AMERICAN ACADEMY OF OPHTHALMOLOGY®

Acanthamoeba Keratitis Risk Factors for Daily Wear Contact Lens Users

A Case–Control Study

Nicole Carnt, PhD,[1,2,4] Darwin C. Minassian, MSc Epidemiol,[3] John K.G. Dart, DM[2,4]

Purpose: This study was designed to establish risk factors for the development of *Acanthamoeba* keratitis (AK) for daily disposable (DD) contact lens (CL) users compared with daily wear (DW) reusable lens users and for risks unique to DD users. This is important because, in many major economies, CL use is the principal cause of microbial keratitis, of which AK accounts for approximately 50% of cases with sight loss. Determining these AK risks informs practitioner advice and consumer behavior.

Design: Case–control study.

Participants: Cases and controls were recruited from an Accident and Emergency Department serving South-East England. Cases were new CL users with AK recruited retrospectively from January 2011 to February 2013 and prospectively thereafter until August 2014. Controls were recruited prospectively from February 2014 to June 2015.

Methods: Analysis of a self-administered questionnaire.

Main Outcome Measures: Independent risk factors and population attributable risk percentage (PAR%) for AK.

Results: A total of 83 AK cases and 122 controls were recruited; DD use was reported by 20 (24%) cases and 66 (54%) controls. In multivariable analyses adjusted for potential confounders, the odds of AK was higher for DW reusable soft lenses (odds ratio [OR], 3.84; 95% confidence interval [CI], 1.75–8.43) and rigid lenses (OR, 4.56; 95% CI, 1.03–20.19) than for DD lenses. Within the DD-using subset, AK was associated with the following modifiable risk factors: less frequent professional follow-up visits (OR, 10.12; 95% CI, 5.01–20.46); showering in lenses (OR, 3.29, 95% CI, 1.17–9.23); lens reuse (OR, 5.41; 95% CI, 1.55–18.89); and overnight wear (OR, 3.93; 95% CI, 1.15–13.46). The PAR% estimated that 30% to 62% of cases could be prevented by switching from reusable soft lens to DD lens use.

Conclusions: *Acanthamoeba* keratitis risks are increased > threefold in DW reusable lens users versus DD lens use. *Acanthamoeba* keratitis risks for DD lens users can be minimized by adherence to safe use guidelines (no reuse, overnight wear, or contamination by water). Safe CL use can be improved by increasing the prominence of risk avoidance information from manufacturers and regulators. Because AK accounts for half of severe keratitis in CL users, these measures can be expected to have public health benefits. *Ophthalmology 2023;130:48-55 © 2022 by the American Academy of Ophthalmology*

Supplemental material available at www.aaojournal.org.

This study was designed both to evaluate whether daily disposable (DD) contact lens (CL) wear was protective for the development of *Acanthamoeba* keratitis (AK) compared with daily wear (DW) reusable lens use and to identify risk factors for AK with DD lens use. *Acanthamoeba* keratitis is important in the context of sight loss in CL users because, although the incidence is low at 0.31 to 0.48:10 000 (United Kingdom [H. Jasmin, unpublished data, 2021, used with permission from "Incidence of *Acanthamoeba* keratitis in the United Kingdom in 2015: a prospective national survey"]) and The Netherlands[1] in 2015), half of these (0.16–0.24:10 000) develop sight loss. Thus, AK accounts for a high proportion of cases of sight loss in CL users, resulting in substantial impacts on quality of life[2,3] and disproportionally higher healthcare costs.[4] This is a public health issue because CL use is the leading cause of microbial keratitis (MK) in patients with otherwise healthy eyes in high per capita income countries where CL use is widespread,[5] resulting in an economic burden both to those affected and to the healthcare system,[6] and inexpensive health protection measures against MK can be effective.[7]

The population penetrance of CL wear in these countries varies at 13.9% (45 million) in the United States in 2016[8] and in 2020 was 9% (6.3 million) in the United Kingdom, increasing to 25% to 30% in The Netherlands and Sweden.[9] A 2017 worldwide user estimate was approximately 300 million.[10] This is an important market for manufacturers, valued at $8.69 billion in 2019,[11] in

https://doi.org/10.1016/j.ophtha.2022.08.002
ISSN 0161-6420/22

which economic imperatives may have mitigated against the promotion of preventive information relating to MK. Microbial keratitis is the only sight-threatening complication of CL use, and despite the introduction of new lens materials and DD lenses, the incidence has remained unchanged at 2 to 4 per 10 000 over many decades,[12] of whom 0.2 to 0.6 per 10 000 will have sight loss.[13,14]

