Disclaimer

The following report(s) provides findings from an FDA-initiated query using Sentinel. While Sentinel queries may be undertaken to assess potential medical product safety risks, they may also be initiated for various other reasons. Some examples include determining a rate or count of an identified health outcome of interest, examining medical product use, exploring the feasibility of future, more detailed analyses within Sentinel, and seeking to better understand Sentinel capabilities.

Data obtained through Sentinel are intended to complement other types of evidence such as preclinical studies, clinical trials, postmarket studies, and adverse event reports, all of which are used by FDA to inform regulatory decisions regarding medical product safety. The information contained in this report is provided as part of FDA's commitment to place knowledge acquired from Sentinel in the public domain as soon as possible. Any public health actions taken by FDA regarding products involved in Sentinel queries will continue to be communicated through existing channels.

FDA wants to emphasize that the fact that FDA has initiated a query involving a medical product and is reporting findings related to that query does not mean that FDA is suggesting health care practitioners should change their prescribing practices for the medical product or that patients taking the medical product should stop using it. Patients who have questions about the use of an identified medical product should contact their health care practitioners.

The following report contains a description of the request, request specifications, and results from the modular program run(s).

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Request ID: cber_mpl1p_wp003

Request Description: We estimated counts and cumulative incidence of postoperative fungal keratitis, antifungal medication use, and both, among patients who have received keratoplasty procedures in the Sentinel Distributed Database (SDD).

Sentinel Routine Querying Module: Cohort Identification and Descriptive Analysis (CIDA) tool, version 8.1.0, with ad hoc programming

Data Source: We distributed this request to 16 Sentinel Data Partners on September 14, 2020. The study period included data from January 1, 2008 through February 29, 2020. Please see Appendix A for a list of dates of available data for each Data Partner.

Study Design: We identified keratoplasty procedures and evaluated the occurrence within 200 days of fungal keratitis diagnosis and/or antifungal treatment of greater than or equal to 15 days, among all patients, and among patients with no fungal keratitis diagnosis in the 90 days prior to their procedure. This is a Type 2 analysis in the Query Request Package (QRP) documentation.

Exposures of Interest: We defined our index exposures of interest, anterior lamellar keratoplasty, penetrating keratoplasty, and endothelial keratoplasty, using Current Procedural Terminology, Fourth Edition (CPT-4) codes. An "any keratoplasty" cohort identified occurrences of any of these three index keratoplasty types. Each qualifying procedure was identified as an index event, with multiple index events allowed per patient. Please see Appendix B for a list of CPT-4 codes to define exposures in this request.

Cohort Eligibility Criteria: We required members to be continuously enrolled in health plans with medical and drug coverage in the 90 days prior to their index date, during which gaps in coverage of up to 45 days were allowed. For all analyses, we included the age groups of 0-17, 18-44, 45-64, 65-74, 75-84, and 85+ years. For cohorts with no prior fungal keratitis diagnosis, we excluded patients with a history of fungal keratitis diagnosis in the 90 days prior to the index-defining keratoplasty procedure. We defined fungal keratitis using International Classification of Diseases, Ninth and Tenth Revisions, Clinical Modification (ICD-9-CM and ICD-10-CM) diagnosis codes. Please see Appendix C for a list ICD-9-CM and ICD-10-CM diagnosis codes used to define exclusion criteria in this request.

Outcomes of Interest: We defined the outcomes of interest as: (1) fungal keratitis, (2) antifungal treatment of greater than or equal to 15 days, (3) fungal keratitis OR antifungal treatment of greater than or equal to 15 days, and (4) fungal keratitis AND antifungal treatment of greater than or equal to 15 days occurring within 90 days of one another. Fungal keratitis was defined using ICD-9/10-CM diagnosis codes and antifungal treatments were defined using National Drug Codes (NDCs). Please see Appendix C for a list ICD-9/10-CM diagnosis codes and Appendix D for a list of brand and generic medical products.

Follow-up Time: For all cohorts, follow-up time was assessed starting on the index-defining keratoplasty procedure date and continued until the first occurrence of any of the following: 1) disenrollment; 2) death; 3) the end of the data provided by each Data Partner; 4) the end of the query period; 5) subsequent keratoplasty procedure; 6) end of the 200-day fixed follow-up window; or 7) outcome occurrence.

Limitations: Algorithms to define exposures, outcomes, and exclusion criteria are imperfect and may be misclassified. Therefore, data should be interpreted with this limitation in mind.

Please see Appendices E and F for the specifications of parameters used in this request.

Notes: Please contact the Sentinel Operations Center (info@sentinelsystem.org) for questions and to provide comments/suggestions for future enhancements to this document. For more information on Sentinel's routine querying modules, please refer to the documentation (https://dev.sentinelsystem.org/projects/sentinel/repos/sentinel-routine-querying-tool-documentation/browse).

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Glossary of Terms for Analyses Using
Cohort Identification and Descriptive Analysis (CIDA) Tool*

Amount Supplied - number of units (pills, tablets, vials) dispensed. Net amount per NDC per dispensing.

Blackout Period - number of days at the beginning of a treatment episode that events are to be ignored. If an event occurs during the blackout period, the episode is excluded.

Care Setting - type of medical encounter or facility where the exposure, event, or condition code was recorded. Possible care settings include: Inpatient Hospital Stay (IP), Non-Acute Institutional Stay (IS), Emergency Department (ED), Ambulatory Visit (AV), and Other Ambulatory Visit (OA). For laboratory results, possible care settings include: Emergency Department (E), Home (H), Inpatient (I), Outpatient (O), or Unknown or Missing (U). The Care Setting, along with the Principal Diagnosis Indicator (PDX), forms the Care Setting/PDX parameter.

    Ambulatory Visit (AV) - includes visits at outpatient clinics, same-day surgeries, urgent care visits, and other same-day ambulatory hospital encounters, but excludes emergency department encounters.

    Emergency Department (ED) - includes ED encounters that become inpatient stays (in which case inpatient stays would be a separate encounter). Excludes urgent care visits.

    Inpatient Hospital Stay (IP) - includes all inpatient stays, same-day hospital discharges, hospital transfers, and acute hospital care where the discharge is after the admission date.

    Non-Acute Institutional Stay (IS) - includes hospice, skilled nursing facility (SNF), rehab center, nursing home, residential, overnight non-hospital dialysis and other non-hospital stays.

    Other Ambulatory Visit (OA) - includes other non overnight AV encounters such as hospice visits, home health visits, skilled nursing facility visits, other non-hospital visits, as well as telemedicine, telephone and email consultations.

Charlson/Elixhauser Combined Comorbidity Score - calculated based on comorbidities observed during a requester-defined window around the exposure episode start date (e.g., in the 183 days prior to index).

Cohort Definition (drug/exposure) - indicates how the cohort will be defined: 01: Cohort includes only the first valid treatment episode during the query period; 02: Cohort includes all valid treatment episodes during the query period; 03: Cohort includes all valid treatment episodes during the query period until an event occurs.

Computed Start Marketing Date - represents the first observed dispensing date among all valid users within a GROUP (scenario)

Days Supplied - number of days supplied for all dispensings in qualifying treatment episodes.

Eligible Members - number of members eligible for an incident treatment episode (defined by the drug/exposure and event washout periods) with drug and medical coverage during the query period.

Enrollment Gap - number of days allowed between two consecutive enrollment periods without breaking a "continuously enrolled" sequence.

Episodes - treatment episodes; length of episode is determined by days supplied in one dispensing or consecutive dispensings bridged by the episode gap.

Episode Gap - number of days allowed between two (or more) consecutive exposures (dispensings/procedures) to be considered

Event Deduplication - specifies how events are counted by the Modular Program (MP) algorithm: 0: Counts all occurrences of a health outcome of interest (HOI) during an exposure episode; 1: de-duplicates occurrences of the same HOI code and code type on the same day; 2: de-duplicates occurrences of the same HOI group on the same day (e.g., de-duplicates at the group level).

Exposure Episode Length - number of days after exposure initiation that is considered "exposed time."

Exposure Extension Period - number of days post treatment period in which the outcomes/events are counted for a treatment episode. Extensions are added after any episode gaps have been bridged.

Lookback Period - number of days wherein a member is required to have evidence of pre-existing condition (diagnosis/procedure/drug dispensing).

Maximum Episode Duration - truncates exposure episodes after a requester-specified number of exposed days. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Member-Years - sum of all days of enrollment with medical and drug coverage in the query period preceded by an exposure washout period all divided by 365.25.

Minimum Days Supplied - specifies a minimum number of days in length of the days supplied for the episode to be considered.

Minimum Episode Duration - specifies a minimum number of days in length of the episode for it to be considered. Applied after any gaps are bridged and extension days added to the length of the exposure episode.

Monitoring Period - used to define time periods of interest for both sequential analysis and simple cohort characterization requests.

Principal Diagnosis (PDX) - diagnosis or condition established to be chiefly responsible for admission of the patient to the hospital. 'P' = principal diagnosis, 'S' = secondary diagnosis, 'X' = unspecified diagnosis, '.' = blank. Along with the Care Setting values, forms the Caresetting/PDX parameter.

Query Period - period in which the modular program looks for exposures and outcomes of interest.

Switch Evaluation Step Value - value used to differentiate evaluation step. Each switch pattern can support up to 2 evaluation steps (0 = switch pattern evaluation start; 1 = first evaluation; 2 = second evaluation).

Switch Gap Inclusion Indicator - indicator for whether gaps in treatment episodes that are included in a switch episode will be counted as part of the switch episode duration.

Switch Pattern Cohort Inclusion Date - indicates which date to use for inclusion into the switch pattern cohort of interest as well as optionally as the index date of the treatment episode initiating the switch pattern. Valid options are the product approval date, product marketing date, other requester defined date, or computed start marketing date.

Switch Pattern Cohort Inclusion Strategy - indicates how the switch pattern cohort inclusion date will be used: 01: used only as a switch cohort entry date. First treatment episode dispensing date is used as index for computing time to first switch; 02: used as switch cohort entry date and as initial switch step index date for computing time to first switch.

Treatment Episode Truncation Indicator - indicates whether the exposure episode will be truncated at the occurrence of a requester-specified code.

Washout Period (drug/exposure) - number of days a user is required to have no evidence of prior exposure (drug dispensing/procedure) and continuous drug and medical coverage prior to an incident treatment episode.

Washout Period (event/outcome) - number of days a user is required to have no evidence of a prior event (procedure/diagnosis) and continuous drug and medical coverage prior to an incident treatment episode.

Years at Risk - number of days supplied plus any episode gaps and exposure extension periods all divided by 365.25.

*not all terms may be used in this report

Table 1a. Aggregated Baseline Table for Patients with Anterior Lamellar Keratoplasty Exposure in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Characteristic[1]	Number	
Number of episodes	7,249	
Number of unique patients	6,467	
Demographics	**Mean**	**Standard Deviation**
Mean Age (Years)	62.0	17.1
Age (Years)	**Number**	**Percent**
0-17	119	1.6%
18-44	1,388	19.1%
45-64	1,765	24.3%
65-74	1,864	25.7%
75-84	1,514	20.9%
85+	599	8.3%
Sex		
Female	3,452	53.4%
Male	3,015	46.6%
Race		
Unknown	2,384	36.9%
American Indian or Alaska Native	27	0.4%
Asian	173	2.7%
Black or African American	535	8.3%
Native Hawaiian or Other Pacific Islander	15	0.2%
White	3,333	51.5%
Ethnicity		
Hispanic Origin	330	5.1%
Year		
2008	598	8.2%
2009	*****	*****
2010	643	8.9%
2011	679	9.4%
2012	621	8.6%
2013	644	8.9%
2014	592	8.2%
2015	619	8.5%
2016	637	8.8%
2017	633	8.7%
2018	624	8.6%
2019	527	7.3%
2020	*****	*****
Index-Date Keratoplasty Type Distribution	**Number**	**Percent**
Anterior lamellar keratoplasty	7,249	100.0%
Penetrating keratoplasty	1,302	18.0%
Endothelial keratoplasty	796	11.0%
Health Service Utilization Intensity within 183 Days Prior to the Index Date	**Mean**	**Standard Deviation**
Mean number of ambulatory encounters (AV)	14.1	12.8
Mean number of emergency room encounters (ED)	0.3	0.7
Mean number of inpatient hospital encounters (IP)	0.1	0.4

Table 1a. Aggregated Baseline Table for Patients with Anterior Lamellar Keratoplasty Exposure in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Health Service Utilization Intensity within 183 Days Prior to the Index Date	Mean	Standard Deviation
Mean number of other ambulatory encounters (OA)	3.0	6.4
Mean number of unique drug classes	8.0	4.8
Mean number of generics	8.7	5.5
Mean number of filled prescriptions	19.6	17.7

†All metrics are based on total number of episodes per group, except for sex, race, and hispanic origin which are based on total number of unique patients

