



Trends in the utilization of erythropoiesis-stimulating agents among Medicare beneficiaries with kidney disease

Erythropoietins

Data Points #4

Chronic renal disease affects more than 26 million Americans¹ and is the cause of significant morbidity, hospitalization, and mortality.² Anemia, a common complication, conveys significant risk for cardiovascular disease, faster progression of renal failure, and decreased quality of life.³ In fact, most patients with chronic renal disease become anemic.⁴ Correction of anemia in such patients is associated with improved outcomes,³ such as forestalling target organ damage.⁴

Erythropoiesis-stimulating agents (ESAs) are recombinant hematopoietic drugs that stimulate the production of red blood cells. Epoetin alfa received Food and Drug Administration (FDA) approval in 1989, with darbepoetin alfa following in 2001. Thereby, modalities became available for the treatment of anemia in chronic renal failure, chemotherapy-treated cancer, and zidovudine-treated HIV-infected patients.⁵ Furthermore, ESAs have allowed the reduction of allogeneic blood transfusions in surgery patients. ESA dosing is individualized to achieve and maintain hemoglobin levels within the range of 10 to 12 grams per dL.⁵ A number of published studies, beginning in the late 1990s,⁶ suggested potential adverse cardiovascular outcomes arising from ESA therapy. Studies amassing over the past decade have led to a number of clinical and policy changes regarding the use of ESAs.

The goal of this *Data Points* brief was to examine practice trends in the use of ESAs among Medicare beneficiaries with kidney disease (KD) and to relate these trends to the timing of clinical practice and policy events that had the potential to affect ESA use. Secondarily, we examined the use of ESAs in a subpopulation of beneficiaries with KD and cancer.

The work described herein was commissioned for presentation at the March 24, 2010, Medicare Evidence Development & Coverage Advisory Committee meeting to discuss ESAs in anemia related to KD. Additional information on this meeting, including the agenda, presentations, and meeting minutes, can be found at: www.cms.gov/FACA/02_MEDCAC.asp (under Index of Meetings).



The findings described herein were presented by Thomas MaCurdy, Ph.D., at the Medicare Evidence Development & Coverage Advisory Committee meeting held on March 24, 2010, in Baltimore, Maryland.



FINDINGS

ESA Use Among Medicare’s Kidney Disease Population

We first examined the use of ESAs among Medicare fee-for-service (FFS) Parts A or B-enrolled beneficiaries affected by KD, stratified by dialysis and nondialysis subpopulations. From July 2006 to September 2009 (hereafter referred to as the study period), there was a slight rise in all Medicare beneficiaries (regardless of FFS or KD status) from about 44 million to 46 million individuals. The number of Medicare FFS beneficiaries remained static at approximately 35 million people. Also unchanged during this period was the size of the Medicare FFS Parts A/B pool of enrolled beneficiaries, at around 31 million individuals. We classified this latter subpopulation, Medicare’s FFS A/B-enrolled population, by KD status into four mutually exclusive and exhaustive groups: (1) beneficiaries without KD (those with no KD codes); (2) beneficiaries with intermittent KD (beneficiaries with occasional diagnoses indicating KD); (3) beneficiaries with predialysis (those with KD not on dialysis); and (4) beneficiaries on dialysis (those with KD on dialysis). These groups are more thoroughly described in the subsequent Definitions and Methodology section. During the study period, the number of beneficiaries without KD (i.e., non-KD beneficiaries) remained the same at about 30 million; the number on dialysis grew minimally, from about 250,000 to about 263,000; the number with intermittent KD increased from about 210,000 to more than 300,000; and the number in a state of predialysis increased from about 280,000 to nearly 500,000. The greatest absolute increase in a subpopulation during this period occurred among those with Stage III chronic KD (see Definitions and Methodology section), increasing from 125,092 beneficiaries to 286,928 beneficiaries over the study period.

We further examined the proportion of beneficiaries in each aforementioned group with ESA use. An extremely small proportion of non-KD beneficiaries used ESAs (<0.4%), and this proportion decreased over the study period. The use of ESAs among beneficiaries with intermittent KD declined from more than 10 percent to 5 percent during the study period. The use of ESAs among beneficiaries in a state of predialysis declined from 23 percent to 16 percent. The use of ESAs among beneficiaries on dialysis remained constant over the study period at around 90 percent. In considering the proportion of ESA users by early-stage chronic KD, usage fell: from 17 percent to 8 percent among beneficiaries in Stage I; from 13 percent to 7 percent in Stage II; from 23 percent to 16 percent in Stage III; and from 35 percent to 27 percent in Stage IV.

