H.3.2 Tools for triage, diagnosis and informed treatment

Review question

RQ4: What tools are useful for triage, diagnosis, informing treatment and determining management in people with suspected AMD?

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	LRs	Effect size (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Diagnostic tools for use in detecting drusen											
Fundus photograph (grading criteria) to detect drusen											
1 (Lim 2002)	Prospective case series	33 eyes (17 people)	50.0% (9.4, 90.6)	98.4% (79.4, 99.9)	LR+	32.00 (1.64, 626.10)	Very serious[1,2]	N/A	Not serious	Serious[3]	VERY LOW
					LR-	0.51 (0.16, 1.58)	Very serious[1,2]	N/A	Not serious	Serious[3]	VERY LOW
Diagnostic tools for use in detecting age-related macular degeneration											
Optical coherence tomography vs Fundus photograph to detect age-related macular degeneration(the presence of ≥10 small (≤63µm) hard druse and pigmentary changes or at least intermediate or large drusen inside the 6mm ETDRS grid)											
1 (Mokwa 2013)	Retrospective case-control	120 eyes (66 people)	89.3% (81.5, 95.2)	75.6% (62.2, 86.8)	LR+	3.65 (2.17, 6.14)	Very serious[4]	N/A	Not serious	Not serious	LOW
					LR-	0.14 (0.07, 0.28)	Very serious[4]	N/A	Not serious	Not serious	LOW
Fluorescein angiography vs Fundus photograph to detect age-related macular degeneration(the presence of ≥10 small (≤63µm) hard druse and pigment changes or at least intermediate or large drusen inside the 6mm ETDRS grid)											
1 (Mokwa 2013)	Retrospective case-control	120 eyes (66 people)	92.0% (84.9, 97.0)	82.2% (69.9, 91.8)	LR+	5.18 (2.75, 9.73)	Very serious[4]	N/A	Serious[5]	Not serious	VERY LOW
					LR-	0.10	Very	N/A	Serious[5]	Not serious	VERY LOW

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	LRs	Effect size (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
						(0.04, 0.21)	serious[4]				
Diagnostic tools for use in detecting dry age-related macular degeneration											
Fundus photography vs clinical assessment to detect geographic atrophy											
1 (Pirbhai 2004)	Prospective case series	223 eyes (118 people)	66.0% (51.5, 78.0)	86.9% (81.1, 91.2)	LR+	5.05 (3.27, 7.78)	Serious[4]	N/A	Serious[5]	Not serious	LOW
					LR-	0.39 (0.26, 0.59)	Serious[4]	N/A	Serious[5]	Serious[3]	VERY LOW
Diagnostic tools for use in detecting pigment epithelial detachment(PED)											
Fundus photography vs clinical assessment to detect pigment epithelial detachment(PED)											
1 (Pirbhai 2004)	Prospective case series	223 eyes (118 people)	40.0% (21.44, 61.6)	94.1% (90.5, 96.9)	LR+	6.77 (3.14, 14.58)	Serious[4]	N/A	Serious[5]	Not serious	LOW
					LR-	0.64 (0.45, 0.91)	Serious[4]	N/A	Serious[5]	Serious[3]	VERY LOW
Fundus photograph (grading criteria) to detect pigment epithelial detachment (PED)											
1 (Lim 2002)	Prospective cross sectional	33 eyes(17 people)	50.0% (18.5, 81.5)	98.2% (77.0, 99.9)	LR+	28.00 (1.63, 481. 68)	Very serious[1,2]	N/A	Not serious	Serious[3]	VERY LOW
					LR-	0.51 (0.24, 1.07)	Very serious[1,2]	N/A	Not serious	Serious[3]	VERY LOW
Diagnostic tools for use in detecting neovascular age-related macular degeneration/choroidal neovascularation											
Optical coherence tomography vs fluorescein angiography to detect choroidal neovascularisation (see figure 1, meta analysis)											
4 (Talks 2007; Wilde 2015;	Retrospective	30/128/ 476/130 /120 eyes (759	93.5% (72.2, 98.8)	89.2% (74.8, 95.8)	LR+	6.72 (3.19, 14.14)	Serious[4]	Serious[6]	Not serious	Not serious	LOW
					LR-	0.08 (0.02, 0.30)	Serious[4]	Serious[6]	Not serious	Not serious	LOW