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented

Table 1b. Aggregated Baseline Table for Patients with Penetrating Keratoplasty Exposure in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Characteristic[1]	Number	
Number of episodes	67,117	
Number of unique patients	52,950	
Demographics	**Mean**	**Standard Deviation**
Mean Age (Years)	66.2	15.6
Age (Years)	**Number**	**Percent**
0-17	422	0.6%
18-44	9,088	13.5%
45-64	14,954	22.3%
65-74	18,596	27.7%
75-84	16,694	24.9%
85+	7,363	11.0%
Sex		
Female	27,981	52.8%
Male	24,969	47.2%
Race		
Unknown	15,901	30.0%
American Indian or Alaska Native	223	0.4%
Asian	1,337	2.5%
Black or African American	5,959	11.3%
Native Hawaiian or Other Pacific Islander	99	0.2%
White	29,431	55.6%
Ethnicity		
Hispanic Origin	2,246	4.2%
Year		
2008	3,473	5.2%
2009	2,615	3.9%
2010	5,818	8.7%
2011	6,562	9.8%
2012	6,485	9.7%
2013	6,504	9.7%
2014	6,395	9.5%
2015	6,280	9.4%
2016	6,256	9.3%
2017	6,057	9.0%
2018	5,637	8.4%
2019	4,961	7.4%
2020	74	0.1%
Index-Date Keratoplasty Type Distribution	**Number**	**Percent**
Anterior lamellar keratoplasty	1,302	1.9%
Penetrating keratoplasty	67,117	100.0%
Endothelial keratoplasty	4,221	6.3%
Health Service Utilization Intensity within 183 Days Prior to the Index Date	**Mean**	**Standard Deviation**
Mean number of ambulatory encounters (AV)	15.8	13.9
Mean number of emergency room encounters (ED)	0.3	0.9
Mean number of inpatient hospital encounters (IP)	0.1	0.5
Mean number of non-acute institutional encounters (IS)	0.1	0.4

Table 1b. Aggregated Baseline Table for Patients with Penetrating Keratoplasty Exposure in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Health Service Utilization Intensity within 183 Days Prior to the Index Date	Mean	Standard Deviation
Mean number of other ambulatory encounters (OA)	3.4	7.2
Mean number of unique drug classes	9.1	5.0
Mean number of generics	10.0	5.7
Mean number of filled prescriptions	24.4	19.9

[1]All metrics are based on total number of episodes per group, except for sex, race, and hispanic origin which are based on total number of unique patients

Table 1c. Aggregated Baseline Table for Patients with Endothelial Keratoplasty Exposure in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Characteristic[1]	Number	
Number of episodes	115,530	
Number of unique patients	83,789	
Demographics	**Mean**	**Standard Deviation**
Mean Age (Years)	74.5	9.2
Age (Years)	**Number**	**Percent**
0-17	42	0.0%
18-44	990	0.9%
45-64	12,785	11.1%
65-74	44,908	38.9%
75-84	40,796	35.3%
85+	16,009	13.9%
Sex		
Female	51,776	61.8%
Male	32,013	38.2%
Race		
Unknown	14,261	17.0%
American Indian or Alaska Native	187	0.2%
Asian	1,350	1.6%
Black or African American	5,349	6.4%
Native Hawaiian or Other Pacific Islander	97	0.1%
White	62,545	74.6%
Ethnicity		
Hispanic Origin	1,552	1.9%
Year		
2008	*****	*****
2009	1,888	1.6%
2010	6,584	5.7%
2011	8,487	7.3%
2012	9,324	8.1%
2013	10,856	9.4%
2014	11,609	10.0%
2015	12,488	10.8%
2016	13,130	11.4%
2017	13,368	11.6%
2018	13,943	12.1%
2019	13,685	11.8%
2020	*****	*****
Index-Date Keratoplasty Type Distribution	**Number**	**Percent**
Anterior lamellar keratoplasty	796	0.7%
Penetrating keratoplasty	4,221	3.7%
Endothelial keratoplasty	115,530	100.0%
Health Service Utilization Intensity within 183 Days Prior to the Index Date	**Mean**	**Standard Deviation**
Mean number of ambulatory encounters (AV)	14.1	10.5
Mean number of emergency room encounters (ED)	0.2	0.6
Mean number of inpatient hospital encounters (IP)	0.1	0.3
Mean number of non-acute institutional encounters (IS)	0.0	0.3

Table 1c. Aggregated Baseline Table for Patients with Endothelial Keratoplasty Exposure in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Health Service Utilization Intensity within 183 Days Prior to the Index Date	Mean	Standard Deviation
Mean number of other ambulatory encounters (OA)	2.6	5.1
Mean number of unique drug classes	8.6	4.4
Mean number of generics	9.3	4.9
Mean number of filled prescriptions	20.9	16.4

[1]All metrics are based on total number of episodes per group, except for sex, race, and hispanic origin which are based on total number of unique patients

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Table 1d. Aggregated Baseline Table for Patients with Any Keratoplasty Exposure in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Characteristic[1]	Number	
Number of episodes	183,583	
Number of unique patients	131,328	
Demographics	**Mean**	**Standard Deviation**
Mean Age (Years)	71.1	12.8
Age (Years)	**Number**	**Percent**
0-17	556	0.3%
18-44	11,009	6.0%
45-64	28,442	15.5%
65-74	63,392	34.5%
75-84	57,039	31.1%
85+	23,145	12.6%
Sex		
Female	76,378	58.2%
Male	54,950	41.8%
Race		
Unknown	29,754	22.7%
American Indian or Alaska Native	406	0.3%
Asian	2,522	1.9%
Black or African American	10,673	8.1%
Native Hawaiian or Other Pacific Islander	190	0.1%
White	87,783	66.8%
Ethnicity		
Hispanic Origin	3,699	2.8%
Year		
2008	3,833	2.1%
2009	4,545	2.5%
2010	12,348	6.7%
2011	15,061	8.2%
2012	15,819	8.6%
2013	17,423	9.5%
2014	18,037	9.8%
2015	18,795	10.2%
2016	19,517	10.6%
2017	19,530	10.6%
2018	19,721	10.7%
2019	18,710	10.2%
2020	244	0.1%
Index-Date Keratoplasty Type Distribution	**Number**	**Percent**
Anterior lamellar keratoplasty	7,249	3.9%
Penetrating keratoplasty	67,117	36.6%
Endothelial keratoplasty	115,530	62.9%
Health Service Utilization Intensity within 183 Days Prior to the Index Date	**Mean**	**Standard Deviation**
Mean number of ambulatory encounters (AV)	14.7	12.0
Mean number of emergency room encounters (ED)	0.2	0.7
Mean number of inpatient hospital encounters (IP)	0.1	0.4
Mean number of non-acute institutional encounters (IS)	0.0	0.3

Table 1d. Aggregated Baseline Table for Patients with Any Keratoplasty Exposure in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Health Service Utilization Intensity within 183 Days Prior to the Index Date	Mean	Standard Deviation
Mean number of other ambulatory encounters (OA)	2.9	6.0
Mean number of unique drug classes	8.8	4.7
Mean number of generics	9.5	5.3
Mean number of filled prescriptions	22.1	17.9

[1]All metrics are based on total number of episodes per group, except for sex, race, and hispanic origin which are based on total number of unique patients

Table 1e. Aggregated Baseline Table for Patients with Anterior Lamellar Keratoplasty Exposure with No Keratitis in 90 Days Prior to the Index Event in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Characteristic[1]	Number	
Number of episodes	7,234	
Number of unique patients	6,455	
Demographics	**Mean**	**Standard Deviation**
Mean Age (Years)	62	17.1
Age (Years)	**Number**	**Percent**
0-17	119	1.6%
18-44	1,387	19.2%
45-64	1,758	24.3%
65-74	1,862	25.7%
75-84	1,510	20.9%
85+	598	8.3%
Sex		
Female	3,447	53.4%
Male	3,008	46.6%
Race		
Unknown	2,378	36.8%
American Indian or Alaska Native	27	0.4%
Asian	173	2.7%
Black or African American	534	8.3%
Native Hawaiian or Other Pacific Islander	15	0.2%
White	3,328	51.6%
Ethnicity		
Hispanic Origin	330	5.1%
Year		
2008	598	8.3%
2009	*****	*****
2010	640	8.8%
2011	679	9.4%
2012	620	8.6%
2013	643	8.9%
2014	591	8.2%
2015	617	8.5%
2016	636	8.8%
2017	631	8.7%
2018	623	8.6%
2019	526	7.3%
2020	*****	*****
Index-Date Keratoplasty Type Distribution	**Number**	**Percent**
Anterior lamellar keratoplasty	7,234	100.0%
Penetrating keratoplasty	1,298	17.9%
Endothelial keratoplasty	795	11.0%
Health Service Utilization Intensity within 183 Days Prior to the Index Date	**Mean**	**Standard Deviation**
Mean number of ambulatory encounters (AV)	14.1	12.8
Mean number of emergency room encounters (ED)	0.3	0.7
Mean number of inpatient hospital encounters (IP)	0.1	0.4

Table 1e. Aggregated Baseline Table for Patients with Anterior Lamellar Keratoplasty Exposure with No Keratitis in 90 Days Prior to the Index Event in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Health Service Utilization Intensity within 183 Days Prior to the Index Date	Mean	Standard Deviation
Mean number of non-acute institutional encounters (IS)	0.0	0.3
Mean number of other ambulatory encounters (OA)	3.0	6.4
Mean number of unique drug classes	7.9	4.8
Mean number of generics	8.7	5.5
Mean number of filled prescriptions	19.5	17.7

[1]All metrics are based on total number of episodes per group, except for sex, race, and hispanic origin which are based on total number of unique patients

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented

Table 1f. Aggregated Baseline Table for Patients with Penetrating Keratoplasty Exposure with No Keratitis in 90 Days Prior to the Index Event in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Characteristic[1]	Number	
Number of episodes	66,784	
Number of unique patients	52,773	
Demographics	**Mean**	**Standard Deviation**
Mean Age (Years)	66.2	15.6
Age (Years)	**Number**	**Percent**
0-17	421	0.6%
18-44	9,057	13.6%
45-64	14,862	22.3%
65-74	18,479	27.7%
75-84	16,626	24.9%
85+	7,339	11.0%
Sex		
Female	27,889	52.8%
Male	24,884	47.2%
Race		
Unknown	15,847	30.0%
American Indian or Alaska Native	222	0.4%
Asian	1,337	2.5%
Black or African American	5,951	11.3%
Native Hawaiian or Other Pacific Islander	99	0.2%
White	29,317	55.6%
Ethnicity		
Hispanic Origin	2,240	4.2%
Year		
2008	3,467	5.2%
2009	2,603	3.9%
2010	5,795	8.7%
2011	6,527	9.8%
2012	6,452	9.7%
2013	6,483	9.7%
2014	6,369	9.5%
2015	6,242	9.3%
2016	6,223	9.3%
2017	6,025	9.0%
2018	5,591	8.4%
2019	4,934	7.4%
2020	73	0.1%
Index-Date Keratoplasty Type Distribution	**Number**	**Percent**
Anterior lamellar keratoplasty	1,298	1.9%
Penetrating keratoplasty	66,784	100.0%
Endothelial keratoplasty	4,217	6.3%
Health Service Utilization Intensity within 183 Days Prior to the Index Date	**Mean**	**Standard Deviation**
Mean number of ambulatory encounters (AV)	15.7	13.8
Mean number of emergency room encounters (ED)	0.3	0.9
Mean number of inpatient hospital encounters (IP)	0.1	0.5
Mean number of non-acute institutional encounters (IS)	0.1	0.4

Table 1f. Aggregated Baseline Table for Patients with Penetrating Keratoplasty Exposure with No Keratitis in 90 Days Prior to the Index Event in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Health Service Utilization Intensity within 183 Days Prior to the Index Date	Mean	Standard Deviation
Mean number of other ambulatory encounters (OA)	3.4	7.2
Mean number of unique drug classes	9.0	5.0
Mean number of generics	9.9	5.7
Mean number of filled prescriptions	24.3	19.9

[1]All metrics are based on total number of episodes per group, except for sex, race, and hispanic origin which are based on total number of unique patients

Table 1g. Aggregated Baseline Table for Patients with Endothelial Keratoplasty Exposure with No Keratitis in 90 Days Prior to the Index Event in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Characteristic[1]	Number	
Number of episodes	115,505	
Number of unique patients	83,781	
Demographics	**Mean**	**Standard Deviation**
Mean Age (Years)	74.5	9.2
Age (Years)	**Number**	**Percent**
0-17	42	0.0%
18-44	990	0.9%
45-64	12,780	11.1%
65-74	44,899	38.9%
75-84	40,789	35.3%
85+	16,005	13.9%
Sex		
Female	51,771	61.8%
Male	32,010	38.2%
Race		
Unknown	14,261	17.0%
American Indian or Alaska Native	187	0.2%
Asian	1,350	1.6%
Black or African American	5,348	6.4%
Native Hawaiian or Other Pacific Islander	97	0.1%
White	62,538	74.6%
Ethnicity		
Hispanic Origin	1,552	1.9%
Year		
2008	*****	*****
2009	1,888	1.6%
2010	6,583	5.7%
2011	8,487	7.3%
2012	9,322	8.1%
2013	10,853	9.4%
2014	11,604	10.0%
2015	12,486	10.8%
2016	13,127	11.4%
2017	13,368	11.6%
2018	13,939	12.1%
2019	13,680	11.8%
2020	*****	*****
Index-Date Keratoplasty Type Distribution	**Number**	**Percent**
Anterior lamellar keratoplasty	795	0.7%
Penetrating keratoplasty	4,217	3.7%
Endothelial keratoplasty	115,505	100.0%
Health Service Utilization Intensity within 183 Days Prior to the Index Date	**Mean**	**Standard Deviation**
Mean number of ambulatory encounters (AV)	14.1	10.5
Mean number of emergency room encounters (ED)	0.2	0.6
Mean number of inpatient hospital encounters (IP)	0.1	0.3

