# Acute Endophthalmitis Following Cataract Surgery

## *A Systematic Review of the Literature*

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**Objectives:** To determine the reported incidence of acute endophthalmitis following cataract extraction over time and to explore possible contributing factors, such as type of cataract incision.

**Methods:** A systematic review of English-language articles was conducted by performing a broad search of PubMed from 1963 through March 2003 using such terms as *cataract extraction*, *endophthalmitis*, and *postoperative complication*. Additional studies were identified from bibliographies of relevant articles and published proceedings. Surgical approach was recorded, when available. Pooled incidence rates and relative risks of developing endophthalmitis using different incision techniques were assessed.

**Results:** From 4916 unique, potentially relevant citations, 215 studies that addressed endophthalmitis and met the selection criteria were analyzed. A total of 3 140 650 cataract extractions were pooled resulting in an overall rate of 0.128% of postcataract endophthalmitis. However, the incidence of acute endophthalmitis changed over time, with a significant increase since 2000 compared with previous decades (relative risk, 2.44 [95% confidence interval, 2.27-2.61]). The rate of endophthalmitis was 0.265% in the 2000-2003 period, 0.087% in the 1990s, 0.158% in the 1980s, and 0.327% during the 1970s. Furthermore, an upward trend in rates after 1992 was noted, compared with 1991 and prior. Incision type appeared to significantly influence risk, as endophthalmitis following clear corneal cataract extraction during the 1992-2003 period was 0.189% compared with 0.074% (relative risk, 2.55 [95% confidence interval, 1.75-3.71]) for scleral incision and 0.062% (relative risk, 3.06 [95% confidence interval, 2.48-3.76]) for limbal incision.

**Conclusions:** This systematic review indicates that the incidence of endophthalmitis associated with cataract extraction has increased over the last decade. This upward trend in endophthalmitis frequency coincides temporally with the development of sutureless clear corneal incisions.

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In the past 4 decades, cataract surgery has undergone remarkable technical refinement, with simplified postoperative care and faster visual recovery as consequences.[1,2] With improved instrumentation, small-incision phacoemulsification became possible in the late 1980s, leading to the current state of the art of sutureless phacoemulsification surgery with foldable intraocular lens implantation.[3-6]

*See also page 605*

Removal of the lens through a corneal incision was reported as early as 1668[7]; however, the current self-sealing clear corneal incision was first introduced in 1992 by I. Howard Fine, MD.[8] Since then, increasing popularity of clear corneal incisions over limbal and scleral tunnel incisions among cataract surgeons across the United States and Europe has resulted in greater intraoperative control, decreased surgical time, simplified postoperative care, less induction of astigmatism, and faster visual recovery.[8] In the most recent survey of American Society of Cataract and Refractive Surgery members (2003), Leaming[3] reported that clear corneal incision was preferred by 72% of US surgeons and the no-suture closure was preferred by 92%. This acceptance is part of a gradual uptrend from 1.5%, 12.4%, 30%, 40%, and 47% in 1992, 1995, 1997, 1999, and 2000, respectively.[4] Among European surgeons, a similar 51.4% prefer clear corneal incisions,[9] while a 1999 French survey reported a more than 86% preference for clear corneal incisions.[10] Furthermore, sutureless cataract incisions are reportedly preferred among 92%, 94%, and 58% of cataract surgeons in the United States, New Zealand, and Japan, respectively.[3-6]

**Table 1. PubMed Search Strategy**

| Description | No. of Articles |
|---|---|
| PubMed keyword searches | |
| Search 1, *cataract extraction** | 16 243 |
| Search 2, *cataract surgery** | 16 314 |
| Search 3, *lens, intraocular** | 8431 |
| Search 4, *lens implantation** | 5326 |
| Search 5, *endophthalmitis* | 3684 |
| Search 6, *eye infection** | 17 192 |
| Search 7, *surgical wound infection** | 17 208 |
| Search 8, *panophthalmitis* | 282 |
| Search 9, *postoperative complication** | 249 356 |
| Combined searches | |
| (1 or 2 or 3 or 4) and (5 or 6 or 7 or 8 or 9) | 6235 |
| Exclusion criteria | |
| Limit by language type (English only) | 4564 |

*Searches also include the plural.

Endophthalmitis is an uncommon but serious intraocular infection that occurs most commonly as a complication of intraocular surgery and often causes severe visual impairment or even the loss of an eye.[11] The reported incidence of postoperative endophthalmitis varies by the specific surgical procedure and across studies, but the overall incidence has been declining since the late 19th to late 20th century. The incidence of endophthalmitis after cataract surgery was approximately 5% to 10% in the late 1800s and early 1900s,[12-14] 1.5% to 2% during the 1930s,[14-16] 0.5% to 0.7% in the mid 1900s,[14,16,17] and 0.06% to 0.09% according to nationwide patient registries in the early 1990s.[18,19] Improvements in microsurgical and aseptic techniques, advancements in surgical materials, and use of prophylactic broad-spectrum antibiotics, in combination with a better understanding of causes of the infection, may explain this favorable trend.

