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Retrospective analysis on the outcomes of contact lens-associated keratitis in a tertiary centre: an evidence-based management protocol to optimise resource allocation

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ABSTRACT

Background/aims Contact lens-associated keratitis (CLAK) is a common sight-threatening complication of contact lens use. Current management protocols in the UK are based on historical practice and necessitate a review for every patient within 48 hours regardless of severity, increasing the treatment burden on a resource-limited healthcare service. Our study aims to identify the different risk factors associated with CLAK, categorise CLAK using a novel grading system and recommend modifications to current management protocols based on the outcomes in the individual subgroups.

Methods The retrospective cohort study identified 161 eyes from 153 patients with CLAK from the electronic patient records of a tertiary eye centre between 1 July 2021 and 28 February 2022. Patients were categorised based on epithelial defect size (grade 1: <1.0 mm, grade 2: 1.0–2.0 mm, grade 3: >2.0 mm) and their risk factors, clinical features, treatments and outcomes were analysed.

Results The most significant risk factors for CLAK include extended-wear contact lens, poor hygiene and prolonged duration of wear. Grades 1 and 2 CLAKs have excellent outcomes following an empirical treatment regime with topical moxifloxacin with 96% discharged within 48 hours and 94.1% discharged in 2 weeks, respectively. Grade 3 CLAKs require prolonged average duration of treatment.

Conclusion We recommend typical grade 1 and 2 CLAKs can be discharged with empirical fluoroquinolone treatment. Grade 3 and all CLAKs with atypical features require monitoring for resolution, further diagnostics or treatment. We provide an evidence-based approach to reduce unnecessary patient visits and optimise resource allocation in an urban setting.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Contact lens-associated keratitis (CLAK) is a common presentation with a rising incidence due to increased contact lens use. Current management protocols in the UK are based on historical practice and necessitate a review within 48 hours, which places a significant burden on ophthalmology units.

WHAT THIS STUDY ADDS

⇒ Typical grade 1 (<1.0 mm) and 2 CLAKs (<2.0 mm) with no atypical features can be safely discharged with empirical fluoroquinolone treatment and easy access to review. Grade 3 (>2.0 mm) and all CLAKs with atypical features require further monitoring and management.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our study provides a safe, evidence-based management protocol to improve resource allocation by reducing the number of reviews in low-risk patients which comprise the majority of patients with CLAK. This approach delivers benefits of decreasing unnecessary patient visits and allows ophthalmology units to cope with the increasing demand for emergency eye care services.

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INTRODUCTION

Microbial keratitis is a common ocular disorder that poses a significant burden on affected populations and if untreated, can lead to blindness.[1] Contact lens-associated keratitis (CLAK) is defined as microbial keratitis (MK) secondary to contact lens (CL) usage and it has a global incidence rate of 2–20 cases per 10 000 CL wearers each year.[1] CL wear is often cited as the most common risk factor with studies reporting it being implicated in up to 50.3% of MK cases and other common risk factors include ocular surface disorders, trauma and immunosuppression.[2 3] The risk of CLAK is influenced primarily by CL hygiene but is also dependent on the type of CLs worn, online availability and social behaviours.[4]

The population penetrance of CL usage varies at 13.9% (45 million) in the USA in 2016 and 9% (6.3 million) in the UK in 2020, increasing to 25%–30% in the Netherlands and Sweden.[5] With CL wear of all types in the UK being on a steady yearly rise, CLAK poses a significant burden on eye emergency services, contributing 18% of attendances annually.[6 7] Additionally, the current management protocol across the UK is based on historical practice and dictates that every patient with CLAK requires review in 48 hours, further increasing the burden on a resource-limited healthcare service. We

aimed to quantify this burden on services at our local tertiary centre and provide evidence to support our hypothesis that the majority of patients with low-risk CLAK are being followed up unnecessarily and can be discharged in the first instance.

METHODS

Participants

All patients who attended the Eye Casualty at Moorfields Eye Unit, St Georges Hospital, London with a primary diagnosis of CLAK between 1 July 2021 and 28 February 2022 (8 months) were included in the study. The exclusion criteria were a primary diagnosis other than CLAK and a lack of or indeterminate primary diagnosis.

