Prevalence of Corneal Dystrophies in the United States: Estimates from Claims Data

David C. Musch,[1,2] *Leslie M. Niziol,*[1] *Joshua D. Stein,*[1] *Roheena M. Kamyar,*[1,3] *and Alan Sugar*[1]

Purpose. To estimate the prevalence of corneal dystrophies.

Methods. Records of almost 8 million enrollees in a national managed-care network throughout the United States who had an eye care visit in 2001 to 2009 were searched for a recording of corneal dystrophy on a claim submitted by an ophthalmologist or optometrist from January 1, 2001, through December 31, 2007.

Results. Unique individuals (n = 27,372) received two or more diagnoses of any type of corneal dystrophy, for an overall corneal dystrophy prevalence rate of 897 per million (10^6) covered lives. Endothelial and anterior corneal dystrophies accounted for most of the reported dystrophies, and granular corneal dystrophy was the least common, being reported in 167 enrollees. Age, sex, and race variations among the various corneal dystrophies were observed. The mean age of those with macular corneal dystrophy (47.3 years) was 15 years younger than the age of those with endothelial dystrophy (62.9 years), and females were most highly represented (68.5%) among those with lattice corneal dystrophy. Hispanics and blacks were underrepresented relative to enrollees undergoing eye care for reasons other than corneal dystrophy. Keratoplasty was most frequently coded among those with lattice dystrophy.

Conclusions. Although caveats must be considered in using claims data to estimate prevalence in a population, these data provide an indication of corneal dystrophy's prevalence within insured subjects across the United States. Variations in age, sex, and race, within and between the different types of corneal dystrophies, raise questions that warrant further study. (*Invest Ophthalmol Vis Sci.* 2011;52:6959–6963) DOI:10.1167/iovs.11-7771

Corneal dystrophies were defined by Duke-Elder as "hereditary degenerations of the cornea of unknown etiology occurring bilaterally, manifesting themselves occasionally at birth but more usually during the first or second decades and sometimes later, either stationary or slowly progressive throughout life."[1] More recently, The American Academy of Ophthalmology's Basic and Clinical Science Course's definition did not include reference to manifestation and added associative information, in defining corneal dystrophies as "a group of inherited corneal diseases that are typically bilateral, symmetric, slowly progressive, and without relationship to environmental or systemic factors."[2] Weiss et al.[3] noted exceptions to elements of these definitions, such as the lack of a hereditary component for most epithelial basement membrane dystrophies, the typical unilaterality of posterior polymorphous dystrophy, and some indications of a systemic etiology for macular corneal dystrophy. Even so, many of the corneal dystrophies are recognizable, and codes for them are included in the International Classification of Diseases, Ninth Revision Clinical Modification (ICD-9-CM).[4] Therefore, people who have these relatively uncommon conditions can be identified in large administrative health care claims databases, which allows for an evaluation of the epidemiology of corneal dystrophies.

Previous estimates of the relative frequency and importance of corneal dystrophies have relied primarily on information from two sources: corneal transplant registries and large case series from corneal surgeons. Both sources have substantial limitations, such as an evident bias toward more severe cases in transplant registries and referral and selection biases in data stemming from corneal surgeons' referral-based practices. Although administrative databases that encompass nationwide data are not immune from bias and inaccuracy, their use permits a more comprehensive look at the prevalence of corneal dystrophies over a defined time and within a defined region. We present information from a large administrative health care claims database to describe the prevalence of corneal dystrophies.

Methods

Data Source

The i3 InVision Data Mart database (Ingenix, Eden Prairie, MN) contains detailed records of all the insured in a national managed-care network throughout the United States. The dataset we accessed contains information on a subset comprising those who had one or more ICD-9-CM codes for eye-related diagnoses (360-379.9); one or more Current Procedural Terminology (CPT)[5] codes for any eye-related visits, diagnostic or therapeutic procedures (65091-68899 or 92002-92499); or any other claim submitted by an ophthalmologist or optometrist from January 1, 2001, through December 31, 2007. For each enrollee, we had access to all medical claims for ocular and nonocular conditions and sociodemographic information including age, sex, race, education level, and household net worth.

