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Racial Differences in Medication Utilization for Secondary Prevention of Cardiovascular Disease in Kidney Transplant Recipients: A Post Hoc Analysis of the FAVORIT Trial Cohort

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# Racial Differences in Medication Utilization for Secondary Prevention of Cardiovascular Disease in Kidney Transplant Recipients: A Post Hoc Analysis of the FAVORIT Trial Cohort

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**Rationale & Objective:** Black kidney transplant recipients have higher prevalences of cardiovascular disease (CVD) risk factors and less intensive risk factor control than White kidney transplant recipients. Our objective was to evaluate racial disparities in receipt of statins and aspirin for secondary CVD prevention among kidney transplant recipients in the Folic Acid for Vascular Outcome Reduction in Transplantation (FAVORIT) trial.

**Study Design:** Cohort study.

**Setting & Participants:** FAVORIT participants of White, Black, and Other races from the United States and Canada with a history of CVD at study entry or who experienced a nonfatal CVD event during follow-up.

**Predictor:** Race.

**Outcome:** Receipt of statins and aspirin for secondary CVD prevention.

**Analytical Approach:** We used parametric (Weibull), proportional-hazards, interval-censored survival models to evaluate the independent

association of race with receipt of statins and aspirin for secondary CVD prevention.

**Results:** Of the 4,110 kidney transplant recipients enrolled in FAVORIT trial, 978 met the inclusion criteria (78% White, 17% Black, and 6% Other race). Compared with the White race, Black and Other races were associated with lower hazards of receiving statins (Black race: adjusted HR, 0.76 [95% CI, 0.60-0.97]; Other race: adjusted HR, 0.87 [95% CI, 0.60-1.27]) and aspirin (Black race: adjusted HR, 0.85 [95% CI, 0.67-1.08]; Other race: adjusted HR, 0.63 [95% CI, 0.43-0.94]).

**Limitations:** Lack of granular information on potential indications or contraindications for aspirin or statin use for secondary CVD prevention.

**Conclusions:** Post hoc findings from the FAVORIT trial demonstrated that Black race was associated with a lower likelihood of receiving statins and Other race was associated with a lower likelihood of receiving aspirin for secondary CVD prevention. This represents a potential target to improve CVD care in non-White kidney transplant recipients.

## Visual Abstract included

Complete author and article information provided before references.

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Kidney transplantation is the optimal treatment for individuals with kidney failure and substantially improves quality of life and decreases early mortality compared to dialysis.<sup>1</sup> Cardiovascular disease (CVD) is the most common cause of death with a functioning graft among kidney transplant recipients.<sup>2,3</sup> The high risk of CVD in kidney transplant recipients is multifactorial and includes nonmodifiable risk factors, such as age and family history, as well as modifiable risk factors, such as hypertension, dyslipidemia, obesity, diabetes mellitus, and immunosuppression. Many kidney transplant recipients do not receive guideline-concordant CVD care after transplant to manage these modifiable factors, with some studies suggesting only a small portion of prevalent kidney transplant recipients receive optimal CVD management.<sup>4-6</sup>

Compared with White kidney transplant recipients, Black kidney transplant recipients have a greater burden of comorbid conditions at the time of transplant, including CVD and CVD risk factors, such as hypertension, diabetes, and dyslipidemia.<sup>7-10</sup> Furthermore, single-center observational studies and 1 larger study from the Veterans Affairs Healthcare System have shown that Black kidney transplant recipients have worse control of these CVD risk factors

after transplant.<sup>6,8-10</sup> Preventive care to mitigate CVD risk may thus be of particular importance among Black kidney transplant recipients to improve health outcomes. In this study, we examined receipt of statins and aspirin for secondary prevention of CVD by race in kidney transplant recipients enrolled in the FAVORIT trial. We specifically looked at the secondary prevention of CVD because at the time the FAVORIT trial was conducted (2002-2009), primary CVD prevention with statins and aspirin in kidney transplant recipients was controversial and not universally recommended. The Kidney Disease Improving Global Outcomes (KDIGO) Clinical Practice Guideline for Lipid Management in Chronic Kidney Disease published in 2013 was the first guideline that suggested treating all adult kidney transplant recipients with a statin.<sup>11</sup> There continues to be no recommendation regarding aspirin use for primary CVD prevention in kidney transplant recipients.<sup>12</sup> Although secondary CVD prevention with statins and aspirin has not been well studied in kidney transplant recipients, the benefits of secondary CVD prevention with these medications have long been well established in the general population.<sup>13</sup> Given that kidney transplant recipients are at higher risk of CVD than the general