The absolute number of ESA-using beneficiaries in each of the aforementioned groups is presented in Figure 1. In general, the number of users remained relatively stable over the study period, except for the non-KD group, in which the number of users declined significantly. Of note, the absolute number of users rose minimally among the predialysis and dialysis groups, each increasing by about 15,000 beneficiaries. The composition of the ESA user population changed over the study period, as the dialysis group grew from 51 percent to 65 percent of all beneficiaries using ESAs, the predialysis group grew from 15 percent to 22 percent, the intermittent KD group fell from 6 percent to 4 percent, and the non-KD group fell from 28 percent to 9 percent. Of interest, 75 percent of the non-KD beneficiaries had cancer.

ESA Use Among Medicare’s Cancer Population With and Without Concomitant Kidney Disease

In examining the size of the Medicare cancer population by KD group and the trends in ESA use, we classified Medicare’s FFS A/B-enrolled cancer population into four mutually exclusive and exhaustive groups: (1) cancer only (beneficiaries with cancer but no KD codes); (2) cancer and intermittent KD (beneficiaries with cancer and occasional KD diagnoses); (3) cancer and predialysis (beneficiaries with cancer and non-dialysis KD); and (4) cancer and dialysis (beneficiaries with cancer and KD requiring dialysis).

During the study period, the size of the cancer and dialysis group remained stable, the cancer only group dipped and spiked but maintained its average,

Figure 1: Size of the ESA user population, by kidney disease group

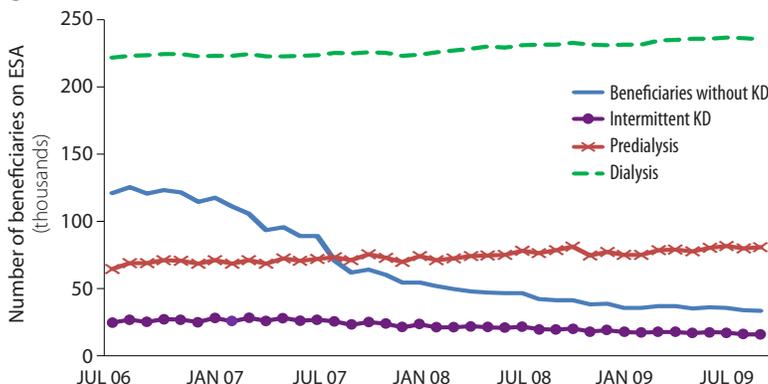


Figure 2: Number of beneficiaries in kidney disease groups among the Medicare cancer population

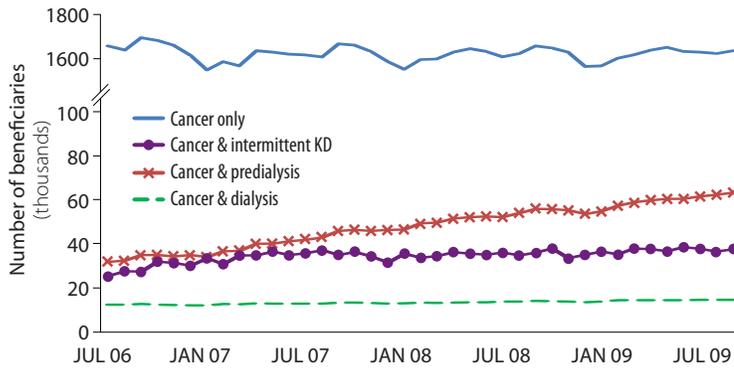


Figure 3: Size of the ESA user cancer population, by kidney disease status

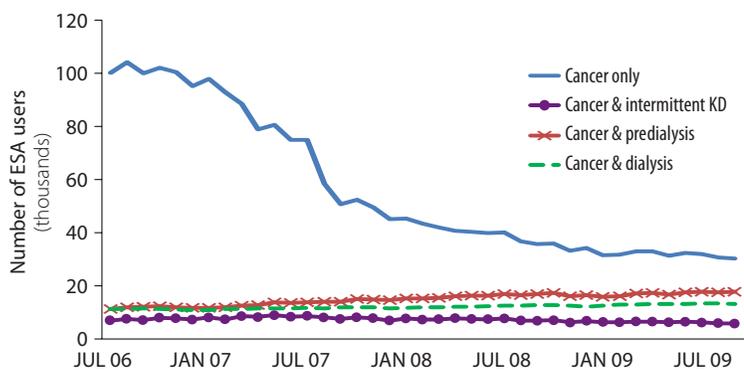


Figure 4: Proportion of nonchronic kidney disease ESA users with cancer having diagnoses of intermittent kidney disease

