Factors Affecting the Morbidity of Contact Lens–Related Microbial Keratitis: A Population Study

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Purpose. To examine factors influencing the severity of soft contact lens (SCL)–related microbial keratitis.

Methods. Cases were detected via surveillance studies in Australia and New Zealand. Factors affecting disease severity (costs, days of symptoms, and 2 or more lines of vision loss) were examined and included age; gender; delay in SCL removal, seeking consultation, or receiving treatment; overnight wear; SCL material (hydrogel or silicone hydrogel [SiH]); and causative organism.

Results. Two hundred ninety-seven cases were identified: 61% female, age: 35 ± 13 years (mean ± SD). Treatment costs were (median [interquartile range]) $760 [1859] and indirect costs were $468 [1810]. Patients were symptomatic for 7 [11] days, and vision loss occurred in 14.3% of cases. Cases with pathogenic causative organisms (66/297, 22%) were 11.4 times (95% confidence interval [CI], 4.2–30.9) more likely to result in vision loss, had longer duration of symptoms (21 [40] vs. 6 [8] days, $P < 0.001$) and incurred higher costs (5,512 [14,733] vs. 1,048[8,325], $P < 0.001$). Delays (>12 hours) before treatment increased the likelihood of vision loss ($P = 0.048$) disease duration ($P = 0.004$), and associated costs ($P = 0.009$). Remoteness increased the risk of vision loss (odds ratio [OR] = 5.1; 95% CI 1.6–16.6), and individuals over 28 years of age had longer disease duration ($P = 0.02$). In overnight wear and after adjustment for culture result and treatment delays, SiH wearers had slightly shorter disease duration (4 [4] vs. 7 [10] days, $P = 0.02$) but a rate of vision loss and cost similar to those of hydrogel wearers.

Conclusions. The causative organism was the major determinant of severity; however, modifiable factors such as delays in treatment had considerable influence. Duration of symptoms was shorter in SiH wearers, but other factors dominated disease outcome in this population study. (*Invest Ophthalmol Vis Sci.* 2006;47:4302–4308) DOI:10.1167/iovs.06-0564

Contact lenses are a major cause of microbial keratitis in all countries where they are widely available, particularly in young adults.[1–3] The condition ranges widely in severity from a painful episode that resolves quickly with intensive antibiotic therapy to an infection requiring long periods of hospitalization and surgery for restoration of vision. Loss of vision is infrequent in contact lens–related microbial keratitis, reported in 11% to 13% of cases.[4,5]

National surveillance studies of contact lens–related microbial keratitis conducted in Australia (Stapleton et al. *IOVS* 2005;46:ARVO E-Abstract 5025) and New Zealand in 2003 and 2004 provided a unique opportunity to review the severity of disease including hospital cases and those managed in the community. The purpose of this analysis was to document the morbidity of contact lens–associated microbial keratitis in a large case series and to determine the factors that increased the likelihood of a poor outcome.

The morbidity of contact lens–related keratitis is strongly influenced by the pathogenicity of the causative organisms. For example, *Pseudomonas* infections are of larger diameter, require more outpatient visits, and are more likely to be associated with vision loss and hospital admission.[4] Gram-negative keratitis is associated with greater treatment costs.[3] In addition to the causative organism, the time taken to receive treatment can have a major impact on disease outcome. Microbial keratitis, which presents >24 hours after the onset of symptoms, has been shown to incur higher treatment costs.[3] Delay in referral is associated with the eventual need for penetrating keratoplasty,[6] and initial inappropriate therapy is associated with severe disease[7] and treatment failure.[8]

Silicone hydrogels (SiH) are new soft contact lenses that allow higher levels of oxygen to the cornea, providing benefits for corneal health during contact lens wear. Recent research has shown that the risk of infection in overnight wear is the same as for hydrogel contact lenses (Stapleton et al. *IOVS* 2005;46:ARVO E-Abstract 5025; Radford et al. *IOVS* 2005;46: ARVO E-Abstract 5026). One study has suggested that events with SiH contact lenses are less severe.[9]

Although several studies of contact lens–related microbial keratitis have documented the rate of vision loss,[4,5,10] cost analysis is a novel approach to measuring the outcome of the disease. Other studies have quoted rate of hospitalization, hospital bed days, or number of outpatient visits[4]; however, only a minority of patients with contact lens–related microbial keratitis are hospitalized for treatment—30% of cases in this study. Cost analysis offers the possibility of a continuous scale for resources involved in disease treatment, both hospital based and in private clinics.

