Age and Other Risk Factors for Corneal Infiltrative and Inflammatory Events in Young Soft Contact Lens Wearers from the Contact Lens Assessment in Youth (CLAY) Study

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Purpose. To describe age and other risk factors for corneal infiltrative and inflammatory events (CIEs) in young, soft contact lens (SCL) wearers and to model the age-related risk.

Methods. A multicenter, retrospective chart review of 3549 SCL wearers (8–33 years at first observed visit, +8.00 to −12.00D, oversampling <18 years) captured CIEs from January 2006 to September 2009. The review noted age, sex, SCL worn, use of lens care products, and SCL wearing history. Event diagnoses were adjudicated to consensus by reviewers masked to wearer identity, age, and SCL parameters. Significant univariate risk factors for CIEs were subsequently tested in multivariate generalized estimating equations.

Results. Charts from 14,305 visits observing 4,663 SCL years yielded 187 CIEs in 168 wearers. Age was a significant nonlinear risk factor, peaking between 15 and 25 years ($P < 0.008$). Less than 1 year of SCL use was protective versus longer years of wear ($P < 0.0003$). Use of multipurpose care products (2.86×), silicone hydrogels (1.85×), and extended wear (2.37×) were significantly associated with CIEs in the multivariate model ($P < 0.0001$ each).

Conclusions. Patient age, years of lens wear, use of multipurpose care products, silicone hydrogels, and extended wear were all significantly associated with CIEs with SCL wear. Use of SCLs in young patients aged 8 to 15 years was associated with a lower risk of infiltrative events compared with teens and young adults. In terms of safety outcomes, SCLs appear to be an acceptable method of delivering optics designed to manage myopia progression in children and young teens in the future. (*Invest Ophthalmol Vis Sci.* 2011;52:6690–6696) DOI: 10.1167/iovs.10-7018

Contact lens wearers younger than 25 years are at increased risk of corneal inflammatory events (CIEs) during continuous wear of silicone hydrogel SCLs, as shown in controlled, randomized, prospective clinical trials and observational studies.[1,2] In addition to age under 25 years, overnight wear and smoking have also been confirmed as risk factors for CIEs with various types of SCLs and wearing schedules.[3–6] Unlike microbial keratitis (MK), CIEs are not sight threatening, but they warrant careful study because they can be painful and difficult to differentiate from MK. These inflammatory and infiltrative events also require medical resources in the form of extra eye care visits and pharmaceutical management and may jeopardize the patient's ability or willingness to continue SCL wear.

Although it is widely accepted that SCL wearers younger than 25 years are at higher risk for CIEs, SCL wearers younger than 18 have not been studied in sufficient numbers to establish the risk among children and teens or the lower age at which the risk abates. Because young patients are often excluded from registration trials for devices that are not specifically intended for pediatric use, there is a paucity of information on children and teenaged SCL wearers, except in controlled clinical trials.[7,8]

Current studies of human myopia suggest that progression of myopia is linked to peripheral hyperopic defocus.[9,10] Early reports from animal and human trials suggested that the rate of myopia progression may be slowed by correcting peripheral refractive error, either binocularly or monocularly.[11–14] Treatments to prevent myopia progression will most likely require the application of adaptive optics directly on the corneal surface via SCLs, to maintain proper relationship with the defocus of the peripheral retina and to maximize the child's ability to wear lenses for more waking hours.[15] With several SCL designs in development for the management of myopia progression in children and teens,[11] there could be a sizeable increase in SCL prescriptions for myopic children and teens in the near future.[16,17]

In preparation for this potential increase in young SCL wearers who must wear SCLs for years, it is essential to establish the safety profiles for SCLs in children and teens outside of controlled clinical trials.[18,19] In a recently published retrospective clinical chart review, the risk profile by age for all complications capable of interrupting lens wear was found to peak at younger than age 25, although that estimate did not control for

