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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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Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

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Prepared by:

Pacific Northwest Evidence-Based Practice Center
Oregon Health & Science University
3181 SW Sam Jackson Park Road
Portland, OR 97239
www.ohsu.edu/epc

Investigators:

Roger Chou, MD
Tracy Dana, MLS
Christina Bougatsos, MPH
Sara Grusing, BS
Ian Blazina, MPH

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Structured Abstract

Background: Impaired visual acuity is common in older adults. In 2009, the United States 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 report 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 for 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 February 2015), 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 report) 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 (for example, 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 non-invasively 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 report 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 report 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, fundoscopic examination, and intraocular pressure measurement) or are considered part of diabetes followup and management. For this report, 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 report, “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 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 by 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 20/40⁶ or 20/50⁷ 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 report, 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 U.S., 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 as 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 over 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 age 65 to 74 years, and 15.2 percent age 75 years or greater reported having vision loss.¹¹ Prevalence of impaired visual acuity rises significantly with age in older adults, from 1.1 percent in persons 65 to 69 years of age to 16.7 percent in persons older than 80 years of age,¹² and the prevalence of both blindness and impaired visual acuity increases with age, especially among people ages 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 greater than 40 years of age and increased with age (2.8% in people aged 40 to 59 years and 11.1% in those ≥ 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 and older were estimated to have cataracts (not necessarily associated with vision impairment) in 2011,¹⁷ and 50 percent of Americans age 80 and older are estimated to have cataracts. In white women, prevalence increases from 27.7 percent in people ages 65 to 69 years to 76.6 percent in people age 80 years or older. In black women, respective prevalence rates are 28.5 percent and 60.9 percent, in white men 22.4 percent and 71.3 percent, and in black men 17.5 percent 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 of 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 and 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 compared to men. For example, among white men, the prevalence of hyperopia +3.0 D or more is 3.6 percent among those 40 to 49 years of age, 14.1 percent among those 65 to 69 years of age, and 23.5 percent among those greater than 80 years of age. Respective rates for white women are 3.7 percent, 17.8 percent, and 27.2 percent, and for black women are 3.1 percent, 10.6 percent, 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 over 65 years of age, the prevalence of myopia is relatively stable with increasing age, though prevalence varies among different ethnic/racial groups. For example, the prevalence of myopia less than -1.0 D in black men aged 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 diopters also tends to decrease with age and ranges from about 27.1 percent in U.S. adults 50 to 54 years, to 14.7 percent in adults 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, 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 impacts.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 inter-individual 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 adults in the U.S. 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 increases³⁰⁻³² and the number of older adults (\geq age 65 years) increases.^{13,20,30,33} Direct medical expenses for older adults with impaired visual acuity in the U.S. 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 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 comorbidities. 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 (PRK), 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 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 Fundoscopic 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 fundoscopic 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 levels of self-reported access to eye care services, approximately half of U.S. adults over the age of 65 years reported an eye exam 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 exam conducted by an optometrist for all adults over 60 years of age, and the American Academy of Ophthalmology recommends a comprehensive exam conducted by an ophthalmologist every 1 to 2 years in patients 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 report. 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 age-related macular degeneration?
4. Does treatment of early impairment in visual acuity due to uncorrected refractive error, cataracts or age-related macular degeneration 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 age-related macular degeneration?

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 report. MEDLINE search strategies are listed in **Appendix A1**. 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 65 years of age 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 studies and case-control studies) that evaluated vision screening performed in primary care of 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 USPSTF⁶⁸ 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, 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 report as well as new evidence.

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 report 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 report found vision screening by an optometrist in frail elderly persons associated with an increased risk for falls (RR 1.57, 95% CI 1.20 to 2.05) and a trend towards increased risk for fractures (RR 1.74, 95% CI 0.97 to 3.11). No study published since the prior report 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 report 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 report 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=3,249) 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 report 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 (RR 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 report 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 report addressed harms of vision screening in asymptomatic older adults. As described above in Key Question 1, the prior report 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 report 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 Age-Related Macular Degeneration?

Summary

The prior USPSTF report 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 report found that a computerized vision screening tool or a flipchart version were not accurate compared with a detailed eye examination (sensitivity 0.80 and specificity 0.68) and one study found the Minimum Data Set 2.0 Vision Patterns section associated with poor diagnostic accuracy compared with an eye chart exam.

Evidence

The prior report 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 (PLR) ranged from 1.19 to 3.23 and negative likelihood ratios (NLR) ranged from 0.23 to 0.78; diagnostic odds ratios (DOR; 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 [$\{ \text{true positives} / \text{false negatives} \} / \{ \text{false positives} / \text{true negatives} \}$]) were similarly weak, ranging from 1.60 to 9.45. Four studies reported low diagnostic accuracy of visual acuity tests compared to complete ophthalmologic 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 that ranged from 0.32 to 1.00, resulting in DORs less than 10. The exception was one study that found presenting distance acuity $\leq 20/40$ associated with a DOR of 18.9 (95% confidence interval [CI] 13.64 to 26.26) for identifying any visual condition.⁸¹ However, three other studies^{74,77,80} found the same distance acuity threshold associated with 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 (AUROC) 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 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 and 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 report 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 flip-chart 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, 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 aged

65 years or older (mean age 77 to 80 years), of which ~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 fundoscopic 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 >0.39 logMAR), or near visual acuity ($>N11.9$), resulting in a PLR 2.5 and a NLR of 0.29 (DOR 8.6). The flip chart instrument performed similarly, based on the low contrast visual acuity test alone (sensitivity 0.75 and specificity 0.77, for a PLR of 3.26, NLR of 0.32, and DOR of 10.2).

A third study (n=371) compared the scores on the Minimum Data Set 2.0 (MDS) Vision Patterns section against a standard visual acuity (Early Treatment Diabetic Retinopathy Study [ETDRS] chart) test for detecting impaired visual acuity.⁸³ Participants aged 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 ~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 on the MDS Visual Patterns score. Using a cutoff score of 1 (adequate vision), sensitivity of the MDS Visual Patterns section for detecting visual acuity worse than 20/40 was 0.52 and specificity 0.25, for a PLR of 0.69 and an NLR of 1.96. Using a cutoff score of 2 (impaired vision), sensitivity was 0.35 and specificity 0.80, for a PLR of 1.73, NLR of 0.81, and DOR of 2.1. Using a cutoff score of 3 (moderately impaired vision), sensitivity was 0.11 and specificity was 0.96, for a PLR of 2.47, NLR of 0.93, and DOR of 2.7.

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

Summary

For uncorrected refractive error and cataracts, the prior USPSTF report 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 report included two randomized trials of corrective lenses that reported beneficial effects on vision-related quality of life, but not in 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 report found evidence from observational studies that over 90 percent of patients undergoing cataract surgery achieve visual acuity of 20/40 or better, and one trial that found immediate cataract surgery associated with decreased risk of falls (RR 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 report 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 report included one large randomized trial, the Age-Related Eye Disease Study (AREDS) study, that found an antioxidant and zinc combination effective for lower likelihood of AMD progression (adjusted odds ratio [OR] 0.68, 95% CI 0.49 to 0.93), though the difference in the likelihood of losing ≥ 15 letters of visual acuity was not statistically significant (adjusted OR 0.77, 95% CI 0.58 to 1.03) 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 report included systematic reviews that found laser photocoagulation associated with lower likelihood of ≥ 6 lines visual acuity loss versus placebo (five trials; relative risk [RR] 0.67, 95% CI 0.53 to 0.83) and PDT associated with lower likelihood of ≥ 3 lines visual acuity loss 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 report.

The prior USPSTF report included four trials of intravitreal injection with VEGF inhibitors versus sham therapy; an updated meta-analysis based on these trials found VEGF inhibitors associated with greater likelihood for ≥ 15 letters of visual acuity gain (RR 2.92, 95% CI 1.20 to 7.12) and greater likelihood of having vision 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 intravitreal injection with VEGF inhibitors associated with small improvements in vision-related function and likelihood of driving among those 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 report 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 report 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 65 years of age or older,⁸⁴ mean baseline visual acuity was 20/63; in the other,⁸⁵ which evaluated nursing home patients 55 years of age or older, about 30 percent were moderately myopic (-0.50 to -2.00 diopters), 30 percent moderately hyperopic (+0.50 to +2.00 diopters), and about 25 percent had minimum impaired visual acuity (-0.50 to +0.50 diopters). Both trials reported improvements in vision-related quality of life in patients with immediate eyeglasses versus delayed treatment and one of the trials⁸⁵ 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 studies⁸⁵ published subsequent to the USPSTF report 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 report also included a large systematic review⁸⁷ 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 achieving visual acuity 20/40 or better) (**Appendix B5**), and three observational studies that found refractive surgery associated with improved quality of life.⁸⁸⁻⁹⁰

Cataracts

The prior USPSTF report identified no trials of cataract surgery versus no surgery, but included one systematic review of observational studies that found cataract surgery associated with improved visual acuity to 20/40 or better in over 90 percent of patients and in 89 percent of all eyes (n=17,390) (**Appendix B6**).⁹¹ One trial found immediate cataract surgery associated with a decreased risk of second (but not first) fall, resulting in a lower overall risk of falls (RR 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 report 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 ≥55 years of age found no differences between cataract surgery and no surgery in measures of function and cognition after 2 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 0.74 logMAR at baseline versus 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 versus 1.5 points without cataract surgery, p=0.004 after adjustment for age).⁹⁶ Another study (n=301) conducted in ophthalmology clinics in the U.S. of cataract patients ≥55 years of age found no differences between cataract surgery versus no surgery in cognitive function (based on the Mattis Organic Mental Syndrome Screening Examination score), 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 score). Visual acuity improved following cataract surgery (visual acuity in worse eye 0.55 logMAR at baseline and 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, comorbidities, 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 report¹ included results from the large, good-quality AREDS⁹⁷ 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 report, longer followup from the AREDS trial⁹⁹ and an updated version of the antioxidant systematic review¹⁰⁰ with four additional trials (total n=6,510),¹⁰¹⁻¹⁰⁴ has been published. We also identified three other recently published, placebo-controlled trials¹⁰⁵⁻¹⁰⁷ 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=3,640 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 (logMAR 0.073) to 20/80 (logMAR 0.60). 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 (n=1,480), zinc (n=903), a combination of antioxidant supplement and zinc (n=887) or placebo (n=1,483). Nearly half of AREDS participants were ≥70 years of age at baseline, 56 percent were women, and 96 percent were white. Over 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 review¹⁰⁵⁻¹⁰⁷ 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 alone¹⁰⁵ or in combination with zeaxanthin,¹⁰⁶ while the third evaluated fish oil supplementation (containing 840 mg DHA, 270 mg EPA, and 2 mg vitamin E).¹⁰⁷ Mean age of participants ranged from 69 to 74 years, and over 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} 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] versus 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 report¹ included 6-year results from AREDS, which found a daily combined antioxidant supplement to be associated with reduced risk of AMD progression versus placebo (OR 0.72, 99% CI 0.52 to 0.98).⁹⁷ 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 review¹⁰⁰ 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 report (**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 4.79¹⁰⁹ and OR 2.31, 95% CI 0.58 to 9.26),¹¹⁰ and one larger trial (n=1179) evaluated vitamin E alone (OR 1.11, 95% CI 0.80 to 1.55).¹¹¹

The prior USPSTF report included 6-year results from AREDS, which found use of an antioxidant supplement associated with a non-statistically reduction in risk of loss of ≥ 15 letters of visual acuity versus placebo (adjusted OR 0.77, 95% CI 0.58 to 1.03).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 report found no difference between supplementation with fish oil capsules versus placebo in risk of visual acuity loss of ≥ 15 letters 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 versus -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 study 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 a daily fish oil supplement 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 report¹ 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 report 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 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 (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 review¹¹³ found laser photocoagulation more effective than no treatment at preventing loss of >6 lines of visual acuity loss 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.