The purpose of this study was to explore different indicators of severity and to examine factors influencing the severity of contact lens–related microbial keratitis. The effect on disease severity of causative organism and treatment delay was examined, in combination with the effect of newly available SiH materials.

Methods

Inclusion and Exclusion Criteria

Cases of contact lens–related microbial keratitis in 15- to 64-year-olds, wearing contact lenses for the correction of simple refractive error were detected through surveillance of ophthalmic practitioners in

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Australia and New Zealand. As this analysis was not designed to produce incidence rates, cases were included from a 4-month pilot study in Australia and New Zealand involving 67 practitioners[11] and 12-month national surveillance studies of Australia and New Zealand. This research was conducted in compliance with the tenets of the Declaration of Helsinki as revised in 2000. The protocol was approved by the Human Research Ethics Committee at the University of New South Wales and at local committees of regional health districts in Australia and New Zealand.

All the cases reported in these surveillance studies were reviewed for their eligibility. Aphakes, keratoconics, and wearers using lenses for medical indications were excluded. Diagnostic criteria were a corneal infiltrate with overlying epithelial defect, which was either culture proven or was associated with at least one of the following: lesion within the central 4 mm, anterior chamber reaction, or significant progressive pain. Cases were excluded from analysis when it was not possible to assess eligibility, because of lack of information.

Detailed information was sought on clinical presentation, microbiologic testing, treatment, and disease resolution. Subjects were interviewed by telephone, at least 1 month after the event, regarding healthcare and symptoms experienced.

Indicators of Disease Severity

Visual Outcome. Any reduction in vision was assessed using best corrected Snellen letter acuity or pinhole acuity if available. Loss of vision was gauged in comparison to the unaffected eye. Nearly all cases were unilateral; however, when both eyes were affected, the amount of vision loss was calculated using the worse eye and a standard referent of 6/6 Snellen acuity. Similarly, if there was amblyopia in the unaffected eye, a standard referent of 6/6 was used for comparison. As cases were reported from many clinics across Australia and New Zealand, it was not possible to standardize the measurement of visual acuity including the type of chart used. Visual outcome was categorized as loss of 2 or more lines, 10 or more lines of letter acuity, or no loss of vision.

Cost Analysis. Component costs were estimated by reviewing the cost of treatment of a series of cases of microbial keratitis at an Australian tertiary referral hospital.[3] This analysis yielded values for components of treatment—namely, hospital bed days, hospital outpatient clinic visits, and emergency department visits. Medications and pathology testing costs were estimated from commercial sources, as these are subsidized by the Australian government under the National Health Insurance Scheme. In cases that were treated in private clinics, costs of visits to general medical practitioners, optometrists, and private ophthalmologists were estimated from scheduled fees.

Indirect costs were calculated for each case and included days off work for the patient, carers' days off work, and purchase of spectacles. Days off work were allocated a value from the Australian average national wage in 2004 (Australian Bureau of Statistics). New spectacles when required were allocated a value estimated from retail prices. If not stated, days off work were estimated from hospital bed days and number of medical visits. If not stated, carers' days were estimated by using 0.1 days per visit (if patient was admitted or had more than five visits) and full days for administering intensive antibiotic therapy.

All costs were calculated in Australian dollars. New Zealand cases were costed using the estimates of component costs from Australia. There would be some differences in component costs between the two countries; however, better comparability of the cases was anticipated by this methodology. There is also considerable similarity between the level of training and mode of practice between ophthalmologists and optometrists in the two healthcare systems.

Disease Duration. Disease duration was defined by the number of days that symptoms including blurred vision, discomfort, photophobia, discharge, and ocular redness and swelling were experienced. If the patient and the practitioner both supplied data on disease duration, the maximum value was taken.

Factors Affecting Disease Outcome

Causative Organisms. There were multiple laboratories from which results for microbial analysis of corneal scrape samples were supplied so the criteria for a positive culture could not be standardized. In some cases, the laboratory report was available. In these cases results were considered culture negative if the report stated that the organism was grown on one medium only or only after extended periods of incubation, if the organism was considered a contaminant, or if there was no growth on any media. Other results were reported by the treating practitioner and would have been subject to interpretation of the laboratory report.

Treatment. Information from interviews with patients ($n = 90$) or from case histories (190) was used to determine the delays in contact lens removal, seeking consultation, and receiving treatment.

