Racial/ethnic and gender disparities in the use of erythropoiesis-stimulating agents and blood transfusions: cancer management under Medicare's reimbursement policy

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What is already known about this subject

- A Medicare reimbursement policy change was associated with a reduction in the use of erythropoiesis-stimulating agents (ESAs).
- Different gender and racial/ethnic groups are distinct in hemoglobin levels, anemia prevalence, and cancer treatment patterns.

What this study adds

- Gender and racial/ethnic disparities were associated with the implementation of a Medicare reimbursement policy change for ESAs in cancer patients.
- The effect of the policy change on the use of ESAs was intended, but the effect on the use of blood transfusions was possibly indirect and unintended.

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ABSTRACT

BACKGROUND: Because of increasing safety concerns related to erythropoiesis-stimulating agents (ESAs), the Centers for Medicare & Medicaid Services issued a Medicare reimbursement policy change regarding these medications in cancer patients. However, the policy established an absolute hemoglobin or hematocrit threshold to qualify for reasonable use but did not take the effect of gender and racial/ethnic differences in hemoglobin levels into consideration.

OBJECTIVE: To examine disparities in the use of ESAs and blood transfusions after the Medicare policy change.

METHODS: This study was an exploratory treatment effectiveness study and used the SEER-Medicare linked database. The treatment group was composed of cancer patients, whereas the control group was composed of chronic kidney disease patients. An interrupted time series design was used to examine the effect of the Medicare policy change on the use of ESAs and blood transfusions in different gender and racial/ethnic groups.

RESULTS: The Medicare reimbursement policy change had an immediate effect on reducing the use of ESAs by 50% and increasing the use of blood transfusions by 10%. The immediate effect of the policy change on the monthly utilization of ESAs was 2 times greater in females (60% reduction) than

males (30% reduction). Females had a 10% immediate increase in the monthly utilization of blood transfusions after the policy change. The policy change had the same immediate effect of a 50% reduction on the use of ESAs for Whites, African Americans/Blacks, and Latinos. African Americans/Blacks had a 50% immediate increase in the monthly utilization of blood transfusions after the policy change.

CONCLUSIONS: Gender and racial/ethnic disparities were associated with the Medicare reimbursement policy change in the use of ESAs and blood transfusions. Thus, future policy considerations should keep biologic differences across gender and racial/ethnic groups in mind.

Anemia can be treated with the transfusion of red blood cells or administration of erythropoiesis-stimulating agents (ESAs).^{1,2} ESAs are commonly prescribed for cancer patients with chemotherapy-induced anemia or patients with chronic kidney disease (CKD) with low levels of hemoglobin. Epoetin alfa and darbepoetin alfa are 2 ESAs available in the United States. Among Medicare beneficiaries with cancer who received chemotherapy, the annual use of ESAs increased substantially in the past 2 decades.³ ESAs are efficacious in increasing hemoglobin and hematocrit levels and reducing or avoiding future requirements of blood transfusions in cancer patients with chemotherapy-induced anemia.⁴⁻⁹ However, ESAs are associated with increased risks of tumor progression or recurrence, mortality, thrombovascular events, and cardiovascular events in several clinical trials.¹⁰⁻¹⁸

The American Society of Clinical Oncology (ASCO) and the American Society of Hematology (ASH) published clinical practice guidelines for the use of epoetin alfa and darbepoetin alfa in adult patients with cancer in 2002, 2007, and 2010.¹⁹⁻²¹ The ASCO/ASH guidelines recommended that ESAs should be initiated in cancer patients with chemotherapy-induced anemia when the hemoglobin level has been decreased to <10 g/dL. When the hemoglobin level is ≥ 10 g/dL but <12 g/dL, whether ESAs should be initiated cannot be definitively determined. The target hemoglobin level was defined as near 12 g/dL in the 2002 and 2007 guidelines but defined as the lowest level needed to avoid blood transfusions in the 2010 guidelines. The National Kidney Foundation developed the Kidney Disease Outcomes Quality Initiative (KDOQI) clinical practice guidelines for anemia in chronic kidney disease in 2006 and updated the hemoglobin target in 2007.^{22,23} The KDOQI guidelines recommended that the target hemoglobin level should be in the range of 11 g/dL to 12 g/dL and not exceed 13.0 g/dL. The KDOQI guidelines did not specify an anemia threshold for initiating ESAs.