Photodynamic therapy. The prior USPSTF report¹ 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 report.

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) trial¹¹⁸ 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 report found no difference between PDT with verteporfin versus placebo in risk of all-cause mortality, based on the TAP (3% versus 4%; RR 0.84, 95% CI 0.35 to 1.99) and VIP (2% versus 3%; RR 0.68, 95% CI 0.15 to 2.97) trials.^{115,118} The VIM trial¹¹⁹ 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 PDT with verteporfin associated with lower likelihood of ≥ 3 lines of visual acuity loss 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 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 report included a good-quality Cochrane systematic review¹²⁰ 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] trial¹²¹ and two VEGF Inhibition Study in Ocular Neovascularization [VISION] trials, reported in one publication¹²²; total n=1,906) compared VEGF inhibitors versus sham (**Appendix B8**). The prior USPSTF report 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 trial¹²⁵ comparing VEGF inhibitors to PDT. Our literature search identified additional long-term followup from the MARINA trial (n=716) (**Appendix C9**).¹²⁶

The four trials¹²¹⁻¹²³ 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 over 75 years of age. 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 non-ocular health outcomes. The MARINA trial previously found no difference between ranibizumab versus placebo in all-cause (2% versus 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 (MI; 2% versus 2%; RR 1.12, 95% CI 0.35 to 3.60) or cerebrovascular accident (CVA; RR 2.24, 95% CI 0.49 to 10) (**Table 5**).¹²¹ The PIER trial reported no MI or CVA 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 report found 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) 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 to gain more than 15 letters of visual acuity (RR 2.92, 95% CI 1.20 to 7.12) (**Appendix D1**) and to experience less than 15 letters of visual acuity loss (RR 1.46, 95% CI 1.22 to 1.75) (**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 20/200 or better after one-year followup versus sham injection (RR 1.47, 95% CI 1.30 to 1.66; $I^2=42\%$) (**Appendix D3; Table 5**). Only the MARINA trial¹²¹ reported effects of VEGF inhibitors versus sham at 2-year followup; ranibizumab was associated with greater likelihood of ≥ 15 letters gain in visual acuity (RR 7.86, 95% CI 4.08 to 15), loss of <15 letters (RR 1.72, 95% CI 1.52 to 1.94), and in likelihood of 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% versus 10.6%; RR 2.64, 95% CI 1.41 to 4.92) or 2-year (31.9% versus 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% versus 56.4% at 2 years; RR 1.37, 95% CI 1.14 to 1.64).

Vision-related function. The prior USPSTF report found ranibizumab 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 published since the prior USPSTF report on driving status found ranibizumab 0.3 mg and 0.5 mg associated with increased likelihood of driving at 24 months in patients who were driving at baseline versus sham (81% versus 78% versus 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 versus 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 Age-Related Macular Degeneration?

Summary

The prior USPSTF report 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%, based on six studies of LASIK and 4 studies of LASEK. No study published since the prior USPSTF report assessed harms of treatment of uncorrected refractive error compared to no treatment.

The prior USPSTF report 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 report assessed the harms of cataract surgery versus no surgery.

The prior USPSTF report included systematic review that found laser photocoagulation associated with greater risk of acute loss of ≥ 6 lines visual acuity versus no treatment (3 months; RR 1.41, 95% CI 1.08 to 1.82) and PDT associated with increased risk of ≥ 20 letters visual acuity loss within 7 days of treatment versus placebo (three trials; RR 3.75, 95% CI 0.87 to 16). One of two trials found intravitreal VEGF inhibitor therapy 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 study¹²⁸ included in the prior USPSTF report 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 studies¹²⁹⁻¹³¹ found incidence of infectious keratitis ranges from 0.3 to 3.6 cases per 10,000 contact lens wearers; one study found incidence to be higher in persons over 50 years old.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 6 studies of LASIK and 4 studies of LASEK.⁸⁷

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

Cataracts

The prior USPSTF report 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 report assessed harms of cataract surgery versus no treatment or usual care.

AMD

Antioxidant vitamins and minerals and other supplements. The prior USPSTF report¹ 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 use of zinc 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 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 report 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 report¹ found laser photocoagulation associated with an increased risk for acute loss of ≥ 6 lines 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.

Photodynamic therapy. Based on a good-quality systematic review¹¹⁴ included in the prior USPSTF report,¹ PDT was associated with an increased risk of severe acute loss of visual acuity (defined as loss ≥ 20 letters within seven 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 report,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 1.70¹²¹) and VISION (RR 1.00, 95% CI 0.27 to 3.66¹²²) 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 RR 3.67, 95% CI 0.20 to 65) or endophthalmitis (two trials; RR 5.49, 95% CI 0.30 to 99 and RR 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, a 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 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 3 lines 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 studies that evaluate effects of changes in visual acuity on vision-related function. Studies using the NEI-VFQ to assess vision-related function, including the 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 cut-off as indicative of a clinically meaningful difference.¹⁴¹ For example, in people undergoing cataract surgery with mild (acuity 20/63 or better) to moderate (acuity 20/80 to 20/160)¹³⁷ impaired visual acuity, evidence suggests that clinically meaningful changes in visual acuity following surgery can range from ~40 letters 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 a 15 letter change in visual acuity 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 (logMAR 0.04 to 0.19), 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 probability of representing a true

difference in visual acuity, while for someone with baseline acuity worse than 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 (logMAR 0.2; two lines 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 report¹ that enrolled over 4,700 patients found vision screening in older adults as part of a multi-component screening intervention in primary care settings to be no more effective than no vision screening, delayed screening, or usual care.⁶⁹⁻⁷¹ A fourth trial found optometrist screening 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 report. 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 report 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 remains the most widely used tool to measure visual acuity in primary care settings, no clinically relevant reference standard exists to determine its diagnostic accuracy, in part because the Snellen is often considered the standard for assessing visual acuity in clinical practice. There remains insufficient evidence to assess the accuracy or utility of pinhole testing, the Amsler grid, visual acuity tests other than the Snellen, physical examination, or fundoscopic examination performed in primary care settings.

Conclusions from the prior USPSTF report 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 report, a very high proportion of patients experience favorable vision-related outcomes following treatment for impaired visual acuity due to refractive error and cataracts.¹ Over half of 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 over 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 E¹⁵⁰) 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 report found intravitreal injection with VEGF inhibitors and PDT with verteporfin to be effective treatment options with a relatively low incidence of serious harms, although 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 report 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 found that exclusion of non-English language studies had little effect on conclusions of review of non-complementary 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 AMD. The small (n=114) Age-related Maculopathy Statin Study (ARMSS) trial of simvastatin 40 mg/day versus placebo, found simvastatin associated with lower risk of AMD progression after 3 years of followup, although the difference was not statistically significant (54.4% versus 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 in AMD.¹⁵⁶

Relevance for Priority Populations

The focus of this review was on screening in older adults, a priority population at particular risk impaired visual acuity as well as sequelae from impaired visual acuity. Although black men are at higher risk of 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 fundoscopic 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 dry AMD remains largely dependent on a single large trial reporting a posthoc subgroup analysis⁹⁷ 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 non-invasively 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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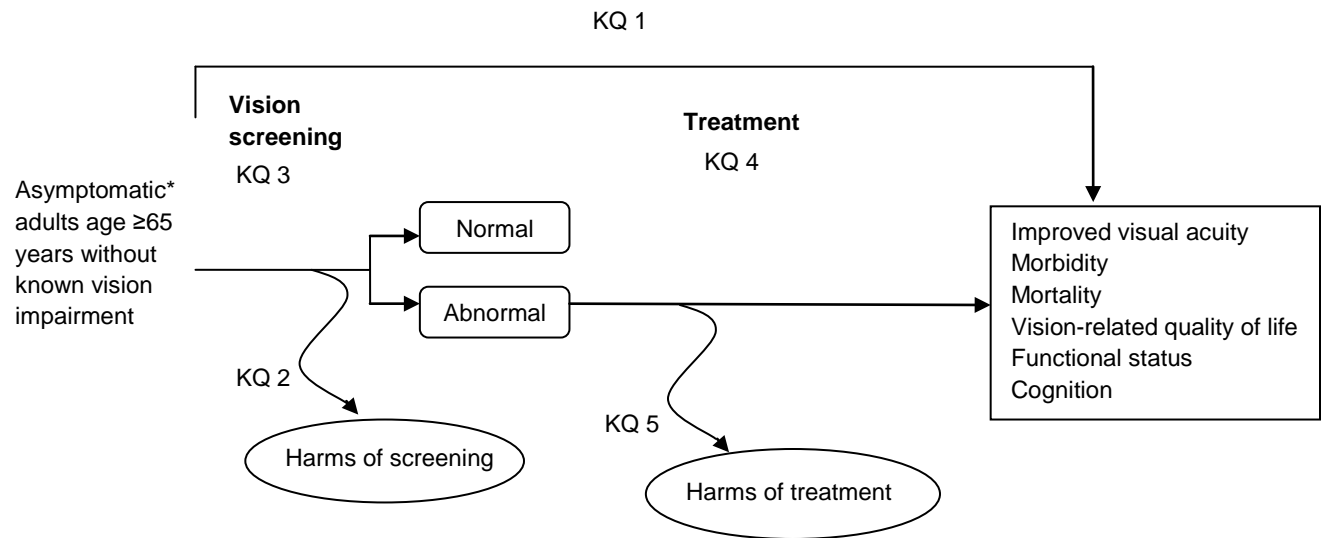
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Figure 1. Analytic Framework