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	LRs	Effect size (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Mathew 2014; Mokwa 2013)		people)									
3 (Do 2012; Padnick 2012; Sandhu 2005)	Prospective cohort	295 eyes: 87/77/131 eyes (282 people)	84.4% (49.0, 96.8)	75.0% (48.6, 90.5)	LR+	3.27 (1.27, 8.43)	Serious[7]	Serious[6]	Not serious	Serious[3]	VERY LOW
					LR-	0.21 (0.05, 0.96)	Serious[7]	Serious[6]	Not serious	Serious[3]	VERY LOW
Optical coherence tomography angiography vs fluorescein angiography to detect choroidal neovascularisation											
1 (De Carlo 2015)	Retrospective	30 eyes (24 people)	50.0% (20, 80%)	90.9% (70, 97.9%)	LR+	5.50 (1.24, 24.5)	Serious[4]	N/A	Not serious	Serious[3]	LOW
					LR-	0.55 (0.27, 1.11)	Serious[4]	N/A	Not serious	Serious[3]	LOW
Optical coherence tomography angiography vs fluorescein angiography to detect neovascular AMD											
1 (Gong 2016)	Retrospective	86 eyes (53 people)	86.5% (76.1-94.3%)	79.4% (64.5-91.0%)	**LR+**	4.20 (2.15,8.20)	Serious[8]	N/A	Not serious	Not serious	MODERATE
					LR-	0.17 (0.08, 0.35)	Serious[8]	N/A	Not serious	Not serious	MODERATE
Fluorescein angiography vs Indocyanine green angiography to detect wet age-related macular degeneration (predominantly classic, minimally classic, serous pigment epithelial detachment, disciform scar, branch retinal vein occlusion, retinal macroaneurysm, occult CNV, late leak, vascularised PED)											
1 (Talks 2007)	Retrospective audit	111 people	93.5% (87.9, 97.4)	96.2% (81.5,100.0)	LR+	24.31 (1.60, 368.47)	Very serious[4,8]	N/A	Not serious	Serious[3]	VERY LOW
					LR-	0.07 (0.03, 0.14)	Very serious[4,8]	N/A	Not serious	Not serious	LOW

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	LRs	Effect size (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
Fundus photography vs Fluorescein angiography to detect neovascular age-related macular degeneration – cohort study											
1 (Maberley 2005)	Prospective cross sectional	74 eyes (40 people)	97.0% (89.1, 99.9)	86.6% (74.8, 95.1)	LR+	7.23 (3.31, 15.77)	Serious[9]	N/A	Not serious	Not serious	MODERATE
					LR-	0.03 (0.01, 0.24)	Serious[9]	N/A	Not serious	Not serious	MODERATE
Fundus photography vs Fluorescein angiography to detect neovascular age-related macular degeneration – case-control study											
1 (Mokwa 2013)	Retrospective case control	120 eyes (66 people)	77.9% (67.4, 86.9)	98.1% (93.0, 100)	LR+	40.53 (5.79, 283,49)	Very serious[4]	N/A	Not serious	Not serious	LOW
					LR-	0.22 (0.14, 0.35)	Very serious[4]	N/A	Not serious	Not serious	LOW
Fundus photography + clinical information vs Fluorescein angiography to detect neovascular age-related macular degeneration											
1 (Maberley 2005)	Prospective cross sectional	74 eyes (40 people)	98.5% (92.7, 100)	76.2% (62.4, 87.6)	LR+	4.14 (2.41, 7.12)	Serious[9]	N/A	Not serious	Not serious	MODERATE
					LR-	0.02 (0.00, 0.30)	Serious[9]	N/A	Not serious	Not serious	MODERATE
Fundus photography vs clinical assessment to detect neovascular age-related macular degeneration											
1 (Pirbhai 2004)	Prospective case series	223 eyes (118 people)	82.1% (43.3, 89.5)	79.1% (72.0, 85.5)	LR+	3.94 (2.81, 5.53)	Serious[4]	N/A	Not serious	Not serious	MODERATE
					LR-	0.23 (0.14, 0.36)	Serious[4]	N/A	Not serious	Not serious	MODERATE
Fundus photograph (grading criteria) to detect CNV											
1 (Lim 2002)	Prospective cross sectional	33 eyes (17 people)	64.0% (44.7, 81.2)	87.5% (59.0, 99.6)	LR+	5.12 (0.80, 32.78)	Very serious[1,2]	N/A	Not serious	Serious[3]	VERY LOW
					LR-	0.41	Very	N/A	Not serious	Serious[3]	VERY LOW

