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The First Increase in Live Kidney Donation in The United States in 15 Years

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Abstract

The first sustained increase in live kidney donation in the US in 15 years was observed from 2017–2019. To help sustain this surge, we studied 35,900 donors (70.3% white, 14.5% Hispanic, 9.3% black, 4.4% Asian) to understand the increase in 2017–2019 vs. 2014–2016 using Poisson regression. Among biologically related donors aged <35, 35–49, and 50 years, the number of donors did not change across race/ethnicity but increased by 38% and 29% for Hispanic and black 50. Among unrelated donors <35, 35–49, and 50, white donors increased by 18%, 14%, and

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Study concept and design: Al Ammary, Yu, Massie, Muzaale. Acquisition of data: Al Ammary, Massie, Segev. Analysis and interpretation of data: Al Ammary, Yu, Ferzola, Massie, Thomas, Segev, Muzaale. Drafting of the manuscript: Al Ammary, Yu, Massie, Segev, Muzaale. Critical revision of the manuscript for important intellectual content: Al Ammary, Yu, Ferzola, Massie, Motter, Henderson, Thomas, Crews, Segev, Muzaale. Statistical analysis: Al Ammary, Yu, Muzaale, Massie, Segev. Obtained funding: Segev. Administrative, technical, and material support: Massie. Study supervision: Muzaale.

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27%; Hispanic donors <35 did not change but increased by 22% and 35% for 35–49 and 50; black donors <35 declined by 23% and did not change for 35–49 and 50; Asian donors did not change. Among kidney paired donors <35, 35–49, and 50, white donors increased by 42%, 50%, and 68%; Hispanic donors <35 and 35–49 increased by 36% and 55% and did not change for 50; black donors did not change; Asian donors <35 did not change but increased by 107% and 82% for 35–49 and 50. The increase in donation was driven predominantly by unrelated and paired white donors. Donation among unrelated black individuals should be promoted.

Keywords

Living kidney Donors; Annual Trends; Unrelated Donors; Donor Nephrectomy

INTRODUCTION

An alarming trend between 2005 and 2017 was the decline in the annual number of live kidney donors in the United States.^{1–4} This was driven exclusively by the decline in biologically related donors who have historically been the majority of this population.¹ In this changing landscape of live kidney donation, however, there was a steady growth in the number of unrelated donors.^{1,5} While these observed trends differed by donor-recipient relationship, they were similar across race/ethnicity.

However, with excitement, the transplant community has witnessed a sustained increase in the overall number of donors from 2017 to 2019, a trend which has not been seen in the United States since 2004.⁶ No study has examined the donor characteristics associated with this recent increase in live donation. Furthermore, no study has characterized the kidney paired donor phenotype in these trends, an emerging phenotype that may not readily be described as biologically related or unrelated in national registry data.^{7,8} Understanding these trends in donation may provide opportunities to effectively sustain or even enhance this recent increase in donors.⁹ Such a goal is timely since 2020 is on course to have a negative impact on live kidney donation given the COVID-19 pandemic and transplant programs limiting procedures.^{10,11}

The objective of this study was to use national registry data to understand the first increase in live kidney donation in the United States in 15 years. We hypothesize that unrelated donors have become the majority of live kidney donors and are driving this recent surge in live donation. We studied three donor subgroups including biologically related, unrelated, and kidney paired donors, to identify the donor characteristics underlying the increase in number of donors in 2017 to 2019 vs. 2014–2016.

METHODS

Data Source

This study used data from the Scientific Registry of Transplant Recipients (SRTR) external release made available in April 2020. The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN), and has been

described elsewhere.^{12,13} The Health Resources and Services Administration (HRSA), U.S. Department of Health and Human Services provides oversight to the activities of the OPTN and SRTR contractors.

Study Population

The study population included 35,900 live kidney donors between January 1, 2014, and December 31, 2019. We stratified our study population by donor type as being related, unrelated, or kidney paired donors because the annual number of donors in the US has substantially varied by donor-recipient relationship.^{1,5} We also recognized the potential influence of the expansion of kidney paired donation, and thus we included paired donors as a unique subgroup.^{7,14} Donors were considered related if they had a biological relationship to the recipient such as a parent, child, sibling, or non-first degree biologically related, as reported by transplant centers to the SRTR. Kidney paired donation primarily represented the exchange of kidneys between incompatible (ABO or human leukocyte antigen) living donor-recipient pairs, so the recipients can receive compatible kidneys. Some kidney paired donation systems do incorporate immunologically compatible pairs in order to maximize the number of transplants or improve other clinical donor characteristics for the recipient. While the transplanted pairs in kidney paired donation are non-biologically related to one another, it is important to note that a proportion of kidney paired donors have a biological relationship to their intended recipient (i.e. an incompatible recipient that entered the exchange with the donor).¹⁵ We compared donor demographics and health characteristics, including age, race, sex, body mass index [BMI], hypertension, preoperative serum creatinine and estimated glomerular filtration rate [eGFR], and highest level of education. We compared donor demographics and health characteristics using χ^2 for categorical variables, and Wilcoxon Rank Sum Test for continuous variables.

Change in Number of Donors in 2017–2019 vs. 2014–2016

The outcome of interest was the change in live kidney donation over time. Based on OPTN data as of March 30, 2020, there was a continuous increase in the number of live kidney donors from 2017 to 2019.^{6,16} Thus, we compared trends in specific donor subpopulations in 2017–2019 vs. 2014–2016. A priori, we stratified the analyses by donor type (related, unrelated, and kidney paired donor), donor race (white, Hispanic, black, Asian), and donor age (<35, 35–49, and ≥50 years) to reflect younger, typical, and older donors, respectively. Because of limited sample size, we were not able to perform distinct analyses for other races including American Indian, Alaskan Native, Native Hawaiian, other Pacific Islander, and multiracial (all together <1.5%). We used this stratified approach because of the evolving knowledge of increased risks of end-stage kidney disease for specific donor subgroups, including those associated with family history of kidney disease, APOL1 high-risk genotypes, and younger age.^{17–26}

Statistical analysis

We used Poisson regression to estimate the change in number of donors over time (incidence rate ratio [IRR]). The IRR indicates the proportional decline or increase in the number of donors in 2017–2019 vs. 2014–2016, based on aggregated data. We used Louis and Zeger's method to report confidence intervals.²⁷ We used a 2-sided α level of 0.05 to indicate a

statistically significant difference.²⁷ All analyses were performed using Stata/MP for Linux, version 16.0.