* “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 Report

Author, year Study design Quality	Population	Screening Test	Reference Standard	Results
Jessa, 2012 ⁸² (Study 1) Cross-sectional Fair	46% male 12% seen in community 10% no spectacles 46.6% multifocal 23.9% distance vision 38.3% near vision n=180	6-item Computer Vision Screener	"Gold standard eye exam," including computerized high-contrast visual acuity and low-contrast visual acuity tests	Optimal cut-off (high-contrast visual acuity >0.19 LogMAR or near visual acuity) Sensitivity: 79.5% (95% CI, 71.5 to 85.7) Specificity: 67.9% (95% CI, 57 to 77.3) Positive likelihood ratio: 2.5 Negative likelihood ratio: 0.29
Jessa, 2012 ⁸² (Study 2) Cross-sectional Fair	31% male 31.5% seen in community 15.5% no spectacles 44.5% multifocal 22.5% distance vision 31.5% near vision n=200	Flip-chart Vision Screener	"Gold standard eye exam," including computerized high-contrast visual acuity and low-contrast visual acuity tests	Optimal cut-off (high-contrast visual acuity >0.19 LogMAR or near visual acuity) Sensitivity: 75.4% (95% CI, 67.1 to 82.2) Specificity: 69.2% (95% CI, 58.3 to 78.4) Positive likelihood ratio: NR Negative likelihood ratio: NR
Swanson, 2009 ⁸³ Cross-sectional Fair	Mean age: 80.7 years 80.6% female 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 n=371	Minimum Data Set Vision Patterns section	ETDRS chart	Sensitivity Adequate: 51.6% (95% CI, 44.2 to 58.9) Impaired: 35.1% (95% CI, 28.3 to 42.4) Moderately impaired: 10.5% (95% CI, 6.7 to 15.4) Severely to highly impaired: 1.6% (95% CI, 0.4 to 4.6) Specificity Adequate: 24.7% (95% CI, 18.2 to 32.2) Impaired: 79.8% (95% CI, 72.6 to 85.7) Moderately impaired: 95.8% (95% CI, 91.5 to 98.3) Severely to highly impaired: 100% (95% CI, 97.7 to 100) Positive likelihood ratio Adequate: 0.69 (95% CI, 0.58 to 0.81) Impaired: 1.73 (95% CI, 1.20 to 2.50) Moderately impaired: 2.47 (95% CI, 1.08 to 5.64) Severely to highly impaired: not calculable Negative likelihood ratio Adequate: 1.96 (95% CI, 1.44 to 2.67) Impaired: 0.81 (95% CI, 0.71 to 0.93) Moderately impaired: 0.93 (95% CI, 0.88 to 0.99) Severely to highly impaired: 0.98 (95% CI, 0.97 to 1.00)

Abbreviations: CI = confidence interval; ETDRS = Early Treatment Diabetic Retinopathy Study; LogMAR = logarithm of the minimum angle of resolution; MMSE = Mini Mental State Examination; NR = not reported; USPSTF = U.S. Preventive Services Task Force.

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

Author, year Study n Duration of followup Quality	Interventions	Population	Vision-Related Outcomes	Other Outcomes	Adverse Events
Chew, 2013 ⁹⁹ AREDS (Report #35) n=4,757 10 years Good	A. Antioxidant supplement (vitamin C 500 mg + vitamin E 400 IU + beta-carotene, 15 mg/day; n=1,480) B. Zinc 80 mg/day (n=903) C. Antioxidant supplement + zinc (n=887) D. Placebo (n=1,483)	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%	A vs. D† Loss of visual acuity ≥15 letters: ETDRS logMAR: 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 logMAR: 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 logMAR: 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)	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 Up to 11 years (mean duration NR) Good	A. Any AREDS active treatment (n=3,137) B. Placebo (n=1,467)	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 Report

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 (n=26) B. Lutein 20 mg/day (n=27) C. Lutein 10 mg/day + zeaxanthin 10 mg/day (n=27) D. Placebo (n=27)	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 NR BCVA 0.30 vs. 0.28 vs. 0.28 vs. 0.31 logMAR 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 (n=36 for effectiveness; 42 for harms) B. Placebo (n=37 for effectiveness; 42 for harms)	A vs. B Mean age 71.9 vs. 69.1 years 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 (n=134) B. Placebo (olive oil 602 mg) (n=129)	A vs. B Mean age 74 vs. 73 years 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 to 20: 17% vs. 22% >20: 81% vs. 76% Smoking history: Current: 7% vs. 9% Former: 14% vs. 17% Nonsmoker: 79% vs. 74%	A vs. B 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 decrease >15 letters ETDRS logMAR: 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 Report

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 (Category 3 and 4); results for other categories of AMD reported in Appendix.

‡ Results for participants with AMD Category 2, 3, or 4.

§ Adjusted for age, sex, race, education, smoking status, body mass index, and presence of diabetes, angina, cancer, and hypertension.

|| 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 Published Since the Prior USPSTF Report

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	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*	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: 58.7% (522/890) vs. 44.3% (131/296); 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 Published Since the Prior USPSTF Report

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 1 year	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: 73.6% (89/121) vs. 44.4% (28/63); 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

Main Findings From 2009 USPSTF Report	Number and Type of Studies Identified for Update	Limitations	Consistency	Applicability	Summary of Findings	Overall Quality*
Key Question 1. Does vision screening in asymptomatic older adults result in improved vision, morbidity or mortality, quality of life, functional status, or cognition?						
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 vision screening by an optometrist in frail elderly persons was associated with an increased risk of falls (RR, 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	All studies had different types of comparators	Consistent	Good (mainly primary care—applicable settings, as part of multi-component screening intervention)	Unchanged from the prior report; no new studies.	Fair
Key Question 2. Are there harms of vision screening in asymptomatic older adults?						
See KQ1 for evidence on falls.	None	1 study	Not applicable	Moderate (screening was done by an optometrist)	Unchanged from the prior report; no new studies.	Poor
Key Question 3. What is the accuracy of screening for early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD?						
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 examination. 1 study found that the Amsler grid is not accurate for identifying the presence of vision conditions compared to a detailed ophthalmologic examination. 1 very small (n=50) study found nonophthalmologists are as accurate as ophthalmologists for identifying presence of cataracts.	3 fair-quality cross-sectional studies	Sometimes unclear if the reference standards were interpreted independently of the target test; lack of predefined thresholds for positive results	Consistent	Moderate (tests are practical for primary care but were sometimes performed by optometrists)	2 new studies found that a computerized vision screening tool or a flip-chart version were not accurate compared with a detailed eye examination, and a third study found the Minimum Data Set 2.0 Vision Patterns section associated with poor diagnostic accuracy compared with an eye chart examination; overall conclusions unchanged from the prior report.	Fair

Table 6. Summary of Evidence

Main Findings From 2009 USPSTF Report	Number and Type of Studies Identified for Update	Limitations	Consistency	Applicability	Summary of Findings	Overall Quality*
Key Question 4. Does treatment of early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD lead to improved visual acuity, morbidity or mortality, vision-related quality of life, functional status, or cognition?						
Uncorrected Refractive Error In 1 large population-based study, 60% of older adults with vision impairment achieved visual acuity 20/40 or better with refractive correction. 2 RCTs found use of corrective lenses associated with improvements in vision-related function, but effects on overall function were inconsistent. Numerous observational studies show that >85% of patients achieved visual acuity 20/40 or better following photorefractive surgery for myopia or hyperopia.	None	Mainly observational data and accumulated clinical experience	Consistent	Moderate	Unchanged from the prior report; no new studies.	Fair
Cataracts Numerous observational studies found that >90% of patients achieved visual acuity 20/40 or better following cataract extraction and intraocular lens implantation. 3 observational studies found cataract surgery associated with improved vision-related function. 1 trial found immediate first-eye cataract surgery associated with a decreased rate of second (but not first) fall compared to delayed surgery, resulting in a lower overall rate of falls (rate ratio, 0.66 [95% CI, 0.40 to 0.96]; p=0.03), but a second trial found no effect of second-eye cataract surgery on falls.	2 fair-quality prospective cohort studies	Mainly observational data	Consistent (for visual acuity)	Moderate	2 new studies reported improved visual acuity with surgery with no differences between groups on cognitive function or quality of life; overall conclusions unchanged from the prior report.	Fair

Table 6. Summary of Evidence

Main Findings From 2009 USPSTF Report	Number and Type of Studies Identified for Update	Limitations	Consistency	Applicability	Summary of Findings	Overall Quality*
Dry AMD—Vitamin and Mineral Supplements A large randomized trial (AREDS) found a multivitamin and zinc combination effective for slowing progression of AMD (adjusted OR, 0.68 [99% CI, 0.49 to 0.93]), though the difference in the likelihood of losing ≥ 15 letters of visual acuity was not statistically significant (adjusted OR, 0.77 [95% CI, 0.58 to 1.03]). A systematic review of 9 trials (including the AREDS trial) 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, adding 4 new RCTs) 3 RCTs + 2 additional reports from the AREDS trial with longer (10-year) followup	Substantial heterogeneity in interventions assessed and outcomes reported	Consistent	Good (participants in AREDS and other studies generally had mild visual impairment at baseline)	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 unchanged from the prior report.	Good
Wet AMD—Laser Photocoagulation 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	No new trials published since the prior report; 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	Consistent	Moderate	Unchanged from the prior report; no new studies.	Fair

Table 6. Summary of Evidence

Main Findings From 2009 USPSTF Report	Number and Type of Studies Identified for Update	Limitations	Consistency	Applicability	Summary of Findings	Overall Quality*
Wet AMD–Photodynamic Therapy 1 systematic review found verteporfin in patients undergoing PDT 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	No new trials published since the prior report; evidence limited to 4 older trials, 1 of which enrolled a younger population than the others (mean age 49 vs. 75–79 years)	Consistent	Moderate	Unchanged from the prior report; no new studies.	Fair
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).	None	No new trials published since the prior report; study population in the 4 included trials was older (age >75 years) with moderate to severe impaired visual acuity at baseline	Consistent	Moderate	Unchanged from the prior report; no new studies.	Fair
Key Question 5. Are there harms of treating early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD?						
Uncorrected Refractive Error 1 small prospective study found multifocal lenses associated with a higher risk of falls in older adults compared to unifocal lenses (OR, 2.09 [95% CI, 1.06 to 4.92]). 3 studies found incidence of infectious keratitis ranged 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, keratitis rates ranged from 0% to 3.4% in 6 studies of LASIK and 4 studies of LASEK.	None	Only 1 study on corrective lenses	Corrective lenses: NA (1 study) Contact lenses; refractive surgery: Consistent	Moderate	Unchanged from the prior report; no new studies.	Corrective lenses: Poor Contact lenses; refractive surgery: Fair

Table 6. Summary of Evidence

Main Findings From 2009 USPSTF Report	Number and Type of Studies Identified for Update	Limitations	Consistency	Applicability	Summary of Findings	Overall Quality*
Cataracts 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	Mainly observational studies	Consistent	Moderate	Unchanged from the prior report; no new studies.	Fair
Dry AMD—Vitamin and Mineral Supplements The large AREDS trial found zinc 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 associated with increased risk of yellow skin compared to nonuse of antioxidants (RR, 1.38 [95% CI, 1.09 to 1.75]).	2 RCTs	Neither trial was designed to assess harms and sample sizes were relatively small (n=94 and 300)	Consistent	Good (participants in both studies had relatively mild visual impairment at baseline)	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 associated with zinc or antioxidants; overall conclusions unchanged from the prior report.	Good
Wet AMD—Laser Photocoagulation Visual acuity loss ≥ 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	Included studies were not designed to assess harms and duration of followup was short in some studies	Consistent	Moderate	Unchanged from the prior report; no new studies.	Fair
Wet AMD—Photodynamic Therapy Increased risk of acute severe visual acuity loss (20 letter loss within 7 days of treatment) compared to placebo (2% vs. 0.2%; 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	Evidence limited to 4 older trials; few adverse events reported	Consistent	Moderate	Unchanged from the prior report; no new studies.	Fair

Table 6. Summary of Evidence

Main Findings From 2009 USPSTF Report	Number and Type of Studies Identified for Update	Limitations	Consistency	Applicability	Summary of Findings	Overall Quality*
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	Evidence limited to 4 older trials; few adverse events reported	Consistent	Moderate	Unchanged from the prior report; no new studies.	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 pediater\$ 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

Appendix A1. Search Strategies

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 pediater\$ or neonat\$ or prematur\$).mp.

