Associations of Race and Ethnicity with Anemia Management among Patients Initiating Renal Replacement Therapy

Steven D. Weisbord, MD, MSc; Linda F. Fried, MD, MPH; Maria K. Mor, PhD; Abby L. Resnick, MA; Paul L. Kimmel, MD; Paul M. Palevsky, MD; and Michael J. Fine, MD, MSc

Financial support: There was no direct funding source for this work. Dr. Weisbord was supported by a Veterans Affairs Health Services Research and Development Career Development Award (RCD 03-176). Dr Fried was supported by a VA Advanced Career Development Award. Dr. Fine was supported in part by a mid-career development award (K24 AI001769) from the National Institute of Allergy and Infectious Diseases. Weisbord is on the speakers bureau of Amgen and has received research support from Roche Pharmaceuticals.

Background: Many patients initiate renal replacement therapy with suboptimal anemia management. The factors contributing to this remain largely unknown. The aim of this study was to assess the associations of race and ethnicity with anemia care prior to the initiation of renal replacement therapy.

Methods: Using data from the medical evidence form filed for patients who initiated renal replacement therapy between 1995–2003, we assessed racial and ethnic differences in pre-end-stage renal disease hematocrit levels, the use of erythropoiesis stimulation agents (ESAs), the proportion of patients with hematocrit levels ≥33% and the proportion of patients with hematocrit levels <33% that did not receive ESA. We also examined secular trends in racial and ethnic differences in these parameters.

Results: In multivariable analyses, non-Hispanic blacks had lower hematocrit levels (Δ hematocrit = -0.97%, 95% CI: -1.00–-0.94%), and were less likely to receive ESA (OR=0.82, 95% CI: 0.81–0.84), to initiate renal replacement therapy with hematocrit ≥33% (OR=0.78, 95% CI: 0.77–0.79) or to receive ESA if the hematocrit was <33% (OR=0.79, 95% CI: 0.77–0.80) than non-Hispanic whites. White Hispanics also had lower hematocrit levels (Δ hematocrit = -0.42%, 95% CI:-0.47% to -0.37%), and were less likely to receive ESA (OR=0.86, 95% CI: 0.85–0.88), to have hematocrit levels ≥33% (OR=0.91, 95% CI: 0.89–0.93) or to receive ESA if the hematocrit was <33% (OR=0.85, 95% CI: 0.83–0.87) than non-Hispanic whites. These disparities persisted over the eight-year study period.

Conclusions: African-American race and Hispanic ethnicity are associated with suboptimal pre-end-stage renal disease anemia management. Efforts to improve anemia care should incorporate targeted interventions to decrease these disparities.

Key words: health disparities ■ end-stage renal disease ■ kidney ■ race/ethnicity

 From the Center for Health Equity Research and Promotion (Weisbord, Fried, Mor, Resnick, Fine), Renal Section, Medical Specialty Service Line (Weisbord, Fried, Palevsky), VA Pittsburgh Healthcare System, Pittsburgh, PA; Renal-Electrolyte Division (Weisbord, Fried, Palevsky) and Division of General Internal Medicine (Fine), Department of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA; Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA (Mor); and Division of Renal Diseases and Hypertension, Department of Medicine, George Washington University Medical Center, Washington, DC (Kimmel). Send correspondence and reprint requests for *J Natl Med Assoc.* 2007;99:1218–1226 to: Dr. Steven D. Weisbord, VA Pittsburgh Healthcare System, Mailstop 111F-U, 7E Room 120, Pittsburgh, PA 15240; phone: (412) 688-6000 ext. 815911; fax: (412) 688-6908; e-mail: weisbordsd@upmc.edu