Appropriate therapy was defined as intensive antimicrobial therapy such as fluoroquinolone monotherapy, an aminoglycoside and cephalosporin duotherapy for bacterial keratitis, or accepted therapy for fungal or amoebic keratitis. Presumed microbial keratitis which was initially treated with chloramphenicol (Chloromycetin; Pfizer Australia Pty Ltd., West Ryde, NSW, Australia) fucithalmic acid, or over-the-counter preparations or were self-medicated were classified as initial inappropriate therapy.

The effect of rural versus metropolitan healthcare was examined using the Accessibility and Remoteness Index of Australia (ARIA).[12] Cases were grouped into those highly accessible to healthcare versus the remainder (accessible to very remote) for the Australian cases. The remoteness of the locations of New Zealand cases could not be analyzed quantitatively, as no parallel index was available for New Zealand.

The case histories of the patients with treatment delays were examined individually. Reasons for delays were categorized as time delays (waiting for appointments, waiting to see a doctor in emergency departments), travel time, or delays because the initial treatment was inappropriate. The proportion where the delay was because initial treatment was inappropriate was determined, and the types of treatments received were documented.

Contact Lens Group. Contact lens wear was grouped into overnight use or daily wear and further by hydrogel and SiH materials. Hydrogel lenses were all soft contact lenses excluding SiH lenses.

Statistical Analysis

Univariate analyses were performed using Fisher exact test, χ^2, *t*-test, and one-way ANOVA based on binary or continuous outcome variables. Log transformation was performed on total costs and duration of symptoms due to their large variance before analysis. The association of factors with binary outcomes was summarized using odds ratios (ORs), their confidence intervals, and population-attributable risk. The association of factors with continuous outcomes was summarized by using R^2. Multivariate analysis was performed with logistic and linear regression for binary and continuous outcome variables, respectively. Standard modeling procedures such as stepwise backward followed by the forward method were adopted. Confounders and interactions were explored. Measures of calibration and discrimination were reported. Analyses were performed with commercial software (SPSS ver. 12 for Windows; SPSS Inc., Chicago, IL, and STATA ver. 7, Intercooled STATA for Windows; STATA Corp., College Station, TX).

The effect of contact lens material in overnight wear was examined further with a paired *t*-test, matching cases for causative organism and treatment delays, with the investigator masked to disease outcome.

Results

A total of 388 cases of contact lens–related microbial keratitis were reported to the study center. There were 38 (9.8%) cases that did not meet the eligibility criteria and 53 (13.7%) in which there was insufficient information to grade the severity. Data were analyzed for 260 cases from Australia and 37 from

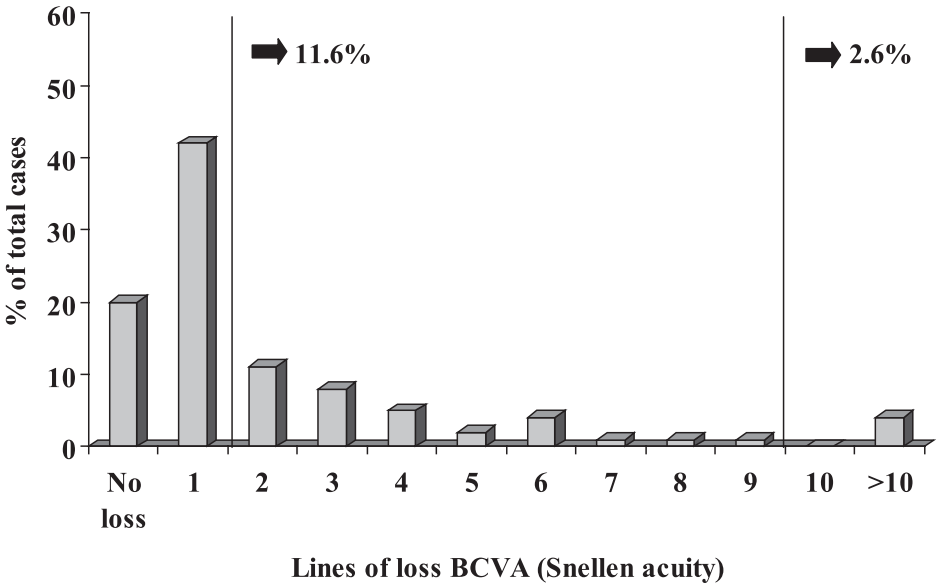

FIGURE 1. Rate of reduction in visual acuity, limited to cases detected during a 12-month surveillance period in Australia ($n = 221$).