RESULTS

Study population

From 1/1/2014 to 12/31/2016, a total of 16,797 donors were identified within the SRTR. Forty-seven percent were related, 42% were unrelated, and 11% were paired donors. Compared to unrelated and paired donors, related donors were more likely to be younger (median age: 40 vs. 45 vs. 45 years, $p < 0.001$), male (40% vs. 34% vs. 36%, $p < 0.001$), have higher eGFR (median eGFR: 100.6 vs. 95.6 vs. 97.6 ml/min/m², $p < 0.001$); and were less likely to be white (62% vs. 78% vs. 72%, $p < 0.001$), and less likely to attend college/post-secondary school (46% vs. 50% vs. 49%, $p < 0.001$).

From 1/1/2017 to 12/31/2019, a total of 19,103 donors were identified within the SRTR. Forty-one percent were related, 45% were unrelated, and 14% were paired donors. Compared to unrelated and paired donors, related donors were more likely to be younger (median age: 41 vs. 46 vs. 45 years, $p < 0.001$), male (40% vs. 33% vs. 35%, $p < 0.001$), to have higher BMI (median BMI: 27.1 vs. 26.6 vs. 26.4, $p < 0.01$), and higher eGFR (median eGFR: 99.5 vs. 95.4 vs. 95.7 ml/min/m², $p < 0.001$); and were less likely to be white (61% vs. 81% vs. 74%, $p < 0.001$), and less likely to attend college/post-secondary school (49% vs. 55% vs. 57%, $p < 0.001$) (Table 1).

Observed Number of live kidney donors over the study period

The overall annual number of donors increased from 5,539 in 2014 to 6,858 in 2019 (24% increase). The change in annual number of donors varied by donor type. From 2014 to 2019, related donors declined from 2,702 to 2,605 (4% decline); unrelated donors increased from 2,261 to 3,120 (38% increase); and paired donors increased from 576 to 1,117 (94% increase) [Figure 1].

Among related donors from 2014 to 2019, the number of white donors declined from 496 to 415 for age <35 group (16% decline), declined from 692 to 603 for age 35–49 group (13% decline), and slightly declined from 530 to 524 for age 50 group (0.1% decline). The number of Hispanic donors increased from 232 to 240 for age <35 group (3% increase), from 171 to 194 for age 35–49 group (13% increase), and from 63 to 101 for age 50 group (60% increase). The number of black donors declined from 177 to 132 for age <35 group (25% decline), from 141 to 132 for age 35–49 group (6% decline) and increased from 46 to 76 for age 50 group (65% increase). The number of Asian donors increased from 38 to 56 for age <35 group (47% increase), slightly declined from 53 to 52 for age 35–49 group (0.2% decline), and increased from 28 to 36 for age 50 group (29% increase) [Figure 2A].

Among unrelated donors from 2014 to 2019, the number of white donors increased from 373 to 487 for age <35 group (31% increase), from 720 to 927 for age 35–49 group (29% increase) and from 657 to 1,056 for age 50 group (61% increase). The number of Hispanic donors increased from 85 to 108 for age <35 group (27% increase), from 105 to 146 for age 35–49 group (39% increase), and from 44 to 68 for age 50 group (55% increase). The

number of black donors declined from 47 to 36 for age <35 group (23% decline), from 87 to 84 for age 35–49 group (3% decline) and increased from 34 to 54 for age 50 group (59% increase). The number of Asian donors increased from 19 to 25 for age <35 group (32% increase), increased from 41 to 51 for age 35–49 group (24% increase), and from 25 to 35 for age 50 group (40% increase) [Figure 2B].

Among paired donors from 2014 to 2019, the number of white donors increased from 84 to 174 for age <35 group (107% increase), from 169 to 296 for age 35–49 group (75% increase), and from 176 to 354 for age 50 group (102% increase). The number of Hispanic donors increased from 24 to 52 for age <35 group (117% increase), from 24 to 58 for age 35–49 group (142% increase), increased from 15 to 30 for age 50 group (100% increase). The number of black donors increased from 22 to 29 for age <35 group (32% increase), declined from 27 to 37 for age 35–49 group (37% decline) and increased from 12 to 17 for age 50 group (42% increase). The number of Asian donors unchanged (8 to 8) for age <35 group, increased from 8 to 29 for age 35–49 group (262% increase), and from 2 to 10 for age 50 group (400% increase) [Figure 2C].

IRR of Live Kidney Donation in 2017–2019 vs. 2014–2016

The number of related donors did not increase across all race/ethnicity subgroups in 2017–2019 vs. 2014–2016, except in black and Hispanic older donors. The number of related white donors did not change significantly for age <35 group (IRR: 0.87 0.94 1.01), age 35–49 group (IRR: 0.93 1.00 1.06), or age 50 group (IRR: 0.92 0.99 1.06). The number of related Hispanic donors did not change significantly for age <35 group (IRR: 0.89 1.00 1.11) and age 35–49 group (IRR: 0.91 1.02 1.15) but increased by 38% for age 50 group (1.16 1.38 1.65). Similarly, the number of related black donors did not change significantly for age <35 group (IRR: 0.80 0.92 1.05) and age 35–49 group (IRR: 0.83 0.96 1.11), but increased by 29% for age 50 group (IRR: 1.04 1.29 1.60). The number of related Asian donors did not change significantly for age <35 group (IRR: 0.88 1.10 1.38), age 35–49 group (IRR: 0.83 1.03 1.27), or age 50 group (0.83 1.09 1.42) [Figure 3A].