Hemoglobin and hematocrit levels are associated with gender and race/ethnicity. Compared with males of the same age and race, females have lower hemoglobin levels.²⁴ In general, African Americans/Blacks and Latinos have lower hemoglobin levels than Whites, and anemia is more prevalent in females, African Americans/Blacks, and Latinos in the United States.²⁴ The prevalence of anemia and moderate to severe anemia in females was 2 and 5 times higher than males, respectively.²⁵ African Americans/Blacks had the highest prevalence of anemia for all age groups and both genders; Latinos had a higher prevalence of anemia than Whites in general.²⁵ Different gender and racial/ethnic groups have distinct utilization patterns of ESAs. In the Medicare population, females had higher utilization of ESAs

than males.³ African Americans/Blacks had the highest utilization of ESAs in all racial groups.³ Cancer treatment patterns are also distinct in different gender and racial/ethnic groups. Differences in gender and race/ethnicity were found in different types of cancer treatment.^{26,27}

Because of increasing safety concerns, the Centers for Medicare & Medicaid Services (CMS) issued a national coverage determination (NCD) for ESAs in cancer and related neoplastic conditions on July 30, 2007.²⁸⁻³¹ Specifically, for chemotherapy-induced anemia, when patients had solid tumors, multiple myeloma, lymphoma, or lymphocytic leukemia, ESA treatment was reasonable and necessary only when the hemoglobin level was <10g/dL or the hematocrit level was <30%. Except for the hemoglobin requirements for the initiation, NCD requirements were more rigid than recommendations in the ASCO/ASH guidelines. The full implementation of the NCD was on April 7, 2008. Since then, Medicare contractors have been required to review claims to ensure implementation of the NCD. Medicare reimbursement policy change on ESAs was applicable only in cancer and related neoplastic conditions. ESA use in renal disease indications was not regulated by this policy. However, the eligibility criteria of reasonable and necessary ESA use defined in the NCD did not take gender and racial/ethnic differences in hemoglobin levels into consideration. Because females, African Americans/Blacks, and Latinos are more likely to be anemic and use ESAs, they are more likely to be affected by the NCD. Using the same cut-off point regardless of biological differences in gender and race/ethnicity could lead to disparities in patient access to ESAs.

Some previous studies have examined the change in the use of ESAs and blood transfusions in cancer patients before and after the implementation of the Medicare reimbursement policy change.³²⁻³⁷ Documented in the literature is a 26%-57% reduction in the use of ESAs after the policy change.³²⁻³⁵ Results are mixed regarding the change in the use of blood transfusions.³²⁻³⁷ These studies, however, lack control groups, which cast doubt on the validity of the study results. In addition, no studies have examined disparities associated with the Medicare reimbursement policy change. Because of gender and racial/ethnic differences in hemoglobin levels, anemia prevalence, and cancer treatment patterns, the policy change could have different effects on different gender and racial/ethnic groups. Therefore, to fill gaps identified in the literature, this study examined gender and racial/ethnic disparities in the utilization of ESAs and blood transfusions after the

implementation of Medicare reimbursement policy change in cancer patients.

Methods

DATA SOURCE

This study used the Surveillance, Epidemiology, and End Results (SEER)-Medicare linked database. The SEER program is a large population-based cancer registry that collects information on cancer incidence and mortality. The SEER program includes cancer registries across 14 states and covers 28% of the U.S. population. The SEER-Medicare linked data include 2 cohorts of people: cancer cohort and noncancer cohort. The cancer cohort is defined as Medicare beneficiaries in the SEER program. The noncancer cohort is defined as a random 5% sample of Medicare beneficiaries who do not have cancer but reside in the same SEER geographic areas. The noncancer cohort is used for comparison purposes.

