Costs associated with the administration of erythropoiesis-stimulating agents for the treatment of anemia in patients with non-dialysis-dependent chronic kidney disease: a US societal perspective

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What is already known about this subject

- Needle-based erythropoiesis-stimulating agents (ESAs) are commonly used to treat anemia resulting from chronic kidney disease (CKD).
- Despite the clinical utility of ESAs, their use is associated with a considerable economic and societal burden resulting from the logistics of therapy administration for both patients and caregivers, especially for non-dialysis-dependent (NDD) patients who do not have prescheduled regular visits for dialysis during which ESAs can be administered.
- The magnitude of the administration costs that could potentially be avoided with the introduction of a new oral treatment for anemia due to CKD with comparable safety and efficacy to ESAs has not been assessed.

What this study adds

- This study estimated the direct and indirect excess costs associated with the needle-based administration of ESAs for the treatment of anemia due to NDD-CKD at \$2.5 billion in the United States in 2019, or \$5,399 per treated patient.
- More than 90% of this excess cost was due to in-clinic ESA administration, suggesting that resources associated with ESA administration visits account for the vast majority of costs that could potentially be avoided with the introduction of novel oral medications.
- Direct health care costs and patients' work productivity loss costs, particularly those resulting from in-clinic ESA administration, were the 2 main drivers of total excess costs, respectively, accounting for 54.9% and 33.9% of total excess costs.

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ABSTRACT

BACKGROUND: Erythropoiesis-stimulating agents (ESAs) are commonly used to treat anemia due to chronic kidney disease (CKD). In addition to drug acquisition costs, the administration of ESAs can include direct and

indirect costs due to the needle-based route of administration (eg, time spent by health care staff administering therapy, and patients' and caregivers' time spent receiving or assisting with therapy). However, a comprehensive assessment of the costs associated with the administration of ESAs is lacking.

OBJECTIVE: To estimate the excess costs associated with the needle-based administration of ESAs for the treatment of anemia due to non-dialysis-dependent (NDD) CKD in the United States in 2019 from a societal perspective.

METHODS: Excess costs associated with ESA administration were estimated as the sum of annual costs that could be avoided with the introduction of an oral treatment with comparable safety and efficacy to ESAs. Cost components included direct health care costs, transportation costs, and work productivity loss costs from the perspective of both patients and caregivers (as applicable). Costs were estimated based on scientific publications, governmental agencies, and the results of a recent survey of US patients and caregivers of patients with anemia and CKD. The setting of the administration (ie, at home vs in clinic), frequency of administration, and insurance type were considered.

RESULTS: At the societal level, annual excess costs associated with ESA administration were estimated at \$2.5 billion in the United States in 2019, based on an estimated 462,005 patients with anemia and NDD-CKD treated with ESAs. Overall, 94.4% (\$2.4 billion) of these costs were incurred from in-clinic ESA administration. When stratifying costs by insurance type, Medicare-insured patients accounted for 79.4% (\$2.0 billion) of total annual excess costs. The largest contributor to total annual excess costs was direct health care costs (\$1.4 billion, 54.9%), followed by patient work productivity loss costs (\$846 million, 33.9%), caregiver work productivity loss costs (\$197 million, 7.9%), and transportation costs (\$81 million, 3.3%). Total annual excess costs of in-clinic administration ranged from \$2,572 per patient receiving monthly administration to \$20,948 per patient receiving thrice-weekly administration, while the total annual excess costs of at-home administration ranged from \$1,123 per patient receiving monthly administration to \$2,109 per patient receiving thrice-weekly administration. At the ESA administration level (ie, for each ESA administration), total excess costs were estimated at \$128 per in-clinic ESA administration and \$7 per at-home ESA administration, excluding monitoring costs.

CONCLUSIONS: The needle-based administration of ESAs in patients with NDD-CKD is associated with a substantial economic burden. The introduction of an oral treatment has the potential to result in important cost savings from a societal perspective.

