The Economic Burden of Anemia in Cancer Patients Receiving Chemotherapy

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ABSTRACT

Background: Anemia is one of the most common hematologic complications of cancer and cytotoxic treatment. The economic burden associated with anemia in patients with malignancy has not yet been extensively studied.

Methods: Patients receiving chemotherapy within 6 months of initial cancer diagnosis were identified in a database of commercial health-care service claims and encounters. Patients with anemia were identified through a coded diagnosis of anemia, transfusion, or erythropoietin treatment. Exponential conditional mean models and a decomposition analysis were used to analyze mean 6-month health-care expenditures.

Results: Twenty-six percent (26%) of 2760 cancer patients with recently diagnosed invasive cancer treated with chemotherapy had anemia. Mean (SD) 6-month unadjusted total expenditures were $62,499 ($78,016) for anemic patients and $36,871 ($52,308) for nonanemic patients (P < 0.0001), with inpatient services representing the largest cost differential between the groups. The adjusted mean 6-month expenditure for the average anemic patient receiving chemotherapy was $57,209. If anemic patients had the same average health status as nonanemic patients, their predicted 6-month expenditures would have been 19% lower ($46,237). Alternatively, if anemic patients had the same expenditure structure or parameter estimates as nonanemic patients, their predicted expenditures would have been 51% lower ($27,847). Thus, for any given health status, treating a patient who is anemic is associated with considerably higher expenditures.

Conclusions: Anemia among cancer patients receiving chemotherapy is associated with a substantial burden in terms of direct medical costs. Implications for the treatment of anemia are suggested by this research and should be confirmed in prospective studies.

Keywords: anemia, cancer, cost-of-illness.

Background

Approximately 8.4 million Americans have cancer or a history of cancer, accounting for roughly 10% of total health-care costs [1,2]. Anemia is one of the most common hematologic complications associated with cancer, estimated to affect at least 50% of patients with cancer at some point in their disease course [3]. Anemia symptoms include fatigue, lethargy, tiredness, or lack of energy. Among patients with cancer, the severity of anemia is influenced by the type of malignancy and treatment regimen. A high incidence of anemia has been reported across the major nonmyeloid tumors treated with the most commonly used chemotherapy agents and combinations [4].

Although anemia is one of the most common complications affecting patients with cancer, researchers have only recently attempted to assess the true prevalence and economic burden of anemia. Two recent claims-based database studies estimated anemia prevalence at between 9.5% and 27% of patients with cancer, with the highest rates occurring among patients with hematologic malignancies, those treated with chemotherapy, or having distant metastasis [5,6]. Barnett et al. [6] found that the additional cost of anemia in patients with cancer was $3775 per year, with approximately 36% of the costs attributable to the actual diagnosis and treatment of the anemic condition.
The main objective of this study is to assess the impact of early anemia within 6 months of cancer diagnosis on resource utilization and expenditures in patients with cancer receiving chemotherapy. A secondary objective is to identify demographic and clinical characteristics associated with anemia in this patient population.

Methods

The data used for this analysis were derived from 1999 Commercial Claims and Encounters and Medicare Supplemental and Coordination of Benefits MarketScan® databases maintained by Medstat, Inc. (Ann Arbor, MI, USA). The MarketScan databases represent the medical experience of approximately three million covered employees and their dependents, early retirees, Consolidated Omnibus Reconciliation Act (COBRA) continues, and a small group of Medicare-eligible retirees. COBRA requires employers with 20 or more employees to continue to offer coverage in their group health plan to certain former employees, retirees, spouses, and dependent children. A variety of fee-for-service, fully capitated, and partially capitated health plans, including exclusive provider organizations, preferred provider organizations, point of service plans, indemnity plans, and health maintenance organizations, are represented in the databases. Each database provides detailed cost and utilization data for health-care services performed in both inpatient and outpatient settings. Outpatient prescription drug data were linked, via unique patient identifiers, with inpatient and outpatient claims files. The outpatient prescription drug file provides information on drugs used (i.e., National Drug Codes), therapeutic class, and pharmacy service payments. Expenditures for all service types include the total gross payment to a provider for specific services before application of deductibles, copayments, and coordination of benefits, but after applying pricing guidelines such as fee schedules and discounts.