STUDY DESIGN

This study was an exploratory treatment effectiveness study. This study used a repeated cross-sectional design to estimate the monthly utilization of ESAs and blood transfusions, which were compared before and after the policy change. The period between January 1, 2003, and June 30, 2007, was selected as the prepolicy period; the period between July 1, 2007, and April 30, 2008, was selected as the policy period; and the period between May 1, 2008, and December 31, 2009, was selected as the postpolicy period. January 1, 2003, was selected as the starting point because darbepoetin alfa was fully available on the U.S. market starting in 2003 for the treatment of anemia associated with cancer chemotherapy. December 31, 2009, was selected as the ending point because ESA Risk Evaluation and Mitigation Strategies (REMS), a policy change for ESAs by the U.S. Food and Drug Administration (FDA), came into effect after that. The selection of the policy period was based on the timeline of the policy change.

CONTROL GROUP

The treatment group was composed of cancer patients, and the control group was composed of CKD patients. CKD patients were selected as the control group because ESAs are used in CKD patients with low levels of hemoglobin, and Medicare reimbursement policy change on ESAs was applicable only to cancer patients. The policy change had no effect on ESA use in CKD patients. Therefore, using CKD patients as the control group could eliminate possible threats

to internal validity due to history (FDA's black box warning) when evaluating the use of ESAs and blood transfusions.

STUDY POPULATION

The study population was selected based on several inclusion and exclusion criteria in each month. The study population of the treatment group in each month was selected from individuals who were aged 65 years or older; were eligible for Medicare because of age; had a primary diagnosis of breast cancer, colorectal cancer, lung cancer, lymphomas, ovarian cancer, or prostate cancer; and received chemotherapy after a cancer diagnosis as recorded in the cancer cohort. Individuals who enrolled in health maintenance organization (HMO) plans, were not covered by Medicare Parts A and B, or had a diagnosis of CKD were excluded from the treatment group in each month. The study population of the control group in each month was selected from individuals who were aged 65 years or older and had a diagnosis of CKD as recorded in the noncancer cohort. Individuals enrolled in HMO plans who were not covered by Medicare Parts A and B or who had a diagnosis of cancer were excluded from the control group in each month.

MEASUREMENT

Gender and race/ethnicity were collected from Medicare enrollment data. The use of ESAs, including epoetin and darbepoetin, was measured from relevant Healthcare Common Procedure Coding System (HCPCS)/Current Procedural Terminology (CPT) and revenue center codes from Medicare claims. The use of blood transfusions was measured from relevant *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) and HCPCS/CPT codes from Medicare claims. Variables in the inclusion and exclusion criteria were measured from the SEER registries and Medicare enrollment and claims.

STATISTICAL ANALYSIS

Percentages of patients who received ESAs or blood transfusions each month were compared before and after the policy change and plotted in graphs. An interrupted time series design was used to examine the effect of the policy change on the use of ESAs and blood transfusions. The interrupted time series design is a particularly strong quasi-experimental design with a high degree of internal validity when evaluating the effect of a policy change. This study design could control for confounding omitted variables and autocorrelation.³⁸⁻⁴⁰ A segmented regression analysis was used in the interrupted time series design. The policy period was included in the graphic illustration but censored in the statistical analysis of the interrupted time series design. The interaction term between policy change and

TABLE 1 Characteristics of Users of ESAs and Blood Transfusions Between the Pre- and Postpolicy Periods