In a meta-analysis of studies published from 1979 to 1991, a period that predates the use of self-sealing clear corneal incisions, Powe et al[20] reported a 0.13% incidence of acute postoperative endophthalmitis following cataract extraction. However, recent reports suggest that the postcataract endophthalmitis rate may be substantially higher, suggesting a greater risk of endophthalmitis coincident with the increase in self-sealing clear corneal incisions.[21-27] Colleaux and Hamilton[21] reported a 0.129% and 0.05% incidence of endophthalmitis following cataract extraction with sutureless clear corneal and scleral tunnel incisions, respectively. Similarly, 3 retrospective, comparative, case-controlled studies found a significantly higher endophthalmitis rate associated with clear corneal incisions compared with scleral tunnel incisions.[22,23,27] In a study from the Massachusetts Eye and Ear Infirmary (Boston), the incidence of endophthalmitis was 0.68% for clear corneal incisions vs 0.18% for scleral tunnel incisions.[24] More recently, Nakagi et al[25] reported a statistically increased risk with clear corneal incisions (0.29%) compared with sclerocorneal incisions (0.05%). Various other anecdotal reports by cataract surgeons and retinal specialists have also claimed a higher incidence of endophthalmitis with clear corneal incisions.[24] These studies indicate an apparently increased occurrence of endophthalmitis in the last decade and a several-fold increase in endophthalmitis risk associated with self-sealing clear corneal incisions compared with scleral tunnel and sclerocorneal wounds. However, the relative rarity of endophthalmitis following intraocular surgery poses significant difficulty in ascertaining accurate incidence rates or in analyzing effects of multiple risk factors. Most reports regarding the rates of endophthalmitis are based on the experience of individual institutions or groups of surgeons and are limited by the small sample sizes, thereby making comparisons and statistical validity of data difficult. Only more appropriate methods such as extensive reviews or multicenter, prospective studies can help reveal clinical and statistical trends for this adverse outcome. Depending on the projected incidence, a study would need to include as many as 100 000 patients to have sufficient study power to detect even a 50% difference in the risk of endophthalmitis between 2 groups of patients.[22]

To obtain the best available perspective, as reflected by the medical literature, and a better understanding of the recent trends in postoperative endophthalmitis following cataract surgery, we conducted a systematic review of the literature. The purpose of our study was to detect changes in the trends of endophthalmitis after cataract extraction and to determine, if present, possible associations of these changes with specific surgical approaches in cataract surgery. In light of the recent reports suggesting an increased incidence of endophthalmitis with clear corneal incisions, we analyzed possible differences in rates according to the date of the publication and the surgical techniques used (eg, clear corneal incision).

## METHODS

### STUDY DESIGN

We performed a systematic review of the literature to identify all published reports pertaining to the outcome of cataract surgery or penetrating keratoplasty. Studies were identified through a search consisting of: (1) a computerized search of Cochrane and PubMed (National Library of Medicine) databases from 1963 through March 2003, using a specific search strategy (**Table 1**); (2) manual search of reference lists of original reports and review articles, retrieved through the electronic search, that met the selected criteria; (3) review of major ophthalmic textbooks; and (4) review of key published proceedings and scientific session electronic abstracts (ie, Association for Research in Vision and Ophthalmology [ARVO] [Rockville, Md] and American Academy of Ophthalmology [AAO] [San Francisco, Calif]) in 2001 through 2003. Because of the low occurrence of endophthalmitis, the importance of obtaining each published report addressing this potential complication was clearly apparent. Therefore, an intentionally broad search strategy was developed to identify all possible studies that met the eligibility criteria. Keywords were selected based on expert opinion and evaluation of selected review articles on endophthalmitis and cataract surgery.

### SELECTION CRITERIA

Reports were considered eligible for our review if they satisfied our selection criteria. Each article had to meet all of the following inclusion criteria: (1) the article was written in English; (2) the study examined human cases; (3) the study examined primary or secondary cataract surgery with or without intraocular lens implantation ("secondary cataract surgeries" were those cases

involving secondary lens implantation or intraocular lens exchange); and (4) the article addressed postcataract endophthalmitis occurrence (reported the number of procedures and the number of postsurgical endophthalmitis cases even if zero or the numbers could be derived according to reported percentages). We chose to include clinically diagnosed (both culture-positive and culture-negative) cases because it allowed for the inclusion of more studies in order to generate more power for analyzing this relatively rare complication.