Participants and Sample Selection

Individuals were included in the analysis if records were available from at least one visit to an eye care provider (ophthalmologist or optome-

From the [1]Department of Ophthalmology and Visual Sciences, Kellogg Eye Center, and the [2]Department of Epidemiology, University of Michigan, Ann Arbor, Michigan; and the [3]Eye Center, University of Pittsburgh, Pittsburgh, Pennsylvania.

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Corresponding author: David C. Musch, University of Michigan Medical School, Dept. of Ophthalmology and Visual Sciences, Kellogg Eye Center, 1000 Wall Street, Ann Arbor, MI 48105-1912; dmusch@umich.edu.

trist) from 2001 through 2007. Two prevalence estimates were generated: the first based on requiring only one coding of the specified corneal dystrophy and the second a more conservative estimate requiring at least two consistent codings for the specific corneal dystrophy during the defined time period. Since the second estimate required two codings, a prevalence estimation for 2001 would not capture a code recorded in 2000, and so estimates were not included for 2001. Figure 1 shows the basis for our identification of enrollees who had a corneal dystrophy diagnosis (i.e., numerator data for prevalence rates), which began with 7,977,385 enrollees who had an eye-related visit between 2002 and 2007, inclusive, excluded those enrollees with noncontinuous follow-up and/or data discrepancies, and thereby resulted in 6,626,976 eligible enrollees. Of these, 27,372 had two or more codes for a corneal dystrophy, and an additional 14,250 had one such code. Denominator data relied on the average number of all covered lives in the database, with exclusion for noncontinuous follow-up and data discrepancies.

The following corneal dystrophies were identified, based on ICD-9-CM billing codes: juvenile epithelial dystrophy (Meesmann corneal dystrophy; 371.51), anterior corneal dystrophy (371.52), granular corneal dystrophy (371.53), lattice corneal dystrophy (371.54), macular corneal dystrophy (371.55), and endothelial corneal dystrophy (371.57). Individuals who had codes for the following corneal dystrophies— hereditary corneal dystrophies (371.5), corneal dystrophy, unspecified (371.50), other stromal corneal dystrophies (371.56), and other posterior corneal dystrophies (371.58)— could not be classified as a specific dystrophy and were assigned to a category called unspecified. Since we also wished to characterize the most frequent corneal therapeutic procedures performed in enrollees with corneal dystrophies from 2002 through 2007, these procedures were grouped into keratoplasty (CPT-4 codes 65710, 65730, 65750, 65755, and 65756) and other corneal procedures (codes 65400, 65435, 65600, and 65770). During this time, there was no CPT-4 code distinction between penetrating, lamellar, and endothelial keratoplasty or other keratoplasty approaches.

Analyses

Participant characteristics were summarized for the entire sample by using means and standard deviations for continuous variables and frequencies and percentages for categorical variables. We calculated the period prevalence for each corneal dystrophy by averaging the annual prevalence rates from 2002 through 2007. Prevalence rates were calculated by dividing the number of individuals in the plan with the condition by the number of covered lives, in millions. Continuous variables (e.g., age) were compared by analysis of variance, with pairwise contrasts performed with the Bonferroni adjustment for multiple comparisons. Categorical variables (e.g., race) were compared by χ^2 tests with a Tukey-type adjustment for multiple comparisons. To compare independent groups, enrollees with more than one corneal dystrophy code were not included. Statistical analyses were performed with a commercial program (SAS software, ver. 9.2; SAS Institute, Cary, NC). Since all data were de-identified, the University of Michigan Institutional Review Board determined that this study was exempt from approval. The de-identification and use of the records was in compliance with the Declaration of Helsinki.