Data collection

In our retrospective cohort study, data were collected from the local electronic patient record (OpenEyes) to identify patients with CLAK. A query targeting the keywords, "Contact Lens", "Keratitis" and "Ulcer" in patient notes was generated during the aforementioned time period and patients who met this criterion had their notes manually screened to determine the nature of their presentation. The following data were collected from patients meeting the inclusion criteria in the following categories:

Patient demographics

Age, sex, ethnicity, and ocular history.

Diagnosis and follow-up

Dates of diagnosis and follow-ups, corneal scrape and PCR if performed and culture results, outcomes of follow-up visits.

CLAK features

Visual acuity (VA) (LogMAR), laterality, size of epithelial defect(s) (ED), size of infiltrate(s), anterior chamber inflammation (cells or flare), corneal oedema, presence of blepharitis and any other pertinent features.

CLAK risk factors

Previous CLAK diagnosis, use of extended wear CL, duration of wear, history of sleeping, showering and swimming in CL, presence of blepharitis and presence of punctate epithelial erosions.

Treatment

Medication prescribed and length of courses, changes over course of treatment/follow-up.

Study design and statistical methods

1. Patients were divided into three gradings of CLAK based on the size of either the ED or infiltrate, whichever was larger: grade 1—<1.0 mm.
2. Grade 2—1.0–2.0 mm.
3. Grade 3—>2.0 mm.

Descriptive statistics and linear regression were performed using Microsoft Excel (Microsoft Corp) and patients who were lost to follow-up in each group were excluded from the statistical analysis of treatment only.

RESULTS

Demographics

153 patients were included in the study with a total of 161 eyes and 8 patients had bilateral CLAK (68 right eyes, 93 left eyes). The mean age was 39.84 ±14.0 (range 12–79) and the male-to-female ratio was 3.1:1. Figure 1 shows the number of attendances by months with the highest number of presentations in October (n=34). The mean best documented VA was 0.23 ±0.52 LogMAR.

Risk factors associated with CLAK

The most significant risk factor in our cohort was the use of extended-wear CLs (83, 51.55%) such as two-weekly, monthly and rigid gas permeable lenses, five of which wore CLs overnight which were suitable for night use and none of our patients used therapeutic CLs. This is followed by a history of showering with CLs (51, 31.68%), prolonged duration of wear

