Supplementary Methods

<u>**Review Protocol**</u>

Review question: Do prospective studies suggest an increased risk of all-cause dementia or key dementia subtypes (Alzheimer's disease, vascular dementia, dementia with Lewy bodies, frontotemporal dementia) associated with visual impairment and eye diseases?

Population: Adults (≥18 years)

Exposure: Visual impairment and eye conditions (e.g. glaucoma, age-related macular degeneration, cataract and retinopathy)

Comparators: No visual impairment (i.e. normal vision) or no eye condition

Outcomes: Incident all-cause dementia or key dementia subtypes

Search strategy:

- Searching the following databases: Medline, Embase, PsycINFO (via OvidSP)
- Backward and forward citation searching of included studies via Web of Science
- Alerts to identify studies published after the search date

Study selection criteria:

Inclusion criteria:

- Prospective studies on the association between visual impairment or eye diseases and incident all-cause dementia or key dementia subtypes
- Only publications in English

Exclusion criteria:

- Studies with outcomes that are not directly dementia-related (e.g. neuroimaging or biomarkers)
- Studies with no comparison group or comparison group other than no visual impairment or no eye disease
- Studies using only a single cognitive instrument or self-reported dementia to define incident all-cause dementia or key dementia subtypes
- studies investigating aspects of visual perception (e.g. color vision deficiency)
- Animal studies
- Case reports, narrative reviews, letters, editorials, opinions, book chapters
- Conference abstracts
- Duplicate publications using the same data

Study selection: Two reviewers (EK & TJL) will independently screen titles and abstracts based on the inclusion/exclusion criteria. The same two reviewers will also review

independently full-texts of potentially relevant studies. Any discrepancies will be resolved by discussion, if necessary with a third reviewer (UT).

Risk of bias assessment: Two reviewers (EK & TJL) will independently assess the risk of bias using the Quality Assessment Tool for Quantitative Studies [1]. Seven components will be rated individually as strong, moderate or weak in the following way:

1. **Selection bias** will be rated as strong if study participants are likely to be representative of the target population and the participation rate at baseline is greater than 80%, as moderate if participants are at least somewhat likely to be representative of the target population and the participation rate at baseline is 60-79%, and as weak if participants are not likely to be representative of the target population or the participation rate at baseline is less than 60% or selection and participation rate at baseline are not described,

2. **Design** will be rated as strong for randomized controlled trials and controlled clinical trials, as moderate for cohort studies, case control studies or interrupted time series and as weak for any other method or if method is not described.

3. **Confounders**. We consider adjusting analyses for sociodemographic confounders (age, sex, education and / or socioeconomic status, and ethnicity in case of a heterogenous sample) as essential. Studies will be rated as strong if analyses are adjusted for sociodemographic and at least three additional confounders and as moderate if adjustment strategy includes sociodemographic and one or two additional confounders. Studies will receive a weak rating if only sociodemographic or not all relevant sociodemographic confounders are adjusted for.

4. **Blinding** will be rated as strong if the outcome assessor is not aware of participants' visual status and participants are not aware of the research question / assessment of visual function for research purposes, as moderate if the outcome assessor is not aware of participants' visual status or participants are not aware of the research question / assessment of visual function for research purposes or blinding is not described and as weak if the outcome assessor is aware of participants' visual status and participants are aware of the research question / assessment of visual function for research purposes.

5. **Data collection methods** will be rated as strong if data collection tools have been shown or are widely known to be valid and reliable, as moderate if data collection tools have been shown or are widely known to be valid but not reliable or reliability is not described and as weak if data collection tools have been shown or are widely known not to be valid or both validity and reliability are not described.

6. **Withdrawals and drop-outs (attrition bias)** will be rated as strong if the follow-up rate is at least 80%, as moderate if the follow-up rate is 60-79% or follow-up rate cannot be assessed due to study design (not applicable) and as weak if the follow-up rate is less than 60% or withdrawals and drop-outs are not described.

Any discrepancies will be resolved by discussion, if necessary with a third reviewer (UT). We will include funnel plots to investigate publication bias if there are at least ten studies included in a meta-analysis [2].

Data extraction: One reviewer (EK) will extract key data including study design, assessment of exposures and outcomes, population, adjusted estimates of the association between exposure and outcome, adjustment strategy and sources of data. Data extraction will be checked by the second reviewer (TJL). Any discrepancies will be resolved by discussion, if necessary with a third reviewer (UT).

Evidence synthesis methods: The identified evidence on the associations between visual impairment and all-cause dementia and key dementia subtypes will be synthesized narratively and using random effects meta-analysis if appropriate. We will investigate heterogeneity between studies using the x^2 test for homogeneity and I^2 statistic, and meta-regression if appropriate. We will also explore small study effects including publication bias using funnel plots and Egger's statistic if appropriate.

Contacting corresponding authors

Corresponding authors of 26 studies [3-28] were contacted for clarification or additional or not fully reported data. We received additional data or clarification for 11 studies [3-5, 7, 13-16, 19, 23, 25], no response from 14 studies [6, 8, 9, 11, 12, 17, 18, 20-22, 24, 26-28] and for one study [10] the email delivery was unsuccessful.

Supplementary Results

Extended results for visual impairment, glaucoma, age-related macular degeneration (AMD) and diabetic retinopathy

Visual impairment

Ten cohort studies investigated the association between VI and incident all-cause dementia [3, 5, 9, 16, 19, 25, 26, 29, 30, 31] (Supplementary Table 2). The pooled estimate of seven studies [3, 5, 19, 25, 29-31] indicated a higher risk of all-cause dementia in those with at least mild VI compared to no VI (37,705 participants, 3,415 dementia cases, pooled adjusted RR = 1.38, 95% CI: 1.19-1.59, p<0.001, I^2 = 28.6%; Figure 2). After excluding three studies [5, 30, 31] using self-reported VI, the pooled estimate remained similar (26,381 participants, 2,651 dementia cases, pooled adjusted HR = 1.35, 95% CI: 1.10-1.67, p = 0.005, I^2 = 38.7%; Supplementary Figure 4).The same pattern of results was also observed in a sensitivity analysis with two studies with a global risk of bias rating of moderate [19] or strong [29] (23,312 participants, 2,231 cases, pooled adjusted HR = 1.32, 95% CI: 0.97-1.79, p = 0.08, I^2 = 64.6). Two studies [16, 26] could not be included in the meta-analysis as they did not define VI based on the WHO classification [32]. Results provided by Maruta and colleagues [16] (2,190 participants, 1,153 dementia cases) suggested no association (HR = 1.04, 95% CI: 0.85-1.26] whereas Paik and colleagues [26] (6,029,657 participants, 165,293 dementia cases) reported increased dementia risk in those with mild (HR=1.45, 95% CI: 1.42-1.48), moderate (HR=1.74, 95% CI: 1.70-1.78) and severe VI/blindness (HR=1.75, 95% CI: 1.71-1.79) compared to normal vision. Two studies [3, 9] assessed VI based on contrast sensitivity. The pooled estimate of these two studies [3, 9] was similar to our main finding although not statistically significant (3,892 participants,

565 dementia cases, pooled adjusted HR = 1.42, 95% CI: 0.82-2.48, p = 0.21, I^2 = 79.7%; Supplementary Figure 5).

Three studies [18, 26, 31] investigated the association with AD (Supplementary Table 2) although one study [18] could not be included in a meta-analysis due to a substantial difference in the definition of exposure that did not include mild VI. The pooled estimate of two studies [26, 31] indicated an increased risk of AD in those with at least mild VI compared to no VI (6,031,708 participants, 123,717 AD cases, pooled adjusted HR = 1.47, 95% CI: 1.43-1.50, p<0.001, I^2 = 0.0%; Supplementary Figure 6). Results reported by Klaver and colleagues [18] (1,438 participants, 62 AD cases; not included in the meta-analysis) suggested no associations of AD risk with moderate/severe VI (RR =1.01, 95% CI: 0.35-2.88) and with blindness (RR=0.96, 95% CI: 0.68-7.05) compared to normal vision/mild VI, though there was considerable uncertainty around the estimates due to wide CIs (Supplementary Table 2).

Two studies [26, 31] investigated the association with VaD (Supplementary Table 2). The pooled estimate of these two studies [26, 31] indicated an increased risk of VaD in those with at least mild VI compared to no VI (6,031,708 participants, 20,764 VaD cases, pooled adjusted HR = 1.40, 95% CI: 1.33-1.47, p<0.001, I^2 = 0.0%; Supplementary Figure 6).

