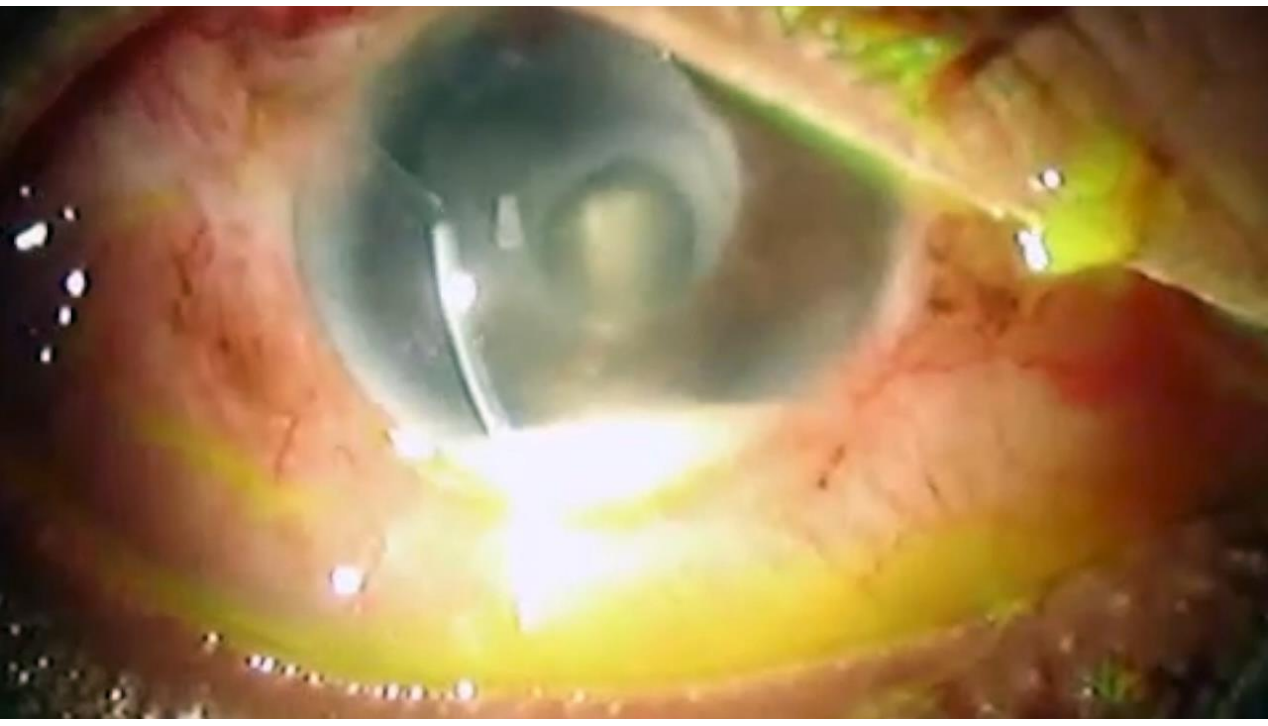


Feasibility Randomised Controlled Trial of Early Vitrectomy and Intravitreal Antibiotics for Post-operative Exogenous Endophthalmitis



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Study Population/Design

Pragmatic, open label, multicentre, randomised feasibility study national UK study
1:1 randomisation, with intervention vs. control group, 4-year study
Sample size: up to 64 participants
Duration: March 2020 to March 2025
Follow-up period: 6 months
Funder: NIHR RfPB Grant Award

Main Inclusion Criteria: ALL patients with exogenous endophthalmitis diagnosed following ANY type of intraocular surgery/procedure, intravitreal injection, or intravitreal implant.

Ophthalmic criteria:
Symptomatic visual loss attributable to bacterial POE
Visual acuity worse than 35 ETDRS letters (6/60)