Table 1g. Aggregated Baseline Table for Patients with Endothelial Keratoplasty Exposure with No Keratitis in 90 Days Prior to the Index Event in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Health Service Utilization Intensity within 183 Days Prior to the Index Date	Mean	Standard Deviation
Mean number of non-acute institutional encounters (IS)	0.0	0.3
Mean number of other ambulatory encounters (OA)	2.6	5.1
Mean number of unique drug classes	8.6	4.4
Mean number of generics	9.3	4.9
Mean number of filled prescriptions	20.9	16.4

[1]All metrics are based on total number of episodes per group, except for sex, race, and hispanic origin which are based on total number of unique patients

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented

Table 1h. Aggregated Baseline Table for Patients with Any Keratoplasty Exposure with No Keratitis in 90 Days Prior to the Index Event in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Characteristic[1]	Number	
Number of episodes	183,219	
Number of unique patients	131,156	
Demographics	**Mean**	**Standard Deviation**
Mean Age (Years)	71.1	12.8
Age (Years)	**Number**	**Percent**
0-17	555	0.3%
18-44	10,978	6.0%
45-64	28,341	15.5%
65-74	63,265	34.5%
75-84	56,964	31.1%
85+	23,116	12.6%
Sex		
Female	76,288	58.2%
Male	54,868	41.8%
Race		
Unknown	29,697	22.6%
American Indian or Alaska Native	405	0.3%
Asian	2,522	1.9%
Black or African American	10,665	8.1%
Native Hawaiian or Other Pacific Islander	190	0.1%
White	87,677	66.8%
Ethnicity		
Hispanic Origin	3,693	2.8%
Year		
2008	3,827	2.1%
2009	4,531	2.5%
2010	12,322	6.7%
2011	15,026	8.2%
2012	15,784	8.6%
2013	17,399	9.5%
2014	18,007	9.8%
2015	18,753	10.2%
2016	19,482	10.6%
2017	19,497	10.6%
2018	19,670	10.7%
2019	18,678	10.2%
2020	243	0.1%
Index-Date Keratoplasty Type Distribution	**Number**	**Percent**
Anterior lamellar keratoplasty	7,234	3.9%
Penetrating keratoplasty	66,784	36.5%
Endothelial keratoplasty	115,505	63.0%
Health Service Utilization Intensity within 183 Days Prior to the Index Date	**Mean**	**Standard Deviation**
Mean number of ambulatory encounters (AV)	14.7	11.9
Mean number of emergency room encounters (ED)	0.2	0.7
Mean number of inpatient hospital encounters (IP)	0.1	0.4

Table 1h. Aggregated Baseline Table for Patients with Any Keratoplasty Exposure with No Keratitis in 90 Days Prior to the Index Event in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020

Health Service Utilization Intensity within 183 Days Prior to the Index Date	Mean	Standard Deviation
Mean number of non-acute institutional encounters (IS)	0.0	0.3
Mean number of other ambulatory encounters (OA)	2.9	6
Mean number of unique drug classes	8.7	4.7
Mean number of generics	9.5	5.3
Mean number of filled prescriptions	22.0	17.9

[1]All metrics are based on total number of episodes per group, except for sex, race, and hispanic origin which are based on total number of unique patients

Table 2. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, Overall

	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Anterior lamellar keratoplasty							
Fungal keratitis diagnosis	6,467	210,403,320	7,249	0.34	1,294,973	25	3.45
Antifungal medications (15+ days)	6,467	210,403,320	7,249	0.34	1,289,634	67	9.24
Fungal keratitis diagnosis OR antifungal medications (15+ days)	6,467	210,403,320	7,249	0.34	1,287,338	82	11.31
Fungal keratitis diagnosis AND antifungal medications (15+ days)	6,467	210,403,320	7,249	0.34	1,297,252	*****	*****
Penetrating keratoplasty							
Fungal keratitis diagnosis	52,950	210,403,320	67,117	3.19	12,015,923	400	5.96
Antifungal medications (15+ days)	52,950	210,403,320	67,117	3.19	11,935,026	1,045	15.57
Fungal keratitis diagnosis OR antifungal medications (15+ days)	52,950	210,403,320	67,117	3.19	11,902,624	1,274	18.98
Fungal keratitis diagnosis AND antifungal medications (15+ days)	52,950	210,403,320	67,117	3.19	12,045,364	166	2.47
Endothelial keratoplasty							
Fungal keratitis diagnosis	83,789	210,403,320	115,530	5.49	19,883,232	167	1.45
Antifungal medications (15+ days)	83,789	210,403,320	115,530	5.49	19,886,873	173	1.50
Fungal keratitis diagnosis OR antifungal medications (15+ days)	83,789	210,403,320	115,530	5.49	19,863,174	325	2.81
Fungal keratitis diagnosis AND antifungal medications (15+ days)	83,789	210,403,320	115,530	5.49	19,906,829	15	0.13
Any keratoplasty							
Fungal keratitis diagnosis	131,328	210,403,320	183,583	8.73	31,748,210	569	3.10
Antifungal medications (15+ days)	131,328	210,403,320	183,583	8.73	31,672,982	1,225	6.67
Fungal keratitis diagnosis OR antifungal medications (15+ days)	131,328	210,403,320	183,583	8.73	31,617,212	1,611	8.78
Fungal keratitis diagnosis AND antifungal medications (15+ days)	131,328	210,403,320	183,583	8.73	31,800,977	178	0.97
Anterior lamellar keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis	6,455	210,403,302	7,234	0.34	1,293,191	20	2.76
Antifungal medications (15+ days)	6,455	210,403,302	7,234	0.34	1,287,179	66	9.12
Fungal keratitis diagnosis OR antifungal medications (15+ days)	6,455	210,403,302	7,234	0.34	1,285,556	77	10.64
Fungal keratitis diagnosis AND antifungal medications (15+ days)	6,455	210,403,302	7,234	0.34	1,294,797	*****	*****
Penetrating keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis	52,773	210,403,302	66,784	3.17	11,985,503	240	3.59
Antifungal medications (15+ days)	52,773	210,403,302	66,784	3.17	11,898,012	932	13.96
Fungal keratitis diagnosis OR antifungal medications (15+ days)	52,773	210,403,302	66,784	3.17	11,879,197	1,074	16.08
Fungal keratitis diagnosis AND antifungal medications (15+ days)	52,773	210,403,302	66,784	3.17	12,002,442	96	1.44

Table 2. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, Overall

	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Endothelial keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis	83,781	210,403,302	115,505	5.49	19,879,987	160	1.39
Antifungal medications (15+ days)	83,781	210,403,302	115,505	5.49	19,882,788	171	1.48
Fungal keratitis diagnosis OR antifungal medications (15+ days)	83,781	210,403,302	115,505	5.49	19,859,936	317	2.74
Fungal keratitis diagnosis AND antifungal medications (15+ days)	83,781	210,403,302	115,505	5.49	19,902,737	14	0.12
Any keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis	131,156	210,403,302	183,219	8.71	31,714,176	400	2.18
Antifungal medications (15+ days)	131,156	210,403,302	183,219	8.71	31,631,116	1,110	6.06
Fungal keratitis diagnosis OR antifungal medications (15+ days)	131,156	210,403,302	183,219	8.71	31,590,178	1,401	7.65
Fungal keratitis diagnosis AND antifungal medications (15+ days)	131,156	210,403,302	183,219	8.71	31,753,196	107	0.58

[1]Some patients had multiple types of keratoplasty during the study period. Thus, the sum of patients across all types of keratoplasty is greater than the count of patients in the "Any keratoplasty" cohort

[2]Eligible Members and Member-Years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period

[3]Patients with both fungal keratitis diagnosis and antifungal medications within greater than 90 days of one another are not included in outcome counts for "Fungal keratitis diagnosis AND antifungal medications." Therefore, this combined outcome might not include all instances of procedures that resulted in both individual outcomes