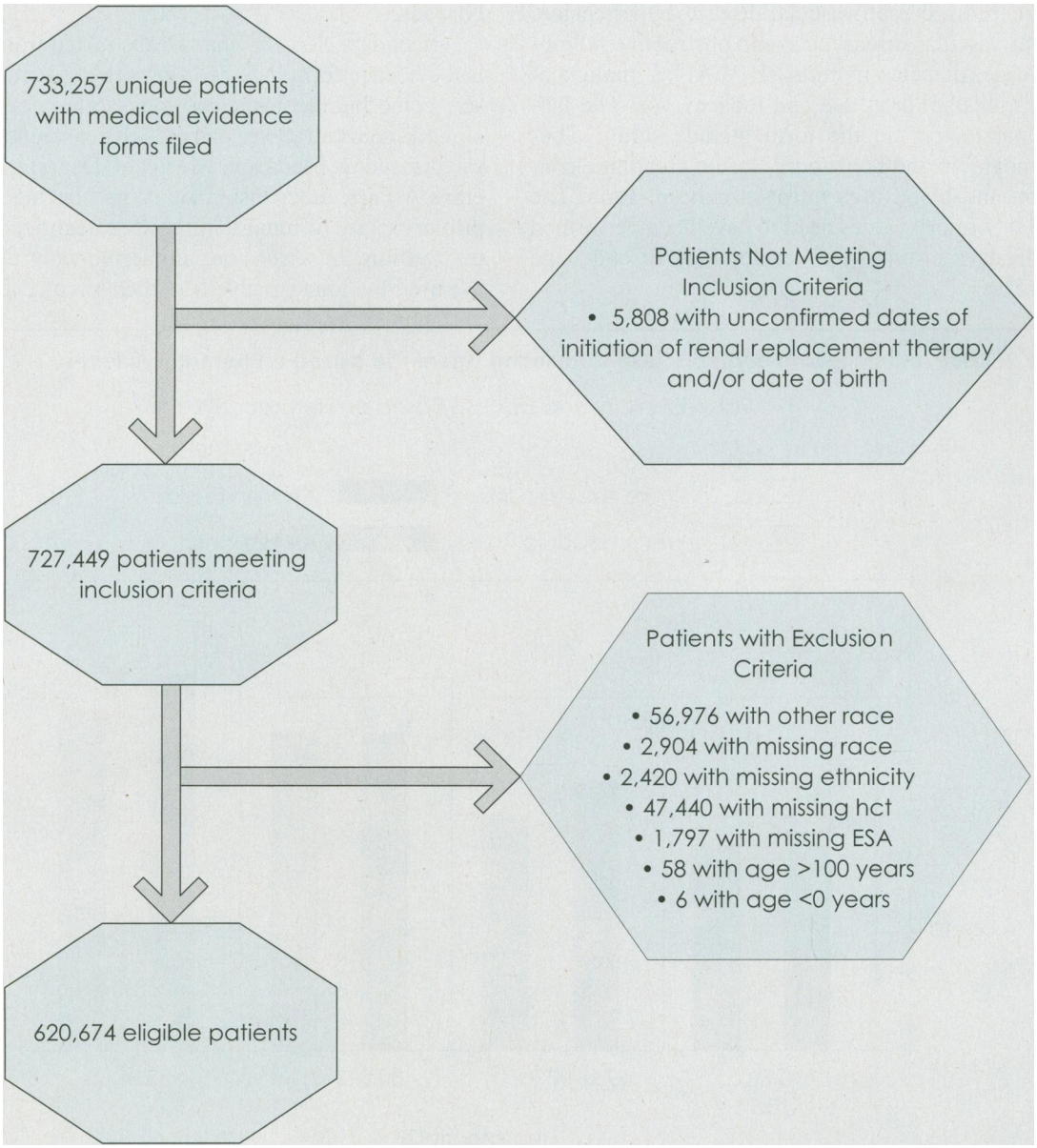
BACKGROUND

Anemia is a well-recognized complication of chronic kidney disease; contributes to impairments in quality of life; and has been linked in observational studies to increased health resource utilization, morbidity and mortality.[1-6] The introduction of recombinant human erythropoietin (rHuEpo) into clinical practice nearly two decades ago transformed the management of anemia for patients with end-stage renal disease by reducing the need for routine blood transfusions and improving overall quality of life, cognition and sexual function.[2,3,7-9] Similar benefits have been recognized in patients with earlier stages of chronic kidney disease.[10,11] As a result, rHuEpo and newer bioengineered agents, which collectively constitute erythropoietin stimulating agents (ESAs), have become standard treatment for the anemia of chronic kidney disease.

Despite the widespread clinical benefits of ESA

therapy and recommendations of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative Clinical Practice Guidelines to use ESA to maintain the hematocrit of patients with chronic kidney disease between 33–36%, studies have found that the majority of patients who initiate renal replacement therapy (RRT), including hemodialysis, peritoneal dialysis and renal transplantation, have hematocrit values well below recommended target levels and do not receive ESA in the pre-RRT period.[12,13] In epidemiological studies, Obrador and colleagues demonstrated that a majority of incident dialysis patients received suboptimal management of anemia and that white patients had higher hematocrit levels and were more likely to receive ESA than African Americans.[12,13] However, ethnic differences were not examined, and these studies only included patients who initiated RRT up through 1999, precluding a meaningful assessment of the potential impact of the National Kidney Foundation's guidelines on the management of anemia in chronic kidney disease that were initially published in 1997.[14] Whether racial differences in hematocrit and ESA use persisted beyond 1999 is unknown, and it remains unclear whether ethnic disparities exist in this important facet of chronic kidney disease care. The aim of the current study was to assess racial and ethnic differences in pre-RRT anemia and its management among patients who initiated RRT between 1995 and 2003.