The most widely used lens types are DD (single use) and DW reusable soft (stored overnight and renewed after 2–4 weeks or longer), which together account for > 90% of all lenses fitted.[15] Daily disposable lenses have steadily increased in popularity[11] and now account for more than half the lenses fitted in some countries (61% in the United Kingdom).[15] The widespread use of DD lenses is both because of convenience and because data suggest that the risk for severe MK with vision loss, including that caused by *Acanthamoeba*, is probably reduced for DD compared with reusable CL wear,[12,16–18] although this has not been confirmed for either predominantly bacterial[12] or AK.[19,20] Identifying modifiable risk factors for CL users is important, particularly with regard to AK, for which, unlike bacterial keratitis in CL users, 90% of cases are associated with avoidable risks.[21] Given this background to our study, we expect our findings to be generalizable to other high per capita income countries where CL use is widespread. This analysis complements our previous publication on risk factors for AK associated with reusable CL.[22]

Methods

Ethics approval was from the National Research Ethics Service Committee London-Hampstead, REC Reference 13/LO/0032, and the Moorfields Eye Hospital Research Governance Committee on February 18, 2013. All research adhered to the tenets of the Declaration of Helsinki. All participants provided informed consent.

Cases were DW reusable or DD lens users diagnosed with AK. These included both self-referrals and secondary (general practitioner and optometric) and tertiary (other ophthalmology centers) referrals between January 2011 and August 2014. Cases diagnosed before ethics approval was given in February 2013 were recruited after diagnosis, following which cases were recruited prospectively at the time of diagnosis. Inclusion criteria before January 2014 were a positive *Acanthamoeba* culture, histopathological confirmation of trophozoites or cysts, culture-negative cases shown to have *Acanthamoeba* cysts on confocal microscopy, and those with a typical clinical course and response to treatment.[21] From January 2014, *Acanthamoeba* DNA identification by polymerase chain reaction was added to the diagnostic tests as an additional inclusion criterion.

Controls were DW reusable or DD CL users recruited between February 2014 and June 2015 attending the Accident and Emergency Department as new patients but with a disorder thought to be unrelated to CL wear (listed in Table S1, available at www.aaojournal.org), for which the diagnosis was derived from the hospital records.

Both cases and controls completed a 5-part (CL wear history, disinfectant solution history, lens use environment, eye care, and demographics) self-administered questionnaire with 48 multiple-part questions. Case questionnaires included 15 additional questions, encompassing a section about events leading up to the episode of keratitis and for which the data were not included in the case–control study analysis. The questionnaires were modified from those used in a previous study.[16] Cases and controls were excluded if they had insufficient questionnaire data despite attempts to contact them to clarify or complete data, had not used a CL during the previous 30 days, had a medical indication for CL wear, or had any previous attendance at Moorfields. The questionnaire data were entered into a database for analysis.

Analysis of the Association between AK and the CL Type (DD versus DW Reusable)

The DW reusable lens cases are those already described in our previous analysis of AK risks for reusable CL wearers in which the hygiene scoring methodology (summarized in Table S2, available at www.aaojournal.org) is described.[22] The hygiene scores for DD lens users were compared with those for reusable lens users by allocating all the DD users who reused their lenses to the highest score for poor hygiene; none of the other hygiene parameters were relevant to DD users.

Analysis of Risk Factors for AK among DD Lens Users

To explore risk factors for AK among DD users, a separate case–control analysis was performed restricted to the study population subset who were DD users. Users of DD who reused their lenses were categorized as DD users because this was considered a behavioral issue (such as overnight wear) that required assessment as a risk factor for DD lens use.

Statistical Analysis

The sample size calculation (including all DD and DW reusable subjects) indicated a sample size of 86 AK cases and 111 controls to detect a true odds ratio (OR) of 3.0 or more with 80% power, alpha (2-sided) set at 0.05, specifying a control/case ratio of 1.3 assuming an exposure proportion of 10% in controls (larger proportions requiring smaller sample sizes).

Analyses were performed using Stata software, version 17 (StataCorp LP). Variables with > 3 categories were grouped for analysis. The descriptive and crude (unadjusted) analyses of the characteristics of cases and controls and their association with risk of AK were evaluated one at a time without adjustment for confounding. Logistic regression was used to estimate ORs as a measure of association. The ORs are regarded as estimates of relative risk throughout.

The main analysis used multivariable logistic modeling to evaluate ORs for a variable of interest, with adjustment for effects of potential confounders (covariates). Variables of interest were chosen because they were associated with higher odds of having AK in the unadjusted analysis ($P < 0.05$) or they had been found to be potential risk factors or confounders in previous studies. Least absolute shrinkage and selection operator (LASSO) inferential logistic models for binary outcome data were fitted via cross-fit partialing out using plugins. The LASSO was our preferred method for selection of covariates because, unlike stepwise procedures, it does not tend to produce biased estimates of regression coefficients (away from zero), deals better with problems of collinearity, and was appropriate for our datasets where the sample sizes were modest and number of potential covariates relatively large. These models were used for evaluation of adjusted ORs for each exposure of interest, taking all other candidate variables as potential confounders. Data on occupation were missing in > 10% (9/86) of the DD lens users. Because this could be a considerable source of bias, the variable was not included in the main LASSO analyses as a covariate; however, subsequent inclusion of the variable in the modeling process did not result in material change of ORs for other variables of interest but did reduce precision of the estimated ORs considerably (details not reported but available).