Study Population Criteria

The population for this study consisted of patients who have received a diagnosis of cancer, excluding those with carcinoma in situ or nonmelanomatous skin cancer, during the period January to June 1999 who also had a 3-month “clean” period free of cancer diagnosis, chemotherapy, or radiation treatment before the initial 1999 cancer diagnosis, hereafter referred to as the “preperiod,” and had at least one claim for chemotherapy treatment in the 6 months after the initial cancer diagnosis. Patients were followed for up to 6 months after the initial 1999 cancer diagnosis, hereafter referred to as the “study period.” The final study population consisted of 2760 patients.

Outcome Measures and Covariates

This analysis compared health-care resource utilization and expenditures of cancer patients receiving chemotherapy treatment, by anemia status. Patients were classified as anemic if they had at least one claim with a diagnosis of anemia (ICD-9 CM code) or anemia treatment, erythropoietin or red blood cell transfusion, in the 3 months before or the 6 months after the initial cancer diagnosis. Patients with transfusions were not excluded from the analysis. Otherwise, patients were classified as “non-anemic,” patients with a diagnosis of anemia, erythropoietin use or red blood cell transfusion within 30 days before or after surgery were not classified as having anemia for the purposes of this analysis. We note that hemoglobin values were not available in these data.

Resource utilization was summarized for each patient in the study period, and categorized into four types of service: inpatient services, emergency department services, outpatient services, and outpatient pharmaceutical prescriptions. The associated expenditures for these categories of service were computed, as was an overall measure of total expenditures. For patients with capitated insurance coverage, payments were imputed using the mean payments per procedure among all patients with noncapitated insurance coverage in 1999.

Demographic characteristics available for patients included age, sex, geographic region, and plan type. Clinical characteristics included summary information on comorbidities, cancer type, and treatments. A Charlson Comorbidity Index (CCI) score for estimating a patient’s concurrent illnesses was constructed from the preperiod and the study period to adjust for expected resource utilization associated with major comorbid health conditions. The CCI score was calculated using a modification of the method developed by D’Hoore et al. [7] for use in analyzing retrospective claims data, where the CCI, covering 19 conditions, was adapted to the International Classification of Disease (ICD-9) codes. Both primary and secondary diagnoses were searched in the patient’s claims history for presence of comorbidities. A categorical variable was created to classify the type of initial cancer observed for each patient in the study population. The following groups were used to classify the initial cancer type:
breast, central nervous system (CNS), endocrine, gastrointestinal, genitourinary or gynecologic, head and neck, hematologic (includes leukemia, lymphoma, and multiple myeloma), respiratory/thoracic, sarcoma, and other (secondary, not otherwise specified, not elsewhere classified). Indicator variables were also created to identify patients treated with radiation therapy or cancer-related surgery in addition to their chemotherapy treatment during the study period. Further, indicator variables were created to identify patients with metastases involving lymph nodes or distant sites to serve as a proxy for disease severity.

**Statistical Analysis**

To assess statistical differences between the anemia and nonanemic cohorts, chi-square tests were employed for categorical variables, whereas two-tailed t-tests and median rank tests were used for continuous variables. All multivariate analyses were conducted using fixed models based on a priori hypotheses specified in an analysis plan. A logistic regression model was estimated to determine which patient characteristics are associated with anemia. The model included demographic characteristics (age and sex), presence of hematologic malignancy, metastases to lymph nodes and to distant sites, CCI score during the preperiod, use of radiotherapy or cancer-related surgery, and type of health-care coverage (capitated vs. noncapitated).

Health-care expenditure models commonly have been estimated with log-transformed dollars as the outcome or dependent variable [8,9]. Researchers have routinely retransformed from log-dollars back to dollars to assess mean expenditures through the incorporation of a “smearing” term into the retransformation [10]. Yet, this method is unbiased only if the errors in the equation have constant variance—a situation that is rare in the analyses of health-care expenditures [11]. To account for the non-negative nature of health-care costs, we used exponential conditional mean (ECM) models to analyze mean 6-month health-care expenditures.