Glaucoma

Eight cohort studies investigated the association between glaucoma and incident all-cause dementia [4, 7, 10, 14, 20, 23, 27, 33] (Supplementary Table 3). The pooled estimate of five studies [7, 14, 20, 27, 33] suggested no association between glaucoma and all-cause dementia (175,357 participants, 44,144 dementia cases, pooled adjusted HR = 0.97, 95% CI: 0.90-1.04, p=0.38, I^2 = 51.5%; Figure 3). A sensitivity analysis with two studies [27, 33] with a global risk of bias rating of moderate revealed the same pattern of results (43,707 participants, 2,472 dementia cases, HR = 1.38, 95% CI: 0.58-3.31, p = 0.47, I^2 = 80.2%). Three studies [4, 10, 23] could not be included in the main analysis: one study [10] due to substantial methodological differences (estimate of effect) and two studies [4, 23] due to use of the same source of data, the Taiwan National Health Insurance Research Database (TNHIRD; Supplementary Table 3). In the study by Helmer and colleagues [10], open-angle glaucoma was associated with significantly increased odds of all-cause dementia compared to no open-angle glaucoma (812 participants, 41 dementia cases, odds ratio = 3.9, 95% CI: 1.5-10.4). The studies based on data from the TNHIRD (32,545 participants, 1,601 dementia cases [23] and 76,585 participants, number of dementia cases not reported [4]) indicated increased dementia risk associated with glaucoma (HR = 1.13, 95% CI: 1.01-1.27), primary open-angle glaucoma (HR = 1.21, 95% CI: 1.02-1.43) [23] and normal tension glaucoma (HR = 1.39, 95% CI: 1.25-1.46) [4] but not with primary angle-closure glaucoma (HR = 1.09, 95% CI: 0.95-1.26) [23]. However, the study by Kuo and colleagues [33] (42,048 participants, 2,304 dementia cases; results for any glaucoma included in the meta-analysis) also based on data from the TNHIRD reported additional results for normal tension glaucoma (HR = 1.17, 95% CI: 0.98-1.40) and angle-closure glaucoma (HR = 0.91, 95% CI: 0.81-1.02) that were statistically not significant. In a sensitivity analysis restricting to studies on open-angle glaucoma only, the pooled estimate suggested a reduced risk of all-cause dementia associated with open-angle glaucoma (169,821 participants, 43,006

dementia cases, pooled adjusted HR = 0.93, 95% CI: 0.91-0.95, p<0.001, I^2 = 0.0%) (Supplementary Figure 7).

Eight cohort studies investigated the association between glaucoma and incident AD [4, 12, 14, 15, 17, 20, 27, 33] (Supplementary Table 3). The pooled estimate of six studies [12, 14, 17, 20, 27, 33] suggested no association between glaucoma and AD (2,806,178 participants, 54,070 AD cases, pooled adjusted RR = 1.05, 95% CI: 0.93-1.17, p = 0.45, I^2 = 87.5%; Figure 4) compared to no glaucoma. When we excluded studies with a global risk of bias rating of weak, the pooled estimate of four moderate studies [12, 17, 27, 33] also revealed the same pattern of results (2,675,651 participants, 31,747 AD cases, pooled adjusted RR = 1.20, 95% CI: 0.94-1.55, p = 0.15, I^2 = 82.9%). Two studies [4, 15] could not be included in the main analysis due to use of the same source of data (TNHIRD; Supplementary Table 3). In the study by Lin and colleagues [15], primary open-angle glaucoma was associated with an increased AD risk (19,895 participants, 208 AD cases, HR = 1.40, 95% CI: 1.03-1.90). Chen and colleagues [4] (76,585 participants, 3,597 AD cases) reported an association between normal tension glaucoma and AD (HR = 1.52, 95% CI: 1.41-1.63) but found little evidence of an increased risk of AD associated with high tension glaucoma (HR = 1.12, 95% CI: 0.89-1.36). However, the study by Kuo and colleagues [33] (42,048 participants, 183 AD cases; results for any glaucoma included in the meta-analysis) also based on data from the TNHIRD reported additional results for normal tension glaucoma (HR = 0.93, 95% CI: 0.45-1.92) and angle-closure glaucoma (HR = 0.93, 95% CI: 0.62-1.38) that were statistically not significant. In a sensitivity analysis restricting to studies on open-angle glaucoma only, the pooled estimate suggested a reduced risk of AD associated with open-angle glaucoma (168,698 participants, 21,714 AD cases, pooled adjusted HR = 0.91, 95% CI: 0.89-0.94, p<0.001, I^2 = 0.0%) (Supplementary Figure 7). When we restricted to primary open-angle glaucoma only, there was little evidence of an increased AD risk (2,651,839 participants, 31,648 AD cases, pooled adjusted RR = 1.23, 95% CI: 0.94-1.60, p = 0.13, I^2 =87.7%, Supplementary Figure 8).

Two cohort studies investigated the association between glaucoma and incident VaD [12, 33] (Supplementary Table 3). The pooled estimate suggested no association between open-angle glaucoma and VaD (2,665,178 participants, 31,304 VaD cases, pooled adjusted RR = 0.97, 95% CI: 0.73-1.27, p=0.81, I^2 = 90.7%; Supplementary Figure 7). Kuo and colleagues [33] (42,048 participants, 1,784 VaD cases; results for open-angle glaucoma included in the meta-analysis) also reported results for any glaucoma (HR = 0.93, 95% CI: 0.85-1.02), normal tension glaucoma (HR = 1.07, 95% CI: 0.87-1.33) and angle-closure glaucoma (HR = 0.90, 95% CI: 0.79-1.02) that were statistically not significant.

Age-related macular degeneration

Five cohort studies reported the association between AMD and incident all-cause dementia [11, 14, 24] (n = 3) and/or AD [6, 11, 14, 18] (n = 4; Supplementary Table 4). Pooled estimates of three studies [11, 14, 24] provided little evidence of an association between AMD and all-cause dementia (7,800,692 participants, >2,559 dementia cases [exact number cannot be determined], pooled adjusted RR = 1.15, 95% CI: 0.88-1.50, p = 0.30, I^2 = 91.0%, Figure 3) or AD (8,079,074 participants, >8,249 AD cases [exact number cannot be determined], pooled

adjusted RR = 1.17, 95% CI: 0.88-1.54, p = 0.28, I^2 = 85.2%, Figure 4). One study [18] (1,438 participants, 62 AD cases) could not be included in the latter meta-analysis, as it investigated severity rather than presence of AMD. The RRs were 1.0 (95% CI: 0.6-1.9) and 1.5 (95% CI: 0.6-3.5) for early and advanced AMD, respectively, in association with AD risk compared to no AMD [18]. In a sensitivity analysis, pooling estimates of two studies with a moderate [11] or strong [6] risk of bias rating also provided no evidence of an association between AMD and AD risk (8,075,197 participants, >7,457 AD cases [exact number cannot be determined], pooled adjusted RR = 1.14, 95% CI: 0.67-1.93, p = 0.64, I^2 = 92.6%).

Diabetic retinopathy

Four studies based on one type 1 diabetic cohort [21], one type 2 diabetic cohort [34] and two cohorts including non-diabetic participants [14, 22] investigated the association between diabetic retinopathy and all-cause dementia with one [22] and two [14, 22] studies, respectively, also investigating VaD and AD. The pooled estimate of four [8, 14, 21, 22] and two studies [14, 22], respectively, indicated an increased risk of all-cause dementia (43,658 participants, 7,060 dementia cases, pooled adjusted HR = 1.34, 95% CI: 1.11-1.61, p = 0.002, I^2 =63.9%, Figure 3) and AD (9,955 participants, 1,375 AD cases, pooled adjusted HR = 1.29, 95% CI: 1.03-1.61, p = 0.03, I2 =11.2%, Figure 4) in those with diabetic retinopathy compared to no retinopathy. When we excluded studies with a global risk of bias rating of weak, the pooled estimate of two moderate studies [8, 22] also indicated an increased risk of all-cause dementia associated with diabetic retinopathy (36,039 participants, 5,908 dementia cases, pooled adjusted HR = 1.29, 95% CI: 1.15-1.44, p <0.001, I^2 = 0.0%) Only one study [22] (6,078 participants, 80 VaD cases) investigated diabetic retinopathy and VaD; this provided little evidence of an association (HR = 0.90, 95% CI: 0.39-2.11). One study [8] (29,961 participants, 5,173 dementia cases) of a type 2 diabetic cohort indicated increased dementia risk in those with proliferative diabetic retinopathy (HR = 1.40, 95% CI: 1.12-1.74) and with diabetic macular edema (HR = 1.42, 95% CI 1.23-1.63; Supplementary Table 6).

Supplementary References

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Supplementary Table 1. Quality assessment of included studies

Study	Selection bias	Study design	Confounders	Blinding	Data collection method	Withdrawals and drop-outs	Global rating
Brenowitz et al. (2019)	weak	moderate	strong	moderate	weak	weak	weak
Chen et al. (2018)	moderate	moderate	moderate	moderate	weak	moderate	moderate
Choi et al. (2019)	moderate	moderate	strong	moderate	strong	moderate	strong
Davies-Kershaw et al. (2018)	moderate	moderate	weak	moderate	weak	moderate	weak
Ekström & Kilander (2014)	weak	moderate	weak	moderate	weak	weak	weak
Exalto et al. (2014)	strong	moderate	strong	moderate	strong	weak	moderate
Fischer et al. (2016)	strong	moderate	strong	moderate	weak	moderate	moderate
Helmer et al. (2013)	moderate	moderate	strong	moderate	strong	strong	strong
Hwang et al. (2020)	weak	moderate	strong	weak	strong	strong	weak
Keenan et al. (2015)	moderate	moderate	moderate	moderate	weak	moderate	moderate
Keenan et al. (2014)	moderate	moderate	moderate	moderate	weak	moderate	moderate
Klaver et al. (1999)	moderate	moderate	weak	moderate	strong	weak	weak
Kuo et al. (2020)	moderate	moderate	strong	moderate	weak	moderate	moderate
Lai et al. (2014)	moderate	moderate	weak	moderate	weak	moderate	weak
Lee et al. (2019)	weak	moderate	strong	moderate	strong	weak	weak
Lee et al. (2020)	moderate	moderate	strong	moderate	strong	strong	strong

Lin et al. (2014)	moderate	moderate	strong	moderate	weak	moderate	moderate
Maruta et al. (2020)	moderate	moderate	weak	moderate	weak	weak	weak
Moon et al. (2018)	moderate	moderate	strong	moderate	weak	moderate	moderate
Naël et al. (2019)	weak	moderate	strong	moderate	strong	strong	moderate
Nam et al. (2021)	moderate	moderate	weak	moderate	weak	moderate	weak
Ou et al. (2012)	moderate	moderate	weak	moderate	weak	weak	weak
Paik et al. (2020)	moderate	moderate	weak	moderate	weak	moderate	weak
Rodill et al. (2018)	moderate	moderate	weak	moderate	strong	weak	weak
Rogers & Langa (2010)	weak	moderate	strong	moderate	moderate	weak	weak
Schrijvers et al. (2012)	moderate	moderate	strong	moderate	strong	weak	moderate
Su et al. (2016)	moderate	moderate	weak	moderate	weak	moderate	weak
Tran et al. (2020)	weak	moderate	strong	moderate	moderate	weak	weak
Tsai et al. (2015)	moderate	moderate	weak	moderate	weak	moderate	weak
Xiao et al. (2020)	moderate	moderate	strong	moderate	strong	weak	moderate

Supplementary Table 2. Results of included studies for the association between visual impairment and incident all-cause dementia or key dementia subtypes.