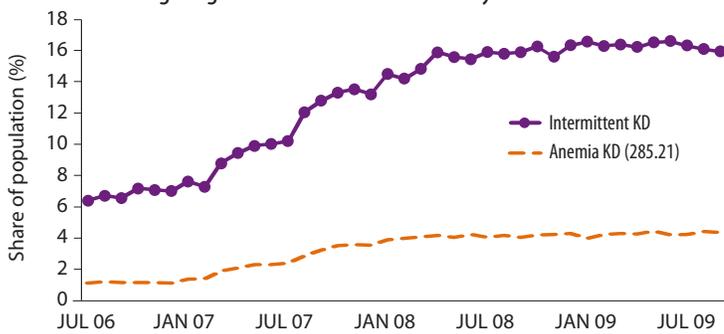
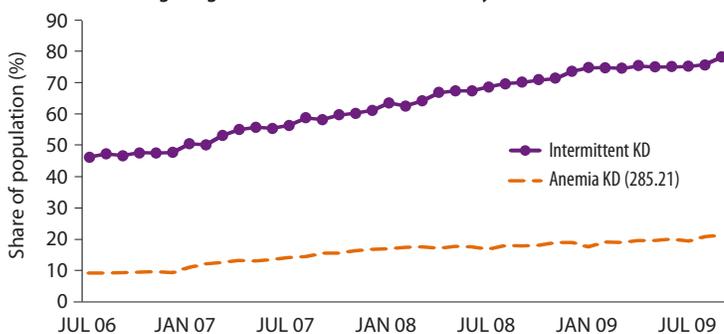


Figure 5: Proportion of nonchronic kidney disease, noncancer ESA users having diagnoses of intermittent kidney disease



the cancer and intermittent KD group rose slightly, and the cancer and predialysis group rose sharply from about 30,000 to more than 60,000 beneficiaries (Figure 2).

We further examined the proportion of beneficiaries in each cancer-KD group having used ESAs. A small proportion of cancer only beneficiaries used ESAs; use declined from 6 percent to about 2 percent over the study period. The use of ESAs among beneficiaries with cancer and intermittent KD declined from nearly 29 percent to 15 percent over the study period. The use of ESAs among beneficiaries with cancer and predialysis declined from 34 percent to 28 percent. The use of ESAs among beneficiaries with cancer and dialysis remained constant over the study period at about 90 percent.

The absolute number of ESA-using beneficiaries with cancer in each of the four groups is presented in Figure 3. Of note, the number of ESA users in the cancer only group dropped precipitously over the study period, while the number of ESA users for the rest of the groups remained fairly stable. The composition of the ESA user population among beneficiaries with cancer also changed over the study period. The cancer and dialysis group grew from 9 percent to 20 percent of all beneficiaries with cancer using ESAs, while the cancer and predialysis group grew from 9 percent to 27 percent. The cancer and intermittent KD group grew from 5 percent to 9 percent, and the cancer only group fell from 77 percent to 44 percent.

Intermittent Kidney Disease and ESA Use

We further examined the diagnosis of intermittent KD (i.e., nonchronic KD) among ESA users with and without cancer. During the study period, while the overall number of ESA users with chronic KD ± cancer was in decline, the proportion of ESA users with intermittent KD was on the rise. Furthermore, the proportion of coded anemia in chronic KD (a subset of intermittent KD) increased. See Figures 4 and 5.

Relating Timing of Practice and Policy Events to Potential Impact on ESA Use

As previously described, we examined the proportion of beneficiaries in each KD group using ESAs, without regard to cancer. These data are presented graphically in **Figure 6** with an overlay of practice and policy events. In general, the proportion of beneficiaries treated with ESAs among the intermittent KD and predialysis populations appears to decline upon publication of relevant studies (e.g., *Cardiovascular Risk Reduction by Early Anemia Treatment With Epoetin Beta [CREATE]*⁷ and *Correction of Hemoglobin and Outcomes in Renal Insufficiency [CHOIR]*⁸) and the modification of the erythropoietin monitoring policy (EMP).⁹

Also, as previously described, we examined the proportion of beneficiaries in each KD-cancer group using ESAs. These data are presented graphically in **Figure 7** with an overlay of practice and policy events. In general, the proportion of beneficiaries treated with ESAs among the cancer only group declined in the face of the National Coverage Determination (NCD), while the proportions increased for the other groups.

