IMPORTANCE A 2016 review for the US Preventive Services Task Force (USPSTF) found that effective treatments are available for refractive errors, cataracts, and wet (advanced neovascular) or dry (atrophic) age-related macular degeneration (AMD), but there were no differences between visual screening vs no screening on visual acuity or other outcomes.

OBJECTIVE To update the 2016 review on screening for impaired visual acuity in older adults, to inform the USPSTF.

DATA SOURCES Ovid MEDLINE, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews (to February 2021); surveillance through January 21, 2022.

STUDY SELECTION Randomized clinical trials and controlled observational studies on screening, vascular endothelial growth factor (VEGF) inhibitors (wet AMD), and antioxidant vitamins and minerals (dry AMD); studies on screening diagnostic accuracy.

DATA EXTRACTION AND SYNTHESIS One investigator abstracted data and a second checked accuracy. Two investigators independently assessed study quality.

RESULTS Twenty-five studies (N = 33 586) were included (13 trials, 11 diagnostic accuracy studies, and 1 systematic review [19 trials]). Four trials (n = 4819) found no significant differences between screening vs no screening in visual acuity or other outcomes. Visual acuity tests (3 studies; n = 6493) and screening question (3 studies; n = 5203) were associated with suboptimal diagnostic accuracy. For wet AMD, 4 trials (n = 2086) found VEGF inhibitors significantly associated with greater likelihood of 15 or more letters visual acuity gain (risk ratio [RR], 2.92 [95% CI, 1.20-7.12]; I² = 76%; absolute risk difference [ARD], 10%) and less than 15 letters visual acuity loss (RR, 1.46 [95% CI, 1.22-1.75]; I² = 80%; ARD, 27%) vs sham treatment, with no increased risk of serious harms. For dry AMD, a systematic review (19 trials) found antioxidant multivitamins significantly associated with decreased risk of progression to late AMD (3 trials, n = 2445; odds ratio [OR], 0.72 [95% CI, 0.58-0.90]) and 3 lines or more visual acuity loss (1 trial, n = 1791; OR, 0.77 [95% CI, 0.62-0.96]) vs placebo. Zinc was significantly associated with increased risk of genitourinary events and beta carotene with increased risk of lung cancer in former smokers; other serious harms were infrequent.

CONCLUSIONS AND RELEVANCE This review found that effective treatments are available for common causes of impaired visual acuity in older adults. However, direct evidence found no significant association between vision screening vs no screening in primary care and improved visual outcomes.
Impaired visual acuity is common in older adults. In 2017, an estimated 53 million US adults older than 65 years were at high risk for serious vision loss, which can result in disability, loss of productivity, and reduced quality of life. Rates of severe vision loss are predicted to double or triple as the number of older adults increases.1–3

In 2016, the US Preventive Services Task Force (USPSTF) concluded that the current evidence was insufficient to assess the balance of benefits and harms of screening for impaired visual acuity in older (≥65 years) adults (I statement).4 Although a 2016 USPSTF review found that screening can identify persons with impaired visual acuity and that effective treatments are available for common causes of impaired visual acuity such as refractive errors, cataracts, and wet (advanced neovascular [caused by leakage of abnormal blood vessels under the macula]) or dry (atrophic [caused by thinning of the macula]) age-related macular degeneration (AMD), direct evidence found no differences between vision screening in older adults in primary care settings vs no screening in visual acuity or other clinical outcomes.5,6 This report was conducted to update the 2016 review on screening for impaired visual acuity in older adults, to inform the USPSTF for an updated recommendation.

Methods

Scope of the Review
Detailed methods and additional study details are available in the full evidence report.7 Figure 1 shows the analytic framework and key questions (KQs) that guided the review.

Data Sources and Searches
Ovid MEDLINE, the Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews were searched from January 2015 to February 9, 2021 (eMethods 1 in the Supplement). Searches were supplemented by reference list review of relevant studies; studies from the prior USPSTF review5,6 that met inclusion criteria were carried forward. Ongoing surveillance was conducted to identify major studies published since February 2021 that may affect the conclusions or understanding of the evidence and the related USPSTF recommendation. The last surveillance was conducted on January 21, 2022, and identified no studies affecting review conclusions.

Study Selection
Two investigators independently reviewed titles, abstracts, and full-text articles using predefined eligibility criteria (eMethods 2 in the Supplement). The population was older adults (65 years or older). Screening was performed with vision tests or questionnaires in primary care settings or were feasible for primary care (did not require eye specialty training or equipment) and compared against no screening. Treatment focused on benefits and harms of wet AMD (intravitreal vascular endothelial growth factor [VEGF] inhibitors) and dry AMD (vitamins and antioxidants). The USPSTF previously determined that treatments for refractive errors and cataracts are effective, and this was not rereviewed.6,9 Treatment was compared against placebo or sham; in addition, newer VEGF inhibitors (aflibercept and brolucizumab-dbll) were compared against older VEGF inhibitors because of the lack of placebo-controlled trials. Outcomes were visual acuity, vision-related quality of life; functional capacity; and harms (including falls and fractures and other treatment-related harms). An updated version10 of a systematic review11 on treatment for dry AMD used in the prior USPSTF review was included. Otherwise this report used primary studies. Inclusion was restricted to English-language articles, and studies published only as abstracts were excluded.