Intervention Arms

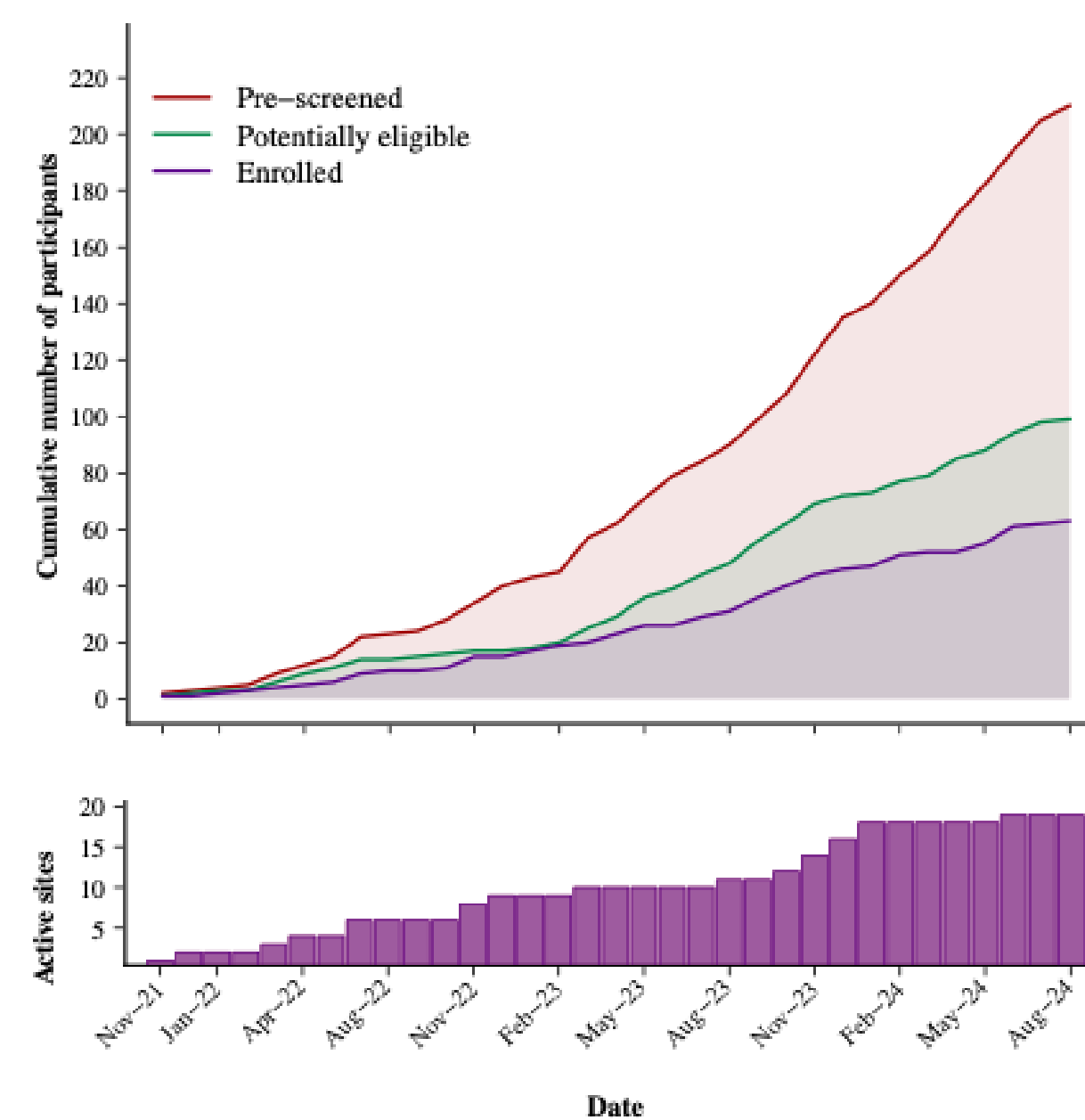
Group 1: Early vitrectomy surgery
Vitrectomy surgery, vitreous biopsy combined with second intravitreal antibiotics performed within 48-72 hours of randomisation

Group 2: Standard of care repeat, immediate intravitreal antibiotic treatments.
According to local hospital “retap and reinjection protocol” Delayed vitrectomy at Day 10-14

Overview: Feasibility study Outcomes

Primary objective: Patient recruitment (Rates of recruitment and retention, rates of participants, including willingness of surgeons to refer patients into the study, and willingness of participants to be randomised)

Secondary objective (s): Distance Best Corrected Visual Acuity, Rate of completed follow up, Number of additional procedures, Quality of life, Rate of complications



Results

- Slow site set-up triggered by post-COVID-19 pandemic
- Restrictions on research capability/capacity at our designated EVIAN clinical sites
- November 2021 to January 2023

Screening & Recruitment

The study was feasible and met the primary endpoint
63 participants were randomized at a 79% recruitment rate (over 2.5 years)
Main Reasons for non-participation: Participant choice (28%), clinician choice (10%), participants deemed ineligible at pre-screening phase (23%).

