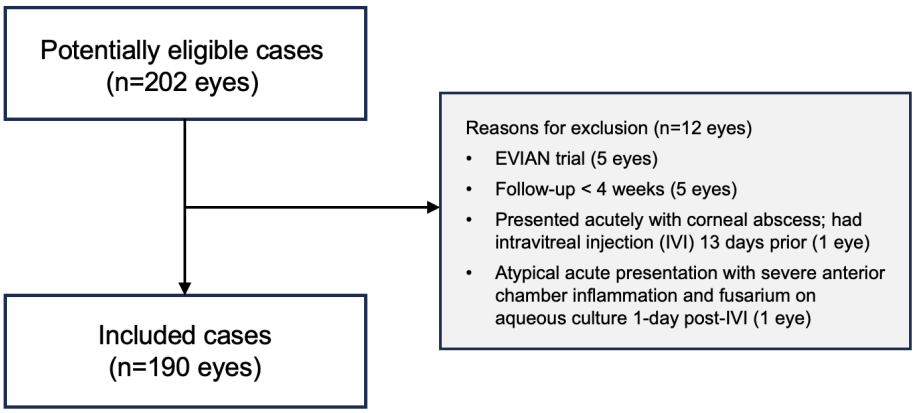
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Supplementary Materials

Supplementary S1: Flow chart depicting cases excluded from analysis and the rationale for exclusion.



Exclusion criteria: Patients with delayed/chronic, endogenous, microbial keratitis-related or post-traumatic endophthalmitis were excluded in the data collection phase, as were those deemed by their treating clinician(s) to have severe postoperative inflammation or toxic anterior segment syndrome (TASS).

On review of potentially eligible cases, 12 patients were excluded.

This comprised 5 patients who were part of the EVIAN trial, a randomised feasibility trial comparing intravitreal antibiotics alone versus antibiotics combined with early vitrectomy for postoperative endophthalmitis. There was a small overlap between the study eligibility period and recruitment to the EVIAN trial[28] at one site. Given the randomised assignment of further treatment, which runs counter to our interest in the rationale for change in subsequent management, these five eyes were excluded from the analysis.

Patients with less than four weeks of follow-up were not eligible for inclusion because of the study's aims - to assess for change in management within four weeks of the initial treatment. This comprised a further five cases seen at these tertiary centres for initial management and discharged back to their local eye unit within 2-4 days of their initial visit.

Two further cases were excluded due to diagnostic uncertainty implicating their eligibility:

One patient presented with a clinical picture typical of endophthalmitis, and was initially included because they had presented 13 days after intravitreal Eylea treatment for diabetic macular oedema. However, they had also developed a suture-related corneal abscess two days prior to presentation (residual suture from phacoemulsification cataract surgery four years prior), and it was felt that this was more likely to have contributed to the presentation, rather than resulting from postoperative endophthalmitis.

The second case presented one day after intravitreal Eylea injection for neovascular age-related macular degeneration. Aqueous culture grew *fusarium* spp. sensitive to voriconazole and amphotericin; however the clinical picture was extremely atypical of fusarium endophthalmitis due to the acute presentation, excellent visual acuity (0.30 logMAR), and significant anterior chamber activity with absence of hypopyon or vitreous activity. Vitreous sampling was unsuccessful ('dry' vitreous tap) at presentation and not repeated. No signs characteristic of fungal infection were evident throughout the clinical course and the visual outcome remained unchanged at final follow-up. There were no significant risk factors for fungal infection such as recent contact lens wear (last worn 3-4 months prior), although the patient was relatively immunosuppressed (on leuprorelin for metastatic prostate cancer) without any other significant past medical history.

Supplementary S2: Typical management of endophthalmitis cases by site.

Vitreous samples were taken via vitreous taps (needle aspiration using a 23- or 25-gauge needle or mechanical vitreous cutter) or PPV according to surgeon choice. Anterior chamber taps were taken according to clinicians' discretion. For four sites (Oxford, Sunderland, Southampton, Sheffield), the intravitreal antibiotics of choice were vancomycin (1-2 mg/0.1 mL) and ceftazidime (2 mg/0.1 mL); intravitreal amikacin (0.4 mg/0.1 mL) was used in place of ceftazidime in those allergic to penicillin or cephalosporins. For one site (Moorfields), intravitreal vancomycin and amikacin were administered according to local treatment protocols. Topical antibiotics, steroids, cycloplegics, and oral antibiotics and steroids were prescribed at the discretion of the treating clinicians.

Supplementary S3: Sensitivity analyses comparing cases with available versus missing antibiotic sensitivity data.

	Antibiotic sensitivities available (n=86)	**Antibiotic sensitivities missing (n=21)**	**p-value**
Age (years) (median, IQR)	75 (62-83)	75 (61-80)	0.746
Female gender (n, %)	48/86 (55%)	10/21 (48%)	0.459
Precipitating procedures (n, %)			0.334
Intravitreal injections	53/86 (62%)	8/21 (38%)	
Cataract surgery	16/86 (19%)	8/21 (38%)	
Vitreoretinal surgery	10/86 (12%)	3/21 (14%)	
Secondary IOL	3/86 (3%)	0/21 (0%)	
Glaucoma surgery	4/86 (5%)	1/21 (5%)	
Squint surgery	1/86 (1%)	0/21 (0%)	
Presenting visual acuity (logMAR) (median, IQR)	2.40 (2.10-2.40)	2.40 (2.10-2.40)	0.926
Final visual acuity (logMAR) (median, IQR)	1.00 (0.48-2.40)	1.18 (0.20-2.70)	0.539
Change in management (n, %)	45/86 (52%)	12/21 (57%)	0.674

Supplementary S4: Further considerations for non-bacterial endophthalmitis

Considerations for suspected cases of non-bacterial endophthalmitis may differ. We excluded one case of ostensible fungal endophthalmitis from our analysis because of diagnostic uncertainty. Aqueous cultures grew *Fusarium spp*., while vitreous samples could not be obtained. The acute presentation, excellent presenting vision and visual outcome, and absence of vitreous inflammation or characteristic vitreous balls made this very unusual. Typical cases of fusarium endophthalmitis tend to present late (4-12 weeks after inoculation), have a fulminant and recurrent course requiring aggressive treatment, and are associated with poor visual outcomes.[29,30] Whether this was truly a case of fungal endophthalmitis or TASS with contaminated cultures remains unclear, particularly as fusarium is not known to be a lid commensal. Nevertheless, this also highlights another important consideration in the management of postoperative endophthalmitis - clinicians' tendency to err on the side of caution and initiate treatment given the risk of a devastating visual outcome, and for the potential for contaminants to complicate clinical decision-making. While careful clinical correlation is essential, it may be difficult to gainsay a positive microbiological culture, and treating for the 'worst case scenario' tends to be the preferred approach.