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## Racial Differences in Rates of Penetrating or Endothelial Keratoplasty for Fuchs Endothelial Corneal Dystrophy Among US Medicare Beneficiaries, 2014

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### Abstract

**Importance**—Fuchs endothelial corneal dystrophy (FECD) is the most common indication for corneal transplant in the United States. The association between race and incidence of advanced FECD, defined by a need for endothelial or penetrating keratoplasty, has not been investigated.

**Observations**—The 2014 US Medicare Limited Data Set (5% sample of 27,163,740 fee-for-service Medicare patients) was analyzed for rate of keratoplasty performed for FECD (*International Classification of Diseases, Ninth Edition, 371.57*) stratified by race. Among all Medicare beneficiaries aged 65 years or older, a diagnosis code for FECD was used in 1.55% (95% CI, 1.51%–1.59%) of white and 1.38% (95% CI, 1.26%–1.50%) of black ( $P=.01$ ) beneficiaries who had an ophthalmologist eye examination in 2014. Among beneficiaries who obtained medical care for FECD, keratoplasty was 1.9-fold more likely in white than black patients (4.7% [95% CI, 4.2%–5.2%] vs 2.5% [95% CI, 1.1%–3.9%]) ( $P<.001$ ) among approximately 6,500 patients undergoing 8,420 procedures.

**Conclusions and Relevance**—In 2014, keratoplasty was 1.9 times more likely in US Medicare fee-for-service white patients than black patients with FECD. This might be due to racial differences in the biology of FECD, access to care, or other unidentified factors.

### Keywords

cornea; endothelial keratoplasty; Fuchs endothelial corneal dystrophy; penetrating keratoplasty; race

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As the most common cause for endothelial and penetrating keratoplasty in the United States, Fuchs endothelial corneal dystrophy (FECD) is likely to have varied phenotypic expressions (1,2). National claims research shows that black patients are as likely or more likely to have

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Michael A. Mahr, MD, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

### Conflict of Interest

No conflicting relationship exists for any author.

a diagnosis of FECD relative to white patients (3). A regional study also showed that black and white patients receive diagnoses of guttae at similar rates, but white patients are more likely to have more severe disease in the form of confluent guttae (2,4). Previous attempts to genetically characterize FECD in African Americans have failed to discern a genetic association relative to a broader population (5). Our aim was to use a national cross-sectional Medicare dataset to test for racial differences in the rates of penetrating or endothelial keratoplasty in FECD.

The Mayo Clinic Institutional Review Board approved this study. Data were derived from the 2014 Medicare Limited Data Set Carrier Standard Analytical File. These data contain a de-identified 5% sample of all claims for approximately 27,163,740 US Medicare fee-for-service (FFS) enrollees after filtering to include age  $\geq$  65 years and race of either black or white. Excluded from this dataset are the approximately 28% of Medicare patients enrolled in non-FFS Medicare Advantage plans. Analysis was performed using Excel 2013 software with PowerPivot and Power Query add-ins (Microsoft) during March and April 2016. After filtering by provider specialty code, we tabulated the number of patients who received any eye care from an ophthalmologist  $\geq$  1 times during 2014. By filtering the primary diagnosis code for FECD (*International Classification of Diseases, Ninth Revision [ICD-9] 371.57*), we determined the number of patients with an FECD diagnosis in the context of any medical care in 2014. Finally, we summed the number of distinct patients who received  $\geq$  1 penetrating (Current Procedural Terminology [CPT] codes 65730, 65750, and 65755) or endothelial (CPT 65756) keratoplasties for an FECD diagnosis specifically. All data were stratified by race (white vs black), which is self-reported by Medicare patients at the time of Social Security enrollment using form SS-5. Percentages were used as a summary for each group, and 95% confidence intervals (CIs) were calculated for the percentages within each group. Overall comparisons between groups were completed using  $\chi^2$  tests.

In 2014, approximately 24,817,940 white and 2,345,800 black patients age  $\geq$  65 years were enrolled in Medicare FFS plans (Table 1). Of these, 34.9% (95% CI, 34.8%–35.0%) of white and 29.6% (95% CI, 29.4%–29.8%;  $P<.001$ ) of black patients received medical care from an ophthalmologist  $\geq$  1 times during that year (Table 2). A diagnosis of FECD as defined by diagnosis code *ICD-9 371.57*, paired with medical claims of any type, was made for an estimated 134,580 white and 9,560 black patients, representing 1.55% (95% CI, 1.51%–1.59%) of white and 1.38% (95% CI, 1.26%–1.50%) of black Medicare beneficiaries ( $P=.01$ ) who had an eye examination by an ophthalmologist in 2014. Among these patients who obtained medical care for FECD, a penetrating or endothelial keratoplasty was 1.9-fold more likely in white patients (4.7% [95% CI, 4.2%–5.2%]) than black patients (2.5% [95% CI, 1.1%–3.9%];  $P<.001$ ). Across all categories, the black patients were more likely to be women (Table 3;  $P<.001$ ). Among all corneal grafts for FECD, 95% (95% CI, 93%–97%;  $P<.001$ ) were endothelial keratoplasties and 5% (95% CI, 2.6%–7.4%;  $P<.001$ ) were penetrating keratoplasties; representing approximately 8,420 procedures in 6,500 patients.