Articles were excluded from this review if they met any of the following exclusion criteria: (1) the study examined fewer than 10 eyes; (2) the article primarily examined cataract surgery in conjunction with vitrectomy or in patients who underwent vitrectomy; (3) the article examined cataract surgery performed with any glaucoma procedure; (4) endophthalmitis cases were associated with an outbreak (eg, contaminated instruments or phacoemulsification tubing causing a series of these infections); or (5) if mentioned, the study had less than 1 week of postoperative follow-up (except if noticeable number of endophthalmitis cases were identified, in which case the study was included).

### IDENTIFICATION OF STUDIES

The process of identifying all possible studies satisfying our eligibility criteria involved several steps. Following the computerized search, we read the titles and abstracts of all retrieved citations. Articles were rejected after review of abstracts only if it could be determined that they did not meet the inclusion criteria or if any of the exclusion criteria applied. A full copy of the article was then obtained and reviewed in detail to determine whether the study satisfied the selection criteria.

### DATA ABSTRACTION

Articles that satisfied the eligibility criteria underwent an intensive, structured review to abstract data on the postsurgical outcome of cataract operations and any potentially significant variables. Data extraction was performed using a standardized review form to record the following: (1) year of publication; (2) journal published; (3) location (ie, country) of trial; (4) the minimum (mean or maximum if minimum was not indicated) duration of follow-up on postsurgical patients; (5) number of eyes undergoing cataract surgery; (6) number of patients who experienced acute endophthalmitis postoperatively (*acute* was defined as onset within 6 weeks); if the timeline was not explicitly reported, then, based on review of the study, a determination was made whether it referred to cases with acute endophthalmitis; and (7) type of cataract wound (limbal, sclerocorneal, and corneoscleral incisions were treated as the same type of incision).

With publications that reported on more than 1 group of patients or surgical procedures, only analysis of the pertinent groups was performed. If it could be determined that 2 or more studies presented the same data from a single participant population, these data were included only once in this review. Furthermore, if the data were published in more than 1 journal, only 1 was chosen for analysis.

### STATISTICAL ANALYSIS

Throughout this report, comparisons of postoperative infection rates were presented using the relative risk statistics. In most cases, the reported relative risk was accompanied by its 95% confidence intervals to provide a consistent criterion by which a difference in infection rates could be construed to be substantial.

Weighted regression analysis was used to portray how the postoperative infection rates were changing during the 40-year period from 1964 to 2003. The period was also divided into 2 subperiods (ie, 1964-1991 and 1992-2003) to reflect the date that clear corneal incision was introduced. Infection rates were then fit by a weighted "piecewise" or "segmented" linear model, which was composed of 2 separate linear approximations of the infection rates reported in the articles published within each subperiod. This method produced 2 slope coefficients, which summarized the change in infection rates over time within the indicated subperiod. In addition to the slope coefficients, the weighted regression analysis also produced a pair of 95% confidence intervals for estimating the true value of each of these slopes.

The weighted regression analyses described earlier were based on units of analysis as defined in 1 of the following ways: either the units of analysis were the 215 qualifying articles or they were the 40 years in which those publications appeared. When publication year was the unit of analysis, the postoperative infection rate for each year was determined by aggregating the data derived from all qualifying articles that were published in that year. In either case, the statistics were then weighted proportional to the number of surgeries reported within each unit of analysis. With this weighting strategy, statistical results can be directly linked to the overall postoperative infection rates, which would not have been the case under an equal case-weighting plan. In other words, the weighting was performed relative to the volume of surgeries both within each study or year, which gave more power to studies with higher numbers of surgeries and less to those with fewer operations. All coefficients for this regression model were computed using the SAS NLIN procedure.

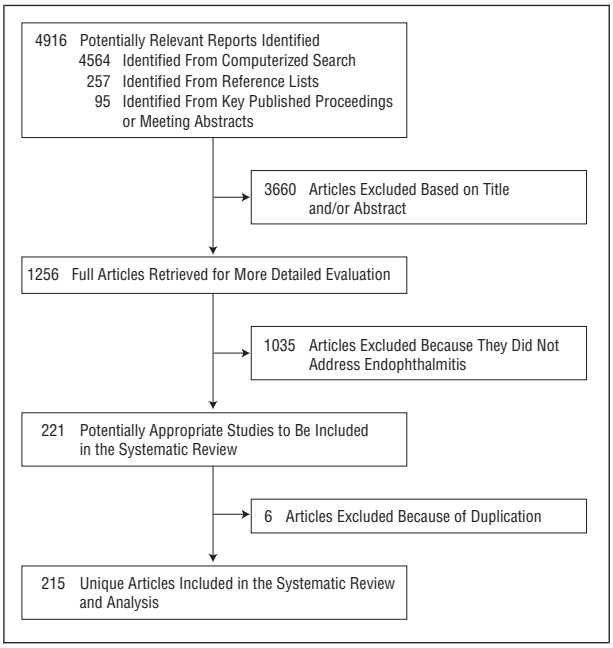


**Figure 1.** Flow of reviewed literature.

## RESULTS

### YIELD OF LITERATURE SEARCH

**Figure 1** illustrates the flow of literature reviewed. Our computerized search identified 4564 unique citations, while manual search of references resulted in 257 additional articles. From these, 215 studies fulfilled our eligibility criteria. The 215 studies were published in 2 text-