Figure 8 depicts a rise in the proportion of ESA users without CKD or cancer who reported intermittent KD.

Figure 6: Rates of ESA use among beneficiaries with kidney disease, by group, with overlay of practice and policy events

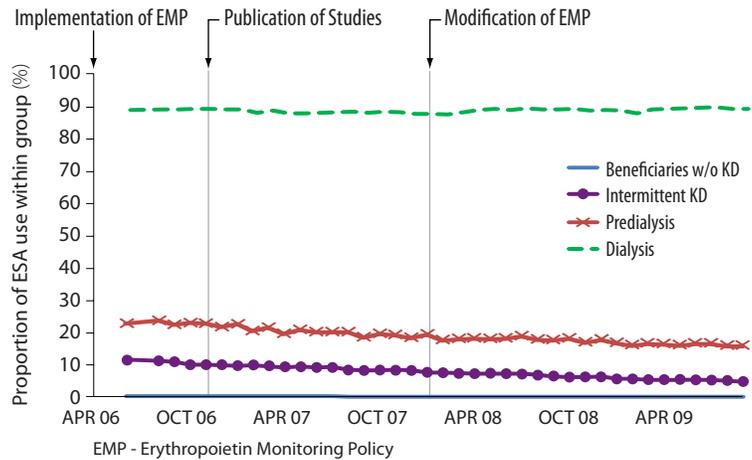


Figure 7: Proportion of cancer beneficiaries with ESA use by kidney disease group, with overlay of practice and policy events

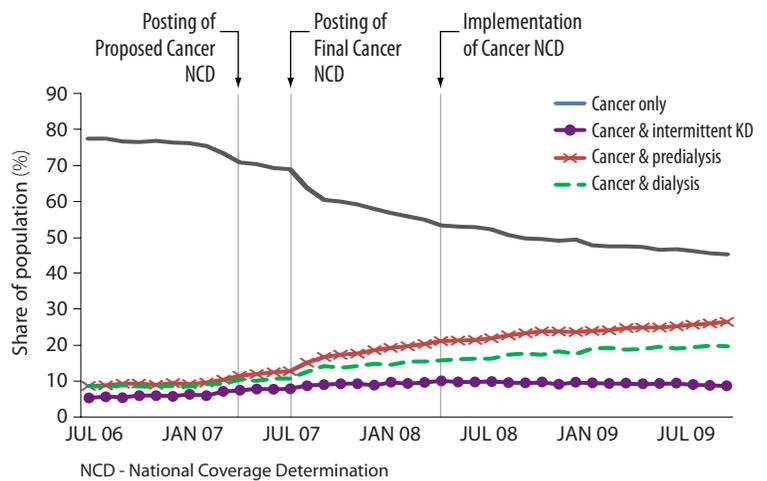
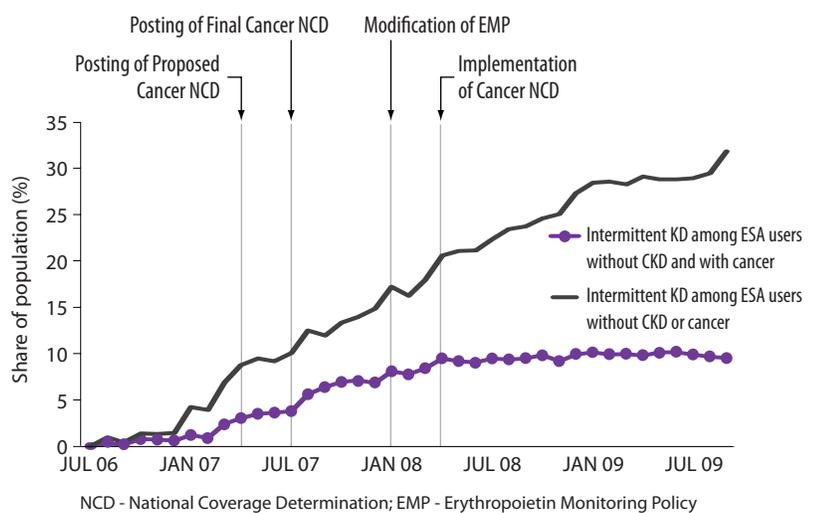


Figure 8: Growth in the proportion of ESA-using beneficiaries without chronic kidney disease, but reporting intermittent kidney disease



DATA SOURCE AND STUDY PERIOD

The Department of Health and Human Services' Medicare data were used for this brief. The use of these data was covered under a project-specific data use agreement with the Centers for Medicare & Medicaid Services.