Figure 2: Study Overview

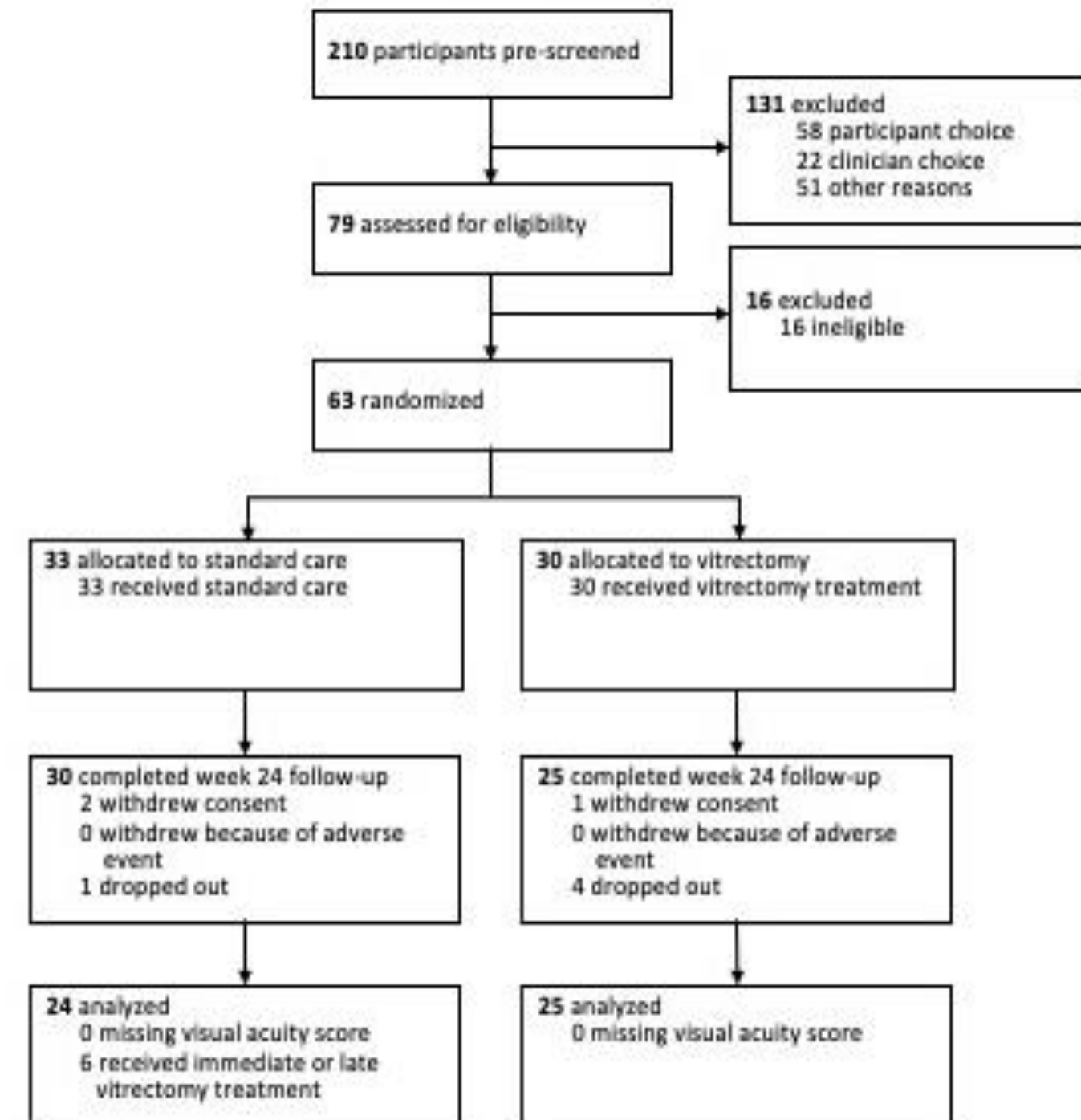