Data Abstraction and Quality Rating
One investigator abstracted details about the study design, patient population, setting, interventions, analysis, follow-up, and results from each study. A second investigator reviewed abstracted data for accuracy. Two independent investigators assessed the quality of each study as good, fair, or poor using predefined criteria (eMethods 3 in the Supplement) developed by the USPSTF.8 Discrepancies were resolved by consensus. In accordance with the USPSTF Procedure Manual,8 studies rated poor quality because of critical methodological limitations were excluded.

Data Synthesis
For all KQs, the overall strength of evidence was rated “high,” “moderate,” “low,” or “insufficient” based on study limitations, consistency, precision, reporting bias, and applicability, using the approach described in the USPSTF Procedure Manual.8 No new evidence suitable for meta-analysis was identified for this review, owing to small numbers of studies and heterogeneity in populations, interventions, and outcomes. However, a random-effects meta-analysis conducted for the prior USPSTF review6 on the effects of VEGF inhibitors remained relevant and was carried forward in this review.

Results
Across all KQs, 25 studies (reported in 51 publications, total N = 33,586 participants) were included (13 randomized clinical trials [RCTs], 11 diagnostic accuracy studies, and 1 systematic review) (Figure 2).12–62 Sixteen studies12,14,21,23,24,27,34,35,39,42,44,46,47,52,53,58,61 were carried forward from the 2016 USPSTF review,5,6 8 studies32,34,39,29,33,41,43,57,61 were new, and an updated Cochrane systematic review10 included 19 studies (the previous Cochrane review11 included 13).15,16,18,22,25,26,28,30,32,36,37,40,49,54–56,59,60

Screening

Key Question 1. What are the effects of vision screening in asymptomatic older adults vs no screening on visual acuity, morbidity or mortality, general or vision-related quality of life, functional status, or cognition?

Four fair-quality RCTs19,23,34,46,47,61 (in 6 publications; n = 4819) compared vision screening in primary care–applicable settings vs no screening, usual care, or delayed screening (eTable 1 in the Supplement; all were included in the 2016 USPSTF review except for 1 small [n = 188] trial.79 The duration of follow-up ranged from 6 months to 5 years. Screening methods varied: a brief screening questionnaire plus the Glasgow visual acuity chart followed by pinhole testing for persons with visual acuity worse than 6/18 (20/60)23; assessment of difficulty in recognizing a face,
None of the trials, including the trials added for this update, found beneficial effects of screening on visual acuity, likelihood of vision disorders, or vision-related functional impairment or quality of life (Table 1). In the largest (n = 3249) trial, universal vision screening identified about 10 times as many patients with impaired visual acuity and correctable impairment compared with targeted screening, but there was no significant difference in the likelihood of visual acuity worse than 20/60 at 3- to 5-year follow-up (relative risk [RR], 1.07 [95% CI, 0.84-1.36]). Another large (n = 1121) trial found no significant difference between immediate vs delayed screening in the likelihood of visual disorders at 2 years (51% [95% CI, 45%-58%] vs 47% [95% CI, 42%-52%]; P = .68). Potential reasons for lack of screening benefit may include attrition (24% to nearly 60% in the larger trials at 2 to 5 years), similar frequency of vision disorder detection and treatment in the screening and control groups, use of a suboptimal method (a question) for initial screening, low uptake of recommended

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**Figure 1. Analytic Framework and Key Questions: Screening for Impaired Visual Acuity in Older Adults**

Key questions:

1. What are the effects of vision screening in asymptomatic older adults vs no screening on visual acuity, morbidity or mortality, general or vision-related quality of life, functional status, or cognition?

2. What are the harms of vision screening in asymptomatic older adults vs no screening?

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

4. What is the accuracy of instruments for identifying patients at higher risk of impaired visual acuity due to uncorrected refractive error, cataracts, or age-related macular degeneration?

5. What are the effects of treatment for wet or dry age-related macular degeneration vs placebo or no treatment on visual acuity, morbidity, mortality, general or vision-related quality of life, functional status, or cognition?

6. What are the effects of newer (aflibercept or brolucizumab-dbll) vs older vascular endothelial growth factor inhibitors for wet age-related macular degeneration on visual acuity, morbidity, mortality, general or vision-related quality of life, functional status, or cognition?

7. What are the harms of treatment for early impaired visual acuity due to wet or dry age-related macular degeneration?
Figure 2. Literature Search Flow Diagram: Screening for Impaired Visual Acuity in Older Adults

- 5170 Abstracts of potentially relevant articles identified through MEDLINE, Cochrane, and other sources
- 4831 Abstracts and background articles excluded
- 339 Full-text articles reviewed for relevance
- 288 Excluded
  - 72 Wrong intervention
  - 54 Wrong study design for KQ
  - 29 Wrong population
  - 26 Wrong outcome
  - 25 Wrong comparator
  - 22 Systematic review or meta-analysis used as a source document only to identify individual studies
  - 13 Wrong screener
  - 12 Ancillary publication not relevant to the current systematic review
  - 10 Wrong setting
  - 8 Not a study
  - 7 Study covered in a systematic review
  - 4 Results not usable or fully reported
  - 3 Wrong publication type
  - 2 Poor quality
  - 1 Wrong country
- 6 Articles (4 studies; 3 carried forward, 1 new) included for KQ1
- 7 Articles (8 studies; 7 carried forward, 1 new) included for KQ3
- 4 Articles (3 studies; 2 carried forward, 1 new) included for KQ4
- 6 Articles (6 trials) and 1 updated systematic review included for KQ5
- 5 Articles (3 trials; new) included for KQ6
- 9 Articles (9 trials) and 1 updated systematic review included for KQ7

