# Incidence of Endophthalmitis after Corneal Transplant or Cataract Surgery in a Medicare Population

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***Objective:*** To estimate the incidence of infectious endophthalmitis after corneal transplant or cataract surgery, to evaluate the trend of endophthalmitis during the study period, and to assess demographic risk factors for endophthalmitis after surgeries.

***Design:*** A retrospective population-based cohort study.

***Participants and Controls:*** Study cohorts were derived from the Medicare claims databases, 2006 to 2011. Patients were continuously enrolled in Medicare Part A, Part B, and Part D. Patients undergoing corneal transplant or cataract surgery were identified using International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) procedure codes.

***Methods:*** Endophthalmitis was defined in 3 different ways: (1) using ICD-9-CM codes (sensitive definition), (2) combining ICD-9-CM codes with Current Procedural Terminology, Fourth Edition (CPT-4) codes (specific definition), or (3) combining ICD-9-CM codes with antifungal prescriptions for endophthalmitis caused by fungal infection. Demographic risk factors for endophthalmitis were examined using multivariate Cox models.

***Main Outcome Measures:*** Incidence rates of endophthalmitis were calculated and compared for each definition of endophthalmitis at 6-week and 6-month intervals after corneal transplant or cataract surgery.

***Results:*** The infectious endophthalmitis incidence rates ranged from 0.11% to 1.05% in the corneal transplant cohort, 0.06% to 0.20% in the cataract surgery cohort, and 0.16% to 0.68% in the concurrent surgery cohort, depending on the definition and time interval after surgery. Compared with the cataract surgery cohort, the corneal transplant cohort had a higher adjusted hazard ratio (HR) of endophthalmitis within the 6-week postoperative interval (HR, 2.744; 95% confidence interval [CI], 1.544−4.880 in the sensitive definition and HR, 2.792; 95% CI, 1.146−6.802 in the specific definition) and within the 6-month postoperative interval (HR, 4.607; 95% CI, 3.144−6.752 for the sensitive definition and HR, 4.385; 95% CI, 2.245−8.566 for the specific definition).

***Conclusions:*** It is possible to monitor the trend of infectious endophthalmitis after corneal transplant or cataract surgery through examining Medicare claims databases as long as a consistent definition of endophthalmitis is used. The annual incidence of endophthalmitis was stable over time during the study period for both corneal transplant and cataract surgery procedures; however, there was a wider year-to-year variation for the corneal transplant cohort. *Ophthalmology 2014;121:290-298 © 2014 by the American Academy of Ophthalmology.*

Endophthalmitis refers to inflammation in the vitreous cavity and anterior chamber inside the eye. Depending on the route, infectious endophthalmitis can be broadly classified as endogenous endophthalmitis usually resulting from hematogenous infection of the eye or exogenous endophthalmitis with organisms introduced to the eye after ocular trauma or surgery. Endophthalmitis may result in extensive corneal melting, perforation, decreased vision, or permanent loss of vision, and patients who subsequently develop a blind and painful eye may require enucleation.[1,2] Although endophthalmitis secondary to fungal infection is rare, patients with fungal endophthalmitis often have a particularly ominous prognosis because the management of fungal endophthalmitis remains a formidable challenge despite recent advances in antifungal therapy. Furthermore, case reports and a passive surveillance study from the Eye Bank Association of America, as well as published case reports, have suggested a possible increased trend of fungal endophthalmitis after corneal transplant.[3−6]

The reported incidence of infectious endophthalmitis in published studies, which are generally derived from individual institutions or groups with limited sample sizes, ranges from 0.142% to 0.453% after corneal transplant and from 0.087% to 0.327% after cataract surgery with or without intraocular lens implant.[7,8] In similar studies, the reported incidence of endophthalmitis secondary to fungal



