E.3.2 Tools for triage, diagnosis and informed treatment

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

Bibliographic reference	**Cachulo,L., Silva,R., Fonseca,P., Pires,I., Carvajal-Gonzalez,S., Bernardes,R., Cunha-Vaz,J.G., Early markers of choroidal neovascularization in the fellow eye of patients with unilateral exudative age-related macular degeneration.Ophthalmologica, 225, 3, 144-149, 2011.**
Country/ies where the study carried out	USA
Study type	Prospective cohort study
Aim of the study	To identify morphological and/or functional early markers of choroidal neovascularization (CNV) development in fellow eyes of patients with exudative age-related macular degeneration (AMD).
Study dates	Not stated
Sources of funding	Not stated
Number of patients	62 patients
Inclusion criteria	Patients were older than 50 years of age Both gender Patients were able to give written consent to make the required visits and to follow instruction Patients had clinical diagnosis of wet AMD in one eye (non-study eye) and the presence of the following characteristics in the second eye (study eye): at least 5 or more intermediate (>63µm) or 1 large soft drusen (>125µm), and /or confluent drusen within 3,000µm of the foveal centre with or within pigmentary changes
Exclusion criteria	Patients had current or past history of a medical condition that would preclude scheduled study visits or completion of the study Patients had current or post history of an ophthalmic disease in the study eye (other than AMD) that would likely compromise the visual acuity of the study eye; Patient had clinical signs of myopic retinopathy or refractive power of >8dpt or funduscopic evidence of degenerative myopia; Patients had past history if intraocular surgery within 60 days prior to enrolling in the study Patients had evidence of past or present CNV in the study eye
Eligible participants characteristics	62 patients were enrolled in the study. 52 patients completed the 2-year follow up

<table>
<tr><th>Bibliographic reference</th><td>Cachulo,L., Silva,R., Fonseca,P., Pires,I., Carvajal-Gonzalez,S., Bernardes,R., Cunha-Vaz,J.G., Early markers of choroidal neovascularization in the fellow eye of patients with unilateral exudative age-related macular degeneration.Ophthalmologica, 225, 3, 144-149, 2011.</td></tr>
<tr><td></td><td>Mean age (SD): 76 (6) years
No. of men: 26 (50%)</td></tr>
<tr><td>Type of test</td><td>Indocyanine green angiography (ICG)
Optical coherence tomography (OCT)
Fundus autoflurescence (FAF)
Imaging and retinal leakage analysis (RLA)</td></tr>
<tr><td>Reference standard</td><td>Fluorescein angiography</td></tr>
<tr><td>Prevalence</td><td>33% of the 52 study eyes (17 eyes) were confirmed with CNV
<table>
<tr><td></td><td></td><td>FA</td><td></td><td></td></tr>
<tr><td>ICG</td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr>
<tr><td></td><td>Positive</td><td>9</td><td>7</td><td>16</td></tr>
<tr><td></td><td>Negative</td><td>8</td><td>28</td><td>36</td></tr>
<tr><td></td><td>Total</td><td>17</td><td>35</td><td>52</td></tr>
</table>
<table>
<tr><td></td><td></td><td>FA</td><td></td><td></td></tr>
<tr><td>FAF</td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr>
<tr><td></td><td>Positive</td><td>15</td><td>2</td><td>17</td></tr>
<tr><td></td><td>Negative</td><td>2</td><td>33</td><td>35</td></tr>
<tr><td></td><td>Total</td><td>17</td><td>35</td><td>52</td></tr>
</table>
<table>
<tr><td></td><td></td><td>FA</td><td></td><td></td></tr>
<tr><td>RLA</td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr>
<tr><td></td><td>Positive</td><td>13</td><td>8</td><td>21</td></tr>
</table></td></tr>
</table>

<table>
<tr><th>Bibliographic reference</th><td colspan="2">Cachulo,L., Silva,R., Fonseca,P., Pires,I., Carvajal-Gonzalez,S., Bernardes,R., Cunha-Vaz,J.G., Early markers of choroidal neovascularization in the fellow eye of patients with unilateral exudative age-related macular degeneration.Ophthalmologica, 225, 3, 144-149, 2011.</td></tr>
<tr><td></td><td colspan="2"><table>
<tr><td></td><td>Negative</td><td>1</td><td>27</td><td>28</td></tr>
<tr><td></td><td>Total</td><td>14 (as examination could not be processed in 3)</td><td>35</td><td>49</td></tr>
</table></td></tr>
<tr><td>Sensitivity</td><td colspan="2"><table>
<tr><td>ICG</td><td>52.9%, 95%CI 29.9 to 75.3%</td></tr>
<tr><td>FAF</td><td>88.2%, 95%CI 69.8 to 98.4%</td></tr>
<tr><td>OCT</td><td>-</td></tr>
<tr><td>RLA</td><td>92.8%, 95%CI 75.3 to 99.8%</td></tr>
</table></td></tr>
<tr><td>Specificity</td><td colspan="2"><table>
<tr><td>ICG</td><td>80.0%, 95%CI 65.5 to 91.3%</td></tr>
<tr><td>FAF</td><td>94.3% 95%CI 84.7 to 99.3%</td></tr>
<tr><td>OCT</td><td>-</td></tr>
<tr><td>RLA</td><td>77.1%, 95%CI 62.1 to 89.3%</td></tr>
</table></td></tr>
<tr><td>Positive predictive values</td><td colspan="2"><table>
<tr><td>ICG</td><td>56.3%, 95%CI 32.3 to 78.7%</td></tr>
<tr><td>FAF</td><td>88.2%, 95%CI 69.8 to 98.4%</td></tr>
<tr><td>OCT</td><td>-</td></tr>
<tr><td>RLA</td><td>61.9%, 95% CI 40.8 to 80.9%</td></tr>
</table></td></tr>
<tr><td>Negative predictive values</td><td colspan="2"><table>
<tr><td>ICG</td><td>80.6%, 95%CI 70.0 to 89.4%</td></tr>
<tr><td>FAF</td><td>94.3%, 95%CI 84.7 to 99.3%</td></tr>
<tr><td>OCT</td><td>-</td></tr>
<tr><td>RLA</td><td>96.4%, 95% CI 87.2 to 99.9%</td></tr>
</table></td></tr>
</table>

Bibliographic reference	**Cachulo,L., Silva,R., Fonseca,P., Pires,I., Carvajal-Gonzalez,S., Bernardes,R., Cunha-Vaz,J.G., Early markers of choroidal neovascularization in the fellow eye of patients with unilateral exudative age-related macular degeneration.Ophthalmologica, 225, 3, 144-149, 2011.**
Comments	Different imagings including OCT, ICG were evaluated for the development of CNV and the progression of early ARM to neovascular AMD Patient selection: Population eligiability was pre-defined (all included participants had a clinical diagnosis of wet AMD in one eye [non-study eye]). Patients satisfying the enrolment criteria completed the baseline/screening assessment and were follow-up for up to 24 months with repeated ophthalmic and imaging assessment performed at 6-month intervals. Patients developing CNV during the study were followed up for 6 months after the conversion to wet AMD and were treated at the discretion of the principlan investigator. Index test: blinding of index test was unclear. Reference standard: blinding of reference standard was unclear. Flow and timing: Patients were examined 6 months, but time intervals of tests were unclear. All patients included in the analysis.

Bibliographic reference	**Cheung,C.M., Laude,A., Wong,W., Mathur,R., Chan,C.M., Wong,E., Wong,D., Wong,T.Y., Lim,T.H., 20151209 Improved specificity of polypoidal choroidal vasculopathy diagnosis using a modified everest criteria.Retina, 35, 7, 1375-1380, 2015**
Country/ies where the study carried out	Singapore
Study type	Retrospective comparative study
Aim of the study	To evaluate the performance of a modified EVEREST criteria using flash fundus camera-based ICGA, and to compare the sensitivity and specificity of individual and combinations of features within the EVEREST criteria with that subretinal focal hyperflurescene alone.
Study dates	Not reported
Sources of funding	National Medical Research Council
Number of patients	230 patients
Inclusion criteria	Patients presenting with untreated exudative maculopathy (either typical neovascular AMD or PCV)
Exclusion criteria	Not reported