Results

From 2002 through 2007, the number of total enrollees (adjusted to discount noncontinuous follow-up and data discrepancies) in the medical plan each year ranged from 12,357,933 to 13,074,104 persons. During the 7-year period, 27,372 unique individuals received two or more diagnoses of any type of corneal dystrophy, for an overall corneal dystrophy prevalence rate of 897 per million (10^6) covered lives, or 0.09%. Reducing the requirement to one diagnosis added another 14,250 enrollees with a corneal dystrophy, thereby increasing the overall prevalence rate estimate to 1,306 per 10^6 covered lives, or 0.13%. Endothelial corneal dystrophy was the most common one, with 16,535 (60.4%) persons with this diagnosis (and recorded at least twice). The second most common was anterior corneal dystrophy with 4268 (15.6%) individuals having this diagnosis. Other less frequent dystrophies (accounting for ≤1%) included 272 enrollees with macular corneal dystrophy, 235 persons with lattice corneal dystrophy, 231 individuals with juvenile epithelial corneal dystrophy, and 167 individuals with granular corneal dystrophy. Codes for unspecified corneal dystrophy accounted for 26.0% (n = 7104) of the enrollees identified with a corneal dystrophy. Summed percentages exceed 100% because some enrollees were coded for more than one corneal dystrophy.

The prevalence estimates reflect the average of annual prevalence estimates calculated for each plan year and so are period prevalence estimates. Table 1 shows that endothelial dystrophy was found in 535.9 per 10^6 covered lives, whereas rates for the least common dystrophies were on the order of 5.3 to 9.7 per 10^6 covered lives. The average age of enrollees at the first recording of the diagnostic code during the time period ranged from 47.3 (SD 18.0) years for those with macular corneal dystrophy to 62.9 (13.2) years for those with endothelial dystrophy. In contrast, the average age of enrollees who had eye care visits for reasons other than corneal dystrophy

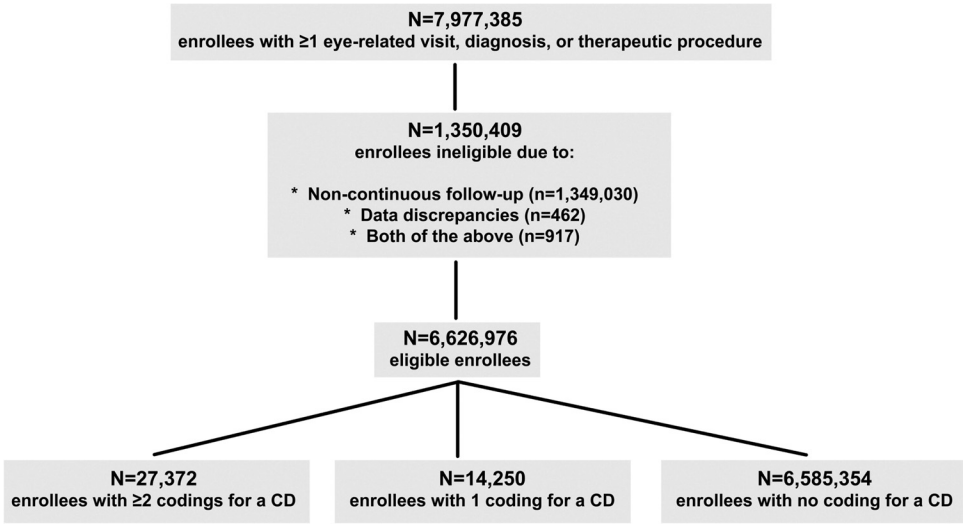

Figure 1. Flow diagram showing selection of corneal dystrophy cases within the InVisionDataMart i3 database (Ingenix, Eden Prairie, MN). CD, corneal dystrophy.

TABLE 1. Prevalence Estimates from the Ingenix Data (2002–2007), Requiring Two Diagnostic Codings for Each Corneal Dystrophy

Corneal Dystrophy	Unique Subjects in 2002–2007 (*n*)	Period Prevalence (Per Million Covered Lives*) Mean (SD)	Prevalence Range over the Period (Min, Max)	Age (y) Mean (SD)	% Female†
Endothelial	16,535	535.9 (137.9)	323.4, 686.4	62.9 (13.2)	64.0
Unspecified‡	7,104	240.5 (57.6)	148.8, 291.8	56.9 (15.8)	63.1
Anterior	4,268	137.9 (42.3)	73.6, 180.8	57.4 (13.9)	66.4
Macular	272	9.7 (1.9)	6.5, 11.2	47.3 (18.0)	56.6
Juvenile Epithelial	231	7.8 (1.7)	5.3, 9.9	51.6 (17.9)	63.2
Lattice	235	6.9 (2.3)	4.0, 10.7	52.3 (15.1)	68.5
Granular	167	5.3 (1.1)	3.8, 6.8	49.9 (17.8)	62.3