Study	Outcome assessment/diagnosis	Visual impairment (VI) assessment/diagnosis	Adjustment	Effect size (95% CI)	*P* value
Brenowitz et al. (2019)	Hospitalization with dementia as primary or secondary diagnosis, dementia medication or at least 1.5 SD decline from baseline in 3MS	Visual acuity of 20/40 or worse measured using corrective lenses with the Bailey-Lovie distance test Contrast sensitivity of <1.55 log units measured using corrective lenses with the Pelli-Robson letter charts	Age, race, sex, education, use of corrective lenses, hypertension, diabetes, cardiovascular disease, cerebrovascular disease, smoking, alcohol use, physical activity	<u>All-cause dementia</u> HR of mild VI to blind[*] = 1.26 (0.90-1.77) HR of contrast sensitivity impairment = 1.11 (0.88-1.38)	0.18[†] 0.38[†]
Davies-Kershaw et al. (2018)	Self- or proxy reported dementia diagnosis, a score <3.5 on IQCODE or dementia medication	Self-reported vision or registered as partially sighted or blind categorized as normal vision (excellent or very good), mild to moderate VI (good or fair), severe VI to blind[*]	Sex, wealth, education, diabetes, hypertension, stroke, smoking[b]	<u>All-cause dementia</u> Aged 50-69: HR of mild to moderate VI[*] = 1.78 (1.04-3.04) HR of severe VI to blind[*] = 3.60 (1.10-11.78) Aged ≥70: HR of mild to moderate VI[*] = 1.22 (0.92-1.64) HR of severe VI to blind[*] = 1.24 (0.69-2.22)	0.036[†] 0.034[†] NR

					NR
Fischer et al. (2016)	MMSE score of <24 or self- or proxy-reported history of dementia or AD	Contrast sensitivity of <1.55 log units in the better eye measured using Pelli-Robson letter charts	Age, sex, education, smoking, BMI, exercise, alcohol consumption, hypertension, diabetes, number of high inflammatory markers, non-HDL-C, mean IMT, frailty	All-cause dementia HR of contrast sensitivity impairment = 1.96 (1.25-3.07)	NR
Hwang et al. (2020)	Adjudicated, DSM-IV, NINCDS-ADRDA, NINDS-AIREN and AD Diagnostic and Treatment Centers criteria	Self-reported visual impairment defined as not being able to see well enough (with or without glasses) to drive and/or to watch TV and/or to read the newspaper and/or to recognize someone across the room	Age, sex, race, education, income, BMI, alcohol consumption, smoking, physical activity, cardiovascular disease, cerebrovascular disease, diabetes, hypertension, clinic site, treatment status, APOE, hearing impairment	All-cause dementia HR of mild to severe VI = 1.32 (1.02-1.71) AD HR of mild to severe VI = 1.32 (0.97-1.80) VaD HR of mild to severe VI = 1.36 (0.82-2.25)	0.04 0.08 0.23
Klaver et al. (1999)	NINCDS-ADRDA criteria based on clinical/diagnostic evaluation, informant interview and medical records	Best-corrected visual acuity measured at a distance of 3m using a modified Early Treatment Diabetic Retinopathy chart categorized as normal to mild VI (≥0.03), moderate	Age, age^2, gender	AD RR of moderate to severe VI[*] = 1.01 (0.35-2.88) RR of blindness = 0.96 (0.68-7.05)	NR NR

		to severe VI (≥0.05 and <0.3) and blind (<0.05)*			
Lee et al. (2020)	Adjudicated, ICD-10 criteria	Visual acuity measured with corrective lenses using line score from the 20-feet Snellen's E chart; Snellen fractions converted to LogMAR with higher scores indicating poorer visual acuity and categorized as normal vision (<0.3) mild VI (0.3-0.47), moderate VI (0.48-0.99) and severe VI to blind (≥1.00)*	Age, sex, education, socioeconomic status, cataract, glaucoma, cardiovascular risk, hearing impairment, poor mobility, depression, physical exercise, intellectual activities, social activities, fruit and vegetable consumption, smoking	All-cause dementia HR of poorer visual acuity = 5.88 (4.04-8.57) HR of mild VI = 1.56 (1.17-2.06) HR of moderate VI = 2.27 (1.68-3.06) HR of severe VI to blindness* = 10.84 (6.60-17.81)	<0.001 0.002 <0.001 <0.001
Maruta et al. (2020)	Medical records, based on eligibility assessment for long-term care insurance (questionnaire supplemented by expert committee review taking into account reports from primary care physicians)‡	Medical records, based on eligibility assessment for long-term care insurance; visual acuity impairment defined as able to see vision testing chart at a distance of about 1m or in front or very poor eyesight compared to normal vision (no hindrance in daily life)	Age, sex, care-need level, degree of independent daily living	All-cause dementia HR of VI = 1.04 (0.85-1.26)	0.73
Naël et al. (2019)	Adjudicated, DSM-IV and NINCDS-ADRDA criteria	Mild near visual acuity impairment: mild VI:	Age, gender, education, center, hearing loss, living	All-cause dementia	

| | | Parinaud 3 or 4 (Snellen equivalent 20/30-20/60), moderate near visual acuity impairment to blind: Parinaud >4 (Snellen equivalent <20/60)[a]; self-reported distance visual function loss defined as inability or difficulty in recognizing a familiar face at 4 meters with corrective lenses | alone, income, depressive symptoms, smoking, BMI, hypertension, stroke history, history of cardiovascular disease, hypercholesterolemia, hypertriglyceridemia, diabetes, APOE e4 | HR of mild VI = 1.14 (0.90-1.43)[†]

HR of moderate VI to blindness[*] = 1.40 (1.05-1.86)[†]

HR of severe distance visual function loss = 1.30 (0.99-1.70)[†]

<2 years follow-up:

HR of mild VI = 1.63 (1.06-2.51)

HR of moderate VI to blindness[*] = 1.95 (1.16-3.28)

HR of severe distance visual function loss = 1.12 (0.63-1.99)

2-4 years follow-up:

HR of mild VI = 1.15 (0.71-1.86)

HR of moderate VI to blindness[*] = 1.82 (1.07-3.08) | 0.28[†]

0.02[†]

0.06[†]

0.027

0.012

0.70

0.57 |

				HR of severe distance visual function loss = 1.22 (0.70-2.13)	0.027
				≥4 years follow-up:	
				HR of mild VI = 1.00 (0.77-1.31)	0.48
				HR of moderate VI to blindness[*] = 1.34 (0.95-1.89)	
				HR of severe distance visual function loss = 1.49 (1.11-2.00)	0.99
					0.095
					0.008
Paik et al. (2020)	Medical records, ICD-10: F00, G30, F01, F02, F03, G23.1, G31.0, G31.1, G31.82, G31.83, G31.88, F10.7 for all-cause dementia, F00 and G30 for AD, and F01 for VaD	Measured best-corrected visual acuity of the worse eye categorized as <0.1 (severe VI to blind), <0.3 (moderate VI), <1.0 (mild VI) or ≥1.0 (normal vision)[*];	Age, sex, smoking, alcohol consumption, physical activity, diabetes, hypertension, lipid levels	All-cause dementia HR of mild VI[*] = 1.45 (1.42-1.48) HR of moderate VI[*] = 1.74 (1.70-1.78)	NR NR

				HR of severe VI to blindness[*] = 1.75 (1.71-1.79)	NR
				AD	
				HR of mild VI[*] = 1.47 (1.44-1.51)	NR
				HR of moderate VI[*] = 1.75 (1.70-1.80)	NR
				HR of severe VI to blindness[*] = 1.75 (1.70-1.80)	NR
				VaD	
				HR of mild VI[*] = 1.40 (1.33-1.47)	NR
				HR of moderate VI[*] = 1.73 (1.63-1.85)	NR
				HR of severe VI to blindness[*] = 1.79 (1.68-1.91)	NR
					NR