**PLAIN-LANGUAGE SUMMARY**

Black kidney transplant recipients have higher prevalences of cardiovascular disease (CVD) risk factors and less intensive risk factor control than White kidney transplant recipients. We conducted this study to evaluate racial disparities in receipt of statins and aspirin for secondary CVD prevention among 978 kidney transplant recipients with a history of CVD. Our study showed that Black kidney transplant recipients were less likely to receive statin and Other race kidney transplant recipients were less likely to receive aspirin for secondary CVD prevention, compared with White kidney transplant recipients. Equitable prescription of aspirin and statin for secondary CVD prevention represents an important potential target to improve CVD care among non-White kidney transplant recipients.

population,<sup>11,14</sup> the secondary prevention of CVD with statins and aspirin in kidney transplant recipients is critically important and is the focus of our study. Although the FAVORIT clinical trial was completed over a decade ago, our results could identify missed opportunities to improve health outcomes among non-White kidney transplant recipients and encourage more examination of this aspect of modern CVD care delivery.

**METHODS**

We conducted a post hoc analysis of the FAVORIT trial, a study testing folate supplementation for CVD prevention among kidney transplant recipients. The details of the FAVORIT design have previously been described.<sup>15</sup> Kidney transplant recipients were enrolled in the FAVORIT trial from 30 clinical sites (27 in the United States, 2 in Canada, and 1 in Brazil) from 2002 to 2007; follow-up concluded in 2009. The enrolled kidney transplant recipients were aged 35-75 years, had functioning allografts, and received the transplant at least 6 months prior. Written informed consent was obtained from all participants. The FAVORIT trial did not show statistically significant differences in graft loss or all-cause mortality between the treatment groups.<sup>16</sup> Therefore, for this post hoc analysis, we combined the data from both treatment groups and treated this as a cohort study. The FAVORIT trial participants were followed by alternating telephone and in-person clinic visits every 6 months to ascertain study outcomes, including CVD events. The medications were self-reported by the participants at each follow-up visit. The follow-up ended with death, loss to follow up, or trial conclusion on June 24, 2009.

**Study Population**

To identify individuals who would be eligible for statin and aspirin prescription for secondary prevention of CVD, we assembled 2 analytic cohorts: 1 for an analysis of statin

initiation and 1 for an analysis of aspirin initiation. Each cohort included FAVORIT trial participants from the United States and Canada who had CVD at study entry and participants without a history of CVD at baseline who experienced a nonfatal CVD event during follow-up. We excluded kidney transplant recipients from Brazil, as racial differences in the presence of modifiable CVD risk factors have primarily been documented in North America.<sup>7-10</sup> The baseline CVD was self-reported or extracted from medical records and was defined as a history of myocardial infarction, coronary artery revascularization, stroke, aortic aneurysm repair, lower extremity arterial revascularization, or amputation above the ankle. Nonfatal CVD during follow-up was defined as a myocardial infarction, resuscitated sudden death, stroke, coronary artery revascularization, or peripheral, carotid, aortic, or renal artery procedures, as previously defined by FAVORIT.<sup>17</sup>

**Study Variables**

The primary predictor was self-reported race, categorized as White, Black, and Other, which included Asian, Mixed, Native Hawaiian/Pacific Islander, and American Indian or Alaska Native races. The primary outcomes were aspirin and statin use. Medication use was ascertained through a self-report, and a review of participant medication lists and container labels during baseline and follow-up study visits.<sup>17</sup> If a medication was ascertained to be used based on any of these 3 sources, that medication was recorded as being used. Ethnicity was self-reported and recorded as Hispanic or not Hispanic. The sources of medical history included the patients themselves, the patients' families, and the patients' medical records. Documentation from participants' transplant clinic charts superseded any information provided by a verbal report. Seated blood pressure was measured twice at 5- to 10-minute intervals in each clinic visit; we report the average blood pressure at the baseline study visit. The estimated glomerular filtration rate was calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) equation.