The number of unrelated donors increased across all race/ethnicity subgroups in the 2017–2019 vs. 2014–2016, except black and Asian donors. The number of unrelated white donors increased by 18% for age <35 group (IRR: 1.09 1.18 1.28), 14% for age 35–49 group (IRR: 1.08 1.14 1.21), 27% for age 50 group (IRR: 1.20 1.27 1.34). The number of unrelated Hispanic donors did not change significantly for age <35 group (IRR: 0.96 1.14 1.36) but increased by 22% for age 35–49 group (IRR: 1.06 1.22 1.41) and by 35% for age 50 group (IRR: 1.10 1.35 1.67). The number of unrelated black donors declined by 23% for age <35 group (IRR: 0.60 0.77 0.98), but did not change significantly for age 35–49 (IRR: 0.88 1.05 1.25) and age 50 group (IRR: 0.95 1.22 1.56). The number of unrelated Asian donors did not change significantly for age <35 group (IRR: 0.73 1.05 1.53), age 35–49 (IRR: 0.91 1.17 1.51) and age 50 group (IRR: 0.99 1.34 1.81) [Figure 3B].

The number of paired donors increased across all race/ethnicity subgroups in 2017–2019 vs. 2014–2016, except black donors. The number of paired white donors increased by 42% for age <35 group (IRR: 1.22 1.42 1.65), 50% for age 35–49 group (IRR: 1.34 1.50 1.68), and 68% for age 50 group (IRR: 1.51 1.68 1.87). The number of paired Hispanic donors increased by

36% for age <35 group (IRR: 1.02 1.36 1.82), by 55% for age 35–49 group (IRR: 1.21 1.55 1.98), and did not change significantly for age ≥ 50 group (IRR: 0.94 1.34 1.91). The number of paired black donors did not change significantly for age <35 (IRR: 0.83 1.18 1.67), age 35–49 (IRR: 0.70 0.96 1.32), and age ≥ 50 (0.72 1.10 1.66). The number of paired Asian donors did not change significantly for age <35 group (IRR: 0.63 1.08 1.84), but increased by 107% for age 35–49 group (IRR: 1.32 2.07 3.25), and 82% for age ≥ 50 group (IRR: 1.08 1.82 3.06). [Figure 3C].

DISCUSSION

In this US national study of live kidney donors, we found that the overall increase in the number of donors in 2017–2019 vs. 2014–2016 was driven predominantly by the increase in unrelated and paired white donors of all ages. Unrelated donors have emerged as the majority of live donors in this period. That said, we continue to observe an overall lack of growth in related donors across all race/ethnicity subgroups except in black and Hispanic older donors. Our study not only reaffirms the reported overall decline in related donors, but also reveals significant declines in unrelated black donors. This is a reminder that national strategies are needed to address racial disparities in access to live donor kidney transplantation.^{28,29}

Unlike studies that have been concerned with the decade-long decline in live kidney donation in the US,^{1,2,4} herein we describe the first sustained increase in donors and in 2019 the highest number of donors to date. Moreover, our study reveals that the rise of kidney paired donors was predominantly among those who were white. While the donor-recipient relationship is not well documented in national registry studies with respect to kidney paired donation, the majority of kidney paired donors are unrelated. In a study of 2,766 transplants using the national kidney registry, 24% were biologically related and 76% were unrelated.¹⁵ Kidney paired donation maximizes utilization of potential donors and overcomes barriers for sensitized kidney transplant recipients. However, we found no substantive increase in kidney paired donation among black donors.¹⁴ Our study calls for efforts to increase awareness among unrelated black individuals about the benefits of kidney paired donation.

The limitations of this study merit consideration. Since this is a national registry study, we were not able to assess the potential impact of center level efforts on these reported trends.³⁰ Also, we did not have data on donor candidates that were considered ineligible, so we cannot rule out the contribution to our inferences of genetic, lifestyle, or other clinical factors not reported to the registry. However, we found it promising that the increase in live kidney donation among related older Hispanic and black donors is non-negligible. We speculate that this might reflect the emerging view wherein related older donors are considered to be beyond the riskiest years in which familial ESRD manifests.⁹ For this reason, we reiterate the call for increased permissiveness for related older donors across race/ethnicity.¹

That said, a key strength of our study is the use of a national registry to capture the entire population of donors and the demonstration of the interdependence among demographic characteristics including donor/recipient relationship, race/ethnicity, and age in the increase

in live kidney donation. Our study highlights the opportunity to target subgroups with a lack of growth in number of donors. This is timely since COVID19 will disrupt the “sustained” increase in live donation from 2017–2019, given the nationwide halt on live donor transplants. Our inferences should remain relevant beyond the COVID-19 crisis since the subgroups with a lack of growth before the pandemic are likely to face similar barriers in the foreseeable future. Our findings potentially direct future interventions to increase live kidney donation among unrelated black individuals in addition to our previous call to promote donation among related older individuals.¹

In conclusion, we report that unrelated and paired white donors were the principal driver of the recent surge in live kidney donation from 2017–2019. Our findings call for efforts to promote live kidney donation and to take more advantage of kidney paired donation programs by unrelated black individuals.

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ABBREVIATIONS

BMI	body mass index
eGFR	estimated glomerular filtration rate
HRSA	The Health Resources and Services Administration
IQR	interquartile range
IRR	Incidence Rate ratio
OPTN	Organ Procurement and Transplantation Network
SRTR	Scientific Registry of Transplant Recipients
US	United States