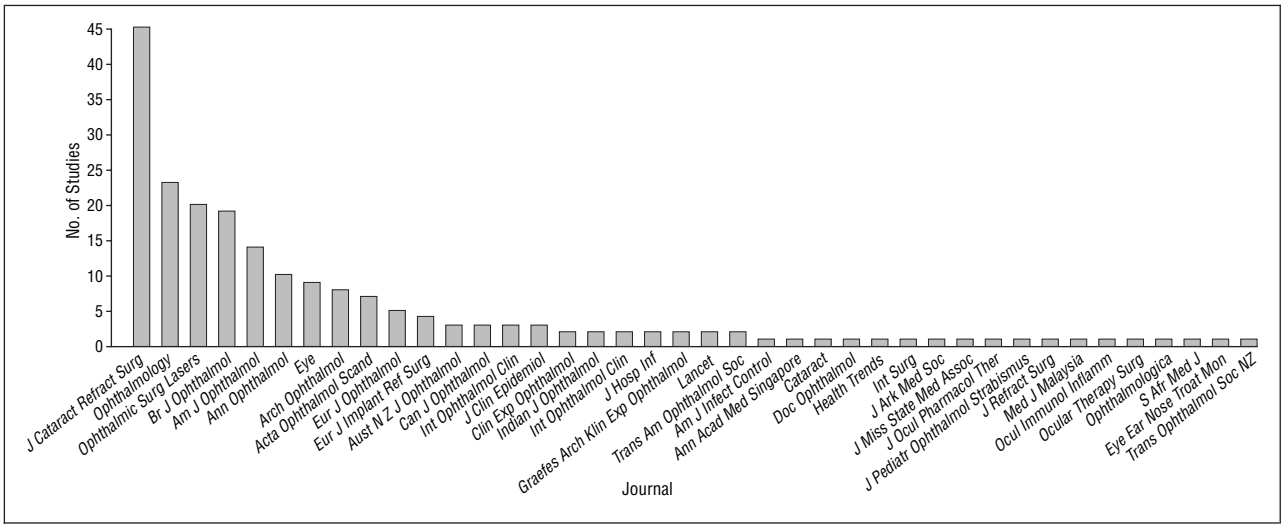


**Figure 2.** Studies from each journal.

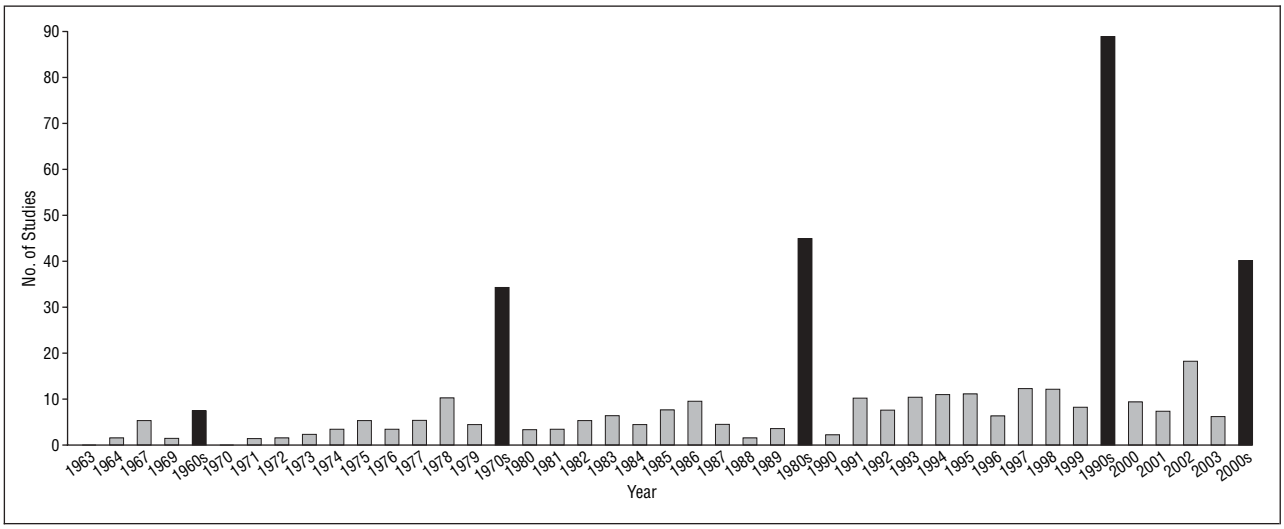


**Figure 3.** Distribution of the 215 studies according to each year.

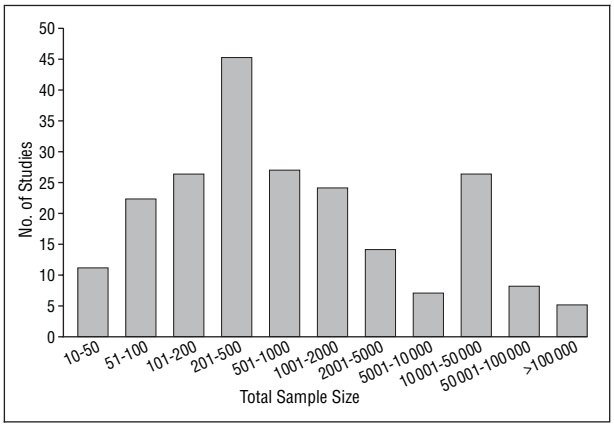


**Figure 4.** Frequency distribution of the total sample sizes (number of eyes studied) in the 215 studies.

books, 3 published proceedings (2 ARVO, 1 AAO, 2 *Eye World*), and 40 journals (**Figure 2**) and were categorized by the year of publication (**Figure 3**). In general, we observed increasing numbers of published reports over time. The highest number of published studies in any single year was 18 in 2002, likely reflecting the fact that there are more investigators and journals in more recent times. The highest number of cataract surgeries was reported in 1997 (n=777 367). There were no studies published in the years 1965, 1966, 1968, and 1970.

## STUDY CHARACTERISTICS

The United States had the highest number of studies conducted (95), followed by the United Kingdom (29), India (9), Canada (7), Germany (7), African countries (6), Australia (6), Denmark (6), Spain (6), Sweden (6), Turkey (5), Belgium (4), Austria (3), Nepal (3), Pakistan (3), Finland (2), France (2), Japan (2), Netherlands (2), and New Zealand (2). Greece, Ireland, Israel, Malaysia, Norway, Russia, Saudi Arabia, Singapore, Switzerland, and Vietnam each contributed 1 study to this analysis.

**Figure 4** shows the distribution of sample sizes. The median number of cataract surgeries included in the 215

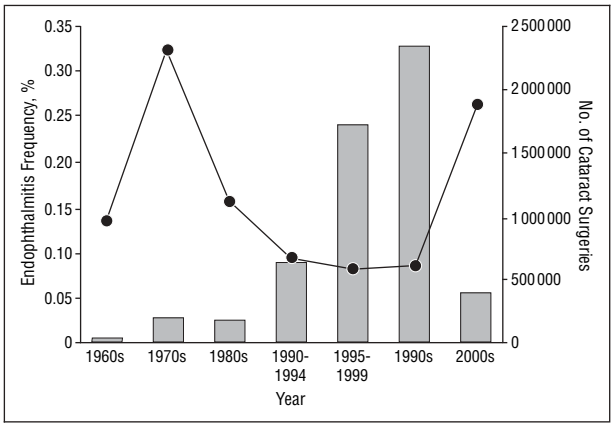


