Screening Older Adults for Impaired Visual Acuity: A Review of the Evidence for the U.S. Preventive Services Task Force

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Background: Impaired visual acuity is common in older adults. Screening for impaired visual acuity could lead to interventions to improve vision, function, and quality of life.

Purpose: To update the 1996 U.S. Preventive Services Task Force evidence review on benefits and harms of screening for impaired visual acuity in primary care settings in adults age 65 years or older.

Data Sources: MEDLINE and the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews were searched for studies published in English from 1996 to July 2008.

Study Selection: Randomized trials and controlled observational studies that directly evaluated screening for impaired visual acuity in older adults were selected. To evaluate indirect evidence on screening, investigators included studies of diagnostic test accuracy and systematic reviews, randomized trials, and controlled observational studies of treatments for uncorrected refractive errors, cataracts, and age-related macular degeneration (AMD).

Data Extraction: Details were abstracted about the patient sample, study design, data analysis, follow-up, and results. Quality was assessed by using predefined criteria.

Data Synthesis: Direct evidence on screening and evidence on accuracy of diagnostic tests were synthesized qualitatively. For benefits and harms of treatments, quantitative estimates for treatment effects from good-quality systematic reviews were reported or relative risks using a random-effects model were calculated. Direct evidence shows that screening for vision impairment in older adults in primary care settings is not associated with improved visual or other clinical outcomes and may be associated with unintended harms, such as increased falls. Effective treatments are available for uncorrected refractive error, cataracts, and AMD. A visual acuity test (for example, the Snellen eye chart) is the standard for screening for vision impairment in primary care, but its diagnostic accuracy is uncertain because no studies compare it against a clinically relevant reference standard. There remains no evidence on accuracy of funduscopic examination.

Limitations: A relatively small number of primary studies and methodological shortcomings made it difficult to reach conclusions with a high degree of confidence. In addition, studies not published in English and studies of community- or home-based screening were not included.

Conclusion: More research is needed to understand why direct evidence shows no benefits of screening, even though impaired visual acuity is common and effective treatments are available.

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The 2002 NHANES (National Health and Nutrition Examination Survey) estimated an 8.8% prevalence of impaired visual acuity (best-corrected vision of 20/50 or worse) in U.S. adults older than 60 years (1). In addition to having a higher incidence and prevalence of primary ocular disease and systemic diseases associated with ocular disease compared with younger adults, older adults also experience normal age-related changes in vision. Because symptoms may be relatively mild or may progress slowly, older adults may be unaware of or underreport impaired visual acuity or have difficulty recognizing or reporting impaired visual acuity because of comorbid conditions, such as cognitive impairment. Impaired visual acuity is consistently associated with decreased functional capacity and quality of life in older persons and can affect the ability to live independently or increase the risk for falls and other accidental injuries (2–5).

Uncorrected refractive errors, cataracts, and age-related macular degeneration (AMD) are common causes of impaired visual acuity. In 2000, among U.S. adults older than 65 years, refractive errors, cataracts, and AMD were estimated to affect 6.7 million (6), more than 5 million (6), and 1.5 million persons (7), respectively. Advanced AMD is the most common cause of blindness in older, white U.S. adults, and cataracts are the most common cause of blindness in older black adults (8).

Screening for vision disorders in primary care settings could identify impaired visual acuity in older adults and lead to treatments that correct or prevent vision loss. In 1996, the U.S. Preventive Services Task Force (USPSTF) recommended routine vision screening with a visual acuity test (for example, the Snellen eye chart) for older adults (a grade B recommendation) (9). In 2008, the USPSTF commissioned a new evidence review on the benefits and harms of screening for impaired visual acuity in adults 65 years or older to update its recommendations. The **Appendix**

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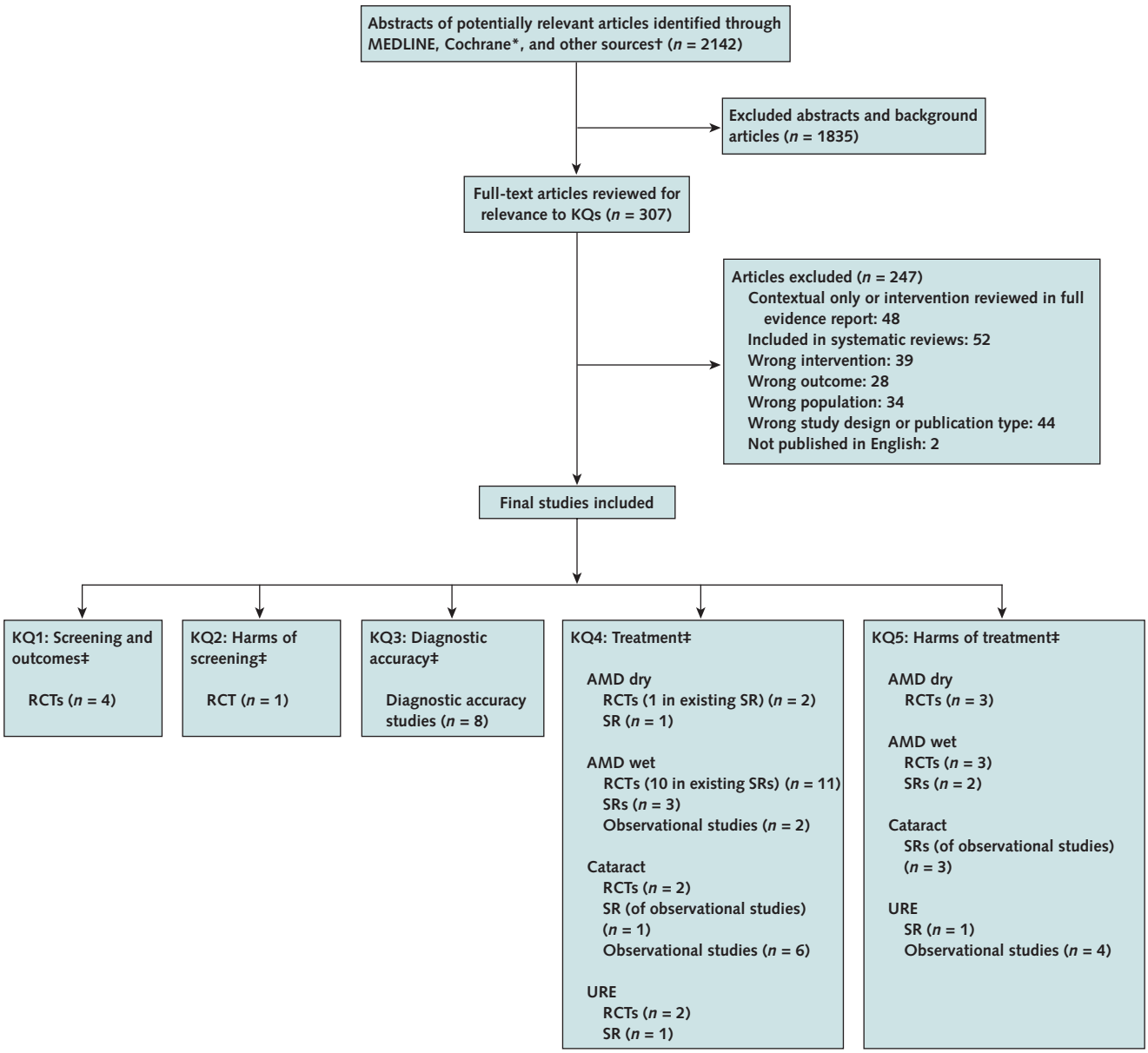
Figure. **Study flow diagram.**



AMD = age-related macular degeneration; KQ = key question; RCT = randomized, controlled trial; SR = systematic review; URE = uncorrected refractive error.
* Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews.
† Identified from reference lists suggested by experts.
‡ Some studies were included for >1 KQ.

Figure (available at www.annals.org) shows the analytic framework and key questions used to guide our review.

Methods

Data Sources

We searched the Cochrane Central Register of Controlled Trials and the Cochrane Database of Systematic Reviews (through Issue 3, 2008) and MEDLINE databases (1996 to July 2008) for relevant studies (see **Appendix Table 1**, available at www.annals.org, for the full search strategy). We supplemented these searches with reviews of reference lists of relevant articles, including the previous USPSTF review (9).

Study Selection

The **Figure** shows the flow of studies from initial identification of titles and abstracts to final inclusion or

Table 1. **Interpretation of Likelihood Ratios**

Positive Likelihood Ratio	Negative Likelihood Ratio	Interpretation
>10	≤0.1	Large or strong
>5 and ≤10	>0.1 and ≤2	Moderate
>2 and ≤5	>0.2 and ≤0.5	Small or weak

exclusion. We selected studies pertaining to screening, diagnosis, and treatment of impaired visual acuity in older adults on the basis of predefined inclusion and exclusion criteria (**Appendix Table 2**, available at www.annals.org). Two reviewers evaluated each study at the title or abstract and full-text article stages to determine eligibility for inclusion.

The target sample was adults 65 years of age or older evaluated in primary care settings who were not known to have impaired visual acuity or had known but inadequately corrected refractive error. We defined impaired visual acuity as worse than 20/40 but better than 20/200. We included studies of vision screening in eye specialty settings but evaluated their applicability to primary care settings. We excluded studies of strictly community- or home-based vision screening but included mixed studies of home and clinic-based screening if 70% or more of patients were evaluated in clinic settings. For diagnosis, we evaluated accuracy of screening questions, visual acuity testing, the Amsler grid, and physical examination. For treatments, we evaluated corrective lenses and photorefractive surgery for uncorrected refractive errors; cataract surgery for cataracts; antioxidants or vitamins for dry AMD; and laser photocoagulation, photodynamic therapy, and vascular endothelin growth factor inhibitors for wet AMD. The full evidence report reviews other interventions (10). Outcomes of interest were visual acuity, vision-related function or quality of life, general function or quality of life, falls, accidents, death, and harms related to screening or treatment. We excluded studies of glaucoma or diabetes (11, 12). Screening for glaucoma is not based on evaluations of visual acuity and is addressed elsewhere by the USPSTF (11). Screening for diabetic retinopathy typically occurs in patients known to have diabetes.

For diagnostic accuracy, we included studies that compared a screening test with a reference standard. We used randomized, controlled trials (RCTs) to assess the effectiveness and harms of screening and various treatments. If RCTs were not available or evidence was sparse, we also used controlled observational studies. Because many systematic reviews have been conducted on treatments for impaired visual acuity, we included good-quality systematic reviews of randomized trials on the effectiveness or harms of treatment and fair- or good-quality systematic reviews of observational studies when no randomized trials were available (after verifying data abstraction and statistical analyses).