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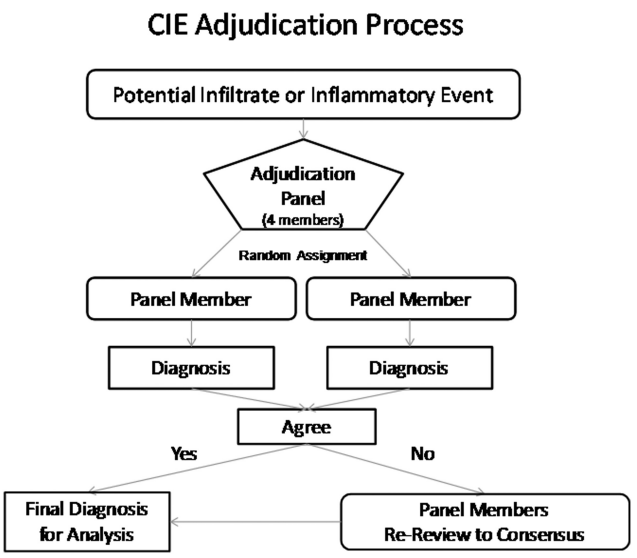

FIGURE 1. The adjudication process.

overnight wear, which may be more common in that age group.[20] In that study, it appeared that the risk for CIEs was lower among the preteens (9–12), but the lower age where the risk began could not be precisely established due to the small sample size of children in that clinical population. The purpose of this analysis is to determine the role of age between 8 and 33 years in the development of CIEs relative to other significant risk factors in a large, multicenter, retrospective chart review in which young SCL wearers (aged 8–18) were oversampled relative to their presence in the normal clinical population.

METHODS

The methods for this retrospective chart review and baseline characteristics of the observed population have been described elsewhere.[21] The diagnoses of interest for this analysis include MK, symptomatic corneal infiltrative events, and iritis; all events that are reportable to the U.S. Food and Drug Administration (FDA) as serious and significant events. The events were classified according to the Cornea and Contact Lens Research Unit (CCLRU) Classification System[22] and include MK; contact lens peripheral ulcer (CLPU); contact lens acute red eye (CLARE), with and without infiltrates; infiltrative keratitis (IK); and iritis. This is an analysis of 187 events with the above diagnoses, a subset of the 522 complications, described elsewhere,[23] that caused interruption of lens wear in the Contact Lens Assessment in Youth (CLAY) study

Briefly, six North American eye care clinics affiliated with schools or colleges of optometry were identified as study sites after successfully completing feasibility exercises to demonstrate the availability of enough SCL wearers aged 8 to 12 years in their patient pool. Institutional Review Board (IRB) approval was obtained before data collection began, and the study complied with the Declaration of Helsinki. Because this was a retrospective chart review, the IRBs determined that no informed consent was required to access the clinical charts, as all information was deidentified before submission to the study Coordinating Center.

Event Adjudication

In addition to data that were gathered for all wearers at all visits, each time a clinical complication occurred that resulted in the eye care practitioner's recommending an interruption in SCL wear, the site scanned the deidentified medical charts for those and all event-related follow-up visits. These scans were submitted to the Event Adjudication Center. After SCL brands, powers, and patient age were redacted at the Event Adjudication Center, each chart was reviewed by two randomly assigned members of the study team to identify those cases that were potentially MK or CIEs. Events that were potentially CIEs or MK were then adjudicated by an expert panel (Adjudication Panel) to consensus, as shown in Figure 1. Disagreements of diagnosis between reviewers were adjudicated to consensus during a face-to-face meeting.