AMD indicates Age-Related Macular Degeneration; AREDS, Age-Related Eye Disease Study; KQ, key question; VEGF, vascular endothelial growth factor.

a Number of articles includes the studies in the systematic review. The number of included studies does not sum to the number shown because some studies are included for more than 1 KQ.
Table 1. Screening Trials

<table>
<thead>
<tr>
<th>Source</th>
<th>Intervention</th>
<th>Screening tools</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eekhof et al,46,47</td>
<td>A: Vision screening (n = 576)</td>
<td>Validated diagnostic tests:</td>
<td>A vs B:</td>
</tr>
<tr>
<td>2000</td>
<td>B: Delayed screening (n = 545)</td>
<td>Assessment of difficulty in recognizing a face at 4 m and/or reading normal letters in a newspaper, and/or impaired vision with both eyes by Snellen eye chart or not being able to read normal newspaper letters at 25 cm distance</td>
<td>Vision disorder detected: 4% (95% CI, 43% to 54%) vs NR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vision was measured with glasses usually worn</td>
<td>Visual disorder in second year: 51% (95% CI, 45%-58%) vs 47% (42%-52%); P = .68</td>
</tr>
<tr>
<td>Moore et al,34</td>
<td>A: Vision screening, coupled with clinical summaries (n = 112)</td>
<td>Question, “Do you have difficulty driving or watching television or reading or doing any of your daily activities because of your eyesight (even while wearing glasses)?”*</td>
<td>A vs B:</td>
</tr>
<tr>
<td>1997</td>
<td>B: Usual care (n = 149)</td>
<td>followed by Snellen eye chart if affirmative</td>
<td>Vision problem detected: 20% vs 19%; P = .84</td>
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<tr>
<td></td>
<td></td>
<td>Improvement in vision at 6 mo: 20% (20/99) vs 24% (31/131); RR, 0.85 (95% CI, 0.52-1.40)</td>
<td></td>
</tr>
<tr>
<td>MRC Trial</td>
<td>A: Universal screening (brief health assessment plus detailed health assessment, latter of which included measurement of VA (n = 1565))</td>
<td>Detailed health assessment: VA measured using Glasgow acuity eye chart (Snellen equivalent provided in results), and pinhole testing if VA worse than 6/18 in either eye; referral to ophthalmologist when appropriate</td>
<td>A vs B:</td>
</tr>
<tr>
<td>Smeeth et al,23</td>
<td>B: Targeted screening (brief health assessment (n = 1684, 120 of which had a detailed assessment due to severity of problems, although 150 were eligible))</td>
<td>Brief health assessment: Covered all areas specified in the general practitioner contract, including a question about difficulty seeing, but did not include measurement of VA; those with a specified range and level of problems were eligible to have a detailed assessment</td>
<td>Eligible for referral to ophthalmologist: 14% (220/1565) vs 1.7% (29/1684)</td>
</tr>
<tr>
<td>2003</td>
<td></td>
<td>Reporting difficulty seeing was not on its own sufficient to lead to a detailed assessment</td>
<td>Eligible for referral to optician: 5% (79/1565) vs 0.4% (8/1684)</td>
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<tr>
<td></td>
<td></td>
<td>At follow-up:</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>VA worse than 6/18 (20/60) in either eye: 2% (451/1565) vs 3.1% (53/1684)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>VA worse than 6/12 binocular vision: 14% (114/817) vs 17% (160/962); RR, 0.84 (95% CI, 0.64-1.10)</td>
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<tr>
<td></td>
<td></td>
<td>VA worse than 6/12 in either eye: 59% (486/829) vs 60% (584/978); RR, 0.98 (95% CI, 0.82-1.17)</td>
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<tr>
<td></td>
<td></td>
<td>VA worse than 6/12 binocular vision: 31% (256/817) vs 37% (311/962); RR, 0.86 (95% CI, 0.65-1.13)</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>NEI-VFQ mean composite score (scale 0-100; higher score = better quality of life): 86.0 vs 85.6; mean difference, 0.4 (95% CI, −1.7 to 2.5)</td>
<td></td>
</tr>
<tr>
<td>ACCS</td>
<td>Routine aged care assessment and interview using a standardized questionnaire, plus</td>
<td>LogMAR chart for presenting VA for distance (with glasses, if worn) using letters read correctly using ETDRS-Fast protocol</td>
<td>A vs B:</td>
</tr>
<tr>
<td>Tay et al,19</td>
<td>A: Vision screening (n = 96)</td>
<td>Binocular near vision and visual field using confrontation method</td>
<td>Mean VA: 39 letters vs 35 letters; P = .25</td>
</tr>
<tr>
<td>2006</td>
<td>B: No vision screening (n = 92)</td>
<td>Self-report questions: Did you notice any deterioration in one or both eyes? Are you able to recognize a friend across the street? Can you read the ordinary print in the newspaper reasonably well, with or without glasses?</td>
<td>Bilateral visual impairment: 35% vs 47%; P = .17</td>
</tr>
</tbody>
</table>

Abbreviations: ACCS, Aged Care Client pilot Study; ETDRS, Early Treatment Diabetic Retinopathy Study; LogMAR, logarithmic minimum angle of resolution; MRC, Medical Research Council; NEI-VFQ, National Eye Institute Visual Function Questionnaire; NR, not reported; RR, relative risk; VA, visual acuity.

follow-up or interventions,23,47 or high rates of antecedent eye professional care.19

Key Question 2. What are the harms of vision screening in asymptomatic older adults vs no screening?