During the examination of utilization and expenditures, preliminary analysis revealed that the relationship between the total expenditures dependent variable and the explanatory variables differed by anemia status. A test of parameter equality was conducted to test the hypothesis that the regression coefficients were equal for patients with and without anemia treatment. The Wald test statistic rejected the null hypothesis of parameter equality (Wald chi-square with 15 degrees of freedom = 358.61; \( P < 0.01 \)). Next, specification testing was conducted to determine the proper functional form for the multivariate estimation of total expenditures. Ordinary least squares (OLS) models with log transformation, ECM, and two-part models were considered. Because no patients had zero total expenditure in the 6 months after cancer diagnosis, two-part models and OLS models with log transformation are indistinguishable. As suggested by Manning and Mullahy [12], to examine the appropriateness of ECM versus OLS with log transformation, we assessed the OLS log-scale residuals for heteroscedasticity; chi-square statistic was 22.16 for the anemic sample and 286.05 for the nonanemic sample, and kurtosis, coefficient of kurtosis was 5.81 for the anemic sample and 7.02 for the nonanemic sample. This implies that the log-scale residuals are both heteroscedastic and heavily tailed. The performance of ECM and OLS with heteroscedastic retransformation was compared using the Schwartz and Akaike information criteria (AIC; see Manning [13] and Ai and Norton [14] for OLS with heteroscedastic retransformation). Both tests slightly favored ECM over OLS with log transformation (anemic sample OLS: Schwarz criterion = 22.63 and AIC = 22.53, ECM: Schwarz criterion = 22.53 and AIC = 22.43; for the nonanemic sample OLS: Schwarz criterion = 21.78 and AIC = 21.74, ECM: Schwarz criterion = 21.29 and AIC = 21.25). This justifies use of the ECM model.

With parameter estimates from the ECM models, we computed separate adjusted mean expenditures for the anemia and no anemia comparison groups. Multivariate analyses were conducted using STATA software.

Each model included age, sex, preperiod CCI score, cancer type, metastasis with lymph node involvement, metastasis to distant site, duration of chemotherapy during the study period, cancer-related surgery, and radiation therapy. Medicare enrollment was not included in the models given its correlation with age. Age, CCI scores, and duration of chemotherapy (in days) were entered as continuous variables. Further, a quadratic term for age reflecting the observed nonlinear relationship with expenditures was included. Given small sample sizes in some of the cancer type subgroups, cancer type was categorized as hematologic malignancy, breast, gastrointestinal, respiratory/thoracic, genitourinary/gynecology, and all remaining subgroups combined; CNS, endocrine, head and neck, melanoma, sarcoma, or other. The genitourinary/gynecologic subgroup served as the reference group in the models because it represented the most common cancer type in the study population. All other
variables in the models were dichotomous indicator variables.

A decomposition of differences in expenditures between the anemic and nonanemic cohort was also conducted [15–18]. In this analysis, the difference in expenditures between anemic and nonanemic patients was decomposed into two parts; 1) differences in health status profile (different average levels of the covariates); and 2) differences in their expenditure structure (different parameter estimates). To evaluate the relative magnitude of each component, expenditures for the anemia group were predicted given the nonanemic patients’ health status, holding the covariates fixed at the average level of the nonanemic patients, and given the nonanemic patients’ expenditure structure, holding the parameter coefficients at the level of the nonanemic patients.

Results

Prevalence of Anemia and Factors Associated with Anemia

The final study sample included 2760 patients with cancer receiving chemotherapy treatment, 731 (26%) of which had evidence of anemia in the 3 months before or the 6 months after the initial cancer diagnosis. Of these 731 patients, 412 (56%) were classified as anemic solely on the basis of having an anemia diagnosis during the preperiod or study period. The remaining 44% had evidence of being treated for anemia with erythropoietin or blood transfusions during this period. In total, 17.1% of the study population had capitated insurance coverage; the proportion of patients with this type of insurance was similar in both the anemic and nonanemic groups.

Descriptive analyses indicated that the anemic patients in the sample were slightly younger in age than nonanemic patients (Table 1). The mean age of all patients was 62.4 years; whereas the mean age of anemic patients was 61.2 years. The average CCI score among the study population in the study period was 7.3, with anemic patients having significantly (P < 0.0001) higher CCI scores (9.4) than nonanemic patients (6.6), indicating greater pre-existing comorbidity. The most common cancer types were genitourinary/gynecologic cancer (28.8%) followed by breast cancer (19.2%) and gastrointestinal cancer (16.4%). Anemic patients were significantly more likely to have gastrointestinal, hematologic, respiratory/thoracic and sarcoma cancers than nonanemic patients, and were more likely to have metastasis to distant sites (all, P < 0.05). With respect to cancer-related treatments, anemic patients were significantly more likely to have received a longer duration of chemotherapy treatment in the follow-up period than nonanemic patients (93 days vs. 74 days; P < 0.0001). Rates of radiation and cancer-related surgery did not vary significantly by anemia status.