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Anterior lamellar keratoplasty							
Fungal keratitis diagnosis							
2008	550	49,770,084	598	0.12	105,647	0	0.00
2009	395	49,221,343	*****	*****	73,984	*****	2.36
2010	614	64,695,998	643	0.10	120,610	*****	*****
2011	642	64,536,563	679	0.11	126,286	*****	*****
2012	587	66,243,699	621	0.09	114,100	*****	*****
2013	608	73,174,976	644	0.09	117,776	*****	*****
2014	560	76,383,090	592	0.08	108,743	*****	*****
2015	586	78,491,704	619	0.08	111,258	*****	*****
2016	598	81,527,197	637	0.08	114,505	*****	*****
2017	598	82,218,767	633	0.08	115,925	*****	*****
2018	590	79,755,141	624	0.08	116,442	*****	*****
2019	502	75,419,323	527	0.07	69,526	*****	*****
2020	*****	18,893,071	*****	*****	171	0	0.00
Antifungal medications (15+ days)							
2008	550	49,770,084	598	0.12	105,174	*****	*****
2009	395	49,221,343	*****	*****	73,981	*****	2.36
2010	614	64,695,998	643	0.10	120,559	*****	*****
2011	642	64,536,563	679	0.11	125,604	*****	*****
2012	587	66,243,699	621	0.09	114,453	*****	*****
2013	608	73,174,976	644	0.09	117,234	*****	*****
2014	560	76,383,090	592	0.08	108,565	*****	*****
2015	586	78,491,704	619	0.08	110,573	*****	*****
2016	598	81,527,197	637	0.08	114,071	*****	*****
2017	598	82,218,767	633	0.08	114,106	13	20.54
2018	590	79,755,141	624	0.08	116,178	*****	*****
2019	502	75,419,323	527	0.07	68,965	*****	*****
2020	*****	18,893,071	*****	*****	171	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
2008	550	49,770,084	598	0.12	105,174	*****	*****
2009	395	49,221,343	*****	*****	73,981	*****	2.36
2010	614	64,695,998	643	0.10	120,354	*****	*****
2011	642	64,536,563	679	0.11	125,493	*****	*****
2012	587	66,243,699	621	0.09	113,693	*****	*****
2013	608	73,174,976	644	0.09	117,035	*****	*****
2014	560	76,383,090	592	0.08	108,565	*****	*****
2015	586	78,491,704	619	0.08	110,196	11	17.77
2016	598	81,527,197	637	0.08	113,872	*****	*****
2017	598	82,218,767	633	0.08	114,106	13	20.54
2018	590	79,755,141	624	0.08	115,809	*****	*****
2019	502	75,419,323	527	0.07	68,889	*****	*****
2020	*****	18,893,071	*****	*****	171	0	0.00
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
2008	550	49,770,084	598	0.12	105,647	0	0.00
2009	395	49,221,343	*****	*****	73,981	*****	2.36
2010	614	64,695,998	643	0.10	120,807	*****	*****
2011	642	64,536,563	679	0.11	126,394	*****	*****
2012	587	66,243,699	621	0.09	114,860	0	0.00
2013	608	73,174,976	644	0.09	117,975	0	0.00
2014	560	76,383,090	592	0.08	108,740	*****	*****
2015	586	78,491,704	619	0.08	111,635	*****	*****
2016	598	81,527,197	637	0.08	114,704	*****	*****
2017	598	82,218,767	633	0.08	115,925	*****	*****
2018	590	79,755,141	624	0.08	116,811	0	0.00
2019	502	75,419,323	527	0.07	69,602	0	0.00
2020	*****	18,893,071	*****	*****	171	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Penetrating keratoplasty							
Fungal keratitis diagnosis							
2008	3,171	49,770,084	3,473	0.70	610,071	*****	*****
2009	2,427	49,221,343	2,615	0.53	462,616	*****	*****
2010	5,486	64,695,998	5,818	0.90	1,071,634	22	3.78
2011	6,123	64,536,563	6,562	1.02	1,210,128	46	7.01
2012	6,064	66,243,699	6,485	0.98	1,195,106	41	6.32
2013	6,111	73,174,976	6,504	0.89	1,190,601	29	4.46
2014	5,934	76,383,090	6,395	0.84	1,165,873	32	5.00
2015	5,877	78,491,704	6,280	0.80	1,145,296	53	8.44
2016	5,826	81,527,197	6,256	0.77	1,141,102	37	5.91
2017	5,682	82,218,767	6,057	0.74	1,109,803	35	5.78
2018	5,283	79,755,141	5,637	0.71	1,024,937	48	8.52
2019	4,673	75,419,323	4,961	0.66	687,175	40	8.06
2020	73	18,893,071	74	0.04	1,581	*****	*****
Antifungal medications (15+ days)							
2008	3,171	49,770,084	3,473	0.70	608,663	19	5.47
2009	2,427	49,221,343	2,615	0.53	461,012	24	9.18
2010	5,486	64,695,998	5,818	0.90	1,067,969	54	9.28
2011	6,123	64,536,563	6,562	1.02	1,203,448	90	13.72
2012	6,064	66,243,699	6,485	0.98	1,189,088	89	13.72
2013	6,111	73,174,976	6,504	0.89	1,185,490	76	11.69
2014	5,934	76,383,090	6,395	0.84	1,156,832	102	15.95
2015	5,877	78,491,704	6,280	0.80	1,135,629	124	19.75
2016	5,826	81,527,197	6,256	0.77	1,130,650	115	18.38
2017	5,682	82,218,767	6,057	0.74	1,100,042	118	19.48
2018	5,283	79,755,141	5,637	0.71	1,014,321	135	23.95
2019	4,673	75,419,323	4,961	0.66	680,257	99	19.96
2020	73	18,893,071	74	0.04	1,625	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
2008	3,171	49,770,084	3,473	0.70	607,709	*****	*****
2009	2,427	49,221,343	2,615	0.53	460,463	28	10.71
2010	5,486	64,695,998	5,818	0.90	1,066,484	67	11.52
2011	6,123	64,536,563	6,562	1.02	1,199,879	118	17.98
2012	6,064	66,243,699	6,485	0.98	1,185,012	118	18.20
2013	6,111	73,174,976	6,504	0.89	1,182,967	94	14.45
2014	5,934	76,383,090	6,395	0.84	1,154,109	117	18.30
2015	5,877	78,491,704	6,280	0.80	1,131,869	149	23.73
2016	5,826	81,527,197	6,256	0.77	1,127,575	136	21.74
2017	5,682	82,218,767	6,057	0.74	1,096,645	137	22.62
2018	5,283	79,755,141	5,637	0.71	1,010,415	163	28.92
2019	4,673	75,419,323	4,961	0.66	677,916	121	24.39
2020	73	18,893,071	74	0.04	1,581	*****	*****
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
2008	3,171	49,770,084	3,473	0.70	611,020	*****	*****
2009	2,427	49,221,343	2,615	0.53	463,110	*****	*****
2010	5,486	64,695,998	5,818	0.90	1,072,903	*****	*****
2011	6,123	64,536,563	6,562	1.02	1,212,966	18	2.74
2012	6,064	66,243,699	6,485	0.98	1,198,941	12	1.85
2013	6,111	73,174,976	6,504	0.89	1,193,075	11	1.69
2014	5,934	76,383,090	6,395	0.84	1,168,394	16	2.50
2015	5,877	78,491,704	6,280	0.80	1,148,702	26	4.14
2016	5,826	81,527,197	6,256	0.77	1,144,110	15	2.40
2017	5,682	82,218,767	6,057	0.74	1,113,023	16	2.64
2018	5,283	79,755,141	5,637	0.71	1,028,475	20	3.55
2019	4,673	75,419,323	4,961	0.66	689,020	18	3.63
2020	73	18,893,071	74	0.04	1,625	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Endothelial keratoplasty							
Fungal keratitis diagnosis							
2008	*****	49,770,084	*****	*****	24	0	0.00
2009	1,641	49,221,343	1,888	0.38	321,642	0	0.00
2010	5,868	64,695,998	6,584	1.02	1,173,844	*****	*****
2011	7,508	64,536,563	8,487	1.32	1,525,355	*****	*****
2012	8,320	66,243,699	9,324	1.41	1,687,514	0	0.00
2013	9,593	73,174,976	10,856	1.48	1,942,993	*****	*****
2014	10,183	76,383,090	11,609	1.52	2,069,596	*****	*****
2015	10,938	78,491,704	12,488	1.59	2,223,785	*****	*****
2016	11,391	81,527,197	13,130	1.61	2,331,527	*****	*****
2017	11,600	82,218,767	13,368	1.63	2,366,873	*****	*****
2018	12,007	79,755,141	13,943	1.75	2,437,213	74	5.31
2019	11,886	75,419,323	13,685	1.81	1,798,946	59	4.31
2020	165	18,893,071	*****	*****	3,920	0	0.00
Antifungal medications (15+ days)							
2008	*****	49,770,084	*****	*****	24	0	0.00
2009	1,641	49,221,343	1,888	0.38	321,256	*****	*****
2010	5,868	64,695,998	6,584	1.02	1,173,887	*****	*****
2011	7,508	64,536,563	8,487	1.32	1,524,845	*****	*****
2012	8,320	66,243,699	9,324	1.41	1,686,133	13	1.39
2013	9,593	73,174,976	10,856	1.48	1,940,894	17	1.57
2014	10,183	76,383,090	11,609	1.52	2,068,485	13	1.12
2015	10,938	78,491,704	12,488	1.59	2,222,198	19	1.52
2016	11,391	81,527,197	13,130	1.61	2,329,710	17	1.29
2017	11,600	82,218,767	13,368	1.63	2,363,872	30	2.24
2018	12,007	79,755,141	13,943	1.75	2,445,891	36	2.58
2019	11,886	75,419,323	13,685	1.81	1,805,758	14	1.02
2020	165	18,893,071	*****	*****	3,920	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
2008	*****	49,770,084	*****	*****	24	0	0.00
2009	1,641	49,221,343	1,888	0.38	321,256	*****	*****
2010	5,868	64,695,998	6,584	1.02	1,173,673	*****	*****
2011	7,508	64,536,563	8,487	1.32	1,524,591	11	1.30
2012	8,320	66,243,699	9,324	1.41	1,686,133	13	1.39
2013	9,593	73,174,976	10,856	1.48	1,940,543	21	1.93
2014	10,183	76,383,090	11,609	1.52	2,068,229	17	1.46
2015	10,938	78,491,704	12,488	1.59	2,221,500	24	1.92
2016	11,391	81,527,197	13,130	1.61	2,329,477	19	1.45
2017	11,600	82,218,767	13,368	1.63	2,363,372	34	2.54
2018	12,007	79,755,141	13,943	1.75	2,433,070	108	7.75
2019	11,886	75,419,323	13,685	1.81	1,797,386	71	5.19
2020	165	18,893,071	*****	*****	3,920	0	0.00
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
2008	*****	49,770,084	*****	*****	24	0	0.00
2009	1,641	49,221,343	1,888	0.38	321,642	0	0.00
2010	5,868	64,695,998	6,584	1.02	1,174,058	0	0.00
2011	7,508	64,536,563	8,487	1.32	1,525,608	*****	*****
2012	8,320	66,243,699	9,324	1.41	1,687,514	0	0.00
2013	9,593	73,174,976	10,856	1.48	1,943,318	*****	*****
2014	10,183	76,383,090	11,609	1.52	2,069,852	*****	*****
2015	10,938	78,491,704	12,488	1.59	2,224,453	*****	*****
2016	11,391	81,527,197	13,130	1.61	2,331,733	*****	*****
2017	11,600	82,218,767	13,368	1.63	2,367,359	*****	*****
2018	12,007	79,755,141	13,943	1.75	2,450,032	*****	*****
2019	11,886	75,419,323	13,685	1.81	1,807,316	*****	*****
2020	165	18,893,071	*****	*****	3,920	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Any keratoplasty							
Fungal keratitis diagnosis							
2008	3,477	49,770,084	3,833	0.77	667,025	*****	*****
2009	4,037	49,221,343	4,545	0.92	778,744	*****	*****
2010	11,152	64,695,998	12,348	1.91	2,212,077	25	2.02
2011	13,450	64,536,563	15,061	2.33	2,710,009	49	3.25
2012	14,146	66,243,699	15,819	2.39	2,850,446	42	2.66
2013	15,553	73,174,976	17,423	2.38	3,114,046	34	1.95
2014	15,952	76,383,090	18,037	2.36	3,213,755	37	2.05
2015	16,599	78,491,704	18,795	2.39	3,340,670	61	3.25
2016	17,093	81,527,197	19,517	2.39	3,460,512	40	2.05
2017	17,144	82,218,767	19,530	2.38	3,465,495	43	2.20
2018	17,196	79,755,141	19,721	2.47	3,458,417	123	6.24
2019	16,426	75,419,323	18,710	2.48	2,471,502	97	5.18
2020	241	18,893,071	244	0.13	5,512	*****	*****
Antifungal medications (15+ days)							
2008	3,477	49,770,084	3,833	0.77	665,600	20	5.22
2009	4,037	49,221,343	4,545	0.92	776,874	27	5.94
2010	11,152	64,695,998	12,348	1.91	2,208,353	58	4.70
2011	13,450	64,536,563	15,061	2.33	2,702,727	101	6.71
2012	14,146	66,243,699	15,819	2.39	2,843,816	101	6.38
2013	15,553	73,174,976	17,423	2.38	3,106,993	93	5.34
2014	15,952	76,383,090	18,037	2.36	3,203,774	114	6.32
2015	16,599	78,491,704	18,795	2.39	3,329,910	142	7.56
2016	17,093	81,527,197	19,517	2.39	3,448,580	135	6.92
2017	17,144	82,218,767	19,530	2.38	3,453,084	149	7.63
2018	17,196	79,755,141	19,721	2.47	3,456,534	171	8.67
2019	16,426	75,419,323	18,710	2.48	2,471,181	114	6.09
2020	241	18,893,071	244	0.13	5,556	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
2008	3,477	49,770,084	3,833	0.77	664,646	*****	*****
2009	4,037	49,221,343	4,545	0.92	776,325	31	6.82
2010	11,152	64,695,998	12,348	1.91	2,206,724	74	5.99
2011	13,450	64,536,563	15,061	2.33	2,698,945	131	8.70
2012	14,146	66,243,699	15,819	2.39	2,839,541	131	8.28
2013	15,553	73,174,976	17,423	2.38	3,104,030	116	6.66
2014	15,952	76,383,090	18,037	2.36	3,200,795	133	7.37
2015	16,599	78,491,704	18,795	2.39	3,325,461	174	9.26
2016	17,093	81,527,197	19,517	2.39	3,445,276	158	8.10
2017	17,144	82,218,767	19,530	2.38	3,449,375	172	8.81
2018	17,196	79,755,141	19,721	2.47	3,439,966	272	13.79
2019	16,426	75,419,323	18,710	2.48	2,460,616	192	10.26
2020	241	18,893,071	244	0.13	5,512	*****	*****
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
2008	3,477	49,770,084	3,833	0.77	667,974	*****	*****
2009	4,037	49,221,343	4,545	0.92	779,235	*****	*****
2010	11,152	64,695,998	12,348	1.91	2,213,490	*****	*****
2011	13,450	64,536,563	15,061	2.33	2,713,059	19	1.26
2012	14,146	66,243,699	15,819	2.39	2,854,480	12	0.76
2013	15,553	73,174,976	17,423	2.38	3,116,960	11	0.63
2014	15,952	76,383,090	18,037	2.36	3,216,532	17	0.94
2015	16,599	78,491,704	18,795	2.39	3,344,746	27	1.44
2016	17,093	81,527,197	19,517	2.39	3,463,747	16	0.82
2017	17,144	82,218,767	19,530	2.38	3,469,013	20	1.02
2018	17,196	79,755,141	19,721	2.47	3,474,615	22	1.12
2019	16,426	75,419,323	18,710	2.48	2,481,570	19	1.02
2020	241	18,893,071	244	0.13	5,556	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Anterior lamellar keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
2008	550	49,770,080	598	0.12	105,647	0	0.00
2009	393	49,221,341	*****	*****	73,584	*****	2.38
2010	612	64,695,992	640	0.10	120,208	*****	*****
2011	642	64,536,555	679	0.11	126,286	*****	*****
2012	586	66,243,694	620	0.09	113,900	*****	*****
2013	607	73,174,971	643	0.09	117,576	*****	*****
2014	559	76,383,085	591	0.08	108,543	*****	*****
2015	584	78,491,700	617	0.08	111,082	*****	*****
2016	597	81,527,193	636	0.08	114,504	*****	*****
2017	596	82,218,762	631	0.08	115,724	0	0.00
2018	589	79,755,132	623	0.08	116,441	*****	*****
2019	501	75,419,311	526	0.07	69,525	0	0.00
2020	*****	18,893,063	*****	*****	171	0	0.00
Antifungal medications (15+ days)							
2008	550	49,770,080	598	0.12	105,174	*****	*****
2009	393	49,221,341	*****	*****	73,581	*****	2.38
2010	612	64,695,992	640	0.10	120,157	*****	*****
2011	642	64,536,555	679	0.11	125,604	*****	*****
2012	586	66,243,694	620	0.09	114,253	*****	*****
2013	607	73,174,971	643	0.09	117,034	*****	*****
2014	559	76,383,085	591	0.08	108,365	*****	*****
2015	584	78,491,700	617	0.08	110,198	*****	*****
2016	597	81,527,193	636	0.08	113,871	*****	*****
2017	596	82,218,762	631	0.08	113,905	12	19.02
2018	589	79,755,132	623	0.08	115,978	*****	*****
2019	501	75,419,311	526	0.07	68,888	*****	*****
2020	*****	18,893,063	*****	*****	171	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
2008	550	49,770,080	598	0.12	105,174	*****	*****
2009	393	49,221,341	*****	*****	73,581	*****	2.38
2010	612	64,695,992	640	0.10	119,952	*****	*****
2011	642	64,536,555	679	0.11	125,493	*****	*****
2012	586	66,243,694	620	0.09	113,493	*****	*****
2013	607	73,174,971	643	0.09	116,835	*****	*****
2014	559	76,383,085	591	0.08	108,365	*****	*****
2015	584	78,491,700	617	0.08	110,020	*****	*****
2016	597	81,527,193	636	0.08	113,871	*****	*****
2017	596	82,218,762	631	0.08	113,905	12	19.02
2018	589	79,755,132	623	0.08	115,808	*****	*****
2019	501	75,419,311	526	0.07	68,888	*****	*****
2020	*****	18,893,063	*****	*****	171	0	0.00
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
2008	550	49,770,080	598	0.12	105,647	0	0.00
2009	393	49,221,341	*****	*****	73,581	*****	2.38
2010	612	64,695,992	640	0.10	120,405	*****	*****
2011	642	64,536,555	679	0.11	126,394	*****	*****
2012	586	66,243,694	620	0.09	114,660	0	0.00
2013	607	73,174,971	643	0.09	117,775	0	0.00
2014	559	76,383,085	591	0.08	108,540	*****	*****
2015	584	78,491,700	617	0.08	111,260	*****	*****
2016	597	81,527,193	636	0.08	114,504	*****	*****
2017	596	82,218,762	631	0.08	115,724	0	0.00
2018	589	79,755,132	623	0.08	116,611	0	0.00
2019	501	75,419,311	526	0.07	69,525	0	0.00
2020	*****	18,893,063	*****	*****	171	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Penetrating keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
2008	3,166	49,770,080	3,467	0.70	609,199	*****	*****
2009	2,419	49,221,341	2,603	0.53	461,333	*****	*****
2010	5,467	64,695,992	5,795	0.90	1,069,131	14	2.42
2011	6,095	64,536,555	6,527	1.01	1,206,160	29	4.44
2012	6,038	66,243,694	6,452	0.97	1,191,405	29	4.49
2013	6,096	73,174,971	6,483	0.89	1,188,449	20	3.08
2014	5,913	76,383,085	6,369	0.83	1,163,669	18	2.83
2015	5,849	78,491,700	6,242	0.80	1,142,233	28	4.49
2016	5,805	81,527,193	6,223	0.76	1,137,477	23	3.70
2017	5,655	82,218,762	6,025	0.73	1,107,345	15	2.49
2018	5,257	79,755,132	5,591	0.70	1,022,111	28	5.01
2019	4,649	75,419,311	4,934	0.65	685,411	25	5.07
2020	72	18,893,063	73	0.04	1,580	0	0.00
Antifungal medications (15+ days)							
2008	3,166	49,770,080	3,467	0.70	607,680	18	5.19
2009	2,419	49,221,341	2,603	0.53	459,825	19	7.30
2010	5,467	64,695,992	5,795	0.90	1,065,206	47	8.11
2011	6,095	64,536,555	6,527	1.01	1,199,282	77	11.80
2012	6,038	66,243,694	6,452	0.97	1,185,102	78	12.09
2013	6,096	73,174,971	6,483	0.89	1,182,722	70	10.80
2014	5,913	76,383,085	6,369	0.83	1,153,741	92	14.44
2015	5,849	78,491,700	6,242	0.80	1,131,015	111	17.78
2016	5,805	81,527,193	6,223	0.76	1,126,557	106	17.03
2017	5,655	82,218,762	6,025	0.73	1,095,914	107	17.76
2018	5,257	79,755,132	5,591	0.70	1,010,712	122	21.82
2019	4,649	75,419,311	4,934	0.65	678,676	85	17.23
2020	72	18,893,063	73	0.04	1,580	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
2008	3,166	49,770,080	3,467	0.70	606,837	23	6.63
2009	2,419	49,221,341	2,603	0.53	459,615	21	8.07
2010	5,467	64,695,992	5,795	0.90	1,064,186	56	9.66
2011	6,095	64,536,555	6,527	1.01	1,196,965	98	15.01
2012	6,038	66,243,694	6,452	0.97	1,182,648	98	15.19
2013	6,096	73,174,971	6,483	0.89	1,180,816	84	12.96
2014	5,913	76,383,085	6,369	0.83	1,152,442	99	15.54
2015	5,849	78,491,700	6,242	0.80	1,129,418	122	19.55
2016	5,805	81,527,193	6,223	0.76	1,124,722	119	19.12
2017	5,655	82,218,762	6,025	0.73	1,094,671	114	18.92
2018	5,257	79,755,132	5,591	0.70	1,008,227	140	25.04
2019	4,649	75,419,311	4,934	0.65	677,070	100	20.27
2020	72	18,893,063	73	0.04	1,580	0	0.00
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
2008	3,166	49,770,080	3,467	0.70	610,042	*****	*****
2009	2,419	49,221,341	2,603	0.53	461,488	*****	*****
2010	5,467	64,695,992	5,795	0.90	1,069,984	*****	*****
2011	6,095	64,536,555	6,527	1.01	1,208,233	*****	*****
2012	6,038	66,243,694	6,452	0.97	1,193,639	*****	*****
2013	6,096	73,174,971	6,483	0.89	1,190,329	*****	*****
2014	5,913	76,383,085	6,369	0.83	1,164,788	*****	*****
2015	5,849	78,491,700	6,242	0.80	1,143,641	17	2.72
2016	5,805	81,527,193	6,223	0.76	1,139,225	*****	*****
2017	5,655	82,218,762	6,025	0.73	1,108,529	*****	*****
2018	5,257	79,755,132	5,591	0.70	1,024,298	*****	*****
2019	4,649	75,419,311	4,934	0.65	686,666	*****	*****
2020	72	18,893,063	73	0.04	1,580	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Endothelial keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
2008	*****	49,770,080	*****	*****	24	0	0.00
2009	1,641	49,221,341	1,888	0.38	321,642	0	0.00
2010	5,867	64,695,992	6,583	1.02	1,173,662	*****	*****
2011	7,508	64,536,555	8,487	1.32	1,525,355	*****	*****
2012	8,318	66,243,694	9,322	1.41	1,687,114	0	0.00
2013	9,592	73,174,971	10,853	1.48	1,942,666	*****	*****
2014	10,182	76,383,085	11,604	1.52	2,068,596	*****	*****
2015	10,937	78,491,700	12,486	1.59	2,223,611	*****	*****
2016	11,388	81,527,193	13,127	1.61	2,331,126	*****	*****
2017	11,600	82,218,762	13,368	1.63	2,366,873	*****	*****
2018	12,006	79,755,132	13,939	1.75	2,437,002	72	5.17
2019	11,885	75,419,311	13,680	1.81	1,798,396	57	4.17
2020	165	18,893,063	*****	*****	3,920	0	0.00
Antifungal medications (15+ days)							
2008	*****	49,770,080	*****	*****	24	0	0.00
2009	1,641	49,221,341	1,888	0.38	321,256	*****	*****
2010	5,867	64,695,992	6,583	1.02	1,173,705	*****	*****
2011	7,508	64,536,555	8,487	1.32	1,524,845	*****	*****
2012	8,318	66,243,694	9,322	1.41	1,685,733	13	1.39
2013	9,592	73,174,971	10,853	1.48	1,940,480	17	1.57
2014	10,182	76,383,085	11,604	1.52	2,067,485	13	1.12
2015	10,937	78,491,700	12,486	1.59	2,221,829	19	1.52
2016	11,388	81,527,193	13,127	1.61	2,329,110	17	1.30
2017	11,600	82,218,762	13,368	1.63	2,363,872	30	2.24
2018	12,006	79,755,132	13,939	1.75	2,445,488	34	2.44
2019	11,885	75,419,311	13,680	1.81	1,805,041	14	1.02
2020	165	18,893,063	*****	*****	3,920	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
2008	*****	49,770,080	*****	*****	24	0	0.00
2009	1,641	49,221,341	1,888	0.38	321,256	*****	*****
2010	5,867	64,695,992	6,583	1.02	1,173,491	*****	*****
2011	7,508	64,536,555	8,487	1.32	1,524,591	11	1.30
2012	8,318	66,243,694	9,322	1.41	1,685,733	13	1.39
2013	9,592	73,174,971	10,853	1.48	1,940,216	20	1.84
2014	10,182	76,383,085	11,604	1.52	2,067,229	17	1.47
2015	10,937	78,491,700	12,486	1.59	2,221,326	23	1.84
2016	11,388	81,527,193	13,127	1.61	2,329,076	18	1.37
2017	11,600	82,218,762	13,368	1.63	2,363,372	34	2.54
2018	12,006	79,755,132	13,939	1.75	2,432,866	105	7.53
2019	11,885	75,419,311	13,680	1.81	1,796,836	69	5.04
2020	165	18,893,063	*****	*****	3,920	0	0.00
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
2008	*****	49,770,080	*****	*****	24	0	0.00
2009	1,641	49,221,341	1,888	0.38	321,642	0	0.00
2010	5,867	64,695,992	6,583	1.02	1,173,876	0	0.00
2011	7,508	64,536,555	8,487	1.32	1,525,608	*****	*****
2012	8,318	66,243,694	9,322	1.41	1,687,114	0	0.00
2013	9,592	73,174,971	10,853	1.48	1,942,904	*****	*****
2014	10,182	76,383,085	11,604	1.52	2,068,852	*****	*****
2015	10,937	78,491,700	12,486	1.59	2,224,084	*****	*****
2016	11,388	81,527,193	13,127	1.61	2,331,133	*****	*****
2017	11,600	82,218,762	13,368	1.63	2,367,359	*****	*****
2018	12,006	79,755,132	13,939	1.75	2,449,622	*****	*****
2019	11,885	75,419,311	13,680	1.81	1,806,599	*****	*****
2020	165	18,893,063	*****	*****	3,920	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Any keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
2008	3,472	49,770,080	3,827	0.77	666,153	*****	*****
2009	4,028	49,221,341	4,531	0.92	777,061	*****	*****
2010	11,133	64,695,992	12,322	1.90	2,209,190	17	1.38
2011	13,422	64,536,555	15,026	2.33	2,706,059	32	2.13
2012	14,119	66,243,694	15,784	2.38	2,846,345	30	1.90
2013	15,538	73,174,971	17,399	2.38	3,111,759	24	1.38
2014	15,931	76,383,085	18,007	2.36	3,210,751	23	1.28
2015	16,571	78,491,700	18,753	2.39	3,337,257	34	1.81
2016	17,071	81,527,193	19,482	2.39	3,456,686	25	1.28
2017	17,119	82,218,762	19,497	2.37	3,462,837	23	1.18
2018	17,171	79,755,132	19,670	2.47	3,455,379	100	5.08
2019	16,401	75,419,311	18,678	2.48	2,469,188	80	4.28
2020	240	18,893,063	243	0.13	5,511	0	0.00
Antifungal medications (15+ days)							
2008	3,472	49,770,080	3,827	0.77	664,617	19	4.96
2009	4,028	49,221,341	4,531	0.92	775,287	22	4.86
2010	11,133	64,695,992	12,322	1.90	2,205,206	51	4.14
2011	13,422	64,536,555	15,026	2.33	2,698,579	88	5.86
2012	14,119	66,243,694	15,784	2.38	2,839,430	90	5.70
2013	15,538	73,174,971	17,399	2.38	3,104,003	87	5.00
2014	15,931	76,383,085	18,007	2.36	3,199,883	104	5.78
2015	16,571	78,491,700	18,753	2.39	3,324,552	129	6.88
2016	17,071	81,527,193	19,482	2.39	3,444,087	126	6.47
2017	17,119	82,218,762	19,497	2.37	3,448,756	138	7.08
2018	17,171	79,755,132	19,670	2.47	3,452,322	156	7.93
2019	16,401	75,419,311	18,678	2.48	2,468,883	100	5.35
2020	240	18,893,063	243	0.13	5,511	0	0.00