No screening study reported harms.

Key Question 3. What is the diagnostic accuracy of screening for impaired visual acuity due to uncorrected refractive error, cataracts, or AMD?

Eight fair-quality studies (n = 7398) examined the accuracy of screening tests for impaired visual acuity due to visual conditions such as cataracts, refractive error, and AMD in older adults (eTables 3-4 in the Supplement). Seven (reported in 6 publications)12,14,21,35,39,58 were in the prior USPSTF review and 1 study (n = 104)27 was added. Screening was conducted using an eye chart (Snellen or logarithm of the minimum angle of resolution [LogMAR], 3 studies),12,14,58 a computerized tool based on 4 tests of vision function (2 studies),39 the Minimum Data Set Vision Patterns section score (1 study),21 geriatrician examination (1 study),35 the Amsler grid (a grid of horizontal and vertical lines used for central visual field monitoring) (1 study),1,58 or a mobile application.57 Methodological limitations included failure to apply the reference standard in all patients, interpretation of the reference standard not independent from screening test results, and thresholds for a positive screening test result not prespecified (eTable 5 in the Supplement).

Three studies (n = 6493) evaluated screening visual acuity tests compared with a complete ophthalmologist examination. Based on a visual acuity threshold on screening of less than 20/30 or less than...
20/40, sensitivity ranged from 0.27 to 0.75 and specificity from 0.51 to 0.87. One study each found low accuracy of a computer-based screening tool or the Minimum Data Set MDS Vision Patterns section score.²¹,²³ One study (n = 50) in the prior USPSTF review found a geriatric examination had sensitivity of 1.0 (95% CI, 0.69-1.0) for cataract and 0.80 (95% CI, 0.28-0.99) for AMD compared with ophthalmologist examination, with no false-positive results, but estimates were imprecise.³⁵ One new study found visual acuity screening using a mobile application associated with sensitivity of 0.98 (95% CI, 0.91-1.00) and specificity of 0.94 (95% CI, 0.82-0.99) for identifying visual acuity 20/40 or less compared with a visual acuity chart.⁵⁷

**Key Question 4.** What is the accuracy of instruments for identifying patients at higher risk of impaired visual acuity due to uncorrected refractive error, cataracts, or AMD?

Two studies²⁴,²⁶,⁴⁷ (n = 1121 and n = 3997) included in the prior USPSTF review and 1 new study³³ (n = 85), all fair quality, found that screening questions were not accurate for identifying older persons with impaired visual acuity compared with an eye chart; all studies reported low sensitivity, low specificity, or both (eTables 6-8 in the Supplement). Sensitivities ranged from 0.17 to 0.81 and specificities from 0.19 to 0.84. Questions included asking about trouble recognizing faces, reading the newspaper, or seeing.

**Treatment**

**Key Question 5.** What are the effects of treatment for wet or dry AMD vs placebo or no treatment on visual acuity, morbidity, mortality, general or vision-related quality of life, functional status, or cognition?

**VEGF Inhibitors for Wet AMD**

Four good-quality RCTs (n = 2086; reported in 5 publications), all included in the prior USPSTF review, evaluated intravitreal injection with VEGF inhibitors vs sham injection.²⁴,²⁷,⁴⁴,⁵²,⁵³ At 1 year, intravitreal VEGF inhibitors were significantly associated with greater likelihood vs sham of 15 letters or more of visual acuity gain (RR, 2.92 [95% CI, 1.20-7.12]; I² = 76%; absolute risk difference [ARD], 10%); less than 15 letters of visual acuity loss (RR, 1.46 [95% CI, 1.22-1.75]; I² = 80%; ARD, 27%); and having vision 20/200 or better (RR, 1.47 [95% CI, 1.30-1.66]; I² = 42%; ARD, 24%) (eFigures 1-3 and eTables 9-10 in the Supplement).²⁴,²⁷,⁴⁴ In 1 trial,²⁴ VEGF inhibitors were significantly associated with better vision-related function and quality-of-life measures vs sham injection at 1 and 2 years. Differences on the National Eye Institute–Vision Function Questionnaire 25 (NEI-VFQ) composite and subscales were about 8 points on a 0 to 100 scale, or above the proposed threshold for a clinically important difference (4 to 6 points).⁶³

**Antioxidant Vitamins and Minerals for Dry AMD**

The large (n = 3640), good-quality Age-Related Eye Disease Study⁵⁹ (AREDS), included in prior USPSTF reviews,³⁶ remains the key trial on treatment for dry AMD (eTables 11-12 in the Supplement). At 6.3 years, it found an antioxidant plus zinc combination significantly associated with decreased risk of progression to advanced AMD vs placebo (odds ratio [OR], 0.72 [99% CI, 0.52-0.98]).³⁹ In patients with more advanced (category 3 or 4) AMD, antioxidants plus zinc were significantly associated with decreased risk of visual acuity loss of 15 lines or more on the ETDRS (OR, 0.73 [99% CI, 0.54-0.99]). Ten-year results⁶⁴ were consistent with 6.3-year results.