Data Extraction and Quality Assessment

One investigator abstracted data, and another checked the abstracted data. We abstracted details about the patient sample, study design, data analysis methods, follow-up, and results. We used predefined criteria developed by the USPSTF to assess the internal validity of primary studies (13). We independently abstracted and rated all placebo-controlled RCTs, regardless of inclusion status in previously published systematic reviews (14). For randomized trials, we assessed methods of randomization, allocation concealment, and blinding; loss to follow-up; and use of intention-to-treat analysis. For cluster randomized trials (trials that randomly assigned patients in groups according to which clinic they attended), we also evaluated whether the study adjusted for the effects of clustering (cluster-correlation correction) (15). For systematic reviews, we abstracted information on search methods, dates of searches, selection of studies, and data synthesis methods. We rated quality by using criteria described in **Appendix Table 3** (available at www.annals.org). Two authors independently rated the internal validity of each study as "good," "fair," or "poor," on the basis of the number and seriousness of methodological shortcomings (13). We assessed the potential applicability of studies to primary care on the basis of whether patients were recruited from primary care settings, the proportion of patients with mild to moderate vision impairment, and whether the screening intervention was or could be done in most primary care settings. We resolved discrepancies in quality ratings by discussion and consensus.

For diagnostic accuracy studies, we used the diagti procedure in Stata, version 10 (StataCorp, College Station, Texas), to calculate sensitivities, specificities, and likelihood ratios. We used the cci procedure to calculate diagnostic odds ratios (ORs) with exact CIs. We classified likelihood ratios as "large," "moderate," or "small" on the basis of the criteria shown in **Table 1** (16).

Data Synthesis and Analysis

We assessed the overall strength of each body of evidence by using methods developed by the USPSTF (13). For screening and diagnostic accuracy, we did not attempt to pool results of individual studies owing to heterogeneity in study samples, screening interventions, or diagnostic tests and results. For efficacy of treatments, we reported quantitative estimates for treatment effects from previously published systematic reviews that met quality criteria (14). When we identified RCTs not included in previous reviews, we calculated updated, pooled relative risks (RRs) by using the Mantel–Haenszel random-effects model (Review Manager, version 4.2.8, The Nordic Cochrane Center, Copenhagen, Denmark).

RESULTS

Key Question 1

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

Three fair- or fair-to-good–quality cluster randomized trials ($n = 4728$) evaluated vision screening as part of a multicomponent screening intervention, with high applicability to screening in primary care settings (**Table 2**) (17–19). Methodological shortcomings of all trials included lack of intention-to-treat analysis, unclear blinding status of outcomes assessors, and high loss to follow-up, which was due in part to advanced age and death in enrollees (**Appendix Table 4**, available at www.annals.org). Only 1 (19) of the 3 trials applied a cluster-correlation correction (15). The screening intervention varied: 1 trial compared universal visual acuity testing (Glasgow acuity chart followed by pinhole testing for persons with visual acuity worse than 6/18) with targeted screening (19), 1 compared immediate with delayed vision screening (17), and 1 compared use of a screening question followed by visual acuity testing if positive with usual care (18). Duration of follow-up ranged from 6 months to 5 years. None of the trials found vision screening to be associated with beneficial effects on vision, likelihood of vision disorders, or functional impairment related to vision.

The highest-quality trial (rated fair to good) also evaluated the largest sample ($n = 3249$) and followed patients for the longest duration (19). Investigators found that universal vision screening identified about 10 times as many patients with impaired visual acuity and correctable impairment as did targeted screening, yet no difference in likelihood of visual acuity worse than 20/60 after 3- to 5-year follow-up. Reasons for the negative findings are not

Table 2. **RCTs of Vision Screening in Older Adults**

Study, Year (Reference)	Screening Intervention	Study Design	Setting	Patient Population	Results	Loss to Follow-up, *n/n (%)*	Quality Rating*
Cumming et al, 2007 (20)	Visual acuity assessed with ETDRS chart† at 2.4 m; contrast sensitivity with the CSV-1000 E chart† 1 at 2.4 m; visual fields with Humphrey automated visual field unit‡; Perkins applanation tonometer§; intraocular pressure with slit-lamp examination and direct ophthalmoscopy	RCT	Eye clinic (71%) or home (29%)	Age ≥70 y ($n = 616$); Australia	Vision screening vs. none: falls (rate ratio, 1.57 [95% CI, 1.20–2.05]); fractures (RR, 1.74 [CI, 0.97–3.11])	84/616 (14)	Fair
Eekhof et al, 2000 (17)	Assessment of difficulty in recognizing a face at 4 m or reading normal letters in a newspaper, or impaired vision with both by Snellen eye chart or inability to read normal newspaper letters at 25 cm	Cluster RCT	Primary care clinic	Age ≥75 y ($n = 1121$); Netherlands	Immediate vs. delayed vision screening: visual disorder in second year (51% vs. 47%; $P = 0.68$)	93/576 (16) of patients who had immediate screening did not participate in second year; otherwise unclear	Fair
Moore et al, 1997 (18)	Vision screening: question to assess difficulty doing everyday activities, followed by Snellen eye chart test if positive	Cluster RCT	Primary care clinic	Age ≥70 y ($n = 261$); United States	Vision screening vs. usual care: improvement in vision at 6 mo, 20% (20/99) vs. 24% (31/131); RR, 0.85 (CI, 0.52–1.40)	31/261 (12) at 6 mo	Fair
Smeeth et al, 2003 (19)	Detailed health assessment by a trained nurse, including Glasgow eye chart and pinhole testing if visual acuity is <6/18 in either eye (targeted screening only consisted of a brief health assessment)	Cluster RCT	Primary care clinic	Age ≥75 y ($n = 3249$); United Kingdom	Universal vs. targeted vision screening: visual acuity <6/18 in either eye at median 3.9 y (RR, 1.07 [CI 0.84–1.36]); National Eye Institute visual function questionnaire at median 3.9 y (mean score [0–100 scale], 86.0 vs. 85.6; $P = 0.69$)	1807/3249 (56) did not complete outcome assessment (1465 deaths)	Good to fair

ETDRS = Early Treatment Diabetic Retinopathy Study; RCT = randomized, controlled trial; RR = relative risk.
* See **Appendix Table 4** (available at www.annals.org) for details on quality ratings.
† VectorVision Products, Arcanum, Ohio.
‡ Zeis-Meditec, Dublin, California.
§ Clement Clarke International, Harlow, Essex, United Kingdom.

Table 3. **Studies of Diagnostic Test Accuracy**

Study, Year (Reference)	Reference Standard	Target Vision Condition	Screening Test
Amsler grid			
Ariyasu et al, 1996 (22)	Ophthalmologic examination	Any ocular disease, excluding refractive error	Amsler grid
Physical examination			
McMurdo and Baines, 1988 (23)	Ophthalmologic examination	Cataract	Positive finding on physical examination
		AMD	Positive finding on physical examination
Screening questions			
Eekhof et al, 2000 (24)	Snellen eye chart	Visual acuity ≤0.3 (about 20/60 on the Snellen eye chart test)	Trouble recognizing face, by questionnaire
		Difficulty with low vision chart at reading distance	
Hiller and Krueger, 1983 (25)	Snellen eye chart	Visual acuity ≤20/50	Trouble seeing, by questionnaire
	Snellen eye chart	Visual acuity ≤20/100	Trouble seeing, by questionnaire
Chu-Ai Teh et al, 2006 (26)	Snellen eye chart	Visual acuity ≤20/40	Problem with vision, by questionnaire
Wang et al, 1998 (27)	Ophthalmologic examination	Any ocular disease	Problem with vision, by questionnaire
			Problem with vision, by questionnaire followed by visual acuity ≤20/40
Visual acuity testing			
Ariyasu et al, 1996 (22)	Ophthalmologic examination	Any ocular disease, excluding refractive error	Near visual acuity ≤20/30
			≤20/40
			≤20/60
Ariyasu et al, 1996 (22)	Ophthalmologic examination	Any ocular disease, excluding refractive error	Presenting distance visual acuity ≤20/30
			≤20/40
			≤20/60
Ivers et al, 2001 (28)	Ophthalmologic examination	Nuclear cataract	Pinhole distance acuity ≤20/30
		Early AMD	Pinhole distance acuity ≤20/30
		Any eye disease	Pinhole distance acuity ≤20/30
		Nuclear cataract	≤20/40
		Early AMD	≤20/40
		Any eye disease	≤20/40
		Nuclear cataract	≤20/60
		Early AMD	≤20/60
		Any eye disease	≤20/60
Ivers et al, 2001 (28)	Ophthalmologic examination	Nuclear cataract	Presenting distance visual acuity ≤20/30
		Early AMD	Presenting distance visual acuity ≤20/30
		Any eye disease	Presenting distance visual acuity ≤20/30
		Nuclear cataract	≤20/40
		Early AMD	≤20/40
		Any eye disease	≤20/40
		Nuclear cataract	≤20/60
		Early AMD	≤20/60
		Any eye disease	≤20/60
Ivers et al, 2001 (28)	Ophthalmologic examination	Nuclear cataract	Reading acuity ≤20/30
		Early AMD	Reading acuity ≤20/30
		Any eye disease	Reading acuity ≤20/30
		Nuclear cataract	≤20/40
		Early AMD	≤20/40
		Any eye disease	≤20/40
		Nuclear cataract	≤20/60
		Early AMD	≤20/60
		Any eye disease	≤20/60
Wang et al, 1998 (27)	Ophthalmologic examination	Any ocular disease	Presenting distance visual acuity ≤20/40
Woods et al, 1998 (29)	Ophthalmologic examination	Any ocular disease, excluding refractive error	Near visual acuity ≤20/30
Woods et al, 1998 (29)	Ophthalmologic examination	Any ocular disease, excluding refractive error	Presenting distance visual acuity ≤20/30

AMD = age-related macular degeneration; LR = likelihood ratio; OR = odds ratio.

entirely clear. However, only half of the patients advised to see an eye care provider after vision screening actually received new glasses. Other reasons for lack of benefit in the screening trials may include the high loss to follow-up in all trials, similar frequency of vision disorder detection and treatment in the screening and control groups in 1 trial (18), use of a screening question to identify persons for further testing in 1 trial (18), and low uptake of recommended interventions in 1 trial (17).