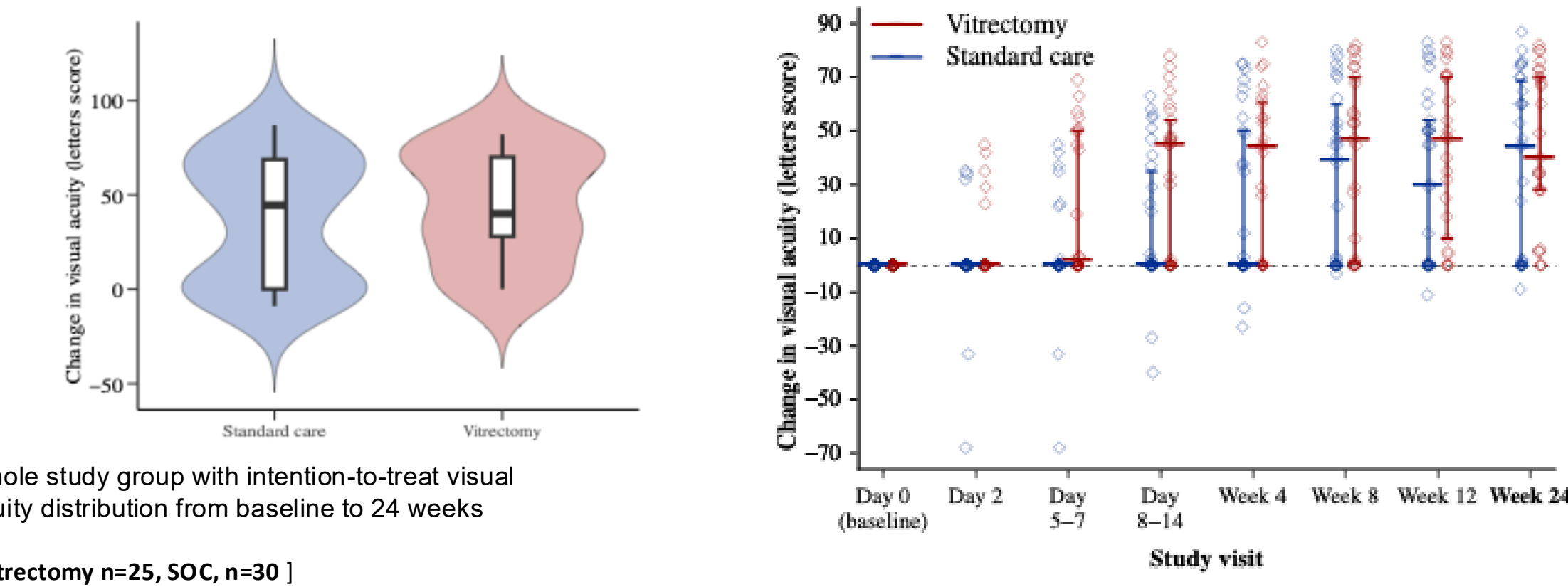