Calculation of the population attributable risk percentage (PAR%) for the potentially remediable AK risk factors was based on the OR estimate and the proportion of cases exposed to the risk factor at issue.

Results

Recruitment

Eighty-three AK cases and 122 controls were recruited. Table S3 (available at www.aaojournal.org) shows the numbers of cases recruited retrospectively (21) as opposed to prospectively (62) and the differences in contemporaneity of recruitment for cases and controls resulting in 81controls recruited after cases. Table 1 summarizes the numbers in the DD and reusable CL datasets. Case recruitment was limited by researcher availability; only 1 case refused to participate, whereas a second was unsuitable having no English language use. Control recruitment was limited by researcher availability and the inclusion criteria requirements and fell behind the recruitment of cases; further recruiter resources were found to recruit the additional controls required for the analysis resulting in an extension of the period of control recruitment for 10 months beyond the recruitment of cases.

Analysis of the Association between AK and the CL Type (DD versus DW Reusable)

Table S4a (available at www.aaojournal.org) shows the characteristics of the cases and controls together with unadjusted ORs as crude measures of association with risk of AK. Table 1 shows both unadjusted and adjusted analyses, which are similar. Reusable soft CLs were associated with higher odds of AK than DD CL, as were the rigid lenses. The adjusted analysis includes the covariates (potential confounders) in the LASSO model-building process, which are listed in the footnote of Table 1. The adjusted ORs indicated a significantly higher risk of AK for both reusable soft (OR, 3.84; 95% confidence interval [CI], 1.75−8.43) and rigid CLs (OR, 4.56; 95% CI, 1.03−20.19) than for DD lenses.

Analysis of Risk Factors for AK among DD Lens Users

Table S4b (available at www.aaojournal.org) shows the characteristics of the cases and controls together with unadjusted ORs as crude measures of association with risk of AK. Variables included in the multivariable LASSO modeling process are marked by asterisks in Table S4b.

Multivariable Analysis (with Adjustment for Confounding) Findings

Results of the multivariable analysis, with adjustment for the confounding effects of covariates, for identified independent risk factors are shown in Table 2 (Table S5 shows full analysis results, available at www.aaojournal.org). Six independent risk factors were identified by the adjusted analysis:

1. White British DD users had a higher risk (∼fivefold) of AK (OR, 5.07; 95% CI, 1.10−23.44, $P = 0.038$).
2. Wearing DD lenses for longer periods (12−18 hours) was protective for AK compared with shorter periods of wear (OR, 0.22; 95% CI, 0.06−0.88, $P = 0.032$).
3. Having a CL check > 30 days before their attendance at the hospital was associated with a 10-fold higher risk of developing AK (OR, 10.12; CI, 5.01−20.46, $P < 0.001$).
4. Showering while wearing CLs was associated with an approximately threefold increase in odds of having AK (OR, 3.29; 95% CI, 1.17−9.23; $P = 0.024$).
5. Reuse of CLs increased odds of AK by approximately fivefold (OR, 5.41; 95% CI, 1.55−18.89; $P = 0.008$).
6. Overnight CL wear was associated with an approximately fourfold increase in odds of AK (OR, 3.93; 95% CI, 1.15−13.46; $P = 0.030$).

Population Attributable Risk Percentage Calculations

The PAR% was calculated to estimate the proportion of AK cases due to each of the risk factors. These are shown in Table 3 for the remediable AK risks. These are substantial for most exposures but with wide confidence limits: for reusable soft lenses versus DD lenses, 51.7% (95% CI, 29.9−61.6); for rigid gas permeable lenses versus DD lenses, 4.7% (95% CI, 0.2−5.7). Within the DD lens user subset, the PAR% for a CL check > 30 days before was 85.4% (95% CI, 75.8−90.1); for showering in CL was 45.2% (95% CI, 9.4−58.0); for CL reuse was 48.9% (95% CI, 21.3−56.8); and overnight CL wear was 26.1% (95% CI, 4.6−32.4).

Discussion

This study has identified DD lenses as protective for AK compared with both reusable soft and rigid lenses with the PAR%, suggesting that approximately 30% to 62% of AK could be prevented by switching from reusable soft to DD lens use. It has also identified 5 modifiable factors that increased risk for AK in users of DD lens users: shorter wearing time, not having a recent appointment with a CL professional, showering while wearing lenses, and lens reuse and overnight wear.

The use of DD in comparison with reusable DW lenses has been shown to increase the risk of predominantly bacterial keratitis 1.56-fold[16] or not to reduce its incidence.[14] However, both of these studies showed a reduction in severe MK for DD users that was significant in univariate analysis[16] probably because of elimination of the lens case. Our findings for AK show DW reusable lens users to have a 4.14-fold higher risk than DD lens users after multivariable analysis, and this was similar for both soft and rigid lens users. This reduction in AK risk for DD users may also relate to the elimination of the lens storage case, which commonly harbors *Acanthamoeba* spp. and their bacterial food source.[23] Contact lens solutions are regulated for antibacterial efficacy but not for anti-*Acanthamoeba* efficacy because of the absence of an agreed test standard.[24] This lack of regulation may be responsible for the periodic outbreaks of AK due to disinfection solution failures.[18,22,25] Given that this study provides evidence that DD use protects against AK and the probability that it also protects against severe bacterial keratitis, DD lens wear should be encouraged.