A fourth, fair-quality trial was less applicable to primary care because it involved vision screening by an optometrist (visual acuity, contrast sensitivity, and visual field testing; slit-lamp examination; and direct ophthalmoscopy) (20). In frail older adults (n = 309), vi-

Table 3—**Continued**

Sensitivity (95% CI)	Specificity (95% CI)	Positive LR (95% CI)	Negative LR (95% CI)	Diagnostic OR (95% CI)
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)
1.0 (9/9 patients)	1.0 (41/41 patients)	Not calculated	Not calculated	Not calculated
0.75 (3/4 patients)	1.0 (46/46 patients)	Not calculated	Not calculated	Not calculated
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)
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)
0.34 (0.28–0.41)	0.84 (0.82–0.86)	2.15 (1.72–2.69)	0.78 (0.71–0.86)	2.75 (2.00–3.78)
0.48 (0.32–0.63)	0.82 (0.80–0.84)	2.69 (1.94–3.74)	0.64 (0.48–0.84)	4.24 (2.33–7.72)
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)
0.90 (0.85–0.94)	0.44 (0.37–0.51)	1.60 (1.41–1.83)	0.23 (0.15–0.36)	6.88 (4.06–11.7)
0.57 (0.50–0.64)	0.79 (0.73–0.84)	2.72 (2.03–3.65)	0.54 (0.46–0.65)	5.00 (3.23–7.74)
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)
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)
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)
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)
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)
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)
0.31 (0.28–0.34)	0.89 (0.87–0.91)	2.83 (2.35–3.40)	0.78 (0.74–0.81)	3.65 (2.93–4.55)
0.45 (0.37–0.53)	0.79 (0.78–0.80)	2.16 (1.80–2.59)	0.69 (0.60–0.80)	3.11 (2.26–4.30)
0.34 (0.31–0.37)	0.86 (0.84–0.87)	2.43 (2.14–2.76)	0.77 (0.74–0.80)	3.17 (2.69–3.73)
0.13 (0.11–0.15)	0.98 (0.97–0.99)	6.57 (4.29–10.1)	0.89 (0.87–0.91)	7.40 (4.78–11.5)
0.21 (0.15–0.28)	0.92 (0.91–0.93)	2.59 (1.87–3.58)	0.86 (0.80–0.93)	3.01 (2.01–4.49)
0.15 (0.13–0.17)	0.96 (0.95–0.97)	3.74 (2.95–4.73)	0.89 (0.86–0.91)	4.22 (3.27–5.45)
0.08 (0.06–0.10)	0.99 (0.98–1.00)	8.07 (4.44–14.7)	0.93 (0.91–0.95)	8.69 (4.76–15.8)
0.10 (0.06–0.16)	0.95 (0.94–0.96)	2.01 (1.24–3.28)	0.95 (0.90–1.00)	2.13 (1.25–3.63)
0.09 (0.07–0.11)	0.97 (0.96–0.98)	2.98 (2.23–3.97)	0.94 (0.92–0.96)	3.17 (2.34–4.30)
0.44 (0.41–0.47)	0.77 (0.74–0.79)	1.91 (1.69–2.16)	0.73 (0.68–0.77)	2.63 (2.20–3.15)
0.56 (0.48–0.64)	0.66 (0.64–0.68)	1.65 (1.42–1.90)	0.67 (0.56–0.80)	2.47 (1.79–3.40)
0.47 (0.44–0.50)	0.74 (0.72–0.76)	1.81 (1.65–1.98)	0.72 (0.68–0.76)	2.53 (2.19–2.92)
0.25 (0.22–0.28)	0.90 (0.88–0.92)	2.50 (2.05–3.05)	0.83 (0.80–0.87)	3.00 (2.38–3.79)
0.34 (0.27–0.42)	0.82 (0.81–0.83)	1.89 (1.50–2.37)	0.80 (0.72–0.90)	2.34 (1.67–3.28)
0.27 (0.24–0.29)	0.87 (0.86–0.88)	2.07 (1.81–2.38)	0.84 (0.81–0.87)	2.47 (2.08–2.94)
0.13 (0.11–0.15)	0.96 (0.95–0.97)	3.22 (2.35–4.41)	0.91 (0.88–0.93)	3.55 (2.54–4.96)
0.13 (0.08–0.20)	0.92 (0.91–0.93)	1.65 (1.09–2.49)	0.94 (0.89–1.00)	1.75 (1.09–2.80)
0.14 (0.12–0.16)	0.94 (0.93–0.95)	2.33 (1.89–2.88)	0.92 (0.89–0.94)	2.55 (2.02–3.21)
0.97 (0.96–0.98)	0.03 (0.02–0.04)	1.00 (0.99–1.01)	1.00 (0.63–1.60)	1.00 (0.62–1.61)
0.99 (0.96–1.00)	0.03 (0.02–0.04)	1.02 (1.00–1.04)	0.42 (0.10–1.69)	2.42 (0.65–8.98)
0.98 (0.97–0.99)	0.03 (0.02–0.04)	1.01 (1.00–1.02)	0.66 (0.42–1.03)	1.53 (0.97–2.42)
0.88 (0.86–0.90)	0.20 (0.18–0.22)	1.10 (1.06–1.14)	0.60 (0.49–0.73)	1.84 (1.46–2.32)
0.95 (0.90–0.98)	0.16 (0.15–0.17)	1.13 (1.09–1.18)	0.32 (0.16–0.62)	3.59 (1.78–7.26)
0.89 (0.87–0.91)	0.19 (0.18–0.21)	1.10 (1.07–1.13)	0.58 (0.49–0.68)	1.90 (1.55–2.32)
0.57 (0.54–0.60)	0.59 (0.56–0.62)	1.39 (1.28–1.52)	0.73 (0.67–0.79)	1.91 (1.62–2.26)
0.70 (0.62–0.77)	0.53 (0.51–0.55)	1.48 (1.33–1.65)	0.57 (0.45–0.72)	2.61 (1.85–3.68)
0.59 (0.56–0.62)	0.59 (0.57–0.61)	1.44 (1.35–1.54)	0.70 (0.64–0.75)	2.07 (1.80–2.38)
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)
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)
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)

sion screening did not reduce risk for falls (RR, 1.57 [95% CI, 1.20 to 2.05]) or fractures (RR, 1.74 [CI, 0.97 to 3.11]) after 1 year compared with usual care; in fact, 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. Possible explanations for an increased risk for falls could be the need for a prolonged period of readjustment in frail older adults after receiving new eyeglasses or increased activities after treatment of vision impairment that could place persons at higher risk.

No study directly evaluated effects of screening for impaired visual acuity in asymptomatic older adults at different intervals. One cohort study found that after a normal baseline eye examination, the likelihood of experiencing no significant visual field or visual acuity loss after 5

years was 97% in persons age 60 to 69 years, and 93% in persons age 70 to 79 years (21).

Key Question 2

Are there harms of vision screening in asymptomatic older adults?

Potential harms associated with vision screening include anxiety, complications of treatment, or exposure to unnecessary interventions due to false-positive screening test results. However, none of the screening studies in primary care settings evaluated harms associated with vision screening (17–19). One study, described above, reported an increased risk for falls after screening by an optometrist (20).

Key Question 3

What is the accuracy of screening for early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD?

Eight cross-sectional studies evaluated the accuracy of various diagnostic tests or screening questions for impaired visual acuity compared with a reference standard (**Appendix Table 5**, available at www.annals.org) (22–29). All of the studies had at least 2 methodological shortcomings (**Appendix Table 6**, available at www.annals.org). Only 1 study clearly reported independent interpretation of the reference standard (23), 2 studies clearly applied the reference standard to all patients (23, 24), and 1 study reported sufficient information to determine that an appropriately broad spectrum of patients was evaluated (25). Four of 8 studies reported diagnostic accuracy specifically in older adults; the remainder enrolled mixed samples of older and younger adults (23–26).

Screening Questions or Questionnaires

Four studies found various screening questions or questionnaires to have low accuracy for identifying impaired visual acuity compared with visual acuity testing (24–26) or a detailed ophthalmologic examination (27) (**Table 3**). In all studies, positive and negative likelihood ratios were relatively weak (range, 1.19 to 3.23 and 0.23 to 0.78, respectively) because of suboptimal combinations of sensitivity and specificity.

Visual Acuity Tests

Four studies found various visual acuity screening tests (near, distance, pinhole, or reading acuity) to have low accuracy compared with a full ophthalmologic examination for identifying the presence of any visual condition (**Table 3**) (22, 27–29). Interpretation of diagnostic accuracy based on this reference standard is a challenge because the clinical significance of visual conditions not necessarily associated with impaired visual acuity is unclear. For 3 of 4 studies, positive likelihood ratios ranged from 1.00 to 8.07 and negative likelihood ratios ranged from 0.32 to 1.00, with diagnostic ORs less than 10 (22, 27, 28). One study reported diagnostic accuracy of visual acuity testing to specifically identify cataracts or early AMD, with results similar to those for identifying any visual condition (28). No studies compared the Snellen eye chart with a reference standard for impaired visual acuity, possibly because it is often considered the clinical standard for evaluating visual acuity.

Other Screening Tests

One study found that the Amsler grid was associated with poor accuracy as a screening test for identifying any visual condition (**Table 3**) (22). One very small ($n = 50$) study found that among patients age 64 to 97 years not known to have eye disease, 100% (9 of 9) of patients with cataracts and 75% (3 of 4) of patients with AMD were correctly identified by a geriatrician compared with an ophthalmologist (23). No study evaluated the accuracy or yield of dilated fundus examination by primary care providers.

Key Question 4

Does treatment of early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD lead to improved morbidity or mortality or quality of life?

Uncorrected Refractive Error

Corrective Lenses. In the large, population-based NHANES, more than 60% of persons older than 60 years presenting with visual acuity worse than 20/50 could achieve visual acuity better than 20/40 with refractive correction (1). Because NHANES used a cross-sectional design, the proportion that would have optimal visual acuity at later follow-up is not known. Two fair-quality randomized trials ($n = 131$ and $n = 151$) found that immediate correction of refractive error with eyeglasses in older adults (mean age, 80 years) was associated with moderate improvements in short-term (2- to 3-month follow-up), vision-related quality of life or function compared with delayed treatment (30, 31). In both trials, general vision subscale scores of the National Eye Institute Visual Functioning Questionnaire were improved by a mean of about 10 (of 100) points in the immediate-treatment groups.

Refractive Surgery. A good-quality systematic review of 157 primarily uncontrolled observational studies found laser in situ keratomileusis (LASIK), laser epithelial keratomileusis (LASEK), and photorefractive keratectomy to be similarly effective at improving refractive errors, with 92% to 94% of persons with myopia and 86% to 96% of persons with hyperopia achieving visual acuity of 20/40 or better (32). Almost half of the observational studies included in this review did not use a prospective design, and most studies did not clearly enroll a consecutive series of patients. Applicability of results to older adults is uncertain because studies generally enrolled younger persons (mean age, 20 to 50 years). Several fair-quality observational stud-

ies also found refractive surgery to be associated with improved quality of life (33–35).