An updated (2017) Cochrane systematic review⁵² included 19 trials, including 13 trials in the prior [2012] version)⁶³ of antioxidant multivitamins, zinc, lutein and zeaxanthin, or vitamin E for dry AMD; results were heavily influenced by AREDS (eTables 13-14 in the Supplement). Besides AREDS, the systematic review included the large (n = 4203) AREDS2 trial,⁵¹,⁶⁰ which evaluated the AREDS formulation or a variation of it (elimination of beta carotene, lowering of zinc dose, or both), and the Vitamin E, Cataract, and Age-related Maculopathy (VECAT) study (n = 1193).³⁸ In the other trials, sample sizes ranged from 14 to 433. The review found antioxidant multivitamins significantly associated with decreased risk of progression to late AMD (3 trials, n = 2445; OR, 0.72 [95% CI, 0.58-0.90]; 73% of patients from AREDS) and 3 lines or more visual acuity loss (1 trial [AREDS], n = 1791; OR, 0.77 [95% CI, 0.62-0.96]) vs placebo. Vitamin E was significantly associated with decreased risk of progression to late AMD vs placebo (3 trials, n = 3790; OR, 0.83 [95% CI, 0.70-0.98]; 96% of patients from AREDS) and decreased risk of 3 lines or more of visual acuity loss that was of borderline statistical significance (2 trials, n = 3791; RR, 0.87 [95% CI, 0.75-1.00]; 96% of patients from AREDS). Lutein and zeaxanthin or vitamin E were associated with little or no effect on risk of AMD progression. Data on effects of multivitamins on vision-related function were limited, with most trials showing no statistically significant differences.³⁸,⁴⁵,⁴⁹,⁵⁰,⁶⁵ AREDS found no differences between antioxidants, zinc, both, or placebo in measures of cognition at 6.9 years.³⁸

Two additional fair-quality trials not included in the systematic review²⁰,²⁹ evaluated an antioxidant combination or α-lipoic acid, but were small (n = 80 and 100) with imprecise estimates, and did not affect the findings of the systematic review (eTables 15-16 in the Supplement).

**Key Question 6.** What are the effects of newer (afiblercept or brolucizumab-dbll) vs older VEGF inhibitors for wet AMD on visual acuity, morbidity, mortality, general or vision-related quality of life, functional status, or cognition?

Three new good-quality trials (n = 2738; reported in 5 publications) compared afiblercept vs the older VEGF inhibitor ranibizumab (eTables 9-10 in the Supplement).¹⁷,⁴¹,⁴³,⁴⁵,⁶² The duration of follow-up ranged from 1 year to 4 years. Afiblercept was noninferior to ranibizumab in likelihood of less than 15 ETDRS letters of visual acuity loss or 15 letters or more of visual acuity gain, and 2 trials (n = 2457) found similar improvements in vision-related function. No trial compared brolucizumab-dbll vs an older VEGF inhibitor.

**Key Question 7.** What are the harms of treatment for early impaired visual acuity due to wet or dry AMD?

**VEGF Inhibitors for Wet AMD**

There were no significant differences between VEGF inhibitors vs sham treatment in likelihood of withdrawal due to adverse events (eTables 9-10 in the Supplement). Evidence on the effects of VEGF inhibitors on other harms was limited.⁶ Serious ocular harms were infrequent, and incidence of endophthalmitis (2 trials, n = 1924; RR, 5.49 [95% CI, 0.30-99] and RR, 8.33 [95% CI, 0.50-140]), ocular hemorrhage (1 trial, n = 184; RR, 0.52 [95% CI, 0.08-3.61]), and retinal detachment (2 trials, n = 1924; RR, 0.17 [95% CI, 0.01-4.07], and RR, 3.67 [95% CI, 0.20-65]) were similar in VEGF and sham
treatment groups. The studies were not sufficiently powered to assess rates of cardiovascular events or other serious adverse events, although no statistically significant differences were reported.

Newer vs Older VEGF Inhibitors for Wet AMD

Three trials (n = 2738; reported in 2 publications) found that serious ocular adverse events and cardiovascular events were infrequent and occurred in similar proportions of patients randomized to aflibercept or ranibizumab (eTables 9-10 in the Supplement). Antioxidant Vitamins and Minerals for Dry AMD

AREDS found zinc use associated with increased risk of hospitalization due to genitourinary causes vs nonuse (7.5% vs 4.9%; RR, 1.47 [95% CI, 1.19-1.80]). Zinc and antioxidant use significantly associated with increased risk of yellow skin vs nonuse (8.3% vs 6.0%; RR, 1.38 [95% CI, 1.09-1.75]). No active treatment in AREDS (antioxidants, zinc, or both) was associated with increased risk of other serious adverse events, which were uncommon (eTable 17 in the Supplement). In AREDS2, there were no differences between AREDS formulation variations and risk of serious adverse events. However, in an analysis in which current smokers were excluded, the AREDS formulation with beta carotene was significantly associated with increased risk of lung cancer vs without beta carotene (2.0% vs 0.9%, P = .04). Almost all (91%) of the lung cancers occurred in former smokers.