* Covered lives per year (2002–2007) ranged from 12,357,933 to 13,074,103 (after adjustment by 10.21% for ineligible subjects).
† 55.3% of all enrollees (n = 6.6 million) in 2002–2007 were women.
‡ See text for included codes.

was significantly younger (34.5 [21.8] years; $P < 0.0001$). Within the corneal dystrophies, the average ages differed significantly ($P < 0.0001$). On pairwise comparison, those with endothelial dystrophy were significantly older than those with all other types of corneal dystrophies (all $P < 0.05$), those with anterior dystrophy were significantly older than those with lattice dystrophy ($P < 0.05$), and those with macular dystrophy were significantly younger than those with lattice dystrophy ($P < 0.05$). All corneal dystrophies were more common among females. The percentage of female enrollees with a specific corneal dystrophy was highest (68.5%) for lattice corneal dystrophy and lowest (56.6%) for macular corneal dystrophy. The difference in the percentage of females in the macular versus lattice dystrophy groups was statistically significant ($P < 0.05$). The percentage of females observed in the enrollees without a corneal dystrophy code was 55.2%.

Racial distributions for the various dystrophies are shown in Table 2. Relative to that reported for enrollees without a corneal dystrophy, of whom whites accounted for 82.5% of eye care visits, the percentage of whites was significantly higher ($P < 0.05$) for anterior corneal dystrophy (92.6%) and endothelial corneal dystrophy (88.2%). Blacks accounted for 4.8% of enrollees with eye care visits for causes other than corneal dystrophy, whereas they represented only 0.7% of those with granular dystrophy and 2.2% of those with anterior corneal dystrophy. Relative to enrollees who had eye care visits for reasons other than corneal dystrophy, the percentage of blacks was significantly lower ($P < 0.05$) for anterior corneal dystrophy (2.2%) and higher ($P < 0.05$) for endothelial corneal dystrophy (5.4%). Hispanics made up 8.1% of enrollees without a corneal dystrophy diagnosis, which was higher than the percentages of Hispanics with any of the corneal dystrophies, and significantly so for anterior and endothelial dystrophies. Asians made up 3.5% of enrollees without a corneal dystrophy diagnosis. A significantly lower percentage of Asians were found among those with anterior and endothelial corneal dystrophies (1.6% and 2.0%, respectively), and somewhat higher percentages (but not statistically different) were observed among those with macular and lattice corneal dystrophies (4.6% and 4.3%, respectively).

Using CPT codes, we identified the frequency of keratoplasties and other corneal procedures among the various corneal dystrophies. Table 3 displays the frequency and percentage of participants with diagnoses who underwent these procedures during their time in the plan, stratified by the participant's age at the first recording of the corneal dystrophy. As expected, the percentage undergoing keratoplasty increased from the youngest to the oldest age categories. The percentage undergoing keratoplasty in lattice and granular dystrophies was relatively higher in each age category, when contrasted with endothelial dystrophy percentages. For example, of 1117 enrollees with endothelial dystrophy in the 25- to 44-year age group, 3.1% (n = 35) had a keratoplasty, whereas 9.5% (n = 6) of 63 enrollees with lattice dystrophy in this age group underwent keratoplasty.