Wearing DD lenses for longer periods per day (12−18 hours) was protective for AK versus shorter periods. This finding is mirrored by a study showing an increased risk of corneal infiltrates in overnight wear lens users unable to adapt to >21 days of wear[26] and might relate to factors like dry eye and microtrauma from insertion and removal difficulty in subjects unable to wear lenses comfortably for longer periods.

The association of AK with the frequency of DD CL follow-up appointments is consistent with findings in other studies showing that internet purchase[14] or poor aftercare

Table 1. Comparison of the Risks for the Development of AK in DD versus Reusable CL Wearers: Unadjusted and Adjusted Analyses

Exposure Variables	Controls, n = 122	AK Cases, n = 83	Unadjusted OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value
Type of CL						
DD	66	20	Referent		Referent	
Reusable	56	63	3.71 (2.00–6.88)	**<0.001**	4.14 (1.92–8.9)	**<0.001**
Type of CL: Detailed						
DD	66	20	Referent		Referent	
Reusable soft	51	58	3.75 (2.01–7.02)	**<0.001**	3.84 (1.75–8.43)	**0.001**
Rigid gas permeable	5	5	3.30 (0.87–12.56)	0.080	4.56 (1.03–20.19)	**0.046**
Total	122	83				

AK = *Acanthamoeba* keratitis; CI = confidence interval; CL = contact lens; DD = daily disposable; OR = odds ratio.
The adjusted OR estimates are from least absolute shrinkage and selection operator (LASSO) inferential logistic models for the combined dataset of 205 patients. Statistically significant values <0.05 are in bold typeface. Covariates included in the LASSO model-building process were mean hygiene score (described in Table S2, available at www.aaojournal.org); where CLs were purchased (from the internet via a CL website versus all optician-associated purchases); handwashing before handling CL; showering with CL in; swimming/water activities with CL in; routine CL check-up periods; and ethnicity.

instruction and recall is associated with predominantly bacterial MK,[10,25] which are all surrogates for education on risks of lens wear. The PAR% CI of 76% to 90% suggests that improving education could have a substantial effect.

Exposure to contaminated water as a risk factor for AK has been acknowledged since the first case–control study, with limited multivariable analysis, investigated the US outbreak of AK in 1985 to 1986.[27] Subsequent case reports both in CL users and after corneal trauma have associated AK with contaminated sea, lake, swimming pool, and domestic water.[28–30] However, confirmation of these probable risks for AK, using multivariable analysis, has only been confirmed recently for reusable CL wearers with a 3.5-fold increase in risk while wearing lenses in hot tubs and swimming pools[22] and, in our current study in DD lens users, a 3.3-fold increased risk for showering in lenses

Table 2. Adjusted OR Estimates for Independent Risk Factors Associated with the Development of AK in Daily Disposable CL Users from the Multivariable Analysis (Using LASSO Inferential Logistic Models)

Exposure Variable	Controls, n (%)	AK Cases, n (%)	Adjusted OR	95% CI for OR	*P* Value
Ethnicity	31 (48.4)	16 (84.2)	5.07	1.10–23.44	**0.038**
British White	33 (51.6)	3 (15.8)	Referent		
Other	2	1			
Unknown					
Hours of CL wear per day (median = 12 hrs)	26 (39.4)	13 (65.0)	Referent	0.06–0.88	**0.032**
4–11 hrs	40 (60.6)	7 (35.0)	0.22		
12–18 hrs					
Routine CL check	13 (19.7)	1 (5.3)	Referent	5.01–20.46	**<0.001**
1–30 days ago	53 (80.3)	18 (94.7)	10.12		
>1 mo ago	0	1			
Unknown					
Showering with CLs in	41 (62.1)	7 (35.0)	Referent	1.17–9.23	**0.024**
No	25 (37.9)	13 (65.0)	3.29		
Yes/unsure					
CL reuse	53 (81.5)	8 (40.0)	Referent	1.55–18.89	**0.008**
No	12 (18.5)	12 (60.0)	5.41		
Yes	1	0			
Unknown					
Overnight CL wear	56 (88.9)	13 (65.0)	Referent	1.15–13.46	**0.030**
Never	7 (11.1)	7 (35.0)	3.93		
Sometimes	3	0			
Unknown					

AK = *Acanthamoeba* keratitis; CI = confidence interval; CL = contact lens; LASSO = least absolute shrinkage and selection operator; OR = odds ratio. Statistically significant values <0.05 are in bold typeface. Table S4 (available at www.aaojournal.org) shows a list of covariates (potential confounders) included in the LASSO model-building process, and Table S5 (available at www.aaojournal.org) shows the full results of the adjusted analysis.