A logistic regression was performed to identify factors associated with anemia among cancer patients receiving chemotherapy treatment (Table 2). This analysis indicated that anemia was positively associated (P < 0.05) with each of the following: hematologic malignancies, metastasis to a distant site, a preperiod CCI score >0, female sex, and noncapitated health insurance. The analysis did not find a significant association with anemia for age ≥ 65 years, radiation therapy, cancer-related surgery, or metastasis to the lymph nodes during the study period.

### Table 1 Demographic and clinical characteristics of study population by anemia status

<table>
<thead>
<tr>
<th></th>
<th>Anemia (N = 731)</th>
<th>No anemia (N = 2029)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age ≥ 65 years</td>
<td>323 (44.2)</td>
<td>1113 (54.9)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Capitated insurance coverage</td>
<td>310 (42.4)</td>
<td>998 (49.2)</td>
<td>0.0016</td>
</tr>
<tr>
<td><strong>Cancer type</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breast</td>
<td>96 (13.1)</td>
<td>434 (21.4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CNS</td>
<td>8 (1.1)</td>
<td>31 (1.5)</td>
<td>0.3946</td>
</tr>
<tr>
<td>Endocrine</td>
<td>8 (1.1)</td>
<td>14 (0.7)</td>
<td>0.2918</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>166 (22.7)</td>
<td>286 (14.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Genitourinary/ gynecologic</td>
<td>89 (12.2)</td>
<td>705 (34.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Head &amp; neck</td>
<td>5 (0.7)</td>
<td>34 (1.7)</td>
<td>0.0514</td>
</tr>
<tr>
<td>Hematologic†</td>
<td>170 (23.3)</td>
<td>157 (7.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Melanoma</td>
<td>0 (0.0)</td>
<td>24 (1.2)</td>
<td>0.0031</td>
</tr>
<tr>
<td>Respiratory/thoracic</td>
<td>93 (12.7)</td>
<td>185 (9.1)</td>
<td>0.0055</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>13 (1.8)</td>
<td>14 (0.7)</td>
<td>0.0104</td>
</tr>
<tr>
<td>Other</td>
<td>83 (11.4)</td>
<td>145 (7.2)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Metastasis</td>
<td>301 (41.2)</td>
<td>590 (29.1)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lymph node involvement</td>
<td>109 (14.9)</td>
<td>258 (12.7)</td>
<td>0.1339</td>
</tr>
<tr>
<td><strong>Duration (Days) of chemotherapy in study period</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>61.2 (14.7)</td>
<td>62.8 (13.7)</td>
<td>0.0118</td>
</tr>
<tr>
<td>CCI score</td>
<td>9.4 (6.8)</td>
<td>6.6 (5.7)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Duration (Days)</td>
<td>92.6 (54.0)</td>
<td>74.4 (55.6)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*The P value represents the results of the statistical comparison of anemic to nonanemic patients using chi-square tests for categorical variables and t-tests for continuous variables.
†Includes lymphoma, leukemia, and multiple myeloma.
CCI, Charlson Comorbidity Index.
**Table 2** Probability of anemia: logistic regression analysis

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>Lower CI†</th>
<th>Upper CI‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preperiod CCI† score &gt;0</td>
<td>1.386§</td>
<td>1.118</td>
<td>1.719</td>
</tr>
<tr>
<td>Male</td>
<td>0.682</td>
<td>0.567</td>
<td>0.821</td>
</tr>
<tr>
<td>Age &gt; 65</td>
<td>0.825</td>
<td>0.676</td>
<td>1.005</td>
</tr>
<tr>
<td>Hematologic malignancy</td>
<td>4.464</td>
<td>3.464</td>
<td>5.752</td>
</tr>
<tr>
<td>Metastasis to lymph node</td>
<td>1.158</td>
<td>0.891</td>
<td>1.506</td>
</tr>
<tr>
<td>Metastasis to distant site</td>
<td>2.267</td>
<td>1.856</td>
<td>2.768</td>
</tr>
<tr>
<td>Cancer-related surgery</td>
<td>1.180</td>
<td>0.973</td>
<td>1.431</td>
</tr>
<tr>
<td>Radiation therapy</td>
<td>1.000</td>
<td>0.831</td>
<td>1.204</td>
</tr>
<tr>
<td>Capitated health insurance</td>
<td>0.759</td>
<td>0.590</td>
<td>0.977</td>
</tr>
</tbody>
</table>

