

ORIGINAL RESEARCH

Hematologic Complications, Healthcare Utilization, and Costs in Commercially Insured Patients with Myelodysplastic Syndrome Receiving Supportive Care

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Background: Myelodysplastic syndrome (MDS) is rare in people aged <50 years. Most patients with this disorder experience progressive worsening of blood cytopenias, with an increasing need for transfusion. The more advanced and severe the disorder, the greater the risk that it will progress to acute myeloid leukemia. Therapy is typically based on the patient's risk category, age, and performance status. Supportive care alone is a major option for lower-risk, older patients with MDS or those with comorbidities. The only potentially curative treatment option is hematopoietic stem-cell transplantation, which is typically used to treat high-risk, younger patients.

Objective: To describe and compare the hematologic complications, healthcare utilization, and costs of supportive care in patients with MDS aged <50 years and in older patients aged ≥50 years.

Methods: Using the i3/Ingenix LabRx claims database, this retrospective study included patients who were continuously enrolled (ie, 6 months preindex through 1 year postindex) in the study and who had an initial claim of MDS (index date) between February 1, 2007, and July 31, 2008. Patients treated with hypomethylating agents or thalidomide analogues were excluded. Claims included information on office visits, medical procedures, hospitalizations, drug use, and tests performed. The hematologic complications, costs, and utilization analyses were stratified by age into 2 age-groups—patients aged <50 years and those aged ≥50 years. The MDS-related diagnoses, utilization, and costs were analyzed postindex. The data used in this study spanned the period from August 1, 2006, to July 31, 2009.

Results: We identified 1133 newly diagnosed patients with MDS who received supportive care only during the study period; of these, 19.5% were younger than age 50 years. These younger patients included more females (62.0% vs 52.5%; $P = .011$) and had fewer comorbidities (mean Charlson comorbidity index, 1.2 vs 2.4; $P < .001$) and physician office visits than those aged ≥50 years. Postindex, compared with the older patients, the younger patients had less use of erythropoietin therapy and fewer transfusions, anemia diagnoses, and potential complications of neutropenia and pneumonia diagnoses; however, more diagnoses of neutropenia and of decreased white blood cell counts were seen in the younger patients than in the older patients ($P \leq .034$ for all comparisons). Furthermore, younger patients had fewer mean office visits in the postindex period than older patients (17.5 vs 24.2, respectively; $P < .001$) and fewer hospitalizations (32.1% vs 44.6%, respectively; $P = .004$), but they had a longer (although not statistically significant) mean length of hospital stay (21 vs 14 days, respectively; $P = .131$). Mean total healthcare charges were \$96,277 (median, \$21,287) in younger patients compared with \$84,102 (median, \$39,402) in older patients, although this difference, too, was not significant.

Conclusions: MDS is associated with frequent and prolonged hospitalizations, frequent outpatient visits, and high costs in younger and in older patients who are receiving supportive care. Although this study shows that younger patients aged <50 years do not have significantly higher costs overall, a small proportion may have a higher healthcare utilization and cost-related burden of MDS than patients aged ≥50 years.

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Myelodysplastic syndrome (MDS) encompasses a heterogeneous group of clonal disorders of hematopoiesis and is characterized by dysplastic morphology of marrow and blood cells, ineffective hematopoiesis, and peripheral blood cytopenias.^{1,2} Most patients with MDS experience progressive worsening of blood cytopenias, with an increasing need for transfusion.² These patients also have an increasing number of potentially fatal infections and hemorrhagic complications.² The more advanced and severe the MDS is, the greater the risk that the disease will progress to acute myeloid leukemia (AML).³ The disease may be classified into 1 of 5 subtypes—refractory anemia, refractory anemia with ringed sideroblasts (RARS), refractory anemia with excess of blasts (RAEB), RAEB in transformation (RAEB-T), or chronic myelomonocytic leukemia.³ Approximately 5% to 15% of the relatively lower-risk patients with refractory anemia/RARS transform to AML; by contrast, 40% to 50% of the high-risk patients with RAEB/RAEB-T transform to AML.³