Cataract

Surgery. No randomized trial evaluated visual outcomes associated with cataract surgery versus no surgery. A good-quality systematic review of 57 generally lower-quality observational studies published from 1979 to 1991 found cataract surgery associated with postoperative visual acuity of 20/40 or better in 88.9% (CI, 88.1% to 89.8%) of all eyes (n = 17 390) and 95.2% (CI, 94.7% to 95.7%) of eyes without preoperative ocular comorbidity (n = 10 003) after results were weighted by sample size and quality score (36). Only 4 of the studies included in the systematic review used a controlled design. Other common shortcomings included potentially biased methods of patient selection, differential duration of follow-up, and poor description or handling of attrition.

A large, prospective cohort study (n = 4819) found that 85% of persons 85 years or older had improved visual acuity (37). Three good-quality prospective observational studies (n = 45, n = 464, and n = 772) found cataract surgery to be associated with moderate improvements in vision-related quality of life and function (38–40). The effect of cataract surgery on functional status or quality of life not directly related to vision was less consistent, with some studies showing no benefits (38, 40–42).

One good-quality trial found first cataract surgery to be associated with no significant difference compared with delayed surgery in risk for first fall (hazard ratio, 0.95 [CI, 0.69 to 1.35]) (43). However, the risk for second fall was reduced (hazard ratio, 0.60 [CI, 0.36 to 0.98]), resulting in a lower overall risk for falls (RR, 0.66 [CI, 0.40 to 0.96]). Cataract surgery was also associated with a lower risk for fracture (RR, 0.33 [CI, 0.1 to 1.0]). In another good-quality trial by the same group of investigators, cataract surgery of the second eye was not associated with a reduction in incidence of falls or fractures, although statistical power was limited (44).

A well-designed prospective cohort study of older drivers with cataracts (n = 277) found cataract surgery to be associated with a lower risk for motor vehicle accidents compared with no surgery (RR, 0.47 [CI, 0.23 to 0.94]; absolute risk reduction, 4.74 crashes per million miles driven) (45). Another well-designed prospective cohort study (n = 384) found that patients with cataracts who did not have surgery had increased all-cause mortality risk for up to 6 years of follow-up (6.8 deaths per 100 patient-years) compared with persons with cataracts who had surgery (3.6 deaths per 100 patient-years) or those without cataracts (0.9 deaths per 100 patient-years) (RR, 3.2 [CI, 1.2 to 9.0] for persons with cataracts who did not have surgery vs. those with no cataracts) (46).

Dry (Nonexudative) AMD

Antioxidant Vitamins and Minerals. The large, good-quality AREDS (Age-Related Eye Disease Study) (n = 3640) (47) found that a multivitamin (vitamins C and E and β-carotene) plus zinc was associated with reduced likelihood of progression to advanced AMD (adjusted OR, 0.68 [CI, 0.49 to 0.93]), although the difference in the likelihood of losing 15 or more letters of visual acuity did not reach statistical significance (adjusted OR, 0.77 [CI, 0.58 to 1.03]) (47). A good-quality systematic review included 9 poor- or fair-quality RCTs (n = 5569) of various antioxidant treatment regimens (48). Results were highly influenced by AREDS, and the systematic review found insufficient evidence to determine efficacy of other vitamin and mineral combinations. A small (n = 101), fair-quality trial not included in the systematic review found the combination of acetyl-L-carnitine, ω-3 fatty acids, and coenzyme Q10 was associated with a lower likelihood of deterioration in visual acuity (23% vs. 45%; RR, 0.51 [CI, 0.28 to 0.92]), but effects on clinically significant visual acuity loss were not reported (49).

Wet (Exudative) AMD

Laser Photocoagulation. A good-quality systematic review found laser photocoagulation to be superior to no treatment for progression of vision loss (loss of ≥6 lines of visual acuity) after 2 years (pooled RR, 0.67 [CI, 0.53 to 0.83]; 5 trials [n = 1413]) (50). We rated all trials poor quality (51–55) because of methodological shortcomings (open-label design, incomplete follow-up, and lack of intention-to-treat analysis). In addition, clinical and statistical heterogeneity (I^2 = 58%) were present in the pooled analysis. The trials enrolled persons with visual acuity ranging from normal to worse than 20/200, and the proportion of patients with baseline vision worse than 20/200 ranged from 0% to 34%. In addition, the location of choroidal neovascularization (foveal, juxtafoveal, or extrafoveal) varied. Nonetheless, all trials found a benefit in favor of laser photocoagulation.

Photodynamic Therapy With Verteporfin. Two good-quality systematic reviews of photodynamic therapy found verteporfin to be superior to placebo for preventing loss of visual acuity, based on either 2 (56) or 3 (57) fair- (58) or good-quality (59, 60) trials. The systematic review that pooled 3 trials (n = 1065) (58–60) found that verteporfin reduced the likelihood of 3 or more lines of visual acuity loss after 2 years (RR, 0.22 [CI, 0.13 to 0.30]), with a number needed to treat of 7 (57). Three- and 5-year open-label extension results of 1 of the trials (59) were similar to 2-year results (61, 62). Quality of life was not assessed in any of the trials.

Intravitreal Injection of Vascular Endothelial Growth Factor Inhibitors. A good-quality systematic review (63) found pegaptanib at doses of 0.3, 1, or 3 mg to be more effective than placebo at 12 months for visual acuity loss

Table 4. **Summary of Evidence**

Study Type	Overall Quality Rating	Limitations	Consistency	Primary Care Applicability	Summary of Findings
KQ1: Does vision screening in asymptomatic older adults result in improved morbidity or mortality or improved quality of life?					
4 RCTs	Fair	Vision screening assessed as part of a multicomponent intervention in most studies; methodological shortcomings in trials; fairly small number of trials	Consistent	High	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 to be associated with an increased risk for falls (RR, 1.57 [95% CI, 1.20–2.05]) and a trend toward increased risk for fractures (RR, 1.74 [CI, 0.97–3.11])
KQ2: Are there harms of vision screening in asymptomatic older adults?					
1 RCT	Fair	NA	NA	NA	See KQ1 for evidence on falls
KQ3: What is the accuracy of screening for early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD?					
8 studies of diagnostic accuracy	Fair	Methodological shortcoming in trials; no studies assessed accuracy or use of Amsler grid, funduscopic examination, or pinhole testing in primary care settings	Consistent	Moderate (some studies conducted in mixed samples of younger and older adults or in non–primary care settings)	4 studies found that screening questions are not accurate for identifying persons with vision impairment compared with the Snellen eye chart; 4 studies found that visual acuity testing is not accurate for identifying the presence of vision conditions compared with a detailed ophthalmologic examination; 1 study found that the Amsler grid is not accurate for identifying the presence of vision conditions compared with a detailed ophthalmologic examination
KQ4: Does treatment of early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD lead to improved morbidity or mortality or quality of life?					
AMD (dry)					
2 RCTs (1 in an existing SR); 1 SR	Fair	Results of 1 large trial heavily influenced conclusions	Some inconsistency	High	1 large RCT found a multivitamin and zinc combination effective for slowing progression of AMD (adjusted OR, 0.68 [CI, 0.49–0.93]), although the difference in the likelihood of losing ≥15 lines of visual acuity was not statistically significant (adjusted OR, 0.77 [CI, 0.58–1.03])
AMD (wet)					
11 trials (10 in existing SRs); 3 SRs; 2 observational studies	Fair to good	Relatively small number of trials	Consistent	High	Laser photocoagulation: RR for ≥6 lines visual acuity loss, 0.67 [CI, 0.53–0.83] for 5 RCTs (poor quality but consistent); photodynamic therapy: RR for ≥3 lines visual acuity loss, 0.22 [CI, 0.13–0.30] for 3 RCTs (fair to good quality); VEGF inhibitors: RR, 0.71 [CI, 0.61–0.84] for 2 RCTs for pegaptanib; RR for ≥3 lines visual acuity loss, 0.21 [CI, 0.16–0.27]) for 2 RCTs for ranibizumab (fair to good quality)
Cataracts					
2 RCTs; 1 SR (of observational studies); 6 observational studies	Fair	2 trials compared immediate with delayed cataract surgery for effects on falls; most observational studies have methodological shortcomings	Consistent	High	Many observational studies found that >90% of patients achieve visual acuity of 20/40 or better after cataract extraction and intraocular lens implantation; 3 observational studies found cataract surgery associated with improved vision-related function
Uncorrected refractive error					
2 RCTs; 1 SR	Fair	Few trials compared treatments of uncorrected refractive error vs. placebo or no therapy	Consistent	High	1 large population-based study found that 60% of older adults with vision impairment can achieve visual acuity of 20/40 or better with refractive correction; many observational studies show that >85% of patients achieve visual acuity of 20/40 or better after photorefractive surgery for myopia or hyperopia in younger adults

Continued on following page

Table 4—**Continued**

Study Type	Overall Quality Rating	Limitations	Consistency	Primary Care Applicability	Summary of Findings
KQ5: Are there harms of treating early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD?					
AMD (dry)					
3 trials	Fair	Data on harms poorly reported	Consistent	High	The large AREDS found zinc to be associated with significantly increased risk for hospitalization for genitourinary causes compared with nonuse of zinc (11.1% vs. 7.6%; RR, 1.47 [CI 1.19–1.80]) and antioxidants to be associated with increased risk for yellow skin compared with nonuse of antioxidants (8.3% vs. 6.0%; RR, 1.38 [CI, 1.09–1.75])
AMD (wet)					
3 RCTs; 2 SRs	Fair to good	Some data on harms are not yet published; data on long-term effects of photodynamic therapy and VEGF inhibitors are limited	Consistent	High	Laser photocoagulation: visual acuity loss ≥6 lines compared with observation 3 mo after treatment (absolute rate, 16.6%; RR, 1.41 [CI, 1.08–1.82] for 5 trials); photodynamic therapy: increased risk for acute severe visual acuity loss (20-letter loss within 7 d of treatment) compared with placebo (2% vs. 0.2%; RR, 0.02 [CI, 0.01–0.03]) and increased risk for infusion-related back pain compared with placebo (3.4% vs. 0.3%; RR 6.50 [CI, 1.52–27.78]) VEGF inhibitors: more cases of endophthalmitis and uveitis compared with placebo, but fewer events; no increase in risk for systemic hypertension or arterial thromboembolic events
Cataracts					
3 SRs (of observational studies)	Fair	No data on harms from placebo-controlled trials	Some inconsistency in reported rates	High	SRs of many observational studies of cataract surgery found a pooled rate of posterior capsule opacification of 28% after 5 y, and a pooled rate of 0.13% for endophthalmitis
Uncorrected refractive error					
1 SR; 4 observational studies	Poor to fair	Few data on harms for corrective lenses; many observational studies did not report rates of harms associated with photorefractive surgery	Consistent	High	1 small prospective study found multifocal lenses to be associated with a higher risk for falls in older adults compared with unifocal lenses (OR, 2.09 [CI, 1.06–4.92]); 3 studies found an incidence of infectious keratitis of 0.3 to 3.6 cases per 10 000 persons who wear contact lenses; corneal ectasia rates range from 0% to 0.87% in 5 studies of LASIK; keratitis rates range from 0% to 3.4% in 6 studies of LASIK and 4 studies of LASEK

AMD = age-related macular degeneration; AREDS = Age-Related Eye Disease Study; KQ = key question; LASEK = laser-assisted subepithelial keratomileusis; LASIK = laser-assisted in situ keratomileusis; NA = not applicable; OR = odds ratio; RCT = randomized, controlled trial; RR = relative risk; SR = systematic review; VEGF = vascular endothelial growth factor.