*Lower (upper) CI = lower (upper) values of the 95% confidence interval for the odds ratio.
†Dummy variable for Charlson Comorbidity Index score greater than 0 in preperiod.
‡Number of hospital days (among users) indicates mean (SD) number of days of hospitalization among all patients who were analyzed.
§Number of hospital days (among users) indicates mean (SD) number of days of hospitalization among patients who were hospitalized.

**Health-Care Utilization and Expenditures**

Tables 3 and 4 present study period health-care utilization and expenditures for patients by anemia status. Rates of inpatient, outpatient, and outpatient prescription drug utilization were significantly higher for the anemic than the nonanemic group. Anemic patients had about twice as many hospital admissions and emergency department visits, and one third more outpatient service days and prescription drug claims than nonanemic patients (all \( P < 0.0001 \)). The mean length of stay among patients who were hospitalized in the study period was 10.9 days for anemic patients, compared with 6.4 days for nonanemic patients (\( P < 0.0001 \)).

Patients with anemia had significantly higher total expenditures than nonanemic patients across each of the four service areas: inpatient, emergency department, outpatient, and outpatient prescription drugs (Table 4). Mean 6-month unadjusted total expenditures were $62,499 for anemic patients and $36,871 for nonanemic patients (\( P < 0.0001 \)) (Table 4). Although patients with anemia represented just 26% of the study population, their health-care expenditures accounted for 46% of total hospitalization expenditures and 38% of total expenditures across the full study population. Erythropoietin treatment accounted for less than 2% of total expenditures in the anemia group. Inpatient services were the largest driver of differences in costs between the two groups. Mean inpatient costs for anemic patients were more than twice that for nonanemic patients ($30,639 vs. $13,152) (Table 4).

Total expenditures were modeled as a function of sociodemographic characteristics, preperiod comorbidity, cancer type and treatments, metastases, and duration of chemotherapy for the anemic and nonanemic cohorts (Table 5). Based on parameter estimates from Table 5, the mean (SE) adjusted 6-month expenditures for the anemic and nonanemic cohorts were $63,694 ($33,623) and $28,955 ($41,332), respectively. For patients with anemia, hematologic malignancy (\( P < 0.01 \)), and respiratory/thoracic cancer (\( P < 0.05 \)) were significantly associated with increased expenditures relative to the genitourinary/gynecologic cancer reference group. Cancer-related surgery also significantly increased expenditures (\( P < 0.01 \)). The other cancer type group included CNS, endocrine, head and neck, melanoma, sarcoma, and other unspecified cancers. For the nonanemic cohort, higher comorbidity scores, longer duration of chemotherapy,
each cancer type (except for other), metastasis to distant sites, and radiotherapy were significantly associated with increased expenditures whereas other cancer types and metastasis to lymph nodes were associated with decreased expenditures ($P < 0.01$).

A decomposition of the difference in costs by anemia status was also conducted. Evaluating the covariates at the sample means, the predicted 6-month expenditures for chemotherapy patients with anemia were $57,209. Applying the health status of the nonanemic patients (i.e., nonanemic average levels of covariates) to the anemia estimated model, predicted 6-month expenditures were $46,237, approximately 19% lower. Applying the expenditure structure of the nonanemic patients (i.e., the nonanemic parameter estimates) to the anemia cohort (i.e., anemic average levels of covariates), predicted 6-month expenditures were $27,847, approximately 51% lower than the original prediction. The implication of this analysis is that for any given health status, treating a patient who, in addition, is anemic is associated with considerably higher expenditures.

### Discussion

Using a retrospective database of the reimbursed health-care claims of roughly three million covered lives, this study estimates the burden of anemia in terms of direct medical costs among chemotherapy-treated cancer patients ($N = 2760$). Twenty-six percent of these patients ($n = 731$) were identified as anemic by diagnosis codes or treatment for anemia. Anemic patients’ 6-month mean (SE) health-care expenditures, adjusted for covariates, were $63,694 ($33,623) compared with $28,955 ($41,332) for nonanemic patients.