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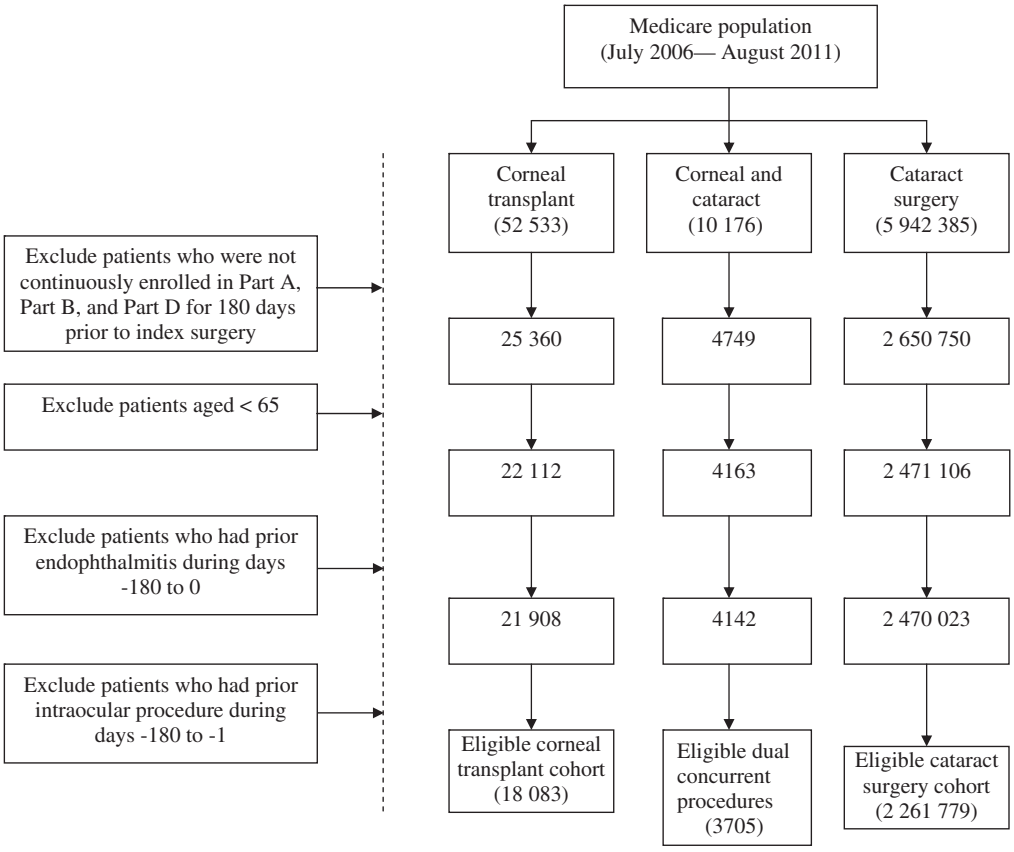


**Figure 1.** Flow chart of cohort selection.

infection is approximately 0.10% to 0.16% after corneal transplant.[4,9,10] In each of these studies, fewer than 5 cases of fungal endophthalmitis were recorded among 1000 to 3000 corneal transplant procedures. Given these small numbers, the precision of the reported incidence of fungal endophthalmitis from these studies is questionable. To our knowledge, no publication has reported the incidence of fungal endophthalmitis after cataract surgery. The use of administrative claims data for the analysis of endophthalmitis after cataract extraction was first reported in 1991 by Javitt et al[11] at Johns Hopkins University and the Medicare Health Standards Quality Bureau. At the time, only Medicare Part A data were available for analysis. Several years later, similar data were used to report the rate of endophthalmitis after corneal transplant in 1993.[12]

In the current study, we used the Medicare claims database including Part A, Part B, and Part D to estimate the rates of endophthalmitis after corneal transplant or cataract surgery and to evaluate trends in the rates of endophthalmitis over a 5-year period. We also assessed demographic risk factors for endophthalmitis after these surgeries.

## Methods

### Data Source

Study cohorts were derived from the Medicare claims databases from July 2006 to August 2011. Medicare is a federal health insurance program in the United States. It provides coverage for approximately 50 million Americans, including virtually all people aged 65 years or more and some younger adults with permanent disabilities or end-stage renal disease.[13] Medicare is composed of 4 parts: Parts A, B, C, and D. Part A covers inpatient hospital care and some long-term care. Part B helps pay for physician services, outpatient care, tests, and durable medical equipment. Part C, also called the Medicare Advantage plan, allows beneficiaries to enroll in private insurance plans. Medicare Advantage plans cover all Part A and Part B services and usually include Part D benefits in the same plan. Part D provides prescription drug benefits.

The computerized Medicare databases are billing claims for Parts A, B, and D and are linked with the Medicare Enrollment Database. These databases provide information about diagnoses, procedures, prescription drugs, and medical equipment use, as well as demographic and enrollment characteristics for each beneficiary. Part A claims contain up to 25 International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes, Current Procedural Terminology, Fourth Edition (CPT-4) codes, and Healthcare Common Procedure Coding System (HCPCS) codes for each inpatient stay. Clinical procedures provided by noninstitutional providers are coded with CPT-4/HCPCS codes in Part B claims. Claims submitted by ambulatory care centers in institutional outpatient settings would be covered under Part A, in which both CPT-4/HCPCS and ICD-9-CM procedure codes are recorded in the databases. Prescription drugs in Part D can be identified through National Drug Codes. Patients in Part C were not included in the study because Part C claims are submitted to private insurers and not maintained in the Medicare databases.