<table>
<tr><th>Bibliographic reference</th><th>Cheung,C.M., Laude,A., Wong,W., Mathur,R., Chan,C.M., Wong,E., Wong,D., Wong,T.Y., Lim,T.H., 20151209 Improved specificity of polypoidal choroidal vasculopathy diagnosis using a modified everest criteria.Retina, 35, 7, 1375-1380, 2015</th></tr>
<tr><td>Characteristics of diagnosed of polypoidal choroidal vasculopathy and typical age-related macular degeneration based on EVEREST criteria</td><td>
<table>
<tr><td></td><td>Polypoidal choroidal vasculopathy</td><td>Typical AMD</td></tr>
<tr><td>Number of eyes</td><td>131</td><td>110</td></tr>
<tr><td>Mean age (SD)</td><td>67.6 (8.8)</td><td>69.2 (10.0)</td></tr>
<tr><td>Percentage of men</td><td>64%</td><td>55%</td></tr>
<tr><td>Presenting vision, logMAR, mean (SD)</td><td>0.8 (0.6)</td><td>0.9 (0.6)</td></tr>
<tr><td>Fluorescein angiography</td><td></td><td></td></tr>
<tr><td>CNV less than 50% of lesion</td><td>39.7%</td><td>29.0%</td></tr>
<tr><td>CNV at least 50% of lesion</td><td></td><td></td></tr>
<tr><td>Classic/predominantly classic</td><td>21.5%</td><td>42.3%</td></tr>
<tr><td>Minimally classic/occult</td><td>78.5%</td><td>57.7%</td></tr>
</table>
</td></tr>
<tr><td>Type of test</td><td>Flash fundus camer-based ICGA
ICGA, applying modified EVEREST grading criteria: PCV diagnosis was made if, in addition to the presence of subretinal focal hyperfluorescence at least one of the following angiographic or clinical criteria was met (“additional” criteria):
branching vascular network
nodular appearance when viewed stereoscopically
the presence of hypoflurescent halo
orange subretinal nodule on color photograph
association with massive submacular haemorrhage</td></tr>
<tr><td>Reference standard</td><td>Confocal scanning laser ophthalmscope-based ICGA
PCV diagnosis was made if, in addition to the presence of subretinal focal hyperfluorescence (“essential criterion”)</td></tr>
<tr><td>Prevalence</td><td>241 eyes were included in the study.
PCV was in 131 eyes (54%) and typical AMD was in 110 eyes (46%).
<table>
<tr><td></td><td></td><td>Essential criteria</td><td></td></tr>
<tr><td>Modified criteria</td><td></td><td>Positive</td><td>Negative</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	**Cheung,C.M., Laude,A., Wong,W., Mathur,R., Chan,C.M., Wong,E., Wong,D., Wong,T.Y., Lim,T.H., 20151209 Improved specificity of polypoidal choroidal vasculopathy diagnosis using a modified everest criteria.Retina, 35, 7, 1375-1380, 2015**
	<table><tr><td></td><td>Positive</td><td>103</td><td>14</td></tr><tr><td></td><td>Negative</td><td>28</td><td>96</td></tr><tr><td></td><td></td><td>131</td><td>110</td></tr></table>
Sensitivity	78.6%, 95%CI 71.2 to 85.2%
Specificity	87.3%, 95%CI 80.5 to 92.8%
Positive predictive values	88.0%, 95%CI 81.6 to 93.2%
Negative predictive values	77.4%, 95%CI 69.7 to 84.3%
Comments	This is a restrospective comparative study. The study reviewed colour fundus photograph, fluorescein angiography, and ICGA image from consecutive patients with untreated exudative maculopathy. Patients selection: pateints were recruited from retinal clinics, but the inclusion/exclusion criteria were not reported in the study. Indext test: Two independent retinal specialists graded imaging results, but masking between index test and reference standards were unclear. Reference standards: Two independent retinal specialists graded imaging results, but masking between index test and reference standards were unclear. Flow and timing: Time intervals between index test and reference standard were unclear.

Bibliographic reference	**Cheung C M. G; Yanagi Y ; Mohla A ; Lee S Y; Mathur R ; Chan C M; Yeo I ; Wong T Y. Characterization and differentiation of polypoidal choroidal vasculopathy using swept source optical coherence tomography angiography. Retina 2016**
Country/ies where the study carried our	Singapore
Study type	Prospective cross sectional study
Aim of the study	To determine the correlation and agreement between swept-source optical coherence tomography angiography (SS-OCT-A) with fluorescein angiography (FA), indocyanine green angiography (ICGA) and spectral domain OCT (SD-OCT) in characterizing polypoidal choroidal vasculopathy (PCV) and in differentiating eyes with typical age-related macular degeneration (t-AMD).
Study dates	Published 2016

<table>
<tr><th>Bibliographic reference</th><th>Cheung C M. G; Yanagi Y ; Mohla A ; Lee S Y; Mathur R ; Chan C M; Yeo I ; Wong T Y. Characterization and differentiation of polypoidal choroidal vasculopathy using swept source optical coherence tomography angiography. Retina 2016</th></tr>
<tr><td>Sources of funding</td><td>Not reported</td></tr>
<tr><td>Number of patients</td><td>86 eyes</td></tr>
<tr><td>Inclusion criteria</td><td>Patients presenting with untreated exudative maculopathy (either typical neovascular AMD or PCV)</td></tr>
<tr><td>Exclusion criteria</td><td>Not reported</td></tr>
<tr><td>Characteristics of diagnosed of polypoidal choroidal vasculopathy and typical age-related macular degeneration based on EVEREST criteria</td><td>
<table>
<tr><td></td><td>Polypoidal choroidal vasculopathy</td><td>Typical AMD</td></tr>
<tr><td>Number of eyes</td><td>54</td><td>32</td></tr>
<tr><td>Mean age (SD)</td><td>68.9 (9.4)</td><td>74.8 (7.0)</td></tr>
<tr><td>Percentage of men</td><td>63%</td><td>59%</td></tr>
<tr><td>Treatment naïve, n(%)</td><td>17 (31.5%)</td><td>14 (43.8%)</td></tr>
<tr><td>ICGA, n (%)</td><td></td><td></td></tr>
<tr><td>Polypidl lesions</td><td>42 (77.8)</td><td>0</td></tr>
</table>
</td></tr>
<tr><td>Type of test</td><td>Swept-source optial coherence tomography angiography (OCT-A)</td></tr>
<tr><td>Reference standard</td><td>Indocyanine green aniogrpahy (ICGA)</td></tr>
<tr><td>Prevalence</td><td>86 eyes were included in the study.

<table>
<tr><td></td><td></td><td>ICGA</td><td></td><td>Total</td></tr>
<tr><td>OCT-A</td><td></td><td>Positive</td><td>Negative</td><td></td></tr>
<tr><td></td><td>Positive</td><td>17</td><td>9</td><td>26</td></tr>
<tr><td></td><td>Negative</td><td>25</td><td>35</td><td>60</td></tr>
<tr><td></td><td></td><td>42</td><td>44</td><td>86</td></tr>
</table>
</td></tr>
<tr><td>Sensitivity</td><td>40.5%, 95%CI 26.3 to 55.5%</td></tr>
<tr><td>Specificity</td><td>81.4%, 95%CI 68.6 to 91.4%</td></tr>
<tr><td>Positive predictive values</td><td>68.0%, 95%CI 48.9 to 84.4%</td></tr>
</table>

Bibliographic reference	Cheung C M. G; Yanagi Y ; Mohla A ; Lee S Y; Mathur R ; Chan C M; Yeo I ; Wong T Y. Characterization and differentiation of polypoidal choroidal vasculopathy using swept source optical coherence tomography angiography. Retina 2016
Negative predictive values	58.3%, 95%CI 45.7 to 70.4%
Comments	Patient selection: prospectively a consecutive selection of patients with exudative AMD were recruited. Index test and reference standard: All patients had a standardized history,clinical examination and underwent fluoresce in angiography (FA) and ICGA. Swept-source optical coherence tomography angiography imaging was performed in all patients at the same visit as their conventional angiography,together withSD-OCT. Swept- source optical coherence tomography angiography images were evaluated by a retinal specialist(GC) independent of conventional angiography and masked to Diagnosis of AMD and PCV and FA/ICGA findings. Flow and timing: patients had their tests on the same visit.

Bibliographic reference	de Carlo,T.E., Bonini Filho,M.A., Chin,A.T., Adhi,M., Ferrara,D., Baumal,C.R., Witkin,A.J., Reichel,E., Duker,J.S., Waheed,N.K., Spectral-domain optical coherence tomography angiography of choroidal neovascularization.Ophthalmology, 122, 6, 1228-1238, 2015
Country/ies where the study carried out	USA
Study type	Retrospective cohort
Aim of the study	To describe the characteristics and the sensitivity and specificity of detection of choroidal neovascularization (CNV) on optical coherence tomography angiography (OCTA) using spectral-domain optical coherence tomography.
Study dates	2014
Sources of funding	Not reported
Number of patients	61 (a cohort of 24 patients who had suspected CNV underwent OCTA and FA)
Inclusion criteria	Not reported
Exclusion criteria	Not reported
Eligible participants characteristics	Mean age, range: 64 years, 29 to 91 years Percentage of female: 50% (n=12)
Type of test	Optical coherence tomography

Bibliographic reference	de Carlo,T.E., Bonini Filho,M.A., Chin,A.T., Adhi,M., Ferrara,D., Baumal,C.R., Witkin,A.J., Reichel,E., Duker,J.S., Waheed,N.K., Spectral-domain optical coherence tomography angiography of choroidal neovascularization.Ophthalmology, 122, 6, 1228-1238, 2015
Reference standard	Fluorescein angiography
Prevalence	<table><tr><td></td><td></td><td>FA</td><td></td><td></td></tr><tr><td>SD-OCT</td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr><tr><td></td><td>Positive</td><td>4</td><td>2</td><td>6</td></tr><tr><td></td><td>Negative</td><td>4</td><td>20</td><td>24</td></tr><tr><td></td><td>Total</td><td>8</td><td>22</td><td>30 (eyes)</td></tr></table>
Sensitivity	50.0%, 95%CI 18.4 to 81.6%
Specificity	90.9%, 95%CI 76.2 to 98.8%
Positive predictive values	66.7%, 95%CI 28.4 to 94.7%
Negative predictive values	83.3%, 95%CI 66.4 to 95.0%
Comments	In the restropsective review, patients who underwent OCTA to evluate the sensitivity and specificity of detection of choroidal neovascularisation. Patient selection: all patients in whom CNV was identified on OCTA underwent further review of the medical records for underlying diagnosis. Detailed inclusion and exclusion criteria were not reported. Index test: The results of OCTA were evaluated independently by 2 trained readers Reference standard: FAs of the selected patients were evaluated independently from the OCTAs fro presences or absences of CNV. Flow and time: all selected patients had OCTA and FA on the same day.