TABLE 1. Description of Observed Cohort by Age Group

Age at First Visit (y)	Enrolled *N* = 3549 *n* (col%)	Wearers with Follow-Up *N* = 3164 *n* (col%)	Observed Months Mean (SD)	Male *n* (row %)	Silicone Hydrogel *n* (row %)	EW at First Visit *n* (row %)
08–12	260 (7)	243 (8)	20.3 (13.2)	120 (46)	117 (45)	36 (14)
13–17	879 (25)	811 (26)	20.3 (12.7)	360 (41)	567 (58)	132 (15)
18–25	1274 (36)	1129 (36)	16.2 (12.6)	408 (32)	803 (63)	204 (16)
26–33	1136 (32)	981 (31)	16.5 (12.8)	398 (35)	670 (59)	136 (12)

TABLE 2. Diagnosis for Events by Age and Overnight Wear

		EW Lens Use		Age at Event			
	Total *n* (%)	EW Previous Night *n* (%)*	Any EW *n* (%)†	8–12 y *n*	13–17 y *n*	18–25 y *n*	>26 y *n*
Microbial keratitis	8 (4)	2 (25)	4 (50)	0	2	5	1
Infiltrative keratitis	110 (59)	21 (19)	39 (35)	2	33	46	29
CLPU	41 (22)	17 (41)	24 (59)	2	8	20	11
CLARE w/infiltrates	14 (8)	10 (71)	13 (93)	0	2	8	4
CLARE w/o infiltrates	13 (7)	4 (31)	5 (39)	0	5	7	1
Iritis	1 (1)	0	0	0	0	1	0
Total by age group	187 (100)	54 (29)	85 (47)	4	50	87	46

All events for all wearers are included. EW, overnight wear. Statistical significance by Fisher's exact test.
* $P = 0.0006$.
† $P = 0.0001$.

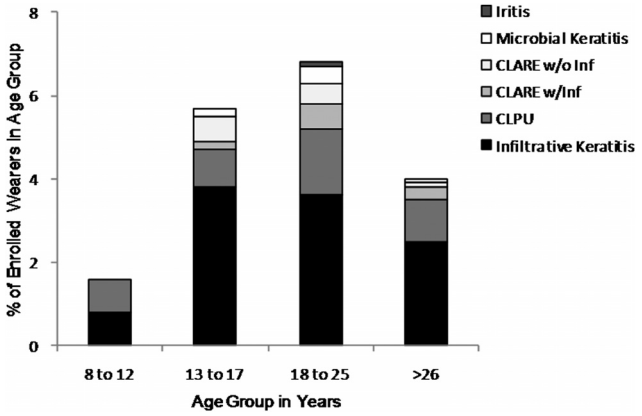

FIGURE 2. Specific CIE diagnoses by age group.

Sample Size Calculation

Although the CLAY study was designed to characterize the risk of many different conditions related to CL wear, the most conservative sample size calculation was based on the estimated incidence of CIEs in the 18- to 25-year-olds from a university clinic, as a subset of historical data from a recently published study.[20] The sample size was calculated with the outcome of interest the presence of a CIE (including MK and iritis), comparing age groups 8 to 17 (this group was subdivided into 8–12 and 13–17 years for CIE comparison), 18 to 25, and 26 to 33 years of age (NCSS and PASS; Number Cruncher Statistical Systems, Kaysville, UT). The assumed proportion of wearers with events in the 18- to 25-year-olds was 6.7% for CIEs and 16.9% for all events from the historical data. Thus, to detect a 40% reduction in the rate of CIEs compared to the 18- to 25-year-olds, we planned to sample 3324 SCL wearers, with oversampling ($n = 243$) in the youngest group aged 8 to 12 years. to enable us to observe a 50% decrease in all events in that age group. By sizing the study this way and including an oversampling of the youngest SCL wearers, we achieved both goals: to detect differences in overall and CIEs. The table of sample size assumptions is shown in Appendix B.

Analysis

Generalized estimating equations (GEEs) were used to characterize the risk of an event with respect to demographic and clinical measures while controlling for the potential for multiple visits per subject.[23] Univariate models were used to test the independent effect of each measure on the odds of experiencing an infiltrative event. A multivariate model was then determined incorporating all significant factors ($P < 0.05$) from the univariate models (all analyses, SAS, ver. 9.2; SAS, Cary, NC). Visits in which a noninfiltrative event was identified ($n = 335$) and visits of subjects with no previous history of lens wear (i.e., new lens wearers at baseline, $n = 754$) were excluded from the analysis as they had no exposure to SCLs at that time and thus no opportunity to develop complications at those visits. Among wearers with multiple events, data from only the first event were used in the analysis ($n = 19$ events excluded).