The study findings suggest that in white FFS Medicare patients, the rate of Medicare claims-based diagnoses of FECD is slightly higher, but clinically similar, to the rate in black patients after correcting for the generally lower overall rate at which black Medicare patients saw ophthalmologists. The 1.9-fold higher rate of endothelial or penetrating keratoplasties in

white patients than black patients suggests that racial differences may be present in the manifestation or treatment, or both, of more severe FECD. Whether this difference represents underlying genetic influence vs environmental influences, access to care, or other unknown or confounding factors merits further investigation.

This study represents, to our knowledge, the largest cross-sectional analysis of racial differences in rate of keratoplasties for FECD. The nature of our CPT and diagnosis code pairing may tend to underestimate the total number of keratoplasties in eyes with FECD because some procedures may have been coded with other, less specific diagnostic codes, such as *corneal edema* or *pseudophakic bullous keratopathy*. We do not expect this factor to influence relative racial differences in the reported corneal graft rates because it is less plausible that race-based differences in physician coding behavior took place. Although disparities in the availability of ophthalmologic surgical care may potentially explain some of this observation, underlying racial differences in the biology of FECD may be present. FECD is a genetically heterogeneous phenotype. Racial differences in the genetic basis of FECD are known to occur, with trinucleotide repeat expansion in the transcription factor 4 gene as the genetic variant found in the majority of US and European populations but in only a small percentage of Asian and Indian populations (6–11). Furthermore, rates of disease progression and severity may reflect the associated genetic variant.

Because FECD is known to also be present in patients younger than 65 years, our Medicare study has an age-based sampling bias. General limitations of Medicare claims data in evaluating disease frequency and expression are well known. Potential confounding factors include access to care, provider coding behavior, potential coding errors, and lack of further clinical detail or data in the Medicare claims data. According to the 2010 Census Data, 8.5% of the US population older than 65 years was black (12), which is consistent with the 8.6% Medicare proportion, suggesting that there is not a race-based difference in Medicare enrollment rates. At birth in 2014, US blacks had a life expectancy that was 3.4 years less than that for whites (13), which introduces the possibility of a race-based survivor bias in the Medicare data set for persons aged 65 or older.

Future additional insights and geographic or sex data stratifications may be possible by expanding this work to encompass more patients over a longer period or by soliciting data sets of the Medicare 100% Research Identifiable File data sets, which are more difficult to obtain. Elucidation of the genetic variants associated with FECD in US whites vs US blacks may also shed light on the pathogenic mechanism of this genetically heterogeneous trait.

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## Abbreviations

<b>CI</b>	confidence interval
<b>CPT</b>	Current Procedural Terminology
<b>FECD</b>	Fuchs endothelial corneal dystrophy
<b>FFS</b>	fee-for-service
<b>ICD-9</b>	<i>International Classification of Diseases, Ninth Edition</i>