	ESAs, n=54,370						Blood Transfusions, n=48,165					
	Prepolicy, n=44,322			Postpolicy, n=10,048			Prepolicy, n=32,179			Postpolicy, n=15,986		
	Cancer n=36,995	CKD n=7,327	P Value	Cancer n=5,607	CKD n=4,441	P Value	Cancer n=20,623	CKD n=11,556	P Value	Cancer n=9,316	CKD n=6,670	P Value
	%	%		%	%		%	%		%		
Age, years												
65-69	27.70	21.40	<0.0001	29.61	26.86	<0.0001	21.17	11.05	<0.0001	21.88	12.79	<0.0001
70-74	28.27	19.05		28.11	18.69		26.14	15.38		25.24	15.31	
75-79	23.64	22.18		23.06	20.92		24.47	21.11		23.44	18.49	
80+	20.39	37.37		19.23	33.53		28.22	52.47		29.44	53.42	
Gender												
Male	39.59	44.93	<0.0001	38.83	42.51	0.0002	50.57	39.12	<0.0001	48.75	39.10	<0.0001
Female	60.41	55.07		61.17	57.49		49.43	60.88		51.25	60.90	
Race/ethnicity												
White	86.92	70.21	<0.0001	85.42	68.01	<0.0001	86.84	76.62	<0.0001	86.38	77.30	<0.0001
African American/ Black	7.63	18.20		8.12	18.63		7.44	14.67		7.67	13.62	
Latino	1.15	3.63		1.12	4.31		1.25	2.90		1.29	2.96	
Other	4.30	7.95		5.34	9.05		4.46	5.81		4.66	6.11	
Residence												
Metropolitan	83.79	84.94	0.0141	82.72	84.82	0.0046	81.88	83.31	0.0013	81.96	82.18	0.7191
Nonmetropolitan	16.21	15.06		17.28	15.18		18.12	16.69		18.04	17.82	
Region												
Northeast	20.15	20.81	<0.0001	21.17	20.27	0.1711	18.57	20.19	<0.0001	19.61	19.53	<0.0001
Midwest	11.95	10.01		10.61	9.76		15.49	13.16		13.27	12.33	
South	27.53	29.75		28.50	30.15		24.36	29.58		24.76	29.62	
West	40.37	39.43		39.72	39.82		41.59	37.08		42.36	38.53	
Education												
1st quartile	26.72	20.66	<0.0001	26.05	20.24	<0.0001	26.52	21.24	<0.0001	27.48	21.63	<0.0001
2nd quartile	25.49	22.78		25.09	23.73		26.01	23.19		25.94	23.49	
3rd quartile	24.85	25.80		24.86	25.35		24.60	25.99		23.72	25.17	
4th quartile	22.94	30.76		24.00	30.69		22.86	29.58		22.86	29.71	
Poverty												
1st quartile	24.92	20.50	<0.0001	24.90	20.03	<0.0001	25.01	22.11	<0.0001	25.43	21.26	<0.0001
2nd quartile	25.20	22.87		24.27	23.42		24.76	22.05		24.49	22.37	
3rd quartile	25.19	23.49		25.54	23.35		25.17	23.61		25.25	25.31	
4th quartile	24.69	33.14		25.29	33.19		25.05	32.23		24.83	31.07	

CKD = chronic kidney disease; ESA = erythropoiesis-stimulating agent.

group estimated the difference in the difference in the level in the monthly utilization between the pre- and postpolicy periods between the treatment and control groups. The

interaction term between month after policy change and group estimated the difference in the difference in the trend in the monthly utilization between the pre- and postpolicy

FIGURE 1 Change in the Monthly Utilization of ESAs Before and After Implementation of the Medicare Reimbursement Policy in Cancer and CKD Patients

CKD=chronic kidney disease; ESA=erythropoiesis-stimulating agents.

periods between the treatment and control groups. We conducted unadjusted analyses without the control group and adjusted analyses with the control group.

Results

This study identified 54,370 users of ESAs, including 44,322 (81.52%) users in the prepolicy period and 10,048 (18.48%) users in the postpolicy period, and 48,165 users of blood transfusions, including 32,179 (66.81%) users in the prepolicy period and 15,986 (33.19%) users in the postpolicy period (Table 1). During the prepolicy period, users of ESAs were significantly different between cancer patients and CKD patients. Except for region, users of ESAs were significantly different between cancer patients and CKD patients during the postpolicy period. During the prepolicy period, users of blood transfusions were significantly different between cancer patients and CKD patients. Except for residence, users of blood transfusions were significantly different between cancer patients and CKD patients during the postpolicy period (Table 1).

After the Medicare reimbursement policy change, the monthly utilization of ESAs declined sharply in the treatment group but declined only slightly in the control group (Figure 1). In the unadjusted analysis, the level in the monthly utilization of ESAs decreased by 2.96% ($P<0.0001$). When including the control group in the segmented regression analysis, the level in the monthly utilization of ESAs decreased by 2.13% ($P<0.0001$), a relative reduction of 50%

after the policy change. In the unadjusted and adjusted analyses, the trend in the monthly utilization of ESAs did not change significantly (Table 2). The monthly utilization of blood transfusions increased in the treatment and control groups after the Medicare reimbursement policy change (Figure 2). In the unadjusted analysis, the level in the monthly utilization of blood transfusions increased by 0.10% ($P=0.0004$), and the trend in the monthly utilization of blood transfusions increased by 0.01% ($P=0.0035$). When including the control group in the segmented regression analysis, the level in the monthly utilization of blood transfusions increased by 0.10% ($P=0.0186$), a relative increase of 10%, after the policy change. The trend in the monthly utilization of blood transfusions did not change significantly (Table 2).