Bibliographic reference	De,Salvo G., Vaz-Pereira,S., Keane,P.A., Tufail,A., Liew,G., Sensitivity and specificity of spectral-domain optical coherence tomography in detecting idiopathic polypoidal choroidal vasculopathy.American Journal of Ophthalmology, 158, 6, 1228-1238, 2014
Country/ies where the studies carried out	UK
Study type	Retrospective case-control study

<table>
<tr><th>Bibliographic reference</th><th>De,Salvo G., Vaz-Pereira,S., Keane,P.A., Tufail,A., Liew,G., Sensitivity and specificity of spectral-domain optical coherence tomography in detecting idiopathic polypoidal choroidal vasculopathy.American Journal of Ophthalmology, 158, 6, 1228-1238, 2014</th></tr>
<tr><td>Aim of the study</td><td>To evaluate the efficacy of spectral-domain optical coherence tomography (SD-OCT) compared with indocyanine green angiography (ICGA) in detecting idiopathic polypoidal choroidal vasculpathy (PCV) and in differentiating between PCV and occult choroidal neovascularization (CNV).</td></tr>
<tr><td>Study dates</td><td>January 2012 and December 2012</td></tr>
<tr><td>Sources of funding</td><td>Not reported</td></tr>
<tr><td>Number of patients</td><td>44 patients (51 eyes)</td></tr>
<tr><td>Inclusion criteria</td><td>Patients have 1 or more pigment epithelial detachment (PEDs) in at least 1 eye.</td></tr>
<tr><td>Exclusion criteria</td><td>Patients with classic exudative age-related macular degeneration
Myopic CNV
Other secondary CNVs
Central serous chorioretinopathy (CSCR)</td></tr>
<tr><td>Eligible participants characteristics</td><td>Median age, range: 70 year, 48-95 years
Percentage of male: 32% (n=14)</td></tr>
<tr><td>Type of test</td><td>Spectral-domain optical coherence tomography (SD-OCT)</td></tr>
<tr><td>Reference standard</td><td>indocyanine green angiography (ICGA)</td></tr>
<tr><td>Prevalence</td><td>73% (n=32 patients)

<table><tr><td></td><td></td><td>ICGA</td><td></td><td></td></tr><tr><td>OCT</td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr><tr><td></td><td>Positive</td><td>35</td><td>1</td><td>36</td></tr><tr><td></td><td>Negative</td><td>2</td><td>13</td><td>15</td></tr><tr><td>Total</td><td></td><td>37</td><td>14</td><td>51 (eyes)</td></tr></table></td></tr>
<tr><td>Sensitivity</td><td>94.6%, 95%CI 85.5 to 99.3%</td></tr>
<tr><td>Specificity</td><td>92.9%, 95%CI 75.3 to 99.8%</td></tr>
<tr><td>Positive predictive values</td><td>97.2%, 95%CI 90.0 to 99.9%</td></tr>
</table>

Bibliographic reference	De,Salvo G., Vaz-Pereira,S., Keane,P.A., Tufail,A., Liew,G., Sensitivity and specificity of spectral-domain optical coherence tomography in detecting idiopathic polypoidal choroidal vasculopathy.American Journal of Ophthalmology, 158, 6, 1228-1238, 2014
Negative predictive values	86.7%, 95%CI 66.1 to 98.2%
Comments	This is an observational case study evaluating the accuracy of OCT in detecting and differentiating PCV from occult CNV. Patient selection: The study reviewed 44 consecutive patients with 1 or more serous/hemorrhagic PED retrospectively. The study excluded patients with classic exudative AMD. Index test and reference standard: all patients underwent OCT, FFA and ICGA in both eyes. FFA and ICGA were reviewed by 2 authors masked to the results of the OCT grading. Disagreements were resolved by open adjusticatioon between the 2 authors. Flow and timing: Time interval between index test and reference standard was unclear.

Bibliographic reference	Do,D.V., Gower,E.W., Cassard,S.D., Boyer,D., Bressler,N.M., Bressler,S.B., Heier,J.S., Jefferys,J.L., Singerman,L.J., Solomon,S.D. Detection of new-onset choroidal neovascularization using optical coherence tomography: the AMD DOC Study.Ophthalmology, 119, 4, 771-778, 2012
Country/ies where the study carried out	USA
Study type	Prospective cohort
Aim of the study	To determine the sensitivity of time domain optical coherence tomography (OCT) in detecting conversion to neovascular age-related macular degeneration n eyes with high risk for choroidal neovascularization(CNV), compared with detection using fluorescein angiography (FA) as the gold standard.
Study dates	2007
Sources of funding	Lincy Foundation to the Johns Hopkins University
Number of patients	98 patients enrolled (89 included)
Inclusion criteria	Patients aged 50 years and/over Patients have best-corrected ETDS visual acuity letter score≥65 Patients have neovascular AMD in the nonstudy eye Patients are absence of CNV in participants' study eyes confirmed on fluorescein angiography Patients have at least 1 large drusen(>125μm) and focal hyperpigmentation within 3600μ of the center of the macular Media are sufficiently clear to permit study imaging

<table>
<tr><th>Bibliographic reference</th><td>Do,D.V., Gower,E.W., Cassard,S.D., Boyer,D., Bressler,N.M., Bressler,S.B., Heier,J.S., Jefferys,J.L., Singerman,L.J., Solomon,S.D. Detection of new-onset choroidal neovascularization using optical coherence tomography: the AMD DOC Study.Ophthalmology, 119, 4, 771-778, 2012</td></tr>
<tr><td>Exclusion criteria</td><td>Patients are allergy to fluorescein dye
Patients have advanced AMD with CNV in both eyes, confirmed on fluorescein angiography
Patients have geographic atrophy which extends through the center of the macular in the participants’ study eye
Patients have macular disease other than AMD in their study eyes
Patients had prior surgical or laser treatment to the macular in their study eye</td></tr>
<tr><td>Eligible participants characteristics</td><td>
<table>
<tr><td></td><td>Included</td><td>Excluded</td></tr>
<tr><td>Median age, range</td><td>79.0, 58 to 91</td><td>78.0, 70 to 86</td></tr>
<tr><td>No. of male (%)</td><td>31 (36)</td><td>4 (36)</td></tr>
<tr><td>No. of White, not of Hispanic origin (%)</td><td>84 (97)</td><td>11 (100)</td></tr>
<tr><td>Current smokers</td><td>3 (3)</td><td>0</td></tr>
<tr><td>Never smokers</td><td>33 (38)</td><td>6 (55)</td></tr>
<tr><td>Median visual acuity in study eye, range</td><td>80, 66 to 95</td><td>84, 77 to 90</td></tr>
<tr><td>Median visual acuity in fellow eye, range</td><td>35, 0 to 84</td><td>39, 7 to 75</td></tr>
<tr><td>Cataract surgery in study eye (%)</td><td>26 (30)</td><td>4 (36)</td></tr>
</table>
</td></tr>
<tr><td>Type of test</td><td>Time-domain optical coherence tomography</td></tr>
<tr><td>Reference standard</td><td>Fluorescein angiography</td></tr>
<tr><td>Prevalence</td><td>
<table>
<tr><td></td><td></td><td>FA</td><td></td><td></td></tr>
<tr><td>OCT</td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr>
<tr><td></td><td>Positive</td><td>9</td><td>32</td><td>41</td></tr>
<tr><td></td><td>Negative</td><td>6</td><td>40</td><td>46</td></tr>
<tr><td></td><td>Total</td><td>15</td><td>72</td><td>87</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	**Do,D.V., Gower,E.W., Cassard,S.D., Boyer,D., Bressler,N.M., Bressler,S.B., Heier,J.S., Jefferys,J.L., Singerman,L.J., Solomon,S.D. Detection of new-onset choroidal neovascularization using optical coherence tomography: the AMD DOC Study.Ophthalmology, 119, 4, 771-778, 2012**
	<table><tr><td>PHP</td><td>Positive</td><td>7</td><td>11</td><td>18</td></tr><tr><td></td><td>Negative</td><td>8</td><td>61</td><td>69</td></tr><tr><td></td><td>Total</td><td>15</td><td>72</td><td>87</td></tr></table>
Sensitivity	OCT: 60.0%, 95%CI 35.1 to 82.3% PHP: 46.7%, 95%CI 23.0 to 71.1%
Specificity	OCT: 55.6%, 95%CI 44.0 to 66.8% PHP: 84.7%, 95%CI 75.6 to 92.0%
Positive predictive values	OCT: 22.0%, 95%CI 10.8 to 35.6% PHP: 38.9%, 95%CI 18.4 to 61.7%
Negative predictive values	OCT: 87.0%, 95%CI 75.9 to 94.9% PHP: 88.4%, 95%CI 79.9 to 92.8%
Comments	This study aimed to determine the sensitivity of OCT in detecting conversion to neovascular AMD in eye at risk of choroidal neovascular, compared with FA. Patient selection: a sample of 227 inviduals who had neovascular AMD in 1 eye (non-study eye) were included. Index test: The OCT were graded by 2 trained, maksed graders at the Reading centre. References standard: Am independent assessment of fluorescein leakage that could represent new onset CNV was performed by 2 trained, masked graders at the Reading Centre. A consensus grade was developed with input from the Reading Centre prinicipal investigator when unresolved discrepancies arose between the graders/ Flow and timing: Time intervals between index test and reference standard were unclear.