RESULTS

Observed Cohort

Charts from 3,549 patients (14,305 visits and 4,663 years of SCL wear observed) resulted in 187 events of interest in 168 patients (4.7% of enrolled). A description of demographics, length of observed follow-up, and key SCL features are shown in Table 1. The median number of visits per wearer was three or four in all age groups. The mean follow-up time was significantly longer for the wearers who began the study at age 8 to 17 years (20.3 months) compared with the other age groups (16.2 months for 18- to 25-year-olds and 16.5 months for those ≥26 years of age). The specific diagnoses for all events by age group and extended wear (EW) status are shown in Table 2 and Figure 2.

Risk Factors for Inflammatory and Infiltrative Events

Figure 3 shows the percentage of CIE visits by age, normalized to all visits by patients of that age, a reflection of the relative risk of those events by year of age. The risk of a CIE increased in a nonlinear fashion up to age 21 and then decreased similarly, with the peak years at risk from age 15 to 25 years. The solid line shows a quadratic equation function that best represents the data. Since

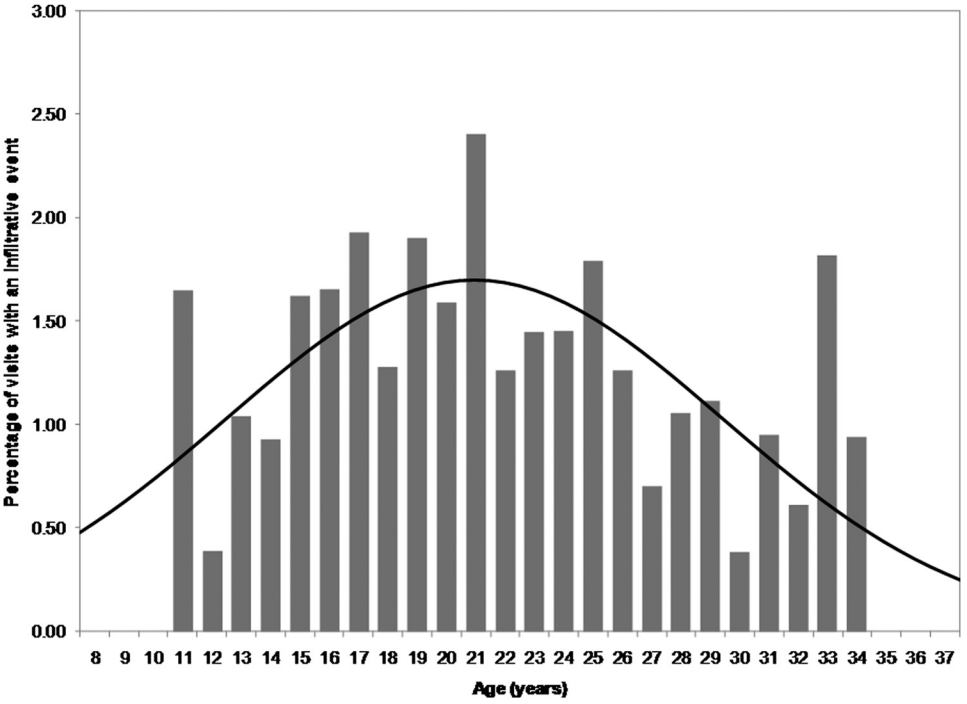

FIGURE 3. Percentage of clinical visits with a CIE by year of age. *Solid line*: the quadratic equation model for age as a risk factor for CIEs.