8 limit 7 to new reviews

9 limit 8 to full systematic reviews

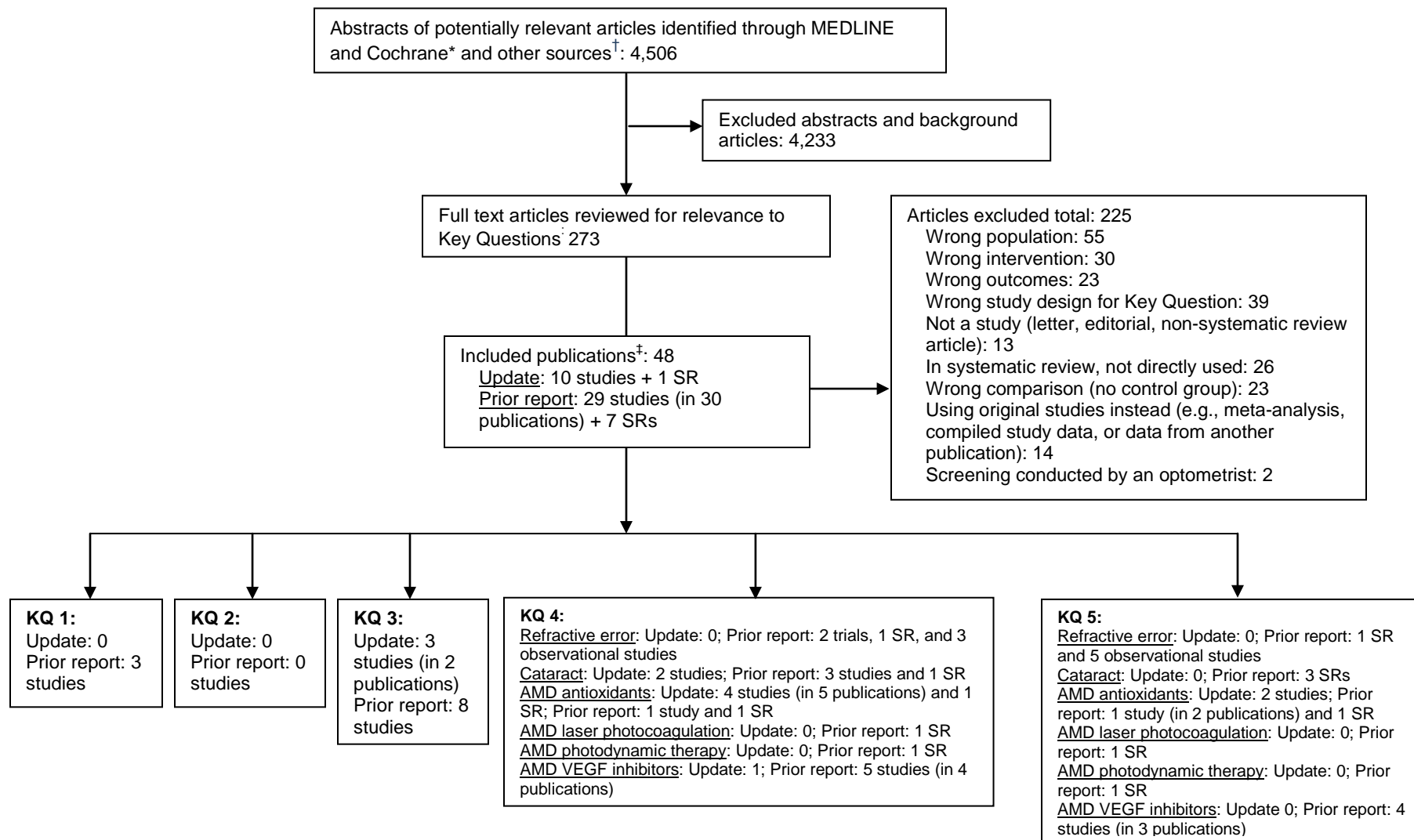
10 9 not diabet\$.mp.

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).

Age-Related Eye Disease Study 2 Research G. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. *JAMA*. 2013;309(19):2005-15. Excluded: wrong comparison (no control group).

Age-Related Eye Disease Study 2 Research G, Chew EY, Clemons TE, et al. Secondary analyses of the effects of lutein/zeaxanthin on age-related macular degeneration progression: AREDS2 report No. 3. *JAMA Ophthalmol*. 2014;132(2):142-9. Excluded: wrong comparison (no control group).

Age-Related Eye Disease Study 2 Research G, Chew EY, SanGiovanni JP, et al. Lutein/zeaxanthin for the treatment of age-related cataract: AREDS2 randomized trial report no. 4. *JAMA Ophthalmol*. 2013;131(7):843-50. Excluded: wrong comparison (no control group).

Ahmadi A, Ghanbari H, Soheilian M, et al. The Effect of HESA-A (natural drug) on visual acuity in age related macular degeneration: a randomized double blind controlled clinical trial. *Afr J Tradit Complement Altern Med*. 2009;6(4):549-53. Excluded: wrong intervention.

Ahn JK, Moon HJ. Changes in aqueous vascular endothelial growth factor and pigment epithelium-derived factor after ranibizumab alone or combined with verteporfin for exudative age-related macular degeneration. *Am J Ophthalmol*. 2009;148(5):718-24.e1. Excluded: wrong population.

Akuffo KO, Beatty S, Stack J, et al. Central Retinal Enrichment Supplementation Trials (CREST): design and methodology of the CREST randomized controlled trials. *Ophthalmic Epidemiol*. 2014;21(2):111-23. Excluded: wrong study design for Key Question.

Alliance for Aging Research, Inventor. Independence for Older Americans: An Investment for Our Nation's Future 1999. Excluded: not a study (letter, editorial, non-systematic review article).

American Optometric Association. Adult Vision: Over 60 Years of age. 2013; <http://www.aoa.org/patients-and-public/good-vision-throughout-life/adult-vision-19-to-40-years-of-age/adult-vision-over-60-years-of-age>. Accessed January 10th, 2014. Excluded: not a study (letter, editorial, non-systematic review article).

Anderson AJ, Shuey NH, Wall M. Rapid confrontation screening for peripheral visual field defects and extinction. *Clin Exp Optom*. 2009;92(1):45-8. Excluded: not a study (letter, editorial, non-systematic review article).

Andonegui J, Berastegui L, Serrano L, et al. [Agreement among ophthalmologists and primary care physicians in the evaluation of retinographies of diabetic patients]. *Arch Soc Esp Oftalmol*. 2008;83(9):527-31. Excluded: wrong population.

Andonegui J, Serrano L, Eguzkiza A, et al. Diabetic retinopathy screening using tele-ophthalmology in a primary care setting. *J Telemed Telecare*. 2010;16(8):429-32. Excluded: wrong population.

Andonegui J, Zurutuza A, de Arcelus MP, et al. Diabetic retinopathy screening with non-mydratic retinography by general practitioners: 2-year results. *Prim Care Diabetes*. 2012;6(3):201-5. Excluded: wrong population.

Anstey KJ, Horswill MS, Wood JM, et al. The role of cognitive and visual abilities as predictors in the Multifactorial Model of Driving Safety. *Accid Anal Prev*. 2012;45:766-74. Excluded: wrong outcomes.

Antoszyk AN, Tuomi L, Chung CY, et al. Ranibizumab combined with verteporfin photodynamic therapy in neovascular age-related macular degeneration (FOCUS): year 2 results. *Am J Ophthalmol*. 2008;145(5):862-74. Excluded: wrong intervention.

Appendix A4. Excluded Studies

Applegate W, Miller S, Elam J, et al. Impact of cataract surgery with lens implantation on vision and physical function in elderly patients. *JAMA*. 1987;257:1064-6. Excluded: in systematic review, not directly used.

AREDS Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E and beta carotene for age-related cataract and vision loss: AREDS report no. 9. *Arch Ophthalmol*. 2001;119(10):1439-52. Excluded: in systematic review, not directly used.

Armbrecht AM, Aspinall P, Dhillon B. A prospective study of visual function and quality of life following PDT in patients with wet age related macular degeneration. *Br J Ophthalmology*. 2004;88:1270-3. Excluded: wrong study design for Key Question.

Arnold C, Winter L, Frohlich K, et al. Macular xanthophylls and [omega]-3 long-chain polyunsaturated fatty acids in age-related macular degeneration: a randomized trial. *JAMA Ophthalmol*. 2013;131(5):564-72. Excluded: wrong outcomes.

Asbell PA, Dualan I, Mindel J, et al. Age-related cataract. *Lancet*. 2005;365:599-609. Excluded: not a study (letter, editorial, non-systematic review article).

Askew D, Schluter PJ, Spurling G, et al. Diabetic retinopathy screening in general practice: a pilot study. *Aust Fam Physician*. 2009;38(8):650-6. Excluded: wrong population.

Attebo K, Ivers RQ, Mitchell P. Refractive errors in an older population: the Blue Mountains Eye Study. *Ophthalmology*. 1999;106(6):1066-72. Excluded: wrong outcomes.

Au Eong KG, Chan EW, Luo N, et al. Validity of EuroQOL-5D, time trade-off, and standard gamble for age-related macular degeneration in the Singapore population. *Eye*. 2012;26(3):379-88. Excluded: wrong outcomes.

Avery RL, Ho AC. Good News for Anti-VEGF Therapy. 2008; Available at: http://www.retinatoday.com/issues/0308/0308_01.php. Accessed November, 2008. Excluded: not a study (letter, editorial, non-systematic review article).

Axer-Siegel R, Bor E, Bourla DH, et al. Intravitreal bevacizumab treatment for exudative age-related macular degeneration with good visual acuity. *Retina*. 2012;32(9):1811-20. Excluded: wrong study design for Key Question.

Azab M, Boyer DS, Bressler NM, et al. Verteporfin therapy of subfoveal minimally classic choroidal neovascularization in age-related macular degeneration: 2-year results of a randomized clinical trial. *Arch Ophthalmol*. 2005;123(4):448-57. Excluded: in systematic review, not directly used.

Baker ML, Wang JJ, Rogers S, et al. Early age-related macular degeneration, cognitive function, and dementia: the Cardiovascular Health Study. *Arch Ophthalmol*. 2009;127(5):667-73. Excluded: wrong study design for Key Question.