Bibliographic reference	**Gong Jingwen; Yu Suqin ; Gong Yuanyuan ; Wang Fenghua ; Sun Xiaodong. The Diagnostic Accuracy of Optical Coherence Tomography Angiography for Neovascular Age-Related Macular Degeneration: A Comparison with Fundus Fluorescein Angiography. Journal of ophthalmology 2016**
Country/ies where the study carried out	China

<table>
<tr><th>Bibliographic reference</th><th>Gong Jingwen; Yu Suqin ; Gong Yuanyuan ; Wang Fenghua ; Sun Xiaodong. The Diagnostic Accuracy of Optical Coherence Tomography Angiography for Neovascular Age-Related Macular Degeneration: A Comparison with Fundus Fluorescein Angiography. Journal of ophthalmology 2016</th></tr>
<tr><td>Study type</td><td>Retrospective case study</td></tr>
<tr><td>Aim of the study</td><td>To describe the morphological characteristics and efficacy of OCTA in detecting CNV in nAMD</td></tr>
<tr><td>Study dates</td><td>Published in 2016</td></tr>
<tr><td>Sources of funding</td><td>Health and Family Planning Commission of Zhejiang Province of China and major scientific and technological project of Science Technology Department of Zhejiang Province</td></tr>
<tr><td>Number of patients</td><td>53 patients (86 eyes)</td></tr>
<tr><td>Inclusion criteria</td><td>Patients aged 50 years and/over with clinical features of age-related maculopathey
Patients have macular exudative signs on at least one of 2 imaging examiniation (FA or SD-OCT)</td></tr>
<tr><td>Exclusion criteria</td><td>Patients without OCTA or FA results available for analysis or the OCTA/FA not being performed within 7 days of each other
Patients have advanced AMD with CNV in both eyes, confirmed on fluorescein angiography
Patients with CNV secondary to pathological myopia, angioid streaks, chorioretinitis, central serous chorioretinopathy, tumors, or trauma
Patients with media opacities, such as cataracts, preventing detailed imaging</td></tr>
<tr><td>Eligible participants characteristics</td><td><table><tr><td></td><td>Included</td></tr><tr><td>Median age, range</td><td>67 years, 50 to 85</td></tr><tr><td>No. of male (%)</td><td>33 (62.3)</td></tr></table></td></tr>
<tr><td>Type of test</td><td>Optical coherence tomography angiography</td></tr>
<tr><td>Reference standard</td><td>Fluorescein angiography</td></tr>
<tr><td>Prevalence</td><td><table><tr><td></td><td></td><td>FA</td><td></td><td></td></tr><tr><td>OCT-A</td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr><tr><td></td><td>Positive</td><td>45</td><td>11</td><td>56</td></tr><tr><td></td><td>Negative</td><td>7</td><td>23</td><td>30</td></tr><tr><td></td><td>Total</td><td>52</td><td>34</td><td>86</td></tr></table></td></tr>
</table>

Bibliographic reference	Gong Jingwen; Yu Suqin ; Gong Yuanyuan ; Wang Fenghua ; Sun Xiaodong. The Diagnostic Accuracy of Optical Coherence Tomography Angiography for Neovascular Age-Related Macular Degeneration: A Comparison with Fundus Fluorescein Angiography. Journal of ophthalmology 2016
Sensitivity	OCTA: 86.5%, 95%CI 76.1 to 94.3%
Specificity	OCTA: 79.4%, 95%CI 64.5 to 91.0%
Positive predictive values	OCTA: 86.5%, 95%CI 76.1 to 94.3%
Negative predictive values	OCTA: 79.4%, 95%CI 64.5 to 91.0%
Comments	Patient selection: a review of consecutive patients with maculopathy who visited the study clinic. Index test and reference standard: All the patients underwent a comprehensive eye examination, which included slitlamp biomicroscopy, color fundus photography, FA, spectraldomainOCT (SD-OCT), andOCTangiography. Two independent and trained readers evaluated each set of images (IR, FA, SD-OCT, and OCTA). The readers were blinded to any clinical patient information, such as the patient's history, visual acuity, and which eye was the index eye, if not both. If there was disagreement between the two readers, a third ophthalmologist was asked to adjudicate. Flow and timing: patients whose OCTA/FA not being performed within 7 days of each other were excluded.

Bibliographic reference	Lim,J.I., Labree,L., Nichols,T., Cardenas,I., Comparison of nonmydriatic digitized video fundus images with standard 35-mm slides to screen for and identify specific lesions of age-related macular degeneration.Retina (Philadelphia, Pa.)Retina, 22, 1, 59-64, 2002
Country/ies where the study carried out	USA
Study type	Prospective case series
Aim of the study	To compare nonmydriatic digitized images obtained using a digital imaging system with 35-mm slide images for detecting specific findings of age-related macular degeneration and to evaluate its usefulness as a screening tool in detecting signs of AMD.
Study dates	Not reported

Bibliographic reference	**Lim,J.I., Labree,L., Nichols,T., Cardenas,I., Comparison of nonmydriatic digitized video fundus images with standard 35-mm slides to screen for and identify specific lesions of age-related macular degeneration.Retina (Philadelphia, Pa.)Retina, 22, 1, 59-64, 2002**
Sources of funding	The National Eye Institute and Research to Prevent blindness
Number of patients	17 patients (33 eyes)
Inclusion criteria	Patients were recruited in the study if they had diagnosis of AMD. Patients were 50 years or older Patients had one or more large drusen (>63µm), retinal pigment epithelial (RPE) change (mottling or atrophy) or disciform scar in at least one eye
Exclusion criteria	Not stated
Eligible participants characteristics	Median age, range: 79 years, 64-88 years
Type of test	Eligible patients underwent nonmydriatic digital fundus photography using a modified nonmydriatic, 45 degree video fundus camera for digital image capture.
Reference standard	Patients underwent mydriatic fundus photography using Zeiss 30-degree fundus camera. The 35-mm film images were processed, and the colour slides were labelled. The same retinal specialist then reviewed all images (digital and 35-mm slide)
Prevalence	Drusen CNV

Drusen

		Photo		
Digital		Positive	Negative	Total
	Positive	16	1	17
	Negative	9	7	16
	Total	25	8	33

CNV

		Photo		
Digital		Positive	Negative	Total
	Positive	3	0	3
	Negative	3	27	30

Bibliographic reference	Lim,J.I., Labree,L., Nichols,T., Cardenas,I., Comparison of nonmydriatic digitized video fundus images with standard 35-mm slides to screen for and identify specific lesions of age-related macular degeneration.Retina (Philadelphia, Pa.)Retina, 22, 1, 59-64, 2002

	Total	6	27	33

PED

		Photo		
Digital		Positive	Negative	Total
	Positive	1	0	1
	Negative	1	31	32
	Total	2	31	33

Sensitivity

	Sensitivity
Drusen	64.0%, 95%CI 44.7 to 81.2%
CNV	50.0%, 95%CI 16.7 to 83.3%
PED	50.0%, 95%CI 6.1 to 93.9%

Specificity

	Specificity
Drusen	87.5%, 95%CI 59.0 to 99.6%
CNV	98.2%, 95%CI 91.2 to 100%
PED	98.4%, 95%CI 92.3 to 100.0%

Positive predictive values

	PPV
Drusen	94.1%, 95%CI 79.4 to 99.8%
CNV	87.5%, 95%CI 46.4 to 100%
PED	75.0%, 95%CI 14.7 to 100.0%

Negative predictive values

	NPV
Drusen	43.8%, 95%CI 21.3 to 67.7%
CNV	88.7%, 95%CI 75.7 to 97.1%

Bibliographic reference	**Lim,J.I., Labree,L., Nichols,T., Cardenas,I., Comparison of nonmydriatic digitized video fundus images with standard 35-mm slides to screen for and identify specific lesions of age-related macular degeneration.Retina (Philadelphia, Pa.)Retina, 22, 1, 59-64, 2002**
	PED: 95.5%, 95%CI 86.3 to 99.7%
Comments	Patient selection: patients were recruited who met inclusion critieria including a patients having AMD who had one or more large drusen, RPE, or disciform scar in at least one eye. Index test and reference standard: eligible patients underwent nonmydriatic, digit fundus photography, a cerified ophthalmic photographer trained in the used of the nonmydriatic camera. After compleing the digital photographs, the patient's pupil was dilated. Then patient underwent mydriatic fundus photography. The film images were processed. Flow and time: Readings of the slide and the digitised images were sperpated by at least 2 days.