Rogers & Langa (2009)	Adjudicated, DSM-III-R and DSM-IV criteria	Self-reported vision categorized as normal vision (excellent or very good) or mild to severe VI or blind (good or fair or poor or blind) vision	Age, gender, race, education, APOE e4, head injury, diabetes, hypertension, stroke, heart disease	All-cause dementia RR of mild to severe VI or blind vision = 2.70 (1.25-5.56)§	0.014
Tran et al. (2020)	Adjudicated, DSM-IV criteria	Nonpinhole visual acuity of 20/40 or worse in at least 1 eye; self-reported moderate to severe VI* based on a visual function questionnaire	Age, race, hormone therapy, education, physical activity, hearing loss, smoking, baseline 3MS score, depression, cardiovascular disease, congestive heart failure, hypertension, hyperlipidemia, chronic pulmonary disease, peptic ulcer disease, liver disease, leukemia or lymphoma, diabetes	All-cause dementia HR of mild VI to blindness* = 2.14 (1.08-4.21) HR of moderate to severe VI* = 1.22 (0.56-2.66)	0.03 0.61

AD, Alzheimer's disease; BMI, body mass index; CI, confidence interval; DSM-III-R, Diagnostic and Statistical Manual of Mental disorders, Third Edition, Revised; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; HR, hazard ratio; ICD-10, International Statistical Classification of Diseases and Related Health Problems, Tenth Revision; IMT, intima-media thickness, IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; LogMAR, Logarithm of the Minimum Angle of Resolution; MMSE, Mini-Mental State Examination; non-HLC-C, NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association; NINDS-AIREN, National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences; non-high-density lipoprotein cholesterol; NR, not reported; RR, risk ratio; SD, standard deviation; 3MS, Modified Mini-Mental State Examination; VI, visual impairment; 3MS, Modified Mini-Mental State Examination;

* Description of categories based on the WHO definition of visual impairment [32] to enable comparability with other studies

†Additional information provided by the authors

‡As previously described [34, 35]

§Comparison group reversed for comparability of results; better vision reported as normal and worse vision described as mild to poor/blind to allow comparisons with other studies; better versus worse vision: RR = 0.37 (0.18-0.80)

Supplementary Table 3. Results of included studies for the association between glaucoma and incident all-cause dementia or key dementia subtypes.

Study	Outcome assessment/diagnosis	Glaucoma assessment/diagnosis	Adjustment	Effect size (95% CI)	*P* value
Chen et al. (2018)	Medical records, ICD-9-CM: 290.x, 291.2, 292.82, 294.x, 331.0 for all-cause dementia[*] and 331.0 for AD	Medical records, ICD-9-CM: 365.12 for NTG and 365.11 for HTG[*]	Age, sex, diabetes, hypertension, hyperlipidemia, coronary artery disease, stroke	<u>All-cause dementia</u> HR of NTG = 1.39 (1.25 – 1.46) <u>AD</u> HR of NTG = 1.52 (1.41-1.63) HR of HTG = 1.12 (0.89-1.36)	<0.0001 <0.0001 0.38[*]
Ekström & Kilander (2013)	Medical records, NINCDS-ADRDA criteria	Presence of a reproducible visual field defect on eye examination	Age, sex, deaths, pseudoexfoliation	<u>All-cause dementia</u> HR of OAG = 1.09 (0.69-1.74)	0.71[*]
Helmer et al. (2013)	Adjudicated, DSM-IV criteria	Adjudicated based on eye examination	Age, sex, education, hypertension, diabetes, history of cardiovascular ischemic disease, stroke history, familial history of glaucoma, APOE e4	<u>All-cause dementia</u> OR of OAG = 3.9 (1.5-10.4)	0.0054

Keenan et al. (2015)	Medical records, ICD-10: F00, G30 for AD and F01 for VaD	Medical records, ICD-10: H40.1	Age, sex, calendar year of admission, region of residence, socioeconomic status	AD SRR of POAG = 1.01 (0.96-1.06) VaD SRR of POAG = 1.10 (1.05-1.16)	NR NR
Kuo et al. (2020)	Medical records, diagnoses of AD, VaD, and Parkinson's disease with concurrent dementia according to ICD-9/ICD-10 codes	Medical records diagnosis of glaucoma made by an ophthalmologist according to ICD-9/ICD-10 codes	Age, gender, education, marital status, hypertension, diabetes, ischemic heart disease, hyperlipidemia, congestive heart failure, peripheral vascular disease, cerebrovascular disease, sensorineural hearing loss, AMD, hemiplegia or paraplegia	All-cause dementia HR of any glaucoma = 0.96 (0.89-1.04) HR of OAG = 0.87 (0.76-1.00) HR of NTG = 1.17 (0.98-1.40) HR of ACG = 0.91 (0.81-1.02) AD HR of any glaucoma = 1.02 (0.76-1.36) HR of OAG = 0.83 (0.49-1.39) HR of NTG = 0.93 (0.45-1.92)	0.3443 NR NR NR 0.9025 NR

				HR of ACG = 0.93 (0.62-1.38)	NR
				VaD HR of any glaucoma = 0.93 (0.85-1.02)	NR
				HR of OAG = 0.83 (0.71-0.98)	
				HR of NTG = 1.07 (0.87-1.33)	0.1154
				HR of ACG = 0.90 (0.79-1.02)	NR
					NR
					NR
Lee et al. (2019)	Adjudicated, DSM-IV and NINCDS-ADRDA criteria	Medical records, ICD-9: 365.1*	Age, sex, education, race, APOE e4, smoking, AMD, diabetic retinopathy	All-cause dementia HR of glaucoma = 1.04 (0.89, 1.22) *	0.601[*]
				HR of glaucoma (0-5 yrs) = 1.32 (1.02-1.72)	0.04
				HR of glaucoma (>5 yrs) = 1.00 (0.84-1.20)	0.99

				AD HR of glaucoma = 0.95 (0.80-1.14) HR of glaucoma (0-5 yrs) = 1.46 (1.08-1.91) HR of glaucoma (>5 yrs) = 0.87 (0.71-1.07)	0.61 0.013 0.19
Lin et al. (2014)	Medical records, ICD-9-CM: 365.10, 365.11, 365.12,	Medical records, ICD-9-CM diagnoses	Age, sex, hypertension, diabetes, heart failure, stroke, insurance eligibility group, income, diagnostic year, urbanization level, CCI	AD HR of POAG = 1.40 (1.03-1.90)	0.033
Moon et al. (2018)	Medical records, KCD: F009, G300, G301, G308, G309	Medical records, KCD: H401, E6691 and prescribed glaucoma medication	Age, sex, residential area, income, CCI, hypertension, diabetes, hyperlipidemia, ischemic stroke	AD HR of POAG = 1.40 (1.18-1.67) HR of POAG (aged <65) = 1.17 (0.90-1.52) HR of POAG (aged ≥65) = 1.75 (1.40-2.17)	<0.001 NR NR
Ou et al. (2012)	Medical records, ICD-9-CM: 331.0 for AD and 290, 290.0-4, 290.8-9, 291.0, 291.2, 292.82,	Medical records, ICD-9-CM: 365.1, 365.10, 365.11, 365.12, 365.15	Age, sex, race, CCI, dry AMD, wet AMD, unspecified AMD, background DR,	All-cause dementia	NR

	294.0-1, 294.8, 331.1-2, 331.7, 331.82, 797.xx for other dementia		proliferative DR, vitreous hemorrhage, cataract, pseudophakia/aphakia, cataract surgery	HR of OAG = 0.93 (0.91-0.95) AD HR of OAG = 0.91 (0.88-0.93)	NR
Su et al. (2016)	Medical records, ICD-9-CM: 290, 294.1, 331.0	Medical records, ICD-9-CM: 365.1 for POAG and 365.2 for PACG	Age, gender, hypertension, diabetes, coronary artery disease, hyperlipidemia, head injury	All-cause dementia HR of glaucoma = 1.13 (1.01-1.27) HR of POAG = 1.21 (1.02-1.43) HR of PACG = 1.09 (0.95-1.26)	0.03[*] 0.03[*] 0.23[*]
Xiao et al. (2020)	Adjudicated, DSM-IV and NINCDS-ADRDA criteria	Self-reported and confirmed by participants' medical records	Age, sex, education, APOE e4, baseline MMSE, smoking, alcohol consumption, hypertension, diabetes, BMI, depression, heart disease, cataract	All-cause dementia HR of glaucoma = 2.38 (1.08-5.23) AD HR of glaucoma = 2.77 (1.17-6.56)	0.03 0.02

ACG, angle-closure glaucoma; AD, Alzheimer's disease; AMD, age-related macular degeneration; APOE, apolipoprotein; CCI, Charlson comorbidities index; CI, confidence interval; DR, diabetic retinopathy; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; HR, hazard ratio; HTG, high tension glaucoma; ICD-8, International Classification of Diseases, Eighth Revision; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; ICD-10, International Classification of Diseases, Tenth Revision; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; KCD, Korean Classification of Diseases; MMSE, Mini-Mental State Examination; NR, not reported; NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related

Disorders Association; NTG, normal tension glaucoma; OAG, open-angle glaucoma; PACG, primary angle-closure glaucoma; POAG, primary open-angle glaucoma; SRR, standardized rate ratio; VaD, vascular dementia; yrs, years;

[*]Additional information provided by the authors

Supplementary Table 4. Results of included studies for the association between age-related macular degeneration and incident all-cause dementia or key dementia subtypes