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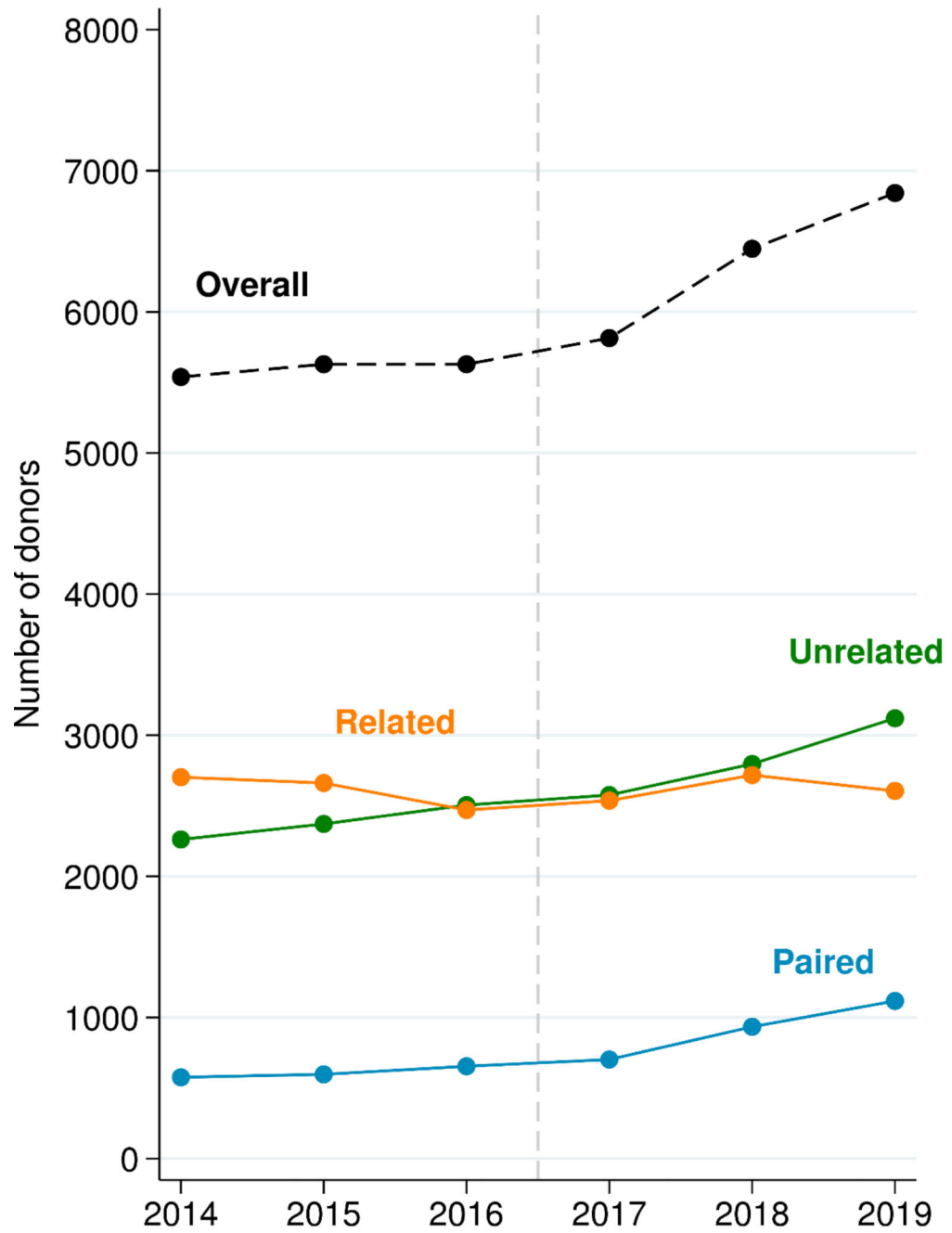


Figure 1: Annual number of live kidney donors in the United States from 2014 to 2019, stratified by donor type (biologically related, unrelated, kidney paired donors).

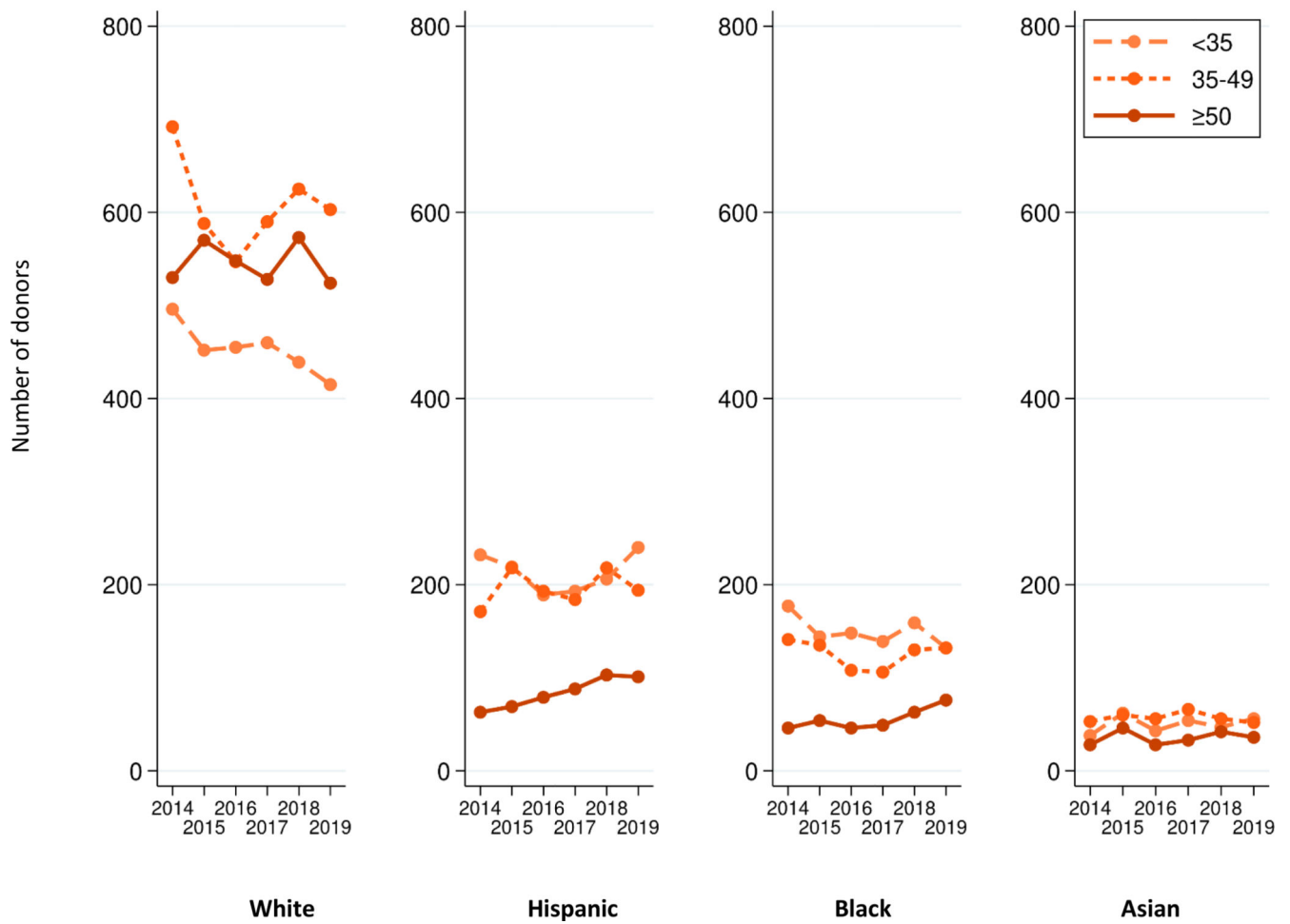
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2A. Related donors