Chronic kidney disease (CKD) is characterized by persistent abnormalities in kidney structure, function, or both, with implications for the health of the affected individual.¹⁻³ The prevalence of CKD increases with age,⁴ such that the prevalence among the Medicare-insured population is estimated to be approximately 22% compared with approximate prevalence of 4% among Medicaid-insured, 1% among commercially insured, and <1% among uninsured populations.⁵ Further, both the prevalence and economic burden of the disease are on the rise,⁶ with total Medicare spending for CKD (including end-stage renal disease) exceeding \$120 billion in 2017, up by 5.3% relative to 2016.⁷

Further, the economic burden of CKD, including health care resource use and costs, significantly increases with

CKD progression, largely due to the emergence of complications.^{8,9} Anemia is a common complication of CKD whose prevalence markedly increases with disease progression; a study by Stauffer et al reported that anemia prevalence increases from 8.4% among patients with stage 1 CKD to 53.4% among those with stage 5 CKD.¹⁰ Anemia due to CKD is characterized by several symptoms (eg, fatigue, weakness, shortness of breath, insomnia, depression, dizziness) that adversely affect patients' health-related quality of life (HRQOL).¹¹

The symptoms associated with anemia and their resulting adverse impact on HRQOL can be alleviated with appropriate treatments of anemia.^{12,13} Treatments currently recommended for anemia due to CKD include iron administration, erythropoiesis-stimulating agents (ESAs), and red blood cell transfusion.¹⁴ ESAs, which can be administered intravenously or subcutaneously, are commonly used for the treatment of anemia due to CKD but may introduce a substantial burden.¹⁴ In addition to drug acquisition costs, the time spent by health care professionals on ESA administration significantly contributes to the total treatment costs.^{15,16} These direct health care costs are further compounded by indirect work productivity loss costs due to patients' time spent receiving therapy. Furthermore, caregivers' time spent accompanying patients to therapy contributes to the societal burden of ESA treatment.¹⁷ The costs associated with ESA administration may be particularly significant in the non-dialysis-dependent (NDD) population since these patients do not have prescheduled regular visits for dialysis during which ESAs can be administered.¹⁸

The direct and indirect costs associated with the needle-based administration of ESAs may be substantially reduced with the introduction of new oral treatments for anemia due to CKD.^{19,20} Hypoxia-inducible factor prolyl hydroxylase inhibitors (HIF-PHIs) are a novel class of oral treatments that have demonstrated promising results in treating anemia due to CKD in recent trials.^{21,22} However, as prior studies have not provided a comprehensive assessment of costs incurred by patients, caregivers, and payers for the needle-based administration of ESAs,^{17,23,24} the potential savings that might result from the introduction of oral HIF-PHIs remain largely unknown. Consistent with the approach advocated by several health technology assessment bodies, assessing costs from a societal perspective is important to reflect the perspective of decision makers, who must take into account the broader impact of health care policies on society in order to appropriately allocate resources.

The goal of this study was to estimate the excess costs associated with the needle-based administration of ESAs for the treatment of anemia due to NDD-CKD

in the United States in 2019 from a societal perspective. This study focused on patients with NDD-CKD, since it is challenging to accurately distinguish costs specific to the administration of ESAs from those associated with dialysis in the dialysis-dependent (DD) population (eg, if ESAs are administered during a visit for dialysis).