Barbazetto I, Saroj N, Shapiro H, et al. Dosing regimen and the frequency of macular hemorrhages in neovascular age-related macular degeneration treated with ranibizumab. *Retina (Philadelphia, Pa)*. 2010;30(9):1376-85. Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

Bartlett HE, F.A. E. Effect of lutein and antioxidant dietary supplementation on contrast sensitivity in age-related macular degeneration: a randomized controlled trial. *Eur J Clin Nutr*. 2001;61(9):1121-7. Excluded: in systematic review, not directly used.

Bergman B, Nilsson-Ehle H, Sjostrand J. Ocular changes, risk markers for eye disorders and effects of cataract surgery in elderly people: a study of an urban Swedish population followed from 70 to 97 years of age. *Acta Ophthalmol Scand*. 2004;82(2):166-74. Excluded: wrong study design for Key Question.

Bernth-Petersen P. Outcome of cataract surgery. A prospective, observational study. *Acta Ophthalmol*. 1982;60:235-42. Excluded: wrong study design for Key Question.

Blaha M, Rencova E, Langrova H, et al. Rheohaemapheresis in the treatment of nonvascular age-related macular degeneration. *Atheroscler Suppl*. 2013;14(1):179-84. Excluded: wrong intervention.

Bourne RRA, French KA, Chang L, et al. Can a community optometrist-based referral refinement scheme reduce false-positive glaucoma hospital referrals without compromising quality of care? The community and hospital allied network glaucoma evaluation scheme (CHANGES). *Eye*. 2010;24(5):881-7. Excluded: wrong intervention.

Appendix A4. Excluded Studies

Boyer D, Heier J, Brown DM, et al. Vascular endothelial growth factor Trap-Eye for macular edema secondary to central retinal vein occlusion: six-month results of the phase 3 COPENICUS study. *Ophthalmology*. 2012;119(5):1024-32. Excluded: wrong population.

Bragge P, Gruen RL, Chau M, et al. Screening for presence or absence of diabetic retinopathy: a meta-analysis. *Arch Ophthalmol*. 2011;129(4):435-44. Excluded: wrong population.

Brenner M, Curbow B, Javitt J, et al. Vision change and quality of life in the elderly; response to cataract surgery and treatment of other chronic ocular conditions. *Arch Ophthalmol*. 1993;111:680-5. Excluded: in systematic review, not directly used.

Bressler NM, Boyer DS, Williams DF, et al. Cerebrovascular accidents in patients treated for choroidal neovascularization with ranibizumab in randomized controlled trials. *Retina*. 2012;32(9):1821-8. Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

Bressler NM, Chang TS, Fine JT, et al. Improved vision-related function after ranibizumab vs photodynamic therapy: a randomized clinical trial. *Arch Ophthalmol*. 2009;127(1):13-21. Excluded: wrong comparison (no control group).

Bressler NM, Chang TS, Suner IJ, et al. Vision-related function after ranibizumab treatment by better- or worse-seeing eye: clinical trial results from MARINA and ANCHOR. *Ophthalmology*. 2010;117(4):747-56.e4. Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

Brown DM, Campochiaro PA, Bhisitkul RB, et al. Sustained benefits from ranibizumab for macular edema following branch retinal vein occlusion: 12-month outcomes of a phase III study. *Ophthalmology*. 2011;118(8):1594-602. Excluded: wrong population.

Brown DM, Campochiaro PA, Singh RP, et al. Ranibizumab for macular edema following central retinal vein occlusion: six-month primary end point results of a phase III study. *Ophthalmology*. 2010;117(6):1124-33.e1. Excluded: wrong population.

Brown DM, Heier JS, Clark WL, et al. Intravitreal aflibercept injection for macular edema secondary to central retinal vein occlusion: 1-year results from the phase 3 COPENICUS study. *Am J Ophthalmol*. 2013;155(3):429-37.e7. Excluded: wrong population.

Brown DM, Kaiser PK, Michels M, et al. Ranibizumab versus verteporfin for neovascular age-related macular degeneration. *New Engl J Med*. 2006;355(14):1432-44. Excluded: wrong comparison (no control group).

Brown DM, Michels M, Kaiser PK, et al. Ranibizumab versus verteporfin photodynamic therapy for neovascular age-related macular degeneration: Two-year results of the ANCHOR study. *Ophthalmology*. 2009;116(1):57-65.e5. Excluded: wrong comparison (no control group).

Burlina P, Freund DE, Dupas B, et al. Automatic screening of age-related macular degeneration and retinal abnormalities. *Conf Proc IEEE Eng Med Biol Soc*. 2011;2011:3962-6. Excluded: wrong intervention.

Burr JM, Mowatt G, Hernandez R, et al. The clinical effectiveness and cost-effectiveness of screening for open angle glaucoma: a systematic review and economic evaluation. *Health Technol Assess*. 2007;11(41):iii-iv, ix-x, 1-190. Excluded: wrong population.

Campochiaro PA, Heier JS, Feiner L, et al. Ranibizumab for macular edema following branch retinal vein occlusion: six-month primary end point results of a phase III study. *Ophthalmology*. 2010;117(6):1102-12.e1. Excluded: wrong population.

Carneiro AM, Falcao MS, Brandao EM, et al. Intravitreal bevacizumab for neovascular age-related macular degeneration with or without prior treatment with photodynamic therapy: one-year results. *Retina*. 2010;30(1):85-92. Excluded: wrong comparison (no control group).

Casparis H, Lindsley K, Kuo IC, et al. Surgery for cataracts in people with age-related macular degeneration. *Cochrane Database Syst Rev*. 2012(7). Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

Caudill SP, Schleicher RL, Pirkle JL. Multi-rule quality control for the age-related eye disease study. *Stat Med*. 2008;27(20):4094-106. Excluded: wrong outcomes.

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- Chang JR, Koo E, Agron E, et al. Risk factors associated with incident cataracts and cataract surgery in the Age-related Eye Disease Study (AREDS): AREDS report number 32. *Ophthalmology*. 2011;118(11):2113-9. Excluded: wrong study design for Key Question.
- Cheng KC, Wu WC, Lin CJ. Intravitreal triamcinolone acetate for patients with macular oedema due to central retinal vein occlusion in Taiwan. *Eye*. 2009;23(4):849-57. Excluded: wrong population.
- Chew EY, Clemons TE, Bressler SB, et al. Randomized trial of a home monitoring system for early detection of choroidal neovascularization home monitoring of the Eye (HOME) study. *Ophthalmology*. 2014;121(2):535-44. Excluded: wrong population.
- Chiu CJ, Klein R, Milton RC, et al. Does eating particular diets alter the risk of age-related macular degeneration in users of the Age-Related Eye Disease Study supplements? *Br J Ophthalmol*. 2009;93(9):1241-6. Excluded: wrong intervention.
- Cho E, Stampfer MJ, Seddon JM, et al. Prospective study of zinc intake and the risk of age-related macular degeneration. *Ann Epidemiol*. 2001;11(5):328-36. Excluded: wrong study design for Key Question.
- Chong EW, Wong TY, Kreis AJ, et al. Dietary antioxidants and primary prevention of age related macular degeneration: systematic review and meta-analysis. *BMJ*. 2007;335(7623):755. Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).
- Christen W, Glynn R, Manson JE, et al. Effects of multivitamin supplement on cataract and age-related macular degeneration in a randomized trial of male physicians. *Ophthalmology*. 2014;121(2):525-34. Excluded: wrong population.
- Christen WG, Glynn RJ, Chew EY, et al. Low-dose aspirin and medical record-confirmed age-related macular degeneration in a randomized trial of women. *Ophthalmology*. 2009;116(12):2386-92. Excluded: wrong population.
- Clemons TE, Rankin MW, McBee WL. Cognitive impairment in the Age-Related Eye Disease Study: AREDS report no. 16. *Arch Ophthalmol*. 2006;124(4):537-43. Excluded: wrong outcomes.
- Cohen S-Y, Bourgeois H, Corbe C, et al. Randomized clinical trial France DMLA2: effect of trimetazidine on exudative and nonexudative age-related macular degeneration. *Retina*. 2012;32(4):834-43. Excluded: wrong intervention.
- Creuzot-Garcher C, Malvitte L, Sicard AC, et al. How to improve screening for diabetic retinopathy: the Burgundy experience. *Diabetes Metab*. 2010;36(2):114-9. Excluded: wrong study design for Key Question.
- Cuadros J, Bresnick G. EyePACS: an adaptable telemedicine system for diabetic retinopathy screening. *J Diabetes Sci Technol*. 2009;3(3):509-16. Excluded: wrong outcomes.
- Cumming RG, Ivers R, Clemson L, et al. Improving vision to prevent falls in frail older people: a randomized trial. *J Am Geriatr Soc*. 2007;55(2):175-81. Excluded: screening conducted by an optometrist.
- Curriero FC, Pinchoff J, van Landingham SW, et al. Alteration of travel patterns with vision loss from glaucoma and macular degeneration. *JAMA Ophthalmol*. 2013;131(11):1420-6. Excluded: wrong study design for Key Question.
- Curtis LH, Hammill BG, Qualls LG, et al. Treatment patterns for neovascular age-related macular degeneration: analysis of 284 380 Medicare beneficiaries. *Am J Ophthalmol*. 2012;153(6):1116-24.e1. Excluded: wrong study design for Key Question.
- Curtis LH, Hammill BG, Schulman KA, et al. Risks of mortality, myocardial infarction, bleeding, and stroke associated with therapies for age-related macular degeneration.[Erratum appears in *Arch Ophthalmol*. 2010 Dec;128(12):1623]. *Arch Ophthalmol*. 2010;128(10):1273-9. Excluded: wrong comparison (no control group).
- Davis MD, Sheetz MJ, Aiello LP, et al. Effect of ruboxistaurin on the visual acuity decline associated with long-standing diabetic macular edema. *Invest Ophthalmol Vis Sci*. 2009;50(1):1-4. Excluded: wrong population.
- Day L, Fildes B, Gordon I, et al. Randomised factorial trial of falls prevention among older people living in their own homes. *BMJ*. 2002;325(7356):128. Excluded: wrong intervention.

Appendix A4. Excluded Studies

Day S, Acquah K, Mruthyunjaya P, et al. Ocular complications after anti-vascular endothelial growth factor therapy in Medicare patients with age-related macular degeneration. *Am J Ophthalmol*. 2011;152(2):266-72. Excluded: wrong study design for Key Question.

de Gaetano G. Low-dose aspirin and vitamin E in people at cardiovascular risk: a randomised trial in general practice. Collaborative Group of the Primary Prevention Project. *Lancet*. 2001;357(9250):89-95. Excluded: wrong outcomes.

de Monchy I, Gendron G, Miceli C, et al. Combination of the Schirmer I and phenol red thread tests as a rescue strategy for diagnosis of ocular dryness associated with Sjogren's syndrome. *Invest Ophthalmol Vis Sci*. 2011;52(8):5167-73. Excluded: wrong population.

de Saint Sardos A, Kamdeu Fansi A, Chagnon M, et al. Intraocular pressure adjusted for central corneal thickness as a screening tool for open-angle glaucoma in an at-risk population. *Can J Ophthalmol*. 2009;44(5):571-5. Excluded: wrong intervention.

de Silva SR, Riaz Y, Evans JR. Phacoemulsification with posterior chamber intraocular lens versus extracapsular cataract extraction (ECCE) with posterior chamber intraocular lens for age-related cataract. *Cochrane Database Syst Rev*. 2014(1). Excluded: wrong intervention.