Figure 1. Identification of study patients



METHODS

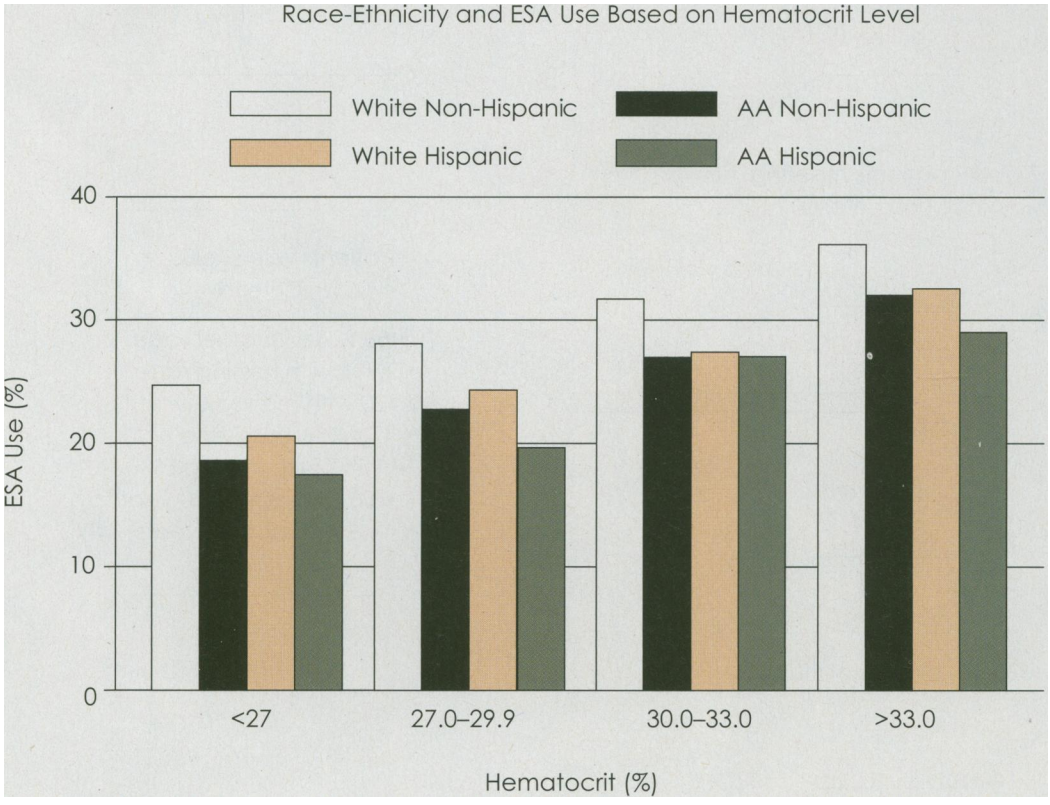
Study Population and Data Collection

This retrospective cohort study identified patients who initiated RRT in the United States between January 1, 1995 and December 31, 2003 using data from the End-Stage Renal Disease Medical Evidence Form from the Centers for Medicare and Medicaid Services. This legally required form is submitted within 90 days of the initiation of RRT for all end-stage renal disease patients in the United States and contains items on demographic characteristics, comorbid medical conditions, metabolic parameters prior to the initiation of RRT and care administered in the pre-RRT period (e.g., use of ESA). The comorbid medical conditions contained on the form include congestive heart failure, myocardial infarction, ischemic heart disease, cardiac arrest, cardiac dysrhythmia, pericarditis, cerebrovascular disease, hypertension, peripheral vascular disease, chronic obstructive pulmonary disease, diabetes mellitus, HIV/AIDS, malignant neoplasm, alcohol/drug use and tobacco use. The laboratory parameters on the form include serum albumin, hemoglobin and hematocrit, serum creatinine concentration and blood urea nitrogen concentration. The reported laboratory values need to have been performed within 45 days prior to the development of end-stage renal disease.

Patients with more than one medical evidence form filed during the study period were included only once using data from the first form filed. Additionally, to ensure that we only included patients who initiated RRT during the target study period and for whom age was known, we cross-referenced data from the medical evidence form to the U.S. Renal Data System Patient Profile. Patients with disparate dates or reported age of <0 or >100 years were not included in the analyses. We excluded patients with race designation other than African American or white, patients with missing race and/or ethnicity designation, and those with missing hematocrit values and/or missing data on the use of ESA. We classified 2,344 patients of Middle-Eastern/Arabian descent as white. Ethnicity was further stratified by racial group into the following categories: white non-Hispanic, white Hispanic, non-Hispanic black and African-American Hispanic.

Other data elements that we abstracted from the medical evidence form included age at the initiation of RRT; sex; comorbid medical conditions; serum creatinine and albumin concentrations; and pre-RRT insurance coverage categorized as Medicare, Medicaid, Department of Veterans Affairs, other insurance or no coverage. Patients' primary cause of renal failure was categorized as diabetes mellitus, hypertension, glomerulonephritis or other. We used the four-variable Modification of Diet in Renal

Figure 2. Race/ethnicity and erythropoiesis stimulating agent use based on hematocrit level



Disease Study equation to determine the estimated glomerular filtration rate at the initiation of RRT.[15]

Outcomes and Statistical Analyses

Our primary analyses were cross-sectional and focused on racial and ethnic comparisons of hematocrit level and ESA use. Because national guidelines were released in 1997 recommending that hematocrit be maintained between 33–36% in patients with chronic kidney disease, we also assessed racial and ethnic differences in the proportion of patients with a pre-RRT hematocrit level ≥33%, and among those with hematocrit levels <33%, the proportion that failed to receive pre-RRT ESA. We used the Student's t test and Chi-squared statistic to conduct univariate comparisons of continuous and categorical variables, respectively.