**Figure 5.** Pooled estimates of endophthalmitis frequency following cataract surgery according to year. The line indicates number of cataract surgeries; the bars indicate endophthalmitis frequency.

studies of our analysis was 567 (range, 18-735 096). The minimum (or mean if minimum was not indicated) duration of follow-up on postsurgical patients in the studies ranged from 4 days to 5 years.

## OVERALL RESULTS

The overall pooled estimate (1964-2003) of the incidence of acute endophthalmitis after cataract surgery was 0.128% based on 3 140 650 cataract extractions. The rate for each decade was as follows: 0.138% in the 1960s, 0.327% in the 1970s, 0.158% in the 1980s, 0.087% in the 1990s, and 0.265% in 2000 and beyond (**Figure 5**). The rate of endophthalmitis from 1963 to 1999 was 0.109%, while the rate from 2000 to 2003 was 0.265%, representing an almost 2.5-fold increase in its incidence (relative risk, 2.44 [95% confidence interval, 2.27-2.61]).

## ENDOPHTHALMITIS FREQUENCY—TRENDS OVER TIME

To assess potential changes in the incidence of acute endophthalmitis, we chose to compare the rates from before 1992 with those from 1992 forward, the year in which the self-sealing clear corneal incision was introduced.[7] A weighted analysis of the mean endophthalmitis rate for each year or article was used, both producing the same results (**Figure 6**A and B). The slope obtained from the regression analysis for the years 1964 to 1991 was –0.0103, suggesting a gradual reduction in the incidence of postoperative endophthalmitis over time. The slope from 1992 to 2003 was 0.0257, indicating a gradual increase in the rate of endophthalmitis over this period. The difference between these slopes was significant (**Figure 7**).