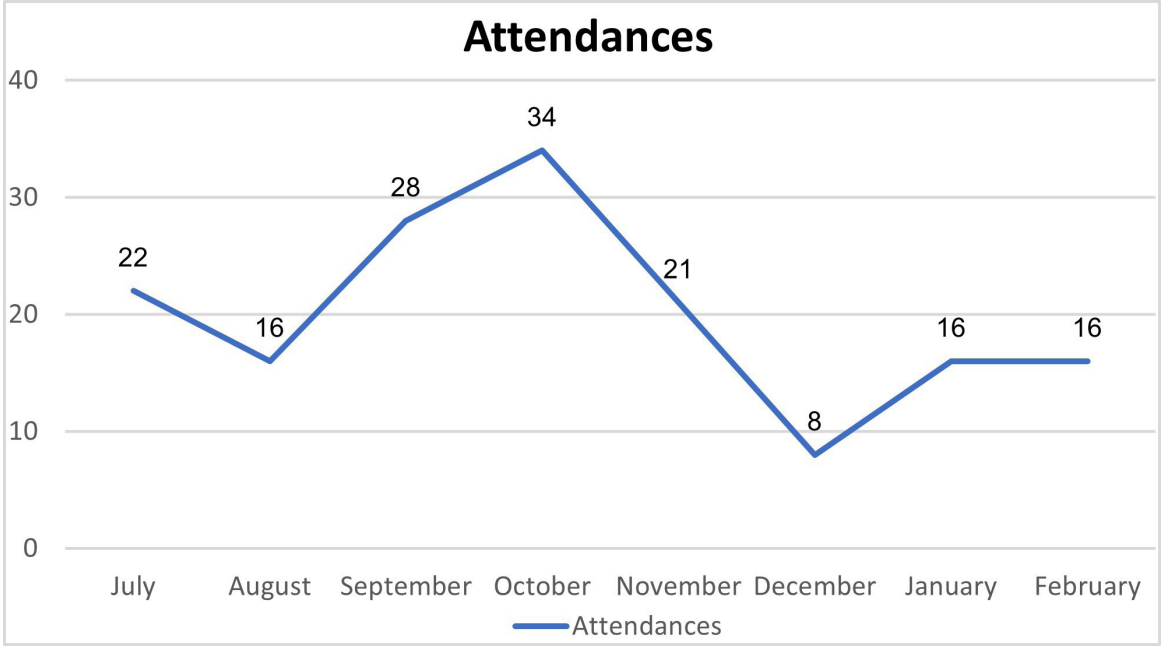

Figure 1 Number of contact lens-associated keratitis (CLAK) attendances by month.

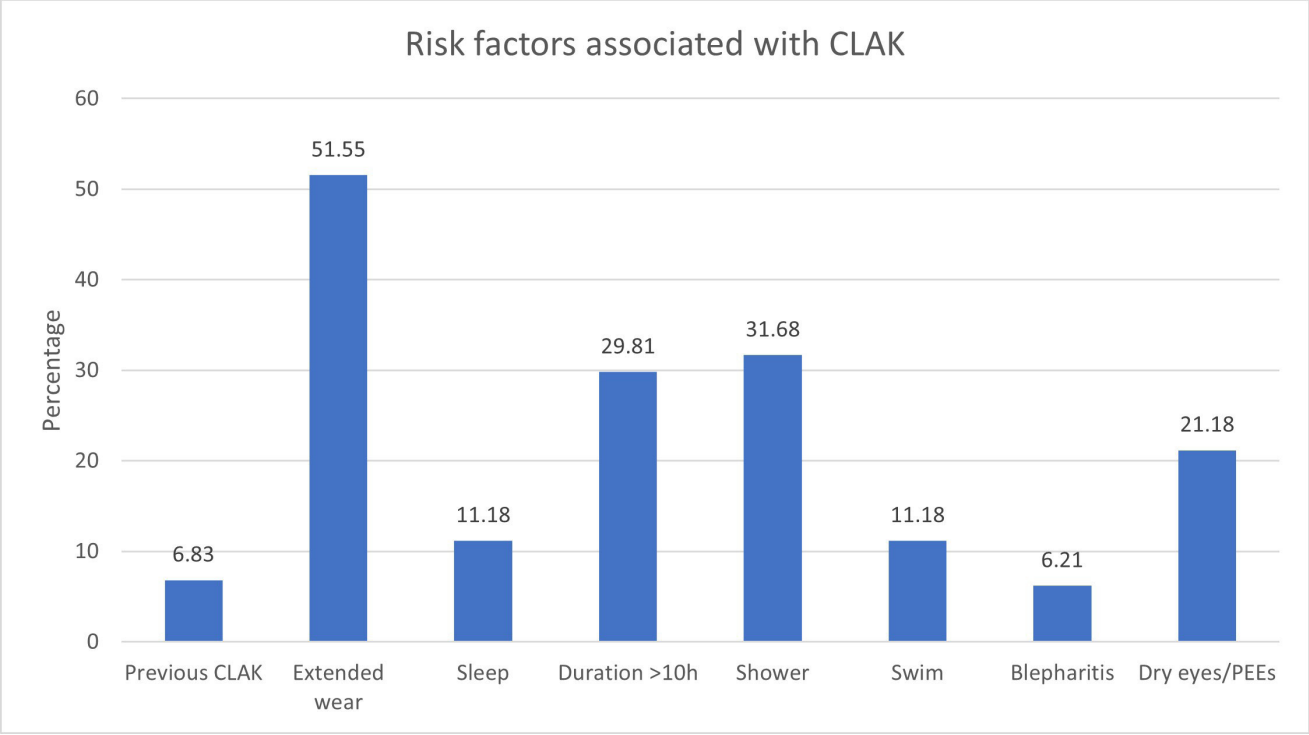

Figure 2 Risk factors associated with contact lens-associated keratitis (CLAK).

over 10 hours (48, 29.81%), dry eyes (34, 21.18%), history of sleeping or swimming with CLs in-situ (sleep 18, 11.18%; swim 18, 11.18%), previous CLAK (11. 6.83%) and blepharitis (10, 6.21%) (figure 2).

