

Supplementary Table S1. List of principal analyses (main and sensitivity analyses, and additional post-hoc analyses of diagnostic accuracy) ^a

Analysis name	Level of Analysis	DME index test positive	DME reference standard	PDR index test positive	PDR reference standard
Main	Person	Ophthalmic graders referral ^b for DME based on SD-OCT images	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy with the addition of SD-OCT scans to assess active DME in either eye	Ophthalmic graders referral for PDR based on ultra-wide field fundus images / Ophthalmic graders referral for PDR based on 7-field ETDRS fundus images	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy to assess active PDR in either eye
Sensitivity analysis 1	Person	Ophthalmic graders identified active DME based on SD-OCT images	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy with the addition of SD-OCT scans to assess active DME in either eye	Ophthalmic graders identified active PDR based on ultra-wide field fundus images / Ophthalmic graders identified active PDR based on 7-field ETDRS fundus images	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy to assess active PDR in either eye
Sensitivity analysis 2	Person	Ophthalmic graders referral for DME based on SD-OCT images	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy with the addition of SD-OCT scans to assess active DME in either eye requiring treatment	Ophthalmic graders referral for PDR based on ultra-wide field fundus images / Ophthalmic graders referral for PDR based on 7-field ETDRS fundus images	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy to assess active PDR in either eye requiring treatment
Sensitivity analysis 3	Person	Ophthalmic graders identified central involving active DME based on SD-OCT images	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy with the addition of SD-OCT scans to assess central involving active DME in either eye
Sensitivity analysis 4	Person	Ophthalmic graders referral for PDR based on ultra-wide field fundus images / Ophthalmic graders referral for PDR based on 7-field ETDRS fundus images	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy to assess active PDR with pre-retinal or vitreous haemorrhage in either eye

Sensitivity analysis 5	Person	Ophthalmic graders referral for PDR based on ultra-wide field fundus images / Ophthalmic graders referral for PDR based on 7-field ETDRS fundus images	Enhanced standard
Sensitivity analysis 6	Person	Ophthalmic graders referral for DME based on SD-OCT images in routine clinic	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy with the addition of SD-OCT scans to assess active DME in either eye in routine clinic	Ophthalmic graders referral for PDR based on ultra-wide field fundus images in routine clinic / Ophthalmic graders referral for PDR based on 7-field ETDRS fundus images in routine clinic	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy to assess active PDR in either eye in routine clinic
Additional 1	Person	Ophthalmologist assessment identified active PDR based on ultra-wide field fundus images / Ophthalmologist assessment identified active PDR based on 7-field ETDRS fundus images	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy to assess active PDR in either eye
Additional 2	Person	Ophthalmologist assessment identified active PDR based on ultra-wide field fundus images / Ophthalmologist assessment identified active PDR based on 7-field ETDRS fundus images	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy to assess active PDR with pre-retinal or vitreous haemorrhage in either eye
Additional 3	Person	Ophthalmic graders referral for PDR based on ultra-wide field fundus images / Ophthalmic graders referral for PDR based on 7-field ETDRS fundus images	Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy to assess active PDR in either eye plus Ophthalmologist assessment identified active PDR in either eye based on ultra-wide field fundus images / Ophthalmologist face-to-face clinical evaluation using slit-lamp biomicroscopy to assess active PDR in either eye plus Ophthalmologist assessment identified active PDR in either eye based on 7-field ETDRS fundus images

Note: Ophthalmologists face-to-face clinical evaluation using slit-lamp biomicroscopy with the addition of SD-OCT scans = reference standard for DME (i.e. standard care); ophthalmologists face-to-face clinical evaluation using slit-lamp biomicroscopy = reference standard for PDR (i.e. standard care).

^a Principal analyses were focused on “eligible participants for the new pathway” and referred to analysis done using data from the eligible eye(s) of each patient included in EMERALD [Note: All patients included in EMERALD were eligible for the purpose of evaluating one or other disease or both (DME, PDR); they may have contributed with data from “eligible eyes” if they have had DME, PDR, or both in one or both eyes which were previously successfully treated, becoming stable at one point following treatment – see Methods section].

Additional post-hoc analyses on PDR (labelled in the table as ‘additional 1-3’) that were not listed in the statistical analysis plan were conducted in light of the main PDR results to understand the content and potential value of the two imaging modalities better along with reliability of the ophthalmologists face-to-face clinical evaluation using slit-lamp biomicroscopy reference standard for PDR.

^b grader referral for DME or PDR= “active” + “unsure” + “ungradable”

SD-OCT = spectral domain optical coherence tomography; DME = Diabetic macular edema; PDR = proliferative diabetic retinopathy; ETDRS = Early treatment diabetic retinopathy study.