Methods

STUDY DESIGN

Total excess costs associated with the administration of ESAs in patients with anemia due to NDD-CKD were estimated as the sum of costs expected to be avoided with an oral treatment instead of a needle-based treatment, assuming a comparable safety and efficacy profile. Inputs used to estimate the total excess costs in the United States (ie, individual costs and prevalence estimates) were obtained from the literature, including scientific publications and governmental agencies, as well as the results of a survey conducted in 2020 among US patients and caregivers of patients with anemia due to CKD (hereafter referred to as the “CKD survey”).²⁵

Total excess costs comprised direct health care costs, transportation costs, and work productivity loss costs. Direct health care costs were reported from a payer’s perspective and included costs associated with ESA administration. Transportation costs and work productivity loss costs included costs incurred by patients and caregivers separately. All costs were expressed in 2019 US dollars, consistent with the most recent complete year (ie, 2019) with the available Consumer Price Index (CPI) at the time the analyses were conducted. Direct health care costs were inflated to 2019 US dollars using the CPI for All Urban Consumers (CPI-U): Medical Care. Transportation costs and work productivity loss costs were inflated to 2019 US dollars using the CPI-U: All Items and CPI-U: Hourly Compensation, respectively.

Total excess costs were reported at the societal level annually, at the patient level annually (ie, per patient), and at the ESA administration level (ie, for each ESA administration). At the societal level, a prevalence-based approach was used to estimate annual costs of ESA administration, where costs per patient were multiplied by the number of prevalent ESA users in the US population. Annual per-patient costs of ESA administration were calculated by multiplying the total cost per administration by the annual number of administrations separately for each available frequency of administration (ie, annual frequency of 12 for once monthly, 26 for every other week, 52 for once weekly, 156 for thrice-weekly administration).²⁵

Total excess costs were reported overall and then stratified by insurance type (ie, commercial, Medicare, Medicaid, Veterans Affairs [VA], and uninsured) and administration setting (ie, in-clinic or at-home administration).

POPULATION

Data on the US adult population in 2019 were obtained from the US Census Bureau.^{26,27} The distribution of the US population by payer type was estimated by classifying individuals into mutually exclusive payer types using the following hierarchy: commercial (including employment-based, direct purchase, TRICARE providers, and patients with dual enrollment in commercial and Medicare or Medicaid), Medicare (including patients with dual enrollment in Medicare and Medicaid), Medicaid, VA, and uninsured.²⁸

The number of adults with NDD-CKD receiving ESAs for the treatment of anemia in 2019 was estimated using publicly available sources that derived payer-specific estimates of the prevalence of diagnosed NDD-CKD and ESA use among patients with NDD-CKD in the United States from claims data.^{4,29} Due to the limited availability of prevalence estimates for certain payer types, the prevalence of diagnosed NDD-CKD among VA-insured patients was assumed to be equal to that of commercially insured patients.⁴ Similarly, the prevalence of ESA use among Medicaid-insured, VA-insured, and uninsured patients was assumed to be equal to that of commercially insured patients.²⁹

The overall number of patients with NDD-CKD receiving ESAs in the United States was calculated as the sum of patients across payer types. Due to the lack of publicly available US-specific estimates, the number of patients receiving in-clinic and at-home ESA administration, as well as the frequency of in-clinic and at-home ESA administration, were estimated based on results from the CKD survey.²⁵ To account for the fact that some population parameters were estimated prior to 2019, these parameters were adjusted for population growth based on data from the US Census Bureau.^{26,27}

DIRECT HEALTH CARE COSTS

Direct health care costs included costs of ESA administration and monitoring costs. These costs were reported from a payer’s perspective and were assumed to be the same across all payer types due to limited data on payer-specific estimates available in the literature.

Costs of ESA administration included fees such as examination fees and facility fees per ESA administration but excluded drug acquisition costs (ie, the cost per ESA unit).¹⁹ Only patients receiving in-clinic ESAs were assumed to incur these costs. It was assumed that at-home ESA administration was conducted by patients or caregivers

FIGURE 1 Total Annual Excess Costs Associated With ESA Administration in Patients With NDD-CKD and Anemia: Population Level^a

^aBased on 2019 US population.

ESA=erythropoiesis-stimulating agent; NDD-CKD=non-dialysis-dependent chronic kidney disease; USD=US dollars; VA=United States Department of Veterans Affairs.

directly, and therefore, was not associated with direct health care costs.