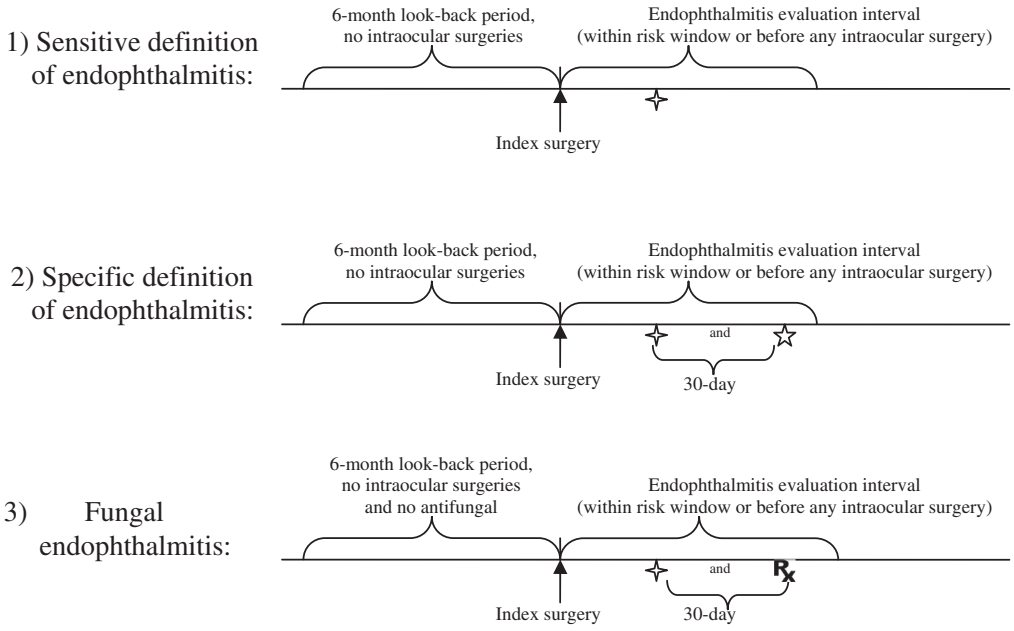


**Figure 2.** Diagram of case definitions. Risk window is 6 weeks or 6 months. CPT-4 = Current Procedural Terminology, Fourth Edition; HCPCS = Healthcare Common Procedure Coding System; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

## Study Cohort

In this study, we identified Medicare patients who underwent corneal transplant or cataract surgery in a hospital or outpatient setting (e.g., ambulatory surgical center) using ICD-9-CM procedure codes and CPT-4/HCPCS codes (Tables 1 and 2, available at http://aaojournal.org). Three cohorts were established, including a corneal transplant cohort, a cataract surgery cohort, and a concurrent surgery cohort. We restricted the Medicare population to persons continuously enrolled in Part A, Part B, and Part D because claims from these sources provide the data needed for research purposes. Patients younger than 65 years were excluded from the study cohort because their Medicare entitlement is generally based on various permanent disabilities or end-stage renal disease, and they are therefore not representative of a more general "Medicare" population. To minimize bias, we excluded patients with diagnoses of endophthalmitis or with other eye surgeries within 180 days before or on the day of the index surgery. All patients were followed in the claims database for up to 180 days after their index surgeries or until another intraocular surgery in the claims database. Figure 1 illustrates the cohort selection process.

## Study Outcome

Endophthalmitis was evaluated using 3 definitions (Fig 2): (1) the sensitive definition using ICD-9-CM codes only, which has high sensitivity to identify outcome cases; (2) the specific definition using ICD-9-CM codes with additional CPT-4/HCPC procedure codes for vitrectomy or intraocular injection of medication, which has high specificity to identify outcome cases; and (3) the fungal endophthalmitis definition using ICD-9-CM diagnosis codes for endophthalmitis and a claim for antifungal medication, which identifies possible fungal endophthalmitis. The ICD-9-CM diagnosis codes for endophthalmitis are listed in Table 3 (available at http://aaojournal.org). For the specific definition, injection of medication in the anterior chamber (CPT-4 66030), intravitreal injection of a pharmacologic agent (CPT-4 67005/67010), anterior vitrectomy (CPT-4 67028), or pars plana vitrectomy (CPT-4 67036) was identified within 30 days after endophthalmitis diagnosis.

Because there is no diagnosis code specific for fungal endophthalmitis secondary to fungal infection, we used prescriptions for antifungal medication as a surrogate identifier for fungal endophthalmitis among patients with a diagnosis of endophthalmitis. The antifungal medications are listed in Table 4 (available at http://aaojournal.org). Patients were presumed to have experienced fungal endophthalmitis if all of the following 3 conditions were met: (1) there were no antifungal prescriptions or endophthalmitis diagnoses within 180 days before reference surgeries; (2) there was at least 1 antifungal prescription within the evaluation interval after index surgeries; and (3) there was at least 1 endophthalmitis diagnosis code within 30 days before the first antifungal prescription.