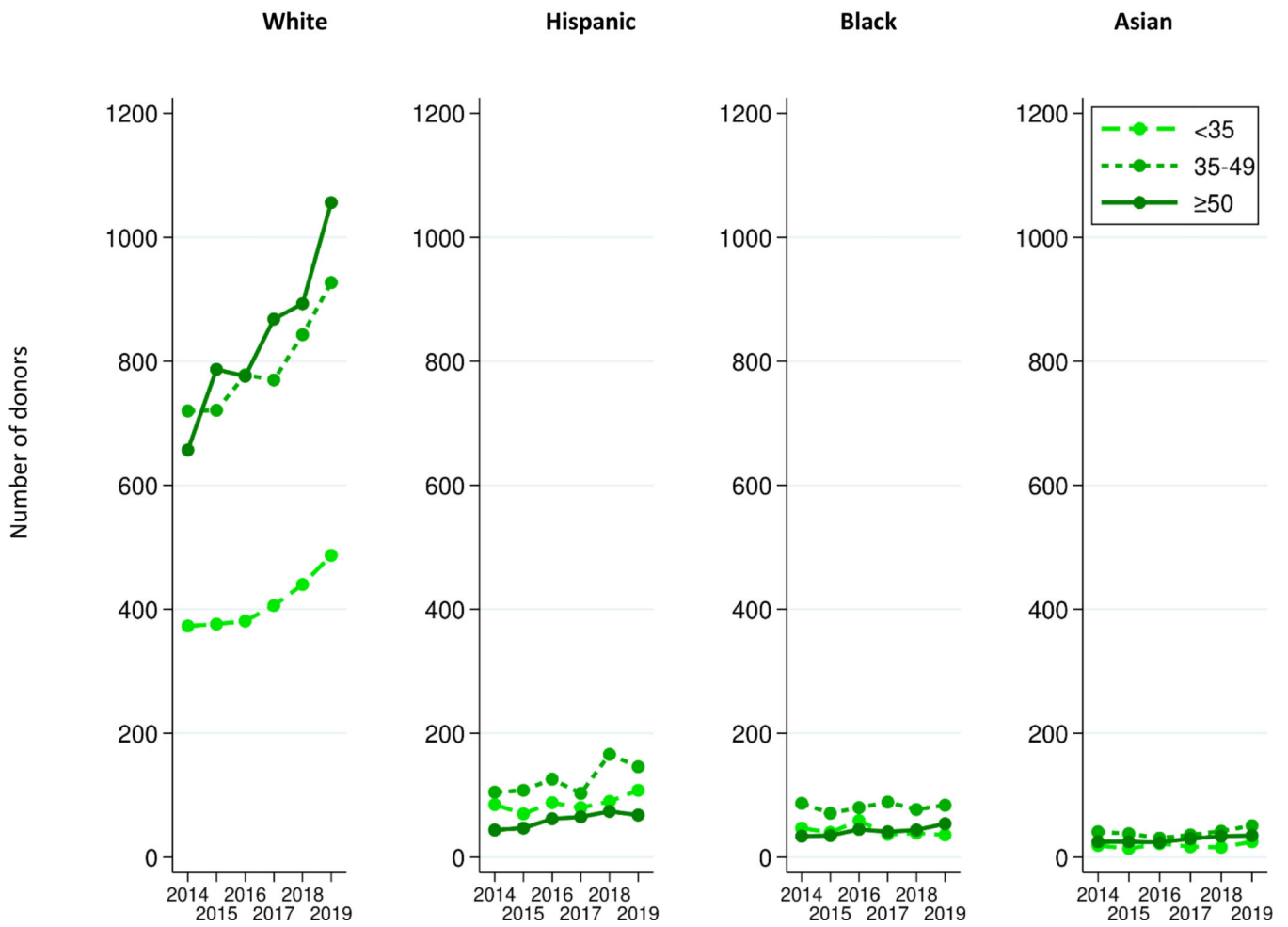
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2B. Unrelated donors