When examining different gender groups, we found that in the unadjusted analysis, the level of ESAs decreased by 1.79% ($P<0.0001$) in males and decreased by 4.64% ($P<0.0001$) in females. By including the control group in the segmented regression analysis, the level of ESAs decreased by 0.79% ($P<0.0001$) in males (a relative reduction of 30%) and decreased by 3.94% ($P<0.0001$) in females (a relative reduction of 60%), after the policy change. The trend of ESAs did not change significantly in males and females (Table 3). In males, the level of blood transfusions increased by 0.07% ($P=0.0298$) in the unadjusted analysis but did not change significantly in the adjusted analysis. In females, the level of blood transfusions increased by 0.15% ($P<0.0001$) in the unadjusted analysis and increased by 0.14% ($P=0.0097$)

TABLE 2 Change in the Monthly Utilization of ESAs and Blood Transfusions Before and After Implementation of the Medicare Reimbursement Policy

	Unadjusted Analysis		Adjusted Analysis	
	β	P Value	β	P Value
Monthly utilization of ESAs				
Intercept	5.78	<0.0001	5.73	<0.0001
Month	-0.03	<0.0001	-0.01	<0.0001
Policy change	-2.96	<0.0001	-0.83	<0.0001
Month after policy change	0.01	0.5528	-0.01	0.1905
Group			0.06	0.5046
Month $\times$ group			-0.02	<0.0001
Policy change $\times$ group (level change)			-2.13	<0.0001
Month after policy change $\times$ group (trend change)			0.02	0.1366
Monthly utilization of blood transfusions				
Intercept	1.25	<0.0001	1.03	<0.0001
Month	-0.01	<0.0001	0.00	0.0020
Policy change	0.10	0.0004	0.00	0.9609
Month after policy change	0.01	0.0035	0.00	0.9194
Group			0.22	<0.0001
Month $\times$ group			-0.01	<0.0001
Policy change $\times$ group (level change)			0.10	0.0186
Month after policy change $\times$ group (trend change)			0.01	0.0524

ESA = erythropoiesis-stimulating agent.

in the adjusted analysis (a relative increase of 10%) after the policy change. The trend of blood transfusions did not change significantly in males and females (Table 3).

When examining different racial/ethnic groups, we found that in the unadjusted analysis, the level of ESAs decreased by 3.02% ($P<0.0001$) in Whites, decreased by 2.86% ($P<0.0001$) in African Americans/Blacks, decreased by 1.95% ($P<0.0001$) in Latinos, and decreased by 2.39% ($P<0.0001$) in others. By including the control group in the segmented regression analysis, the level of ESAs decreased by 2.25% ($P<0.0001$) in Whites (a relative reduction of 50%), decreased by 2.13% ($P<0.0001$) in African Americans/Blacks (a relative

reduction of 50%), decreased by 1.54% ($P<0.0001$) in Latinos (a relative reduction of 50%), but did not change significantly in others after the policy change. The trend of ESAs did not change significantly in all racial/ethnic groups in the unadjusted analysis but increased by 0.03% ($P=0.0277$) in Whites and decreased by 0.07% ($P=0.0013$) in Latinos in the adjusted analysis (Table 3). In the unadjusted analysis, the level of blood transfusions increased by 0.09% ($P=0.0031$) in Whites, increased by 0.36% ($P<0.0001$) in African Americans/Blacks but did not change significantly in Latinos and others. By including the control group, the level of blood transfusions increased by 0.41% ($P=0.0002$) only in African Americans/Blacks (a

relative increase of 50%) after the policy change. The trend of blood transfusions did not change significantly in all racial/ethnic groups (Table 3).