Figure 3 shows a linear regression scatter plot showing a moderate correlation (correlation coefficient (r)=0.457954 (p <0.0001)) between ED and best documented VA (LogMAR) regardless of the location of the lesion. This demonstrates that we cannot estimate the severity or size of CLAK based on the VA alone.

Analysis and outcomes of individual subgroups

The analysis was performed using ED size as insufficient infiltrate size data were documented on patient notes and just one patient had a larger infiltrate size relative to ED which did not affect the CLAK grading. Across all groups, patients were treated with a standard regime of topical antibiotics with hourly topical preservative-free moxifloxacin 0.5% drops followed by a weaning regime (less than hourly frequency) as guided by clinical improvement at the follow-up visits or at discharge based on Moorfields' CLAK treatment guidelines with a degree of variability between prescribers.

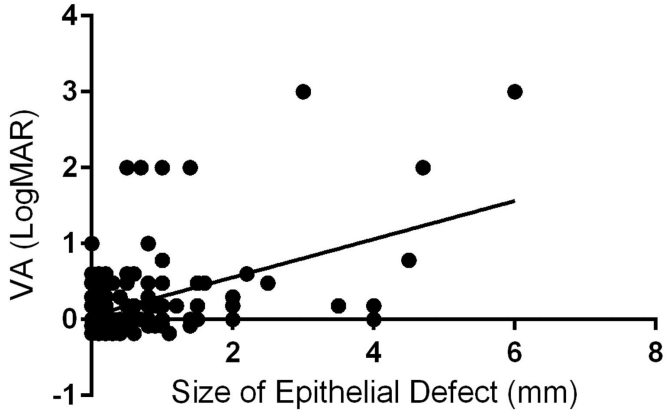

Figure 3 Correlation between epithelial defect size and visual acuity (VA) (LogMAR); correlation coefficient (r)=0.457954 (p <0.0001).

Grade 1 CLAK < 1.0 mm

A total of 127 patients were diagnosed with grade 1 CLAK and 22.0% (n=28) failed to attend their follow-up. The mean best documented VA is 0.1510 (95% CI 0.0900 to 0.2120) and the mean ED size was 0.344mm (95% CI 0.288 to 0.400). Among this group of patients, 96.0% (n=95) of the 99 who were reviewed were discharged at their first appointment or within 48 hours and the remaining 4.04% (n=4) remained under review due to atypical presentations; 3 patients were diagnosed with acanthamoeba of which 2 had positive confocal findings and 1 was positive for PCR, and 1 patient presented with a ring-shaped stromal lesion although subsequent investigations were negative and the patient was eventually diagnosed with a stromal scar. A total of 7 scrapes and 6 PCRs were performed, of which 28.6% of scrapes were positive (2 of 7, 1 Pseudomonas, 1 *Staphylococcus epidermidis* reported as likely contaminant) and 33.3% of PCRs were positive (2 of 6, 1 adenoviral, 1 acanthamoeba). The average treatment regime of the 95 patients discharged comprises a mean hourly regime of topical moxifloxacin 4.14 days (min 0–max 10 days) and an average weaning regime of 9.80 days (min 0–max 36 days).

Grade 2 CLAK 1.0–2.0 mm

A total of 25 patients were diagnosed with grade 2 CLAK and 32.0% (n=8) failed to attend follow-up. The mean best documented VA is 0.2904 (95% CI 0.0621 to 0.5187) and the mean ED size was 1.34mm (95% CI 1.203 to 1.477). Among this group of patients, 94.1% (n=16) of the 17 who were reviewed were discharged within 2 weeks and it is worth noting that one