2C. Kidney paired donors

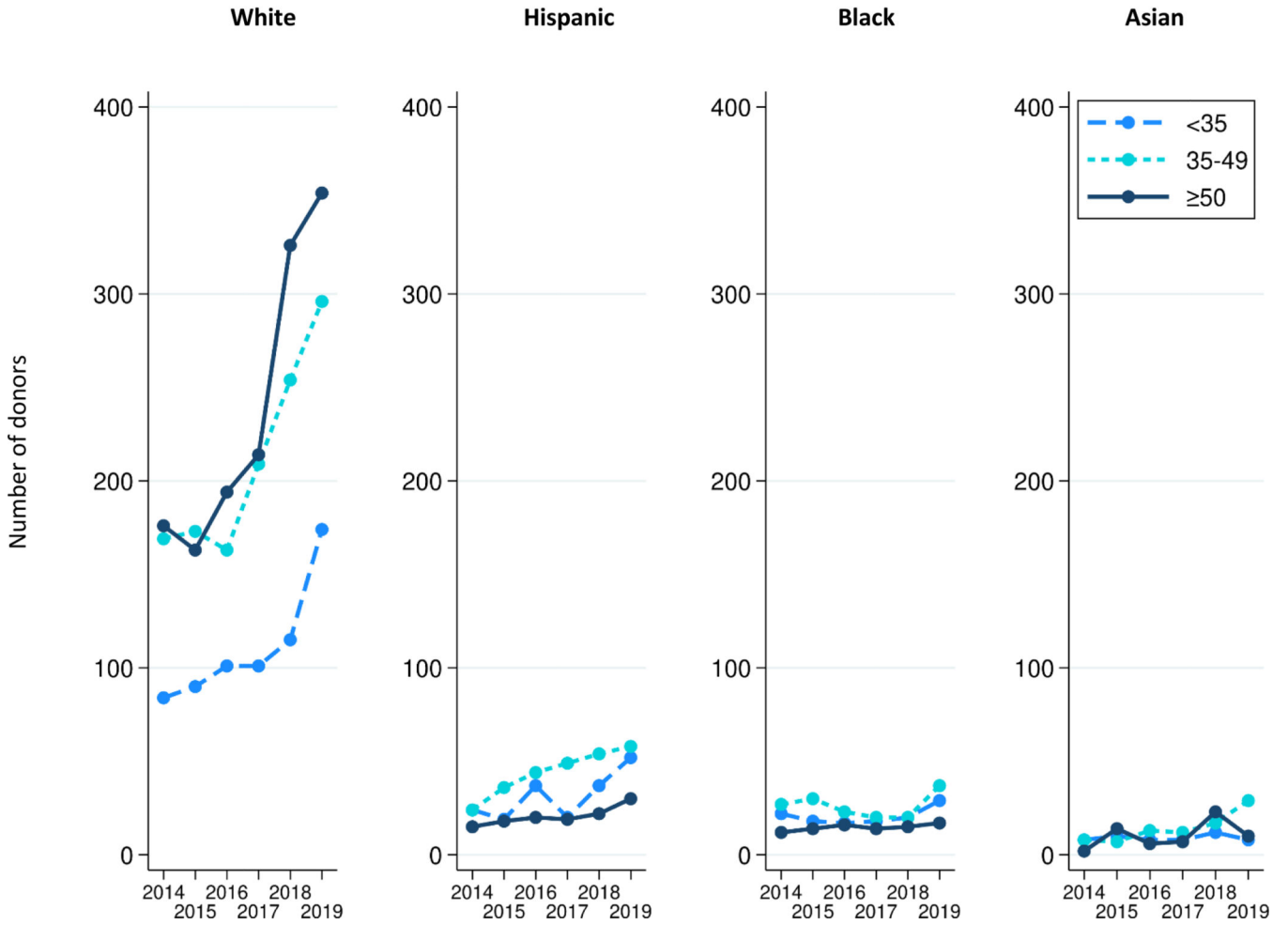


Figure 2: Observed number of live kidney donors in the United States from 2014 to 2019, stratified by donor type (biologically related, unrelated, kidney paired donors), race/ethnicity*, and age. * Other races including American Indian, Alaskan Native, Native Hawaiian, other Pacific Islander, and multiracial were not included in this analysis because of limited sample size (all together N=541).

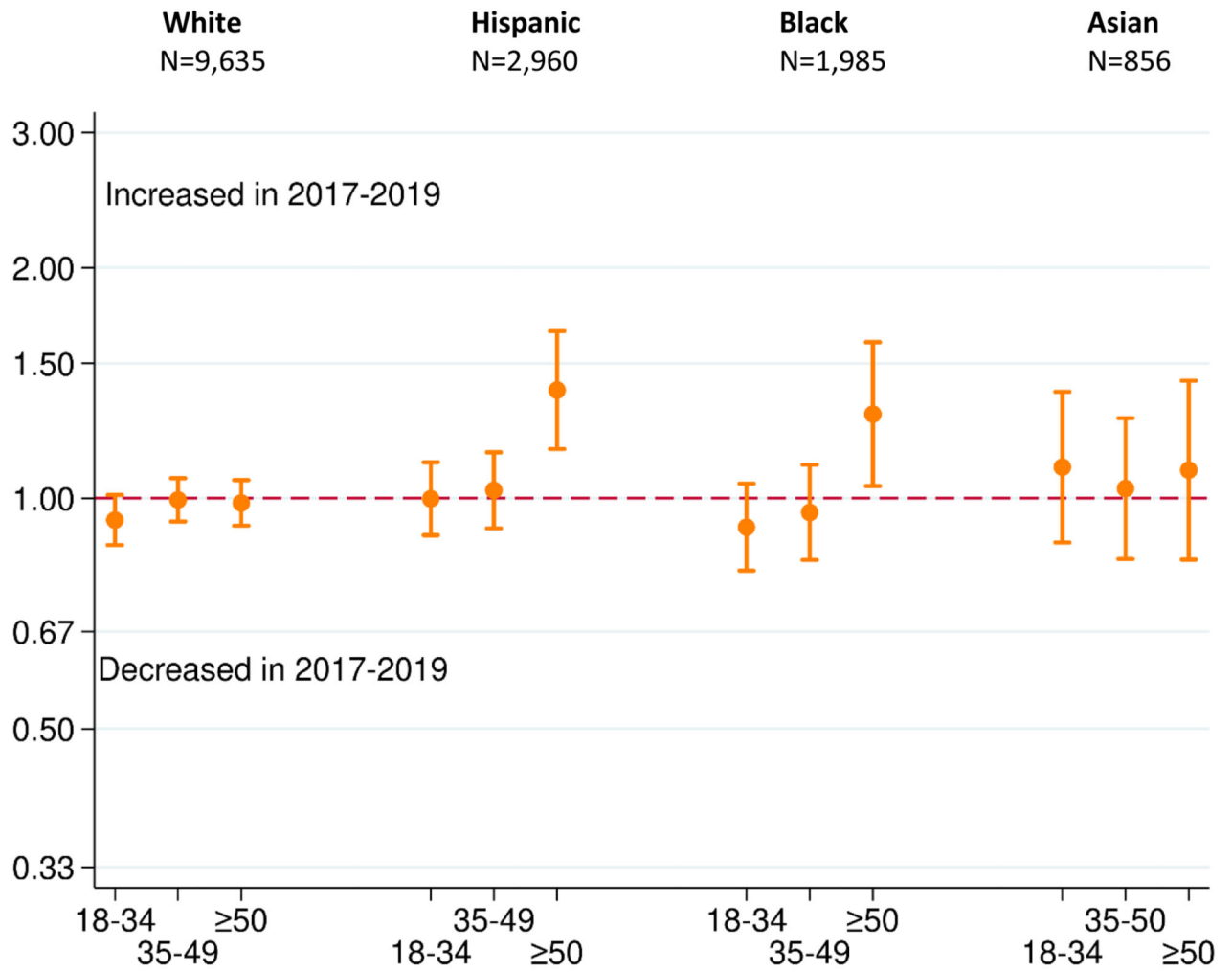
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3A. Related donors