The study period, over which ESA use was examined, included July 2006 to September 2009.

DEFINITIONS AND METHODOLOGY

Eligible Population

Unless otherwise specified, the ESA utilization described in this brief was derived from the Medicare Parts A and B FFS population. The eligible Medicare population included all beneficiaries who were enrolled in Part A or B in the given month, the month prior, and the month after (i.e., enrolled in a 3-month window). Beneficiaries who died in the given month or the month after but were enrolled in the given month and previous month were included.

Definitions of Kidney Disease Groups

Dialysis: The inclusion criteria for the dialysis population included beneficiaries: (1) enrolled in Part A or B in the given month, the month prior, and the month after; and (2) having at least one dialysis procedure in the given month, at least one in the month prior, and at least one in the month after, if the beneficiary did not die and did not have a kidney transplant in the current month or the month after. If the beneficiary died or had a kidney transplant in the current month or the month after, he or she had to have at least one dialysis procedure in the current month and at least one procedure in the month prior. International Classification of Diseases (ICD-9) procedure, Current Procedural Terminology (CPT), and Healthcare Common Procedure Coding System (HCPCS) codes used to identify dialysis are available from the authors.

Predialysis KD: The inclusion criteria for the predialysis KD population included beneficiaries: (1) enrolled in Part A or B in the given month, the month prior, and the month after; (2) not included in the dialysis population; and (3) having ICD-9 diagnosis code 585.1-581.6 on at least two different dates between the month prior and the month after (i.e., in a 3-month window).

Intermittent KD: The inclusion criteria for the intermittent KD population included beneficiaries: (1) enrolled in Part A or B in the given month, the month prior, and the month after; (2) not included in the dialysis or predialysis population; and (3) having an ICD-9 diagnosis code of 285.21 or at least one of 585-585.6 in the current month. Beneficiaries with 285.21 alone were considered to have anemia in KD.

Definitions of Kidney Disease Stages

Stage I: The inclusion criteria for the stage I population included beneficiaries: (1) enrolled in Part A or B in the given month, the month prior, and the month after; (2) not included in the dialysis population; and (3) having ICD-9 diagnosis code 585.1 on at least two different dates between the month prior and the month after (i.e., in a 3-month window).

Stage II: The inclusion criteria for the stage II population included beneficiaries: (1) enrolled in Part A or B in the given month, the month prior, and the month after; (2) not included in the dialysis population; and (3) having ICD-9 diagnosis code 585.2 on at least two different dates between the month prior and the month after (i.e., in a 3-month window).

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Stage III: The inclusion criteria for the stage III population included beneficiaries: (1) enrolled in Part A or B in the given month, the month prior, and the month after; (2) not included in the dialysis population; and (3) having ICD-9 diagnosis code 585.3 on at least two different dates between the month prior and the month after (i.e., in a 3-month window).

Stage IV: The inclusion criteria for the stage IV population included beneficiaries: (1) enrolled in Part A or B in the given month, the month prior, and the month after; (2) not included in the dialysis population; and (3) having ICD-9 diagnosis code 585.4 on at least two different dates between the month prior and the month after (i.e., in a 3-month window).

Stage V: The inclusion criteria for the stage V population included beneficiaries: (1) enrolled in Part A or B in the given month, the month prior, and the month after; (2) not included in the dialysis population; and (3) having ICD-9 diagnosis code 585.5 on at least two different dates between the month prior and the month after (i.e., in a 3-month window).

Stage VI: The inclusion criteria for the stage VI population included beneficiaries: (1) enrolled in Part A or B in the given month, the month prior, and the month after; (2) not included in the dialysis population described above; and (3) having ICD-9 diagnosis code 585.6 on at least two different dates between the month prior and the month after (i.e., in a 3-month window).

Cancer Population

The eligible Medicare population with cancer included beneficiaries: (1) enrolled in Part A or B in the given month, the month prior, and the month after (including beneficiaries who died in the current month or the month after); and (2) having an ICD-9 diagnosis code indicative of cancer on at least two different dates, or at least one procedure code indicative of cancer, in the 3-month window. ICD-9 diagnosis, ICD-9 procedure, HCPCS, and CPT codes used to identify cancer are available from the authors.

ESA Users

Beneficiaries were considered ESA users if they: (1) were enrolled in Part A or B in the given month, the month prior, and the month after (including beneficiaries who died in the current month or the month after); and (2) had at least one HCPCS code for either epoetin alfa or darbepoetin alfa in that month. The HCPCS codes used for identifying ESA treatment are available from the authors.

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