**Statistical Analysis**

Baseline demographic and clinical characteristics were compared by race using a  $\chi^2$  test, analysis of variance, and Kruskal-Wallis test. Our goal was to compare the time to initiation of secondary preventive care following the development of CVD; however, many participants had prevalent CVD at the time of enrollment. To account for the uncertainty in the time of onset of CVD among these patients, we used an interval-censored approach that allowed us to improve power by combining patients having prevalent CVD at enrollment with those developing incident CVD during follow-up period. We used a parametric survival model (Weibull) to accommodate interval censoring.<sup>18</sup> Goodness of fit for survival models was assessed graphically using Cox-Snell residual plots. The time scale in our study was years from the first CVD event.

When CVD was present at the time of enrollment in the FAVORIT trial, we treated CVD onset as occurring in the interval between the age of 30 years and age at enrollment, given that CVD is rare before the age of 30 years among patients with kidney failure.<sup>19</sup> For participants who have incident CVD onset during follow-up, the time to event is either known (if medication was initiated in a later follow-up) or right-censored (if medication was not initiated during follow-up), corresponding to definitions in a conventional survival analysis. Time-to-event definitions for our interval-censored survival analysis are shown in [Table S1](#). As a sensitivity analysis, we repeated our analyses while excluding participants with prevalent CVD at baseline.

All models were adjusted for age, sex, ethnicity, country of enrollment (United States or Canada), and graft vintage. In addition, we controlled for baseline cyclosporin use in the model assessing statin use because of a potential clinician concern for drug-drug interactions between cyclosporin and statins.<sup>20</sup> In the aspirin model, we also controlled for baseline use of nonaspirin antiplatelet agents (eg, clopidogrel) and for baseline anticoagulation use (eg, warfarin). We performed a sensitivity analysis to account for variation in prescription patterns by transplant center by calculating cluster-robust standard errors and including them in the model.

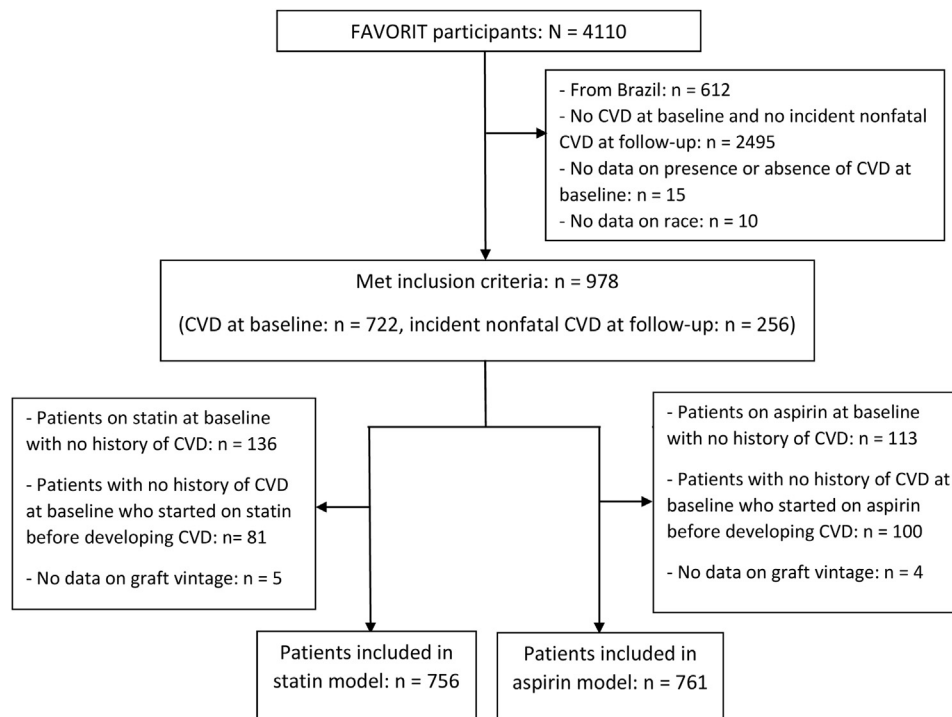
Study data were obtained from the National Institute of Diabetes and Digestive and Kidney Diseases Central Repository in deidentified form. The institutional review

board of University of California, San Francisco, considers this study not human subjects research. All analyses were performed using Stata version 16.1 (Stata Corp).