New Zealand. The smaller case series from New Zealand was because of the smaller population. The mean age of subjects was 35 ± 13 years, and gender distribution was 61% female and 39% male ($n = 297$).

Measures of Disease Severity

Visual Outcome. The proportion with known visual outcome was 269 of 297 subjects. In Figure 1, the data are restricted to the cases reported nationally in Australia within the 12-month surveillance study ($n = 221$). The corresponding rate of vision loss was 14.3%.

Costs. Indirect costs could be calculated for 272 cases. Direct costs correlated well with indirect costs ($R^2 = 0.64$; ANOVA, indirect costs = 0.8 × direct costs + 72; $P < 0.001$), so indirect costs were estimated from direct costs in an additional five cases. Direct costs mainly comprised medical visits and hospital bed days, and medications comprised 15% of total costs on average. The major component of indirect costs were days off work for the subject (2 [9]; median[interquartile range]) and their carer (0.7 [0.5]). Assistance from a carer was required in 60% of cases.

Direct costs ($760 [1859]) were generally higher than indirect costs ($468 [1810], median [inter-quartile range]), and both types of costs were widely distributed (Fig. 2).

Disease Duration. Contact lens–related microbial keratitis had a typical duration of symptoms of 7 [11] days (median [inter-quartile range]), and 60% resolved in 8 days or fewer (Fig. 3). There were some cases with long duration of symptoms, particularly where visual symptoms of blur or photophobia persisted past the resolution of redness, pain, and irritation. Of the cases in which symptoms persisted for longer than 1 month, 70% (17/23) had permanent vision loss.

Factors Affecting Disease Outcome

Causative Organisms. A total of 183 (62%) of 297 subjects had a corneal scrape performed. There were 11 cases in which the results of the corneal scrape were not available and 4 in which the sample was insufficient for conclusive analysis.

Of the remaining 168 cases, there were 83 (49.4%) that were culture proven. There were 53 samples reported as sterile, 29 with growth on one medium only, and a further 3

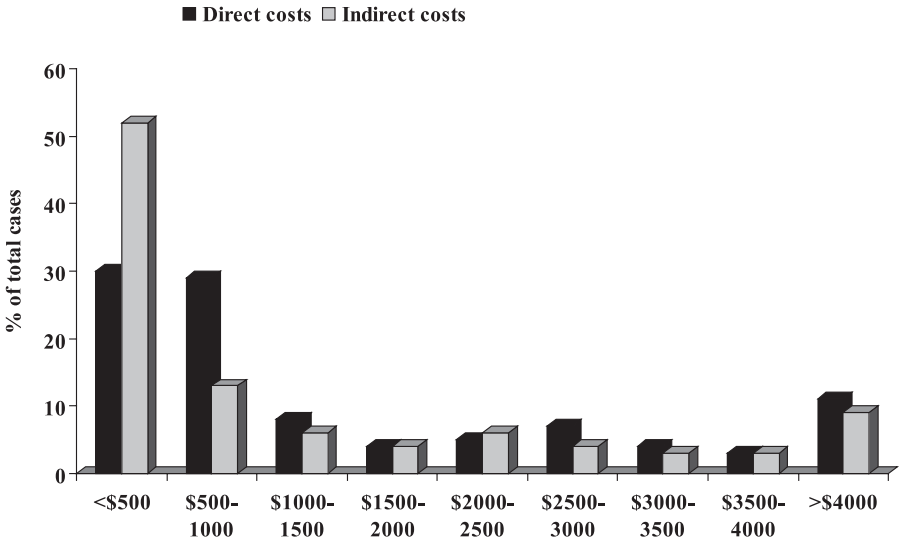

FIGURE 2. Frequency distribution of direct and indirect costs in Australian dollars ($n = 277$).