To account for the potential impact of demographic and clinical variables on the associations of race and ethnicity with anemia and ESA use, we conducted multivariable linear and logistic regression analyses.[16] Covariates in these analyses included demographic characteristics (e.g., age, sex and insurance coverage), comorbid conditions as well as estimated glomerular filtration rate. Potential confounders were inclusively selected a priori based on clinical judgment to include those factors that might potentially impact the outcomes and have an association with race/ethnicity. The analyses of hematocrit level also included an adjustment for ESA use, while analyses of ESA use were adjusted for hematocrit level. HIV/AIDS was not included in the multivariable models because of the very large number of missing data points for this variable. Transformations (e.g., categorization) were considered for continuous predictors without any impact on the estimates of racial and ethnic effects; linear terms were used for ease of interpretation. Based on the recognition that race and ethnicity may be highly correlated and that racial background could confound the associations of ethnicity with anemia management, we used the four ethnic-racial groups as independent variables in the multivariable models. We assessed the

Table 1. Baseline characteristics by race and ethnicity*

	AA† (N=193,115)	White (N=427,559)	White Non-Hispanic (N=367,466)	AA Non-Hispanic (N=190,948)	White Hispanic (N=60,093)	AA Hispanic (N=2,167)
Demographic Characteristics						
Age (Years)§	57.2 ± 16.0	63.6 ± 16.0	64.4 ± 15.7	57.2 ± 16.0	58.2 ± 16.4	57.0 ± 17.0
Gender (% Male)	48.4	56.0	56.5	48.3	52.7	53.0
Type of Insurance (%)‡						
Veterans Affairs	1.6	1.2	1.3	1.6	1.0	2.4
Medicare	44.3	57.7	61.2	44.3	36.3	40.3
Medicaid	34.3	18.0	14.5	34.2	39.2	37.0
Other	18.0	38.9	41.9	18.0	20.5	15.5
No Insurance	11.5	5.5	4.2	11.4	13.4	13.4
Comorbid Illnesses						
Heart Failure (%)	27.4	34.5	35.4	27.4	29.1	26.4
Myocardial Infarction (%)	5.1	10.8	11.7	5.1	5.6	4.7
Ischemic Heart Disease (%)	14.6	29.0	30.6	14.6	18.7	16.0
Pulmonary Disease (%)	4.2	9.2	10.1	4.2	3.2	3.9
Cerebrovascular Disease (%)	8.9	9.4	9.9	8.9	6.6	6.7
Peripheral Vascular Disease (%)	9.6	16.9	17.6	9.6	12.4	10.6
Diabetes Mellitus (%)	47.1φ	47.0φ	44.8	47.2	60.7	45.0
Cancer (%)	3.8	6.6	7.2	3.8	2.6	3.3
HIV/AIDS (%)	5.0	2.3	2.4	5.0	1.3	8.1
Alcohol/Drug Use (%)	4.2	1.4	1.4	4.2	1.6	4.0
Clinical Characteristics						
Dialysis Modality (% Hemodialysis)	93.0	87.4	86.7	93.0	91.6	92.3
Serum Albumin (g/dL)§	3.1 ± 0.7	3.2 ± 0.7	3.2 ± 0.7	3.1 ± 0.7	3.1 ± 0.7	3.1 ± 0.7
eGFR (ml/min/1.73m²)§	8.7 ± 5.0	9.3 ± 5.2	9.4 ± 5.2	8.7 ± 5.0	8.7 ± 5.0	8.7 ± 5.6
Primary Cause of ESRD (%)						
Diabetes Mellitus	42.1	42.8	40.2	42.1	59.2	44.6
Hypertension	33.8	20.7	21.3	33.9	17.2	27.3
Glomerulonephritis	10.7	12.4	12.6	10.7	11.1	12.4
Other	13.4	24.1	25.9	13.3	12.5	15.7

* All p values for comparisons of African Americans to whites and white non-Hispanics to white Hispanics significant at the p value <0.0001 level unless otherwise specified; † AA: African American; ‡ Nonmutually exclusive and does not sum to 100%; § Mean ± standard deviation; φ p value: nonstatistically significant

associations of race with the outcome variables in these models by specifically comparing non-Hispanic blacks to the referent group, white non-Hispanics. The effect of ethnicity on the outcomes of interest was assessed by comparing white Hispanics to the referent group, white non-Hispanics. Additional analyses considered the impact of potential confounders through the use of interaction terms with race and ethnicity. Estimates of racial and ethnic disparities under different covariate configurations were very similar to those from the main effects model without the interaction terms. For the ease of interpretation, main effects models are presented. Lastly, to assess secular trends in race/ethnic differences in anemia and ESA use over the eight-year study period, we examined risk-adjusted two-way interactions of race/ethnicity group with a calendar year using similar multivariable regression analyses.

For univariate comparisons, Bonferroni correction was applied to account for multiple comparisons and a p value of <0.0025 was considered statistically significant. For the multivariable models, 95% confidence intervals (CIs) are described. Statistical analyses were conducted using SAS version 8.2 (Cary, NC) and STATA® version 9 (College Station, TX). All study procedures were approved by the U.S. Renal Data Service and the Veterans Affiars (VA) Pittsburgh Healthcare System institutional review board.

RESULTS

Study Population

Of 733,257 patients with medical evidence forms filed during the study period, 112,583 had ≥1 exclusion criteria and/or missing race, ethnicity, hematocrit or ESA data, leading to a final study population of 620,674 patients (Figure 1). There were a small number of patients (N=9,413) who received pre-emptive renal transplants rather than initiating dialysis that were included in this population. African Americans were younger, were more likely to be female and had less kidney function at the initiation of RRT than whites, while white Hispanics were younger, more likely to be female and had a higher frequency of diabetes mellitus than their white non-Hispanic counterparts. Nearly all racial and ethnic differences in demographic and clinical characteristics met the level of statistical significance because of the very large number of study patients. (Table 1).