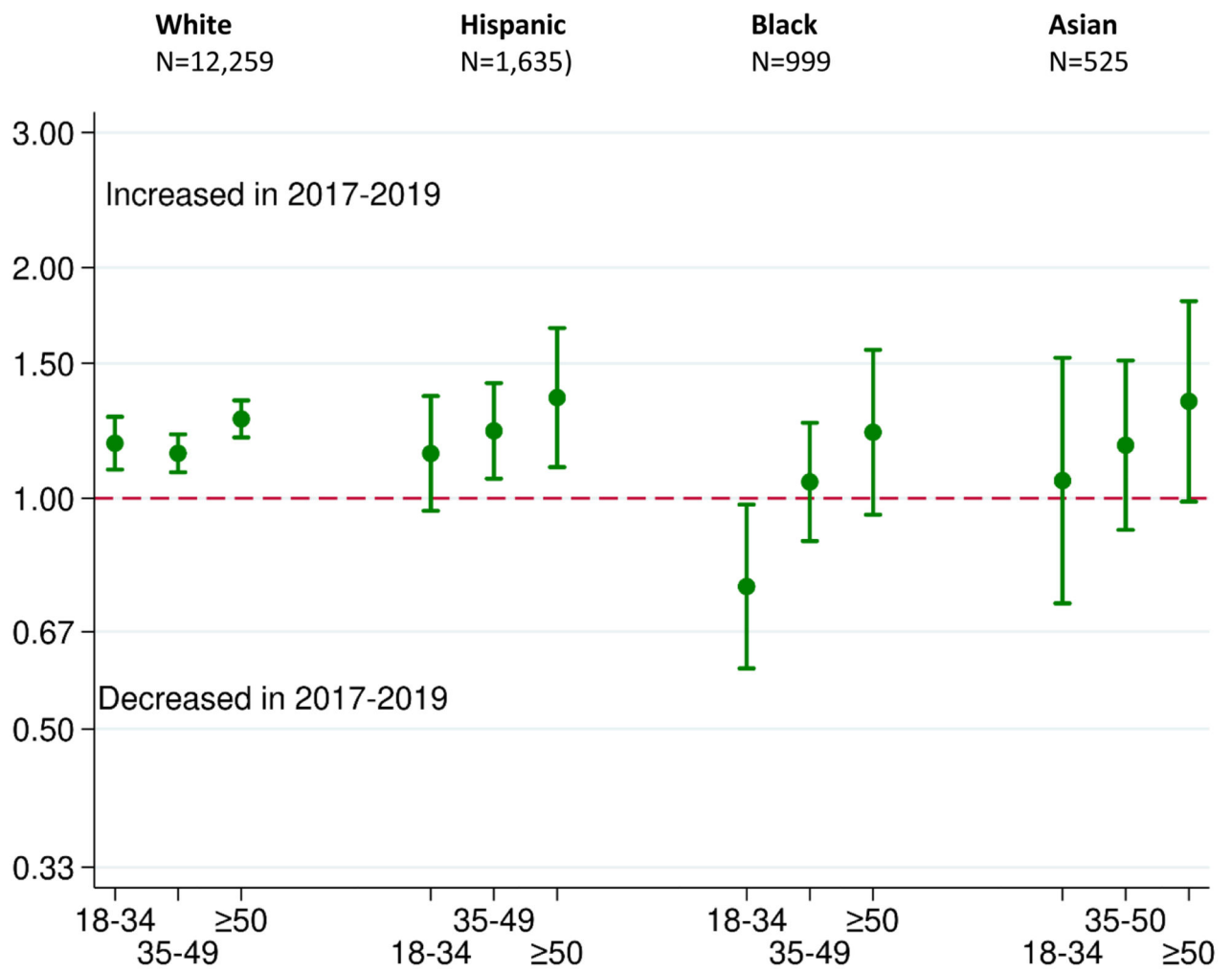
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3B. Unrelated donors