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	LRs	Effect size (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
						(0.23, 0.74)	serious[1,2]				
Fundus autofluoresence vs fluorescein angiography to detect CNV											
1 (Cachulo 2011)	Prospective cohort	58 eyes (52 people)	88.2% (63.2, 97.0)	94.3% (79.8, 98.6)	LR+	15.44 (3.98, 59,97)	Very serious[1,8]	N/A	Not serious	Not serious	LOW
					LR-	0.12 (0.03, 0.46)	Very serious[1,8]	N/A	Not serious	Not serious	LOW
Indocyanine green angiography vs fluorescein angiography to detect choroidal neovascularisation (see figure 2, meta analysis)											
2 (Cachulo 2011; Sallet 1996)	Prospective cohort; retrospective cross sectional	52/58 eyes (104 people)	58.4% (46.2, 69.7)	82.8% (70.0, 90.8)	LR+	3.25 (1.64, 6.45)	Very serious[4,8]	Not serious	Not serious	Serious[3]	VERY LOW
					LR-	0.49 (0.36, 0.66)	Very serious[4,8]	Not serious	Not serious	Serious[3]	VERY LOW
Diagnostic tools for use in detecting polypoidal choroidal vasculopathy (PCV)											
Optical coherence tomography vs Indocyanine green angiography to detect polypoidal choroidal vasculopathy (PCV)											
1 (De Salvo 2014)	Retrospective case-control	51 eyes (44 people)	94.6% (85.5, 99.3)	92.9% (75.3, 99.8)	LR+	13.24 (2.00, 87.68)	Very serious[4]	N/A	Not serious	Not serious	LOW
					LR-	0.06 (0.02, 0.23)	Very serious[4]	N/A	Not serious	Not serious	LOW
Optical coherence tomography angiography (OCT-A) vs Indocyanine green angiography to detect polypoidal choroidal vasculopathy (PCV)											
1 (Cheung 2016)	Prospective cross section	86 eyes	40.5% (26.3, 55.5)	81.4% (68.6, 91.4)	**LR+**	2.18 (1.05, 4.49)	Serious[1]	N/A	Not serious	Serious	LOW
					LR-	0.73 (0.55, 0.98)	Serious[1]	N/A	Not serious	Not serious	MODERATE
Flash fundus camera-based indocyanine green angiography vs confocal scanning laser ophthalmoscope-based iIndocyanine green angiography											

No. of studies	Study design	Sample size	Sensitivity (95%CI)	Specificity (95%CI)	LRs	Effect size (95%CI)	Risk of bias	Inconsistency	Indirectness	Imprecision	Quality
(grading criteria) to detect polypoidal choroidal vasculopathy (PCV)											
1 (Cheung et al. 2015)	Retrospective comparative	241 eyes (230 people)	78.6% (71.2, 85.2)	87.3% (80.5, 92.8)	LR+	6.18 (3.76. 10.16)	Very serious[4,2]	N/A	Not serious	Not serious	LOW
					LR-	0.24 (0.18, 0.34)	Very serious[4,2]	N/A	Not serious	Not serious	LOW
Fundus photography vs clinical assessment to detect choroidal neovascular membrane											
1 (Pirbhai 2004)	Prospective case series	223 eyes (118 people)	89.2% (81.9, 93.8)	85.7% (77.9, 91.1)	LR+	6.24 (3.95, 9.87)	Serious[4]	N/A	Not serious	Not serious	MODERATE
					LR-	0.13 (0.07, 0.22)	Serious[4]	N/A	Not serious	Not serious	MODERATE

1. Downgraded one level for inadequate or unclear blinding between index test and reference standard;
2. Downgraded one level for exclusion criteria not reported;
3. Downgraded one level for confidence interval cross 1 line of defined minimal important difference;
4. Downgraded two levels for case-control study design; downgraded one level for case series, retrospective study;
5. Downgraded one level for reference test was not consistent with protocol reference test (OCT);
6. Downgraded one level for heterogeneity (i2>50%);
7. Downgraded one level for time interval between index test and reference standard unclear;
8. Downgraded one level for selection bias (pre-defined study population or patients being treated with anti-VGF);
9. Downgraded one level for risk of bias due to multiple imaging readers;

Figure 1: Optical coherence tomography vs fluorescein angiography to detect CNV

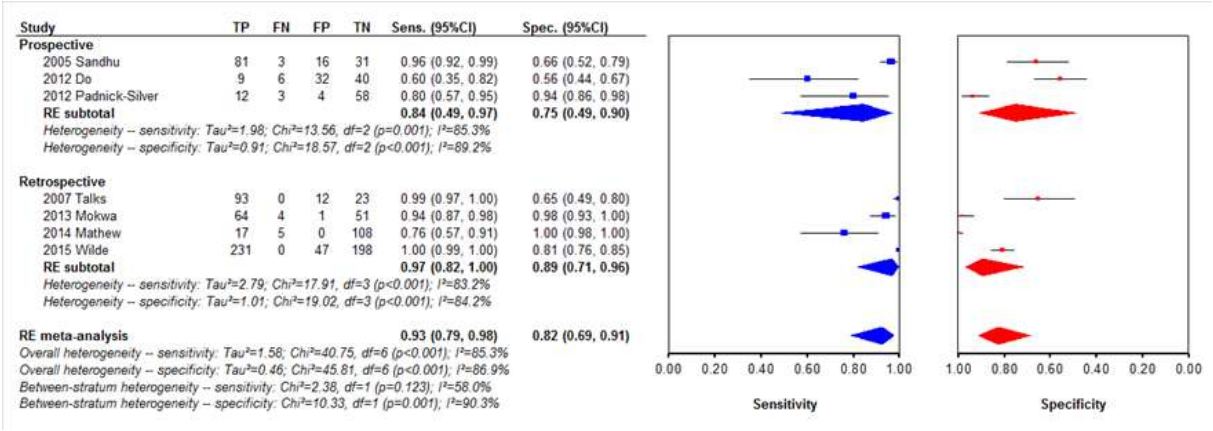

Figure 2: Indocyanine green angiography vs fluorescein angiography to detect CNV