VECAT (n = 1193), the largest trial other than AREDS and AREDS2, reported no serious adverse events with vitamin E or placebo, and no differences in risk of withdrawal due to adverse events or specific adverse events. Evidence on harms from other trials was limited because of suboptimal reporting and imprecision but did not indicate increased risk of serious adverse events or withdrawal due to adverse events.

Discussion

This report evaluated evidence regarding screening for impaired visual acuity in older adults; the findings are summarized in Table 2. As in the prior review for the USPSTF, direct evidence on screening older adults for impaired visual acuity in primary care settings vs no screening, delayed screening, or usual care found no benefits on vision-related or other outcomes. Potential reasons for lack of benefit in the screening trials may include high attrition, use of suboptimal screening interventions, low uptake of recommended interventions, or high rates of antecedent eye professional care. Recent reviews of vision screening in older adults in broader (eg, community and home-based) settings also found no differences between screening vs no screening in vision or vision-related outcomes, even though they included a number of trials that did not meet inclusion criteria for this report because they did not evaluate the vision screening component separately or screening was conducted by an eye specialist and was not primary care feasible.

Conclusions regarding the suboptimal diagnostic accuracy of vision screening tests for identifying conditions associated with impaired visual acuity in primary care settings are also unchanged from the prior review for the USPSTF. No screening question is comparable in accuracy to tests of visual acuity for identifying impaired visual acuity, and visual acuity testing with a chart is inaccurate for identifying visual conditions identified on a comprehensive ophthalmological examination. However, it is not known whether identification of cataracts or AMD prior to the development of impaired visual acuity is associated with improved clinical outcomes compared with identification after the development of mildly impaired visual acuity. Data on other screening tests was limited or indicated suboptimal performance. There remains insufficient evidence to assess the accuracy or utility of pinhole testing, the Amsler grid, visual acuity tests other than the Snellen and ETDRS, physical examination, or funduscopic examination performed in primary care settings.

As in the prior review for the USPSTF, strong evidence supports the effectiveness of treatments for common causes of impaired visual acuity. The USPSTF previously determined that a very high proportion of patients experience favorable vision-related outcomes and improvement in vision-related quality of life following treatment for impaired visual acuity due to refractive error and cataracts; therefore, this evidence was not reviewed for this update. For dry AMD, evidence showing the effectiveness of antioxidant vitamins and minerals for slowing progression of disease or improving visual acuity remains largely based on the large AREDS trials, which included extended (10-year) follow-up. Based on AREDS2 and other evidence indicating an association between use of beta carotene and increased risk of lung cancer in smokers, recommendations for current and former smokers are to avoid the AREDS formula with beta carotene, using lutein and zeaxanthin in its place. For wet AMD, this update focused on VEGF inhibitors, which are first-line treatment in most patients. As in the prior review for the USPSTF, VEGF inhibitors were associated with improvement in visual acuity–related outcomes, with a relatively low incidence of serious harms, although data on effects on vision-related quality of life or function are limited and inconclusive. One area of concern with VEGF inhibitors has been a potential association with increased risk of cardiovascular events. Although randomized trials of VEGF inhibitors for AMD did not report increased risk of cardiovascular events, they were not designed to evaluate these outcomes and the number of events were small. Although new sham-controlled trials of VEGF inhibitors were not identified, head-to-head trials of the recently approved US Food and Drug Administration (FDA)-approved VEGF inhibitor aflibercept vs an older VEGF inhibitor indicated similar effects on visual acuity–related outcomes and no difference in serious harms. No trial of the recently FDA-approved VEGF inhibitor brolucizumab-dbll met inclusion criteria. However, in May 2021, several ongoing brolucizumab-dbll trials were discontinued because of higher rates of intraocular inflammation, including retinal vasculitis and retinal vascular occlusion.

Limitations

This evidence review has several limitations. First, a previously published systematic review on antioxidant multivitamins and minerals for dry AMD was used. The reliability of systematic reviews depends on how well they are designed and conducted. Therefore, the systematic review was required to meet a quality threshold based on predefined criteria, and data abstraction and quality assessment of included trials was independently verified. Second, evidence on effectiveness of treatment for dry AMD relied heavily on results of a single trial—the large, well-conducted AREDS trial.
### Table 2. Summary of Evidence