Table 3. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Year

Year	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
2008	3,472	49,770,080	3,827	0.77	663,774	24	6.27
2009	4,028	49,221,341	4,531	0.92	775,077	24	5.30
2010	11,133	64,695,992	12,322	1.90	2,204,042	63	5.11
2011	13,422	64,536,555	15,026	2.33	2,696,049	111	7.39
2012	14,119	66,243,694	15,784	2.38	2,836,777	111	7.03
2013	15,538	73,174,971	17,399	2.38	3,101,744	105	6.03
2014	15,931	76,383,085	18,007	2.36	3,198,328	115	6.39
2015	16,571	78,491,700	18,753	2.39	3,322,660	145	7.73
2016	17,071	81,527,193	19,482	2.39	3,442,222	140	7.19
2017	17,119	82,218,762	19,497	2.37	3,447,201	149	7.64
2018	17,171	79,755,132	19,670	2.47	3,437,573	245	12.46
2019	16,401	75,419,311	18,678	2.48	2,459,220	169	9.05
2020	240	18,893,063	243	0.13	5,511	0	0.00
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
2008	3,472	49,770,080	3,827	0.77	666,996	*****	*****
2009	4,028	49,221,341	4,531	0.92	777,213	*****	*****
2010	11,133	64,695,992	12,322	1.90	2,210,187	*****	*****
2011	13,422	64,536,555	15,026	2.33	2,708,344	*****	*****
2012	14,119	66,243,694	15,784	2.38	2,848,778	*****	*****
2013	15,538	73,174,971	17,399	2.38	3,113,992	*****	*****
2014	15,931	76,383,085	18,007	2.36	3,212,126	11	0.61
2015	16,571	78,491,700	18,753	2.39	3,338,941	18	0.96
2016	17,071	81,527,193	19,482	2.39	3,458,462	11	0.56
2017	17,119	82,218,762	19,497	2.37	3,464,319	12	0.62
2018	17,171	79,755,132	19,670	2.47	3,469,828	11	0.56
2019	16,401	75,419,311	18,678	2.48	2,478,499	11	0.59
2020	240	18,893,063	243	0.13	5,511	0	0.00