## RESULTS

Of the 4,110 kidney transplant recipients enrolled in the FAVORIT trial, 978 (759 White [78%], 162 Black [17%], and 57 Other [6%]) met the study inclusion criteria; 722 (74%) had baseline CVD and 256 (26%) had no CVD at enrollment and developed nonfatal CVD during follow-up ([Fig 1](#)). The baseline characteristics for this population at the time of enrollment are shown in [Table 1](#). Compared with White participants, Black participants were more likely to be women and to be from the United States ( $P < 0.001$  for both comparisons). Nearly 95% of participants had hypertension, but individuals of Black and Other races had higher prevalences of diabetes than White participants. The median estimated glomerular filtration rate was not different between different racial groups. However, individuals of Black race had higher urine albumin-to-creatinine ratio levels than their White and Other race counterparts.

Among the 978 participants with CVD at baseline or during follow-up, 222 (23%) and 217 (22%) individuals were excluded from the statin and aspirin analytic cohorts, respectively ([Fig 1](#)). The baseline characteristics of the population included in each model at the time of enrollment are shown in [Tables S2](#) and [S3](#). The main reason for



**Figure 1.** Study flow diagram. Abbreviations: CVD, cardiovascular disease; FAVORIT, Folic Acid for Vascular Outcome Reduction in Transplantation.

**Table 1.** Baseline Characteristics of FAVORIT Study Patients Meeting the Inclusion Criteria

	White (n=759)	Black (n=162)	Other Race (n=57)	P Value
Age, y	55.5 ± 9.2	56.0 ± 7.8	56.7 ± 8.1	0.57
Male sex	555 (73.1%)	91 (56.2%)	40 (70.2%)	<0.001
Hispanic ethnicity	14 (1.8%)	0 (0%)	10 (17.5%)	<0.001
Country, United States	666 (87.8%)	160 (98.8%)	49 (86.0)	<0.001
Graft vintage, y	4.41 (1.80-8.04)	2.99 (1.59-6.75)	2.49 (1.05-5.41)	<0.001
Follow-up duration, y	3.18 (2.05-4.83)	2.95 (1.09-4.13)	2.87 (2.03-4.88)	0.01
History of diabetes	456 (60.1%)	112 (69.1%)	40 (70.2%)	0.04
History of hypertension	713 (93.9%)	157 (96.9%)	54 (94.7%)	0.33
Systolic blood pressure, mm Hg	136.1 ± 19.7	141.4 ± 20.4	135.7 ± 19.9	0.008
Diastolic blood pressure, mm Hg	73.8 ± 11.0	76.9 ± 11.5	75.0 ± 9.7	0.006
Body mass index, kg/m <sup>2</sup>	28.6 (25.3-32.8)	30.0 (26.9-35.6)	28.7 (25.0-34.0)	0.002
eGFR, mL/min/1.73 m <sup>2</sup>	43.5 (34.8-54.4)	44.7 (37.5-55.5)	45.0 (34.8-55.3)	0.25
Urinary albumin creatinine ratio (mg/g)	25.6 (9.6-117.2)	58.3 (14.8-242.2)	27.3 (10.7-106.0)	0.008
Immunosuppressive medications				
Cyclosporin	402 (53.0%)	75 (46.3%)	33 (57.9%)	0.20
Tacrolimus	269 (35.4%)	74 (45.7%)	21 (36.8%)	0.05
Sirolimus	62 (8.2%)	13 (8.0%)	5 (8.8%)	0.98
Mycophenolate mofetil (%)	512 (67.5%)	128 (79.0%)	37 (64.9%)	0.01
Azathioprine	97 (12.8%)	15 (9.3%)	7 (12.3%)	0.46
Prednisone	687 (90.5%)	146 (90.1%)	48 (84.2%)	0.31

Note: Continuous data are presented as the mean ± standard deviation if normally distributed and as the median (interquartile range) if not normally distributed, and categorical data are presented as n (%).