Table 3. Population Attributable Risk Percent for the Comparison of DD with Reusable CLs in 205 CL Users and for the 4 Remediable Independent Risk Factors with Adjusted ORs >1.00 in 86 DD Lens Users

Exposure Variable	Adjusted OR	P Value	PAR%*	95% CI for PAR%
Type of CL				
DD	Referent			
Reusable soft	3.84	0.001	51.7	29.9−61.6
Rigid gas permeable	4.56	0.046	4.7	0.2−5.7
For DD lens use				
Routine CL check				
1−30 days ago	Referent			
> 1 mo ago	10.12	<0.001	85.4	75.8−90.1
Showering when wearing CL				
No	Referent			
Yes/unsure	3.29	0.024	45.2	9.4−58.0
CL reuse				
No	Referent			
Yes	5.41	0.008	48.9	21.3−56.8
Overnight CL wear				
Never	Referent			
Sometimes	3.93	0.030	26.1	4.6−32.4

CI = confidence interval; CL = contact lens; DD = daily disposable; OR = odds ratio; PAR% = population attributable risk %.
*The PAR% calculation is based on OR estimate and the proportion of AK cases exposed to the risk factor.

(PAR% CI, 9−58). Exposure to any water when using CL is a risk for AK and should be avoided. By contrast, bacterial keratitis due to swimming in lenses, although reported in case series, has not been proven in large epidemiological studies and is probably relatively uncommon.[14,16] Swimming in lenses is widespread; it is prudent to advise users that the least risk of AK while swimming is without lenses and that the advice to use goggles over lenses[31] and renew lenses immediately afterward may not be safe.

Reuse of DD lenses unsurprisingly increased the risk of AK by 5.4-fold (PAR% CI, 21−57) and probably relates to absent disinfection and the use of nonsterile liquid to maintain lens hydration. Overnight CL wear is a well-established risk factor for predominantly bacterial keratitis in reusable soft and DD lenses; however, it has not been associated with AK before this study. An unmodifiable risk factor was White British ethnicity, associated with a fivefold higher risk of AK, which may be related to cultural differences such as a greater risk-taking propensity.[32]

Limitations and Sources of Bias

Because of the comparative rarity of AK, the sample size for this study limited the detection of ORs ≥threefold unless the exposure of controls was high, as for the risk of AK in DD versus reusable CLs, where the exposure of controls to reusable lenses was 56 of 122 (46%), giving a lowest detectable OR of 2.3-fold. The study was designed to eliminate important sources of potential bias in the selection of cases and controls with little or no subjectivity in ascertainment. Using controls who were referred or self-referred to the same hospital department might be a limitation because the cases can be expected to reduce bias arising from differential referral or attendance patterns because many factors determining attendance are common to both cases and controls; this has held true in a previous and similar study on MK in CL users where no substantive difference in OR estimates were found when comparing hospital with nonhospital controls, which led us to combine these 2 groups.[16] (Sources of Bias are described in the Appendix, available at www.aaojournal.org, which shows a detailed description of this rationale.)

There was a difference in the ethnicity of tertiary referral cases with a higher proportion of these being White British. This is a potential source of bias for the ethnicity findings. In the Appendix Sources of Bias (available at www.aaojournal.org), we have shown that the OR for ethnic group in DD users remains substantial when tertiary AK cases are excluded from the analysis but with loss of power due to small numbers. As a result, we think it probable that the excess risk in British White subjects is present despite the imbalance in the referral pathway.

The disparity in the timing of enrollment of cases and controls, as well as the fact that some cases but no controls were enrolled retrospectively, could have introduced bias through a variety of factors, although we are unaware of any (e.g., weather, pandemics, and changes in the availability of lenses and disinfection solutions) that would have introduced excessive bias.

Regulatory Deficiencies

Contact lenses are designated class IIa (low to medium risk) medical devices in the United Kingdom and European Union and class II in the United States (for DW lenses), requiring manufacturers to include essential information on safe use and risks. However, CL manufacturers in the United Kingdom and European Union are currently using an exception to this requirement, reasoning that CL users will have received this information and training from the regulated professional who dispenses their lenses. Now that lenses are available to consumers on the internet without professional involvement (20/85 in this study) in the United Kingdom and European Union (but not in the United States), many users may have no training or ongoing education in safe CL use. In the United Kingdom and European Union, and for soft lenses in the United States, information on lens safety and risk avoidance recommendations is absent in lens packaging where the "do's and don't's" needed to reduce the risk of keratitis might be reinforced at each purchase.

Instead, users are directed to access "Patient information/ instruction for use" guides on CL company websites or from their practitioner; these provide variable information about MK risks and risk avoidance. Contact lens companies have adopted little of the effort that public health (UK National Health Service and USA Centers for Disease Control, among others) and professional organizations (British Contact Lens Association) have put into campaigning against the use of water with CL wear, apart from advising against this in "Instruction for Use" guides on their websites and in social media feeds.[33] That education can reduce keratitis risks has been discussed in relation to internet purchase[14] or deficient instruction in use,[10,25] and a recent study on the effect of "no water" stickers on CL cases has shown that water exposure was reduced by this simple measure that could be incorporated into all CL packaging, including the capsules containing individual lenses.[7] This evidence should be used by CL manufacturers, or their regulators, to include no water symbols on each lens capsule and case, together with a statement on the packaging, in the language used by the markets into which the lenses are sold, regarding keratitis avoidance (the Appendix shows an example of a risks and precautions statement and graphic, available at www.aaojournal.org). Given that MK is the only sight-threatening complication of lens wear, more accessible and prominent information about MK risks and avoidance should be mandatory.