Unadjusted Associations of Race and Ethnicity with Anemia and Use of Erythropoietin Stimulating Agents

In unadjusted comparisons, African Americans and Hispanics had lower hematocrit levels and were less likely to receive ESA than whites and non-Hispanics, respectively (Table 2). When ethnicity was stratified by race, the ethnic differences in mean hematocrit were greater in whites (29.8% in non-Hispanics vs. 28.8% in Hispanics, p<0.001) than among African Americans (28.1% in non-Hispanics vs. 28.0% in Hispanics, p=0.8), highlighting the confounding effect of race on associations of ethnicity with the study outcomes. Ethnic differences in ESA use were also more pronounced in whites (30.7% in non-Hispanics vs. 25.9% in Hispanics, p<0.0001) than African Americans (24.2% in non-Hispanics vs. 22.4% in Hispanics, p=0.03). Similar patterns are present in the proportion of patients with hematocrit levels <33% and in the use of pre-RRT ESA in such patients. For all ranges of hematocrit, white non-Hispanics were more likely to receive ESA than white Hispanics and African Americans, either Hispanic or non-Hispanic (Figure 2).

Adjusted Associations of Race and Ethnicity with Anemia and rHuEpo Use

The results of multivariable analyses of the associations of race and ethnicity with hematocrit and ESA use are presented in Table 3. Compared to white non-Hispanics, non-Hispanic blacks had lower hematocrit level (Δ hematocrit=-0.97%, 95% CI: -1.00–-0.94) and less pre-RRT ESA use (OR=0.82, 95% CI: 0.81–0.84). White Hispanics also had lower hematocrit levels (Δ hematocrit=-0.42%, 95% CI: -0.47–-0.37) and were less likely to receive ESA (OR=0.86, 95% CI: 0.85–0.88) than white non-Hispanics. Like-

Table 2. Unadjusted associations of race and ethnicity with hematocrit and use of erythropoietin stimulating agents (ESAs) at the initiation of renal replacement therapy*

	African Americans	Whites	White Non-Hispanics	AA Non-Hispanics	White Hispanics	AA Hispanics
Hematocrit (%)†	28.1 ± 5.7	29.6 ± 5.4	29.8 ± 5.3	28.1 ± 5.7	28.8 ± 5.5	28.0 ± 5.6
ESA use (%)	24.2	30.0	30.7	24.2	25.9	22.4
Hematocrit <33% (%)	81.3	74.6	73.9	81.3	78.8	82.8
ESA use if hematocrit <33% (%)	22.3	28.0	28.7	22.4	24.1	21.1
Hematocrit 33–36% (%)	10.3	14.0	14.4	10.3	11.8	8.9
Hematocrit >36% (%)	8.4	11.4	11.7	8.4	9.4	8.3

* All p values for comparisons of African Americans to whites and white non-Hispanics to white Hispanics <0.0001; † Mean ± standard deviation

wise, compared to white non-Hispanics, African-American Hispanics had lower pre-RRT hematocrit levels (Δ hematocrit=-1.11, 95% CI: -1.3– -0.89). Because of the concern that small racial differences in the proportion of patients with near-normal hematocrit levels (>39%) and in the prevalence of primary conditions such as polycystic kidney disease—which is associated with less anemia—could have driven the observed racial disparities, we performed sensitivity analyses excluding such patients. There was no appreciable change in the results.

Compared to white non-Hispanics, non-Hispanic blacks were less likely to initiate RRT with hematocrit levels ≥33% (OR=0.78, 95% CI: 0.77–0.79). Among patients with hematocrit levels <33%, non-Hispanic blacks were less likely than white non-Hispanics to receive ESA (OR=0.79, 95% CI: 0.77–0.80). Similar differences were seen in these outcomes when White Hispanics and African-American Hispanics were compared to white non-Hispanics (Table 4).

There were variables other than race and ethnicity that were associated with hematocrit and ESA use. Most had statistically, albeit seemingly not clinically, significant associations with these outcomes, likely due to the very large sample size. As expected, women and those with cancer had lower hematocrit values and were more likely to receive ESA. Patients without medical insurance also had lower hematocrit levels than those with insurance, yet were much less likely to receive ESA. Alcohol/drug use was associated with higher hematocrit values and greater use of ESA, although these associations were likely reflective of the very small proportion of study patients in this category (<3%).

Time Trends in Hematocrit and Use of Erythropoietin Stimulating Agents

Throughout the study period, African-American race and Hispanic ethnicity were associated with lower hematocrit levels and less ESA use. There was a slightly greater increase in hematocrit levels over time among non-Hispanic blacks than white non-Hispanics (Δ hematocrit/year=0.07%, 95% CI: 0.06–0.08). Likewise, the temporal rise in hematocrit among white Hispanics was slightly greater than that seen in white non-Hispanics (Δ hematocrit/year=0.03%, 95% CI: 0.01–0.05). Use of ESA remained less common in non-Hispanic blacks than white non-Hispanics throughout the eight-year study period; however, over time, the use of ESA increased to a slightly greater extent each year in non-Hispanic blacks than white non-Hispanics (OR=1.01, 95% CI: 1.01–1.02). Conversely, compared to white non-Hispanics, white Hispanics became less likely to receive ESA over time (OR=0.98, 95% CI: 0.98–0.99). Time had no statistically significant impact on the hematocrit level or use of ESA among African Americans Hispanics compared to white non-Hispanics.