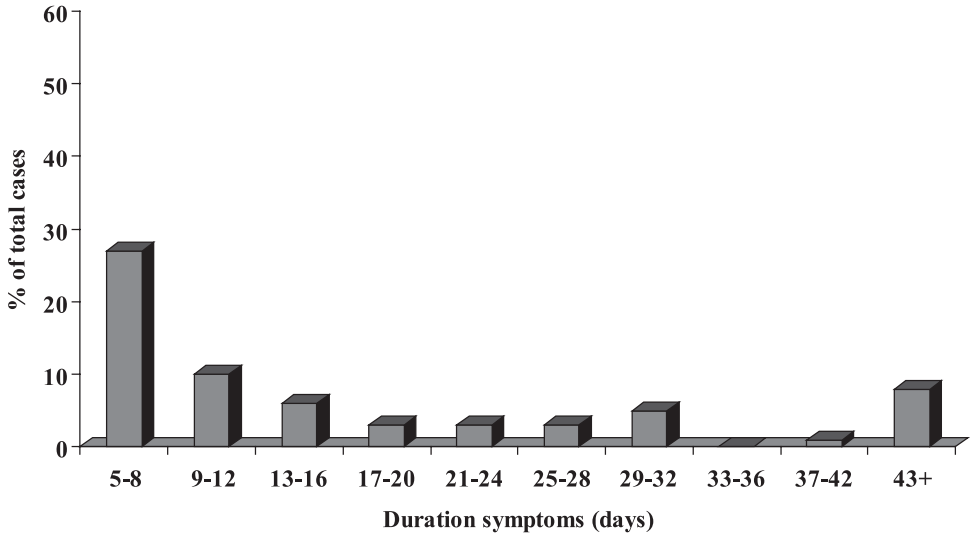

FIGURE 3. Frequency distribution of the duration of symptoms in days.

samples in which the organism isolated was considered to be a contaminant rather than a causative organism.

Among the culture-proven cases, amoeba (4/83, 4.8%) and fungal (3/83, 3.6%) keratitis were rare. The majority of culture-proven cases were Gram-negative keratitis 48/83 (57.8%). Of the Gram-negative samples, *Pseudomonas* spp. were the most commonly isolated organisms present in 37 (77.1%) of 48 followed by *Serratia* spp. In 9 or (18.8%) 48. There were no significant differences in the spectrum of organisms cultured from corneal infections associated with SiH and hydrogel materials (χ^2 test, $P = 0.3$).

Culture proven Gram-negative, *Nocardia*, amoebic, or fungal keratitis cases were grouped together, in the analysis of the effect of causative organism on severity. This group comprised 66 (22.2%) of 297 cases. The group had particularly severe disease outcomes in rate of vision loss, costs of disease, and duration of symptoms (Table 1). A confirmed pathogenic causative organism accounted for 51% of the risk of loss of vision (PAR%).

Treatment. A total of 70 (56%) of 125 of persons delayed >4 hours before removing their contact lenses; the median delay of those who waited before removing contact lenses was over 18 hours (19 [42]; median [IRQ]). There were 103 (61%) of 168 persons who delayed 24 or more hours before seeking consultation (48 [48]). A significant portion, 55 (33%) of 168, experienced a delay of 12 or more hours before commencing appropriate therapy (24 [42]).

Although delays in contact lens removal and seeking consultation did not influence disease severity, delays in receiving appropriate therapy did influence the costs associated with the disease, duration of disease, and rate of loss of best corrected visual acuity (Table 1). When all factors were considered in the mulitvariate models, delays in treatment increased costs associated with disease and disease duration, but did not determine visual outcome. Most cases of infection (85%) occurred in areas of Australia that were highly accessible to healthcare (ARIA category HA). Remoteness to healthcare increased the likelihood of loss of 2 or more lines of vision (Table 1) and accounted for 15% of the risk (PAR%). Remoteness did not correlate with delays in receiving treatment (χ^2 $P = 0.6$).

The group who had delays of 12 or more hours before receiving appropriate therapy predominantly presented to general medical practitioners (30/53, 57%), to optometrists (17/53, 32%), and to hospital accident and emergency departments (6/53, 11%). The majority of the delays (47/55) were due to not receiving appropriate treatment at the initial consultation and included initial treatment with topical chloramphenicol (27/47), fucithalmic ointment (1/47), or miscellaneous low-dose antibiotic drops from general practitioners (8/47); receiving no treatment (1/47); self-medicating (2/47); or using over-the-counter preparations (5/49). Two patients received a steroid as the initial treatment, one from a general practitioner and one from a private ophthalmologist. A case of *Acanthamoeba* keratitis was initially treated with acyclovir before final successful treatment with polyhexylmethyl biguanide, chlorhexidine, and propamidine isethionate (Brolene; Sanofi-Aventis, Ltd., Guildford, UK). Those with delays in treatment were more likely to be treated initially by a nonophthalmic practitioner (32/55, 62%) than were those who did not experience any delays in treatment (9/113, 8%; $P < 0.001$). The delay in time to treatment was accounted for by geographic remoteness or waiting for appointments in a small number (8/55, 15%).

Contact Lens Group. There were a large number of cases in which the soft lens material and overnight wear status were not confirmed ($n = 109$) so the total dataset for this analysis was 178 cases (Fig. 4). Modalities unpopular in Australia and New Zealand such as hydrogel extended wear were used in few cases ($n = 12$).