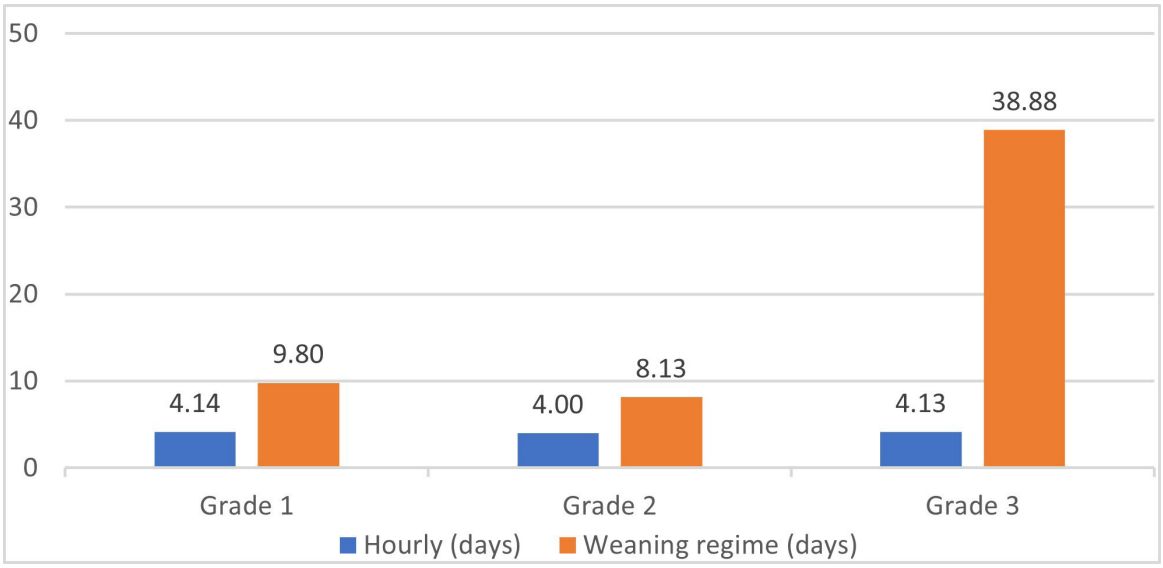

Figure 4 Average treatment duration in each contact lens-associated keratitis grade.

of these patients presented with a 1.6 mm ED with hypopyon and was treated with an extended hourly regime of 10 days. The remaining 5.88% (n=1) remained under review for a prolonged period of time following a presentation with a 1.5 mm by 1.5 mm ED with hypopyon and investigations revealed a polymicrobial infection with scrapes positive for Pseudomonas and Moraxella, and the PCR was positive for Alternaria. He subsequently completed 6 months of moxifloxacin in combination with antifungal drops and required corneal glueing following a microperforation, which was repeated in theatre due to a subsequent leak. A total of 7 scrapes and 4 PCRs were performed, of which 28.6% of scrapes were positive (2 of 7, 1 Pseudomonas and Moraxella, 1 *Staphylococcus aureus* and aspergillus reported as likely contaminant) and 25% of PCRs were positive (1 of 4, alternaria). The average treatment regime of the 16 patients discharged comprises a mean hourly regime of topical moxifloxacin 4.00 days (min 1–max 8 days) and an average weaning regime of 8.13 days (min 0–max 14 days) as shown in figure 4.

Grade 3 CLAK >2.0 mm

A total of 9 patients were diagnosed with grade 3 CLAK and 11.1% (n=1) was referred to an external unit for further management following the presentation visit and 50% (n=4) did not attend their final appointments following signs of improvement at prior follow-ups. The mean best documented VA is 1.1356 (95% CI 0.2076 to 2.0635) and the mean ED size was 3.822mm (95% CI 2.913 to 4.732). Of the eight patients who were followed up, 50% (n=4) presented with typical features of which two were discharged within 2 weeks (one had negative scrape findings and no results were available in the other), one had positive scrapes for *Bacillus oceanisediminis* and one had positive PCR for Staphylococcus. The remaining four patients had presented with atypical features such as cells or fibrin in the anterior chamber, hypopyon, ring infiltrate, feathery infiltrate, sloughing epithelium and corneal oedema with Descemet folds. Positive scrapes were found with Pseudomonas in one patient, polymicrobial infection of Pseudomonas and Candida in another, and one patient had a positive PCR for acanthamoeba. A total of nine scrapes and four PCRs were performed, of which 33.3% of scrapes (3 of 9) and 50% of PCRs (2 of 4) were positive as detailed above. All grade 3 patients were on a prolonged course of topical antimicrobials (more than a total of 12 days as per our protocol) apart from the two patients discharged within 2 weeks. The average treatment regime of the eight patients comprises a mean hourly regime of topical moxifloxacin 4.13 days (min 2–max 6 days) and an average weaning regime of 38.88 days (min 7–max 189 days) as shown in figure 4.