Monitoring costs included fees associated with the assessment of blood hemoglobin levels through laboratory tests and nurse consultations.¹⁹ Monitoring costs were assumed to be the same across administration settings (ie, in clinic and at home). Annual monitoring costs per patient were calculated by multiplying the cost per monitoring event by the expected annual number of monitoring events related to ESA administration. The frequency of monitoring events was estimated based on the US Food and Drug Administration recommendation to monitor patients on a monthly

basis during the maintenance phase (ie, 12 monitoring events per year).^{30,31}

Transportation Costs. Transportation costs included costs incurred for transportation to and from health care facilities to receive in-clinic ESA treatment. Per-patient costs included both patient and caregiver costs and accounted for the proportion of patients who were accompanied by a caregiver during ESA administration visits. It was assumed that no additional transportation costs were incurred for monitoring (eg, monitoring performed during ESA administration visits). The average transportation cost per administration was calculated by multiplying the average total travel

time per visit, as reported by persons seeking ambulatory care in the United States (patients and caregivers separately), by the average driving speed to obtain the average distance traveled,^{32,33} which was then multiplied by the average cost per mile.³⁴ Only patients receiving in-clinic ESAs were assumed to incur these costs.

Work Productivity Loss Costs. Work productivity loss costs were estimated based on a human capital approach, which assumed productivity was valued at an individual's market earnings. Per-patient costs included both patient and caregiver costs, accounting for the proportion of patients who were accompanied to visits by a caregiver.

Patients' work productivity loss costs were estimated using the average time required for ESA administration and patients' mean hourly wage.³² For in-clinic ESA recipients, the time required for ESA administration included all time spent from the moment the patient left his or her residence to the moment he or she returned (eg, including time spent traveling, waiting at the health care facility, and receiving the ESA).³² For at-home ESA recipients, the time required for ESA administration included all time spent preparing and administering ESA treatment at home.²⁵

Caregivers' work productivity loss costs were estimated similarly, using the average time required for ESA administration from the caregivers' perspective, caregivers' mean hourly wage, and the proportion of patients with a caregiver assisting during administration.^{25,32}

SENSITIVITY ANALYSES

Two sensitivity analyses were conducted assuming (1) monitoring requirements were equivalent for needle-based and oral formulations

FIGURE 2 Total Annual Excess Costs Associated With ESA Administration in Patients With NDD-CKD and Anemia: Breakdown by Cost Component^a

^aBased on 2019 US population.

ESA=erythropoiesis-stimulating agent; NDD-CKD=non-dialysis-dependent chronic kidney disease.

(ie, \$0 excess monitoring costs) and (2) the prevalence of ESA use among uninsured individuals was 0% (ie, \$0 excess costs among uninsured patients).

Results

Annual excess costs associated with ESA administration in the United States in 2019 were estimated at \$2.5 billion, or \$5,399 per patient. In-clinic ESA administration accounted for 94.4% (\$2.4 billion) of total annual excess costs, and at-home ESA administration accounted for the remaining 5.6% (\$140 million; Figure 1). Medicare-insured patients accounted for 79.4% of ESA users with NDD-CKD and incurred \$2.0 billion in total annual excess costs. The remaining costs were incurred by commercially insured (\$383 million), Medicaid-insured (\$118 million), VA-insured (\$9 million), and uninsured patients (\$4 million; Figure 1). The largest contributor to total annual excess costs was

direct health care costs (\$1.4 billion, 54.9%), followed by work productivity loss costs (\$1.0 billion, 41.8%), and transportation costs (\$81 million, 3.3%; Figure 2).

Total annual excess costs of in-clinic ESA administration ranged from \$2,572 per patient receiving monthly administration to \$20,948 per patient receiving thrice-weekly administration, while total annual excess costs of at-home ESA administration ranged from \$1,123 for monthly administration to \$2,109 for thrice-weekly administration (Figure 3). At the ESA administration level, total excess costs were estimated at \$128 per in-clinic ESA administration and \$7 per at-home ESA administration, excluding monitoring costs (Supplementary Table 1, available in online article).