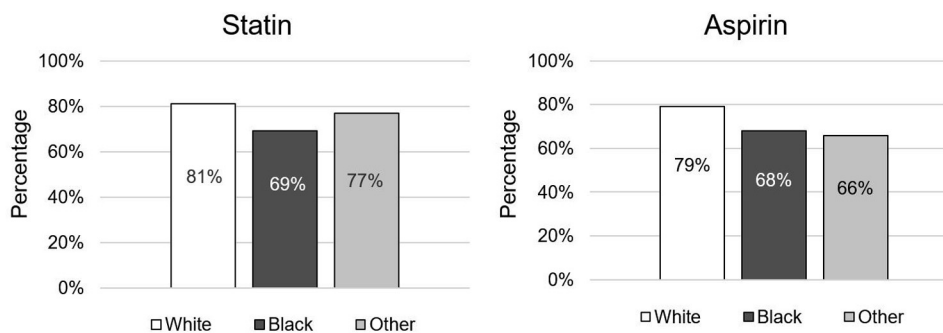
Abbreviations: eGFR, estimated glomerular filtration rate; FAVORIT, Folic Acid for Vascular Outcome Reduction in Transplantation.

exclusion was receiving statin or aspirin at baseline without a history of CVD or being started on statin or aspirin during follow-up before developing CVD. The racial distributions of patients included and excluded from the 2 analytic cohorts were similar (Table S4).

Among 756 kidney transplant recipients included in the final statin analytic cohort, 453 (60%) had CVD and were on statin at the time of enrollment, and 140 (19%) initiated statin during follow-up. In total, 593 (78%) patients included in the statin model received statin. As shown in Fig 2, the prevalence of statin use differed by race, with 471 (81%) of the White participants, 88 (69%) of the Black participants, and 34 (77%) of the Other race participants reporting statin use ( $P = 0.01$ ). The Black race was

independently associated with a significantly lower adjusted hazard of receiving a statin for secondary CVD prevention compared with the White race (adjusted hazard ratio = 0.76; 95% confidence interval, 0.60-0.97). The Other race was associated with a statistically nonsignificant lower hazard of receiving statin than the White race (adjusted hazard ratio = 0.87; 95% confidence interval, 0.60-1.27; Table 2).

Among 761 kidney transplant recipients included in the final aspirin analytic cohort, 458 (60%) had CVD and were on aspirin at the time of enrollment and 120 (16%) initiated aspirin during follow-up. In total, 578 (76%) patients included in the aspirin model received aspirin, including 460 (79%) of the White participants, 89 (68%)



**Figure 2.** Percentages of participants with different races who received statin or aspirin for secondary cardiovascular disease prevention.

**Table 2.** Results of Parametric, Proportional-Hazards, Interval-Censored Survival Model to Evaluate the Association of Race With Self-reported Receipt of Statins in Kidney Transplant Recipients

	Adjusted Hazard Ratio	95% CI	P Value
Black race	0.76	0.60-0.97	0.03
Other race	0.87	0.60-1.27	0.47
Age, y	0.93	0.91-0.94	<0.001
Female sex	1.04	0.86-1.26	0.70
Hispanic ethnicity	1.24	0.70-2.20	0.47
Canada as the country of residence	0.88	0.65-1.19	0.40
Graft vintage, y	1.02	1.00-1.04	0.08
Baseline cyclosporin use	1.10	0.93-1.32	0.27

Abbreviation: CI, confidence interval.

of the Black participants, and 29 (66%) of the Other race participants ( $P = 0.01$ ; Fig 2). Although the Black race was associated with a lower hazard of receiving aspirin compared with the White race, the results did not achieve statistical significance (adjusted hazard ratio = 0.85; 95% confidence interval, 0.67-1.08). The Other race was associated with a statistically significant lower hazard of receiving aspirin compared with White race (adjusted hazard ratio = 0.63; 95% confidence interval, 0.43-0.94; Table 3). The residual plots (Figs S1 and S2) showed good agreement with the assumed Weibull model, with discrepancies only in the longest times, where there are limited data and the plots are imprecise.