Dehghan MH, Ahmadieh H, Ramezani A, et al. A randomized, placebo-controlled clinical trial of intravitreal triamcinolone for refractory diabetic macular edema. *Int Ophthalmol*. 2008;28(1):7-17. Excluded: wrong population.

Desapriya E, Wijeratne H, Subzwari S, et al. Vision screening of older drivers for preventing road traffic injuries and fatalities. *Cochrane Database Syst Rev*. 2011(3):CD006252. Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

Diabetic Retinopathy Clinical Research N. Randomized clinical trial evaluating intravitreal ranibizumab or saline for vitreous hemorrhage from proliferative diabetic retinopathy. *JAMA Ophthalmol*. 2013;131(3):283-93. Excluded: wrong population.

Diabetic Retinopathy Clinical Research N, Beck RW, Edwards AR, et al. Three-year follow-up of a randomized trial comparing focal/grid photocoagulation and intravitreal triamcinolone for diabetic macular edema. *Arch Ophthalmol*. 2009;127(3):245-51. Excluded: wrong population.

Diabetic Retinopathy Clinical Research N, Elman MJ, Aiello LP, et al. Randomized trial evaluating ranibizumab plus prompt or deferred laser or triamcinolone plus prompt laser for diabetic macular edema. *Ophthalmology*. 2010;117(6):1064-77.e35. Excluded: wrong population.

Diabetic Retinopathy Clinical Research N, Elman MJ, Qin H, et al. Intravitreal ranibizumab for diabetic macular edema with prompt versus deferred laser treatment: three-year randomized trial results. *Ophthalmology*. 2012;119(11):2312-8. Excluded: wrong population.

Dupas B, Walter T, Erginay A, et al. Evaluation of automated fundus photograph analysis algorithms for detecting microaneurysms, haemorrhages and exudates, and of a computer-assisted diagnostic system for grading diabetic retinopathy. *Diabetes Metab*. 2010;36(3):213-20. Excluded: wrong intervention.

Eandi CM, Giansanti F, Virgili G. Macular translocation for neovascular age-related macular degeneration. *Cochrane Database Syst Rev*. 2008(4):CD006928. Excluded: wrong intervention.

Epstein DL, Algvere PV, von Wendt G, et al. Benefit from bevacizumab for macular edema in central retinal vein occlusion: twelve-month results of a prospective, randomized study. *Ophthalmology*. 2012;119(12):2587-91. Excluded: wrong population.

Evans J. Antioxidant supplements to prevent or slow down the progression of AMD: a systematic review and meta-analysis. *Eye*. 2008;22(6):751-60. Excluded: using original studies instead (e.g., meta-analysis, compiled study data, or data from another publication).

Evans JR. Ginkgo Biloba extract for age-related macular degeneration. *Cochrane Database Syst Rev*. 2013;1. Excluded: wrong intervention.

Evans JR, Sivagnanavel V, Chong V. Radiotherapy for neovascular age-related macular degeneration. *Cochrane Database Syst Rev*. 2010(5). Excluded: wrong intervention.

Appendix A4. Excluded Studies

Falck A, Kuoppala J, Winblad I, et al. The Pyhajarvi Cataract Study. I. Study design, baseline characteristics and the demand for cataract surgery. *Acta Ophthalmol (Oxf)*. 2008;86(6):648-54. Excluded: wrong study design for Key Question.

Farley TF, Mandava N, Prall FR, et al. Accuracy of primary care clinicians in screening for diabetic retinopathy using single-image retinal photography. *Ann Fam Med*. 2008;6(5):428-34. Excluded: wrong population.

Fies P, Dienel A. Ginkgo extract in impaired vision - treatment with special extract EGb 761 of impaired vision due to dry senile macular degeneration. *Wiener Medizinische Wochenschrift*. 2002;152(15-16):423-6. Excluded: in systematic review, not directly used.

Fisher JB, Jacobs DA, Markowitz CE, et al. Relation of visual function to retinal nerve fiber layer thickness in multiple sclerosis. *Ophthalmology*. 2006;113(2):324-32. Excluded: wrong study design for Key Question.

Forte R, Cennamo G, Finelli ML, et al. Combination of flavonoids with *Centella asiatica* and *Melilotus* for diabetic cystoid macular edema without macular thickening. *J Ocul Pharmacol Ther*. 2011;27(2):109-13. Excluded: wrong population.

Francis BA, Varma R, Vigen C, et al. Population and high-risk group screening for glaucoma: the Los Angeles Latino Eye Study. *Invest Ophthalmol Vis Sci*. 2011;52(9):6257-64. Excluded: wrong population.

Frei A, Woitzek K, Wang M, et al. The chronic care for age-related macular degeneration study (CHARMED): study protocol for a randomized controlled trial. *Trials*. 2011;12:221. Excluded: wrong study design for Key Question.

French DD, Margo CE. Age-related macular degeneration, anti-vascular endothelial growth factor agents, and short-term mortality: a postmarketing medication safety and surveillance study. *Retina*. 2011;31(6):1036-42. Excluded: wrong study design for Key Question.

Friberg TR, Brennen PM, Freeman WR, et al. Prophylactic treatment of age-related macular degeneration report number 2: 810-nanometer laser to eyes with drusen: bilaterally eligible patients. *Ophthalmic Surg Lasers Imaging*. 2009;40(6):530-8. Excluded: wrong study design for Key Question.

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.

Funk M, Schmidinger G, Maar N, et al. Angiogenic and inflammatory markers in the intraocular fluid of eyes with diabetic macular edema and influence of therapy with bevacizumab. *Retina*. 2010;30(9):1412-9. Excluded: wrong population.

Garas A, Kothy P, Hollo G. Accuracy of the RTVue-100 Fourier-domain optical coherence tomograph in an optic neuropathy screening trial. *Int Ophthalmol*. 2011;31(3):175-82. Excluded: wrong population.

Garway-Heath DF, Lascaratos G, Bunce C, et al. The United Kingdom Glaucoma Treatment Study: a multicenter, randomized, placebo-controlled clinical trial: design and methodology. *Ophthalmology*. 2013;120(1):68-76. Excluded: wrong intervention.

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.

Gillies MC, McAllister IL, Zhu M, et al. Pretreatment with intravitreal triamcinolone before laser for diabetic macular edema: 6-month results of a randomized, placebo-controlled trial. *Invest Ophthalmol Vis Sci*. 2010;51(5):2322-8. Excluded: wrong population.

Appendix A4. Excluded Studies

Grahn BH, Paterson PG, Gottschall-Pass KT, et al. Zinc and the eye. *J Am Coll Nutr*. 2001;20(2 Suppl):106-18. Excluded: not a study (letter, editorial, non-systematic review article).

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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.

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- 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.
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- 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).
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Appendix A4. Excluded Studies

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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.

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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.

Appendix A5. USPSTF Quality Criteria

- 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.

Appendix A5. USPSTF Quality Criteria

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>.

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

Author, Year Study Design Country Setting Duration of Followup Quality	Population	Intervention (n)	Results
Cumming, 2007 ⁷² (Also see Swamy, 2009 ⁷³) RCT Australia Optometry clinic 1 year Fair <i>Excluded from update because vision screening conducted by optometrist</i>	Mean age 81 years 67% female Race not reported Self-rated vision poor or very poor: 12.7% vs. 9.4%	A. Screening: visual acuity assessed with Early Treatment Diabetic Retinopathy Study Chart at 2.4 m; contrast sensitivity with the CSV-1000E Chart 1 at 2.4 m; visual fields with Humphrey automated visual field unit; Perkins applanation tonometer; intraocular pressure with slit lamp exam and direct ophthalmoscopy (n=309) B. Usual care (n=307)	A vs. B Number of falls: 758 vs. 516; RR 1.57 (95% CI 1.20 to 2.05) Proportion with fractures: 10% (31/309) vs. 6% (18/307); RR 1.74 (95% CI 0.97 to 3.11) Assessed as needing a vision-related intervention: 44% vs. NR Visual acuity at 1 year (mean, logMAR) at 1 year: 0.27 vs. 0.25 (p=0.32) VFQ-15 at 1 year (mean, 0 to 100): 84 vs. 86 (p=0.49)
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	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 (n=576) B. Delayed screening (n=545)	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: 80% white; other races not reported Baseline visual acuity: Not reported	A. Screening: question to assess difficulty performing everyday activities, followed by Snellen eye chart if positive (n=112) B. Usual care (n=149)	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%	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 (n=1,662) B. Targeted screening: brief health assessment (n=1,684)	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)

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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%	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 (n=1,662) B. Targeted screening: brief health assessment (n=1,684)	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 Report

Study, Year	Type of Study	Age of Enrollees and Sample Size	Proportion With Visual Conditions	Reference Standard	Index 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	Detailed ophthalmologic assessment	Amsler grid Near visual acuity Distance visual acuity	Poor-Fair
Eekhof, 2000 ⁷⁵	Cross-sectional	75 years or older n=1121	Snellen chart <0.3: 10.8%	Snellen chart and low vision chart (testing vision at reading distance)	Screening questions	Fair
Hiller, 1983 ⁷⁶	Cross-sectional	25 to 74 years n=1466 for subgroup 65 to 74 years old	Snellen 20/25 or worse: 69%	Snellen chart	Screening question	Fair
Ivers, 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	Detailed ophthalmologic assessment	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	Geriatrician examination	Fair
Teh, 2006 ⁷⁹	Cross-sectional	60 years or older n=112	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)	Detailed ophthalmologic assessment	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=2522	12% (50 to 64 years) and 23% (>64 years) macular degeneration, 4.9% and 27.2% cataract	Detailed ophthalmologic assessment	Distance visual acuity (Snellen) Near visual acuity (Snellen)	Fair

Abbreviations: 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 Report

Study, Year	Reference Standard	Target Vision Condition	Screening Test	Sensitivity	Specificity	Positive Likelihood Ratio	Negative Likelihood Ratio	Diagnostic Odds Ratio
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 Report

Study, Year	Reference Standard	Target Vision Condition	Screening Test	Sensitivity	Specificity	Positive Likelihood Ratio	Negative Likelihood Ratio	Diagnostic Odds Ratio
Ariyasu, 1996 ⁷⁴	Ophthalmologic examination	Any ocular disease, excluding refractive error	Presenting distance visual acuity $\leq 20/30$	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)
			$\leq 20/40$	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)
			$\leq 20/60$	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 $\leq 20/30$	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)
			$\leq 20/40$	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)
			$\leq 20/60$	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)
			Presenting distance visual acuity $\leq 20/30$	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)
			$\leq 20/40$	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)
			$\leq 20/60$	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)
Ivers, 2001 ⁷⁷	Ophthalmologic examination	A: Nuclear cataract B: Early AMD C: Any eye disease	Presenting distance visual acuity $\leq 20/30$	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)
			$\leq 20/40$	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)
			$\leq 20/60$	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 Report