Study	Outcome assessment/diagnosis	Visual impairment assessment/diagnosis	Adjustment	Effect size (95% CI)	*P* value
Choi et al. (2019)	Medical records, ICD-10: F00, G30	Medical records, ICD-10: H35.3	Age, sex, household income, smoking, alcohol consumption, physical activity, BMI, systolic blood pressure, fasting serum glucose, total cholesterol, CCI	<u>AD</u> HR of AMD = 1.48 (1.25-1.74)	NR
Keenan et al. (2014)	Medical records	Medical records	Age, sex, calendar year of admission, region of residence, socioeconomic status	<u>All-cause dementia</u> SRR of AMD = 0.91 (0.79-1.04) <u>AD</u> SRR of AMD = 0.86 (0.67-1.08)	0.19 0.22
Klaver et al. (1999)	NINCDS-ADRDA criteria based on clinical/diagnostic evaluation, informant interview and medical records	Ophthalmologic screening examination, diagnosis based on grading of fundus transparencies	Age, age^2, gender, smoking, atherosclerosis	<u>AD</u> RR of AMD (stage 1 or 2) = 1.0 (0.6-1.9) RR of AMD (stage 3 or 4) = 1.5 (0.6-3.5)	NR NR

Lee et al. (2019)	Adjudicated, DSM-IV and NINCDS-ADRDA criteria	Medical records, ICD-9: 362.50, 362.51, 362.52	Age, sex, education, race, APOE e4, smoking, glaucoma, DR	All-cause dementia HR of AMD = 1.16 (1.01, 1.34)[*]	0.038[*]
				HR of AMD (0-5 yrs) = 1.25 (1.03-1.53)	0.03
				HR of AMD (>5 yrs) = 1.39 (1.18-1.65) AD	<0.001
				HR of AMD =1.20 (1.02-1.40)	
				HR of AMD (0-5 yrs) = 1.20 (0.95-1.50)	0.03
				HR of AMD (>5 yrs) = 1.50 (1.25-1.81)	0.12
					<0.001
Tsai et al. (2015)	Medical records, ICD-9-CM: 331.0, 290.xx	Medical records, ICD-9-CM: 362.50, 362.51, 362.52	Age[†], sex[†], time of enrolment[†], Parkinson's disease, hypertension, diabetes, dysrhythmia, coronary artery disease, hyperlipidemia, number of insurance claims for outpatients' visits	All-cause dementia HR of AMD = 1.44 (1.26-1.64)	<0.001
				HR of exudative AMD = 1.35 (0.89-2.06)	0.163
				HR of nonexudative AMD = 1.44 (1.26-1.65)	<0.001

AMD, age-related macular degeneration; BMI, body mass index; CI, confidence interval; CCI, Charlson comorbidity index; DR, diabetic retinopathy; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; HR, hazard ratio; ICD-9, International Classification of Disease, Ninth Revision; ICD-10, International Classification of Disease, Tenth Revision; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association; NR, not reported; OAG, open-angle glaucoma; RR, risk ratio; SRR, standardized rate ratio; yrs, years;

*Additional information provided by the authors

†Participants with and without AMD matched for age, sex and time of enrolment

Supplementary Table 5. Results of included studies for the association between cataract diagnosis and incident all-cause dementia or key dementia subtypes

Study	Outcome assessment/diagnosis	Visual impairment assessment/diagnosis	Adjustment	Effect size (95% CI)	*P* value
Ekström & Kilander (2013)	Medical records, NINCDS-ADRDA criteria	Presence of cataract on eye examination	Age, sex	All-cause dementia SRR of cataract = 1.14 (0.83-1.58)	NR
Lai et al. (2014)	Medical records, ICD-9: 331.0	Medical records, ICD-9: 366	Age, sex, diabetes, head injury, hypertension	AD HR of cataract = 1.43 (1.13-1.82)	0.0032*
Lee et al. (2019)	Adjudicated, DSM-IV and NINCDS-ADRDA criteria	Medical records, ICD-9: 366.*	Age, sex, education, race, APOE e4, smoking, glaucoma, AMD, diabetic retinopathy	All-cause dementia HR of cataract = 1.17 (0.94, 1.47)* AD HR of cataract = 1.13 (0.88, 1.45)* HR of cataract (0-5 yrs) = 0.99 (0.73-1.32) HR of cataract (>5 yrs) = 1.21 (0.93-1.57)	0.167* 0.345* 0.92 0.15

| Xiao et al. (2020) | Adjudicated, DSM-IV and NINCDS-ADRDA criteria | Self-reported and confirmed by participants' medical records | Age, sex, education, APOE e4, baseline MMSE, smoking, alcohol consumption, hypertension, diabetes, BMI, depression, heart disease, glaucoma | All-cause dementia

HR of cataract = 1.23 (0.85-1.79)

AD

HR of cataract = 1.14 (0.73-1.77) | 0.28

0.57 |

AMD, age-related macular degeneration; APOE, apolipoprotein; BMI, body mass index; CI, confidence interval; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; HR, hazard ratio; ICD-8, International Classification of Disease, Eighth Revision; ICD-9, International Classification of Diseases, Ninth Revision; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; MMSE, Mini-Mental State Examination; NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association; SRR, standardized rate ratio; yrs, years;

*Additional information provided by the authors

Supplementary Table 6. Results of included studies for the association between diabetic retinopathy and incident all-cause dementia or key dementia subtypes

Study	Outcome assessment/diagnosis	Visual impairment assessment/diagnosis	Adjustment	Effect size (95% CI)	*P* value
Exalto et al. (2014)	Medical records, ICD-9: 290.0, 331.0, 290.4x, 290.1, 290.0, 290.1x, 331.0, 290.1x, 290.2x, 290.3, 290.4x	Medical record, ICD-9: 250.5, 362.02 for DPR and 250.5, 362.53, 250.5, 362.83 for DME	Age, sex, race, education, medical utilization, composite measures of diabetes severity and vascular disease, BMI, smoking Age, gender, race, education, medical utilization, diabetic medication use	<u>All-cause dementia</u> HR of DR = 1.32 (1.17-1.49) HR of proliferative DR = 1.40 (1.12-1.74) HR of DME = 1.42 (1.23-1.63)	NR NR NR
Lee et al. (2019)	Adjudicated, DSM-IV and NINCDS-ADRDA criteria	Medical records, ICD-9: 362.50, 362.51, 362.52	Age, sex, education, race, APOE e4, smoking, glaucoma, AMD	<u>All-cause dementia</u> HR of DR = 1.80 (1.41, 2.29)[*] HR of DR (0-5 yrs) = 1.96 (1.31-2.96) HR of DR (>5 yrs) = 1.87 (1.39-2.51)	<0.001[*] 0.001

				AD	<0.001
				HR of DR = 1.44 (1.08-1.94)	
				HR of DR (0-5 yrs) = 1.67 (1.01-2.74)	0.02
				HR of DR (>5 yrs) = 1.50 (1.05-2.15)	0.045
					0.027
Rodill et al. (2018)	Medical records, ICD-9: 331.0, 290.4x, 290.0, 291.1x, 290.2x, 290.3, 294.1x, 294.2x, 294.8	Medical records, ICD-9:362.02, 362.07, 362.53, 362.83, 250.5x, 362.0x and CPT-4: 67228, 67208, 67210	Age, sex, race, glycosylated hemoglobin, neuropathy, diabetic nephropathy, end-stage renal disease, cardiovascular disease, stroke, hyperglycemic or hypoglycemic episodes	All-cause dementia HR of DR = 1.12 (0.82-1.54)	NR
Schrijvers et al. (2012)	Adjudicated, DSM-III-R, NINCDS-ADRDA and NINDS-AIREN criteria	Ophthalmologic examination, presence of ≥1dot/blot hemorrhages, microaneurysms, or cotton wool spots or evidence of laser treatment for retinopathy	Age, sex, stroke, SBP, antihypertensive medication, education, APOE e4, smoking, diabetes, total cholesterol, CRP, coronary heart disease	All-cause dementia HR of DR = 1.15 (0.89-1.50) AD HR of DR = 1.15 (0.86-1.55) VaD	NR NR NR

				HR of DR = 0.90 (0.39-2.11)	

AMD, age-related macular degeneration; CI, confidence interval; CPT-4, Current Procedural Terminology, 4th edition; CRP, C-reactive protein; DME, diabetic macular edema; DR, diabetic retinopathy; DSM-III-R, Diagnostic and Statistical Manual of Mental disorders, Third Edition, Revised; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition; HR, hazard ratio; ICD-9, International Classification of Disease, Ninth Revision; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification; IQCODE, Informant Questionnaire on Cognitive Decline in the Elderly; NINCDS-ADRDA, National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's Disease and Related Disorders Association; NINDS-AIREN, National Institute of Neurological and Communicative Disorders and Stroke – Association Internationale pour la Recherché et l'Enseigment en Neurosciences; NR, not reported; OAG, open-angle glaucoma; SBP, systolic blood pressure;

[*] Additional information provided by the authors

Supplementary Table 7. Results of included studies for the association between other eye conditions and incident all-cause dementia or key dementia subtypes

Study	Outcome assessment/diagnosis	Visual impairment assessment/diagnosis	Adjustment	Effect size (95% CI)	*P* value
Nam et al. (2021)	Medical records, ICD-10-CM code F00 and/or G30 and a prescription for donepezil, rivastigmine, galantamine and/or memantine for AD; ICD-10-CM code F01 and a prescription for medication for VaD; NINDS-AIREN criteria	Medical record, ICD-10-CM code H34.8 for central retinal vein occlusion or 362.36 for venous tributary occlusion	Age, sex, smoking, alcohol consumption, physical activity, BMI, hypertension, diabetes, dyslipidemia	All-cause dementia HR of RVO = 1.16 (1.12-1.21) AD HR of RVO = 1.15 (1.11-1.20) VaD HR of RVO = 1.24 (1.12-1.37)	NR NR NR