Racial and ethnic disparities in the proportion of patients with pre-RRT hematocrit levels ≥33% and the use of ESA in patients with hematocrit levels <33% also persisted throughout the eight-year study period. There were statistically significant, albeit likely not clinically significant, changes in the magnitude of these disparities over time. The proportion of non-Hispanic blacks with hematocrit levels ≥33% increased to a greater degree over time than the proportion of white non-Hispanics (OR=1.02, 95% CI: 1.01–1.03). The increase in the

Table 3. Adjusted associations of race and ethnicity with hematocrit level and use of erythropoietin stimulating agents

	Association with Hematocrit Level†			Association with rHuEpo Use†		
		95% Confidence Interval			95% Confidence Interval	
Factors	**Δ Hematocrit (%)**	**Lower**	**Upper**	**Odds Ratio**	**Lower**	**Upper**
African-American non-Hispanic*	-0.97	-1.00	-0.94	0.82	0.81	0.84
White Hispanic*	-0.42	-0.47	-0.37	0.86	0.85	0.88
African-American Hispanic*	-1.11	-1.34	-0.89	0.77	0.69	0.85
ESA use	1.06	1.03	1.09	–	–	–
Hematocrit‡	–	–	–	1.04	1.04	1.04
Age‡	0.30	0.29	0.31	0.98	0.98	0.99
Female gender	-0.19	-0.21	-0.16	1.18	1.16	1.19
Estimated GFR‡	0.81	0.79	0.82	0.93	0.93	0.94
Heart failure	-0.26	-0.29	-0.23	0.97	0.96	0.98
Myocardial infarction	0.24	0.19	0.29	0.91	0.89	0.93
Ischemic heart disease	0.25	0.21	0.28	1.05	1.03	1.07
Cancer	-0.33	-0.38	-0.27	1.20	1.18	1.23
Alcohol/drug use	0.34	0.25	0.43	1.43	1.37	1.50
No insurance§	-0.62	-0.68	-0.56	0.52	0.51	0.54

* Referent category is white non-Hispanic; ‡ For ease of interpretation, linear terms for hematocrit, age, and eGFR are presented. Use of detailed categorical strata for these variables did not impact other estimates (age is centered around its median and scaled by 10 years, eGFR is centered around its median and scaled by 5 ml/min); § Referent category is employer group health insurance; † Additional adjustments for pulmonary disease, cerebrovascular disease, peripheral vascular disease, diabetes, Medicare insurance, Medicaid insurance and other insurance not shown in table.

number of white Hispanics who achieved this benchmark was also slightly greater than among white non-Hispanics (OR=1.01, 95% CI: 1.00–1.02). Among patients with hematocrit levels <33%, ESA use increased slightly more in non-Hispanic blacks than in white non-Hispanics over time (OR=1.02, 95% CI: 1.01–1.02), while white Hispanics with this degree of anemia became less likely to receive ESA over time than white non-Hispanics (OR=0.98, 95% CI: 0.97–0.99). No statistically significant temporal changes in either of these outcomes were seen when comparing African-American Hispanics to white non-Hispanics.

DISCUSSION

In this cohort of patients initiating RRT in the United States, African-American race and Hispanic ethnicity were associated with lower pre-RRT hematocrit levels, lower rates of pre-RRT ESA use, a decreased likelihood of initiating RRT with a hematocrit ≥33% and lower probability of receiving ESA therapy despite a hematocrit <33%. Overall, anemia management improved between 1995 and 2003, yet racial and ethnic disparities persisted throughout this time frame.

Our result built upon prior analyses by examining disparities in the attainment of target anemia parameters; assessing the association of ethnicity with anemia care; and determining secular trends in disparities, which allowed for an evaluation of the impact of national guidelines on attenuating disparate care. While our findings raise the specter of clinician prejudice and/or systematic racial/ethnic bias, there are potential explanations for the observed disparities in hematocrit levels. The possibility that unmeasured differences in underlying levels of inflammation, iron stores, prevalence of conditions such as congential hemoglobinopathies, and/or dose of ESA account for the observed differences in hematocrit is suggested by our observation that even after adjusting for ESA use, African Americans and Hispanics had lower hematocrit levels and were significantly less likely to achieve a hematocrit ≥33%. Studies in the general population have shown that African Americans have slightly lower hematocrit levels than whites.[17] Variable compliance with prescribed ESA could also have contributed to the differences in the achieved hematocrit level as studies in populations of patients with diabetes, rheumatologic conditions and cardiovascular disease have shown that African Americans are less likely to adhere to prescribed medications than whites.[18-20] Lastly, cultural differences in trust in the medical system and varying levels of health education could contribute to these disparities.[21] Given the data limitations of the medical evidence form, we were unable to examine such variables in this analysis.