Univariate analysis (Table 1) showed that the class of hydrogel material in combination with an overnight wearing schedule had no effect on disease severity ($P > 0.1$), and multivariate modeling confirmed that the causative organism and delays in receiving treatment were more influential. Paired analysis, controlling for these other factors showed some beneficial effect on disease duration (Table 2). The average age was not different between the two groups (33 ± 14 vs. 32 ± 12; $P = 0.9$) and the SiH group comprised slightly fewer males (8/14 vs. 6/14, $P = 0.4$). There was a shorter disease duration in those who wore SiH lenses overnight (Table 2), but rate of vision loss and associated costs were similar.

Multivariate Analysis

The univariate analysis in Table 1 shows that there were several factors that influenced disease outcome. Delays in receiving appropriate treatment correlated highly with initial treatment by a nonophthalmic practitioner, and so both factors were not used in the multivariate modeling.

Two factors were identified that predicted the likelihood of loss of 2 or more lines of best corrected visual acuity (goodness of fit: $P = 0.690$, area under the receiver operating characteristic [ROC] curve: 0.813 ± 0.045; 95% confidence interval [CI]

TABLE 1. Univariate Analysis of Effect of Various Factors on the Indicators of Severity

Indicator of Severity	Factor				*P*	OR (95% CI) /r^2*
Age	<28 years		≥28 years			
Vision loss (>2 lines)†	12/94 (13%)		35/176 (20%)		0.2	1.7 (0.8–3.4)
Total cost ($AU)‡	1,298 [14,737]		1,297 [8,325]		0.7	0.001
Duration symptoms (days)‡	7 [11]		7 [17]		**0.02**	0.022
Gender	Female		Male			
Vision loss (>2 lines)†	29/167 (17%)		18/102 (18%)		1.0	1.0 (0.5–1.9)
Total cost ($AU)‡	1,336 [14,737]		1,125 [6,627]		0.1	0.009
Duration symptoms (days)‡	7 [11]		7 [11]		0.3	0.004
Corneal scrape	ND/Sterile/Gram positive		Gram negative/Other			
Vision loss (>2 lines)†	18/206 (9%)		29/57 (51%)		**<0.001**	10.8 (5.3–22.0)
Total cost ($AU)‡	1,048 [8,325]		5,512 [14,733]		**<0.001**	0.163
Duration symptoms (days)‡	6 [8]		21 [40]		**<0.001**	0.147
CL Removal	No delay		Delay 4+ hours			
Vision loss (>2 lines)†	7/51 (14%)		9/64 (14%)		1.0	1.0 (0.4–3.0)
Total cost ($AU)‡	1,795 [14,578]		1,529 [6,931]		0.5	0.004
Duration symptoms (days)‡	7 [14]		7 [16]		0.6	0.002
Consultation	No Delay Consultation		Delay 24+ hours			
Vision loss (>2 lines)†	10/59 (17%)		18/97 (19%)		0.8	1.1 (0.5–2.6)
Total cost ($AU)‡	1,541 [14,578]		1,576 [7,310]		0.2	0.009
Duration symptoms (days)‡	7 [11]		7 [15]		0.8	0.000
Treatment	No delay		Delay 12+ hours			
Vision loss (>2 lines)†	14/104 (14%)		14/52 (27%)		**0.048**	2.4 (1.0–5.4)
Total cost ($AU)‡	1,336 [8,305]		3,397 [14,706]		**0.001**	0.070
Duration symptoms (days)‡	6 [11]		10 [23]		**0.001**	0.080
Treating Practitioner	Ophthalmic		Non-ophthalmic			
Vision loss (>2 lines)†	30/181 (17%)		13/59 (22%)		0.3	1.4 (0.7–3.0)
Total cost ($AU)‡	1,257 [14,751]		1,842 [8,252]		**0.04**	0.017
Duration symptoms (days)‡	7 [9]		14 [20]		**0.005**	0.037
Remoteness	Highly Accessible		MA-Very Remote			
Vision loss (>2 lines)†	21/131 (16%)		8/23 (35%)		**0.04**	2.8 (1.1–7.4)
Total cost ($AU)‡	1,488 [14,731]		1,469 [6,792]		0.8	0.000
Duration symptoms (days)‡	7 [14]		10 [24]		0.2	0.012
CL Type and Overnight Wear	SiH EW	H EW	SiH DW	H DW		
Vision loss (>2 lines)†	7/70 (10%)	3/11 (27%)	3/15 (20%)	13/76 (17%)	0.4	§
Total cost ($AU)‡	1,162 [5,897]	1,301 [6,592]	1,361 [5,727]	1,561 [14,744]	0.2	0.026
Duration symptoms (days)‡	5 [9]	7 [8]	7 [10]	7 [15]	0.6	0.011

Bold *P* indicates a significant effect. $AU, Australian dollars; MA, moderately accessible; CL, contact lens; ND, not done; DW, daily wear; EW, extended wear.