POPULATION

The number of adults with diagnosed NDD-CKD in the United States in 2019 was estimated to be 8,916,742 based on an overall prevalence of 3.6% (Table 1). This prevalence was derived from payer-specific estimates of diagnosed NDD-CKD for commercially insured (1.3%; also used for VA-insured patients),³⁵ Medicare-insured (22.0%),³⁵ Medicaid-insured (3.5%),³⁵ and uninsured patients (0.1%).⁵

Among patients with NDD-CKD, it was estimated that 462,005 received ESAs for the treatment of anemia, based on an overall prevalence of ESA use of 5.2% in the NDD-CKD population (Table 1). This prevalence was similarly derived from payer-specific estimates of ESA use among commercially insured patients (3.0%; also used for Medicaid-insured, VA-insured, and uninsured patients) and Medicare-insured patients (6.4%).²⁹

Based on the results of the CKD survey, the numbers of in-clinic and at-home ESA recipients were estimated to be 367,893 and 94,112, respectively (Figure 4). Among in-clinic recipients, the most common dosing frequency was once monthly (34.3%), while once every other week was the most common dosing frequency among at-home recipients (45.5%; Figure 4).

DIRECT HEALTH CARE COSTS

Annual excess direct health care costs associated with ESA administration (ie, costs of ESA administration and monitoring costs) were estimated at \$1.4 billion, or \$2,965 per patient. Annual direct health care costs associated with in-clinic ESA administration ranged from \$1,731 per patient receiving monthly administration to \$10,018 per patient receiving thrice-weekly administration. Annual per-patient direct health care costs associated with at-home ESA administration were \$1,041, regardless of dosing frequency.

Direct costs per in-clinic ESA administration (ie, excluding monitoring costs) were estimated at \$58 (Supplementary Table 1).¹⁹ Annual excess costs of in-clinic ESA administration

FIGURE 3 Annual Excess Costs Associated With ESA Administration in Patients With NDD-CKD and Anemia: Breakdown by Setting of Administration and Dosing Frequency^{a,b,c}

^aThe annual frequency of ESA administration was assumed to be 12 for patients receiving ESA administration 1 time/month, 26 for patients receiving ESA administration once every other week, 52 for patients receiving ESA administration 1 time/week, and 156 for patients receiving ESA administration 3 times/week.

^bBased on 2019 US population.

^cAnnual excess costs are per patient.

ESA=erythropoiesis-stimulating agent; NDD-CKD=non-dialysis-dependent chronic kidney disease; USD=US dollars.

ranged from \$691 per patient receiving monthly administration to \$8,978 per patient receiving thrice-weekly administration. Direct costs of at-home ESA administration (ie, excluding monitoring costs) were assumed to be \$0 ([Supplementary Table 1](#)).

Direct health care costs associated with each monitoring visit were estimated at \$87 ([Supplementary Table 1](#)), corresponding to an annual cost of \$1,041, assuming monthly monitoring visits. Costs per visit included those associated with hemoglobin tests (\$3), the cost of a blood draw (\$3), and the cost of a nurse consultation (\$80).¹⁹

Transportation Costs. Annual excess transportation costs associated with ESA administration were estimated at

\$81 million, or \$176 per patient. At the patient level, annual transportation costs associated with in-clinic ESA administration (including both patient and caregiver costs) ranged from \$63 for monthly administration to \$822 for thrice-weekly administration. At-home administration was assumed to incur \$0 in transportation costs.