Differences in access to care and medical insurance coverage could also explain our findings.[22-24] Access to nephrology care in the pre-ESRD period may vary by race and ethnicity. Moreover, presence and type of insurance can have an impact on patients' eligibility for and means to afford ESA.[25] There was substantial racial and ethnic variation in medical coverage, with Medicaid and lack of coverage being significantly more common among African Americans and Hispanics. In fact, Medicaid and lack of insurance were associated with suboptimal anemia care. However, adjustment for insurance

Table 4. Adjusted associations of race and ethnicity with hematocrit level ≥33% and use of erythropoietin stimulating agents (ESAs) among patients with hematocrit <33%

	Association with Hematocrit ≥33%Ω			Association with rHuEpo Use if Hematocrit <33%Ω		
	95% Confidence Interval			95% Confidence Interval		
Variable	**Odds Ratio**	**Lower**	**Upper**	**Odds Ratio**	**Lower**	**Upper**
African-American non-Hispanic*	0.78	0.77	0.79	0.79	0.77	0.80
White Hispanic*	0.91	0.89	0.93	0.85	0.83	0.87
African-American Hispanic*	0.71	0.63	0.79	0.74	0.66	0.83
ESA	1.45	1.44	1.47	–	–	–
Age‡	1.07	1.06	1.08	0.99	0.98	0.99
Female gender	0.93	0.92	0.94	1.14	1.12	1.15
Estimated GFR	1.24	1.23	1.24	1.00†	0.99	1.00
Heart failure	0.89	0.88	0.90	1.01†	0.99	1.02
Myocardial infarction	1.06	1.03	1.08	0.94	0.92	0.96
Ischemic heart disease	1.05	1.04	1.07	1.06	1.04	1.08
Cancer	0.89	0.87	0.91	1.18	1.14	1.21
Alcohol/drug use	1.11	1.07	1.17	1.39	1.32	1.46
No insurance§	0.85	0.83	0.87	0.53	0.51	0.54

* Referent category is white non-Hispanic; † Denotes nonstatistically significant association; ‡ Age is centered around its median and is scaled by 10 years, eGFR is centered around its median and is scaled by 5 ml/min; § Referent category is employer group health insurance; Ω Additional adjustments for pulmonary disease, cerebrovascular disease, peripheral vascular disease, diabetes, Medicare insurance, Medicaid insurance and other insurance not shown in table.

failed to eliminate the observed disparities. It is possible that such adjustments may not adequately account for broad socioeconomic differences.[26,27]

There were statistically significant, albeit not clinically significant, reductions in some disparities over time. While the publication and dissemination of the National Kidney Foundation guidelines likely explain the overall improvements in anemia management, these guidelines do not appear to have attenuated racial or ethnic inequities in care. The secular constancy of these disparities should prompt efforts to determine if physiologic differences in the response to ESA among racial and ethnic groups underlie this phenomenon.

This study also highlights important issues in the overall quality of anemia care. As recently as 2003, 71% of patients began RRT with hematocrit levels <33%, yet only 32% received ESA. A key question that stems from this study is whether disparate and suboptimal management of anemia exists in patients with less-advanced chronic kidney disease. The optimal target hematocrit for patients with chronic kidney disease remains a matter of ongoing debate, with recently studies suggesting that targeting near-normal hemoglobin levels in patients with moderate levels of chronic kidney disease may be associated with increased cardiovascular morbidity and mortality.[28,29] However, the mean hematocrit values in the present study (28.1–29.6%) were substantially lower than the levels targeted in these trials and far below the lower threshold (33%) established by national guidelines for ESA treatment. While future studies will certainly aim to clarify the optimal target hematocrit, the importance of racial and ethnic disparities in achieved hematocrit in the present study should not be downplayed. Our findings should prompt efforts to examine the equity of anemia management in patients with less-advanced stages of chronic kidney disease.

There are certain limitations to this study. First, although the racial and ethnic differences in hematocrit levels were highly statistically significant due to the large sample size, the clinical significance of these differences would seem to be less robust. Second, our analyses emanate from administrative data and our ability to confirm racial and ethnic designations and verify the hematocrit level and ESA prescription against source documents was not possible. Third, duration and dose of ESA therapy, inflammatory markers and iron status could not be ascertained from the medical evidence form. Fourth, we were not able to determine temporal associations between the reported hematocrit level and the use of ESA, which limited the formulation of conclusions on causality between these two interrelated variables. Lastly, approximately 15% of patients initially identified met exclusion criteria and were not included in our analyses. However, post hoc analyses revealed that the racial and ethnic make-up of patients with missing hematocrit values closely mirrored that of our study population. Moreover, among patients without hematocrit values but with hemoglobin reported, hemoglobin values were similar to those reported for patients included in the study.

In summary, this study demonstrates the presence of significant racial and ethnic disparities in pre-RRT anemia management that persist over time. A large majority of all patients initiate RRT with hematocrit levels that fall substantially below recommended targets and do not received ESA, even when the use of these agents is seemingly clinically indicated. Concerted efforts to address these issues of equity and quality of care will require systematic attempts to identify the root causes of disparate and suboptimal care and, subsequently, the development of interventions targeted at the underlying etiologies.

ACKNOWLEDGEMENTS

The data reported were supplied by the U.S. Renal Data System. The interpretation and reporting of these data are the responsibility of the authors and should in no way be interpreted as official policy of the U.S. Renal Data System or the U.S. government. All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

REFERENCES

1. Sarnak MJ, Tighiouart H, Manjunath G, et al. Anemia as a risk factor for cardiovascular disease in The Atherosclerosis Risk in Communities (ARIC) study. *J Am Coll Cardiol.* 2002;40:27-33.

2. Beusterien KM, Nissenson AR, Port FK, et al. The effects of recombinant human erythropoietin on functional health and well-being in chronic dialysis patients. *J Am Soc Nephrol.* 1996;7:763-773.