* Summary of associations expressed as OR (95% CI) for vision loss, *r* square for total cost and symptom duration.

† % of cases with loss of 2 or more lines best corrected visual acuity.

‡ Median [IQR].

§ SiH EW 0.5 (0.2–1.4), H EW 1.8 (0.4–7.8), SiH DW 1.2 (0.3–4.9), H DW 1 (referent).

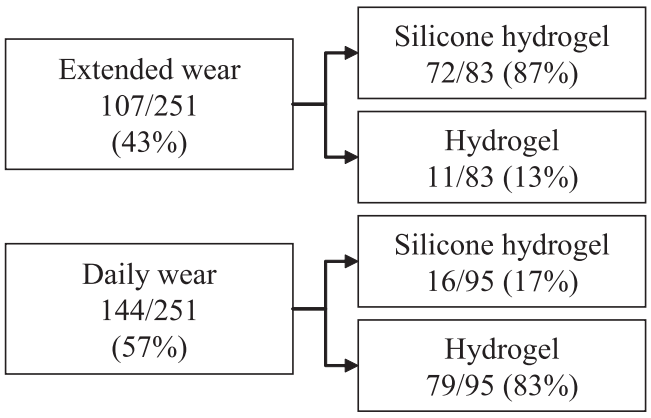

FIGURE 4. Categorization of cases of microbial keratitis in soft contact lens wearers in daily or extended wear ($n = 251$) and hydrogel or SiH ($n = 178$) lenses.

0.72–0.90]). Culture-proven cases in which Gram-negative organisms, *Nocardia* species, fungi, or *Acanthamoeba* were identified were 11.4 times more likely to cause loss of vision (95% CI, 4.2–30.9). The other factor was remoteness of healthcare which increased the likelihood of loss of vision by 5.1 times (95% CI, 1.6–16.6).

Total costs associated with disease were influenced by the causative organism once again but also by delays in treatment ($R = 0.546$; $R^2 = 0.298$; overall significance $F = 33.9$, $P < 0.001$). The causative organism was a more potent factor (partial eta (r) squared = 0.24, $P < 0.001$), but delay in treatment also increased costs (partial eta (r) squared = 0.04, $P = 0.008$).

Similar to costs, disease duration was influenced by the culture result and delays in treatment, but in addition persons over the age of 28 years had longer disease duration ($R = 0.496$; $R^2 = 0.246$; overall significance, $F = 15.5$, $P < 0.001$). The causative organism had the strongest effect (partial eta (r) squared = 0.12, $P < 0.001$). Age (partial eta (r) squared = 0.07, $P = 0.001$) and treatment delays (partial eta (r) squared = 0.06, $P = 0.004$) had similar influence on disease duration.

TABLE 2: Comparison of Outcome Measures for Matched Pairs of Silicone Hydrogel and Hydrogel Cases in Overnight Wear

	Silicone Hydrogel	Hydrogel	*P*
Rate of vision loss (%)	2/13(15.4%)	3/14 (21.4%)	1.0*
Total costs	1,409 [4,688]	1,288 [1,183]	0.5
Symptom duration	4 [4]	7 [10]	0.02

$n = 28$.
* Fisher's exact test.

DISCUSSION

A pathogenic causative organism is the primary determinant of disease outcome in contact lens–related microbial keratitis. However, modifiable factors such as delays in treatment appear to have considerable influence on outcome. Cost analysis and symptom duration are useful measures of morbidity for a condition that ranges widely in severity, but is rarely associated with vision loss.

In this analysis, multivariate modeling was limited by the sample size, comparing within a group of cases of contact lens–related microbial keratitis in which a severe outcome occurs in a small subgroup. The models were poorly predictive for cost and disease duration ($R^2 < 0.3$) but predicted the likelihood of loss of vision from the culture result and remoteness of healthcare with a high level of confidence (area under ROC curve, 81.3%). One of the advantages of this study was the large series of close to 300 cases and the depth of information on both hospital and private clinic cases.