<table>
<thead>
<tr>
<th>Studies</th>
<th>Summary of findings</th>
<th>Evidence consistency and precision</th>
<th>Other limitations</th>
<th>Strength of evidence</th>
<th>Applicability</th>
</tr>
</thead>
<tbody>
<tr>
<td>KQ1: Benefits of screening</td>
<td>Four trials of screening vs no screening, usual care, or delayed screening in older adults found no difference on vision or other clinical outcomes in older adults</td>
<td>Consistent</td>
<td>All studies rated fair quality</td>
<td>Moderate for no benefit</td>
<td>Screening tests feasible for primary care</td>
</tr>
<tr>
<td>4 Trials (3 in prior USPSTF review, 1 new) (4819 observations)</td>
<td></td>
<td>Reasonably precise</td>
<td>Interventions and comparators differed across studies</td>
<td></td>
<td>Studies conducted in the US, Europe, and Australia</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Adherence to recommended follow-up and interventions was low in some trials</td>
<td></td>
<td>Screening conducted in community or general practice settings or a geriatric day hospital</td>
</tr>
<tr>
<td></td>
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<td></td>
<td>Attrition high in some trials</td>
<td></td>
<td>Screening conducted by general practitioners, office staff, or trained nurses; vision screening was conducted as part of a multicomponent health screen</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Reporting bias not detected</td>
<td></td>
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<tr>
<td></td>
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<td></td>
<td>All studies rated fair quality</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Variations in screening tests and testing thresholds; testing thresholds not specified in some studies</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>Clinical relevance of visual conditions identified on ophthalmological examination but not associated with impaired visual acuity unclear</td>
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<tr>
<td></td>
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<td></td>
<td>Some screening tests have not been validated</td>
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<td></td>
<td>Reporting bias not detected</td>
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<tr>
<td>KQ2: Harms of screening</td>
<td>No studies</td>
<td>No included trials reported harms of screening</td>
<td>NA</td>
<td>Insufficient</td>
<td>NA</td>
</tr>
<tr>
<td>8 Cross-sectional studies (7 in prior USPSTF review, 1 new) (7398 observations)</td>
<td>Visual acuity tests (3 studies) were associated with poor diagnostic accuracy for identifying visual conditions compared with a complete examination by an ophthalmologist; evidence on other screening tests was limited</td>
<td>Consistent</td>
<td>All studies rated fair quality</td>
<td>Moderate</td>
<td>Screening tests were feasible for primary care</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Precise</td>
<td>Variability in screening tests and testing thresholds; test threshold not specified in some studies</td>
<td></td>
<td>Studies conducted in the US, UK, and Australia</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Clinical relevance of visual conditions identified on ophthalmological examination but not associated with impaired visual acuity unclear</td>
<td></td>
<td>Variability in screening settings (primary care clinics, general eye clinics, hospitals, community day centers, and nursing homes); screener-trained research staff or unclear in some studies</td>
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<tr>
<td>KQ3: Diagnostic accuracy of screening tests</td>
<td>Three studies found that a screening question was not accurate for identifying older persons with impaired visual acuity compared with a visual acuity chart</td>
<td>Consistent</td>
<td>All studies rated fair quality</td>
<td>Moderate</td>
<td>Screening questions were highly feasible for primary care</td>
</tr>
<tr>
<td>3 Cross-sectional studies (2 in prior USPSTF review, 1 new) (5203 observations)</td>
<td></td>
<td>Reasonably precise</td>
<td>Screening question varied across studies</td>
<td></td>
<td>Studies conducted in the US and Europe</td>
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<td>Reporting bias not detected</td>
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<tr>
<td>KQ4: Diagnostic accuracy of screening instruments</td>
<td>Four trials of VEGF inhibitors were associated with greater likelihood of &gt;15 letters (3 lines) of visual acuity gain (RR, 2.92 [95% CI, 1.20–7.12]; I² = 76%; ARD, 10%), &lt;15 letters (3 lines) of visual acuity loss (RR, 1.46 [95% CI, 1.22–1.75]; I² = 80%; ARD, 27%), and having vision 20/200 or better (RR, 1.47 [95% CI, 1.30–1.66]; I² = 42%; ARD, 24%) at 1 y vs sham injection</td>
<td>Consistent</td>
<td>Data on function or quality of life limited to 1 trial</td>
<td>Moderate for benefit</td>
<td>VEGF inhibitors are considered first-line therapy in the US</td>
</tr>
<tr>
<td>VEGF inhibitors for wet AMD:</td>
<td></td>
<td>(statistical heterogeneity present in pooled analyses, but inconsistency was in magnitude of effect, not direction of effect)</td>
<td>Studies not designed to evaluate mortality or other health outcomes</td>
<td></td>
<td>Baseline visual acuity 20/80 in 3 studies and ranged from 20/40 to 20/200 in 1 study</td>
</tr>
<tr>
<td>4 Trials (all in prior USPSTF review) (2086 observations)</td>
<td>In 1 trial, VEGF inhibitors were associated with better vision-related function and quality-of-life measures vs sham injection at 1 and 2 y; the mean difference was above the threshold for a minimum clinically important difference</td>
<td>Precise</td>
<td>Reporting bias not detected</td>
<td></td>
<td>Studies conducted in the US in 2 trials, and the others had various sites (US, Canada, Europe, Israel, Australia, South America)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Data on function or quality of life limited to 1 trial</td>
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Table 2. Summary of Evidence (continued)

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</tr>
</thead>
<tbody>
<tr>
<td>Vitamin and mineral supplements for dry AMD:</td>
<td>Antioxidant multivitamins associated with decreased risk of progression to late AMD (3 trials, n = 2445; OR, 0.72 [95% CI, 0.58-0.90]) and &gt;3 lines visual acuity loss (1 trial, n = 1791; OR, 0.77 [95% CI, 0.62-0.96]) vs placebo</td>
<td>Consistent</td>
<td>Findings primarily based on 1 study (AREDS)</td>
<td>Moderate for benefit</td>
<td>AREDS was conducted in the US and the AREDS and AREDS2 formulations are widely used in clinical practice</td>
</tr>
<tr>
<td>The prior USPSTF review included a prior version of the systematic review with 13 trials</td>
<td>Zinc was associated with decreased risk of progression to late AMD vs placebo (3 trials, n = 3790; OR, 0.83 [95% CI, 0.70-0.98]; 96% of patients from AREDS) and decreased risk of visual acuity loss &gt;3 lines that was of borderline statistical significance (2 trials, n = 3791; RR, 0.87 [95% CI, 0.75-1.00])</td>
<td>Precise</td>
<td>Heterogeneity in the interventions assessed</td>
<td></td>
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<tr>
<td>≈75% of patients in AREDS had mild to moderate AMD at baseline</td>
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</table>