Study, Year	Reference Standard	Target Vision Condition	Screening Test	Sensitivity	Specificity	Positive Likelihood Ratio	Negative Likelihood Ratio	Diagnostic Odds Ratio
Ivers, 2001 ⁷⁷	Ophthalmologic examination	A: Nuclear cataract B: Early AMD C: Any eye disease	Reading acuity $\leq 20/30$	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)
			$\leq 20/40$	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)
			$\leq 20/60$	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 $\leq 20/40$	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 $\leq 20/30$	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 $\leq 20/30$	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 Report

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 (SD 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 Report

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 Report

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): Endophthalmitis 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 Report

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 0.45 to 0.96; $p=0.03$)	Good

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

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 Report

Study, Year	Aims	Literature Searches	Patients/Trials	Interventions
Evans, 2008 ⁹⁸ <i>Antioxidant vitamin and mineral supplements</i>	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 <i>Ginkgo biloba</i>	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); Lebuissou 1986 (n=20); total n=119	Ginkgo 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 Report

Study, Year	Results	Conclusion	Quality
Evans, 2008 ⁹⁸ <i>Antioxidant vitamin and mineral supplements</i>	<p>All comparisons</p> <p><i>Any multivitamin or antioxidant vs placebo</i></p> <p>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; $p=0.03$)</p> <p>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)</p> <p>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</p> <p>AMD progression as a continuous variable (AMDSG): mean difference -0.06 (CI -0.62 to 0.50)</p> <p>Individual comparisons</p> <p><i>Multivitamin supplements vs placebo (AREDS, Kaiser 1995, Richer 1996, Richer 2004)</i></p> <p>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</p> <p>Mean difference visual acuity (Kaiser 1995, AMDSG, LAST; $I^2=0\%$): pooled SMD 0.16 (CI -0.19 to 0.51)</p> <p>AMD progression as a dichotomous variable (AREDS): adjusted OR 0.68 (CI 0.53 or 0.87)</p> <p>AMD progression as a continuous variable (AMDSG): mean difference -0.06 (CI -0.62 to 0.50)</p> <p><i>Vitamin E vs. placebo (VECAT)</i></p> <p>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)</p> <p>AMD progression: OR 0.11 (CI 0.80 to 1.55)</p> <p><i>Zinc vs. placebo (AREDS, Holz 1993, Newsome 1988, Stur 1996)</i></p> <p>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)</p> <p>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</p> <p>AMD progression as a dichotomous variable (AREDS, Holz 1993, Stur 1996; $I^2=29.0\%$): pooled OR 0.73 (0.58-0.93)</p> <p><i>Lutein vs. placebo (LAST)</i></p> <p>Mean difference visual acuity: 0.04 (-0.15 to 0.23)</p>	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 <i>Ginkgo biloba</i>	<p><i>Ginkgo biloba 160 mg QD vs placebo (1 trial; n=20)</i></p> <p>Change in visual acuity: WMD 1.70 (CI 1.21 to 2.19)</p> <p>Clinical improvement: OR 36.00 (2.72 to 476.28)</p> <p><i>Ginkgo biloba 60 mg QD vs. 240 mg QD (1 trial; n=99)</i></p> <p>Mean visual acuity: WMD 0.05 (CI -0.03 to 0.13)</p> <p>>0.2 improvement in visual acuity score: OR 2.29 (CI 0.90 to 5.80)</p> <p>No serious AEs reported in either trial (headache, blood in stool and abdominal pain reported in 3/99 patients)</p>	There is inadequate evidence from 2 small, short-term trials to draw conclusions regarding the effect of ginkgo biloba on AMD progression. There may be harms associated with ginkgo biloba use, but they have been too inadequately reported.	Good

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

Study, Year	Results	Conclusion	Quality
Vedula, 2008 ¹²⁰	<p><i>Change in visual acuity (% of patients losing ≥ 3 lines of acuity at 1 year)</i></p> <p>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</p> <p>0.3 mg dose, 6.25 1.0 mg dose, 14.28 3.0 mg dose</p> <p>Ranibizumab (both doses) vs sham: RR 0.14 (CI 0.08 to 0.25); NNT 3.13 (both doses)</p> <p><i>Blindness</i></p> <p>Pegaptanib: RR 0.69 (CI 0.59 to 0.82)</p> <p>Ranibizumab: RR 0.28 (CI 0.21 to 0.37)</p> <p><i>Quality of life, mean change in NEI-VFQ score at 2-year followup</i></p> <p>ANCHOR Trial: 5.9 ranibizumab 0.3 mg vs. 8.1 ranibizumab 0.5 mg vs 2.2 verteporfin</p> <p>MARINA Trial: 4.8 ranibizumab 0.3 mg vs. 4.5 0.5 mg ranibizumab vs -6.4 sham injection</p> <p>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)</p> <p>Pegaptanib: Serious ocular AEs (endophthalmitis, retinal detachment, traumatic cataract) in tx groups, none in sham group</p>	Both interventions effective at reducing visual acuity loss and progression to blindness with improved QoL outcomes	Good
Virgili, 2007 ¹¹³	<p><i>Photocoagulation vs no treatment</i></p> <p>Visual acuity, loss of ≥ 6 lines at 3 months (5 trials): RR 1.41 (95% CI 1.08 to 1.82; $I^2=0\%$)</p> <p>Visual acuity, loss of ≥ 6 lines at 2 years (5 trials): RR 0.67 (95% CI 0.53 to 0.83; $I^2=58\%$)</p> <p>Visual acuity 20/200 or better at 1-3 years (3 trials): RR 0.73 (95% CI 0.61 to 0.86; $I^2=43\%$)</p> <p>Visual acuity 20/200 or better at 5 years followup (2 trials): RR 0.77 (95% CI 0.66 to 0.90; $I^2=21\%$)</p>	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	<p><i>Laser photocoagulation vs sham</i></p> <p>Loss of >3 lines of visual acuity at 12 months (4 trials): RR 0.80 (95% CI 0.69 to 0.93; $I^2=30\%$)</p> <p>Loss of >3 lines of visual acuity at 24 months (4 trials): RR 0.80 (95% CI 0.73 to 0.83; $I^2=0\%$)</p> <p>Loss of ≥ 6 lines of visual acuity at 12 months (4 trials): RR 0.70 (95% CI 0.56 to 0.88; $I^2=0\%$)</p> <p>Loss of ≥ 6 lines of visual acuity at 24 months (4 trials): RR 0.66 (95% CI 0.53 to 0.83; $I^2=31\%$)</p> <p>Gain of ≥ 3 lines of visual acuity at 12 months (3 trials): RR 2.19 (95% CI 0.99 to 4.82; $I^2=0\%$)</p> <p>Gain of ≥ 3 lines of visual acuity at 24 months (3 trials): RR 2.55 (95% CI 1.31 to 4.99; $I^2=0\%$)</p> <p><i>Harms</i></p> <p>Severe acute loss of visual acuity (3 trials): RR 3.75 (95% CI 0.87 to 16; $I^2=28\%$)</p> <p>Visual disturbance (3 trials): RR 1.56 (95% CI 1.21 to 2.01; $I^2=7\%$)</p> <p>Injection site reaction (3 trials): RR 2.09 (95% CI 1.29 to 3.39; $I^2=73\%$)</p> <p>Infusion-related back pain (4 trials): RR 9.93 (95% CI 2.82 to 35; $I^2=0\%$)</p> <p>Allergic reaction (2 trials): RR 0.94 (95% CI 0.34 to 2.56; $I^2=0\%$)</p> <p>Photosensitivity (2 trials): RR 5.37 (95% CI 1.01 to 29; $I^2=70\%$)</p>	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 Report

Study, Year	Study Design Purpose of Study	Patients	Intervention Duration of Followup	Results	Quality
AMD (Dry)					
AREDS Research Group, 2001 ⁹⁷ and Johnson 2007 ¹³⁵ <i>AREDS Report No. 8</i>	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: OR 0.68 (0.49 to 0.93; p=0.002) Loss of ≥15 letters of VA: Antioxidants vs. placebo: OR 0.87 (0.67 to 1.15; p=0.20) Zinc vs. placebo: OR 0.82 (0.63 to 1.08; p=0.07) Antioxidants + zinc vs. placebo: OR 0.77 (0.58 to 1.03; p=0.02) ORs adjusted for age, sex, race, baseline 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)	Good
AMD (Wet)					
<i>VEGF inhibitors</i>					
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: 73.6% (89/121) vs. 44.4% (28/63) 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)	Fair
Regillo, 2008 ¹²³ <i>PIER study year 1</i>	To evaluate the effectiveness and safety of ranibizumab for treatment of minimally classic or occult with no classic choroidal neovascularization 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: 58.7% (522/890) vs. 44.3% (131/296) 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)	Good

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

Study, Year	Study Design Purpose of Study	Patients	Intervention Duration of Followup	Results	Quality
Rosenfeld et al, 2006 ¹²¹ <i>MARINA Trial</i>	To evaluate the effectiveness and safety of ranibizumab for treatment of minimally classic or occult with no classic choroidal neovascularization 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	<p><i>Ranibizumab (all doses) vs. sham:</i> 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)</p> <p><i>Ranizumab 0.3 mg vs. 0.5 mg vs. sham</i> 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 $p < 0.01$</p>	Fair

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 Report

Study, Year	Type of Study	Screening Test	Reference Standard	Setting	Screener	Age of Enrollees	N	Proportion With Condition	Subjects
Any eye disease									
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 Report

Study, Year	Sensitivity	Specificity
Any eye disease		
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	Adequate: 51.6% (95% CI 44.2 to 58.9%) Impaired: 35.1% (95% CI 28.3 to 42.4%) Moderately impaired: 10.5% (95% CI 6.7 to 15.4%) Severely to highly impaired: 1.6% (95% CI 0.4 to 4.6%)	Adequate: 24.7% (95% CI 18.2 to 32.2%) Impaired: 79.8% (95% CI 72.6 to 85.7%) Moderately impaired: 95.8% (95% CI 91.5 to 98.3%) Severely to highly impaired: 100% (95% CI 97.7 to 100%)

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

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

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 Report

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 <u>Comorbidities</u> 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 <u>Comorbidities</u> 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 report)	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 $\leq 20/40$, 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 Report

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

Abbreviations: AMD = age-related macular degeneration, CES = Center for Epidemiologic Studies, MMSE = Mini-Mental State Examination, NHVQoL = Nursing Home Vision-Targeted Health-Related Quality of Life Questionnaire, 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 Report

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 report)	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 Report

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 = randomized 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 Report