AD, Alzheimer's disease; BMI, body mass index; ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; NINDS-AIREN, National Institute of Neurological and Communicative Disorders and Stroke – Association Internationale pour la Recherché et l'Enseigment en Neurosciences; RVO, retinal vein occlusion; VaD, vascular dementia;

1   exp Vision/ (27341)
2   vision.ti,ab. (109239)
3   (visual adj (function$ or acuity)).ti,ab. (69747)
4   exp Vision Disorders/ (70736)
5   exp Refractive Errors/ (32169)
6   (presbyop$ or myop$ or astigmati$ or hyperop$).ti,ab. (60460)
7   exp Diabetic Retinopathy/ (23909)
8   diabetic retinopath$.ti,ab. (21700)
9   exp Hypertensive Retinopathy/ (172)
10   hypertensive retinopath$.ti,ab. (622)
11   exp Retinal Artery Occlusion/ (2242)
12   exp Retinal Vein Occlusion/ (4083)
13   (retina$1 adj3 occlu$).ti,ab. (7730)
14   exp Retinal Degeneration/ (41251)
15   (retina$1 adj3 degenerat$).ti,ab. (10185)
16   (macular adj3 degenerat$).ti,ab. (19534)
17   exp Retinal Hemorrhage/ (5177)
18   retina$1 hemorrhage$1.ti,ab. (1754)
19   (armd or amd).ti,ab. (12683)
20   exp Cataract/ (28455)
21   cataract.ti,ab. (46718)
22   (visual$ adj3 impair$).ti,ab. (16022)
23   exp Glaucoma/ (51596)
24   glaucoma.ti,ab. (55325)
25   1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or
21 or 22 or 23 or 24 (432503)
26   exp Dementia/ (160636)
27   exp Alzheimer Disease/ (90897)
28   *dementia, vascular/ or *dementia, multi-infarct/ or *frontotemporal dementia/ or *primary progressive
nonfluent aphasia/ (6357)
29   dement$.ti,ab. (108310)
30   alzheimer$.ti,ab. (138948)
31   ((vascular or frontotemporal) adj dementia).ti,ab. (11808)
32   26 or 27 or 28 or 29 or 30 or 31 (245778)
33   prospective$.ti,ab. (674356)
34   longitudinal.ti,ab. (234819)
35   *Longitudinal Studies/ (1822)
36   *Prospective Studies/ (390)
37   predict$.ti,ab. (1511606)
38   inciden$.ti,ab. (851157)
39   determinant$1.ti,ab. (227114)
40   hazard$1.ti,ab. (212995)
41   risk.ti,ab. (2001927)
42   33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 (4482544)
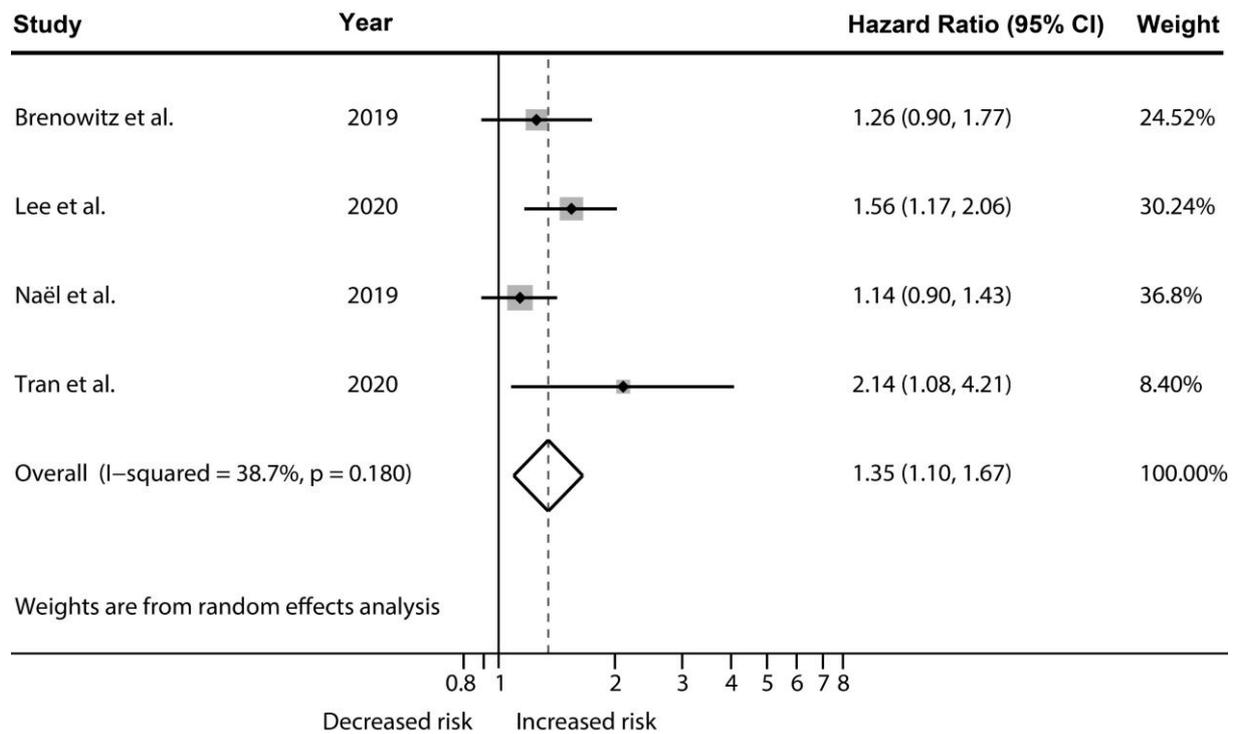43   25 and 32 and 42 (861)

Supplementary Figure 1. Search strategy in Medline

1   exp vision/ (254619)
2   vision.ti,ab. (148236)
3   (visual adj (function$ or acuity)).ti,ab. (91032)
4   exp visual disorder/ (227581)
5   exp refraction error/ (49630)
6   (presbyop$ or myop$ or astigmati$ or hyperop$).ti,ab. (76449)
7   exp diabetic retinopathy/ (40958)
8   diabetic retinopath$.ti,ab. (30108)
9   exp hypertension retinopathy/ (1264)
10   hypertensive retinopath$.ti,ab. (845)
11   exp retina artery occlusion/ (5003)
12   exp retina vein occlusion/ (8442)
13   (retina$1 adj3 occlu$).ti,ab. (10074)
14   exp retina degeneration/ (39552)
15   (retina$1 adj3 degenerat$).ti,ab. (13374)
16   (macular adj3 degenerat$).ti,ab. (26499)
17   exp retina hemorrhage/ (8288)
18   retina$1 hemorrhage$1.ti,ab. (2306)
19   (armd or amd).ti,ab. (18728)
20   exp cataract/ (56717)
21   cataract.ti,ab. (54611)
22   exp visual impairment/ (94245)
23   (visual$ adj3 impair$).ti,ab. (22450)
24   exp glaucoma/ (80573)
25   glaucoma.ti,ab. (65616)
26   1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or
21 or 22 or 23 or 24 or 25 (699521)
27   exp dementia/ (349154)
28   exp Alzheimer disease/ (194250)
29   exp multiinfarct dementia/ (11992)
30   *frontal variant frontotemporal dementia/ or *primary progressive aphasia/ (2236)
31   dement$.ti,ab. (158896)
32   alzheimer$.ti,ab. (192959)
33   ((vascular or frontotemporal) adj dementia).ti,ab. (18311)
34   27 or 28 or 29 or 30 or 31 or 32 or 33 (400689)
35   prospective$.ti,ab. (1037368)
36   longitudinal.ti,ab. (315334)
37   *prospective study/ (23152)
38   *longitudinal study/ (7189)
39   predict$.ti,ab. (2034052)
40   inciden$.ti,ab. (1197569)
41   determinant$1.ti,ab. (274923)
42   hazard$1.ti,ab. (304006)
43   risk.ti,ab. (2913315)
44   35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 (6172643)
45   26 and 34 and 44 (3021)

**Supplementary Figure 2. Search strategy in Embase**

1   exp Vision/ (15506)
2   vision.ti,ab. (44413)
3   (visual adj (function$ or acuity)).ti,ab. (5928)
4   exp Vision Disorders/ (16685)
5   exp Refraction Errors/ (547)
6   (presbyop$ or myop$ or astigmati$ or hyperop$).ti,ab. (3685)
7   diabetic retinopath$.ti,ab. (344)
8   hypertensive retinopath$.ti,ab. (8)
9   (retina$1 adj3 occlu$).ti,ab. (84)
10   (retina$1 adj3 degenerat$).ti,ab. (655)
11   (macular adj3 degenerat$).ti,ab. (597)
12   retina$1 hemorrhage$1.ti,ab. (61)
13   (armd or amd).ti,ab. (388)
14   exp Cataracts/ (303)
15   cataract.ti,ab. (559)
16   (visual$ adj3 impair$).ti,ab. (6803)
17   exp Glaucoma/ (451)
18   glaucoma.ti,ab. (902)
19   1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 (74140)
20   exp Dementia/ (74758)
21   exp Alzheimer's Disease/ (45292)
22   exp vascular dementia/ (2073)
23   exp semantic dementia/ (1906)
24   dement$.ti,ab. (63793)
25   alzheimer$.ti,ab. (57660)
26   ((vascular or frontotemporal) adj dementia).ti,ab. (6442)
27   20 or 21 or 22 or 23 or 24 or 25 or 26 (99711)
28   prospective$.ti,ab. (66174)
29   longitudinal.ti,ab. (108129)
30   *longitudinal studies/ (2952)
31   *prospective studies/ (94)
32   predict$.ti,ab. (436974)
33   inciden$.ti,ab. (77906)
34   determinant$1.ti,ab. (51052)
35   hazard$1.ti,ab. (17471)
36   risk.ti,ab. (338831)
37   28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 (898379)
38   19 and 27 and 37 (303)