## Statistical Analysis

The incidence of endophthalmitis in each definition was calculated on the basis of the number of endophthalmitis cases that occurred during the postoperative period. Two different

Table 5. Baseline Characteristics in Corneal Transplant Cohort, Cataract Surgery Cohort, and Concurrent Corneal Transplant and Cataract Surgery Cohort

| Demographic Variables among Eligible Population | Corneal Transplant (n = 18 083) | Cataract Surgery n = (2 261 779) | Concurrent Corneal Transplant and Cataract Surgery (n = 3705) |
|---|---|---|---|
| Age, yrs | | | |
| 65–69 | 2430 (13.4%) | 446 152 (19.7%) | 1032 (27.9%) |
| 70–74 | 3001 (16.6%) | 589 821 (26.1%) | 1040 (28.1%) |
| 75–79 | 3963 (21.9%) | 568 480 (25.1%) | 813 (21.9%) |
| 80–84 | 4350 (24.1%) | 413 669 (18.3%) | 530 (14.3%) |
| 85+ | 4339 (24.0%) | 243 657 (10.8%) | 290 (7.8%) |
| Sex | | | |
| Male | 5553 (30.7%) | 768 392 (34.0%) | 1063 (28.7%) |
| Female | 12 530 (69.3%) | 1 493 387 (66.0%) | 2642 (71.3%) |
| Ethnicity | | | |
| White | 15 187 (84.0%) | 1 950 349 (86.2%) | 3287 (88.7%) |
| Black | 1372 (7.6%) | 155 275 (6.9%) | 242 (6.5%) |
| Hispanic | 709 (3.9%) | 54 843 (2.4%) | 65 (1.8%) |
| Non-Hispanic other | 815 (4.5%) | 101 312 (4.5%) | 111 (3.0%) |
| Regions | | | |
| Midwest | 4469 (24.7%) | 578 574 (25.6%) | 1055 (28.5%) |
| Northeast | 3429 (19.0%) | 427 647 (18.9%) | 626 (16.9%) |
| South | 7489 (41.4%) | 910 118 (40.2%) | 1526 (41.2%) |
| West | 2656 (14.7%) | 338 753 (15.0%) | 490 (13.2%) |
| Other/unknown | 40 (0.2%) | 6687 (0.3%) | 8 (0.2%) |
| LIS status | | | |
| Not receiving LIS | 12 412 (68.6%) | 1 591 038 (70.3%) | 2849 (76.9%) |
| With 15% copay | 340 (1.9%) | 36 542 (1.6%) | 53 (1.4%) |
| With high copay | 1700 (9.4%) | 214 581 (9.5%) | 282 (7.6%) |
| With low copay | 3184 (17.6%) | 356 766 (15.8%) | 454 (12.3%) |
| With zero copay | 447 (2.5%) | 62 852 (2.8%) | 67 (1.8%) |

LIS = low-income subsidy.
Data are no. (%).

postoperative risk windows were assessed corresponding to 6 weeks or 6 months after index surgeries. There was censoring for any other intraocular procedure in that endophthalmitis after another intraocular procedure within the postoperative period after the index procedures was not considered. Endophthalmitis incidence for each definition was calculated by year and compared across the study period.

Multivariate Cox proportional hazard models were fitted with the first 2 endophthalmitis definitions described earlier to estimate potential risk factors for postoperative endophthalmitis. The models controlled for age, sex, race, socioeconomic status, geographic location, immunosuppressant use, and comorbidities. Socioeconomic status was assessed in the Medicare database through the low-income subsidy indicator, a measure of the level of subsidy that the Medicare beneficiary received for Part D coverage. The occurrence date of an event was defined as the date of diagnosis for that event. Patients were followed from index surgeries to the event date or the end of the study intervals. Patients were censored from observation at the time of subsequent corneal transplant or cataract surgery or other intraocular surgery to prevent incorrect attribution of adverse outcomes to the index surgery rather than to the second procedure. This was especially pertinent because the Medicare data do not indicate which eye underwent the designated diagnosis or treatment.

This study was performed as part of the SafeRx Project, a joint initiative of the Centers for Medicare & Medicaid Services and the US Food and Drug Administration (FDA). Our study was deemed exempt from review by the FDA Research in Human Subjects Committee. All statistical analyses were completed using Stata software version 9.2 (StataCorp LP, College Station, TX). We considered $P$ values less than 0.05 to be statistically significant.

## Results

Table 5 shows the demographic characteristics of the study cohorts. The total study population consisted of 18 083 patients who underwent corneal transplant, 2 261 779 patients who underwent cataract surgery, and 3705 patients who underwent concurrent corneal transplant and cataract surgery on the same day from July 1, 2006, to August 31, 2011. The concurrent surgery cohort represents only 0.2% of total study samples. The corneal transplant cohort (average age, 78.8 years) was, on average, 3 years older than the cataract surgery cohort (average age, 75.8 years). The concurrent cohort was the youngest group (average age, 74.4 years). Female patients accounted for a slightly higher proportion in the corneal transplant cohort (69.3%) than in the cataract surgery cohort (66.0%) and represented 71.3% of patients in the concurrent surgery cohort. The cataract study cohort contained a slightly higher percentage of white patients than the corneal transplant cohort (86.2% vs. 84.0%) but a slightly lower percentage of Hispanic patients (3.9% vs. 2.4%). Other demographic characteristics, such as geographic region and low-income subsidies, were evenly balanced in the corneal transplant and cataract surgery cohorts. The concurrent surgery cohort consisted of more patients who were white (88.7%), from the US Midwest region (28.5%), and not receiving a low-income subsidy (76.9%).