Bibliographic reference	**Maberley,D.A., Isbister,C., Mackenzie,P., Aralar,A. An evaluation of photographic screening for neovascular age-related macular degeneration.Eye, 19, 6, 611-616, 2005**
Country/ies where the study carried out	Canada
Study type	Cross sectional study
Aim of the study	To evaluate the utility of colour fundus photographs for identifying subjects with potentially treatable neovascular AMD.
Study dates	Jan 2002 to March 2002
Sources of funding	Not reported
Number of patients	74 eyes
Inclusion criteria	Patients who had been referred by general ophthalmologist with a diagnosis of "age-related macular degeneration".
Exclusion criteria	Not reported
Eligible participants characteristics	Not reported
Type of test	Colour fundus photography
Reference standard	Fluorescein angiography

Bibliographic reference	**Maberley,D.A., Isbister,C., Mackenzie,P., Aralar,A. An evaluation of photographic screening for neovascular age-related macular degeneration.Eye, 19, 6, 611-616, 2005**
Prevalence	Based on the consensus of the two retinal specialists, 46% (31) noevascular AMD was present, and 54% (43) of eyes displayed no evidence of neovascular AMD.

Reader A		FA		
CFP (colour image)		Positive	Negative	Total
	Positive	5	32	37
	Negative	36	1	37
	Total	41	33	74
CFP (stereo colour image)				
	Positive	8	33	41
	Negative	33	0	33
	Total	41	33	74
CFP (stereo colour image + clinical information				
	Positive	10	33	43
	Negative	31	0	31
	Total	41	33	74

Reader B		FA		
CFP (colour image)		Positive	Negative	Total
	Positive	3	31	34
	Negative	38	2	40

Bibliographic reference	Maberley,D.A., Isbister,C., Mackenzie,P., Aralar,A. An evaluation of photographic screening for neovascular age-related macular degeneration.Eye, 19, 6, 611-616, 2005

	Total	41	33	74
CFP (stereo colour image)				
	Positive	6	32	38
	Negative	35	1	36
	Total	41	33	74
CFP (stereo colour image + clinical information				
	Positive	9	33	42
	Negative	32	0	32
	Total	41	33	74

Sensitivity

	Sensitivity
Reader A	
Colour image	12.2%, 95%CI 4.2 to 23.7%
Stereo colour image	20.2%, 95%CI 9.7 to 33.5%
Stereo colour image +clinical information	25.0%, 95%CI 13.3 to 39.0%
Read B	
Colour image	7.3%, 95%CI 1.6 to 16.9%
Stereo colour image	14.6%, 95%CI 5.7 to 26.8%
Stereo colour image +clinical information	22.6%, 95%CI 11.5 to 36.2%

Specificity

	Specificity
Reader A	
Colour image	3.0%, 95%CI 0.1 to 10.9%

Bibliographic reference	Maberley,D.A., Isbister,C., Mackenzie,P., Aralar,A. An evaluation of photographic screening for neovascular age-related macular degeneration.Eye, 19, 6, 611-616, 2005

Stereo colour image	-
Stereo colour image +clinical information	-
Reader B	
Colour image	6.1%, 95%CI 0.7 to 16.2%
Stereo colour image	3.0%, 95%CI 0.0 to 10.9%
Stereo colour image +clinical information	-

Positive predictive values

	PPV
Reader A	
Colour image	13.5%, 95%CI 4.7 to 26.1%
Stereo colour image	20.2%, 95%CI 9.7 to 33.5%
Stereo colour image +clinical information	23.8%, 95%CI 12.6 to 37.3%
Reader B	
Colour image	8.8%, 95%CI 1.9 to 20.2%
Stereo colour image	15.8%, 95%CI 6.2 to 28.8%
Stereo colour image +clinical information	22.1%, 95%CI 11.2 to 35.4%

Negative predictive values

	NPV
Reader A	
Colour image	2.7%, 95%CI 0.1 to 9.7%
Stereo colour image	-
Stereo colour image +clinical information	-
Reader B	
Colour image	5.0%, 95%CI 0.1 to 13.5%

Bibliographic reference	**Maberley,D.A., Isbister,C., Mackenzie,P., Aralar,A. An evaluation of photographic screening for neovascular age-related macular degeneration.Eye, 19, 6, 611-616, 2005**
	Stereo colour image: 2.8%, 95%CI 0.0 to 10.0% Stereo colour image +clinical information: -
Comments	Patient selection: patients were sent by general ophthalmologists with a diagnosis of age-related macular degeneration Index test and reference standard: for each patient, both eyes were imaged by colour fundus photography and fluorescein angiography. The colour image readings were performed serially and independently by each specialist. The reader were required to predict which colour images would deomonstrated chorodial neovascularisation. A thoird retinal opinion was sought for grader disagree,emt pm the angiographic interpretation. Flow and timing: fluorescein aniograms taken at the same time as colour images were read by the two retinal speclaists at spate reading seesion.

Bibliographic reference	**Mathew,R., Pefkianaki,M., Kopsachilis,N., Brar,M., Richardson,M., Sivaprasad,S. Correlation of fundus fluorescein angiography and spectral-domain optical coherence tomography in identification of membrane subtypes in neovascular age-related macular degeneration.Ophthalmologica, 231, 3, 153-159, 2014**
Country/ies where the study carried out	UK
Study type	Retrospective cross sectional
Aim of the study	To assess the sensitivity and specificity of spectral-domain optical coherence tomography (SDOCT) for determinant of choroidal neovascularization subtypes in neovascular age-related macular degeneration (AMD) compared with fundus fluorescein angiography (FFA).
Study dates	Not reported
Sources of funding	Not reported
Number of patients	130 patients
Inclusion criteria	Patients initiated on ranibizumab therapy for neovascular AMD were selected from the respective AMD databases. Inclusion criteria were: eyes with subfoveal CNV due to neovascular AMD, of any lesion subtype, with lesion size of less than 12 disc areas and a clear media permitting OCT imaging with good signal strength.

Bibliographic reference	**Mathew,R., Pefkianaki,M., Kopsachilis,N., Brar,M., Richardson,M., Sivaprasad,S. Correlation of fundus fluorescein angiography and spectral-domain optical coherence tomography in identification of membrane subtypes in neovascular age-related macular degeneration.Ophthalmologica, 231, 3, 153-159, 2014**
Exclusion criteria	Patietns with CNV secondary to cause other than AMD, other retinal diseases in the study eye including diabetic retinopathy or hereditary retinal dystrophies were excluded. Eyes that presented with predominantly scar and blood that obscured identification of the CNV subtype were also excluded.
Eligible participants characteristics	No. of males: 36, 36% Mean age (SD): 75.6 (2.1) years
Type of test	Spectral-domain optical coherence tomography (SD-OCT)
Reference standard	Fundus fluorescein angiography (FFA)
Prevalence	On FFA, most of the CNV were occult types (62%) followed by RAP (20%0 and classic CNV (14%). Occult

		FFA		
OCT		Positive	Negative	Total
	Positive	75	10	85
	Negative	2	43	45
	Total	77	53	130

RAP

		FFA		
OCT		Positive	Negative	
	Positive	21	2	23
	Negative	5	102	107
	Total	26	104	130

Classic CNV

		FFA		
OCT		Positive	Negative	

Bibliographic reference	Mathew,R., Pefkianaki,M., Kopsachilis,N., Brar,M., Richardson,M., Sivaprasad,S. Correlation of fundus fluorescein angiography and spectral-domain optical coherence tomography in identification of membrane subtypes in neovascular age-related macular degeneration.Ophthalmologica, 231, 3, 153-159, 2014

	Positive	17	0	17
	Negative	5	108	113
	Total	22	108	130

PCV

		FFA		
OCT		Positive	Negative	
	Positive	5	0	5
	Negative	0	125	125
	Total	5	125	130

Sensitivity

	Sensitivity
Occult	97.3%, 95%CI 92.9 to 99.7%
RAP	80.8%, 95%CI 63.9 to 93.1%
Classic CNV	76.1%, 95%CI 57.1 to 90.8%
PCV	100%

Specificity

	Specificity
Occult	81.1%, 95%CI 69.7 to 90.4%
RAP	98.1%, 95%CI 94.7 to 99.8%
Classic CNV	100%
PCV	100%

Positive predictive values

	PPV
Occult	88.2%, 95%CI 80.6 to 94.1%
RAP	91.3%, 95%CI 77.1 to 98.9%

Bibliographic reference	**Mathew,R., Pefkianaki,M., Kopsachilis,N., Brar,M., Richardson,M., Sivaprasad,S. Correlation of fundus fluorescein angiography and spectral-domain optical coherence tomography in identification of membrane subtypes in neovascular age-related macular degeneration.Ophthalmologica, 231, 3, 153-159, 2014**
	Classic CNV: 100% PCV: 100%
Negative predictive values	NPV Occult: 95.6%, 95%CI 88.0 to 99.4% RAP: 95.3%, 95%CI 90.6 to 98.5% Classic CNV: 95.2%, 95%CI 90.6 to 98.3% PCV: 100%
Comments	Patient slection: this retrospective review included patients initiated on ranibizumab therapy for neovascular AMD. Index test and reference standard: Spectralis OCT scans of included patients were obtained. All patients underwent FFA at baseline. All SD-OCT images were assessed independently by two graders. Differences were adjudicated by the senior author (S.S.), after discussion. All anomymise images were evaluated by masked retina specialists. Flow and timing: time intervals between index test and reference standard were unclear.