Table 1: Population Demographics

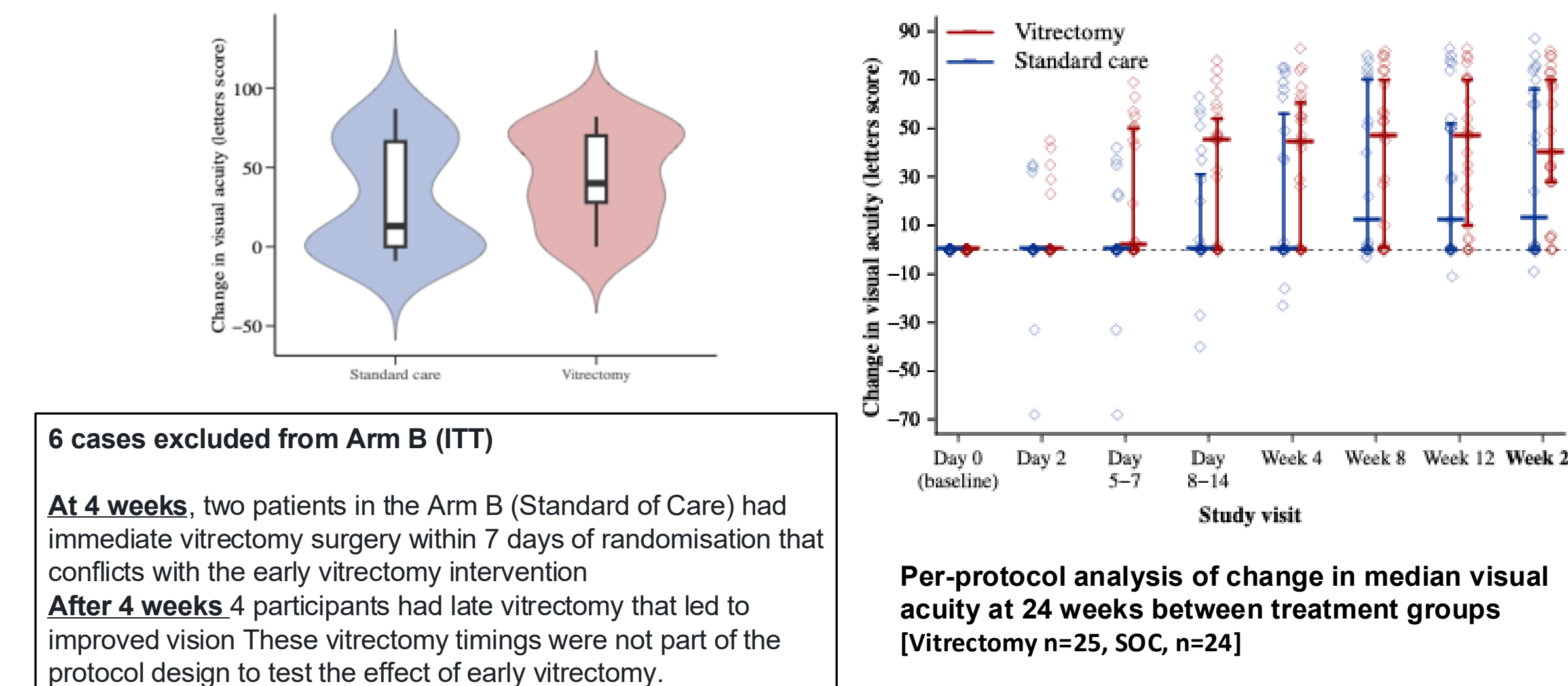
	Standard care (Arm B) (N=33)	Vitrectomy (Arm A) (N=30)	Overall (N=63)
Demographic characteristics			
Age (mean, years)	72.8 (13.5)	70.7 (9.8)	71.8 (11.8)
Female	15 (58%)	15 (50%)	34 (54%)
Ethnicity			
White	28 (85%)	26 (87%)	54 (86%)
Asian	1 (3%)	4 (13%)	5 (8%)
Black	3 (9%)	-	3 (5%)
Other	1 (3%)	-	1 (2%)
Ophthalmic characteristics			
Study eye (left)	11 (33%)	14 (47%)	25 (40%)
Endophthalmitis cause			
Intravitreal injection	13 (39%)	14 (47%)	27 (43%)
Cataract surgery	9 (27%)	8 (27%)	17 (27%)
Vitrectomy surgery	4 (12%)	3 (10%)	7 (11%)
Glaucoma surgery	3 (9%)	1 (3%)	4 (6%)
Lens implant surgery	-	1 (3%)	1 (2%)
Other/unknown	4 (12%)	3 (10%)	7 (11%)
Duration of symptoms (days)*	3 [2-5]	3 [2-3]	3 [2-4]
Bacterial culture	23 (70%)	20 (67%)	43 (68%)
Lens status			
Phakic	13 (39%)	9 (30%)	22 (35%)
Anterior chamber lens implant	1 (3%)	1 (3%)	2 (3%)
Posterior chamber lens implant	19 (58%)	19 (63%)	38 (60%)
Other	-	1 (3%)	1 (2%)
Any ocular co-morbidity	27 (82%)	24 (80%)	51 (81%)
Corneal pathology	3 (10%)	2 (8%)	5 (9%)
Macular pathology	18 (62%)	14 (56%)	32 (59%)
Uveitis	2 (7%)	-	2 (4%)
Glaucoma	8 (28%)	5 (20%)	13 (24%)
Optic nerve disease	1 (3%)	-	1 (2%)
Other [‡]	5 (17%)	10 (40%)	15 (28%)
ETDRS visual acuity (letters score)	3.1 (13.0)	1.1 (5.0)	2.1 (10.0)

Secondary Outcomes: Visual Acuity: Intention-to-Treat (ITT)