(>15 letters or 3 lines of loss), based on a pooled analysis of 2 fair-quality trials (RR, 0.71 [CI, 0.60 to 0.84]; n = 1186) (64). The number needed to treat to prevent 1 case of visual acuity loss ranged from 7 to 14, depending on the dose evaluated (63). Pegaptanib also reduced the risk for blindness (visual acuity worse than 20/200) compared with placebo (RR, 0.69 [CI, 0.59 to 0.82]). In a pooled analysis of 2 good-quality trials (n = 900), we found that ranibizumab, 0.3 or 0.5 mg, was associated with decreased risk for visual acuity loss (RR, 0.21 [CI, 0.16 to 0.27]) and blindness (RR, 0.35 [CI 0.21 to 0.57]) compared with placebo at 12 months, with a number needed to treat to prevent 1 case of visual acuity loss of about 2.5 (65, 66). In 1 of the trials, results were sustained through 24 months (66). Vascular endothelial growth factor inhibitors were associated with mild to moderate improvements in vision-related function in 3 good-quality trials, although differences were not always statistically significant (65, 67, 68).

Appendix Table 7 (available at www.annals.org) summarizes trials of interventions for wet AMD versus placebo

or no treatment, with quality ratings given in **Appendix Table 8** (available at www.annals.org).

Key Question 5

Are there harms of treating early impairment in visual acuity due to uncorrected refractive error, cataracts, or AMD?

Uncorrected Refractive Error

Corrective Lenses. We identified no studies on harms associated with monofocal eyeglasses. One fair-quality prospective study ($n = 87$) found that multifocal lenses (bifocals, trifocals, or progressive lenses) were associated with a higher risk for falls in older adults (adjusted OR, 2.09 [CI, 1.06 to 4.92]) (69).

Two large (each enrolled >10 000 persons), fair-quality, prospective observational studies found that the incidence of vision loss due to infectious keratitis ranged from 0.3 to 0.9 cases per 10 000 persons who wore contact lenses, regardless of age (70, 71). Other fair-quality prospective studies reported a substantially higher risk for keratitis among those who wore extended-wear contact lenses (3.6 [CI, 0.4 to 12.9] cases per 10 000 persons) (72) or found that persons older than 50 years had increased risk for keratitis compared with those 25 years or younger (OR, 2.04 [CI, 1.40 to 2.98]) (73).

Photorefractive Surgery. A good-quality systematic review of 157 primarily uncontrolled observational studies of photorefractive surgery identified 5 studies, all of LASIK, that reported a median rate of corneal ectasia (bulging forward of the cornea due to weakening of supporting structures) of 0.2% (range, 0% to 0.87%) (32). Rates of infectious keratitis ranged from 0% to 0.16% after LASIK and 0% to 3.4% after LASEK but were reported in only 6 LASIK studies (including 4 reporting no cases) and 4 LASEK studies. Estimates of incidence of glare, visual haloes, or worsened night vision after refractive surgery were inconsistent and were based on sparse evidence, with rates ranging from 0% to more than 50%.

Cataract

Posterior capsule opacification of surgically implanted lens is the most common long-term complication after cataract surgery, but it can usually be treated with a brief external laser procedure. A systematic review of 49 primarily uncontrolled observational studies found a pooled incidence of posterior capsule opacification of 11.8% (range, 9.3% to 14.3%) at 1 year, 20.7% (range, 16.6% to 24.9%) at 3 years, and 28.4% (range 16.6 to 24.9%) at 5 years (74).

A fair-quality systematic review of 215 primarily uncontrolled observational studies found a 0.13% rate of endophthalmitis after cataract surgery (75). Additional analyses found a RR of 2.44 (CI, 2.27 to 2.61) for surgeries completed since 2000 compared with surgeries in earlier decades. This trend temporally coincides with increased use of sutureless, clear corneal incisions.

Other major complications associated with cataract surgery include bullous keratopathy (0.3% [CI, 0.2% to 0.4%]), dislocation of intraocular lens (1.1% [CI, 0.9% to 1.2%]), clinical cystoid macular edema (1.4% [CI, 1.2% to 1.6%]), and retinal detachment (0.7% [CI, 0.6% to 0.8%]) (36).

Dry AMD

Antioxidant Vitamins and Minerals. The large, good-quality AREDS found treatment with zinc associated with increased risk for hospitalization for genitourinary causes compared with nonuse (11.1% vs. 7.6%; RR, 1.47 [CI, 1.19 to 1.80]) and treatment with antioxidants associated with increased risk for yellow skin compared with nonuse (8.3% vs. 6.0%; RR, 1.38 [CI, 1.09 to 1.75]) (76, 77). There was no association between antioxidant supplementation and increased hospitalizations, death, or lung cancer. Risk for congestive heart failure was not specifically reported. Other trials of antioxidants for dry AMD found no clear association with adverse events (78, 79), although assessment and reporting of harms were generally suboptimal.

Wet AMD

Laser Photocoagulation. A good-quality systematic review found laser photocoagulation to be associated with increased risk for short-term (3 months after treatment) visual acuity loss of 6 or more lines compared with observation (pooled RR, 1.41 [CI, 1.08 to 1.82]; 5 poor-quality trials) (50). However, laser photocoagulation was superior to observation on visual acuity outcomes by 2 years (see Key Question 4).

Photodynamic Therapy With Verteporfin. A good-quality systematic review of 3 fair- or good-quality trials found verteporfin to be associated with greater risk for acute severe visual acuity loss (20-letter loss within 7 days of treatment) compared with placebo (2% vs. 0.2%; pooled RR, 0.02 [CI, 0.01 to 0.03]; number needed to harm, 50) (57). Verteporfin was also associated with a greater risk for infusion-related back pain compared with placebo (3.4% vs. 0.3%; pooled RR, 6.50 [CI, 1.52 to 27.78]).

Intravitreal Injection of Vascular Endothelial Growth Factor Inhibitors. A large, good-quality trial reported 5 cases of presumed endophthalmitis, 6 cases of uveitis, and 11 cases of elevated intraocular pressure among 477 patients treated with ranibizumab compared with 0 cases for any of these adverse events among 236 patients treated with sham injections (66).

A study that pooled data from 2 similarly designed, fair-quality trials of pegaptanib (892 patients who received pegaptanib) found a rate of 1.3% for endophthalmitis (0.16% per injection; 1 of 12 cases associated with ≥6 lines of vision loss), 0.6% for traumatic cataract (0.07% per injection; 1 of 5 cases associated with severe vision

loss), and 0.7% for retinal detachment (0.08% per injection; no cases associated with severe vision loss) after 1 year of treatment (80). There were no differences between pegaptanib or ranibizumab and placebo in rates of hypertensive or thromboembolic events (66, 80).

The manufacturer of ranibizumab sent a letter to clinicians in January 2007 about preliminary results of an ongoing trial that found increased stroke rates in patients who received higher doses of intravitreal ranibizumab. However, 1-year data reported at a conference in February 2008 showed no difference in stroke rates, regardless of dose (81).

DISCUSSION

Table 4 summarizes the results of this evidence synthesis, by key question. Compared with the 1996 USPSTF evidence synthesis (9), more direct evidence on vision screening in older adults now exists. Three cluster randomized trials that enrolled more than 4700 patients found vision screening in older adults as part of a multicomponent screening intervention in primary care settings to be no more effective than no vision screening, delayed screening, or usual care (17–19). A fourth trial found optometrist screening to be associated with an increased risk for falls in frail elderly patients (20). No studies that evaluate optimal screening intervals exist.

Despite the lack of direct evidence to support vision screening, evidence on effectiveness of treatments for common causes of impaired visual acuity is strong. As the 1996 USPSTF review concluded, a very high proportion of patients have favorable vision-related outcomes after treatment of impaired visual acuity due to refractive error and cataracts (9). For wet AMD, vascular endothelial growth factor inhibitors and photodynamic therapy with verteporfin seem to be effective treatment options with a relatively low incidence of serious harms (57, 63). An important advantage of these treatments is that they are associated with less retinal scarring than laser photocoagulation, which is a particularly important consideration for patients with subfoveal (central) neovascularization. For dry AMD, antioxidant vitamins and minerals seem effective for slowing progression of disease (48), although conclusions are largely based on a single large trial of a specific antioxidant regimen (47). In addition, antioxidants included in the formulation used in this trial have been found to be associated with congestive heart failure (vitamin E [82]) and lung cancer in smokers (β-carotene [83, 84]) when prescribed for prevention of cancer or cardiovascular disease.

Evidence on accuracy of screening tests for impaired visual acuity (or conditions associated with impaired visual acuity) is difficult to interpret. Although the Snellen eye chart is widely used to measure visual acuity in primary care settings, no studies have evaluated its accuracy against a clinically relevant reference standard. Some studies found testing with the Snellen eye chart to be inaccurate compared with a detailed ophthalmologic examination, but the conditions identified on examination were not necessarily associated with impaired visual acuity. It is unclear whether identification of AMD or cataracts before the development of impaired visual acuity is associated with improved clinical outcomes compared with identification of these conditions after the development of early vision changes. No screening question is similar in accuracy to visual acuity testing (24–27), and no studies have assessed the accuracy or utility of pinhole testing, the Amsler grid, visual acuity tests other than the Snellen eye chart, physical examination, or funduscopic examination.