Bibliographic reference	**Mokwa,N.F., Ristau,T., Keane,P.A., Kirchhof,B., Sadda,S.R., Liakopoulos,S. Grading of Age-Related Macular Degeneration: Comparison between Color Fundus Photography, Fluorescein Angiography, and Spectral Domain Optical Coherence Tomography.Journal of ophthalmology, Vol 2013 (2013).**
Country/ies where thte study carried out	Germany
Study type	Retrospective case control
Aim of the study	To compare FP, FA and SDOCT imaging regarding their sensitivity and specificity for detecting AMD, CNV, and CNV activity and to analyse whether SDOCT may have the potential to replace the other imaging techniques.
Study dates	Not reported
Sources of funding	The Retinovit Foundation, Cologne, Germany
Number of patients	66 patients (120 eyes)

<table>
<tr><th>Bibliographic reference</th><th>Mokwa,N.F., Ristau,T., Keane,P.A., Kirchhof,B., Sadda,S.R., Liakopoulos,S. Grading of Age-Related Macular Degeneration: Comparison between Color Fundus Photography, Fluorescein Angiography, and Spectral Domain Optical Coherence Tomography.Journal of ophthalmology, Vol 2013 (2013).</th></tr>
<tr><td>Inclusion criteria</td><td>Eyes with early, intermediate, or late AMD as well as control cases were included. Control eyes were required to show no signs for AMD, but other chorioretinal diseases including CNV secondary to any other disease but AMD was allowed.</td></tr>
<tr><td>Exclusion criteria</td><td>Not reported</td></tr>
<tr><td>Eligible participants characteristics</td><td>Not reported</td></tr>
<tr><td>Type of test</td><td>AMD: Fluorescein angiography, spectral-domain optical coherence tomography
CNV: Fundus photography, spectral-domain optical coherence tomography</td></tr>
<tr><td>Reference standard</td><td>AMD: Fundus photography
CNV: Fluorescein angiography</td></tr>
<tr><td>Prevalence</td><td>AMD
<table>
<tr><td></td><td></td><td>FP</td><td></td><td></td></tr>
<tr><td></td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr>
<tr><td>FA</td><td>Positive</td><td>69</td><td>8</td><td>77</td></tr>
<tr><td></td><td>Negative</td><td>6</td><td>37</td><td>43</td></tr>
<tr><td>Total</td><td></td><td>75</td><td>45</td><td>120</td></tr>
</table>
<table>
<tr><td></td><td></td><td>FP</td><td></td><td></td></tr>
<tr><td></td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr>
<tr><td>OCT</td><td>Positive</td><td>67</td><td>11</td><td>78</td></tr>
<tr><td></td><td>Negative</td><td>8</td><td>34</td><td>42</td></tr>
<tr><td>Total</td><td></td><td>75</td><td>45</td><td>120</td></tr>
</table>
CNV
<table>
<tr><td></td><td></td><td>FA</td><td></td><td></td></tr>
<tr><td></td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr>
</table></td></tr>
</table>

Bibliographic reference	Mokwa,N.F., Ristau,T., Keane,P.A., Kirchhof,B., Sadda,S.R., Liakopoulos,S. Grading of Age-Related Macular Degeneration: Comparison between Color Fundus Photography, Fluorescein Angiography, and Spectral Domain Optical Coherence Tomography.Journal of ophthalmology, Vol 2013 (2013).				
	FP	Positive	53	1	54
		Negative	15	51	66
	Total		68	52	120
			FA		
			Positive	Negative	Total
	OCT	Positive	64	1	65
		Negative	4	51	55
	Total		68	52	120
Sensitivity	AMD	Fluorescein angiography	92.0%, 95%CI 84.9 to 97.0%		
		SD-optical coherence tomography	89.3%, 95%CI 81.5 to 95.2%		
	CNV	Fundus photography	77.9%, 95%CI 67.4 to 86.9%		
		SD-optical coherence tomography	94.1%, 95%CI 87.4 to 98.4%		
Specificity	AMD	Fluorescein angiography	82.2%, 95%CI 70.0 to 91.8%		
		SD-optical coherence tomography	75.6%, 95%CI 62.2 to 86.8%		
	CNV	Fundus photography	98.1%, 95%CI 93.0 to 99.9%		
		SD-optical coherence tomography	98.1%, 95%CI 93.0 to 99.9%		
Positive predictive values	AMD	Fluorescein angiography	89.6%, 95%CI 81.9 to 95.3%		
		SD-optical coherence tomography	86.9%, 95%CI 77.4 to 92.6%		
	CNV	Fundus photography	98.1%, 95%CI 93.2 to 99.9%		
		SD-optical coherence tomography	98.4%, 95%CI 94.4 to 99.9%		
Negative predictive values					
	AMD	Fluorescein angiography	86.0%, 95%CI 74.4 to 94.6%		
		SD-optical coherence tomography	80.9%, 95%CI 67.9 to 91.2%		

Bibliographic reference	**Mokwa,N.F., Ristau,T., Keane,P.A., Kirchhof,B., Sadda,S.R., Liakopoulos,S. Grading of Age-Related Macular Degeneration: Comparison between Color Fundus Photography, Fluorescein Angiography, and Spectral Domain Optical Coherence Tomography.Journal of ophthalmology, Vol 2013 (2013).**
	<table><tr><td>CNV</td><td>Fundus photography</td><td>77.2%, 95%CI 66.5 to 86.5%</td></tr><tr><td></td><td>SD-optical coherence tomography</td><td>92.7%, 95%CI 84.6 to 97.9%</td></tr></table>
Comments	Patient selection: The European Genetic Database (EUGENDA), a database collecting AMD patients as well as healthy controls, was retrospectively reviewed, and and FP, FA,and SDOCT images of 120 eyes of 66 consecutive patients were randomly collected. Index test and reference standard: SDOCT images were acquired using the Spectralis SDOCT instrument. FA images were performed using the SpectralisHRAsystem. Images were independently analyzed by reading center graders at the Cologne Image ReadingCenter (CIRCL),which have been trained and certified in image interpretation of AMDpatients.Discrepancies between graders have been solved by open adjudication. During analysis of one imaging technique, the grader was masked to all other images and grading results of the patient. Flow and timing: To be eligible for this study, all imageshad to be performedonthe same day.

Bibliographic reference	**Padnick-Silver,L., Weinberg,A.B., Lafranco,F.P., Macsai,M.S. Pilot study for the detection of early exudative age-related macular degeneration with optical coherence tomography.Retina, 32, 6, 1045-1056, 2012**
Country/ies where the study carried out	USA
Study type	Prospective cohort study
Aim of the study	To investigate the ability of optical coherence tomography to detect early choroidal neovascularisation in age-related macular degeneration.
Study dates	Not stated
Sources of funding	The NorthShore University HealthSystem
Number of patients	79 patients
Inclusion criteria	Patients with bilateral AMD, who had developed unilateral exudative changes were enrolled in the study.
Exclusion criteria	Patients with other retinal disease in the eye with non exudative age-related macular degeneration were excluded from the study.

<table>
<tr><th>Bibliographic reference</th><th>Padnick-Silver,L., Weinberg,A.B., Lafranco,F.P., Macsai,M.S. Pilot study for the detection of early exudative age-related macular degeneration with optical coherence tomography.Retina, 32, 6, 1045-1056, 2012</th></tr>
<tr><td>Eligible participants characteristics</td><td>79 patients were enrolled in the study, and 62 patients were followed for the full 2 year or until the point of conversion to exudative AMD.