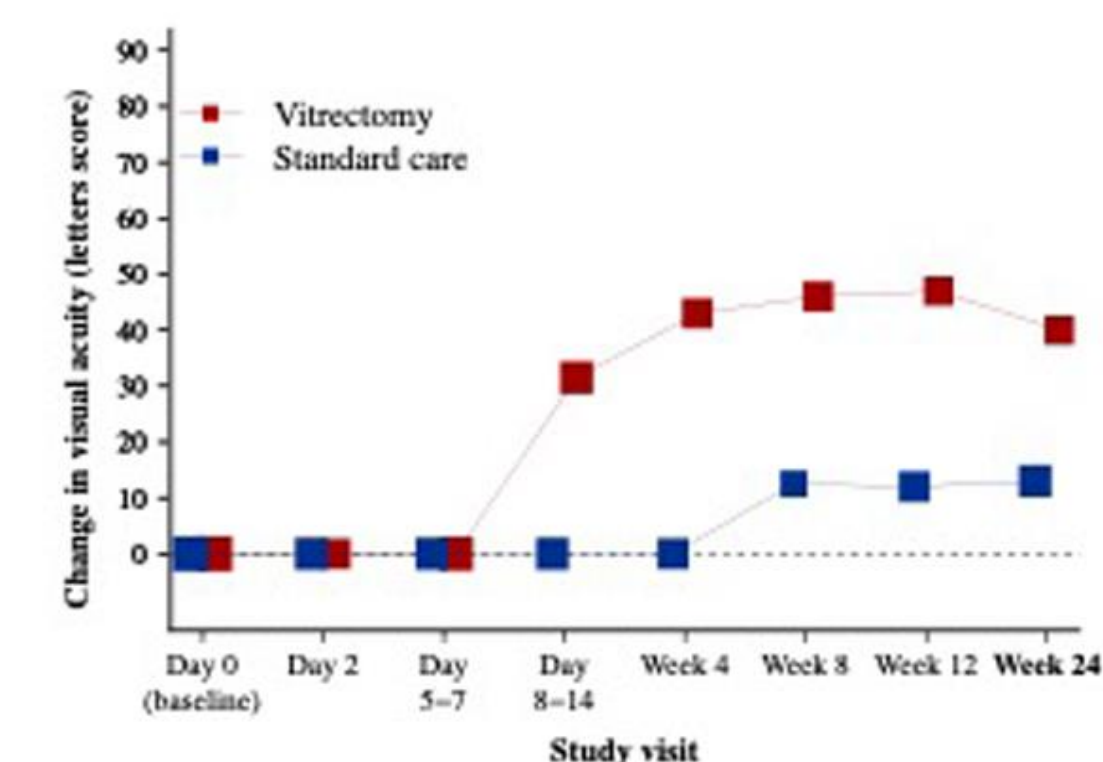
Whole study group with intention-to-treat visual acuity distribution from baseline to 24 weeks
[Vitrectomy n=25, SOC, n=30]
Mean change in VA from baseline to 24 weeks was 36.4 (SD 33.3) letters in SOC Arm (n=30) versus 43.6 letters (SD 29.5) in VITY Arm (n=25).
Median change in VA from baseline to 24 weeks was 46.0 (IQR -0.70) letters in SOC Arm (n=30) versus 40 letters (IQR 28-73) in VITY Arm (n=25).

Secondary Outcomes: Visual Acuity: Per-Protocol (PP)



6 cases excluded from Arm B (ITT)
At 4 weeks, two patients in the Arm B (Standard of Care) had immediate vitrectomy surgery within 7 days of randomisation that conflicts with the early vitrectomy intervention
After 4 weeks 4 participants had late vitrectomy that led to improved vision These vitrectomy timings were not part of the protocol design to test the effect of early vitrectomy.

Per-Protocol Visual Acuity Outcomes



- Median change in VA (IQR) per-protocol from baseline was 40 (28-70) letters in vitrectomy Arm A group (n=25) versus 13 (0-66) letters in standard of care Arm B group (n=24).

As this is a feasibility study, the trial was NOT powered to detect significant differences in VA or other clinical outcomes. However, the PP results provided valuable preliminary estimates of variability, which have been useful to inform the sample size calculations for a future Phase 3 confirmatory trial.