## ENDOPHTHALMITIS FREQUENCY—EFFECT OF INCISION TYPE

The rates for this analysis were obtained from analyzing only those studies that specifically indicated the type of cataract incision performed from 1992 to 2003. This information was specified in 57 of the 117 (approximately 49%) published studies or 421 940 of the 2 232 026 (approximately 19%) cataract procedures reported during this period. The rate of acute endophthalmitis was significantly higher following clear corneal cataract extraction compared with both scleral and limbal incisions (**Table 2**). There was no significant difference between the rates for scleral and limbal incisions.

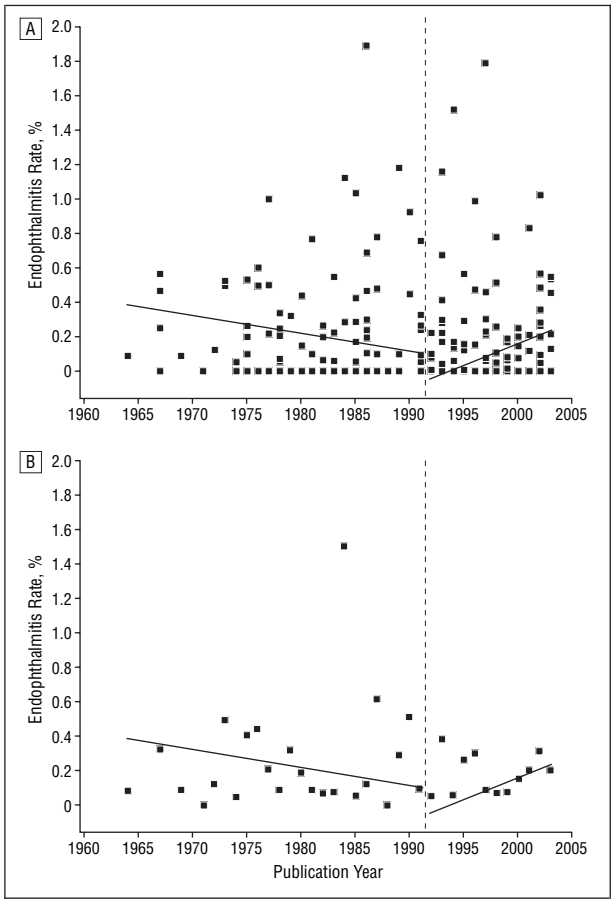


**Figure 6.** Trends of endophthalmitis rate. Slope is best-fit line from weighted regression analysis (see "Methods" section). A, Based on each study/publication (weighted per surgery), 1963-1991 slope, –0.0103; 1992-2003 slope, 0.0257. B, Based on each year (weighted per surgery), 1963-1991 slope, –0.0103; 1992-2003 slope, 0.0257.

## COMMENT

The findings of this literature synthesis demonstrate an apparent increase in the incidence of postoperative endophthalmitis following cataract surgery during the last decade. The increased occurrence of endophthalmitis after cataract extraction has been temporally associated with the use of self-sealing clear corneal incisions, and we detected a statistically significant increase in risk associated with clear corneal incisions when compared with other incision types from 1992 to 2003. Our analysis for trends of endophthalmitis (Figure 6) over time revealed that the postsurgical endophthalmitis after cataract surgery was on the decline from the early 1960s until 1992 when sutureless clear corneal incision was introduced, at which time a statistically significant reversal of this trend was demonstrable. Comparing the overall rates of endophthalmitis following cataract extraction from before and after 2000 also revealed a

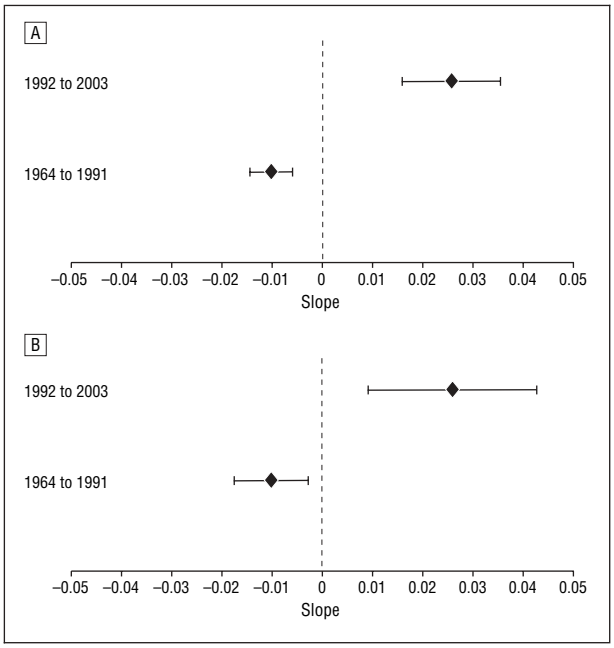


**Figure 7.** Ninety-five percent confidence intervals of trends analysis. Slopes within each period with error bars indicating 95% confidence intervals. A, Based on each study/publication. B, Based on each year.

significant increase with the more recent reports. We chose 2000 for this comparison for 2 reasons: (1) According to an American Society of Cataract and Refractive Surgery survey,[28] this was the year when clear corneal incision was used by about half of US cataract surgeons. (2) There is a natural delay between the introduction of a new technique and the inherent gap between when a study is conducted until the publication of its results; therefore, an article published in 2000 would generally encompass a study conducted several years prior (eg, 1995-1998).