[1]Some patients had multiple types of keratoplasty during the study period. Thus, the sum of patients across all types of keratoplasty is greater than the count of patients in the "Any keratoplasty"

[2]Eligible Members and Member-Years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period

[3]Patients with both fungal keratitis diagnosis and antifungal medications within greater than 90 days of one another are not included in outcome counts for "Fungal keratitis diagnosis AND antifungal medications." Therefore, this combined outcome might not include all instances of procedures that resulted in both individual outcomes

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented

Table 4. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Sex

Sex	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Anterior lamellar keratoplasty							
Fungal keratitis diagnosis							
Female	3,452	108,789,826	3,864	0.36	695,055	11	2.85
Male	3,015	101,613,494	3,385	0.33	599,918	14	4.14
Antifungal medications (15+ days)							
Female	3,452	108,789,826	3,864	0.36	692,547	34	8.80
Male	3,015	101,613,494	3,385	0.33	597,087	33	9.75
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
Female	3,452	108,789,826	3,864	0.36	691,351	41	10.61
Male	3,015	101,613,494	3,385	0.33	595,987	41	12.11
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
Female	3,452	108,789,826	3,864	0.36	696,248	*****	*****
Male	3,015	101,613,494	3,385	0.33	601,004	*****	*****
Penetrating keratoplasty							
Fungal keratitis diagnosis							
Female	27,981	108,789,826	35,607	3.27	6,403,864	203	5.70
Male	24,969	101,613,494	31,510	3.10	5,612,059	197	6.25
Antifungal medications (15+ days)							
Female	27,981	108,789,826	35,607	3.27	6,361,132	551	15.47
Male	24,969	101,613,494	31,510	3.10	5,573,894	494	15.68
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
Female	27,981	108,789,826	35,607	3.27	6,344,363	667	18.73
Male	24,969	101,613,494	31,510	3.10	5,558,261	607	19.26
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
Female	27,981	108,789,826	35,607	3.27	6,418,792	86	2.42
Male	24,969	101,613,494	31,510	3.10	5,626,572	80	2.54
Endothelial keratoplasty							
Fungal keratitis diagnosis							
Female	51,776	108,789,826	71,795	6.60	12,400,823	105	1.46
Male	32,013	101,613,494	43,735	4.30	7,482,409	62	1.42

Table 4. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Sex

Sex	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Antifungal medications (15+ days)							
Female	51,776	108,789,826	71,795	6.60	12,404,060	101	1.41
Male	32,013	101,613,494	43,735	4.30	7,482,813	72	1.65
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
Female	51,776	108,789,826	71,795	6.60	12,389,206	197	2.74
Male	32,013	101,613,494	43,735	4.30	7,473,968	128	2.93
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
Female	51,776	108,789,826	71,795	6.60	12,415,598	*****	*****
Male	32,013	101,613,494	43,735	4.30	7,491,231	*****	*****
Any keratoplasty							
Fungal keratitis diagnosis							
Female	76,378	108,789,826	107,626	9.89	18,670,502	307	2.85
Male	54,950	101,613,494	75,957	7.48	13,077,708	262	3.45
Antifungal medications (15+ days)							
Female	76,378	108,789,826	107,626	9.89	18,631,781	658	6.11
Male	54,950	101,613,494	75,957	7.48	13,041,201	567	7.46
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
Female	76,378	108,789,826	107,626	9.89	18,600,665	871	8.09
Male	54,950	101,613,494	75,957	7.48	13,016,547	740	9.74
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
Female	76,378	108,789,826	107,626	9.89	18,699,749	93	0.86
Male	54,950	101,613,494	75,957	7.48	13,101,228	85	1.12
Anterior lamellar keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
Female	3,447	108,789,815	3,857	0.35	694,252	*****	*****
Male	3,008	101,613,487	3,377	0.33	598,939	*****	*****
Antifungal medications (15+ days)							
Female	3,447	108,789,815	3,857	0.35	691,346	33	8.56
Male	3,008	101,613,487	3,377	0.33	595,833	33	9.77

Table 4. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Sex

Sex	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
Female	3,447	108,789,815	3,857	0.35	690,548	38	9.85
Male	3,008	101,613,487	3,377	0.33	595,008	39	11.55
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
Female	3,447	108,789,815	3,857	0.35	695,047	*****	*****
Male	3,008	101,613,487	3,377	0.33	599,750	*****	*****
Penetrating keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
Female	27,889	108,789,815	35,435	3.26	6,385,394	130	3.67
Male	24,884	101,613,487	31,349	3.09	5,600,109	110	3.51
Antifungal medications (15+ days)							
Female	27,889	108,789,815	35,435	3.26	6,340,802	490	13.83
Male	24,884	101,613,487	31,349	3.09	5,557,210	442	14.10
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
Female	27,889	108,789,815	35,435	3.26	6,330,463	567	16.00
Male	24,884	101,613,487	31,349	3.09	5,548,734	507	16.17
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
Female	27,889	108,789,815	35,435	3.26	6,394,589	53	1.50
Male	24,884	101,613,487	31,349	3.09	5,607,853	43	1.37
Endothelial keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
Female	51,771	108,789,815	71,780	6.60	12,398,841	101	1.41
Male	32,010	101,613,487	43,725	4.30	7,481,146	59	1.35
Antifungal medications (15+ days)							
Female	51,771	108,789,815	71,780	6.60	12,401,719	99	1.38
Male	32,010	101,613,487	43,725	4.30	7,481,069	72	1.65
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
Female	51,771	108,789,815	71,780	6.60	12,387,231	192	2.67
Male	32,010	101,613,487	43,725	4.30	7,472,705	125	2.86

Table 4. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Sex

Sex	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
Female	51,771	108,789,815	71,780	6.60	12,413,250	*****	*****
Male	32,010	101,613,487	43,725	4.30	7,489,487	*****	*****
Any keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
Female	76,288	108,789,815	107,439	9.88	18,650,441	229	2.13
Male	54,868	101,613,487	75,780	7.46	13,063,735	171	2.26
Antifungal medications (15+ days)							
Female	76,288	108,789,815	107,439	9.88	18,609,302	595	5.54
Male	54,868	101,613,487	75,780	7.46	13,021,814	515	6.80
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
Female	76,288	108,789,815	107,439	9.88	18,585,181	765	7.12
Male	54,868	101,613,487	75,780	7.46	13,004,997	636	8.39
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
Female	76,288	108,789,815	107,439	9.88	18,673,390	59	0.55
Male	54,868	101,613,487	75,780	7.46	13,079,806	48	0.63

[1] Some patients had multiple types of keratoplasty during the study period. Thus, the sum of patients across all types of keratoplasty is greater than the count of patients in the "Any keratoplasty" cohort

[2] Eligible Members and Member-Years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period

[3] Patients with both fungal keratitis diagnosis and antifungal medications within greater than 90 days of one another are not included in outcome counts for "Fungal keratitis diagnosis AND antifungal medications." Therefore, this combined outcome might not include all instances of procedures that resulted in both individual outcomes

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented

Table 5. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Age Group

Age Group (Years)	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Anterior lamellar keratoplasty							
Fungal keratitis diagnosis							
0-17	101	40,055,403	119	0.03	20,053	0	0.00
18-44	1,244	84,763,736	1,388	0.16	242,241	*****	*****
45-64	1,570	57,388,079	1,765	0.31	311,367	*****	*****
65-74	1,665	36,595,024	1,864	0.51	334,303	12	6.44
75-84	1,384	19,740,766	1,514	0.77	276,944	*****	*****
85+	552	9,074,028	599	0.66	110,065	*****	*****
Antifungal medications (15+ days)							
0-17	101	40,055,403	119	0.03	20,053	0	0.00
18-44	1,244	84,763,736	1,388	0.16	240,973	11	7.93
45-64	1,570	57,388,079	1,765	0.31	310,364	14	7.93
65-74	1,665	36,595,024	1,864	0.51	332,982	23	12.34
75-84	1,384	19,740,766	1,514	0.77	276,248	*****	*****
85+	552	9,074,028	599	0.66	109,014	*****	*****
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
0-17	101	40,055,403	119	0.03	20,053	0	0.00
18-44	1,244	84,763,736	1,388	0.16	240,972	*****	*****
45-64	1,570	57,388,079	1,765	0.31	309,891	17	9.63
65-74	1,665	36,595,024	1,864	0.51	331,503	31	16.63
75-84	1,384	19,740,766	1,514	0.77	276,102	13	8.59
85+	552	9,074,028	599	0.66	108,817	*****	*****
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
0-17	101	40,055,403	119	0.03	20,053	0	0.00
18-44	1,244	84,763,736	1,388	0.16	242,241	*****	*****
45-64	1,570	57,388,079	1,765	0.31	311,835	*****	*****
65-74	1,665	36,595,024	1,864	0.51	335,771	*****	*****
75-84	1,384	19,740,766	1,514	0.77	277,090	*****	*****
85+	552	9,074,028	599	0.66	110,262	0	0.00

Table 5. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Age Group

Age Group (Years)	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Penetrating keratoplasty							
Fungal keratitis diagnosis							
0-17	329	40,055,403	422	0.11	68,826	*****	*****
18-44	7,357	84,763,736	9,088	1.07	1,567,453	*****	*****
45-64	11,736	57,388,079	14,954	2.61	2,611,848	112	7.49
65-74	15,072	36,595,024	18,596	5.08	3,365,796	136	7.31
75-84	13,802	19,740,766	16,694	8.46	3,056,678	92	5.51
85+	6,257	9,074,028	7,363	8.11	1,345,322	30	4.07
Antifungal medications (15+ days)							
0-17	329	40,055,403	422	0.11	68,341	*****	*****
18-44	7,357	84,763,736	9,088	1.07	1,561,307	*****	*****
45-64	11,736	57,388,079	14,954	2.61	2,589,891	288	19.26
65-74	15,072	36,595,024	18,596	5.08	3,340,241	336	18.07
75-84	13,802	19,740,766	16,694	8.46	3,038,221	241	14.44
85+	6,257	9,074,028	7,363	8.11	1,337,025	92	12.49
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
0-17	329	40,055,403	422	0.11	68,341	*****	*****
18-44	7,357	84,763,736	9,088	1.07	1,559,284	*****	*****
45-64	11,736	57,388,079	14,954	2.61	2,581,243	350	23.41
65-74	15,072	36,595,024	18,596	5.08	3,328,297	417	22.42
75-84	13,802	19,740,766	16,694	8.46	3,030,709	295	17.67
85+	6,257	9,074,028	7,363	8.11	1,334,750	108	14.67
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
0-17	329	40,055,403	422	0.11	68,826	*****	*****
18-44	7,357	84,763,736	9,088	1.07	1,569,226	*****	*****
45-64	11,736	57,388,079	14,954	2.61	2,619,179	48	3.21
65-74	15,072	36,595,024	18,596	5.08	3,377,148	53	2.85
75-84	13,802	19,740,766	16,694	8.46	3,063,558	38	2.28
85+	6,257	9,074,028	7,363	8.11	1,347,427	13	1.77