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3C. Kidney paired donors

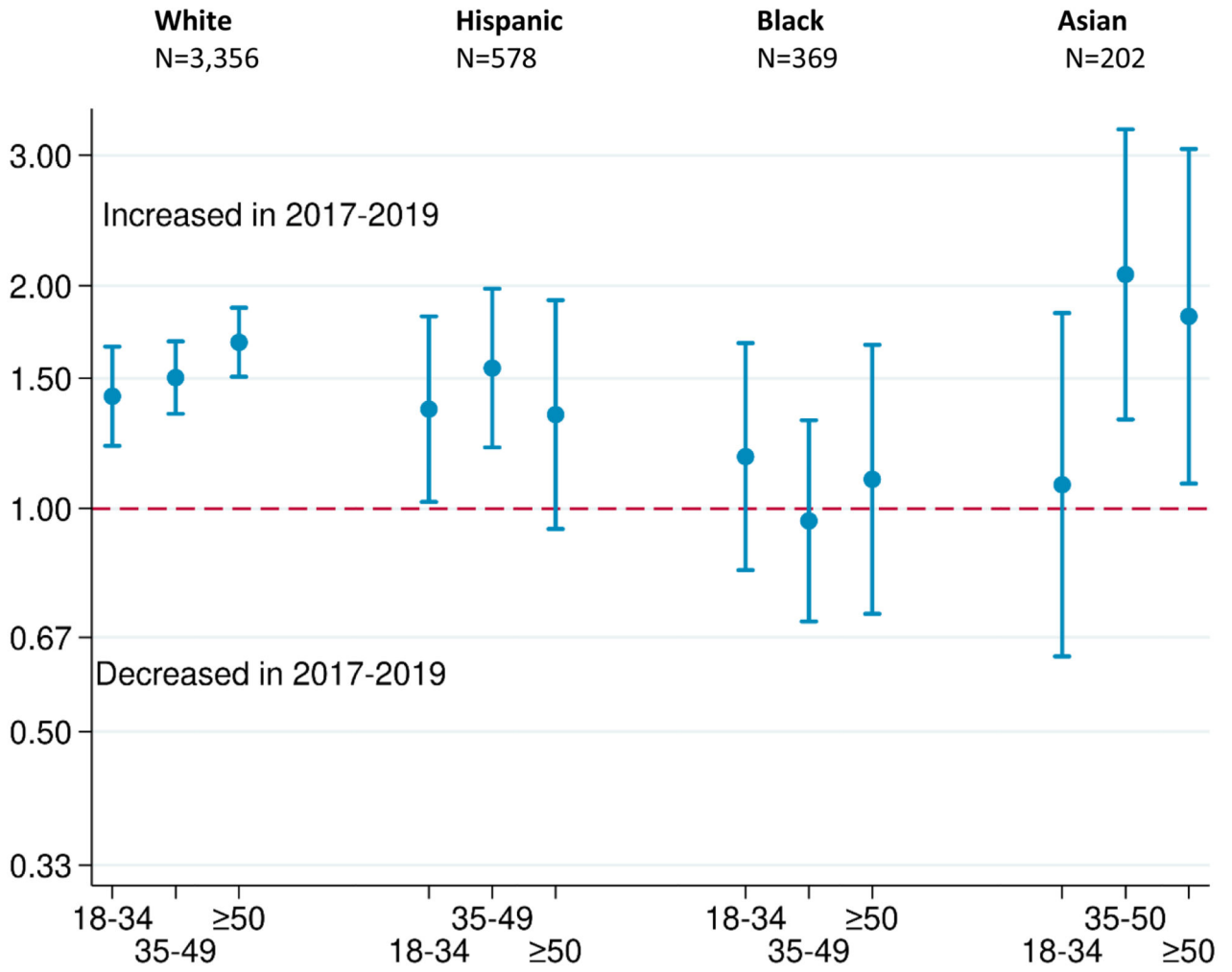


Figure 3: Incidence rate ratio of live kidney donation in the United States in 2017–2019 vs. 2014–2016, stratified by donor type (biologically related, unrelated, kidney paired donors), race/ethnicity*, and age. * Other races including American Indian, Alaskan Native, Native Hawaiian, other Pacific Islander, and multiracial were not included in this analysis because of limited sample size (all together N=541).

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Table 1.

Baseline characteristics of live kidney donors in the United States in 2014–2016 and 2017–2019, stratified by donor type (biologically related, unrelated, kidney paired donors).

Donation period Characteristic ¹	2014–2016			2017–2019		
	Related (N=7,833)	Unrelated (N=7,137)	Paired (N=1,827)	Related (N=7,858)	Unrelated (N=8,492)	Paired (N=2,753)
Race						
White	62%	78%	72%	62%	81%	74%
Hispanic	18%	10%	13%	19%	10%	12%
Black	13%	7%	10%	12%	6%	7%
Asian	5%	3%	4%	6%	2%	5%
Other ²	2%	2%	1%	1%	1%	2%
Age, median (IQR)						
	40.0 (31.0, 50.0)	45.0 (36.0, 54.0)	45.0 (35.0, 53.0)	41.0 (31.0, 51.0)	46.0 (36.0, 55.0)	45.0 (36.0, 55.0)
34	35%	22%	25%	33%	21%	22%
35–49	38%	41%	40%	39%	40%	39%
50	27%	36%	36%	28%	39%	39%
Male sex						
	40%	34%	36%	40%	33%	35%
BMI³, median (IQR)						
	26.8 (23.9, 29.8)	26.6 (23.8, 29.6)	26.6 (23.8, 29.6)	27.1 (24.1, 29.9)	26.6 (23.8, 29.5)	26.4 (23.7, 29.4)
25	34%	34%	35%	32%	35%	37%
25–29	42%	43%	42%	44%	43%	42%
30	23%	22%	23%	24%	22%	21%
Hypertension⁴						
	4%	5%	4%	4%	5%	5%
eGFR⁵, median (IQR)						
	100.6 (88, 112.2)	96.6 (84.6, 108.0)	97.6 (85.6, 109.4)	99.5 (87.0, 111.6)	95.4 (83.8, 107.0)	95.7 (84.0, 107.4)
Creatinine⁵, median (IQR)						
	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)	0.8 (0.7, 0.9)
Highest level of education⁶:						
High School or less	28%	24%	24%	25%	20%	19%
Attended college/ Technical school	26%	26%	27%	27%	25%	25%
College/Post-Secondary school	46%	50%	49%	49%	55%	57%

Abbreviations: IQR, Interquartile Range; BMI, body mass index, calculated as weight in kilograms divided by height in meters squared; eGFR, estimated glomerular filtration rate.

¹Characteristics at the time of donation (2014–2016) and (2017–2019) are shown; age, sex, and race/ethnicity, biological relationship to the recipient were available throughout the study period.

²The category of “Other” included American Indian, Alaskan Native, Native Hawaiian, other Pacific Islander, and multiracial.

³BMI (0.15% missing between 2014–2016; 0.47% missing 2017–2019).

⁴Hypertension was defined as predonation documented use of antihypertensive therapy/history of hypertension (0.11% missing between 2014–2016; 0.07% missing 2017–2019).

⁵eGFR and creatinine (0.09% missing between 2014–2016; 0.18 % missing 2017–2019).

⁶Education (3.17% missing between 2014–2016; 2.24% missing 2017–2019).

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