Conclusions

This article adds new data confirming previously suspected risk factors for AK in CL users and new avoidable risk factors including showering and reuse of DD lenses together with a threefold increased risk of AK in reusable lenses compared with DD lenses. The PAR% calculations suggest that avoiding the remediable risks can be expected to substantially reduce the number of AK cases. These results can be expected to encourage more CL users to switch from reusable CLs, with their associated storage and solution risks, and to practice safer use of DD lenses (without reuse, overnight wear, or contamination by water). Safe CL use could be improved by the inclusion of clear risk avoidance data on lens packaging by manufacturers and advice in public swimming pools on water avoidance while using lenses.

Acknowledgments

The authors thank Ruth Lloyd-Williams, Benefit Risk Evaluation Assessor, Medicines and Healthcare products Regulatory Agency, United Kingdom, for advice on the regulation of class IIa medical devices in the United Kingdom and European Union and for comments on the article; the Moorfields Eye Hospital staff and the Accident and Emergency Department Nurses for their help in identifying control CL users; Melanie Mason and the Corneal Clinic staff for assistance with recruiting cases; and staff in Research and Development for database management.

Footnotes and Disclosures

Originally received: February 14, 2022.
Final revision: August 2, 2022.
Accepted: August 2, 2022.
Available online: August 8, 2022. Manuscript no. OPHTHA-D-22-00281

[1] School of Optometry and Vision Science, University of New South Wales, Sydney, Australia.
[2] Moorfields Eye Hospital NHS Foundation Trust, London, United Kingdom.
[3] EpiVision Ophthalmic Epidemiology Consultants, Penn, United Kingdom.
[4] National Institute of Health Research Moorfields Biomedical Research Centre, London, United Kingdom.

Disclosure(s):
All authors have completed and submitted the ICMJE disclosures form.
The author(s) have no proprietary or commercial interest in any materials discussed in this article.

Financial support: Grants from Fight for Sight (1542/43 and 1465/6), Moorfields Eye Hospital Special Trustees (ST 12 09A), anonymous donors to Moorfields Eye Charities None of the funders had a role in the design or conduct of this research. Part of John Dart's salary was paid by the National Institute of Research (NIHR) Biomedical Research Centre at Moorfields Eye Hospital NIHR BRC. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. Dr Carnt was supported by an NHMRC Early Career CJ Martin Fellowship (APP1036728).

HUMAN SUBJECTS: Human subjects were included in this study. Ethics approval was obtained from the National Research Ethics Service Committee London-Hampstead, REC Reference 13/LO/0032 and the Moorfields Eye Hospital Research Governance Committee 18th February 2013. All research adhered to the tenets of the Declaration of Helsinki. All participants provided informed consent.

No animal subjects were used in this study.

Author Contributions
Conception and design: Carnt, Minassian, Dart
Data collection: Carnt, Dart
Analysis and interpretation: Carnt, Minassian, Dart

Obtained funding: N/A

Overall responsibility: Carnt, Minassian, Dart

Abbreviations and Acronyms:
AK = *Acanthamoeba* keratitis; **CI** = confidence interval; **CL** = contact lens; **DD** = daily disposable; **DW** = daily wear; **LASSO** = least absolute shrinkage and selection operator; **MK** = microbial keratitis; **OR** = odds ratio; **PAR%** = population attributable risk percentage.

Keywords:
Acanthamoeba keratitis, AK, Contact lens, Daily disposable contact lens, Hard contact lens, Reusable soft contact lens, Rigid contact lens, Risk factor.