Supplementary Figure 3. Search strategy in PsycINFO

Study	Year	Hazard Ratio (95% CI)	Weight
Brenowitz et al.	2019	1.26 (0.90, 1.77)	24.52%
Lee et al.	2020	1.56 (1.17, 2.06)	30.24%
Naël et al.	2019	1.14 (0.90, 1.43)	36.8%
Tran et al.	2020	2.14 (1.08, 4.21)	8.40%
Overall (I−squared = 38.7%, p = 0.180)		1.35 (1.10, 1.67)	100.00%

Weights are from random effects analysis

0.8 1   2   3   4   5 6 7 8

Decreased risk   Increased risk

Supplementary Figure 4. Meta-analysis of hazard ratios of at least mild visual impairment compared to normal vision on incident all-cause dementia excluding three studies assessing self-reported vision
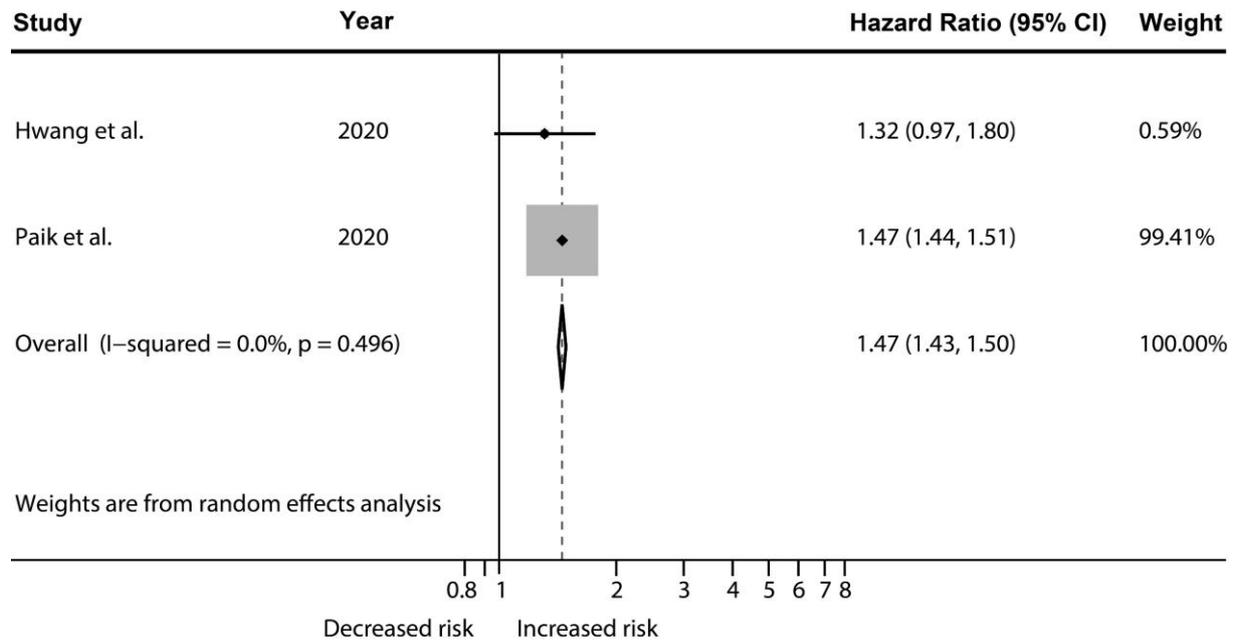
Abbreviations: CI, confidence interval
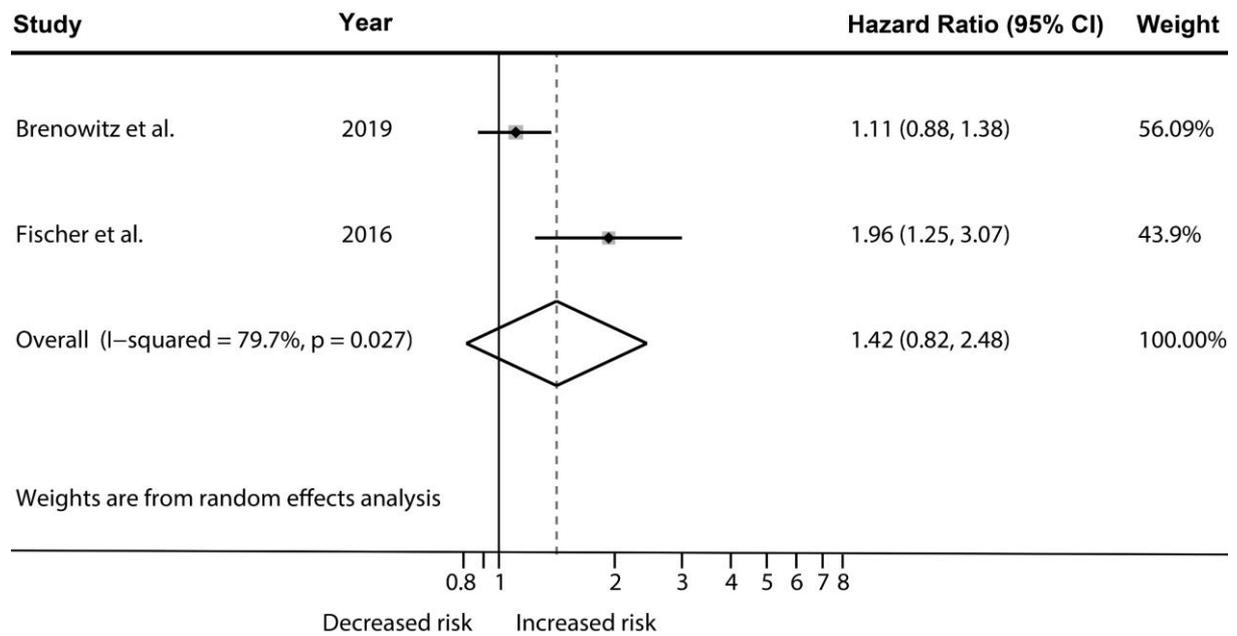
Supplementary Figure 5. Meta-analysis of hazard ratios of low contrast sensitivity compared to normal contrast sensitivity on incident all-cause dementia