Discussion

Medicare reimbursement policy change had an immediate effect of reducing the use of ESAs by 50%. The intended consequence of the policy change was to reduce unreasonable or unnecessary use of ESAs. The effect of the policy change on the use of ESAs found in this study were similar to findings in several previous studies. Through analyzing Medicare claims data, Arneson et al. (2012) and Hershtman et al. (2014) found that the use of ESAs experienced a 51%-57% reduction after the implementation of Medicare reimbursement policy change.^{34,35} Studies conducted by Hess et al. (2010) and Henry et al. (2012) analyzed medical records and found that the use of ESAs had a 29%-36% reduction after the policy change.^{32,33} Using medical records in local settings might reflect the effect of the policy change only at a specific location instead of the national level. The current study used the SEER-Medicare linked database (a nationally representative database) and could provide national estimates on the effect of Medicare reimbursement policy change on the use of ESAs.

Medicare reimbursement policy change had an immediate effect of increasing the use of blood transfusions by 10%. The possibly unintended consequence of the policy change was to increase the use of blood transfusions. Transfusion of red blood cells is a rapid approach to increasing hemoglobin levels in patients with anemia. The safety of blood transfusions (e.g., immunosuppression and transfusion reactions), however, is a significant concern.⁴¹⁻⁴⁶ In addition, transfusion of red blood cells is inconvenient and

FIGURE 2 Change in the Monthly Utilization of Blood Transfusions Before and After Implementation of the Medicare Reimbursement Policy in Cancer and CKD Patients

CKD=chronic kidney disease.

time consuming for patients. Results from the effect of the policy change on the use of blood transfusions found in this study were different from findings in previous studies.

By analyzing Medicare claims data, Arneson et al. and Hershman et al. found that the use of blood transfusions did not change after the Medicare reimbursement policy change.^{34,35} Unlike with the use of ESAs, the use of blood transfusions following the policy change was possibly indirect and unintended. The policy change might have had a delayed effect on the use of blood transfusions. The postpolicy periods used by Arneson et al. and Hershman et al. were shorter than ours and might not have been long enough to observe any delayed effect of the policy change on the use of blood transfusions.^{34,35}

The current study included extended pre- and post-policy periods that enabled researchers to examine the short-term and long-term effects of the policy change. Hess et al. analyzed medical records and found that the use of blood transfusions had increased 31% after the implementation of the Medicare reimbursement policy.³² Using medical records in local settings might reflect the effect of the policy change only at a specific location instead of the national level. The current study used the SEER-Medicare linked database (a nationally representative database) and provided national estimates on the effect of the Medicare reimbursement policy change on the use of blood transfusions.

After the policy change, the increase in the use of blood transfusions was smaller than the decrease in the use of

ESAs. Three reasons might have contributed to this finding. First, unreasonable or unnecessary use of ESAs was reduced after the policy change. The goal of the Medicare reimbursement policy change was to reduce the unsafe use of ESAs. Some patients receiving unreasonable or unnecessary ESA treatments did not require blood transfusions to treat anemia. Second, some patients eligible for the administration of ESAs were not eligible for the transfusion of red blood cells. For example, when patients were severely ill, even though they did not have access to ESA treatment, they would not seek blood transfusions. Third, some patients were worried about adverse events (e.g., immunosuppression and transfusion reactions) associated with blood transfusions. When physicians recommended blood transfusions to them, they might have refused to get transfusion of red blood cells.

In different gender groups, Medicare reimbursement policy change had an immediate effect on the use of ESAs for males (30% reduction) and females (60% reduction), but the effect was 2 times higher in females. The policy change had an immediate effect on increasing the use of blood transfusions by 10% only in females. In different racial/ethnic groups, the Medicare reimbursement policy change had the same immediate effect of a 50% reduction on the use of ESAs by Whites, African Americans/Blacks, and Latinos, and the policy change increased the trend by 0.03% in Whites and decreased the trend by 0.07% in Latinos. The policy change had an immediate effect on increasing the

TABLE 3 Change in the Monthly Utilization of ESAs and Blood Transfusions Before and After Implementation of the Medicare Reimbursement Policy by Gender and Race/Ethnicity

	ESAs				Blood Transfusions			
	Level Change		Trend Change		Level Change		Trend Change	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
Gender								
Male	-1.79 ^a	-0.79 ^a	0.01	0.02	0.07 ^a	0.07	0.01	0.01
Female	-4.64 ^a	-3.94 ^a	0.01	0.02	0.15 ^a	0.14 ^a	0.00	0.00
Race/ethnicity								
White	-3.02 ^a	-2.25 ^a	0.01	0.03 ^a	0.09 ^a	0.08	0.01	0.01
African American/Black	-2.86 ^a	-2.13 ^a	0.01	0.02	0.36 ^a	0.41 ^a	0.00	-0.01
Latino	-1.95 ^a	-1.54 ^a	0.00	-0.07 ^a	0.12	0.04	0.01	0.00
Other	-2.39 ^a	-0.48	-0.01	0.01	0.00	-0.04	0.02	0.01

^aSignificant at 0.05 level.