DISCUSSION

This claims-based estimate of the prevalence of corneal dystrophies provides unique information, as most studies in the literature have reported relative frequencies of corneal transplantation for these corneal dystrophies. Our relative frequency findings are consistent with the Eye Bank Association of America's (EBAA's) 2008 report, in which data are reported on 29,315 corneal transplantations performed in the United States in 2008.[6] The most common dystrophy they recorded was Fuchs endothelial dystrophy, which was the fourth most

TABLE 2. Racial Distribution of Corneal Dystrophies from the Ingenix Data (2002–2007), Requiring Two Diagnostic Codings for Each Corneal Dystrophy

Corneal Dystrophy	Unique Subjects in 2002–2007* (*n*)	White (%)	Black (%)	Hispanic (%)	Asian (%)	Other (%)
Endothelial	13,323	88.2	5.4	3.8	2.0	0.7
Unspecified†	5,745	89.0	3.3	4.9	2.0	0.9
Anterior	3,449	92.6	2.2	2.8	1.6	0.9
Macular	217	85.3	5.1	4.2	4.6	0.9
Juvenile epithelial	200	88.5	4.0	3.0	2.5	2.0
Lattice	186	84.4	4.3	5.9	4.3	1.1
Granular	136	87.5	0.7	5.9	3.7	2.2
No corneal dystrophy	5,050,473	82.5	4.8	8.1	3.5	1.1

* Sample sizes are smaller, because of missing data on race.
† See text for the codes included.

TABLE 3. Corneal Procedures (2002–2007) by Corneal Dystrophy and Age

Age Category/Corneal Procedure	Corneal Dystrophy Type						
	Endothelial (n = 16,535)	Unspecified* (n = 7,104)	Anterior (n = 4,268)	Macular (n = 272)	Juvenile Epithelial (n = 231)	Lattice (n = 235)	Granular (n = 167)
0–24 y	n = 171	n = 280	n = 72	n = 34	n = 19	n = 8	n = 16
Other†	0 (0.0)	9 (3.2)	3 (4.2)	0 (0.0)	1 (5.3)	0 (0.0)	0 (0.0)
Keratoplasty‡	5 (2.9)	7 (2.5)	1 (1.4)	0 (0.0)	1 (5.3)	0 (0.0)	1 (6.3)
25–44 y	n = 1,117	n = 1,035	n = 607	n = 73	n = 48	n = 63	n = 47
Other†	16 (1.4)	45 (4.4)	88 (14.5)	0 (0.0)	1 (2.1)	4 (6.4)	7 (14.9)
Keratoplasty‡	35 (3.1)	48 (4.6)	3 (0.5)	0 (0.0)	1 (2.1)	6 (9.5)	2 (4.3)
45–64 y	n = 7,642	n = 3,632	n = 2,406	n = 128	n = 110	n = 118	n = 71
Other†	87 (1.1)	152 (4.2)	238 (9.9)	0 (0.0)	5 (4.6)	8 (6.8)	3 (4.2)
Keratoplasty‡	394 (5.2)	126 (3.5)	30 (1.3)	3 (2.3)	4 (3.6)	12 (10.2)	14 (19.7)
65–88 y	n = 7,605	n = 2,157	n = 1,183	n = 37	n = 54	n = 46	n = 33
Other†	59 (0.8)	67 (3.1)	89 (7.5)	1 (2.7)	1 (1.9)	2 (4.4)	1 (3.0)
Keratoplasty‡	472 (6.2)	120 (5.6)	27 (2.3)	2 (5.4)	6 (11.1)	7 (15.2)	3 (9.1)

Data are displayed as frequency (percentage of total). Two diagnostic codings required.

* See text for included codes.

† CPT codes: 65400, 65435, 65600, and 65770.

‡ CPT codes: 65710, 65730, 65750, 65755, and 65756.

common indication for corneal transplantation that year. Another large resource of corneal transplantation information, the Australian Corneal Graft Registry, has records on over 17,000 PKs. Their 2007 report[7] provides detail on the percentages of reported corneal transplants that were performed for specific corneal dystrophies. In concert with the EBAA information, Fuchs endothelial dystrophy predominated (84%), followed by granular dystrophy (4%), lattice, polymorphous, and macular dystrophies (~2% each), and other dystrophies (crystalline, juvenile, and anterior) were less common (<1%) indications.