Table 6. Incidence of Postoperative Endophthalmitis after Corneal Transplant and Cataract Surgery, and Concurrent Corneal Transplant and Cataract Surgery Cohort

| Endophthalmitis | Postoperative Interval | Corneal Transplant (n = 18 083) | | Cataract Surgery (n = 2 261 779) | | Concurrent Corneal Transplant and Cataract Surgery (n = 3705) | |
|---|---|---|---|---|---|---|---|
| | | *Cases* | *Incidence* | *Cases* | *Incidence* | *Cases* | *Incidence* |
| Sensitive definition (ICD-9-CM codes only) | 6 wks | 76 | 0.420% | 2874 | 0.127% | 13 | 0.351% |
| | 6 mos | 190 | 1.051% | 4416 | 0.195% | 25 | 0.675% |
| Specific definition (ICD-9-CM codes and CPT/HCPCS codes) | 6 wks | 20 | 0.111% | 1417 | 0.063% | 6 | 0.162% |
| | 6 mos | 63 | 0.348% | 1991 | 0.088% | 10 | 0.270% |
| Fungal endophthalmitis (ICD-9-CM codes and antifungal medication claim) | 6 wks | 6 | 0.033% | 52 | 0.002% | 2 | 0.054% |
| | 6 mos | 12 | 0.066% | 121 | 0.005% | 3 | 0.081% |

CPT-4 = Current Procedural Terminology, Fourth Edition; HCPCS = Healthcare Common Procedure Coding System; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification.

The corneal transplant cohort exhibited higher endophthalmitis rates than the cataract surgery cohort in all 3 definitions of endophthalmitis (Table 6). With the sensitive endophthalmitis definition, the 6-week endophthalmitis rate was more than 3 times higher in the corneal transplant cohort (0.420%) than in the cataract surgery cohort (0.127%). The 6-month endophthalmitis rate was 5 times higher in the corneal transplant cohort (1.051%) than in the cataract surgery cohort (0.195%). With the specific definition, the corneal transplant cohort (0.111%) showed an endophthalmitis rate that was twice as high as in the cataract surgery cohort (0.063%) within 6 weeks after the index surgery and approximately 4 times higher within 6 months (0.348% in the corneal transplant cohort and 0.088% in the cataract surgery cohort). The fungal endophthalmitis definition also showed that the corneal transplant cohort had a higher infection rate than the cataract surgery cohort. The timing of the diagnosis of fungal endophthalmitis ranged from a few days to 6 months after the index surgery. The incidence rates of presumed fungal endophthalmitis were 0.033% and 0.002% in the 6-week interval and 0.066% and 0.005% in the 6-month interval in the corneal transplant and cataract surgery cohorts, respectively. The incidences of endophthalmitis in the concurrent surgery cohort were lower than in the corneal transplant cohort but higher than in the cataract surgery cohort. Estimates for the concurrent cohort should be interpreted with caution in that no more than 25 cases were identified with the sensitive endophthalmitis definition and fewer than 4 cases for fungal endophthalmitis.

One of the study objectives was to evaluate the trend of endophthalmitis after index surgeries for the past 5 years. Figure 3 shows there was no continuously increasing or decreasing trend in the endophthalmitis rates for the corneal transplant cohort and cataract surgery cohort, although the endophthalmitis rates in the corneal transplant cohort were higher for year 2010. Because of the small number of endophthalmitis cases identified, trends for the 5-year period were not plotted for the concurrent surgery cohort.

The Cox regression models (Table 7) consistently showed that age, male sex, low socioeconomic status, and immunosuppressant use were statistically significant risk factors for endophthalmitis after the index surgeries. These risk factors showed similar effect size across all definitions of endophthalmitis (Table 7). After controlling for various risk factors, the corneal transplant cohort had a higher risk of developing endophthalmitis than the cataract surgery cohort. The adjusted hazard ratio (HR) for endophthalmitis within 6 weeks was 2.741 (95% confidence interval [CI], 1.542−4.874) in the sensitive definition of endophthalmitis and 2.796 (95% CI, 1.148−6.813) in the specific definition. The HRs for endophthalmitis within the 6-month interval were 4.602 (95% CI, 3.140−6.744) for the sensitive definition and 4.391 (95% CI, 2.248−8.578) for the specific definition. The concurrent cohort showed the highest adjusted risk of developing endophthalmitis within 6 weeks after surgery (HR, 3.395; 95% CI, 1.816−6.145 for sensitive definition and HR, 3.508; 95% CI, 1.456−8.455 for