3. Evans RW, Rader B, Manninen DL. The quality of life of hemodialysis recipients treated with recombinant human erythropoietin. Cooperative Multicenter EPO Clinical Trial Group. *JAMA.* 1990;263:825-830.

4. Levin A, Thompson CR, Ethier J et al. Left ventricular mass index increase in early renal disease: impact of decline in hemoglobin. *Am J Kidney Dis.* 1999;34:125-134.

5. McClellan WM, Jurkovitz C, Abramson J. The epidemiology and control of anaemia among pre-ESRD patients with chronic kidney disease. *Eur J Clin Invest* 2005;35(suppl 3):58-65.

6. Lefebvre P, Duh MS, Buteau S, et al. Medical costs of untreated anemia in elderly patients with predialysis chronic kidney disease. *J Am Soc Nephrol.* 2006;17:3497-3502.

7. Moreno F, Sanz-Guajardo D, Lopez-Gomez JM, et al. Increasing the hematocrit has a beneficial effect on quality of life and is safe in selected hemodialysis patients. Spanish Cooperative Renal Patients Quality of Life Study Group of the Spanish Society of Nephrology. *J Am Soc Nephrol.* 2000;11:335-342.

8. Nissenson AR. Epoetin and cognitive function. *Am J Kidney Dis.* 1992;20:21-24.

9. Kimmel PL, Greer JW, Milam RA, et al. Trends in erythropoietin therapy in the U.S. dialysis population: 1995 to 1998. *Semin Nephrol.* 2000;20:335-344.

10. Group TURHEPS. Double-Blind, Placebo-Controlled Study of the Therapeutic Use of Recombinant Human Erythropoetin for Anemia Associated With Chronic Renal Failure in Predialysis Patients. *Am J Kidney Dis.* 1991;18:50-59.

11. Ritz E, Laville M, Bilous RW, et al. Target level for hemoglobin correction in patients with diabetes and CKD: primary results of the Anemia Correction in Diabetes (ACORD) Study. *Am J Kidney Dis.* 2007;49:194-207.

12. Obrador GT, Roberts T, St. Peter WL, et al. Trends in anemia at initiation of dialysis in the United States. *Kidney Int.* 2001;60:1875-1884.

13. Obrador GT, Ruthazer R, Arora P, et al. Prevalence of and factors associated with suboptimal care before initiation of dialysis in the United States. *J Am Soc Nephrol.* 1999;10:1793-1800.

14. NKF-DOQI clinical practice guidelines for the treatment of anemia of chronic renal failure. National Kidney Foundation-Dialysis Outcomes Quality Initiative. *Am J Kidney Dis.* 1997;30:S192-S240.

15. Levey A, Greene T, Kusek JW, et al. A simplified equation to predict glomerular filtration rate from serum creatinine. *J Am Soc Nephrol.* 2000 (abstr);11:A0828.

16. Kleinbaum DG KL, Muller KE, Nizam A. Applied Regression Analysis and Other Multivariable Methods, 3rd ed. Pacific Grove, CA: Duxbury Press; 1998.

17. Kent S. Interpretations of differences in population hemoglobin means: a critical review of the literature. *Ethn Dis.* 1997;7:79-90.

18. Charles H, Good CB, Hanusa BH, et al. Racial differences in adherence to cardiac medications. *J Natl Med Assoc.* 2003;95:17-27.

19. Shenolikar RA, Balkrishnan R, Camacho FT, et al. Race and medication adherence in Medicaid enrollees with type-2 diabetes. *J Natl Med Assoc.* 2006;98:1071-1077.

20. Dominick KL, Golightly YM, Bosworth HB. Racial differences in analgesic/anti-inflammatory medication adherence among patients with osteoarthritis. *Ethn Dis.* 2005;15:116-122.

21. Boulware LE, Cooper LA, Ratner LE, et al. Race and trust in the health care system. *Public Health Rep.* 2003;118:358-365.

22. Kirby JB, Taliaferro G, Zuvekas SH. Explaining racial and ethnic disparities in health care. *Med Care.* 2006;44:164-72.

23. Ronsaville DS, Hakim RB. Well child care in the United States: racial differences in compliance with guidelines. *Am J Public Health.* 2000;90:1436-1443.

24. Escarce JJ, Epstein KR, Colby DC, et al. Racial differences in the elderly's use of medical procedures and diagnostic tests. *Am J Public Health.* 1993;83:948-954.

25. Cotter DJ, Thamer M, Kimmel PL, et al. Secular trends in recombinant erythropoietin therapy among the U.S. hemodialysis population: 1990–1996. *Kidney Int.* 1998;54:2129-2139.

26. Owen WF Jr, Chertow GM, Lazarus JM, et al. Dose of hemodialysis and survival: differences by race and sex. *JAMA.* 1998;280:1764-1768.

27. Epstein AM, Ayanian JZ, Keogh JH, et al. Racial disparities in access to renal transplantation—clinically appropriate or due to underuse or overuse? *N Engl J Med.* 2000;343:1537-1544, 2 p preceding 1537.

28. Singh AK, Szczech L, Tang KL, et al. Correction of anemia with epoetin alfa in chronic kidney disease. *N Engl J Med.* 2006;355:2085-2098.

29. Drueke TB, Locatelli F, Clyne N, et al. Normalization of hemoglobin level in patients with chronic kidney disease and anemia. *N Engl J Med.* 2006;355:2071-2084. ■