TABLE 3. Age-Related Risk of CIEs

Reference Age	Age (y) Hazard Ratio (95% CI)											
	12	14	16	18	20	22	24	26	28	30	32	34
10	**1.29 (1.02–1.63)**	**1.58 (1.03–2.42)**	**1.84 (1.03–3.30)**	**2.04 (1.02–4.09)**	**2.15 (1.00–4.64)**	2.16 (0.97–4.79)	2.06 (0.94–4.51)	1.86 (0.90–3.86)	1.61 (0.86–2.98)	1.32 (0.84–2.05)	1.02 (0.84–1.25)	**0.76 (0.62–0.92)**
12		**1.23 (1.01–1.49)**	**1.43 (1.01–2.02)**	**1.58 (1.00–2.51)**	1.67 (0.98–2.84)	1.67 (0.95–2.93)	1.59 (0.92–2.75)	1.45 (0.89–2.34)	1.25 (0.87–1.78)	1.02 (0.84–1.24)	**0.79 (0.65–0.97)**	**0.59 (0.48–0.72)**
14			**1.17 (1.00–1.36)**	1.29 (0.99–1.69)	1.36 (0.97–1.91)	1.37 (0.95–1.97)	1.30 (0.92–1.84)	1.18 (0.90–1.54)	1.02 (0.83–1.24)	0.83 (0.68–1.01)	**0.65 (0.53–0.79)**	**0.48 (0.39–0.58)**
16				1.11 (0.99–1.24)	1.17 (0.97–1.40)	1.17 (0.95–1.44)	1.12 (0.93–1.33)	1.01 (0.83–1.23)	0.87 (0.72–1.06)	**0.71 (0.59–0.87)**	**0.56 (0.46–0.87)**	**0.41 (0.34–0.50)**
18					1.05 (0.98–1.13)	1.06 (0.97–1.15)	1.01 (0.83–1.22)	0.91 (0.75–1.11)	**0.79 (0.65–0.96)**	**0.64 (0.53–0.78)**	**0.50 (0.41–0.61)**	**0.37 (0.27–0.50)**
20						1.00 (0.82–1.22)	0.96 (0.79–1.16)	0.87 (0.71–1.05)	**0.75 (0.61–0.91)**	**0.61 (0.50–0.74)**	**0.48 (0.38–0.60)**	**0.35 (0.23–0.55)**
22							0.95 (0.78–1.16)	0.86 (0.71–1.05)	**0.74 (0.61–0.91)**	**0.61 (0.52–0.71)**	**0.47 (0.35–0.65)**	**0.35 (0.21–0.59)**
24								**0.91 (0.74–1.10)**	**0.78 (0.72–0.84)**	**0.64 (0.53–0.77)**	**0.50 (0.35–0.70)**	**0.37 (0.22–0.63)**
26									**0.86 (0.81–0.92)**	**0.71 (0.59–0.84)**	**0.55 (0.40–0.76)**	**0.41 (0.24–0.68)**
28										**0.82 (0.74–0.91)**	**0.64 (0.49–0.82)**	**0.47 (0.30–0.74)**
30											**0.78 (0.67–0.90)**	**0.58 (0.41–0.81)**
32												**0.74 (0.61–0.89)**

Data are the age in years, with the hazard ratio (95% CI) and show the relative risk for corneal infiltrative events by age in years relative to reference age in years. Bold, $P < 0.05$.