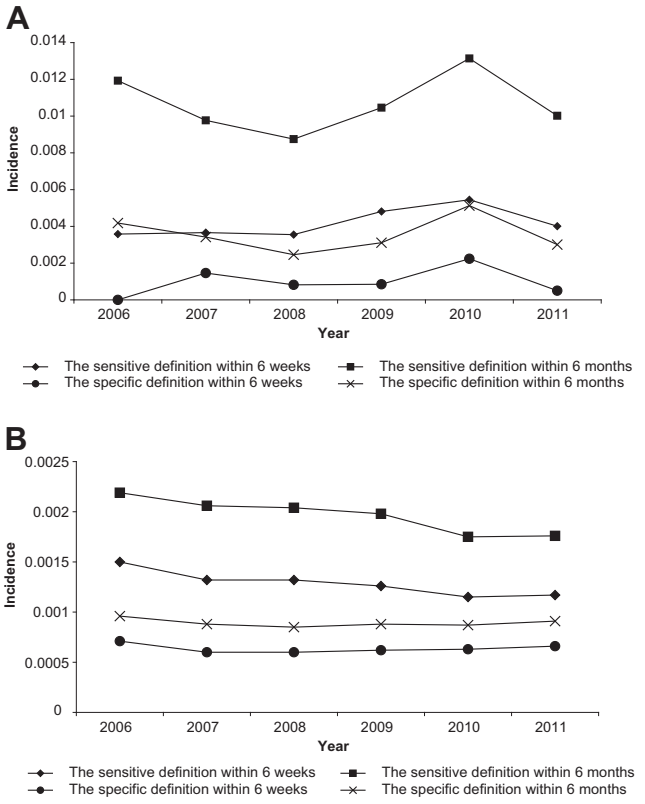


**Figure 3.** Incidence trend of endophthalmitis after (**A**) corneal transplant or (**B**) cataract surgery.

Table 7. Cox Regression Results for Likelihood of Experiencing Endophthalmitis after Index Surgery

| | Six-Week Postoperative Interval | | | | Six-Month Postoperative Interval | | | |
|---|---|---|---|---|---|---|---|---|
| | *Sensitive Definition (ICD-9-CM codes only)* | | *Specific Definition (ICD-9-CM codes + CPT/HCPCS codes)* | | *Sensitive Definition (ICD-9-CM codes only)* | | *Specific Definition (ICD-9-CM codes + CPT/HCPSC codes)* | |
| **Covariates** | *HR* | *95% CI* | *HR* | *95% CI* | *HR* | *95% CI* | *HR* | *95% CI* |
| Procedures | | | | | | | | |
| Cataract surgery | 1.000 | Referent | 1.000 | Referent | 1.000 | Referent | 1.000 | Referent |
| Corneal transplant | 2.744‡ | (1.544–4.880) | 2.792† | (1.146–6.802) | 4.607‡ | (3.144–6.752) | 4.385‡ | (2.245–8.566) |
| Concurrent procedures | 3.395‡ | (1.876–6.145) | 3.508‡ | (1.456–8.455) | 3.617‡ | (2.211–5.918) | 3.125† | (1.297–7.529) |
| Age groups | | | | | | | | |
| ≥75 yrs | 1.000 | Referent | 1.000 | Referent | 1.000 | Referent | 1.000 | Referent |
| 65–74 yrs | 0.787‡ | (0.716–0.864) | 0.720‡ | (0.628–0.826) | 0.809‡ | (0.744–0.881) | 0.732‡ | (0.644–0.831) |
| Sex | | | | | | | | |
| Female | 1.000 | Referent | 1.000 | Referent | 1.000 | Referent | 1.000 | Referent |
| Male | 1.264‡ | (1.153–1.387) | 1.289‡ | (1.128–1.472) | 1.193‡ | (1.098–1.565) | 1.283‡ | (1.133–1.453) |
| LIS status | | | | | | | | |
| Not receiving LIS | 1.000 | Referent | 1.000 | Referent | 1.000 | Referent | 1.000 | Referent |
| With 15% copay | 1.071 | (0.753–1.523) | 1.230 | (0.758–1.995) | 1.183 | (0.873–1.604) | 1.304 | (0.844–2.017) |
| With high copay | 1.196† | (1.028–1.393) | 1.075 | (0.852–1.357) | 1.279‡ | (1.119–1.462) | 1.040 | (0.836–1.295) |
| With low copay | 1.117 | (0.975–1.281) | 1.219† | (1.004–1.481) | 1.213‡ | (1.076–1.366) | 1.198* | (0.999–1.437) |
| With zero copay | 2.078‡ | (1.714–2.519) | 2.153‡ | (1.628–2.846) | 2.189‡ | (1.847–2.594) | 2.050‡ | (1.573–2.671) |
| Immunosuppressant | | | | | | | | |
| No | 1.000 | Referent | 1.000 | Referent | 1.000 | Referent | 1.000 | Referent |
| Yes | 1.346‡ | (1.189–1.523) | 1.347‡ | (1.127–1.610) | 1.334‡ | (1.195–1.488) | 1.323‡ | (1.120–1.562) |

CI = confidence interval; CPT-4 = Current Procedural Terminology, Fourth Edition; HCPCS = Healthcare Common Procedure Coding System; HR = hazard ratio; ICD-9-CM = International Classification of Diseases, Ninth Revision, Clinical Modification; LIS = low-income subsidy.