## THEORIES/MECHANISMS

Theories to account for more frequent postcataract endophthalmitis with sutureless clear corneal incisions are centered on the stability of the surgical wound because its integrity is believed to be a critical factor. In a study by Maxwell et al,[29] up to 80% of postsurgical cases of endophthalmitis were associated with wound defects, such as wound gape and/or malapposition and leakage. Montan et al[30] found wound abnormality to be a statistically significant risk factor in their review of more than 22 000 cataract surgeries. However, problems with clear corneal cataract wounds may not be readily apparent intraoperatively. Furthermore, wound integrity may vary as a function of intraocular pressure (IOP). Intraocular pressure has been known to vary in the postoperative period. In a report by Shingleton et al,[31] 21% of eyes had IOPs of 5 mm Hg or less following clear corneal phacoemulsification. Squeezing of the lids or even normal unconscious blinking have been shown to cause wide variations of IOP in both human and animal subjects.[32-34] Doane[35] demonstrated that dramatic posterior movement of the globe occurs in relation to lid motion. He attributed this to the pressure of the lid on the globe, which resulted in a posterior movement of the globe, ranging between 0.7 to 1.6 mm.[35] These pressure recordings

**Table 2. Relative Risks of Endophthalmitis Rate Among Cataract Incision Type***

| Incision Type | | |
|---|---|---|
| Method 1 (Endo Rate, %) | Method 2 (Endo Rate, %) | Relative Risk (95% Confidence Interval) |
| Clear corneal (0.19) | Scleral (0.07) | 2.55 (1.75-3.71) |
| Clear corneal (0.19) | Limbal (0.06) | 3.06 (2.48-3.76) |
| Scleral (0.07) | Limbal (0.06) | 1.20 (0.82-1.75) |

Abbreviations: endo, endophthalmitis; limbal, limbal or sclerocorneal or corneoscleral.
*Based on the published studies reporting their cataract surgical technique (ie, incision type). This information was specified in approximately 49% of published studies or approximately 19% of the cataract surgeries reported from 1992 to 2003.

thus confirm the clinically apparent fact that large fluctuations in IOP can occur during the postoperative period and blinking or squeezing of the lids can exert tremendous forces on the globe, which may be important following intraocular surgery.

Recent imaging studies of clear corneal incisions using optical coherence tomography may explain the underlying cause of the increased risk of endophthalmitis associated with self-sealing clear corneal incisions.[36,37] Optical coherence tomography reveals that transient fluctuations in IOP of a magnitude not uncommon in the postoperative period result in gaping of the unhealed wound margins. Furthermore, histologic examination of the clear corneal incisions showed that india ink particles could migrate from the ocular surface into the stroma through the wound.[36]

In addition, the lack of conjunctiva covering the clear corneal incisions and a possible increased technical difficulty in constructing a stable, self-sealing incision in the cornea compared with the sclera may contribute to an elevated risk of endophthalmitis with clear corneal incisions relative to scleral tunnel incisions.[22,24] In the light of these findings, although not proven in any controlled study, the use of a suture to seal the wound might be justified if there is any question about the self-sealing properties of a clear corneal cataract incision.

## STUDY LIMITATIONS

There are potential limitations to the present literature synthesis, some inherent to systematic reviews in general and some particular to our review. First, the studies included in this analysis may be subject to some methodological variation. Definitions of endophthalmitis may have varied; in addition, inherent difficulties in the diagnosis of this complication are apparent secondary to the uncommon manifestation of the "classic" form of postsurgical endophthalmitis. Miscoding of endophthalmitis itself could be a serious concern for data quality of any epidemiological analysis, as demonstrated in 1 recent study where Li et al[38] reported that up to 24% of postsurgical endophthalmitis cases were not coded as endophthalmitis. Second, the majority of studies were retrospective and the accumulation of study populations frequently took several years so the quality of data obtained within a single study may be uneven. Third,

sample sizes varied across studies and years. However, using the statistical methods described earlier (eg, regression analysis and the weighting method), we minimized the potential drawbacks for our trends analysis.

The overwhelming number of publications showing retrospective data, and the limited number of prospective, case-controlled studies with appropriate randomization methods, negatively affected the proportion of high-quality articles reviewed. To evaluate a trend in endophthalmitis rates over time, we decided to be more flexible in the article-inclusion criteria in spite of sacrificing the strength of the evidence. This was especially true with older citations, which frequently lacked more rigorous methods. These studies were included so that information from these years would not be missing.