Some geographic differences in the relative frequency of dystrophies as indications for corneal transplantation can be derived from case series reports. One report from Japan[8] indicated that Fuchs endothelial dystrophy was a very infrequent indication for corneal transplantation (18/3972 grafts, or 0.5%), which may correspond to the low frequency of corneal guttata (4.1%) found in 3060 participants of the Kumejima Study.[9] A report from Iceland indicated that macular corneal dystrophy accounts for one third of corneal transplants,[10] and a report from the Czech republic posited that posterior polymorphous corneal dystrophy was one of the most prevalent corneal dystrophies.[11]

Although some of these accounts lack supporting data, the data reported from large graft registries provide information only on corneal dystrophies that are severe enough to require corneal grafting. Our use of claims data from a countrywide resource of health care information gives a much different picture, reflecting dystrophies that were diagnosed and recorded by an eye care professional. Although it is likely that there are many subjects with undiagnosed dystrophies in the underlying population and some corneal dystrophies were missed or diagnosed incorrectly by eye care providers within our claims database, the database we accessed gives more accurate insight than a graft registry into the prevalence of these conditions in the population. The large sample size and capture of health care claims from all regions of the United States provides better coverage of the population. Likewise, the percentage of persons with a diagnosed corneal dystrophy who then underwent keratoplasty or other corneal procedures in this claims database gives an indication of the relative severity of these conditions. This information is lacking in graft registry data. Finally, our results provide some intriguing patterns in the demographic distribution of corneal dystrophies, such as racial differences, that deserve further evaluation.

Claims data analyses rely on information that is recorded for reasons other than research. Weaknesses of claims data when used for clinical research purposes have been reviewed[12] and include lack of capture of potentially valuable data, such as exposures of interest (e.g., smoking, dietary factors); personal information, such as weight and height; and ophthalmic measures such as visual acuity and corneal thickness. Also, claims data come from insured participants in a managed care plan. Although the InVision database captures information on millions of care recipients from all 50 U.S. states, our prevalence information pertains to the insured population, which differs from the entire population of the United States. We found, though, that the percentages of Asians and Latinos in our claims population are very similar to those in the U.S. Census population, whereas percentages of blacks and whites in the claims database are slightly lower and higher, respectively, relative to the U.S. Census population. Another limitation, particularly with endothelial dystrophy, is case definition. Clearly, cases requiring keratoplasty are likely to be correctly classified. However, a code for endothelial dystrophy could have been recorded for much less common conditions, such as posterior polymorphous corneal dystrophy, and enrollees with only a few corneal guttae may also be assigned this diagnosis. Lorenzetti et al.[13] found guttae in 70% of eyes over age 40 and Zoega et al.[14] in 11% of women over age 55. While defining Fuchs endothelial dystrophy based on guttae or on corneal edema will result in great variation, recently published molecular genetic information suggests that both are related to the same genetic variant.[15] Likewise, anterior corneal dystrophy is a code that is not specific, as it includes the more common map-dot-fingerprint dystrophy and several less common anterior corneal dystrophies. Coding dystrophies according to an updated classification system for corneal dystrophies, the International Classification of Corneal Dystrophies (IC3D) system,[3] would greatly enhance the information we now can obtain with ICD-9-CM codes.

With due attention to the limitations and caveats described above, we believe that the prevalence rates we report can be used as an estimate of the expected number of subjects with corneal dystrophies in the United States. The information on procedures provides an estimate of the percentage that will require PK or other corneal procedures, thereby giving some insight to the expected surgical demand arising from these dystrophies and the approximate age at which patients with

specific types of corneal dystrophy experience enough visual dysfunction or intolerable symptoms to require surgical intervention.

Conclusions

A conservative estimate of the overall prevalence of corneal dystrophies in the United States indicates that 897 per 10^6 have one of these conditions, which translates to approximately 278,000 people in a population of 310 million. Approximately 60% of all corneal dystrophies are endothelial, whereas such conditions as macular, lattice, and granular corneal dystrophies are far less prevalent, each making up 1% or less of the total. Differences by age, sex, and race are worthy of considering in these conditions' etiologies. Variations in frequencies of keratoplasty are likely to be reflective of these corneal dystrophies' relative severity. These data can serve as a basis for estimating the cost of care and future demand as the population ages.

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