Table 2: Ocular Adverse Events	Standard care (Arm B) (N=33)	Vitrectomy (Arm A) (N=30)
Anterior Segment		
Iris Bombe	1 (3%)	
Anterior uveitis	3 (9%)	2 (6.7%)
Corneal oedema		
Iris rubeosis	1 (3%)	
Ocular hypertension	3 (9%)	2 (6.7%)
Cataract	2 (6%)	2 (6.7%)
Microbial keratitis	1 (3%)	1 (3.3%)
Glaucoma		1 (3.3%)
Infectious necrotizing scleritis	1 (3%)	
Persistent Corneal epithelium defect	1 (3%)	

Posterior Segment		
Cystoid macular oedema	1 (3%)	1 (3.3%)
Retinal detachment	8 (24%)	2 (6.7%)*
Phthisis bulbi	1 (3%)	
Epiretinal membrane	1 (3%)	
Macular hole	1 (3%)	
Choroidal hemorrhage	1 (3%)	1 (3.3%)
Subretinal hemorrhage	1 (3%)	
Cyclitic membrane	1 (3%)	
Hypotony	2 (6%)	

Conclusions

Although, the PP result was not statistically significant, the PP change in VA reveals a **positive signal of effect** indicating a potential greater effect on patient vision of early vitrectomy compared to standard of care treatment, with an acceptable safety profile of early vitrectomy in the EVIAN trial

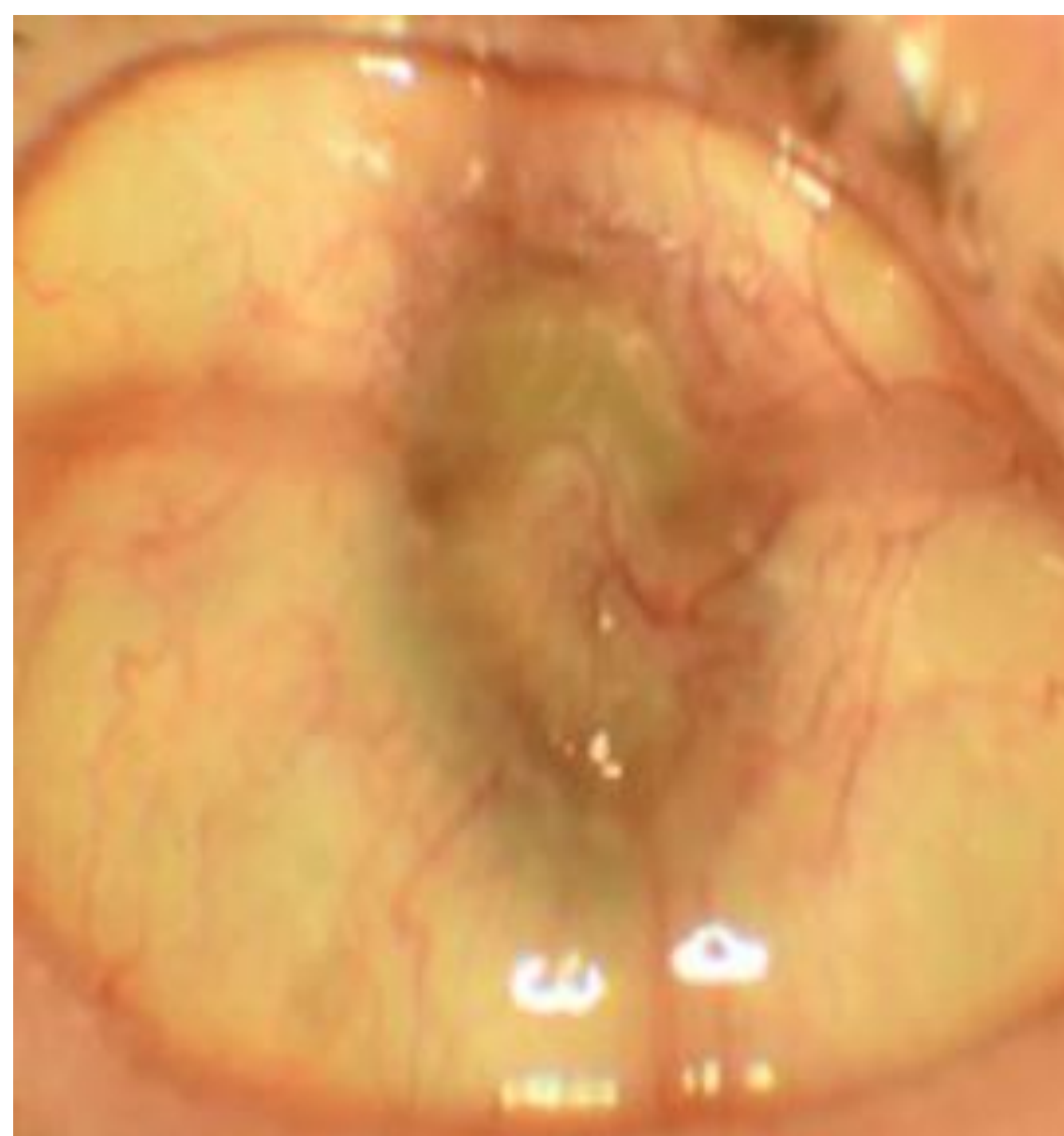