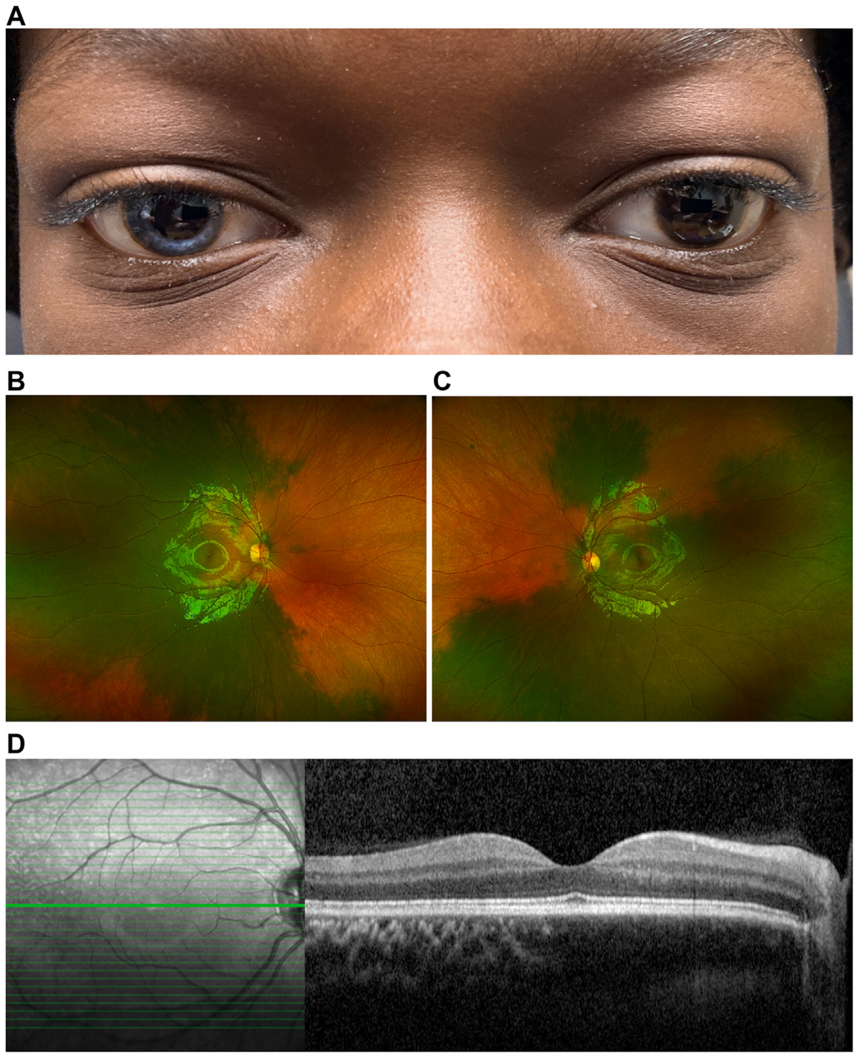
Correspondence:
John K. G. Dart, DM, Moorfields Eye Hospital, 162 City Road, London EC1V 2PD, UK. E-mail: j.dart@ucl.ac.uk.