Although patients with anemia represent just more than a quarter of patients undergoing chemotherapy, their health-care expenditures accounted for 46% of inpatient expenditures and 38% of all expenditures. The expenditure structure of anemic and nonanemic patients differed, most likely resulting from the finding that inpatient-related services were the most important driver of expenditure differentiation between the anemic and nonanemic cohorts. Erythropoietin treatment accounted for less than 2% of total expenditures in the anemia group. In multivariate analyses that controlled for age, sex, preperiod comorbidity (CCI), cancer type, cancer severity, and cancer treatment regimen, total expenditures for anemic patients were higher than those of nonanemic patients. This study provides detailed information concerning the nature and reason that anemic patients are more likely than nonanemic patients to have increased utilization of all types of health-care services. Differences in health status between anemic and nonanemic patients only accounted for 19% of the anemic patients’ expenditures, whereas the remaining expenditures were primarily driven by the nature of incurred expenses, namely inpatient services.
The strongest factor associated with anemia was hematologic malignancies, a finding that has been shown in other research [19,20]. The next strongest factors associated with anemia were the comorbidity indicators and staging; greater preperiod CCI scores and evidence of metastasis to distant sites. Another factor that was found to be associated with increased incidence of anemia was sex; women were more likely than men to have anemia diagnosed. Groopman and Itri [4] have reviewed the literature and found that the incidence of anemia is associated with several different tumor types, stage, and specific chemotherapeutic regimens. It is noteworthy that age is not associated with increased incidence of anemia, either in this research or in other published studies [4,21,22]. Finally, the relationship between anemia and noncapitated health insurance, while not strong, was present. The latter finding may reflect a selection bias. Individuals with long-term illnesses and comorbidities are more likely to have established relationships with medical providers and therefore may be more likely to select fee-for-service programs to preserve those relationships.

Our study has several limitations that stem from the retrospective nature of the data. First, while the sample was drawn from more than three million lives, it may not be representative of the general population, or even of those with health insurance. Second, for untreated anemic patients, we rely on identifying the anemic population based on physician and facility coding of an anemia diagnosis for patients with low hemoglobin values. Untreated low-grade anemic patients may be less likely to receive an ICD-9 diagnostic code for anemia in their health-care claims, and thus would be included in our cohort of nonanemic patients. Additionally, because of data availability, this study only looks at early anemia—anemia that occurs within the first 6 months after initial cancer diagnosis. We are unable to track disease progression over time, which may affect our results.

Another limitation of this study is the absence of hemoglobin or hematocrit data, because this would allow for definitive determination of patients’ anemic status, and a determination of the undertreatment of anemia. Nevertheless, the presence of an anemia diagnosis code in these data does not necessarily indicate that anemia is severe enough to require treatment; it may simply indicate that the anemia was noted in the medical chart and resulted in its entry on the health-care claim. Inclusion of data on actual patient hemoglobin concentration would enable researchers to examine the effectiveness of anemia treatment on changes in hemoglobin and determine if changes in health-care utilization and expenditures result from such treatment.

Finally, the study has some methodological limitations. Although the ECM model used for the analysis does have several advantages, it does not fit well with highly skewed data, such as health-care expenditure. Hence, although the model chosen allows for decomposition of the drivers of skewness; there was a trade-off between bias and robustness in its selection.

Additional research on the effects of anemia with regard to disease prevalence and health-care resource utilization for all patients with cancer is warranted. Results of studies by Glaspy et al. [21] and Demetri et al. [22] demonstrated a relationship between an increase in hemoglobin concentrations and an improvement in quality of life. Additional research is needed to investigate further the impact of anemia treatment or the lack of it on utilization and costs, for both patients with and without chemotherapy treatment.

In summary, this analysis of reimbursed health-care claims suggests that anemia is associated with a substantial burden in terms of direct medical care costs. Anemic cancer patients receiving chemotherapy utilize considerably more health-care resources, both inpatient and outpatient services, even after controlling for many possible confounders. A prospective trial with broad inclusion criteria that is designed to assess the health-care utilization and costs associated with ameliorating anemia of chemotherapy patients in general oncology practice appears to be warranted.

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