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 Report

Author, Year Study Name	Study Design	Country Setting	Inclusion criteria	Randomized Analyzed Attrition	Intervention (n)
Chew, 2013 ⁹⁹ AREDS (Report #35)	RCT (long-term observational followup)	United States Multicenter	Age 55 to 80 years with AMD and BCVA $\geq 20/32$ in at least one eye	Randomized: 4,757 Analyzed (post-trial followup): 3,549 Attrition: NA	A. Antioxidant supplement (vitamin C 500 mg + vitamin E 400 IU + beta-carotene, 15 mg/day; n=1,480) B. Zinc 80 mg/day (n=903) C. Antioxidant supplement + zinc (n=887) D. Placebo (n=1,483)
Chew, 2009 ¹¹² AREDS (Report #25)	RCT (long-term observational followup)	United States Multicenter	Age 55 to 80 years with AMD and BCVA $\geq 20/32$ in at least one eye	Randomized: 4,757 Analyzed (post-trial followup): 4,577 Attrition: NA	A. Any AREDS active treatment (n=3,137) B. Placebo (n=1,467)
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 (n=26) B. Lutein 20 mg/day (n=27) C. Lutein 10 mg/day + zeaxanthin 10 mg/day (n=27) D. Placebo (n=27)
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 (n=36 for effectiveness; 42 for harms) B. Placebo (n=37 for effectiveness; 42 for harms)
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 (n=134) B. Placebo (olive oil 602 mg) (n=129)

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)

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

Author, Year Study Name	Study Participants	Duration of Followup	Results
			<p>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)</p> <p>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) <i>Participants with AMD category 3 or 4 at baseline</i></p> <p>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)</p> <p>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)</p> <p>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) <i>Participants with AMD category 4 at baseline</i></p> <p>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)</p> <p>B vs. D 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)</p> <p>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)</p>
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)	<p>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)</p>

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

Author, Year Study Name	Study Participants	Duration of Followup	Results
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% 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%	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 Report

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 ¹⁰⁸ 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 ¹⁰⁹ 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 Report

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 Report

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%

Author, year	Clinical Health Outcomes	Adverse Events	Quality	Comment
Bressler, 2013 ¹²⁶ MARINA (post-hoc analysis)	<p>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)</p> <p>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)</p> <p>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)</p> <p>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)</p>	<p>A vs B CVA: 3.3% (8/239) vs. 1.3% (3/236); RR 2.63 (95% CI 0.71 to 9.81)</p> <p>B vs. C CVA: 1.3% (3/238) vs. 1.3% (3/326); RR 0.99 (95% CI 0.20 to 4.86)</p>	Good	ANCHOR results outside the scope of this report (ranibizumab vs. verteporfin)

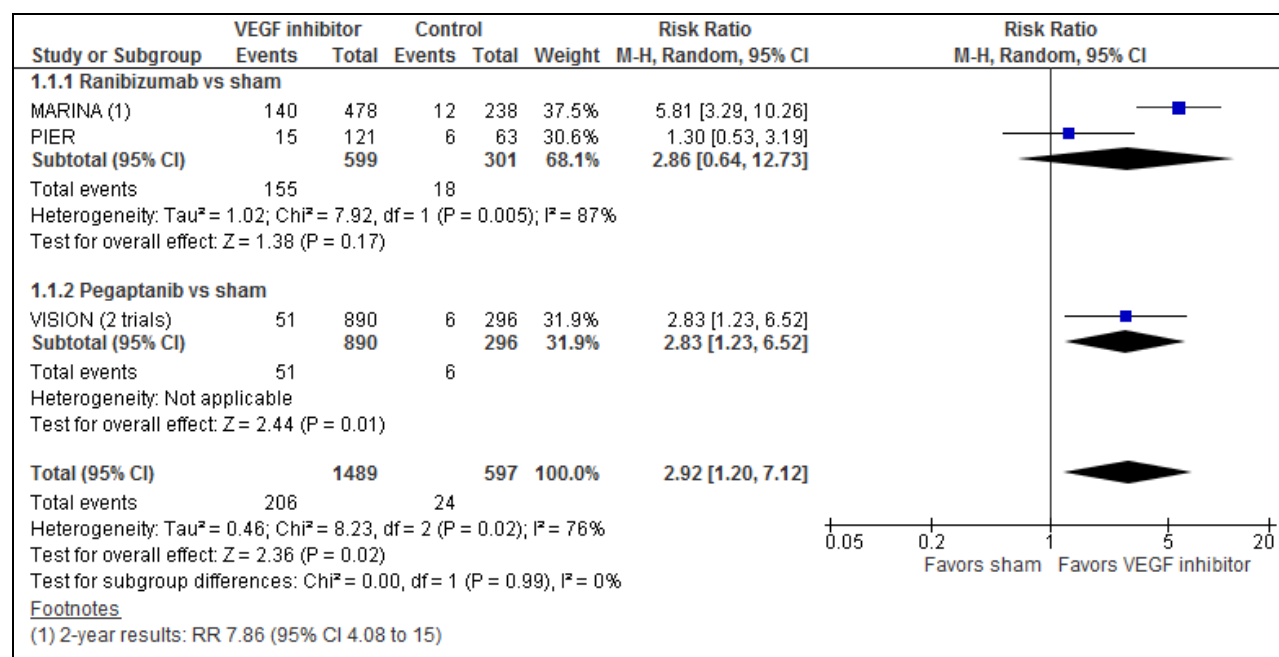
Abbreviations: AMD = age-related macular degeneration; CI = confidence interval, CNV = choroidal neovascularization; CVA = cerebrovascular accident; MI = myocardial infarction, NEI VFQ-25 = National Eye Institute Visual Function Questionnaire 25, RCT = randomized controlled trial, RR = risk ratio, VA = 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 Published Since the Prior USPSTF Report

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

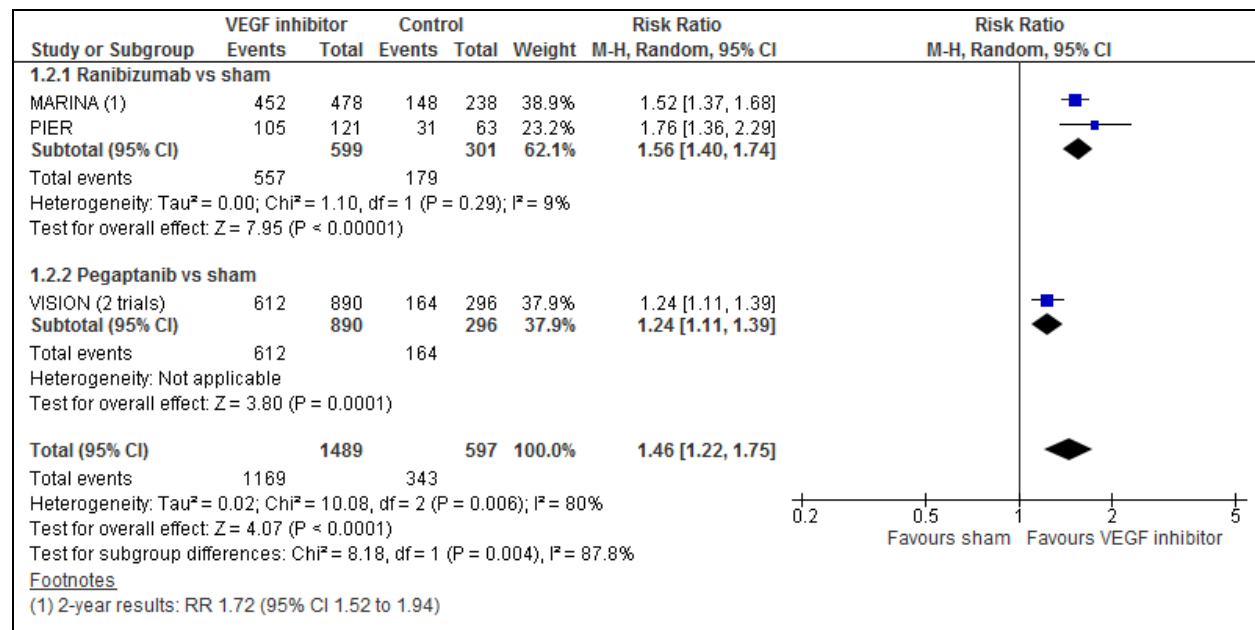
Note: Prior report studies abstracted in Appendix B.

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



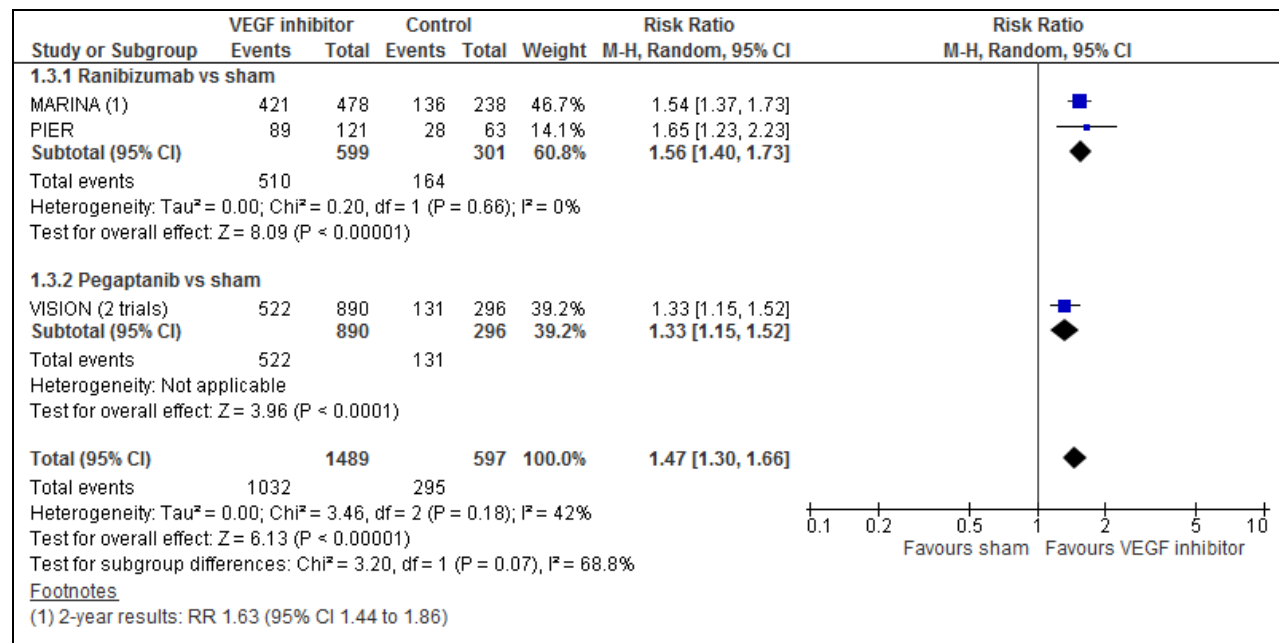
Abbreviation: VEGF = vascular endothelial growth factor.

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 20/20 or Better With Use of Vascular Endothelial Growth Factor Inhibitors at 1-Year Followup



Abbreviation: VEGF = vascular endothelial growth factor.