Abbreviations: CI, confidence interval

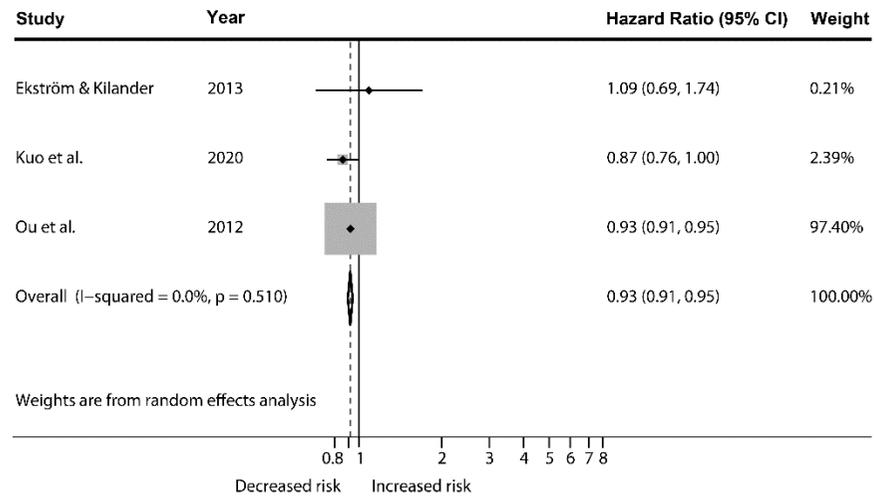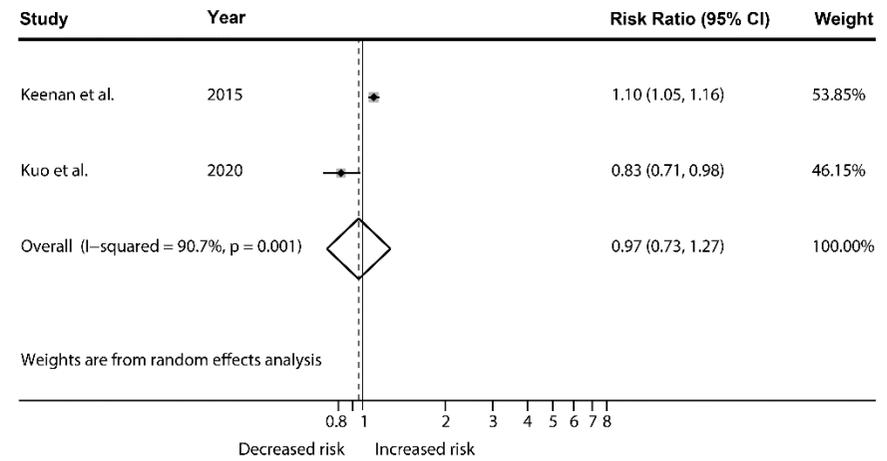**A. Alzheimer's disease**
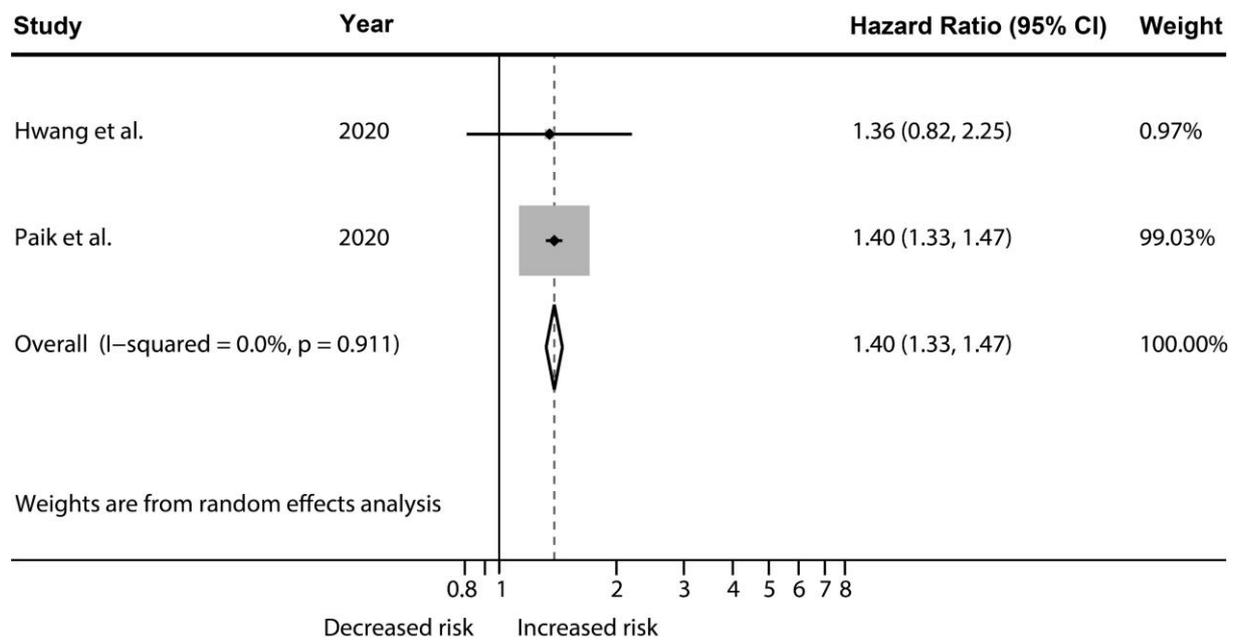
Supplementary Figure 6. Meta-analysis of hazard ratios of mild to severe visual impairment compared to normal vision on incident Alzheimer's disease (A) and vascular dementia (B)

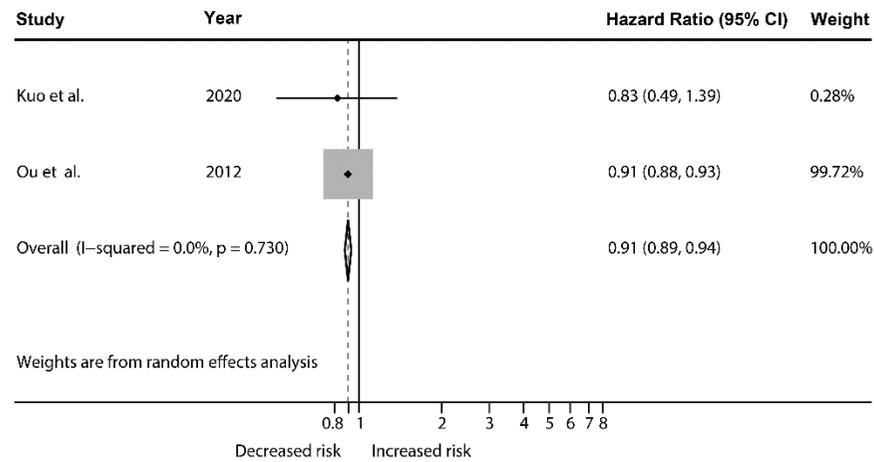Abbreviations: CI, confidence interval

A. All-cause dementia

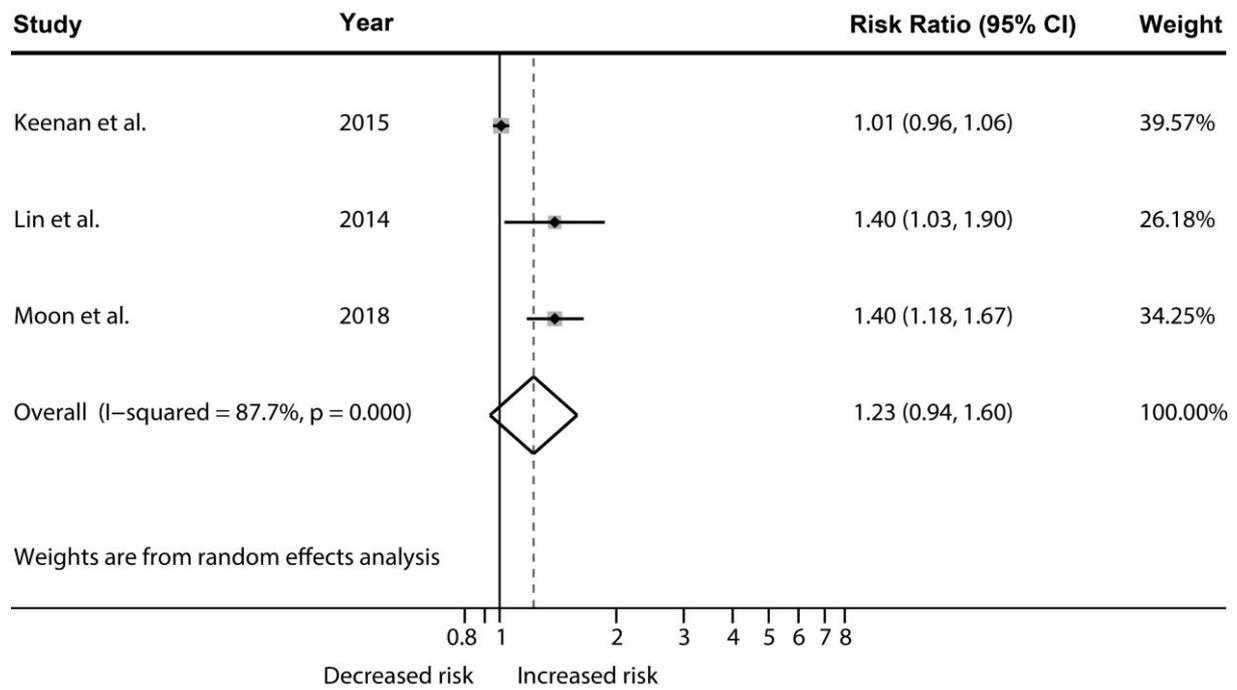| Study	Year		Hazard Ratio (95% CI)	Weight
Ekström & Kilander	2013		1.09 (0.69, 1.74)	0.21%
Kuo et al.	2020		0.87 (0.76, 1.00)	2.39%
Ou et al.	2012		0.93 (0.91, 0.95)	97.40%
Overall (I−squared = 0.0%, p = 0.510)			0.93 (0.91, 0.95)	100.00%

Weights are from random effects analysis

0.8 1   2   3   4   5   6   7   8

Decreased risk   Increased risk

B. Alzheimer's disease

Study	Year		Hazard Ratio (95% CI)	Weight
Kuo et al.	2020		0.83 (0.49, 1.39)	0.28%
Ou et al.	2012		0.91 (0.88, 0.93)	99.72%
Overall (I−squared = 0.0%, p = 0.730)			0.91 (0.89, 0.94)	100.00%

Weights are from random effects analysis

0.8 1   2   3   4   5   6   7   8

Decreased risk   Increased risk

C. Vascular dementia

Study	Year		Risk Ratio (95% CI)	Weight
Keenan et al.	2015		1.10 (1.05, 1.16)	53.85%
Kuo et al.	2020		0.83 (0.71, 0.98)	46.15%
Overall (I−squared = 90.7%, p = 0.001)			0.97 (0.73, 1.27)	100.00%

Weights are from random effects analysis

0.8 1   2   3   4   5   6   7   8

Decreased risk   Increased risk

Supplementary Figure 7. Meta-analysis of risk ratios of open-angle glaucoma compared to no open-angle glaucoma on incident all-cause dementia, Alzheimer's disease and vascular dementia

Abbreviations: CI, confidence interval

Study	Year	Risk Ratio (95% CI)	Weight
Keenan et al.	2015	1.01 (0.96, 1.06)	39.57%
Lin et al.	2014	1.40 (1.03, 1.90)	26.18%
Moon et al.	2018	1.40 (1.18, 1.67)	34.25%
Overall (I−squared = 87.7%, p = 0.000)		1.23 (0.94, 1.60)	100.00%

Weights are from random effects analysis

0.8 1   2   3   4 5 6 7 8

Decreased risk   Increased risk

Supplementary Figure 8. Meta-analysis of risk ratios of primary open-angle glaucoma compared to no primary open-angle glaucoma on incident Alzheimer's disease

Abbreviations: CI, confidence interval