DISCUSSION

Corneal opacity is the fifth leading cause of blindness globally, with an estimated 1.5–2.0 million cases of unilateral blindness annually.[8] Ocular trauma and corneal ulceration are significant causes of corneal blindness that are often under-reported, which accounts for up to 5% of all blindness.[9 10] Capturing epidemiological data for MK, of which CLAK is a subgroup, is difficult because data are reported under the term “corneal blindness” which comprises a range of traumatic, infectious, inflammatory and inherited conditions.[9] This leads to difficulty measuring the true burden of MK, which is likely to be underestimated because the current WHO guidelines define ‘blindness’ as a VA of <3/60 corrected in the better eye and MK often causes disability that is significant but fall short of this standard,[9] hence highlighting an ongoing unchecked burden on human health.[8 11]

The pattern of MK aetiologies varies by region, with bacterial predominance in developed countries and fungal predominance in developing countries.[12–15] The highest proportions of bacterial aetiology (over 85%) have been reported in Europe, North America, Australia and Oceania, where the incidence of CL wear are also the highest.[16–21] MK costs the US healthcare system an estimated 175 million dollars in direct health expenditures and approximately 70 million dollars in Medicare and Medicaid-related costs.[9] However, no such data exist for the developing countries but it is reasonable to conclude that these costs are magnified in the poorest populations due to poor access to healthcare, delayed presentation, under dosage of empirical antibiotics, inappropriate use of steroids and impracticalities of obtaining cultures, and they often occur in the patients’ most productive years.[22 23]

In the UK, many ophthalmology units share a common system of managing CLAK regardless of severity or the size of epithelial defect, whereby patients are started on empirical treatment with topical antibiotics and a follow-up is arranged in 48 hours to

review for improvement or deterioration. Additionally, corneal scrapes are performed for culture and sensitivities for any epithelial defects 1 mm or more in size. With a continuously growing population in London where Moorfields Eye Hospital services are based, there is a sharp rise in demand for eye casualty services where a majority of these patients first present to a medical professional for treatment.[24] Previous studies show that corneal presentations account for over 18% of eye casualty presentations, and up to 50% of MK are secondary to CL wear.[2 25] This further increases the burden of disease on a resource-limited National Health Service and our study provides practitioners with evidence on safe approaches to managing CLAK or MK to optimise clinical efficiency and channel resources to patients who require them most.

First, our analysis on the risk factors of CLAK are corroborated with previous studies showing similar trends with extended-wear CL, poor hygiene and prolonged duration of wear among the most significant risk factors for developing MK.[26–28]

It is generally understood that the pathogenesis of CLAK is complex and multifactorial, and a plausible aetiology is related to a reduction of tear exchange during blinking in combination with tear stagnation under the CL, resulting in adherence and accumulation of microbes on the cornea, and reduced corneal epithelial cell desquamation, and alteration of tear fluid biochemistry.[29 30]

Second, our subgroup analysis of the outcomes in individual CLAK grades show that grades 1 and 2 CLAKs can be classified as low risk as they are predicted to have excellent outcomes with 96% of the grade 1s being discharged at their first appointment or within 48 hours, and 94.1% of the grade 2s were discharged in 2 weeks. Most importantly, the patients discharged in both groups have had a similar average duration of treatment with topical moxifloxacin monotherapy, emphasising that the prognosis of these patients is similar. All the patients that remained under review had presented with atypical features. We describe a typical CLAK as a corneal lesion with classical features of a focal epithelial defect with an underlying subepithelial or stromal infiltrate and an atypical CLAK where additional features of multiple infiltrates, perineual infiltrates, dendritiform lesions, satellite/feathery infiltrate with associated pigment, or endothelial plaques are found that may be suggestive of fungal or acanthamoeba infections. Due to the low number of grade 3 patients, it is difficult to derive useful statistical analysis but the treatment regime in this group of patients is estimated to be higher than average. Therefore, there is a need to review current management protocols in managing CLAKs throughout the UK as low-risk patients (typical grade 1 and 2 CLAK) comprise the majority of patients, and this may also apply globally in other developed countries.