At the ESA administration level, total transportation costs (including both patient and caregiver costs) associated with in-clinic ESA administration were estimated at \$5 ([Supplementary Table 1](#)). From the patient perspective, each in-clinic administration visit incurred \$4 of excess transportation costs. This cost was estimated based on an average self-reported total travel time of 33 minutes for an in-clinic

appointment,³² an average driving speed of 37.1 mph,³³ and an average cost per mile of 20 cents.³⁴ From the caregiver perspective, each in-clinic administration visit incurred an average excess transportation cost of \$1. This cost was estimated based on an average self-reported total travel time of 48 minutes for an in-clinic appointment,³² an average driving speed of 37.1 mph,³³ an average cost per mile of 20 cents,³⁴ and an assumption that 20% of patients were accompanied to visits by a caregiver.³²

Work Productivity Loss Costs. Annual excess work productivity loss costs associated with ESA administration were estimated at \$1.0 billion, or \$2,257 per patient. These costs included \$846 million in patient work productivity loss costs and \$197 million in caregiver work productivity loss costs. Annual work productivity loss costs associated with in-clinic ESA administration (including both patient and caregiver costs) ranged from \$777 per patient receiving monthly administration to \$10,107 per patient receiving thrice-weekly administration; for at-home administration, these costs ranged from \$82 per patient receiving monthly administration to \$1,069 per patient receiving thrice-weekly administration.

For patients, excess work productivity loss costs were estimated at \$53 per in-clinic ESA administration ([Supplementary Table 1](#)). This cost was calculated using an average hourly wage of \$28 (based on the characteristics of an average patient) and an average time of 115 minutes to seek care.³² At-home ESA administration was estimated to incur excess work productivity loss costs of \$5 per administration ([Supplementary Table 1](#)) based on an average hourly wage of \$28 and an average duration of ESA administration of 10 minutes.^{25,32}

TABLE 1 Population and Prevalence of ESA Use Among Adults With NDD-CKD in the United States in 2019

Component	Overall	Commercial	Medicare	Medicaid	VA	Uninsured
US adult population ^a (aged ≥18 years)	251,116,064	175,230,701	26,205,859	20,677,666	4,020,920	24,980,917
Prevalence of NDD-CKD diagnosis, %	3.6	1.3 ^b	22.0 ^b	3.5 ^b	1.3 ^b	0.1 ^b
Number of adults with NDD-CKD	8,916,742	2,348,968	5,765,289	723,718	53,900	24,867
Prevalence of ESA use among adults with NDD-CKD, %	5.2	3.0 ^c	6.4 ^c	3.0 ^c	3.0 ^c	3.0 ^c
Number of adults with NDD-CKD receiving ESAs	462,005	70,958	366,806	21,862	1,628	751

^aPopulation estimates are based on the 2019 civilian non-institutionalized population. The proportion of adults in this population was assumed to be the same as the proportion of adults in the 2019 resident population.^{26,27}

^bThe prevalence of NDD-CKD in the commercial, Medicare, and Medicaid populations was reported based on estimates published by the Centers for Disease Control and Prevention.⁴ The prevalence of NDD-CKD in the VA population was assumed to be equal to that in the commercial population. The prevalence of NDD-CKD in the uninsured population was derived using Medical Expenditure Panel Survey Household Component data.⁵

^cThe prevalence of ESA use in the commercial and Medicare NDD-CKD populations was reported based on estimates obtained using IBM MarketScan and CMS Medicare National 20% Sample data, respectively.²⁹ The prevalence of ESA use in the Medicaid, VA, and uninsured populations was assumed to be equal to that in the commercial population.

CMS=Centers for Medicare & Medicaid Services; ESA=erythropoiesis-stimulating agent; NDD-CKD=non-dialysis-dependent chronic kidney disease; VA=US Department of Veterans Affairs.