References

1. Randag AC, van Rooij J, van Goor AT, et al. The rising incidence of Acanthamoeba keratitis: a 7-year nationwide survey and clinical assessment of risk factors and functional outcomes. *PLoS One*. 2019;14:e0222092.
2. Bonini S, Di Zazzo A, Varacalli G, Coassin M. Acanthamoeba keratitis: perspectives for patients. *Curr Eye Res*. 2021;46:771–776.
3. Carnt NA, Man REK, Fenwick EK, et al. Impact of Acanthamoeba keratitis on the vision-related quality of life of contact lens wearers. *Cornea*. 2022;41:206–210.
4. Keay L, Edwards K, Naduvilath T, et al. Microbial keratitis predisposing factors and morbidity. *Ophthalmology*. 2006;113:109–116.
5. Ung L, Bispo PJM, Shanbhag SS, et al. The persistent dilemma of microbial keratitis: global burden, diagnosis, and antimicrobial resistance. *Surv Ophthalmol*. 2019;64:255–271.
6. Moussa G, Hodson J, Gooch N, et al. Calculating the economic burden of presumed microbial keratitis admissions at a tertiary referral centre in the UK. *Eye (Lond)*. 2021;35:2146–2154.
7. Arshad M, Carnt N, Tan J, Stapleton F. Compliance behaviour change in contact lens wearers: a randomised controlled trial. *Eye (Lond)*. 2021;35:988–995.
8. Cope JR, Collier SA, Nethercut H, et al. Risk behaviors for contact lens-related eye infections among adults and adolescents - United States, 2016. *MMWR Morb Mortal Wkly Rep*. 2017;66:841–845.
9. Michas F. *Share of Individuals Who Wear Contact Lenses in Selected European Countries in 2020*. Hamburg, Germany: Statista2021; 2021.
10. Sauer A, Greth M, Letsch J, et al. Contact lenses and infectious keratitis: from a case-control study to a computation of the risk for wearers. *Cornea*. 2020;39:769–774.
11. Fortune Business Insights. Contact Lenses Market Size, Share & COVID-19 Impact Analysis, By Modality (Reusable and Disposable), By Design (Toric, Multi-focal, and Spherical), By Distribution Channel (Retail Stores, Online Stores, and Ophthalmologists), and Regional Forecast, 2020-2027. Maharashtra, India. *Medical Device Marketing Research Report Fortune Business Insights*. 2020:2021.
12. Szczotka-Flynn LB, Shovlin JP, Schnider CM, et al. American Academy of Optometry Microbial Keratitis Think Tank. *Optom Vis Sci*. 2021;98:182–198.
13. Wu YT, Ho A, Naduvilath T, et al. The risk of vision loss in contact lens wear and following LASIK. *Ophthalmic Physiol Opt*. 2020;40:241–248.
14. Stapleton F, Keay L, Edwards K, et al. The incidence of contact lens-related microbial keratitis in Australia. *Ophthalmology*. 2008;115:1655–1662.
15. Morgan P, Woods CA, Tranoudis IG, et al. International contact lens prescribing 2020: we report on the prescribing trends highlighted by our 19th global survey including more than 20,000 fits. *Contact Lens Spectrum*. 2020;35:26–32.
16. Dart JK, Radford CF, Minassian D, et al. Risk factors for microbial keratitis with contemporary contact lenses: a case-control study. *Ophthalmology*. 2008;115:1647–1654, 54 e1-3.
17. Stapleton F, Naduvilath T, Keay L, et al. Risk factors and causative organisms in microbial keratitis in daily disposable contact lens wear. *PLoS One*. 2017;12:e0181343.
18. Verani JR, Lorick SA, Yoder JS, et al. National outbreak of Acanthamoeba keratitis associated with use of a contact lens solution, United States. *Emerg Infect Dis*. 2009;15:1236–1242.
19. Chew HF, Yildiz EH, Hammersmith KM, et al. Clinical outcomes and prognostic factors associated with acanthamoeba keratitis. *Cornea*. 2011;30:435–441.
20. Thebpatiphat N, Hammersmith KM, Rocha FN, et al. Acanthamoeba keratitis: a parasite on the rise. *Cornea*. 2007;26:701–706.
21. Radford CF, Minassian DC, Dart JK. Acanthamoeba keratitis in England and Wales: incidence, outcome, and risk factors. *Br J Ophthalmol*. 2002;86:536–542.
22. Carnt N, Hoffman J, Verma S, et al. Acanthamoeba keratitis: confirmation of the UK outbreak and a prospective case-control study identifying contributing risk factors. *Br J Ophthalmol*. 2018;102:1621–1628.
23. Wu YT, Willcox M, Zhu H, Stapleton F. Contact lens hygiene compliance and lens case contamination: a review. *Cont Lens Anterior Eye*. 2015;38:307–316.
24. Hampton D, Tarver ME, Jacobs DS, et al. Special Commentary: Food and Drug Administration, American Academy of Ophthalmology, American Academy of Optometry, American Optometric Association and the Contact Lens Association of Ophthalmologists Cosponsored Workshop: Revamping Microbiological Test Methods for Contact Lenses, Products, and Accessories to Protect Health and Ensure Safety. *Eye Contact Lens*. 2015;41:329–333.
25. Radford CF, Bacon AS, Dart JK, Minassian DC. Risk factors for acanthamoeba keratitis in contact lens users: a case-control study. *BMJ*. 1995;310:1567–1570.
26. Chalmers RL, McNally JJ, Schein OD, et al. Risk factors for corneal infiltrates with continuous wear of contact lenses. *Optom Vis Sci*. 2007;84:573–579.
27. Stehr-Green JK, Bailey TM, Brandt FH, et al. Acanthamoeba keratitis in soft contact lens wearers. A case-control study. *JAMA*. 1987;258:57–60.
28. Carnt N, Stapleton F. Strategies for the prevention of contact lens-related Acanthamoeba keratitis: a review. *Ophthalmic Physiol Opt*. 2016;36:77–92.
29. Todd CD, Reyes-Batlle M, Pinero JE, et al. Isolation and molecular characterization of Acanthamoeba genotypes in recreational and domestic water sources from Jamaica, West Indies. *J Water Health*. 2015;13:909–919.
30. Carnt NA, Subedi D, Connor S, Kilvington S. The relationship between environmental sources and the susceptibility of Acanthamoeba keratitis in the United Kingdom. *PLoS One*. 2020;15:e0229681.

31. Zimmerman AB, Richdale K, Mitchell GL, et al. Water exposure is a common risk behavior among soft and gas-permeable contact lens wearers. *Cornea*. 2017;36:995–1001.
32. Carnt N, Keay L, Willcox M, et al. Higher risk taking propensity of contact lens wearers is associated with less compliance. *Cont Lens Anterior Eye*. 2011;34:202–206.
33. Arshad M, Carnt N, Tan J, et al. Water exposure and the risk of contact lens-related disease. *Cornea*. 2019;38:791–797.

Pictures & Perspectives



Iris Heterochromia and Choroidal Hypopigmentation in Waardenburg Syndrome

A 10-year-old Black boy was referred for possible retinal hemorrhages. His visual acuity was 20/20 in both eyes. Examination revealed complete iris heterochromia, with one blue iris and one brown iris (Fig **A**). Fundus examination demonstrated diffuse areas of choroidal hypopigmentation (Fig **B-C**), notably also in the eye with normal iris pigment. OCT showed a loss of choroidal reflectivity in areas of hypopigmentation (Fig **D**). The patient did not have a white forelock or hearing loss, but had facial features of telecanthus and a wide nasal root, consistent with a diagnosis of Waardenburg syndrome (Magnified version of Fig **A**-**D** is available online at www.aaojournal.org).

Jong G. Park, MD
Sandeep Randhawa, MD
Antonio Capone, Jr., MD

Associated Retinal Consultants, Royal Oak, Michigan