There was a variation between different transplant centers in terms of percentages of patients who received statin and aspirin for secondary CVD prevention. Statin use ranged from 50% to 100% (median, 79.2%; interquartile range, 71.4%-92.3%). Aspirin use ranged from 50% to 100% (median, 80.9%; interquartile range, 69.8%-

**Table 3.** Results of Parametric, Proportional-Hazards, Interval-Censored Survival Model to Evaluate the Association of Race With Self-reported Receipt of Aspirin in Kidney Transplant Recipients

	Adjusted Hazard Ratio	95% CI	P Value
Black race	0.85	0.67-1.08	0.18
Other race	0.63	0.43-0.94	0.02
Age, y	0.94	0.93-0.96	<0.001
Female sex	0.88	0.73-1.07	0.21
Hispanic ethnicity	1.23	0.69-2.20	0.48
Canada as the country of residence	1.20	0.87-1.64	0.27
Graft vintage, y	0.99	0.98-1.01	0.57
Baseline nonaspirin antiplatelet use	0.83	0.64-1.06	0.14
Baseline anticoagulant use	0.62	0.45-0.86	0.004

Abbreviations: CI, confidence interval.

86.5%). Results from analyses performed with cluster-robust standard errors to account for variation in prescription patterns by the transplant center showed similar differences in the use of statins and aspirin for secondary CVD prevention by race (Table S5). When analyses were restricted to include only US participants, we found similar differences in the use of statins and aspirin for secondary CVD prevention by race (Tables S6).

In a sensitivity analysis wherein participants with baseline CVD and aspirin or statin use were excluded, we found similar results to our main analyses, albeit with greater uncertainty, as we would expect because of limited power (Table S7).

## DISCUSSION

Our results demonstrate that compared with White race, the Black race was independently associated with a lower hazard of receiving statin and the Other race was associated with a lower hazard of receiving aspirin among kidney transplant recipients with established CVD enrolled in the FAVORIT trial.

There are several potential reasons for less CVD medication use among participants of Black and Other races compared to their White counterparts. Clinicians may prescribe CVD medications differently by race, due to an underestimation of CVD risks among non-White kidney transplant recipients, implicit bias, or a focus on non-CVD strategies like immunosuppression to maximize allograft health. This is consistent with findings from a post hoc analysis of the Patient Outcomes in Renal Transplantation study, which evaluated CVD risks and medications in 23,575 kidney transplant recipients from 14 centers worldwide (including some in the United States and Canada). In the Patient Outcomes in Renal Transplantation study, Black and Asian patients had lower odds of being prescribed statins compared with White patients, and Black patients had lower odds of being prescribed antiplatelet medications compared with White patients.<sup>5</sup> In a study that used Organ Procurement and Transplantation registry data linked to records from a US pharmaceutical claims clearinghouse to evaluate medication use at the first transplant anniversary in 16,157 kidney transplant recipients, the Black race was associated with a higher prevalence of antihypertensive medication use but a lower prevalence of statin use in an adjusted analysis.<sup>21</sup> In a single-center cohort of 987 kidney transplant recipients in South Carolina,<sup>10</sup> there was not a statistically significant difference in prescriptions of statins and  $\beta$ -blockers among Black versus White kidney transplant recipients when there was a compelling indication for receiving these medications. Similarly, in a study of 3,139 US veteran kidney transplant recipients, Black veterans were more likely to be prescribed an angiotensin-converting enzyme inhibitor or  $\beta$ -blocker at 1, 3, and 5 years after transplant than the White veterans. Moreover, there was not a statistically significant racial difference in prescriptions of insulin, oral

hypoglycemic agents, and statins in that study.<sup>7</sup> These studies did not differentiate between prescriptions for primary versus secondary prevention of CVD risk. Further research is needed to understand clinician prescription patterns for CVD risk reduction among non-White kidney transplant recipients.