All multivariate regression models include the following control variables: race, obesity, diabetes, region, Charlson comorbidity score, year, and seasonality.

*$P < 0.1$.

†$P < 0.05$.

‡$P < 0.01$.

specific definition) and slightly lower risk within 6 months after the procedure than the corneal transplant cohort (HR, 3.617; 95% CI, 2.211–5.918 for sensitive definition and HR, 3.125; 95% CI, 1.297–7.529 for specific definition).

## Discussion

Human cells or tissue intended for implantation, transplantation, infusion, or transfer into a human recipient are regulated by the US FDA's Center for Biologics Evaluation and Research as human cells, tissues, and cellular- and tissue-based products (HCT/Ps). The FDA has implemented a risk-based approach to the regulation of HCT/Ps. Under the authority of section 361 of the Public Health Service Act, the FDA established regulations for all HCT/Ps to prevent the introduction, transmission, and spread of communicable diseases. These regulations can be found in Title 21 of the Code of Federal Regulations parts 1270 and 1271.[14,15] Among the regulations are the requirements for tissue establishments to screen and test donors and to follow good tissue practices to ensure that the HCT/Ps do not contain communicable disease agents, are not contaminated, and do not become contaminated during handling. Cell and tissue establishments also are required to report to the FDA infectious adverse reactions involving HCT/Ps if, among other things, the adverse reaction necessitates medical or surgical intervention.[16,17] Despite the requirement to report, there are limitations to the conclusions that can be drawn from a system based on passive surveillance.

We explored the possibility of conducting active surveillance using a claims database as a way to complement the adverse event reporting required by regulation. To compare with previously reported endophthalmitis rates, we evaluated the infection rate on the basis of 2 time periods and 3 definitions of endophthalmitis. The time periods were within 6 weeks or 6 months after the index surgery. The 3 definitions were (1) ICD-9-CM codes only for the sensitive definition, (2) ICD-9-CM codes with CPT-4/HCPCS codes for vitrectomy or intraocular injection of medication for the specific definition, and (3) presumed fungal endophthalmitis. The incidence rates of endophthalmitis in the current study were low (~≤1%, depending on the time interval and definition used) and within the range found in previous published reports.[7,8,12,18–20]

The sensitive definition of endophthalmitis that we used was also used in early studies using Medicare data.[12,21] Our study found that the endophthalmitis rate (1.051%) within 6 months after corneal transplant during 2006 to 2011 was slightly higher than the reported rate of 0.77% for 1984 to 1987.[12] In the earlier study, the authors were able to examine only Medicare inpatients records paid by Medicare Part A. In our study, we included both inpatient services and outpatient services paid by Medicare Part A, as well as patient services

paid by Part B. Over the past 30 years, the setting of corneal transplant procedure has significantly shifted from the hospital setting to the noninstitutional setting. For example, it is estimated that 56% of corneal transplants among Medicare patients were performed in a hospital setting from 1984 to 1987 compared with 38% in the current study.[12] Therefore, we speculated that this shift may contribute to the higher observed rate of endophthalmitis in the current study. Additional research is needed to support such a connection. The endophthalmitis rate (0.420%) within 6 weeks is close to an estimate (0.38%) from a systematic review of data from 1972 to 2002.[7] However, this rate is higher than estimates from individual institutions or groups with limited sample sizes that range from 0.08% to 0.18% and are based on cohorts of approximately 2500 patients.[18–20]

It is possible that this sensitive definition of endophthalmitis may identify some false-positive cases of endophthalmitis. To increase the possibility of identifying true endophthalmitis, we also tested a specific definition that added CPT-4 procedure codes for vitrectomy or intraocular injection of medication to the ICD-9-CM codes. The acute endophthalmitis rate was 0.111% within the 6-week interval after corneal transplant, which is in the range of institution reports (0.08%–0.18%).[18–20] The 6-month endophthalmitis rate was 0.348%, approximately one third of the 6-month endophthalmitis rate under the sensitive definition. There is no report of an acute endophthalmitis rate in the previous Medicare study, and no long-term rate has been reported in previous institutional studies.

There is no ICD-9-CM code designation for fungal endophthalmitis. Yet, patients infected with fungal infection often have poor outcomes if the condition is not treated promptly and aggressively. We explored a third definition of endophthalmitis, specific for fungal infection, using ICD-9-CM codes and an antifungal prescription. We found the incidence rate of presumed acute fungal endophthalmitis was 0.033% and 0.066% in the 6-week and 6-month postoperative intervals, respectively. The incidence rate is consistent with, although lower than, the rates of 0.10% to 0.16% reported in published studies.[4,9] All published studies that we identified involved fewer than 3000 patients, and no study reported more than 4 cases of fungal endophthalmitis.[4,9,10] Although the fungal endophthalmitis incidence from our study may be more precise because of the large sample size, our definition has not been validated with medical record review and may lead to over- or under-identification of cases. Adding a fungal endophthalmitis diagnosis code to the ICD coding system could help to facilitate future investigation of this disease and accurately identify it from claims databases.

