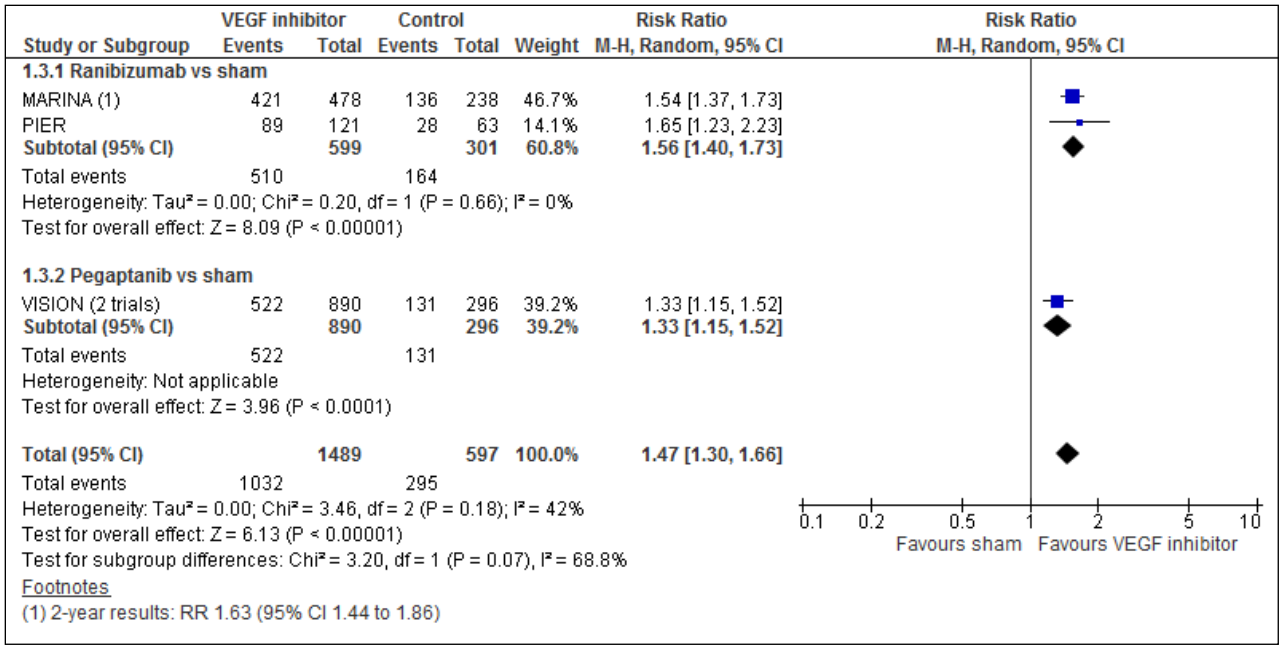
Abbreviation: VEGF = vascular endothelial growth factor.

Appendix D2. Loss of 15 Letters or Less of Visual Acuity With Use of Vascular Endothelial Growth Factor Inhibitors at 1-Year Followup



Abbreviation: VEGF = vascular endothelial growth factor.

Appendix D3. Visual Acuity of 20/200 or Better With Use of Vascular Endothelial Growth Factor Inhibitors at 1-Year Followup



Abbreviation: VEGF = vascular endothelial growth factor.