The patient-level factors that could influence racial differences in CVD medication use include differences in social and economic factors, understanding of complicated posttransplant medication regimens, and access to social support to maximize medication adherence.<sup>22,23</sup> The previously reported factors contributing to racial disparities in access to transplantation and posttransplant outcomes include miscommunication and mistrust between patients and clinicians, patients' lower education and health literacy levels, and patients' lower incomes.<sup>24-26</sup> Although data about health literacy, education, and income are not available in the FAVORIT trial, such factors could translate into lower utilization of CVD medications by non-White study participants, independent of clinician prescription patterns.<sup>27,28</sup> For example, in the aforementioned Veterans Affairs' study,<sup>7</sup> although prescriptions of angiotensin-converting enzyme inhibitors,  $\beta$ -blockers, statins, and insulin were similar or higher among Black than among White veterans, the medication possession ratio (the percentage of time a patient has access to a medication based on refill data) was lower among Black veterans, as was the education level.

Although we found racial differences in medication use for secondary CVD risk reduction in FAVORIT kidney transplant recipients, a prior study found no differences in all-cause mortality or a composite of CVD events and CVD death between Black versus White FAVORIT trial participants.<sup>29</sup> This apparent discrepancy could be explained by insufficient follow-up time in the FAVORIT trial to detect racial differences in CVD mortality and morbidity, given that our study cohort included participants who developed CVD during follow-up. It could also suggest that the use of CVD risk reduction medications may not be as protective in kidney transplant recipients as they are in the general population. Although the efficacy of statins and aspirin in secondary CVD prevention in the general population is well established,<sup>13</sup> the efficacy of these medications in secondary CVD prevention in kidney transplant recipients has not been well studied. The only randomized trial evaluating the effects of statin use for dyslipidemia on CVD outcomes in kidney transplant recipients is the Assessment of Lescol in Renal Transplantation study, in which treatment with fluvastatin compared with placebo led to a nonstatistically significant decrease in the primary composite outcome of fatal and nonfatal CVD after a mean follow-up of 5.1 years.<sup>14,30</sup> In a 2-year, open-label extension of this study, fluvastatin led to a statistically significant reduction in fatal and nonfatal CVD. Fluvastatin was mainly used for primary prevention in this trial. All patients with a history of myocardial infarction within 6 months before enrollment were excluded from the

Assessment of Lescol in Renal Transplantation study, and only a small number of enrolled patients had an established history of CVD. In a post hoc analysis of the FAVORIT trial examining kidney transplant recipients with no known history of CVD, there was not a statistically significant difference in risks for CVD events or all-cause mortality between kidney transplant recipients who were receiving aspirin for primary prevention at baseline compared with those who were not receiving aspirin.<sup>31</sup> Given that kidney transplant recipients are at increased risk of CVD-related morbidity and mortality compared with the general population, studies that explicitly examine the role of medications for secondary CVD prevention are needed to guide practice.

Although other studies evaluating racial disparities in receipt of CVD medications have been cross-sectional, a strength of our study was the use of an interval-censoring design to account for prevalent CVD on enrollment in a time-to-event analysis for secondary CVD prevention. However, the results of this study must be taken in the context of its limitations. The FAVORIT trial was conducted more than a decade ago. Since then, CVD has been increasingly recognized as a major cause of morbidity and mortality in kidney transplant recipients and CVD risk management in this population has intensified.<sup>12</sup> Therefore, the descriptive results of our study may not be directly reflective of modern-day practice, and this is an important limitation of our study. However, compared with other studies that have evaluated racial disparities in CVD care in kidney transplant recipients, the advantage of the FAVORIT trial is that it is a multicenter trial designed to study CVD in kidney transplant recipients who reported medication use during regular follow-ups. Although there are not enough contemporary data about racial disparities in CVD care in kidney transplant recipients, the reasons driving these disparities may not have changed as much over time. Understanding where there are racial differences in CVD care delivery (ie, primary prevention, secondary prevention, use of diagnostic testing) and the mechanisms underlying disparate care delivery is key to developing targeted interventions to mitigate these disparities.<sup>32</sup> Other limitations include a small number of participants included in our final analyses and that the majority of patients (60% in both models) had a diagnosis of CVD and were on statin or aspirin at the time of enrollment, although we accounted for this uncertainty using interval censoring. Also, the lack of granular information on transplant center-specific practices, side effects of aspirin and statin, and potential indications or contraindications for their use for secondary CVD prevention pose the risk for residual confounding and limits interpretation of the results. We did not have information about clinicians' medication prescriptions or patients' adherence. Therefore, the reasons for racial differences in statin or aspirin use for secondary CVD prevention cannot be ascertained. Additionally, the diagnosis of CVD and the receipt of statins and aspirin were largely ascertained