Our results support the safe use of fluoroquinolone monotherapy as first-line treatment which is proven by recent UK studies showing an increasing trend of resistance against penicillin in Gram-positive and Gram-negative bacteria but a maintained moderate and high susceptibility to fluoroquinolone, respectively.[17 31 32] Moorfields Eye Hospital's local recommended empirical regime for CLAKs have been modified to hourly preservative-free moxifloxacin 0.5% for 48 hours, then hourly during the day for 3 days, and four times daily for 7 days. In particular, our findings suggest that patients who present with typical grades 1 and 2 CLAK do not require review in 48 hours and can be discharged on the recommended empirical regime, and patients with atypical features will require follow-up with further diagnostics, additional treatment and monitoring. Furthermore, we need to relook at our threshold for performing corneal scrapes as given our evidence of favourable outcomes of low-risk typical grade 1 and 2 CLAKs (up to 2.0 mm) on fluoroquinolone monotherapy, we should consider performing corneal scrapes for typical lesions with EDs larger than 2.0 mm and have a lower threshold to scrape in the presence of atypical features with the awareness of generally low yields on culture positivity which can vary by region (UK 33.0%–54.0%, Taiwan 49.3%, India 69% and Portuguese 38.4%).[17] A recent study from Liverpool comparing the use of corneal impression membrane (CIM) and corneal scrapes found significantly higher bacterial isolate rates from CIM (65.2% vs 19.4%) with significant increases in the isolations of a number of species, including *S. aureus* (2.4%–11.3%), *Serratia* (0.5%–1.7%), *Streptococcal* species (0.7%–6.9%), *S. epidermidis* (2.1%–26.2%), *S. capitis* (0.4%–2.6%) *and S. warneri* (0.3%–1.6%), demonstrating its superiority as an alternative user-dependent method of investigation over corneal scrapes.[33] Although CIM had not been implemented at our centre at the time of the study, it has now been introduced at Moorfields which is a simpler and faster procedure to perform compared with corneal scrapes and thus allows allied healthcare staff such as nurses to acquire samples.

Our group recognises several limitations with our study methods and the first of which is with regards to patient population. Moorfields St George's covers an area of South London and hence our results and local recommendations have to be interpreted cautiously in other geographies and climates where the incidence of atypical pathogens such as fungal and acanthamoeba, and polymicrobial infections differ.[34] In view of our findings, a local audit of MK in a similar manner to this study should guide local policy. A retrospective study on CLAK in Southern India found that bacterial infections were the predominant cause at 89.2% and a half of which were positive for pseudomonas on cultures.[35] All but one culture of *S epidermis* was sensitive to ciprofloxacin, demonstrating that similar trends can, however, be found in developing countries although more studies are required to guide antimicrobial management in these regions. The documentation of sensitivities on our electronic patient record system (OpenEyes) was low at 4.35% (1 of 23) and hence we were unable to perform an analysis on the sensitivities of our positive scrapes. Also, the small sample size of grade 3 patients precludes any meaningful statistics and further studies are required to better characterise this group of patients by evaluating the causative microorganisms, sensitivities, treatment duration and prognosis. In addition, the nature of our study design introduces a degree of variability in VA assessment as most patients were not assessed with a pinhole if their initial uncorrected or corrected VA is LogMAR 0.0 or better. Further attempts to collect data for patients who were lost to follow-up from other hospitals can also be made to improve the accuracy of our findings but we recognise the challenge in doing so and our results reflect realistic high rates of DNA in the CLAK patient group.

In conclusion, we present a risk-adjusted management protocol for MK by assessing the outcomes of different gradings of CLAK. Our findings reflect results from a real-world setting with a relatively high number of patients lost to follow-up (25.5%, n=41) and we purport that a majority of patients improved with empirical therapy and voluntarily declined subsequent review with a small number of patients seeking further management in other centres. We recommend that typical grade 1 and 2 CLAK can be discharged with empirical treatment of topical fluoroquinolone with easy access to review at a tertiary centre in the presence of worsening signs or symptoms, and the patients planned for follow-up may be reviewed in 4–5 days depending on access to

specialty clinics. In our patient cohort, this would reduce the number of unnecessary reviews in 68.9% (n=111) of all CLAKs and in a healthcare system where demand is steadily on the rise, such measures will go a long way towards optimising the use of resources on patients who need to be seen.

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Patient consent for publication Not applicable.

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