TABLE 4. Univariate Model for Risk of CIEs

Characteristic (Referent)	Factor	OR	95% CI
Patient age		**Nonlinear**	
Lens material, (hydrogel)	Silicone hydrogel	**2.27**	**1.59–3.22**
Lens replacement schedule (daily disposable)	1–2 Weekly	**2.98**	**1.18–7.51**
	Monthly	**3.42**	**1.36–8.57**
	Other	**5.10**	**1.83–14.22**
	Hydrogen peroxide	**0.36**	**0.17–0.65**
Care system (multi-purpose)	Generic	0.90	0.39–2.04
	None/saline	**0.30**	**0.13–0.69**
Extended wear (daily wear)	Yes	**3.21**	**2.32–4.45**
Years of CL wear (<1 Year)	1–5 y	**3.52**	**1.53–8.07**
	6–10 y	2.25	0.89–5.73
	>10 y	**2.95**	**1.04–8.32**
Sex (male)	Female	1.14	0.80–1.49
Lens type (sphere)	Toric	1.42	0.91–1.94
Lens power			
(1 D increase)	1-D increase	0.96	0.91–1.01
(<5 D)	≤5 D	0.80	0.56–1.20

Bold, $P < 0.05$.

each age had a different number of patients and visits, the hazard ratio and 95% CIs of CIEs by year of age is shown in Table 3 for all CIEs relative to each year of age.

The univariate and multivariate risk factors are shown in Tables 4 and 5. In addition to patient age, years of CL wear, use of a multipurpose lens care system, overnight wear, and use of silicone hydrogel lenses (in decreasing order) were all significant risk factors for CIEs in the univariate and multivariate models. These factors were significant in the multivariate analysis when all events or only first events were considered. Lens replacement frequency was the only factor that was significant just in the univariate model, with daily replacement associated with the lowest risk.

CIEs Attributed to Extended Wear

Association of EW just before the CIEs or at any visit during the follow-up varied significantly with different CIE diagnoses ($P = 0.0006$ and $P = 0.0001$, Fisher's exact test), as shown in Table 2. For example, those with CLARE with infiltrates had the highest proportion of EW users (71% immediately preceding the event and 93% at some time during observation), whereas EW immediately preceding the event was associated with 31% of CLARE without infiltrates, and only 39% of those patients reported EW at any visit during observation.

DISCUSSION AND CONCLUSIONS

This study presents the largest postmarket observation of SCL-related CIEs among children and teens ever conducted. The study observed an average of 20.3 months of SCL wear in 1054 patients under age 18 and in more than 2000 young adults with a slightly shorter duration of follow-up. Our chart selection process included an oversampling of child SCL wearers relative to their presence in the SCL population overall. This tactic yielded a sufficient number of SCL wearers who began the study at 8 to 17 years of age to be able to make a meaningful statistical comparison in the proportion in that age group who developed CIEs compared with the number of young adult patients with such events. In addition, the types of SCLs prescribed in these academic clinics are among the most up-to-date SCL types, yielding a result that reflects clinical performance with SCLs that will be prescribed for years to come. The inclusion criteria for refractive error were set between +8.00 and −12.00 D in either meridian in wearers with good ocular health. These two criteria helped to exclude patients with very unusual refractive errors or corneal conditions who may be seen in the academic clinics but would not be representative of a normal patient population. In addition, the proportion of males in the sample and the distribution of refractive error with age showed that the sample of young SCL wearers was similar to the overall population of SCL wearers in North America.[21]

Even though young patients have developed MK with orthokeratology, children and young teens were not included in the original FDA registration trials for orthokeratology lenses because the lenses did not carry a pediatric indication for use.[7,8,24–29] Regardless of reports in case series with young patients, the age-related relative risk with orthokeratology remains unknown, because young orthokeratology patients have not been studied in sufficient numbers.[30] The suspicion of age-related risk with orthokeratology in children stimulates the SCL research community to focus on SCL safety outcomes in

TABLE 5. Multivariate Model for Risk of Corneal Infiltrative Events

		All Events		First Events Only	
Characteristic (Referent)	Factor	OR	95% CI	OR	95% CI
Age		**Nonlinear**			
Lens material (hydrogel)	Silicone Hydrogel	**1.85**	**1.26–2.70**	**1.79**	**1.22–2.63**
Care system (multipurpose)	Hydrogen Peroxide	**0.35**	**0.16–0.76**	**0.33**	**0.14–0.75**
Extended wear (daily wear)	Yes	**2.37**	**1.69–3.32**	**2.39**	**1.67–3.41**
Years of CL wear (<1 y)	1–5 y	**3.25**	**1.41–7.52**	**2.92**	**1.26–6.77**
	6–10 y	1.96	0.75–5.12	1.70	0.64–4.50
	>10 y	**3.04**	**1.03–8.94**	2.64	0.87–7.99

Bold, $P < 0.05$.

children before they are adopted as a mainstream treatment for the management of progressing myopia.