## References

1. Gain P, Jullienne R, He Z, Aldossary M, Acquart S, Cognasse F, et al. Global survey of corneal transplantation and eye banking. *JAMA Ophthalmol*. 2016 Feb 1; 134(2):167–173. [PubMed: 26633035]
2. Eghrari AO, McGlumphy EJ, Iliff BW, Wang J, Emmert D, Riazuddin SA, et al. Prevalence and severity of Fuchs corneal dystrophy in Tangier Island. *Am J Ophthalmol*. 2012 Jun; 153(6):1067–1072. Epub 2012 Feb 8. [PubMed: 22321803]
3. Musch DC, Niziol LM, Stein JD, Kamyar RM, Sugar A. Prevalence of corneal dystrophies in the United States: estimates from claims data. *Invest Ophthalmol Vis Sci*. 2011 Sep 1; 52(9):6959–6963. [PubMed: 21791583]
4. Lorenzetti DW, Uotila MH, Parikh N, Kaufman HE. Central cornea guttata: incidence in the general population. *Am J Ophthalmol*. 1967 Dec; 64(6):1155–1158. [PubMed: 6072991]
5. Baratz KH, Tosakulwong N, Ryu E, Brown WL, Branham K, Chen W, et al. E2-2 protein and Fuchs's corneal dystrophy. *N Engl J Med*. 2010 Sep 9; 363(11):1016–1024. Epub 2010 Aug 25. [PubMed: 20825314]
6. Kuot A, Hewitt AW, Griggs K, Klebe S, Mills R, Jhanji V, et al. Association of TCF4 and CLU polymorphisms with Fuchs' endothelial dystrophy and implication of CLU and TGFBI proteins in the disease process. *Eur J Hum Genet*. 2012 Jun; 20(6):632–638. Epub 2012 Jan 11. [PubMed: 22234156]
7. Nanda GG, Padhy B, Samal S, Das S, Alone DP. Genetic association of TCF4 intronic polymorphisms, CTG18.1 and rs17089887, with Fuchs' endothelial corneal dystrophy in an Indian population. *Invest Ophthalmol Vis Sci*. 2014 Oct 23; 55(11):7674–7680. [PubMed: 25342617]
8. Riazuddin SA, McGlumphy EJ, Yeo WS, Wang J, Katsanis N, Gottsch JD. Replication of the TCF4 intronic variant in late-onset Fuchs corneal dystrophy and evidence of independence from the FCD2 locus. *Invest Ophthalmol Vis Sci*. 2011 Apr 27; 52(5):2825–2829. [PubMed: 21245398]
9. Wang KJ, Jhanji V, Chen J, Law RW, Leung AT, Zhang M, et al. Association of transcription factor 4 (TCF4) and protein tyrosine phosphatase, receptor type G (PTPRG) with corneal dystrophies in southern Chinese. *Ophthalmic Genet*. 2014 Sep; 35(3):138–141. Epub 2013 Jun 12. [PubMed: 23758498]
10. Wieben ED, Aleff RA, Eckloff BW, Atkinson EJ, Baheti S, Middha S, et al. Comprehensive assessment of genetic variants within TCF4 in Fuchs' endothelial corneal dystrophy. *Invest Ophthalmol Vis Sci*. 2014 Aug 28; 55(9):6101–6107. [PubMed: 25168903]
11. Wieben ED, Aleff RA, Tosakulwong N, Butz ML, Highsmith WE, Edwards AO, et al. A common trinucleotide repeat expansion within the transcription factor 4 (TCF4, E2-2) gene predicts Fuchs corneal dystrophy. *PLoS One*. 2012; 7(11):e49083. Epub 2012 Nov 21. [PubMed: 23185296]
12. West, LA.; Cole, S.; Goodkind, D.; He, W. 65+ in the United States: 2010. Washington DC: US Census Bureau; 2014. [Internet]. Available from: <https://www.census.gov/content/dam/Census/library/publications/2014/demo/p23-212.pdf> [cited 2016 Jun 10]
13. Hyattsville (MD): National Center for Health Statistics; 2016. Health, United States, 2015: with special feature on racial and ethnic health disparities. [Internet]. Available from: <http://www.cdc.gov/nchs/data/abus/abus15.pdf> [cited 2016 Jun 10]

**Table 1**

Estimate of Total Number of Medicare Patients With Fee-for-Service Payment Structure and With Diagnosis of FECD, 2014, Based on Medicare Limited Data Set Carrier File 5% Sample (% Female Sex)

Patient Age, y	White Patients, No.		Black Patients, No.	
	Total	FECD Diagnosis	Total	FECD Diagnosis
65–69	7,590,220	27,340	832,300	2,320
70–74	5,686,340	29,880	548,960	2,180
75–79	4,369,560	28,980	403,820	2,240
80–84	3,338,560	24,060	274,760	1,400
>84	3,833,260	24,320	285,960	1,420
Total	24,817,940 (58%)	134,580 (67%)	2,345,800 (62%)	9,560 (73%)

Abbreviation: FECD, Fuchs endothelial corneal dystrophy.

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**Table 2**

Estimates Among 2014 Fee-for-Service Medicare Patients, Based on Medicare Limited Data Set Carrier File  
5% Sample

Patient Grouping	White Patients, No. <sup>a</sup>	Black Patients, No. <sup>a</sup>
Total cohort	24,817,940	2,345,800
Patients who saw an ophthalmologist in 2014	8,661,420 (34.9%) <sup>b</sup>	694,740 (29.6%) <sup>b</sup>
Patients with FECD diagnosis	134,580 (1.6%) <sup>c</sup>	9,560 (1.4%) <sup>c</sup>
Patients receiving 1 endothelial or penetrating keratoplasties for FECD	6,260 (4.7%) <sup>b</sup>	240 (2.5%) <sup>b</sup>

Abbreviation: FECD, Fuchs endothelial corneal dystrophy.

<sup>a</sup> All ratios are expressed as a percentage of the patient category.

<sup>b</sup>  $P < .001$ .

<sup>c</sup>  $P = .01$ .

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**Table 3**

Estimates of Sex Distribution Among 2014 Fee-for-Service Medicare Patients, Based on Medicare Limited Data Set Carrier File 5% Sample

Patient Grouping	Female White Patients, % <sup>a</sup>	Female Black Patients, % <sup>a</sup>
All Medicare patients	58	62
Patients who saw an ophthalmologist in 2014	60	65
Patients with FECD diagnosis	67	73
Patients receiving 1 endothelial or penetrating keratoplasties for FECD	63	77

Abbreviation: FECD, Fuchs endothelial corneal dystrophy.

<sup>a</sup>Percentage of white vs black patients,  $P < .001$  for all categories.

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