**KQ6: Benefits of newer (aflibercept or brolucizumab-dbll) vs older VEGF inhibitors for AMD**

| 3 Trials (all new) (2738 observations) | Afiblercept was noninferior to ranibizumab in likelihood of <15 ETDRS letters of visual acuity loss (3 trials) and <15 letters of visual acuity gain (3 trials) and was similar to ranibizumab for vision-related function (2 trials) | Consistent | No trial of brolucizumab-dbll met inclusion criteria | Moderate for similar benefit | Aflibercept was FDA approved for AMD in 2011 and with a longer dosing schedule in 2018 |
| | | Reasonably precise | Trials not designed to assess mortality or other health outcomes Reporting bias not detected | |
| | | | | |

**KQ7: Harms of treatment for AMD**

| VEGF inhibitors for wet AMD: | No differences between VEGF inhibitors vs sham injection in likelihood of withdrawal due to adverse events, cardiovascular events, or serious ocular adverse events | Consistent | Trials not powered for serious cardiovascular or ocular adverse events Reporting bias not detected | Moderate for no harm | VEGF inhibitors vs sham: VEGF inhibitors are considered first-line therapy in the US Baseline visual acuity 20/80 in 3 studies and ranged from 20/40 to 20/200 in 1 study Studies were conducted in the US in 2 trials, and the others had various sites (US, Canada, Europe, Israel, Australia, South America) Newer vs older VEGF inhibitors: Aflibercept was FDA approved for AMD in 2011 and with a longer dosing schedule in 2018 One trial was conducted in Australia, and the others had various sites (US, Canada, international) |
| VEGF vs sham: 4 trials (all in prior USPSTF review) (2086 observations) | Three trials found that serious ocular adverse events were infrequent and occurred in similar proportions of patients randomized to either aflibercept or ranibizumab | Imprecise | | |
| Newer vs older VEGF inhibitors: 3 trials (all new) (2738 observations) | | | | |

**Vitamin and mineral supplements for dry AMD:**

| 1 Systematic review of 19 trials (n = 11162) and 2 additional trials (180 observations) | The AREDS trial found zinc use associated with increased risk for hospitalization due to genitourinary causes vs nonuse (7.5% vs 4.9%; RR, 1.47 [95% CI, 1.19-1.80]) and antioxidant use associated with increased risk of yellow skin compared with nonuse (8.3% vs 6.0%; RR, 1.38 [95% CI, 1.09-1.75]) The AREDS2 trial found the AREDS formulation with beta carotene associated with increased risk of lung cancer vs the AREDS formulation without beta carotene (2.0% vs 0.9%, P = .04); almost all (91%) of the lung cancers in this analysis occurred in former smokers (current smokers were excluded from the analysis) Evidence on harms of antioxidant vitamins and minerals for dry AMD was otherwise limited but did not indicate increased risk of serious adverse events or withdrawal due to adverse events | Consistent | Trials not designed to evaluate harms, and reporting of harms from some trials was suboptimal | Moderate for harm (for AREDS formulation) | AREDS was conducted in the US and the AREDS and AREDS2 formulations are widely used in clinical practice Baseline visual acuity was 20/32 or better in AREDS ≈75% of patients in AREDS had mild to moderate AMD at baseline |
| The prior USPSTF review included a prior version of the systematic review with 13 trials | | Precise for the AREDS formulation but imprecise for other antioxidant multivitamins and minerals | | |

Abbreviations: AMD, age-related macular degeneration; ARD, absolute risk difference; AREDS, Age-Related Eye Disease Studies; ETDRS, Early Treatment Diabetic Retinopathy Study; FDA, US Food and Drug Administration; KQ, key question; NA, not applicable; OR, odds ratio; RR, risk ratio; USPSTF, US Preventive Services Task Force; VEGF, vascular endothelial growth factor.
Third, non-English-language studies were excluded, which could introduce language bias. However, no relevant non-English-language studies that appeared likely to affect conclusions were identified. Fourth, there were too few randomized trials to perform formal assessments for publication bias with graphical or statistical methods for small sample effects. However, unpublished trials likely to affect findings were not identified. Fifth, there was statistical heterogeneity in some pooled analyses of VEGF inhibitors vs sham. However, inconsistency was in the magnitude of benefit, not direction of effect, which consistently favored VEGF inhibitors. In addition, because of anticipated heterogeneity, a random-effects model was used for pooling. Sixth, trials of screening vs no screening had methodological limitations, including high attrition and use of a suboptimal screening test. In some trials, low uptake of recommended interventions or a high rate of eye specialist care prior to screening could have attenuated potential benefits. In addition, the screening trials were published between 1997 and 2006, potentially reducing applicability to current clinical practice.

Conclusions
This review found that effective treatments are available for common causes of impaired visual acuity in older adults. However, direct evidence found no significant association between vision screening vs no screening in primary care and improved visual outcomes.


47. Bartlett HE, Epejerfi E. Effect of lutein and antioxidant dietary supplementation on contrast sensitivity in age-related macular degeneration.


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