Table 5. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Age Group

Age Group (Years)	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Endothelial keratoplasty							
Fungal keratitis diagnosis							
0-17	33	40,055,403	42	0.01	7,397	0	0.00
18-44	811	84,763,736	990	0.12	164,200	*****	*****
45-64	9,079	57,388,079	12,785	2.23	2,032,731	*****	*****
65-74	32,149	36,595,024	44,908	12.27	7,638,225	46	1.02
75-84	31,497	19,740,766	40,796	20.67	7,180,778	61	1.50
85+	13,243	9,074,028	16,009	17.64	2,859,901	40	2.50
Antifungal medications (15+ days)							
0-17	33	40,055,403	42	0.01	7,397	0	0.00
18-44	811	84,763,736	990	0.12	164,226	*****	*****
45-64	9,079	57,388,079	12,785	2.23	2,033,289	*****	*****
65-74	32,149	36,595,024	44,908	12.27	7,637,621	60	1.34
75-84	31,497	19,740,766	40,796	20.67	7,181,720	71	1.74
85+	13,243	9,074,028	16,009	17.64	2,862,620	25	1.56
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
0-17	33	40,055,403	42	0.01	7,397	0	0.00
18-44	811	84,763,736	990	0.12	164,027	*****	*****
45-64	9,079	57,388,079	12,785	2.23	2,031,190	*****	*****
65-74	32,149	36,595,024	44,908	12.27	7,631,424	101	2.25
75-84	31,497	19,740,766	40,796	20.67	7,172,416	126	3.09
85+	13,243	9,074,028	16,009	17.64	2,856,720	62	3.87
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
0-17	33	40,055,403	42	0.01	7,397	0	0.00
18-44	811	84,763,736	990	0.12	164,399	0	0.00
45-64	9,079	57,388,079	12,785	2.23	2,034,830	*****	*****
65-74	32,149	36,595,024	44,908	12.27	7,644,405	*****	*****
75-84	31,497	19,740,766	40,796	20.67	7,190,042	*****	*****
85+	13,243	9,074,028	16,009	17.64	2,865,756	*****	*****

Table 5. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Age Group

Age Group (Years)	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Any keratoplasty							
Fungal keratitis diagnosis							
0-17	427	40,055,403	556	0.14	90,777	*****	*****
18-44	8,721	84,763,736	11,009	1.30	1,877,367	*****	*****
45-64	20,511	57,388,079	28,442	4.96	4,721,761	132	4.64
65-74	45,343	36,595,024	63,392	17.32	10,879,574	183	2.89
75-84	43,076	19,740,766	57,039	28.89	10,054,434	153	2.68
85+	18,575	9,074,028	23,145	25.51	4,124,297	69	2.98
Antifungal medications (15+ days)							
0-17	427	40,055,403	556	0.14	90,292	*****	*****
18-44	8,721	84,763,736	11,009	1.30	1,870,839	*****	*****
45-64	20,511	57,388,079	28,442	4.96	4,700,038	310	10.90
65-74	45,343	36,595,024	63,392	17.32	10,854,668	396	6.25
75-84	43,076	19,740,766	57,039	28.89	10,038,406	305	5.35
85+	18,575	9,074,028	23,145	25.51	4,118,739	119	5.14
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
0-17	427	40,055,403	556	0.14	90,292	*****	*****
18-44	8,721	84,763,736	11,009	1.30	1,868,616	*****	*****
45-64	20,511	57,388,079	28,442	4.96	4,689,289	390	13.71
65-74	45,343	36,595,024	63,392	17.32	10,836,267	522	8.23
75-84	43,076	19,740,766	57,039	28.89	10,021,953	415	7.28
85+	18,575	9,074,028	23,145	25.51	4,110,795	172	7.43
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
0-17	427	40,055,403	556	0.14	90,777	*****	*****
18-44	8,721	84,763,736	11,009	1.30	1,879,339	*****	*****
45-64	20,511	57,388,079	28,442	4.96	4,731,190	50	1.76
65-74	45,343	36,595,024	63,392	17.32	10,897,379	55	0.87
75-84	43,076	19,740,766	57,039	28.89	10,070,241	43	0.75
85+	18,575	9,074,028	23,145	25.51	4,132,051	15	0.65

Table 5. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Age Group

Age Group (Years)	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Anterior lamellar keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
0-17	101	40,055,403	119	0.03	20,053	0	0.00
18-44	1,243	84,763,733	1,387	0.16	242,041	*****	*****
45-64	1,563	57,388,069	1,758	0.31	310,589	*****	*****
65-74	1,664	36,595,018	1,862	0.51	334,301	*****	*****
75-84	1,382	19,740,761	1,510	0.76	276,342	*****	*****
85+	551	9,074,027	598	0.66	109,865	*****	*****
Antifungal medications (15+ days)							
0-17	101	40,055,403	119	0.03	20,053	0	0.00
18-44	1,243	84,763,733	1,387	0.16	240,773	11	7.93
45-64	1,563	57,388,069	1,758	0.31	309,311	13	7.39
65-74	1,664	36,595,018	1,862	0.51	332,582	23	12.35
75-84	1,382	19,740,761	1,510	0.76	275,646	*****	*****
85+	551	9,074,027	598	0.66	108,814	*****	*****
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
0-17	101	40,055,403	119	0.03	20,053	0	0.00
18-44	1,243	84,763,733	1,387	0.16	240,772	*****	*****
45-64	1,563	57,388,069	1,758	0.31	309,113	14	7.96
65-74	1,664	36,595,018	1,862	0.51	331,501	29	15.57
75-84	1,382	19,740,761	1,510	0.76	275,500	13	8.61
85+	551	9,074,027	598	0.66	108,617	*****	*****
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
0-17	101	40,055,403	119	0.03	20,053	0	0.00
18-44	1,243	84,763,733	1,387	0.16	242,041	*****	*****
45-64	1,563	57,388,069	1,758	0.31	310,782	*****	*****
65-74	1,664	36,595,018	1,862	0.51	335,371	*****	*****
75-84	1,382	19,740,761	1,510	0.76	276,488	*****	*****
85+	551	9,074,027	598	0.66	110,062	0	0.00

Table 5. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Age Group

Age Group (Years)	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Penetrating keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
0-17	328	40,055,403	421	0.11	68,825	0	0.00
18-44	7,346	84,763,733	9,057	1.07	1,565,519	19	2.10
45-64	11,681	57,388,069	14,862	2.59	2,604,685	60	4.04
65-74	15,007	36,595,018	18,479	5.05	3,355,649	73	3.95
75-84	13,760	19,740,761	16,626	8.42	3,048,398	66	3.97
85+	6,240	9,074,027	7,339	8.09	1,342,427	22	3.00
Antifungal medications (15+ days)							
0-17	328	40,055,403	421	0.11	68,340	*****	*****
18-44	7,346	84,763,733	9,057	1.07	1,558,956	*****	*****
45-64	11,681	57,388,069	14,862	2.59	2,580,406	256	17.23
65-74	15,007	36,595,018	18,479	5.05	3,327,224	293	15.86
75-84	13,760	19,740,761	16,626	8.42	3,028,397	224	13.47
85+	6,240	9,074,027	7,339	8.09	1,334,689	79	10.76
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
0-17	328	40,055,403	421	0.11	68,340	*****	*****
18-44	7,346	84,763,733	9,057	1.07	1,557,712	*****	*****
45-64	11,681	57,388,069	14,862	2.59	2,575,512	290	19.51
65-74	15,007	36,595,018	18,479	5.05	3,321,173	339	18.35
75-84	13,760	19,740,761	16,626	8.42	3,023,608	262	15.76
85+	6,240	9,074,027	7,339	8.09	1,332,852	93	12.67
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
0-17	328	40,055,403	421	0.11	68,825	0	0.00
18-44	7,346	84,763,733	9,057	1.07	1,566,613	*****	*****
45-64	11,681	57,388,069	14,862	2.59	2,608,838	25	1.68
65-74	15,007	36,595,018	18,479	5.05	3,361,222	27	1.46
75-84	13,760	19,740,761	16,626	8.42	3,052,648	28	1.68
85+	6,240	9,074,027	7,339	8.09	1,344,296	*****	*****

Table 5. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Age Group

Age Group (Years)	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Endothelial keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
0-17	33	40,055,403	42	0.01	7,397	0	0.00
18-44	811	84,763,733	990	0.12	164,200	*****	*****
45-64	9,078	57,388,069	12,780	2.23	2,032,152	*****	*****
65-74	32,145	36,595,018	44,899	12.27	7,637,486	41	0.91
75-84	31,495	19,740,761	40,789	20.66	7,179,651	60	1.47
85+	13,241	9,074,027	16,005	17.64	2,859,101	40	2.50
Antifungal medications (15+ days)							
0-17	33	40,055,403	42	0.01	7,397	0	0.00
18-44	811	84,763,733	990	0.12	164,226	*****	*****
45-64	9,078	57,388,069	12,780	2.23	2,032,717	*****	*****
65-74	32,145	36,595,018	44,899	12.27	7,636,122	60	1.34
75-84	31,495	19,740,761	40,789	20.66	7,180,506	71	1.74
85+	13,241	9,074,027	16,005	17.64	2,861,820	25	1.56
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
0-17	33	40,055,403	42	0.01	7,397	0	0.00
18-44	811	84,763,733	990	0.12	164,027	*****	*****
45-64	9,078	57,388,069	12,780	2.23	2,030,618	*****	*****
65-74	32,145	36,595,018	44,899	12.27	7,630,685	96	2.14
75-84	31,495	19,740,761	40,789	20.66	7,171,289	125	3.06
85+	13,241	9,074,027	16,005	17.64	2,855,920	62	3.87
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
0-17	33	40,055,403	42	0.01	7,397	0	0.00
18-44	811	84,763,733	990	0.12	164,399	0	0.00
45-64	9,078	57,388,069	12,780	2.23	2,034,251	0	0.00
65-74	32,145	36,595,018	44,899	12.27	7,642,906	*****	*****
75-84	31,495	19,740,761	40,789	20.66	7,188,828	*****	*****
85+	13,241	9,074,027	16,005	17.64	2,864,956	*****	*****

Table 5. Summary of Outcomes for Keratoplasty Recipients in the Sentinel Distributed Database (SDD) between January 1, 2008 and February 29, 2020, by Age Group

Age Group (Years)	Number of Patients[1]	Eligible Members[2]	Number of Exposure Procedures	Number of Exposures per 10,000 Eligible Members	Days At Risk	Number of Exposures with an Event[3]	Events per 1,000 Exposures
Any keratoplasty with no keratitis in 90 days prior							
Fungal keratitis diagnosis							
0-17	426	40,055,403	555	0.14	90,776	0	0.00
18-44	8,710	84,763,733	10,978	1.30	1,875,433	21	1.91
45-64	20,456	57,388,069	28,341	4.94	4,713,443	78	2.75
65-74	45,280	36,595,018	63,265	17.29	10,868,687	114	1.80
75-84	43,037	19,740,761	56,964	28.86	10,045,435	126	2.21
85+	18,557	9,074,027	23,116	25.47	4,120,402	61	2.64
Antifungal medications (15+ days)							
0-17	426	40,055,403	555	0.14	90,291	*****	*****
18-44	8,710	84,763,733	10,978	1.30	1,868,488	*****	*****
45-64	20,456	57,388,069	28,341	4.94	4,689,206	276	9.74
65-74	45,280	36,595,018	63,265	17.29	10,839,952	353	5.58
75-84	43,037	19,740,761	56,964	28.86	10,027,776	288	5.06
85+	18,557	9,074,027	23,116	25.47	4,115,403	106	4.59
Fungal keratitis diagnosis OR antifungal medications (15+ days)							
0-17	426	40,055,403	555	0.14	90,291	*****	*****
18-44	8,710	84,763,733	10,978	1.30	1,867,044	*****	*****
45-64	20,456	57,388,069	28,341	4.94	4,682,410	327	11.54
65-74	45,280	36,595,018	63,265	17.29	10,828,403	438	6.92
75-84	43,037	19,740,761	56,964	28.86	10,014,133	381	6.69
85+	18,557	9,074,027	23,116	25.47	4,107,897	157	6.79
Fungal keratitis diagnosis AND antifungal medications (15+ days)							
0-17	426	40,055,403	555	0.14	90,776	0	0.00
18-44	8,710	84,763,733	10,978	1.30	1,876,726	*****	*****
45-64	20,456	57,388,069	28,341	4.94	4,719,495	26	0.92
65-74	45,280	36,595,018	63,265	17.29	10,879,754	29	0.46
75-84	43,037	19,740,761	56,964	28.86	10,058,525	33	0.58
85+	18,557	9,074,027	23,116	25.47	4,127,920	*****	*****

[1] Some patients had multiple types of keratoplasty during the study period. Thus, the sum of patients across all types of keratoplasty is greater than the count of patients in the "Any keratoplasty" cohort

[2] Eligible Members and Member-Years are reflective of the number of patients that met all cohort entry criteria on at least one day during the query period

[3] Patients with both fungal keratitis diagnosis and antifungal medications within greater than 90 days of one another are not included in outcome counts for "Fungal keratitis diagnosis AND antifungal medications."
Therefore, this combined outcome might not include all instances of procedures that resulted in both individual outcomes

*****Data are not presented in these cells due to a small sample size or to assure a small cell cannot be recalculated through the cells presented

Appendix A. Start and End Dates for Each Data Partner (DP) up to Request End Date (February 29, 2020)

DP ID	Start Date[1]	End Date[1]
DP01	1/1/2000	2/28/2019
DP02	1/1/2000	1/31/2019
DP03	1/1/2004	8/31/2019
DP04	1/1/2008	2/29/2020
DP05	1/1/2006	1/31/2020
DP06	1/1/2000	12/31/2017
DP07	1/1/2010	12/31/2019
DP08	1/1/2000	7/31/2019
DP09	6/1/2007	10/31/2019
DP10	1/1/2000	4/30/2018
DP11	1/1/2005	7/31/2018
DP12	1/1/2000	4/30/2019
DP13	1/1/2000	6/30/2019
DP14	1/1/2008	9/30/2019
DP15	1/1/2000	3/31/2019
DP16	1/1/2012	6/30/2018

[1]The start and end dates are based on the minimum and maximum dates within each DP. The month with the maximum date must have at least 80% of the number of records in the previous month.