Systematic reviews have an intrinsic limitation: the quality of the outcome depends on the quality of the inputs. Therefore, their findings must be interpreted with caution. The issue of publication bias is important both from the scientific perspective (complete dissemination of knowledge) and from the perspective of those who combine results from a number of similar studies (literature synthesis). Positive-outcome bias, also termed publication bias, is a widely recognized phenomenon and refers to the higher likelihood of positive results to be published than studies with negative results.[39-43] One reason for this bias is that authors and investigators are less likely to submit manuscripts reporting negative outcomes to journals.[39-41] For example, studies with particularly high frequencies of occurrence of complications may not be reported.[39] Although less clear, there have also been reports that journal reviewers and editors are more likely to publish positive results relative to negative ones (the file drawer problem).[41-43] Evidence also exists that studies with positive results are published on average several years sooner than studies with negative results.[41] Therefore, potentially additional unpublished evidence regarding rates of endophthalmitis following cataract surgery and clear corneal incisions during the past decade may be unavailable for analysis.

Nonetheless, even with these limitations in mind, we believe that our analysis provides clear evidence to support the notion that postsurgical acute endophthalmitis following cataract extraction has been increasing during the past decade. Furthermore, there is evidence that this trend is associated with the increased prevalence of the self-sealing clear corneal incision technique. By synthesizing the results of multiple studies, the present review has allowed us to address the rate of a relatively rare complication using existing data with increased statistical power.

## CONCLUSIONS AND FUTURE DIRECTIONS

Age-related cataract is one of the leading causes of visual impairment worldwide and cataract extraction is one of the most frequently performed surgical procedures in the world.[44] Increasing age is associated with an increasing prevalence of cataract.[44-49] With the projected doubling of the number of people older than 65 years by 2020,[44,50] the volume of cataract surgery will increase dramatically both in developed and developing countries. Etzioni et al[51] recently reported a projected 47% increase in the demand for ophthalmologists by 2020, owing primarily to cataract surgeries. With such a high volume of cataract surgery worldwide, any increase in the incidence of endophthalmitis can lead to large absolute numbers of surgical failures. Considering a current (2002) volume of more than 2.5 and 10 million cataract surgeries performed annually in the United States[4] and worldwide,[52] the recent increase in endophthalmitis occurrence (0.265% from 2000 and later vs 0.109% in 1963-1999) can equate to approximately 4000 and 16 000 additional cases of endophthalmitis annually in the United States and worldwide, respectively. Since postoperative endophthalmitis continues to be a devastating, sight-threatening complication of cataract surgery, the global implications for the need for an effective prevention strategy are obvious. This encompasses the adoption of a surgical technique with the least risk for developing endophthalmitis.

Some other factors inherent to the cataract surgery may also play a role in the increase of endophthalmitis rates in the past few years. These might include changes in outpatient vs inpatient surgery, a move from hospital operating rooms to a freestanding ambulatory setting, changes in anesthesia from injected to topical, changes in intraocular lens design or materials (eg, foldable vs nonfoldable, 1 piece vs 3 piece, rigid acrylic vs silicone vs foldable acrylic), and changes in antibiotic prophylaxis and sensitivity of organisms. In an attempt to control for these variables and minimize bias, we contrasted results of cataract surgery to those obtained after penetrating keratoplasty, because both surgeries have evolved in parallel over time.[53] However, some of the former particular variables, other than incision type, may still be linked to the higher incidence of endophthalmitis and should be more thoroughly studied in large prospective trials in the future.

The results of the present synthesis of the literature indicating an increased risk of endophthalmitis associated with self-sealing clear corneal cataract incisions will need to be confirmed in further studies. Bias inevitably results from the selection of cases included in studies submitted or accepted for publication and hence can potentially affect a review. One approach to elimination of such bias is to attempt the gathering of nonpublished data from the institutions at which the participating studies were conducted. This is, however, logistically impractical and leaves uncorrected errors owing to methodological anomalies. Dickersin and Rennie,[54] among others before them, have proposed the comprehensive registration of all initiated clinical trials. Yet an alternative solution is to test the hypothesis generated by the review in a large-scale prospective trial with defined inclusion criteria, such as surgical technique. Large multicenter, prospective, controlled trials, such as the recent European Society of Cataract and Refractive Surgery–instigated, 16-center European study,[55] are necessary to address the current observation of increased rate of endophthalmitis after cataract surgery and other key issues in postsurgical endophthalmitis. The Internet can provide a fast and easy avenue for the acquisition of scientific data from such a large multicenter trial.[56] The Magdeburg University Eye Hospital (Magdeburg, Germany) recently initiated a national prospective study on "Intraoperative Anti-infective Prophylaxis for Cataract Surgery" using such a resource.[56] This new way of paperless data recording can help realize such a multicenter clinical trial in the United States and worldwide.

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