The clinical information in this retrospective study was captured by a scan of the medical records for all visits in which the patient received treatment or advice to interrupt SCL wear. This method of identifying events erred on the side of including milder events that were then adjudicated by a masked panel of expert reviewers, to arrive at the pool of patients with CIEs. The reviewers diagnosed CIEs according to established criteria from the contact lens literature. All patients in this series were receiving routine or problem-oriented clinical care and were not enrolled in clinical trials. Thus, most of the CIEs analyzed in this study were symptomatic, not the asymptomatic events that are often reported in clinical trials.[31,32] These CIEs were complications that required patients to seek care specifically for the acute symptomatic condition and consumed considerable outpatient medical resources.

The proportion of SCL patients who presented with CIEs in this study and the relative prevalence of specific complications is in the range of other published reports from postmarket studies with modern SCLs.[2,20] In the larger study that reviewed all events that interrupted SCL wear, the CIEs were the most frequent complications, far outstripping the other categories in their frequency (e.g., allergic, conjunctivitis).[23] The CIE conditions were also the most likely to repeat in SCL wearers. Thus, CIEs were worthy of independent analysis based on their prevalence in SCL wearers and also because they include events with the potential for MK and its associated morbidity.

There are several challenges in representing CIEs by age at event in a chart review such as that from which the CLAY dataset was compiled. The clinical data could vary for each lens wearer in terms of total observation time, number, frequency, and reason for visits. Wearers had an unequal chance to be observed with an event, although it is unlikely that this created any systematic bias that pertains to age. In addition, the observed cohort aged slightly during the 3+ years of potential observation. Age at the time of a CIE was known with a high degree of certainty, but the age and number of active wearers without events (the denominator) changed constantly, making it difficult to estimate any incidence of CIEs. The hazard ratio representation is the most appropriate analysis method for this type of data and uses the number of visits for wearers at each age, with and without a CIEs.[23] Note that the confidence intervals vary across age in that model, in particular at the lower and upper ranges where there were few events in that age group, as detailed in Table 3.

The CLAY results highlight the degree to which teenage and young adult SCL wearers merit targeted study because of their tendency to present with a higher rate and higher severity of CIEs. Six (75%) of the eight MK patients in this study were between 15 and 25 years old, and 23 (56%) of the 41 CLPU events were in that age group. An increase in inflammatory events among teenagers may be driven by the upregulation of autoimmune reactions seen in late adolescence (increase rates of acne, allergies, and autoimmune diseases). Inexperience with accessing health care may also contribute to delay in care that can result in worsening of otherwise self-limiting conditions or in resolution of the conditions without presenting for diagnosis.[33–37] The CLAY wearers were drawn from clinical sites at schools of optometry, and so many of the SCL wearers in this study were university students, many of whom lived in on-campus housing. For college students, factors such as lack of parental oversight or availability to purchase and supply SCLs and lens care products may contribute to noncompliance with many aspects of SCL wear. Without targeted counseling at eye care visits, patients between 15 and 25 years old may not know the right self-management steps to optimize the safety of their SCL wear, such as lens removal when they experience a red or painful eye.[34] In addition, North American college students have a reportedly unhealthy lifestyle, with poor nutrition, poor sleep habits, binge drinking, and crowded living conditions. All these factors could drive a higher rate of CIEs in this age group, but that understanding must be gained via carefully designed, prospective study of the behaviors and habits that vary with age across the 15- to 25-year-old population of SCL wearers.