For caregivers, excess work productivity loss costs were estimated at \$12 per in-clinic ESA administration (Supplementary Table 1). This cost was calculated using an average hourly wage of \$26 (based on the characteristics of an average caregiver), an average of 139 minutes spent accompanying patients to receive care, with the assumption that 20% of patients are accompanied by a caregiver.³² Each at-home ESA administration was estimated to incur excess work productivity loss costs of \$2 per administration. This cost was calculated using an average hourly wage of \$26 and an average duration of ESA administration of 10 minutes,³² with the assumption that 53% of patients are assisted by a caregiver for at-home administration.²⁵

SENSITIVITY ANALYSES

Monitoring Costs. Assuming monitoring requirements were equivalent for needle-based and oral formulations (ie, \$0 excess monitoring costs), total annual excess costs associated with ESA administration in the United States in 2019 were estimated at \$2.0 billion, or \$4,358 per patient, which represents a \$0.5 billion (19%) reduction compared with the base-case scenario (Supplementary Figure 1, available in online article).

Prevalence of ESA Use Among Uninsured Patients. Assuming the prevalence of ESA use among uninsured individuals was 0% (ie, \$0 excess costs among uninsured patients), the total estimated number of adults receiving ESAs in the United States was 461,254, which represents a

reduction of 751 (0.2%) patients receiving ESAs. Total annual excess costs were comparable to the base-case scenario (\$2.5 billion).

Discussion

The findings of this study suggest that the needle-based administration of ESAs is associated with a considerable economic burden, which was estimated at \$2.5 billion in the United States in 2019. More than 90% of this excess cost was due to in-clinic ESA administration, suggesting that resources associated with ESA administration visits account for the vast majority of costs that could be avoided with the introduction of novel oral medications. In addition, direct health care costs and patients' work productivity loss costs, particularly those resulting from in-clinic ESA administration, were the 2 main drivers of total excess costs, respectively accounting for 54.9% and 33.9% of total excess costs. Further, in both administration settings, Medicare-insured patients incurred the majority of costs due to the high prevalence of NDD-CKD and ESA use in this population, which resulted in nearly 80% of total excess costs incurred by Medicare-insured patients.

To the best of our knowledge, this study is the first to provide a societal perspective on ESA administration costs that could potentially be avoided with the introduction of a new oral treatment for anemia due to CKD with comparable safety and efficacy to ESAs. Most prior studies that

FIGURE 4 Frequency of ESA Administration in Patients With NDD-CKD by Setting^{a,b}

^aThe prevalence of at-home and in-clinic ESA administration among patients with anemia and CKD was estimated using the results of a survey conducted in parallel with the current study.²⁵ Results were provided from 54 respondents with anemia and CKD (NDD or DD) who reported currently receiving ESA treatment to manage their anemia. Of note, 8 out of 43 respondents receiving ESAs in clinic had an unknown frequency of ESA administration and were excluded from the analyses reported above. Results were largely consistent across NDD-CKD and DD-CKD subgroups.

^bBased on 2019 US population.

DD=dialysis-dependent; ESA=erythropoiesis-stimulating agent; NDD-CKD=non-dialysis-dependent chronic kidney disease.

assessed the economic burden associated with ESAs and their administration did not focus on patients with NDD-CKD, who may incur the greatest excess costs associated with ESA administration.³⁶⁻³⁹

In addition, studies that included patients with NDD-CKD were conducted more than a decade ago and thus may not provide reliable contemporary estimates due to changes in ESA reimbursement policies and prescribing labels over the past decade.^{17,23,24,40-42} Further, most of these studies exclusively assessed the burden associated with ESAs from the patient perspective or only considered direct health care costs,^{17,23,24} which does not allow for a comprehensive assessment of excess costs associated with the needle-based administration of ESAs.

The results of the current study suggest that the needle-based administration of ESAs may account for a notable proportion of the economic burden of ESA-treated patients. A 2007 study by Maddux et al reported that ESA recipients with NDD-CKD incurred total direct health care costs of \$3,876 per month (ie, annual costs of \$46,512),⁴³ an estimate that included costs incurred by patients, payers, and third parties. The present estimate of \$2,965 per year in direct health care costs incurred exclusively by payers due to the needle-based route of administration of ESAs and associated monitoring requirements may account for an important proportion of total health care costs among ESA-treated patients with NDD-CKD.