Our evidence review has some potential limitations. First, the relatively small number of primary studies and methodological shortcomings made it difficult to answer most key questions with a high degree of confidence. We did not grade any key question as being supported by good-quality evidence. Second, we excluded studies not published in English, which could introduce language bias. However, we did not identify any relevant non–English-language studies from literature searches or reference lists. Finally, we excluded trials of community- or home-based vision screening. The inclusion of such studies is unlikely to change our conclusions because their results are consistent with no benefit from screening (85).

Impaired visual acuity is common in older adults, and effective treatments are available for common causes of impaired visual acuity. Nonetheless, direct evidence of vision screening in asymptomatic older adults in primary care settings found no effects in improving visual acuity or other clinical outcomes. Additional studies are needed to determine why trials of vision screening have shown no benefit and to clarify the risk for potential unintended harms from screening (such as increased falls). For any vision-screening program to be effective, optimal screening approaches and intervals need to be defined, and older adults with impaired visual acuity need to be effectively linked to appropriate follow-up care.

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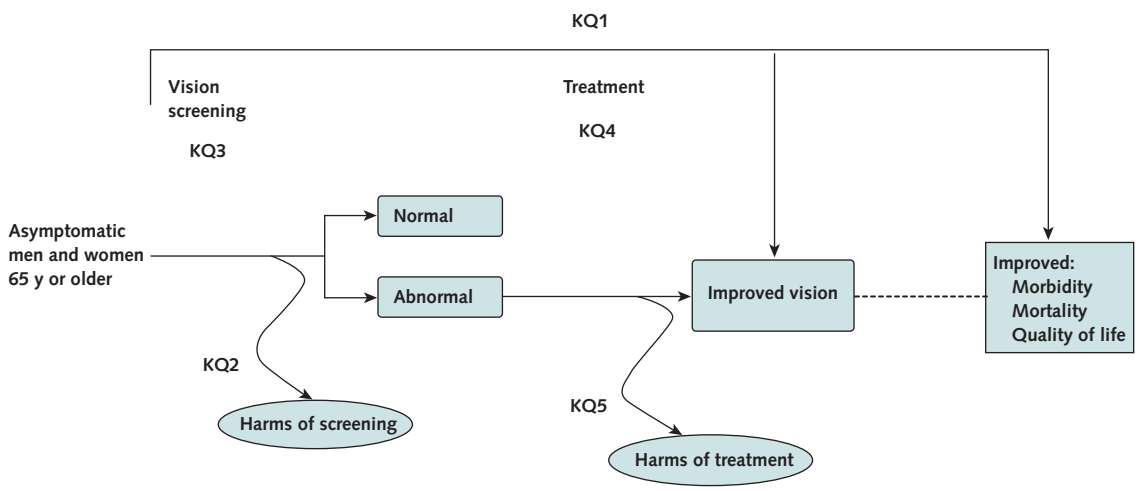
Appendix Figure. **Analytic framework and key questions.**



Key Question 1: Does vision screening in asymptomatic older adults result in improved morbidity or mortality or improved quality of life?
Key Question 2: Are there harms of vision screening in asymptomatic older adults?
Key Question 3: What is the accuracy of screening for early visual impairment due to uncorrected refractive error, cataracts, or age-related macular degeneration?
Key Question 4: Does treatment of early visual impairment due to uncorrected refractive error, cataracts, or age-related macular degeneration lead to improved morbidity or mortality or quality of life?
Key Question 5: Are there harms of treating early visual impairment due to uncorrected refractive error, cataracts, or age-related macular degeneration?

KQ = key question.

Appendix Table 1. Search Strategies

Diagnostic accuracy searches

Ovid MEDLINE

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

EBM Reviews: Cochrane Central Register of Controlled Trials

1. exp Vision/
2. exp Vision Disorders/
3. exp Mass Screening/
4. screen$.mp.
5. exp Refractive Errors/
6. (presbyop$ or myop$ or astigmati$ or hyperop$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
7. exp Macular Degeneration/
8. (degenerat$ adj3 macula$).mp.
9. armd.mp.
10. exp Cataract/
11. cataract.mp.
12. (1 or 2) and (3 or 4)
13. or/5–11
14. 13 and (3 or 4)
15. 12 or 14
16. sensitivity.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
17. specificity.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
18. accura$.mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
19. (16 and 17) or 18
20. 15 and 19
21. (child$ or pediatri$ or infant$ or neonat$).ti.
22. 20 not 21
23. from 22 keep 1–44

EBM Reviews: Cochrane Database of Systematic Reviews

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

Screening searches

Ovid MEDLINE

1. exp Vision/
2. exp Vision Disorders/
3. exp Mass Screening/
4. exp Geriatric Assessment/
5. 1 or 2
6. 3 and 5
7. limit 6 to "all aged (65 and over)"
8. 4 and 5
9. 7 or 8
10. screen$.mp.
11. exp Vision Tests/
12. 10 and 11
13. limit 12 to "all aged (65 and over)"
14. exp Refractive Errors/
15. (presbyop$ or myop$ or astigmati$ or hyperop$).mp. [mp=title, original title, abstract, name of substance word, subject heading word]
16. 14 or 15
17. exp Macular Degeneration/
18. (degenerat$ adj3 macula$).mp.
19. armd.mp.
20. or/17–19
21. exp Cataract/
22. cataract.mp.
23. 21 or 22
24. 16 or 20 or 23
25. 24 and (3 or 4 or 12)
26. limit 25 to "all aged (65 and over)"
27. 7 or 13 or 26
28. limit 27 to English language
29. limit 27 to abstracts
30. 28 or 29
31. from 30 keep 1–498

EBM Reviews: Cochrane Central Register of Controlled Trials

1. ((vision or visual) adj5 screen$).mp.
2. (presbyop$ or myop$ or astigmati$ or hyperop$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]

Continued

Continued on following page

Appendix Table 1—Continued

3. (macula$ adj3 degenerat$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
4. armd.mp.
5. cataract$.mp.
6. screen$.mp.
7. or/2–5
8. 6 and 7
9. 1 or 8
10. (elder$ or old or aged).mp.
11. 9 and 10
12. (child$ or pediatri$ or infant or neonat$).mp.
13. 11 not 12
14. from 13 keep 1–95

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

Treatment searches

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

EBM Reviews: Cochrane Central Register of Controlled Trials
1. exp Vision/
2. exp Vision Disorders/
3. exp Refractive Errors/
4. (presbyop$ or myop$ or astigmati$ or hyperop$).mp. [mp=title, original title, abstract, mesh headings, heading words, keyword]
5. exp Macular Degeneration/

Continued

Appendix Table 1—Continued

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

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

EBM = evidence-based medicine.

Appendix Table 2. Inclusion and Exclusion Criteria

Criteria

All KQs
- Populations
  - Include: Asymptomatic adults ≥65 y (if insufficient data for adults ≥65 y includes studies enrolling adults in general) with vision impairment (visual acuity worse than 20/40 but better than 20/200), uncorrected refractive errors (due to myopia, hyperopia, astigmatism, or presbyopia), age-related macular degeneration, or cataracts
  - Exclude: Persons with known vision impairment, cataracts, age-related macular degeneration, diabetes, or glaucoma
- Languages
  - Include: English language

KQ1 and 2
- Interventions
  - Include: Vision screening done in primary care or eye specialty settings, including multicomponent screening with a distinct vision-screening component
  - Exclude: Community-based or in-home interventions
- Study designs
  - Include: Randomized, controlled trials and controlled observational studies
- Outcomes
  - Include: Visual acuity; quality of life, functional capacity (including ability to drive and driving outcomes), and other measures of morbidity; and mortality
  - Exclude: Falls, reading speed, and other tests of vision function

KQ3
- Interventions
  - Include: Screening questions or diagnostic tests used for vision screening in primary care settings (e.g., Snellen eye chart, other visual acuity charts, physical examination, or funduscopic examination done by a primary care clinician)
  - Exclude: Diagnostic tests used for vision screening in eye specialty settings (including funduscopic examination done by an eye professional and specialized diagnostic testing)
- Study designs
  - Include: Studies evaluating diagnostic accuracy of a screening question or diagnostic test compared with a reference standard
- Outcomes
  - Include: Sensitivity, specificity, positive and negative predictive values, areas under the receiver-operating characteristic curve, and other measures of diagnostic test accuracy

KQ4 and 5
- Interventions
  - Include: Corrective lenses (eyeglasses and contact lenses), reading aids, photorefractive surgery (LASIK, LASEK, photorefractive keratectomy), vitamins and antioxidants, laser therapy, photodynamic therapy, and vascular endothelial growth factor inhibitors
- Study designs
  - Include: Systematic reviews; randomized, controlled trials; and controlled observational studies if there was insufficient evidence from randomized trials
- Outcomes
  - Include: Visual acuity; quality of life, functional capacity (including ability to drive and driving outcomes), other measures of morbidity; and mortality
  - Exclude: Reading speed and other tests of vision function

KQ = key question; LASEK = laser-assisted subepithelial keratomileusis; LASIK = laser-assisted in situ keratomileusis.

Appendix Table 3. Quality Assessment Criteria for Systematic Reviews*

Questions for overall quality rating†
- Search dates reported?
- Search methods reported?
- Comprehensive search?
- Inclusion criteria reported?
- Selection bias avoided?
- Validity criteria reported?
- Validity assessed appropriately?
- Methods used to combine studies reported?
- Findings combined appropriately?
- Conclusions supported by data?

Definitions of ratings (based on above criteria)
- Good: Meets all criteria. Reports comprehensive and reproducible search methods and results; predefined criteria to select studies, and reasons for excluding potentially relevant studies; adequately evaluates quality of included studies and incorporates assessments of quality when synthesizing data; reports methods for synthesizing data and uses appropriate methods to combine data qualitatively or quantitatively; conclusions supported by the evidence reviewed
- Fair: Does not meet ≥1 of the criteria, but the limitations are not judged as being major
- Poor: Includes a major limitation in ≥1 of the above criteria

* Data based on references 13, 86, and 87.
† Questions are answered with either "yes" or "no." Ratings are then summarized as good, fair, or poor on the basis of the extent to which the criteria are met.

Appendix Table 4. Quality Assessment of Randomized, Controlled Trials of Vision Screening in Older Adults

Study, Year (Reference)	Randomly Assigned	Allocation Concealed	Groups Similar at Baseline	Specified Eligibility Criteria	Blinding: Outcome Assessors or Data Analysts	Intention-to-Treat Analysis
Cumming et al, 2007 (20)	Yes, but the method was not described	Yes	Yes	Yes	Cannot tell	Yes
Eekhof et al, 2000 (17)	Yes	NA (cluster)	Yes	Yes	Cannot tell	No
Moore et al, 1997 (18)	Yes	NA (cluster)	Yes	Yes	Cannot tell	No
Smeeth et al, 2003 (19)	Yes	NA (cluster)	Yes	Yes	Cannot tell	No

NA = not applicable.