ESA = erythropoiesis-stimulating agent.

utilization of blood transfusions by 50% only in African Americans/Blacks.

Gender and racial/ethnic disparities associated with the Medicare reimbursement policy change were not examined in previous studies. This study is the first to examine whether the policy change had disproportionate effects on vulnerable groups. It is well documented in the literature that gender and racial/ethnic differences exist in hemoglobin level, anemia prevalence, anemia treatment, and ESA use.^{3,24-27} However, the Medicare reimbursement policy change was applied to all cancer patients regardless of gender and race/ethnicity.

This study found gender disparities in the use of ESAs and blood transfusions after the policy change. Compared with males, females had 2 times greater immediate reduction in the monthly utilization of ESAs after the policy change. In addition, females had a 10% immediate increase in the monthly utilization of blood transfusions, which was not found in males. This study also found racial/ethnic disparities in the use of ESAs and blood transfusions after the policy change. The immediate effect on the reduction in the use of ESAs was the same for Whites, African Americans/Blacks, and Latinos. However, the trend was increased in Whites, was the same in African Americans/Blacks, and was decreased in Latinos. For the monthly utilization of blood transfusions, African Americans/Blacks had a 50% immediate increase, which was equal to the percentage of reduction in the monthly utilization of ESAs.

This study could help inform future health policies to mitigate health disparities and achieve health equity. We

found that the Medicare reimbursement policy change disproportionately affected vulnerable groups. A sound policy should not exacerbate health disparities. Understanding the effect of the policy on health equity is of great significance to policymakers. In addition, we examined the intended and possibly unintended consequences of the Medicare reimbursement policy change. This could help decision makers to have a comprehensive understanding of the potential policy effects and make appropriate policy decisions in the future.

STRENGTHS AND LIMITATIONS

This study has several strengths. First, it incorporated a control group when examining the effect of the Medicare reimbursement policy change on the use of ESAs and blood transfusions. Some published studies did not include control groups and thus were subject to threats to internal validity.^{32-35,37}

Second, this study used the interrupted time series design, which enabled us to examine 2 types of change: the change in the level and the change in the trend. Previous studies examined the change in the level of the average monthly or annual utilization of ESAs and blood transfusions only.^{32-35,37} The change in the trend of utilization was not captured.

Third, this study clearly distinguished among the prepolicy, policy, and postpolicy periods. The postpolicy periods defined in some previous studies were problematic.^{32-35,37} Some studies included some months of the policy period in their postpolicy periods. Including part

of the policy implementation period in the postpolicy period in the analysis might underestimate the true effect of the policy change on the use of ESAs and blood transfusions.

Some possible limitations of this study should be considered when interpreting study findings. First, an ideal control group should be similar to the treatment group in all aspects but is not subject to the policy change. The advantage of the CKD control group is that CKD patients are not subject to the policy change, but a limitation is that the CKD control group is not compatible as the treatment group in all aspects.

Second, the use of ESAs and blood transfusions was counted as a binary event within each population of interest at the aggregate level. So, the patient-level understanding of the effect of the policy change on the number and frequency of the use of ESAs and blood transfusions was not known.

Conclusions

Gender and racial/ethnic disparities were associated with the implementation of the Medicare reimbursement policy change for ESAs in cancer patients. Future policy changes should consider the biologic differences in gender and racial/ethnic groups to explore options to minimize disparities. The effect of the policy change on the use of ESAs was intended, but the effect on the use of blood transfusions was possibly indirect and unintended. When making future policy decisions, in addition to predicting and studying the intended changes caused by the policy, the possibly unintended changes should also be considered and estimated.

DISCLOSURES

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