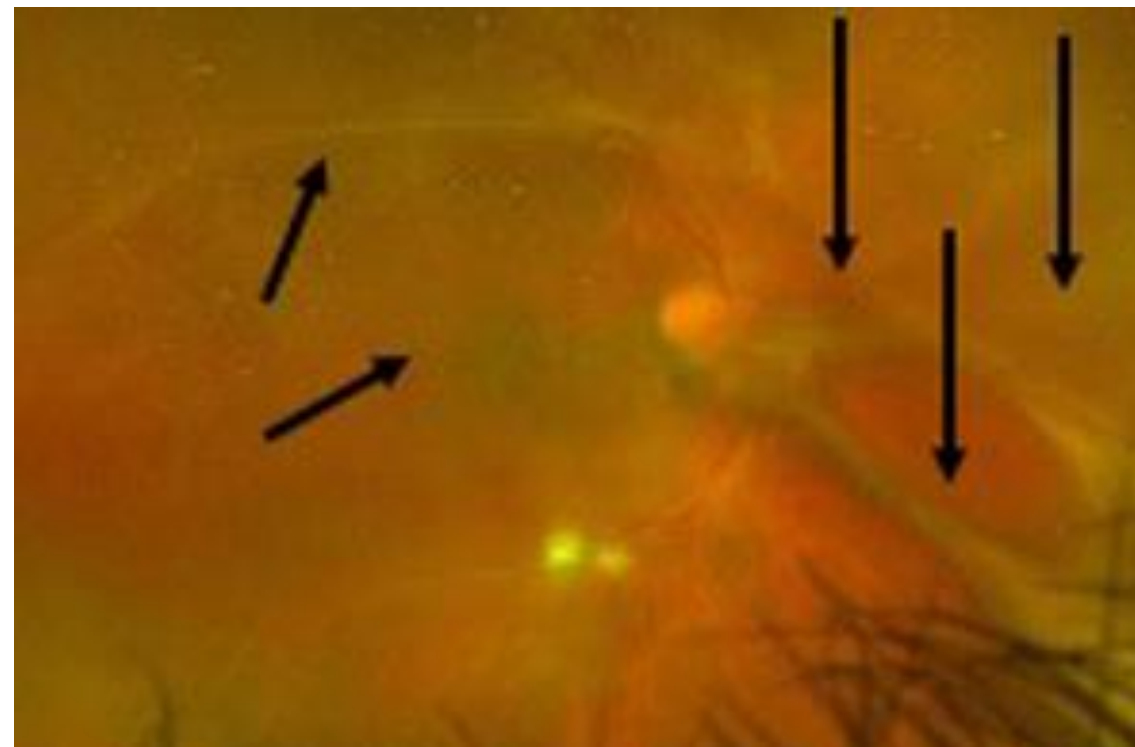
Next step is the definitive trial: “DIAMONDE” Study

Multicentre International RCT to study the Efficacy and Safety of Early Vitrectomy for Exogenous Endophthalmitis

Sponsor: UCL Comprehensive Clinical Trials Unit (CCTU), UK

References

- MMK Muqit, C Pavesio, Y Wang³, S Cobb, C Spink, E Pizzo, G Clare, G Hay, H Wafa, J Wang, H Boston, K Sriharan, EVIAN Study Group, J Bainbridge. Early Vitrectomy and Intravitreal Antibiotics for Post-operative Exogenous Endophthalmitis (EVIAN): A Randomised Control Trial of Feasibility. *Nat Comms Med.* 2026 (in press)
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- Muqit MMK, Pavesio C, Boston H, Sriharan K, Wang Y, Pizzo E, Cobb S, Spink C, Bainbridge J. A Randomised Controlled Trial of Early Vitrectomy and Intravitreal Antibiotics for Post-operative Exogenous Endophthalmitis (EVIAN study): study protocol for a feasibility trial. *NIHR Open Res.* 2023 Sep 28;3:47



Examples of Adverse Events:
Upper: Retinal detachment; Middle: Necrotising scleritis;
Lower: Phthisis bulbi