Appendix Table 5. Studies of Diagnostic Test Accuracy

Study, Year (Reference)	Study Type	Enrollee Age (Sample Size)	Patients With Visual Conditions	Reference Standard	Index Text	Quality Score
Ariyasu et al, 1996 (22)	Cross-sectional	Most patients, 20–59 y (n = 317)	Refractive error (43%); cataract (16%); macular degeneration (4%); strabismus (4%); amblyopia (2%)	Detailed ophthalmologic assessment	Amsler grid; near visual acuity; distance visual acuity	Poor to fair
Eekhof et al, 2000 (24)	Cross-sectional	≥75 y (n = 1121)	Snellen eye chart <0.3: 0.8%	Snellen eye chart and low vision chart (testing vision at reading distance)	Screening questions	Fair
Hiller and Krueger, 1983 (25)	Cross-sectional	25–74 y (n = 1466) for 65–74 y subgroup	Snellen eye chart 20/25 or worse: 69%	Snellen eye chart	Screening questions	Fair
Ivers et al, 2001 (28)	Cross-sectional	≥49 y (n = 3654)	Posterior subcapsular cataract (3.9%); cortical cataract (19.1%); nuclear cataract (47.0%); early AMD (4.5%); refractive error (4.5%); any vision condition (34.5%)	Detailed ophthalmologic assessment	Presenting distance visual acuity (logMAR chart); pinhole distance visual acuity; presenting reading acuity (with current reading glasses)	Poor to fair
McMurdo and Baines, 1988 (23)	Cross-sectional	64–97 y (n = 50)	Previously undiagnosed cataract (18%); previously undiagnosed AMD (8%)	Ophthalmologic examination	Geriatrician examination	Fair
Chu-Ai Teh et al, 2006 (26)	Cross-sectional	≥60 y (n = 112)	Snellen eye chart 6/12 or worse: 81%	Snellen eye chart	Screening questions	Poor to fair
Wang et al, 1998 (27)	Cross-sectional	≥40 y (n = 405)	Any eye disease: 50.7% (of these, 13% have cataracts, AMD, and refractive error not specified)	Detailed ophthalmologic assessment	Screening questionnaire; presenting distance visual acuity, followed by pinhole visual acuity if worse than 20/30	Poor to fair
Woods et al, 1998 (29)	Cross-sectional	≥50 y (n = 2522)	Macular degeneration: 50–64 y (12%) and >64 y (23%) and cataract: 64 y (4.9%) and >64 y (27.2%)	Detailed ophthalmologic assessment	Distance visual acuity (Snellen eye chart); near visual acuity (Snellen eye chart)	Fair

AMD = age-related macular degeneration.

Appendix Table 4—**Continued**

Reporting of Attrition or Contamination	Differential Loss to Follow-up or Overall High Loss to Follow-up	Appropriate Analysis, Including Cluster Correlation	Funding Source	External Validity	Quality Score
Yes	No (14%)	NA	National Health and Medical Research Council of Australia (Melbourne, Victoria, Australia)	Number screened and eligible not reported; mean severity of visual acuity impairment not reported	Fair
Yes	Yes	No	Cannot tell	Seems highly applicable to screening settings in primary care	Fair
Yes	Yes	No	Robert Wood Johnson Clinical Scholars Program; National Institute on Aging Geriatric Academic Program	Seems highly applicable to screening settings in primary care	Fair
Yes	Yes	Yes	Department of Health, Medical Research Council (London, United Kingdom)	Seems highly applicable to screening settings in primary care	Good to fair

Appendix Table 6. **Quality Assessment of Studies of Diagnostic Test Accuracy**

Study, Year (Reference)	Appropriate Spectrum of Patients	Adequate Sample Size (>500)	Credible Reference Standard Used	Reference Standard Applied to All Patients	Screening Test Adequately Described	Reference Standard Interpreted Independently	Quality Score
Ariyasu et al, 1996 (22)	Cannot tell	No	Yes	Cannot tell	Yes	No	Poor to fair
Eekhof et al, 2000 (24)	Cannot tell	Yes	Yes	Yes	Yes	Cannot tell	Fair
Hiller and Krueger, 1983 (25)	Yes	Yes	Yes	Cannot tell	Yes	Cannot tell	Fair
Ivers et al, 2001 (28)	Cannot tell	Yes	Yes	Cannot tell	Yes	Cannot tell	Poor to fair
McMurdo and Baines, 1988 (23)	Cannot tell	No	Yes	Yes	Yes	Yes	Fair
Chu-Ai Teh et al, 2006 (26)	Cannot tell	No	Yes	Cannot tell	Yes	Cannot tell	Poor to fair
Wang et al, 1998 (27)	Cannot tell	No	Yes	No	Yes	Cannot tell	Poor
Woods et al, 1998 (29)	Cannot tell	Yes	Yes	No	Yes	Cannot tell	Poor to fair

Appendix Table 7. **Randomized, Placebo-Controlled Trials of Interventions for Wet AMD**

Study, Year (Reference)	Purpose	Sample Size, *n*	Patient Characteristics	Intervention	Results	Quality Score
Laser photocoagulation						
Macular Photocoagulation Study Group, 1982 (51)	To determine whether argon laser photocoagulation is useful in preventing severe vision loss in eyes with evidence of macular degeneration	224	Mean age not reported; age 50–64 y (23%); age 65–75 y (46%); age >75 y (30%); women (51%); BCVA 20/32 or better: 105/224 (46%)	Laser photocoagulation vs. no treatment	Increase in lines of VA or no change from baseline to 18 mo: 61/100 (61.0%) vs. 30/98 (30.6%) (RR, 1.99 [CI, 1.42–2.79]); loss of 2–5 lines of VA at 18 mo: 23/100 (23.0%) vs. 16/98 (16.3%) (RR, 1.41 [CI, 0.79–2.50]); loss of 6–9 lines of VA at 18 mo: 8/100 (8.0%) vs. 24/98 (24.5%) (RR 0.33 [CI, 0.15–0.69]); loss of ≥10 lines of VA at 18 mo: 8/100 (8.0%) vs. 16/98 (16.3%) (RR, 0.49 [CI, 0.22–1.09])	Poor
Macular Photocoagulation Study Group, 1990 (52)	To determine whether krypton laser photocoagulation would help prevent VA loss in eyes with AMD	496	Mean age not reported; age 50–59 y (5%); age 60–69 y (29%); age 70–79 y (48%); age ≥80 y (17%); women (53%); BCVA 20/40 or better: 157/496 (32%)	Laser photocoagulation vs. no treatment	Increase in lines of VA or no change from baseline to 36 mo: 47/174 (27.0%) vs. 29/169 (17.2%) (RR, 1.57 [CI, 1.04–2.38]); loss of 2–5 lines of VA at 36 mo: 41/174 (23.6%) vs. 42/169 (24.9%) (RR, 0.95 [CI, 0.65–1.38]); loss of 6–9 lines of VA at 36 mo: 55/174 (31.6%) vs. 54/169 (32.0%) (RR, 0.99 [CI, 0.73–1.35]); loss of ≥10 lines of VA at 36 mo: 31/174 (17.8%) vs. group 44/169 (26.0%) (RR, 0.68 [CI, 0.46–1.03])	Poor
Macular Photocoagulation Study Group, 1991 (53)	To determine the effect of laser photocoagulation of subfoveal neovascularization in eyes with AMD but without previous photocoagulation of the macula	373	Mean age not reported; age 50–59 y (4%); age 60–69 y (21%); age 70–79 y (50%); age ≥80 y (24%); women (56%); BCVA 20/20 or better: 106/373 (28%); 20/25–20/100: 190/373 (51%); 20/250 or worse: 76/373 (20%)	Laser photocoagulation vs. no treatment	Loss of <2 lines of VA at 24 mo: 37/114 (32.5%) vs. 20/112 (17.9%) (RR, 1.82 [CI, 1.13–2.93]); loss of 2–3 lines of VA at 24 mo: 27/114 (23.7%) vs. 20/112 (17.9%) (RR, 1.33 [CI, 0.79–2.22]); loss of 4–5 lines of VA at 24 mo: 27/114 (23.7%) vs. 31/112 (27.7%) (RR, 0.86 [CI, 0.55–1.34]); loss of ≥6 lines of VA at 24 mo: 23/114 (20.2%) vs. 41/112 (36.6%) (RR, 0.55 [CI, 0.36–0.85])	Poor
Macular Photocoagulation Study Group, 1991 (54)	To determine the effect on vision of laser treatment of subfoveal neovascular lesions compared with no treatment	206	Mean age not reported; age 50–59 y (2%); age 60–69 y (28%); age 70–79 y (54%); age ≥80 y (16%); women (52%); BCVA 20/20 or better: 70/206 (34%); 20/25–20/100: 73/206 (35%); 20/250 or worse: 63/206 (31%)	Laser photocoagulation vs. no treatment	Loss of <2 lines of VA at 24 mo: 10/35 (28.6%) vs. 15/46 (32.6%) (RR, 0.88 [CI, 0.45–1.71]); loss of 2–3 lines of VA at 24 mo: 10/35 (28.6%) vs. 10/46 (21.7%) (RR, 1.31 [CI, 0.62–2.81]); loss of 4–5 lines of VA at 24 mo: 12/35 (34.3%) vs. 8/46 (17.4%) (RR, 1.97 [CI, 0.90–4.30]); loss of ≥6 lines of VA at 24 mo: 3/35 (8.6%) vs. 13/46 (28.3%) (RR, 0.30 [CI, 0.09–0.98])	Poor
The Moorfields Macular Study Group, 1982 (55)	To determine the effects of argon laser photocoagulation in the treatment of neovascular disciform macular degeneration in elderly persons	128	Baseline characteristics not reported; inclusion criteria required for persons age 50–80 y; no description of BCVA at baseline	Laser photocoagulation vs. no treatment	Loss of <2 lines of VA at 24 mo: 3/51 (5.9%) vs. 3/50 (6.0%) (RR, 0.98 [CI, 0.21–4.63]); loss of 2–3 lines of VA at 24 mo: 11/51 (21.6%) vs. 10/50 (20.0%) (RR, 1.08 [CI, 0.50–2.31]); loss of 4–5 lines of VA at 24 mo: 14/51 (27.4%) vs. 16/50 (32.0%) (RR, 0.86 [CI, 0.47–1.57]); loss of ≥6 lines of VA at 24 mo: 9/51 (17.6%) vs. 14/50 (28%) (RR, 0.63 [CI, 0.30–1.32])	Poor
Photodynamic therapy						
TAP Study Group, 1999 (59); Kaiser and TAP Study Group, 2006 (62); TAP and VIP Report 3, 2004 (88)	To determine whether photodynamic therapy with verteporfin can safely reduce the risk for vision loss in patients with subfoveal choroidal neovascularization	609	Mean age, 75.3 y; women (56%); white (98%), other (2%); mean BCVA, 52.7 letters (approximate Snellen equivalent 20/80); subfoveal lesions (89%)	Verteporfin vs. placebo	Loss of ≥3 lines of VA at 12 mo: 156/402 (39%) vs. 111/207 (54%) (RR, 0.72 [CI, 0.61–0.86]); loss of ≥6 lines of VA at 12 mo: 59/402 (15%) vs. 49/207 (24%) (RR, 0.62 [CI, 0.44–0.87])	Good