The incidence of endophthalmitis after cataract surgery found in this study also matches incidences found in earlier reports. The acute endophthalmitis rate is 0.127% in the sensitive definition, which matches the estimate (0.128%) from a systematic review of publications from 1964 to 2003 that included 3 140 650 cataract extractions.[8] However, our estimate is higher than the estimates from institutional reports. The acute endophthalmitis rates in these institutional reports (from 0.034% to 0.054%) are close to our estimate using the specific definition of endophthalmitis (0.063%).[22,23] Our estimates of 6-month endophthalmitis after cataract surgery (0.195% with the sensitive definition and 0.088% with the specific definition) are similar to earlier studies using Medicare data that reported rates of 0.08% to 0.17% in the 1980s and 0.22% for 1994 to 2001.[11,21,24] Our estimated fungal endophthalmitis rate after cataract surgery was extremely low, 0.002% for acute onset within 6 weeks and 0.005% within 6 months. No fungal endophthalmitis rate after cataract surgery has been reported in the past, although case reports are available.[25,26] The fungal endophthalmitis rate in the cataract surgery cohort was >10 times less than in the corneal transplant cohort.

No study has reported the endophthalmitis incidence after concurrent corneal transplant and cataract surgery. Given that the concurrent surgery cohort accounted for less than 0.2% of total study samples, only a small number of cases were identified. The estimates from the concurrent cohort may not be accurate, but the incidence estimates were in line with findings from each surgery alone.

Under the same endophthalmitis definitions, the rates of endophthalmitis were fairly stable over the study period, although there were relatively bigger variations observed in the corneal transplant cohort than in the cataract cohort (Fig 2). These findings demonstrate the possibility of using claims data to monitor trends in the rate of endophthalmitis after ophthalmology surgery as long as a consistent definition of endophthalmitis is used. However, medical record review would be an important step to validate that the administrative codes used in our study accurately captured both exposures and outcomes.

The higher HRs for endophthalmitis after corneal transplant in the Cox models are consistent with the observed incidence rates and the rates in previous published studies.[7,8,22,23] This finding is not surprising given the differences in the 2 surgery procedures, the size of the postoperative wound, and the implantation of donor tissue in corneal transplant that does not undergo sterilization as does the implant lens. The calculated higher HRs within the 6-month interval compared with the 6-week interval after corneal transplant suggest that the risk of endophthalmitis lasts beyond 6 weeks. Patients should be continuously monitored for signs of endophthalmitis during this period. In addition, all multivariate models consistently suggested that male sex, low socioeconomic status, and immunosuppressant use are risk factors for endophthalmitis after ophthalmology surgeries. This suggests that environmental factors or comorbidities may play an important role for developing endophthalmitis after these surgeries.

This analysis using Medicare claims databases provides several advantages. First, compared with passive surveillance, active surveillance can provide more complete information with both numerator and denominator data. Second, results from Medicare data are representative of the older population given the extremely large population of seniors aged 65 years or more who are covered by Medicare. Last, the health care providers for Medicare patients are not limited to teaching hospitals or research institutes. Thus, the incidence obtained from the current

study reflects performance across a variety of clinical care settings.

### Study Limitations

Our analyses were limited by a number of factors. First, we used the ICD-9-CM code 360.xx to identify endophthalmitis. To our knowledge, this code has not been validated among Medicare patients for this purpose. An early study of 1980−1999 Western Australia data validated the code through chart review and suggested that only 50.3% of ICD-9-CM code 360.xx was correctly coded for true endophthalmitis after eye procedures.[27] If a similar coding accuracy applies to the Medicare population in the current study, we may overestimate the endophthalmitis rates based on only the ICD-9-CM diagnosis code. The endophthalmitis rate derived from the combined use of diagnosis code and procedure codes (e.g., intraocular injection or vitrectomy) could provide a more accurate identification of true cases, but this needs to be validated through chart review. Second, only Medicare beneficiaries who were covered with fee-for-service insurance were included in the current study. Conclusions from this study may not be generalized to managed care patients and other insurance groups or patients younger than 65 years. Finally, we used antifungal prescriptions as an identifier for fungal endophthalmitis. When Medicare beneficiaries hit the Medicare Part D coverage gap—informally known as the Medicare donut hole—patients may receive their prescriptions through other resources (e.g., out-of-pocket spending or secondary insurance) or discontinue the use of their prescribed medications. The Medicare databases do not capture this information. Therefore, we may fail to identify some endophthalmitis cases that were, in fact, fungal infections.

In conclusion, endophthalmitis after corneal transplant or cataract surgery was rare, and the incidence rates identified from the Medicare claims data are consistent with early reports from individual institutions. No consistent trend, either increasing or decreasing, in the endophthalmitis rate over the study period was found after corneal transplant or cataract surgery. It is possible to use a claims database to monitor postoperative endophthalmitis rate; however, more work needs to be done to validate the strategies used to identify these conditions and exposures.

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