The needle-based route of ESA administration may also have an impact on patient and caregiver HRQOL, which was not measured as part of this study. For example, patients' fear of needles and potential injection-site reactions (eg, skin rash) may impact HRQOL and further compound the overall burden of ESA administration.³¹ Furthermore, while the current study assessed the economic impact of time spent receiving therapy, the intrinsic value of an individual's time spent receiving therapy also warrants consideration. Clinic visits, transportation time, and work loss may result in diminished quality of life and add to the already high burden of anemia due to CKD. Therefore, an oral treatment merits consideration as a convenient alternative to ESAs for the treatment of anemia due to CKD.

Despite the cost and burden associated with ESA administration, current treatment options for anemia in patients with CKD requiring ESAs remain limited to needle-based medications. In a recent survey, nearly 50% of patients and caregivers of patients with anemia and NDD-CKD expressed a preference for an oral anemia treatment.²⁵ Therefore, the use of an oral treatment with a safety and efficacy profile comparable to that of ESAs has the potential to improve patients' satisfaction with treatment in addition to avoiding costs associated with ESA administration.

HIF-PHIs have been shown to improve anemia by stimulating endogenous erythropoietin production and restoring iron metabolism in ongoing clinical trials.⁴⁴ Although comparative data are currently limited, it is thought that this novel mechanism will enable a safer and more effective correction of anemia compared with ESAs.⁴⁵ Once additional clinical data are available, further studies will be warranted to account for potential differences in the safety and efficacy of HIF-PHIs compared with ESAs and the potential cost implications of these differences.

LIMITATIONS

The present study is subject to some limitations. For certain payer types, the prevalence of NDD-CKD and ESA use was

assumed to be equal to that of commercially insured patients due to a lack of published payer-specific estimates. This assumption may have underestimated the societal cost associated with ESA administration, as estimates for the commercially insured population were the lowest estimates among available payer types.

Data on the setting (ie, in clinic vs at home) and frequency of ESA administration were derived from a recent survey in which the sample may not be representative of the general US population. Moreover, there was a scarcity of information on certain cost components (ie, transportation costs and work productivity loss costs) specific to the ESA-treated NDD-CKD population. Hence, values derived from the general population receiving ambulatory care were used for these components. However, values in the general population were very similar to CKD-specific estimates found in the CKD survey. For example, 20% of adults in the US general population were reportedly accompanied to ambulatory visits by a caregiver compared with 23.7% of patients accompanied to ESA administration visits as reported in the CKD survey.^{25,32}

Because of the scarcity of publicly available estimates of comparable direct health care costs for all payer types, direct health care costs of Medicare-insured patients were applied to individuals with other types of insurance coverage; this extrapolation may have underestimated health care costs, especially among commercially insured individuals who are known to incur higher costs than Medicare beneficiaries.⁴⁶⁻⁴⁸

Although this analysis adopted a societal perspective, which encompassed costs beyond direct health care costs, this study was limited to specific costs for which estimates were available in the literature.

Accordingly, total excess costs may be underestimated due to additional factors related to the needle-based administration of ESAs (eg, record keeping costs, drug ordering, injection-site reactions, biohazard waste management, disposal of unused medication, and training costs for at-home administration) or potential consequences of increased caregiver burden (eg, depression, sleep disorders), which were not captured in this study due to a lack of cost estimates in the literature.

Finally, this study focused on the NDD-CKD population, and costs may not be generalizable to the DD-CKD population.

Conclusions

The findings of this study suggest that needle-based administration of ESAs in patients with NDD-CKD may be associated with a substantial economic burden. If all ESA-treated patients with NDD-CKD and anemia were to receive an oral treatment with comparable safety and efficacy as when receiving ESAs, potential savings associated with oral administration would amount to approximately \$2.5 billion from a societal perspective. As new data become available, further studies will be warranted to assess excess costs associated with ESA administration, taking into account potential differences between new oral treatments and ESAs in terms of safety and efficacy.

DISCLOSURES

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