Mean age (SD): 79.7 (6.3)
Number of female: 55 (70%)
Mean visual acuity (SD): 0.27 (0.21) in the study eye and 1.4 (0.74) in the follow eye</td></tr>
<tr><td>Type of test</td><td>Optical coherence tomography</td></tr>
<tr><td>Reference standard</td><td>Fluorescence angiography</td></tr>
<tr><td>Prevalence</td><td>Of the 77 patients followed in this study, 15(19%) demonstrated exudative changes (as confirmed by FA) in their study eye.
<table>
<tr><td></td><td></td><td>FA</td><td></td><td></td></tr>
<tr><td>OCT</td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr>
<tr><td></td><td>Positive</td><td>12</td><td>4</td><td>16</td></tr>
<tr><td></td><td>Negative</td><td>3</td><td>58</td><td>61</td></tr>
<tr><td>Total</td><td></td><td>15</td><td>62</td><td>77</td></tr>
</table></td></tr>
<tr><td>Sensitivity</td><td>80.0%, 95%CI 57.2 to 95.3%</td></tr>
<tr><td>Specificity</td><td>93.5%, 95%CI 86.3 to 98.2%</td></tr>
<tr><td>Positive predictive values</td><td>75.0%, 95%CI 51.9 to 92.2%</td></tr>
<tr><td>Negative predictive values</td><td>95.1%, 95%CI 88.4 to 98.9%</td></tr>
<tr><td>Comments</td><td>Patient selection: Patients with bilateral AMD who had developed unilateral exudative changes were included in the study.
Index test and reference standard: patients were monitored at 3-month intervals over a period of 2 years. At each visit, patients underwent eye examination. If the examination raised suspicious of or demonstrated signes of EMA, an GA was perfomed as a standard care of measure. In these cases, patients also underwent OCT imaging as part of the study. Masking of index test and reference standard was unclear.
Flow and timing: If anigiography was negative for CNV, interim evaluation (OCT) and FA as requested by the physician) at 4-weeks to 6-weeks intervals were performed.</td></tr>
</table>

Bibliographic reference	**Pirbhai,A., Sheidow,T., Hooper,P. Prospective evaluation of digital non-stereo colour fundus photography as a screening tool in age-related macular degeneration. American journal of ophthalmology, 139, 3, 455-461, 2005**
Country/ies where the study carried out	Ontario, Canada
Study type	Prospective case series
Aim of the study	To compare the expert evaluation of mydriatic, non-stereo digital colour fundus photographs with clinical examination and fluorescein angiography in identifying and classifying exudative age-related macular degeneration (AMD)
Study dates	September 2001 and June 2002
Sources of funding	Not reported
Number of patients	118 patients (236 eyes)
Inclusion criteria	Patients were seen in the AMD screening clinic
Exclusion criteria	Patients for whom fundus photographs were not available Patients deemed not to require angiography or fundus photography on reference Patients for whom the time between obtaining a fundus photograph and clinical examination was greater than 3 month Patients seen in the AMD screening clinical for a condition other than AMD
Eligible participants characteristics	Median age, range: 79.2, 45 to 93 years
Type of test	Fundus photograph
Reference standard	Clinical examination (final clinical assessment for each eye was derived from information obtained from patient charts, including review of fluorescein angiograms).
Prevalence	The presence of specific lesion in age-related macular degeneration RPE (retinal pigment epithelium) geographic atrophy

		Clinical examination		
FP		Positive	Negative	Total
	Positive	31	23	54
	Negative	16	153	169

Bibliographic reference	Pirbhai,A., Sheidow,T., Hooper,P. Prospective evaluation of digital non-stereo colour fundus photography as a screening tool in age-related macular degeneration. American journal of ophthalmology, 139, 3, 455-461, 2005

Total		47	176	223

PED (pigment epithelial detachment)

		Clinical examination		
FP		Positive	Negative	Total
	Positive	8	12	20
	Negative	12	191	203
Total		20	203	223

CNVM (choroidal neovascular membrane)

		Clinical examination		
FP		Positive	Negative	Total
	Positive	99	16	115
	Negative	12	96	108
Total		111	112	223

Exudative age-related macular degeneration

		Clinical examination		
FP		Positive	Negative	Total
	Positive	69	29	98
	Negative	15	110	125
Total		84	139	223

Bibliographic reference	Pirbhai,A., Sheidow,T., Hooper,P. Prospective evaluation of digital non-stereo colour fundus photography as a screening tool in age-related macular degeneration. American journal of ophthalmology, 139, 3, 455-461, 2005	
Sensitivity		
	Exudative AMD	82.1%, 95%CI 73.3 to 89.5%
	Presences of lesion in AMD	
	RPE geographic atrophy	65.9%, 95%CI 51.9 to78.6%
	PED	40.0%, 95%CI 20.3 to 61.6%
	CNVM	89.2%, 95%CI 82.8 to 94.2
Specificity	Exudative AMD	79.1%, 95%CI 72.0 to 85.4%
	Presences of lesion in AMD	
	RPE geographic atrophy	86.9%, 95%CI 81.6 to 91.5%
	PED	94.1%, 95%CI 90.4 to 96.8%
	CNVM	85.7%, 95%CI 78.7 to 91.5%
Positive predictive values	Exudative AMD	70.4%, 95%CI 61.0 to 79.0%
	Presences of lesion in AMD	
	RPE geographic atrophy	57.4%, 95%CI 44.1 to70.2%
	PED	40.0% 95%CI 20.3 to 61.6%
	CNVM	86.1%, 95%CI 78.7 to 91.5%
Negative predictive values	Exudative AMD	88%, 95%CI 81.8 to 93.1%
	Presences of lesion in AMD	
	RPE geographic atrophy	90.5%, 95%CI 85.7 to 94.5%
	PED	94.1%, 95%CI 90.4 to 96.9%
	CNVM	88.9%, 95%CI 82.4 to 94.1%
Comments	Patient selection: patients seen in AMD screening clinic between Septermaber 2001 and June 2002. Index test and reference standard: Colour fundus photographys for each patient were randomly labeld before being read by a vitreoretinal surgeon. The readers was masked to other patient infomraiton and status of the fellow eye. Agreement between final clinical assessment and digital photography was calculated using a kappa coeffieicent.	

Bibliographic reference	Pirbhai,A., Sheidow,T., Hooper,P. Prospective evaluation of digital non-stereo colour fundus photography as a screening tool in age-related macular degeneration. American journal of ophthalmology, 139, 3, 455-461, 2005
	Flow and timing: Fundus photographs were taken at the time of fluorescein angiography, either berfore or after the clinicl visit.

Bibliographic reference	Sallet,G., Lafaut,B.A., De Laey,J.J., Indocyanine green angiography and age-related serous pigment epithelial detachment.Graefes Archive for Clinical & Experimental Ophthalmology, 234, 1, 25-33, 1996
Country/ies where the study carried out	Belgium
Study type	Retrospective case
Aim of the study	To examine whether indocyanine green angiography (ICG-A) provides a better visualisation of choroidal circulation and of CNV than fluorescein angiography.
Study dates	Not reported
Sources of funding	Supported by a grant form Les amis des Aveugles (Ghlin Belgium)
Number of patients	52 patients (58 eyes)
Inclusion criteria	Patients with age-related macular degeneration presenting a PED without classic CNV on fluorescein angiography Evidence of CNV such as haemorrhage, exudate, regional masking on FA not related to hyperpigmentation, a notch at the edge of the PED and ill-defined hyperfluorescence with late diffusion Serious PED of at least on disc diameter without signs of CNV on FA
Exclusion criteria	Patients with other macular diseases associated with CNV and patients with absence of signs of ARMD in the fellow eyes
Eligible participants characteristics	Mean age, range: 72, 58 and 86 years. Number of males: 25 (48%)
Type of test	Indocyanine green angiography (ICG-A)
Reference standard	Fluorescein angiography (FA)
Prevalence	

		FA		
ICG-A		Positive	Negative	Total
	Positive	29	2	31

Bibliographic reference	**Sallet,G., Lafaut,B.A., De Laey,J.J., Indocyanine green angiography and age-related serous pigment epithelial detachment.Graefes Archive for Clinical & Experimental Ophthalmology, 234, 1, 25-33, 1996**
	<table><tr><td></td><td>Negative</td><td>19</td><td>8</td><td>27</td></tr><tr><td>Total</td><td></td><td>48</td><td>10</td><td>58</td></tr></table>
Sensitivity	60.4%, 95%CI 46.4 to73.6%
Specificity	89.5%, 95%CI 72.7 to98.6%
Positive predictive values	93.5%, 95%CI 82.8 to 99.2%
Negative predictive values	47.2%, 95%CI 31.4 to 63.4%
Comments	Patient selection: patients with ARMD presenting a PED without classic CNV or FA were studied. Index test and reference standard: ICG-A was perfomed following designed procedures. FA was also performed. Grading and masking of index test and reference standard were not described in the study. Flow and timing: FA and ICG-A were performed on the same day.

Bibliographic reference	**Sandhu,S.S., Talks,S.J. Correlation of optical coherence tomography, with or without additional colour fundus photography, with stereo fundus fluorescein angiography in diagnosing choroidal neovascular membranes.British Journal of Ophthalmology, 89, 8, 967-970, 2005**
Country/ies where the study carried out	UK
Study type	Prospective cross sectional
Aim of the study	To assess the diagnostic accuracy of optical coherence tomography (OCT), with/without colour funds photographs, in predicting fundus fluorescein angiography (FFA) findings in patients suspected of having choroidal neovascularisation (CNV).
Study dates	2002
Sources of funding	Not reported
Number of patients	118 patients (131 eyes) included in the analysis
Inclusion criteria	Patients with suspected choroidal neovascularisaiton
Exclusion criteria	Not reported
Eligible participants characteristics	Mean age (SD): 73.2 (13.7) years