Continued on following page

Appendix Table 7—**Continued**

Study, Year (Reference)	Purpose	Sample Size, n	Patient Characteristics	Intervention	Results	Quality Score
VIP Study Group, 2001 (89)	To determine whether photodynamic therapy with verteporfin can safely reduce the risk for vision loss compared with placebo	339	Mean age, 75 y; white (99%); other (1%); mean BVCA, 66 letters (approximate Snellen equivalent 20/50); subfoveal lesions (83.4%)	Verteporfin vs. placebo	Loss of ≥3 lines of VA at 12 mo: 114/225 (51%) vs. 62/114 (54%) (RR, 0.44 [CI, 0.25–0.77])	Good
Visudyne in Minimally Classic Choroidal Neovascularization Study Group, 2005 (90)	To compare the treatment effect and safety of photodynamic therapy with verteporfin using SF or RF light fluence rate with that of placebo in patients with subfoveal minimally classic choroidal neovascularization with AMD	117	Mean age, 78 y; mean BCVA, 20/80; subfoveal lesions (92%)	Verteporfin vs. placebo	Loss of ≥3 lines of VA at 12 mo: verteporfin SF 10/36 (27.8%) vs. verteporfin RF 5/36 (13.9%) vs. placebo 18/38 (47%); loss of ≥6 lines of VA at 12 mo: verteporfin SF 3/36 (8%) vs. verteporfin RF 0/36 (0%) vs. placebo 6/38 (16%); loss of ≥3 lines of VA at 24 mo: verteporfin SF 17/32 (8%) vs. verteporfin RF 9/34 (26.4%) vs. placebo 18/37 (48.6%); loss of ≥6 lines of VA at 24 mo: verteporfin SF 4/32 (12.5%) vs. verteporfin RF 6/34 (17.6%) vs. placebo 13/37 (35.1%)	Good
VEGF inhibitors						
Gragoudas et al, 2004 (64); V.I.S.I.O.N. Clinical Trial Group, 2006 (80); Leys et al, 2008 (68)	To test the short-term safety and effectiveness of pegaptanib	1208	Mean age not reported; age range, 50–64 y (6%); 65–74 y (32%); 75–84 y (52%); ≥85 y (10%); women (58%); white (96%); other mean VA (4%); study eye, 51.8 letters (SD, 12.8)	Pegaptanib vs. sham injection, 0.3 mg, 1.0 mg, or 3.0 mg	Loss of >3 lines of VA at 12 mo: pegaptanib, 0.3 mg, 88/294 (29.9%) vs. pegaptanib, 1.0 mg, 87/300 (29.0%) vs. pegaptanib, 3.0 mg, 103/296 (34.8%) vs. sham injection 132/296 (44.6%); combined doses pegaptanib vs. sham injection (RR, 0.77 [CI, 0.65–0.92])	Fair
Regillo et al, 2008 (65)	To evaluate the effectiveness and safety of ranibizumab for the treatment of minimally classic or occult with no classic choroidal neovascularization associated with AMD; prospective, double-blind, randomized, controlled trial	184	Mean age, about 78 y; women (60%); neovascular AMD	Ranibizumab vs. sham injection, 0.3 mg or 0.5 mg	Loss of >3 lines of VA at 12 mo: 0.3 mg 10/60 (16.7%) vs. 0.5 mg 6/61 (9.8%) vs. sham injection 32/63 (50.8%); combined doses ranibizumab vs. sham injection (RR, 0.35 [CI, 0.20–0.60; $P < 0.001$]); gain of ≥3 lines of VA at 12 mo: 0.3 mg 7/60 (11.7%) vs. 0.5 mg 8/61 (13.1%) vs. sham injection 6/63 (9.5%); mean change from baseline VA to 12 mo: 0.3 mg, −1.6 letters vs. 0.5 mg, −0.2 letters vs. sham injection −16.3 letters; patients with VA worse than 20/200 at 12 mo: 0.3 mg 14/60 (23.3%) vs. 0.5 mg 15/61(24.6%) vs. sham injection 33/63 (52.4%)	Good
Rosenfeld et al, 2006 (66); Boyer et al, 2007 (91)	To evaluate the effectiveness and safety of ranibizumab for the treatment of minimally classic or occult with no classic choroidal neovascularization associated with AMD; double-blind, placebo-controlled trial	716	Mean age, 77 y (SD, 8); women (65%); AMD	Ranibizumab vs. sham injection, 0.3 mg or 0.5 mg	Loss of >3 lines of VA at 12 mo: ranibizumab 0.3 mg 13/238 (5.5%) vs. ranibizumab 0.5 mg 13/240 (5.4%) vs. sham injection 90/238 (37.8%); combined doses of ranibizumab vs. sham injection (RR, 0.19 [CI, 0.12–0.28]); loss of >3 lines of VA at 24 mo: ranibizumab, 0.3 mg, 19/238 (8.0%) vs. ranibizumab, 0.5 mg, 24/240 (10.0%) vs. sham injection 112/238 (47.1%); combined doses of ranibizumab vs. sham injection (RR, 0.26 [CI, 0.19–0.36])	Fair

AMD = age-related macular degeneration; BCVA = best corrected visual acuity; RF = reduced fluence; RR = relative risk; SD = standard deviation; SF = standard fluence; TAP = Treatment of Age-Related Macular Degeneration With Photodynamic Therapy; VA = visual acuity; VIP = Verteporfin in Photodynamic Therapy; V.I.S.I.O.N. = VEGF Inhibition Study in Ocular Neuvascularization; VEGF = vascular endothelial growth factor.

Appendix Table 8. **Quality Assessment of Randomized, Controlled Trials of Wet AMD**

Study, Year (Reference)	Randomly Assigned	Allocation Concealed	Groups Similar at Baseline	Specified Eligibility Criteria	Blinding		
					Patient	Provider	Outcome Assessors or Data Analysts
Gragoudas et al, 2004 (64)	Yes, but method not described	Cannot tell	Yes	Yes	Yes	No	Yes
Macular Photocoagulation Study Group, 1982 (51)	Yes	Cannot tell	No	Yes	No	No	No
Macular Photocoagulation Study Group, 1991 (53)	Yes, but method not described	Cannot tell	Yes	Yes	No	No	No
Macular Photocoagulation Study Group, 1991 (54)	Yes, but method not described	Cannot tell	No	Yes	No	No	No
Macular Photocoagulation Study Group, 1990 (52)	Yes, but method not described	Cannot tell	No	Yes	No	No	No
The Moorfields Macular Study Group, 1982 (55)	Yes, but method not described	Cannot tell	Cannot tell	Yes	Cannot tell	Cannot tell	Cannot tell
Regillo et al, 2008 (65)	Yes	NA	Yes	Yes	Yes	No	Yes
Rosenfeld et al, 2006 (66)	Yes, but method not described	Cannot tell	Yes	Yes	Yes	No	Yes
TAP Study Group, 1999 (59)	Yes	Yes	No	Yes	Yes	Yes	Yes
Verteporfin in Photodynamic Therapy Study Group, 2001 (89)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Visudyne in Minimally Classic Choroidal Neovascularization Study Group, 2005 (90)	Yes, but method not described	Yes	Yes	Yes	Yes	Yes	Yes

AMD = age-related macular degeneration; BCVA = best corrected visual acuity; MRC = Medical Research Council; NA = not applicable; NEI, NIH = National Eye Institute, National Institutes of Health; TAP = Treatment of Age-Related Macular Degeneration With Photodynamic Therapy.
* New York, NY.
† Bethesda, MD.
‡ London, United Kingdom.
§ San Francisco, CA.
¶ Basel, Switzerland.
** Vancouver, British Columbia.
†† Duluth, GA.

Appendix Table 8—**Continued**

Reporting of Attrition, Contamination	Differential Loss to Follow-Up, Overall High Loss to Follow-up, or Incomplete Follow-up	Funding Source	External Validity	Intention-to-Treat Analysis	Quality Score
Partial (reasons for patients who withdrew or loss to follow-up not reported)	No	Eyetech Pharmaceuticals and Pfizer*	Mean visual acuity, 51–53	Yes	Fair
Yes	Yes	NEI, NIH†	BCVA 20/32 or better: 105/224 patients (47%)	No	Poor
Yes	Yes	NEI, NIH†	BCVA 20/20 or better: 106/373 patients (28%); 20/25–20/100: 190/373 patients (51%); 20/250 or worse: 76/373 patients (20%)	No	Poor
Yes	Yes	NEI, NIH†	BCVA 20/20 or better: 70/206 patients (34%); 20/25–20/100: 73/206 patients (35%); 20/250 or worse: 63/206 patients (31%)	No	Poor
No	Yes	NEI, NIH†	BCVA 20/40 or better: 157/496 patients (32%)	No	Poor
Yes	No	NEI, NIH†; MRC‡	Inclusion criteria required age 50–80 y; no description of BCVA at baseline	No	Poor
Yes	No	Genentech§; Novartis¶	Mean baseline visual acuity, 20/63–20/80; most patients with a new diagnosis of AMD (87% ≤1 y of diagnosis)	Yes	Good
Yes	No	Genentech§; Novartis¶	>85% had visual acuity >20/200	Yes	Fair
Yes	No	QLT**; CIBA Vision††	Mean BCVA, 52.7 letters (approximate Snellen equivalent 20/80); 89% subfoveal lesions	Yes	Good
Yes	No	Novartis¶; QLT**	Mean BCVA, 66 letters (approximate Snellen equivalent 20/50); 83.4% subfoveal lesions	Yes	Good
Yes	No	Novartis¶; QLT**	Mean BCVA, 20/80; 92% subfoveal lesions	No	Good