Appendix B. List of Current Procedural Terminology, Fourth Edition (CPT-4) Codes Used to Define Exposures in this Request

Code	Description	Code Category	Code Type
Anterior Lamellar Keratoplasty			
65710	Keratoplasty (corneal transplant); anterior lamellar	Procedure	CPT-4
Penetrating Keratoplasty			
65730	Keratoplasty (corneal transplant); penetrating (except in aphakia or pseudophakia)	Procedure	CPT-4
65750	Keratoplasty (corneal transplant); penetrating (in aphakia)	Procedure	CPT-4
65755	Keratoplasty (corneal transplant); penetrating (in pseudophakia)	Procedure	CPT-4
Endothelial Keratoplasty			
65756	Keratoplasty (corneal transplant); endothelial	Procedure	CPT-4

Code	Description	Code Category	Code Type
	Keratitis		
370.05	Mycotic corneal ulcer	Diagnosis	ICD-9-CM
H16.061	Mycotic corneal ulcer, right eye	Diagnosis	ICD-10-CM
H16.062	Mycotic corneal ulcer, left eye	Diagnosis	ICD-10-CM
H16.063	Mycotic corneal ulcer, bilateral	Diagnosis	ICD-10-CM
H16.069	Mycotic corneal ulcer, unspecified eye	Diagnosis	ICD-10-CM

Appendix D. List of Generic and Brand Name Medical Products Used to Define Outcomes in this Request

Generic Name	Brand Name
Antifungal Medications	
amphotericin B	Amphocin
voriconazole	Vfend
voriconazole	Vfend IV
natamycin	Natacyn
voriconazole	voriconazole
amphotericin B liposome	AmBisome
amphotericin B	amphotericin B (bulk)
amphotericin B	amphotericin B
voriconazole	voriconazole (bulk)
amphotericin B lipid complex	Abelcet
amphotericin B cholesteryl sulfate	Amphotec

Appendix E. Specifications Defining Parameters for this Request

The Center for Biologics Evaluation and Research (CBER) has requested execution of the Cohort Identification and Descriptive Analysis (CIDA) tool, version 8.1.0 with ad hoc programming, to estimate counts and proportions of postoperative fungal keratitis, antifungal medication use, and both, among patients who have received keratoplasty procedures in the Sentinel Distributed Database (SDD).

Query period:	January 1, 2008 - February 29, 2020
Coverage requirement:	Medical and Drug Coverage
Pre-index enrollment requirement:	0
Post-index enrollment requirement:	0
Enrollment gap:	45
Age group restrictions:	0-17, 18-44, 45-64, 65-74, 75-84, ≥85
Sex restrictions:	Female, Male, Other
Stratifications:	Overll, Age, Sex, Year
Envelope macro:	No reclassification of encounters during an inpatient stay
Exposure washout:	None

	Exposure					Inclusion / Exclusion						
Scenario	Exposure (index)	Exposure care setting	Cohort definition	Exposure episode length	Censor enrollment at earliest evidence of:	Condition	Include/ exclude:	Evaluation period start	Evaluation period end	Inclusion/ Exclusion care setting	Inclusion/Exclusion evaluation should search for evidence of:	Number of instances the criterion should be found in evaluation period
1	Anterior lamellar keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
2	Anterior lamellar keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
3	Anterior lamellar keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
4	Anterior lamellar keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---

Appendix E. Specifications Defining Parameters for this Request

Scenario	Exposure (index)	Exposure care setting	Cohort definition	Exposure episode length	Censor enrollment at earliest evidence of:	Condition	Include/ exclude:	Evaluation period start	Evaluation period end	Inclusion/ Exclusion care setting	Inclusion/Exclusion evaluation should search for evidence of:	Number of instances the criterion should be found in evaluation period
		Exposure						**Inclusion / Exclusion**				
5	Penetrating keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
6	Penetrating keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
7	Penetrating keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
8	Penetrating keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
9	Endothelial keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
10	Endothelial keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
11	Endothelial keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
12	Endothelial keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---

	Exposure					Inclusion / Exclusion						
Scenario	Exposure (index)	Exposure care setting	Cohort definition	Exposure episode length	Censor enrollment at earliest evidence of:	Condition	Include/ exclude:	Evaluation period start	Evaluation period end	Inclusion/ Exclusion care setting	Inclusion/Exclusion evaluation should search for evidence of:	Number of instances the criterion should be found in evaluation period
13	Any keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
14	Any keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
15	Any keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
16	Any keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	---	---	---	---	---	---	---
17	Anterior lamellar keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
18	Anterior lamellar keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
19	Anterior lamellar keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
20	Anterior lamellar keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1

Appendix E. Specifications Defining Parameters for this Request

Appendix E. Specifications Defining Parameters for this Request

	Exposure					Inclusion / Exclusion						
Scenario	Exposure (index)	Exposure care setting	Cohort definition	Exposure episode length	Censor enrollment at earliest evidence of:	Condition	Include/ exclude:	Evaluation period start	Evaluation period end	Inclusion/ Exclusion care setting	Inclusion/Exclusion evaluation should search for evidence of:	Number of instances the criterion should be found in evaluation period
21	Penetrating keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
22	Penetrating keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
23	Penetrating keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
24	Penetrating keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
25	Endothelial keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
26	Endothelial keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
27	Endothelial keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
28	Endothelial keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1

Appendix E. Specifications Defining Parameters for this Request

	Exposure					Inclusion / Exclusion						
Scenario	Exposure (index)	Exposure care setting	Cohort definition	Exposure episode length	Censor enrollment at earliest evidence of:	Condition	Include/ exclude:	Evaluation period start	Evaluation period end	Inclusion/ Exclusion care setting	Inclusion/Exclusion evaluation should search for evidence of:	Number of instances the criterion should be found in evaluation period
29	Any keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
30	Any keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
31	Any keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1
32	Any keratoplasty	Any	All valid episodes	200 days	Death; Data Partner End Date; Query End Date	Fungal keratitis diagnosis	Exclude	-90	-1	Any	Admission date of the diagnosis	1

Appendix E. Specifications Defining Parameters for this Request

Scenario	Outcome	Outcome Definition	Time-to-Outcome	Gap allowed for antifunal episodes	Combo Outcome Definition	Outcome care setting	Blackout period	Baseline Characteristics
	Outcome							**Baseline Characteristics**
1	Fungal keratitis diagnosis	First valid outcome only	Calculate follow-up time from the closest exposure episode	N/A	N/A	Any	0	---
2	Antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
3	Fungal keratitis diagnosis or antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
4	Fungal keratitis diagnosis and antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	Time window: 90 days between events. Event order: either or. Final event date: first event date.	Any	0	---
5	Fungal keratitis diagnosis	First valid outcome only	Calculate follow-up time from the closest exposure episode	N/A	N/A	Any	0	---
6	Antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
7	Fungal keratitis diagnosis or antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
8	Fungal keratitis diagnosis and antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	Time window: 90 days between events. Event order: either or. Final event date: first event date.	Any	0	---

Appendix E. Specifications Defining Parameters for this Request

Scenario	Outcome	Outcome Definition	Time-to-Outcome	Outcome Gap allowed for antifunal episodes	Combo Outcome Definition	Outcome care setting	Blackout period	Baseline Characteristics Baseline Characteristics
9	Fungal keratitis diagnosis	First valid outcome only	Calculate follow-up time from the closest exposure episode	N/A	N/A	Any	0	---
10	Antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
11	Fungal keratitis diagnosis or antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
12	Fungal keratitis diagnosis and antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	Time window: 90 days between events Event order: either or. Final event date: first event date.	Any	0	---
13	Fungal keratitis diagnosis	First valid outcome only	Calculate follow-up time from the closest exposure episode	N/A	N/A	Any	0	See Appendix F
14	Antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	See Appendix F
15	Fungal keratitis diagnosis or antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	See Appendix F
16	Fungal keratitis diagnosis and antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	Time window: 90 days between events Event order: either or. Final event date: first event date.	Any	0	See Appendix F

Appendix E. Specifications Defining Parameters for this Request

Scenario	Outcome							Baseline Characteristics
								Baseline Characteristics
	Outcome	Outcome Definition	Time-to-Outcome	Gap allowed for antifunal episodes	Combo Outcome Definition	Outcome care setting	Blackout period	Baseline Characteristics
17	Fungal keratitis diagnosis	First valid outcome only	Calculate follow-up time from the closest exposure episode	N/A	N/A	Any	0	---
18	Antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
19	Fungal keratitis diagnosis or antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
20	Fungal keratitis diagnosis and antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	Time window: 90 days between events. Event order: either or. Final event date: first event date.	Any	0	---
21	Fungal keratitis diagnosis	First valid outcome only	Calculate follow-up time from the closest exposure episode	N/A	N/A	Any	0	---
22	Antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
23	Fungal keratitis diagnosis or antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
24	Fungal keratitis diagnosis and antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	Time window: 90 days between events. Event order: either or. Final event date: first event date.	Any	0	---

Appendix E. Specifications Defining Parameters for this Request

Scenario	Outcome	Outcome Definition	Time-to-Outcome	Gap allowed for antifunal episodes	Combo Outcome Definition	Outcome care setting	Blackout period	Baseline Characteristics
25	Fungal keratitis diagnosis	First valid outcome only	Calculate follow-up time from the closest exposure episode	N/A	N/A	Any	0	---
26	Antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
27	Fungal keratitis diagnosis or antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	---
28	Fungal keratitis diagnosis and antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	Time window: 90 days between events Event order: either or. Final event date: first event date.	Any	0	---
29	Fungal keratitis diagnosis	First valid outcome only	Calculate follow-up time from the closest exposure episode	N/A	N/A	Any	0	See Appendix F
30	Antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	See Appendix F
31	Fungal keratitis diagnosis or antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	N/A	Any	0	See Appendix F
32	Fungal keratitis diagnosis and antifungal medications (15+ days)	First valid outcome only	Calculate follow-up time from the closest exposure episode	3	Time window: 90 days between events Event order: either or. Final event date: first event date.	Any	0	See Appendix F

Note: International Classification of Diseases, Ninth Revision (ICD-9), International Classification of Diseases, Tenth Revision (ICD-10), Healthcare Common Procedure Coding System (HCPCS), and Current Procedural Terminology (CPT) codes are provided by Optum360. National Drug Codes (NDCs) are checked against First Data Bank's "National Drug Data File (NDDF®) Plus"

Appendix F. Specifications Defining Baseline Characteristics in this Request

Baseline Characteristics

Baseline characteristic	Baseline Period Start	Baseline Period End	Principal diagnosis position	Number of instances the covariate should be found in evaluation period
Anterior lamellar keratoplasty	Day 0	Day 0	Any	At least 1
Penetrating keratoplasty	Day 0	Day 0	Any	At least 1
Endothelial keratoplasty	Day 0	Day 0	Any	At least 1

Type 2 Design Diagram
(Cohort definition: multiple index events allowed per patient)

Cohort entry date: *Keratoplasty Procedure* (Day 0)

Subsequent index date

1/1/2008   2/29/2020

Enrollment requirement *Required coverage type*

Pre-index: [-90, 0] *Medical and Drug Coverage*

Allowed coverage gap   45 days

Exclusion criteria*   [-90, -1]

Baseline Characteristics**

A

B

C: [-183, 0]

Episode length***   Capture evidence of fungal outcomes**** within a fixed risk window of 200 days

Capture evidence of fungal outcomes**** within a fixed risk window of 200 days

*Exclusion Criteria
Fungal keratitis diagnosis

**Baseline Characteristics
Window A: Age, sex, race, ethnicity, year
Window B: Keratoplasty Type Distribution
Window C: Health Service Utilization Intensity

***Episode Length
This request has been custom programmed to 1) remove the implicit washout when using **fixed risk windows (ITT)** and 2) truncate exposure episodes upon subsequent exposure episodes

****Fungal outcomes
1. Fungal keratitis diagnosis,
2. Antifungal medications (15+ days),
3. Fungal keratitis diagnosis **OR** antifungal medications (15+ days), or
4. Fungal keratitis diagnosis **AND** antifungal medications (15+ days)