through participant self-report, which is prone to recall bias or social desirability bias. However, investigator confirmation with medical records, medication lists, and bottle labels likely mitigated this potential bias. Also, our study population had a small number of patients with Hispanic ethnicity, precluding any meaningful analyses for this important population.

In summary, post hoc findings from a large, multicenter cohort showed that non-White kidney transplant recipients with CVD had lower hazards of using statin and aspirin than their White counterparts. Because participants in research studies are often more engaged in their care and receive greater guideline-concordant care than the general population,<sup>33,34</sup> the existence of racial disparities in CVD care delivery in the FAVORIT trial is particularly concerning, as it may underestimate the magnitude of disparities in the general population. While over a decade old, these data highlight the importance of optimizing CVD risk reduction medications, as they represent a potential target to improve CVD care in non-White kidney transplant recipients. Further research should examine modern patterns in CVD care delivery and factors contributing to racial disparities for deployment of targeted interventions.

## SUPPLEMENTARY MATERIAL

### Supplementary File (PDF)

**Figure S1:** Goodness-of-fit plot for statin model.

**Figure S2:** Goodness-of-fit plot for aspirin model.

**Table S1:** Definition of censoring intervals for enrolled patients.

**Table S2:** Baseline characteristics of FAVORIT study participants who were included in the statin model.

**Table S3:** Baseline characteristics of FAVORIT study participants who were included in the aspirin model.

**Table S4:** Racial distribution of patients meeting inclusion criteria who were included in and excluded from the analytic models.

**Table S5:** Results of parametric, proportional-hazards, interval-censored survival model with clustering by transplant centers to evaluate the association of race with self-reported receipt of statins and aspirin in kidney transplant recipients.

**Table S6:** Results of parametric, proportional-hazards, interval-censored survival model to evaluate the association of race with self-reported receipt of statins and aspirin in kidney transplant recipients enrolled in the United States.

**Table S7:** Results of parametric, proportional-hazards, interval-censored survival model to evaluate the association of race with self-reported receipt of statins and aspirin in kidney transplant recipients after excluding patients who had a baseline history of cardiovascular disease and were receiving a statin or aspirin at the time of enrollment.

## ARTICLE INFORMATION

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# Racial differences in medication utilization for secondary prevention of cardiovascular disease in kidney transplant recipients



## Cohort Study (post-hoc analysis)

- FAVORIT Trial Cohort Study participants (USA & Canada)
- 30 clinical sites
- Kidney Transplant Recipients
- CVD at diagnosis or during follow-up
- Enrollment 2002 - 2007
- N = 978

Follow-up until 2009

## Analysis

Parametric (Weibull) proportional hazards interval-censored survival models

- Statins
- Aspirin

## Results

	White race	Black race	Other race
Statins	Ref	HR 0.76 95%CI 0.60 - 0.97	HR 0.87 95%CI 0.60 - 1.27
Aspirin	Ref	HR 0.85 95%CI 0.67 - 1.08	HR 0.63 95%CI 0.43 - 0.94

**Conclusion:** Post-hoc findings from FAVORIT demonstrated that Black race was associated with lower likelihood of receiving statins and Other race with lower likelihood of receiving aspirin for secondary CVD prevention. This represents a potential target to improve CVD care in kidney transplant recipients.

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