In addition to age, the other risk factors that were significant in this study have been noted previously with SCLs. Extended wear is the most established risk factor for CIEs and the threefold increase relative to daily wear found here is in accordance with many other studies.[5] Some studies have also shown that the use of silicone hydrogel lenses significantly increases the risk of CIEs, although the mechanism is not known.[20,31] A patient's being new to SCL wear was recently reported as a protective factor for CIEs, regardless of overnight wear schedule.[20]

Smoking was not a significant risk factor in this study, although it has been shown to be significant in other studies.[3,6] This result could be due to the manipulated age distribution of the observed wearers; one third of our wearers were under the legal age for smoking and may have been reluctant to report smoking to their eye care practitioner, in particular if they were accompanied by their parents.

Another significant factor in this analysis, the use of multipurpose solutions tripled the risk of a CIE. This is a new finding and may be related to studying SCL wearers in the era after manufacturers of many solutions stopped instructing users to rub the lens surface during cleaning and disinfection. Even though hydrogen peroxide solutions do not carry a rubbing step, the volume of solution required and agitation created by the oxidation process may provide a less antigenic lens surface.

In summary, the CLAY study results suggest that the age-related risk for CIEs that interrupt SCL wear peaks in adolescence and early adulthood and that SCL wearers between ages 15 and 25 are at increased risk. Relative to teens and young adults, patients 8 to 15 years old presented with significantly fewer CIEs. Soft contact lenses appear to be an acceptable method to manage refractive error in children and the safety profile with use in this uncontrolled, postmarket study shows promise for them as a means of delivering advanced optics designed to manage progression of myopia in children.

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Appendix A

Clay Study Structure

Executive Committee: Robin L. Chalmers, Co-chair, Heidi Wagner, Co-chair, and G. Lynn Mitchell.

Event Review Team: Robin L. Chalmers, Meredith E. Jansen, Beth T. Kinoshita, Dawn Y. Lam, Kathryn Richdale, Luigina Sorbara, and Heidi Wagner.

CIE Event Adjudication Team: Mark A. Bullimore, Robin L. Chalmers, Timothy T. McMahon, and Heidi Wagner.

Clinical Sites

Indiana University School of Optometry, *Bloomington*, *IN*: Meredith E. Jansen, Principal Investigator, Angelina Bonner, Kristen Burkholder, and Carolyn Masters, Data Entry.

Nova Southeastern University College of Optometry, *Fort Lauderdale*, *FL*: Heidi Wagner, Principal Investigator, Steven Warne, and Margi A. Patel, Data Entry.

The Ohio State University College of Optometry, Columbus, OH: Kathryn Richdale, Principal Investigator, and Austin L.Tanner, Data Entry.

Pacific University College of Optometry, *Forest Grove, OR*: Beth T. Kinoshita, Principal Investigator, and Evelyn Y. Hu, Data Entry.

Southern California College of Optometry, *Fullerton*, *CA*: Dawn Y. Lam, Principal Investigator, and Jamie Lam, Data Entry.

University of Waterloo School of Optometry, *Waterloo*, *ON*, *Canada*: Luigina Sorbara, Principal Investigator, Gerry Giddens, and Jyotsna Maram, Data Entry.

Resource Centers

Data Coordinating Center: The Ohio State University College of Optometry, Columbus, OH: G. Lynn Mitchell, Director.

Event Data Management Center: Robin L. Chalmers, Director, Julia Purser, and Lucas Henneman, Data Management.

Appendix B

Table A1. Sample Size Calculation

	Inflammatory Events 6.7%	**All Events 16.9%**
30%	2086	751
35%	1490	538
40%	**1108**	401
45%	849	308
50%	667	*243*

Data are the number required per age group, to detect a decrease in rate of 6.7% and 16.9%. Bold, sample required to show 50% difference between larger age groups (8–17, 18–25, and 26–33 years) to compare all events. Italic, sample to show 40% difference in CIE events between 8–12-year-olds and other age groups.