<table>
<tr><th>Bibliographic reference</th><td>Sandhu,S.S., Talks,S.J. Correlation of optical coherence tomography, with or without additional colour fundus photography, with stereo fundus fluorescein angiography in diagnosing choroidal neovascular membranes.British Journal of Ophthalmology, 89, 8, 967-970, 2005</td></tr>
<tr><td></td><td>% of female: 57.6%</td></tr>
<tr><td>Type of test</td><td>Optical coherence tomography</td></tr>
<tr><td>Reference standard</td><td>Fundus fluorescein angiography (FFA)</td></tr>
<tr><td>Prevalence</td><td>CNV
<table>
<tr><td></td><td></td><td>FFA</td><td></td><td></td></tr>
<tr><td>OCT</td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr>
<tr><td></td><td>Positive</td><td>81</td><td>16</td><td>97</td></tr>
<tr><td></td><td>Negative</td><td>3</td><td>31</td><td>34</td></tr>
<tr><td>Total</td><td></td><td>84</td><td>47</td><td>131</td></tr>
</table>
<table>
<tr><td></td><td></td><td>FFA</td><td></td><td></td></tr>
<tr><td>OCT + stereo images (fundus)</td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr>
<tr><td></td><td>Positive</td><td>79</td><td>5</td><td>84</td></tr>
<tr><td></td><td>Negative</td><td>5</td><td>42</td><td>47</td></tr>
<tr><td>Total</td><td></td><td>84</td><td>47</td><td>131</td></tr>
</table></td></tr>
<tr><td>Sensitivity</td><td>
<table>
<tr><td>OCT alone</td><td>96.4%, 95%CI 91.6 to 99.2%</td></tr>
<tr><td>OCT with stereo imaged</td><td>94.4%, 95%CI 88.1 to 98.0%</td></tr>
</table></td></tr>
<tr><td>Specificity</td><td>
<table>
<tr><td>OCT alone</td><td>65.9%, 95%CI 52.0 to 78.6%</td></tr>
<tr><td>OCT with stereo imaged</td><td>89.3%, 95%CI 79.2 to 96.4%</td></tr>
</table></td></tr>
<tr><td>Positive predictive values</td><td>
<table>
<tr><td>OCT alone</td><td>83.5%, 95%CI 75.5 to 90.2%</td></tr>
<tr><td>OCT with stereo imaged</td><td>94.0%, 95%CI 88.1 to 98.0%</td></tr>
</table></td></tr>
</table>

Bibliographic reference	**Sandhu,S.S., Talks,S.J. Correlation of optical coherence tomography, with or without additional colour fundus photography, with stereo fundus fluorescein angiography in diagnosing choroidal neovascular membranes.British Journal of Ophthalmology, 89, 8, 967-970, 2005**
Negative predictive values	<table><tr><td>OCT alone</td><td>91.2%, 95%CI 79.8 to 98.1%</td></tr><tr><td>OCT with stereo imaged</td><td>89.4%, 95%CI 79.2 to 96.4%</td></tr></table>
Comments	Patient selection: patients presented with suspected CNV. Detailed inclusion and exclusion critiera were not reported in the study. Index test and reference standard: Imagings were reviewed by 2 independent observers, one assigning the OCT and then the OCT plus colour photography, the other the FFA. Each masked to the other's diagnositic classification and the clinicald disagnosis. Flow and timing: Time intervals of index tests and reference standard were unclear.

Bibliographic reference	**Talks,J., Koshy,Z., Chatzinikolas,K., Use of optical coherence tomography, fluorescein angiography and indocyanine green angiography in a screening clinic for wet age-related macular degeneration.British Journal of OphthalmologyBr.J.Ophthalmol., 91, 5, 600-601, 2007.**
Country/ies where the study carried out	UK
Study type	Retrospective audit
Aim of the study	To assess the utility of optical coherence tomography in a nurse-led, fast-track clinic for new age-related macular degeneration referrals, and to see how often indocyanine green angiography led to an additional diagnosis to that provided by fluorescein angiography.
Study dates	Not reported
Sources of funding	Not reported
Number of patients	111 patients
Inclusion criteria	Patients were referred from optometrists and GPs with symptoms suggestive of wet AMD
Exclusion criteria	Not reported
Eligible participants characteristics	Mean age, range: 84.6, 58 to 97 years % of female: 60.4%

<table>
<tr><th>Bibliographic reference</th><th>Talks,J., Koshy,Z., Chatzinikolas,K., Use of optical coherence tomography, fluorescein angiography and indocyanine green angiography in a screening clinic for wet age-related macular degeneration.British Journal of OphthalmologyBr.J.Ophthalmol., 91, 5, 600-601, 2007.</th></tr>
<tr><td>Type of test</td><td>OCT</td></tr>
<tr><td>Reference standard</td><td>Fundus fluorescein angiography
indocyanine green angiography</td></tr>
<tr><td>Prevalence</td><td>
<table>
<tr><td></td><td></td><td>FFA/ICG</td><td></td></tr>
<tr><td>OCT</td><td></td><td>Positive</td><td>Negative</td></tr>
<tr><td></td><td>Positive</td><td>93</td><td>12</td></tr>
<tr><td></td><td>Negative</td><td>0</td><td>23</td></tr>
<tr><td>Total</td><td></td><td>93</td><td>35</td></tr>
</table>
<table>
<tr><td></td><td></td><td>FFA/ICG</td><td></td></tr>
<tr><td>FFA</td><td></td><td>Positive</td><td>Negative</td></tr>
<tr><td></td><td>Positive</td><td>93</td><td>0</td></tr>
<tr><td></td><td>Negative</td><td>6</td><td>12</td></tr>
<tr><td>Total</td><td></td><td>99</td><td>12</td></tr>
</table>
</td></tr>
<tr><td>Sensitivity</td><td>OCT: 100%
FFA: 93.5%, 95%CI 87.9 to 97.4%</td></tr>
<tr><td>Specificity</td><td>OCT: 65.0%, 95%CI 49.2 to 79.7%
FFA:100.0%</td></tr>
<tr><td>Positive predictive values</td><td>OCT: 88.2%, 95%CI 81.4 to 93.6%
FFA: 100.0%</td></tr>
<tr><td>Negative predictive values</td><td>OCT: 100%
FFA: 65.8%, 95%CI 43.7 to 84.7%</td></tr>
<tr><td>Comments</td><td>Patient selection: a selection of new patients referred wth wet AMD to a nurse-led, fast-tracl screening clinic.
Index test and reference standard: patients underwent simultaneous FFA and ICGA. Masking of index test and reference standard were unclear.</td></tr>
</table>

Bibliographic reference	Talks,J., Koshy,Z., Chatzinikolas,K., Use of optical coherence tomography, fluorescein angiography and indocyanine green angiography in a screening clinic for wet age-related macular degeneration.British Journal of OphthalmologyBr.J.Ophthalmol., 91, 5, 600-601, 2007.
	Flow and timing: patients underwent simultaneous FFA and ICGA.

Bibliographic reference	Wilde,C., Patel,M., Lakshmanan,A., Amankwah,R., Dhar-Munshi,S., Amoaku,W., Medscape, The diagnostic accuracy of spectral-domain optical coherence tomography for neovascular age-related macular degeneration: a comparison with fundus fluorescein angiography.Eye, 29, 5, 602-610, 2015
Country/ies where the study carried out	UK
Study type	Retrospective cross sectional
Aim of the study	To evaluate the diagnostic accuracy of spectral-domain optical coherence tomography (SD-OCT) for neovascular age-related macular degeneration (nAMD).
Study dates	February 2009 to February 2013
Sources of funding	The Macular Society UK
Number of patients	411 patients (822 eyes)
Inclusion criteria	Patients were over 50 years Patients were referred for suspected nAMD Patients had symptoms of reduced vision, metamorphopsia, or signs suggestive of nAMD
Exclusion criteria	All patients that had either no SD-OCT or FP/FFA available for analysis Patients whose imaging modality was deemed ungradable. If SD-OCT or FFA were not performed within 7 days of each other Patients with CNV secondary to angioid streaks or evidence of chorioretinitis
Eligible participants characteristics	Not reported
Type of test	Spectral-domain optical coherence tomography (SD-OCT)
Reference standard	Fundus fluorescein angiography (FFA)
Prevalence	

Bibliographic reference	**Wilde,C., Patel,M., Lakshmanan,A., Amankwah,R., Dhar-Munshi,S., Amoaku,W., Medscape, The diagnostic accuracy of spectral-domain optical coherence tomography for neovascular age-related macular degeneration: a comparison with fundus fluorescein angiography.Eye, 29, 5, 602-610, 2015**
	<table><tr><td></td><td></td><td>FFA</td><td></td><td></td></tr><tr><td>OCT</td><td></td><td>Positive</td><td>Negative</td><td>Total</td></tr><tr><td></td><td>Positive</td><td>231</td><td>47</td><td>278</td></tr><tr><td></td><td>Negative</td><td>0</td><td>198</td><td>198</td></tr><tr><td>Total</td><td></td><td>231</td><td>245</td><td>476</td></tr></table>
Sensitivity	100.0%
Specificity	80.6%, 95%CI 75.5 to 85.3%
Positive predictive values	83.0%, 95%CI 78.3 to 87.1%
Negative predictive values	100.0%
Comments	Patient selection: A consecutive patietsn who were referraed to a rapid access clinic over 4-year period. Patientswho may have had treatment 6 or more months previously with PDT or anti-VEGF but were thought to have new CNV were included. Index test and reference standard: OCT and FA were performed. OCT images were reviewed without reference to the FFA. The grader was blind to any clinical patient information. Side by side independent grading took place withi immediate open discussion and adjudication. If there was disagrrement beween the two grading ophthamologists then adustification by a third ophthalmologist would take place. Flow and timing: patients who had OCT or FFA were not performed within 7 days of each other were excluded.