The major determinant of disease outcome in contact lens–related microbial keratitis is the causative organism, which affects rate of vision loss, associated costs, and duration of symptoms. Similar to previous studies,[3,4,9,13–16] we found that *Pseudomonas* species were the most common causative organism in contact lens–related microbial keratitis, accounting for approximately half of the culture-proven infections. Other rare but highly pathogenic organisms implicated in contact lens–related infections were *Nocardia* species, *Acanthamoeba*, and fungi.

Treatment delays after presentation to a healthcare provider affected visual outcome, associated costs, and duration of disease. As delay in treatment is a modifiable factor, better education of primary healthcare providers about timely diagnosis, treatment, and appropriate referral of contact lens–related microbial keratitis is indicated.[17] Remoteness of healthcare also affected the likelihood of loss of vision. The fact that remoteness did not correlate with treatment delays suggests that other factors may be at play in remote Australia, which differs in climate and other environmental factors such as water supply. This finding has implications for advice to contact lens wearers in rural communities and for those traveling to remote locations.

The length of time from onset of symptoms to contact lens removal or presentation to a healthcare provider did not correlate with outcome. Both of these actions are taken by the individual and would be in response to the symptoms experienced. In effect, people would seek advice sooner in severe disease, which is typically associated with higher levels of pain and distress. In milder, less-progressive disease, they may delay longer before seeking treatment or removing their contact lenses, with limited effect on disease outcome. A study of corneal infiltrative events associated with contact lens wear also found that long delays in presentation were associated with milder disease.[18]

In this study, we found that cases in those aged 28 years and older had longer disease duration than did those in younger persons. More severe outcome has been shown in patients older than 60 years[6,19]; however, we found an age effect, even within a younger age range.

Although the cases in the population study showed some trends toward less-severe outcome with SiH materials, the relatively low number of cases in hydrogel extended wear (11 cases) in this population study limited the full exploration of these differences. In Australia and New Zealand, extended wear of hydrogel materials is not recommended by contact lens practitioners and consequently comprises as little as 2% of the lens-wearing population.[20] Population studies therefore yield fewer cases of infections in hydrogel extended wear.

In the paired analysis, when the effect of high oxygen permeability in SiH lenses was isolated, there was a small but statistically significant reduction in disease duration compared with hydrogel lenses in overnight wear. Although this is encouraging, it remains that very serious infections can still occur with SiH contact lenses, especially with highly pathogenic organisms and delays in receiving treatment.

Our rate of reduction in best corrected visual acuity of 2 or more lines (14%) is similar to that found in other population-based studies not restricted by age (12%–13%).[4,5] Cost analysis was used to measure severity and the purpose was not to estimate definitively the cost of treating contact lens–related keratitis, but rather to investigate relative costs and identify factors that increase costs. Both cost analysis and disease duration identified delays in treatment as a factor contributing to poor outcome, whereas vision loss was only predicted by the pathogenicity of the causative organism and remoteness.

There are always limitations to the accuracy of cost analysis in healthcare, particularly when multiple centers are involved that may have different protocols for treatment. However, both Australia and New Zealand have nationalized health services, and there is some uniformity to the charges associated with medical treatment. A nationalized health service means that there is often a distinction between what a patient is charged for a service and the actual cost of providing that service. In this analysis for in-hospital treatment we used the average cost of a hospital stay, whereas costs of out-of-hospital treatment were estimated using out-of-pocket expenses by patients. Despite limitations, cost analysis offers further perspective on the burden of disease.

Societal costs of days missed at work have been analyzed in other acute diseases,[21] and we chose to include indirect costs in our analysis of the costs of contact lens–related microbial keratitis. The population affected by contact lens–related microbial keratitis is of working age. Indirect costs due to time off work are therefore relevant and were a major component in the financial burden of disease, comprising 44% of total costs.

In this study, we investigated new means of quantifying the severity of contact lens–related microbial keratitis, including cost analysis and duration of symptoms. Successful medical treatment of disease is achieved in a large proportion of cases, with very few progressing to permanent loss of vision, and so supplementary measures of severity have descriptive merit in quantifying disease outcome. The causative organism is the

dominant factor in determining disease severity, but modifiable factors such as delays in receiving appropriate therapy have considerable influence. These findings highlight the importance of availability of high-quality ophthalmic healthcare and specific advice for contact lens wearers to optimize disease outcome in the rare event of a corneal infection associated with contact lens use.

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