The therapeutic options that are tailored for specific MDS subgroups are typically based on factors such as the patient's risk category, age, and performance status.^{3,4} The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology recommend that all patients with MDS receive supportive care,³ which includes blood transfusions, erythropoietin with or without granulocyte colony-stimulating factor, iron chelation therapy, and prophylactic antibiotics.^{4,5} Other therapies indicated for the treatment of patients with MDS include the thalidomide analogue lenalidomide and the hypomethylating agents decitabine and 5-azacytidine.^{3,4} The only potentially curative treatment option is hematopoietic stem-cell transplantation, which is typically used to treat younger, high-risk patients.^{3,4} Supportive care alone remains a leading option for the treatment of lower-risk, older patients with MDS or those with comorbidities.^{3,4}

Data on the distribution of MDS in the general population are inconsistent, possibly because of misdiagnoses and/or underreporting of the disease.^{6,7} The most recent estimates of the annual incidence of MDS in the United States range from 3.3 to 5.0 per 100,000 persons.^{3,7,8} Some studies indicate that the median age of patients with MDS is approximately 65 years, whereas others note that more than 70% of cases occur in patients aged ≥ 70 years in the United States.^{3,6,9} The incidence of MDS in individuals aged ≥ 70 years is between 22 and 45 per 100,000 persons and increases with age.^{3,6,9-11}

Less than 10% of patients with MDS are aged < 50 years; therefore, little is known about this disease in this younger age-group, particularly among patients who receive supportive care only.^{6,11,12} Some data suggest that

KEY POINTS

- The more advanced and severe the myelodysplastic syndrome (MDS) is, the greater the risk of progression to acute myeloid leukemia. Therapy is currently based on risk category, age, and performance status.
- In the United States, the majority of newly diagnosed patients with MDS receive only supportive care, although for younger patients at high-risk, hematopoietic stem-cell transplantation is potentially the only curative option.
- This analysis compares the hematologic complications, healthcare utilization, and cost of care between patients with MDS aged < 50 years and those aged ≥ 50 years who receive supportive care only.
- Although the younger patients had fewer office visits, they had longer mean length of hospital stay than the older group (21 vs 14 days, respectively).
- Mean total healthcare charges were \$96,277 in younger patients compared with \$84,102 in older patients.
- Based on this study, approximately 20% of patients with MDS are under age 50 years.
- The results of this study suggest that a small proportion of younger patients with MDS who receive supportive care only may have a higher healthcare utilization and cost-related burden of MDS than older patients with this condition.

younger patients with MDS have less aggressive disease.^{12,13} We compared hematologic complications, healthcare utilization, and costs in patients aged < 50 years and in those aged ≥ 50 years who were newly diagnosed with MDS and received supportive care only.

Methods

This study was a retrospective cohort analysis using data from the i3/Ingenix LabRx database, which is a Health Insurance Portability and Accountability Act-compliant administrative claims database of 8 million to 10 million covered lives from all major regions of the United States. The database contains deidentified adjudicated pharmacy and medical claims submitted for payment by providers, healthcare facilities, and pharmacies. Claims included information on physician office visits, medical procedures, hospitalizations, drugs dispensed, and on the tests that were performed. In this database, charges are reported, but paid claims and costs are not (although charges and costs are conceptually different, we refer to charges as costs in the discussion of the results, for convenience). Data used in this study spanned the period from August 1, 2006, to July 31, 2009.

Table 1 List of CPT®, GPI, HCPCS, and ICD-9-CM Codes by Study Measure

Study measure	CPT®, GPI, HCPCS, or ICD-9-CM code
Acute myeloid leukemia	ICD-9-CM: 205.0x, 205.2x-205.9x, 206.0x, 206.2x-206.9x, 207.0x, 207.2, 208.0x, 208.2x-208.9x
Anemia	
Anemia diagnosis	ICD-9-CM: 281.9, 283.9, 284.8, 284.9, 285.0, 285.2x, 285.9, V78.1
Use of erythropoietin	HCPCS: J0885, J0881, Q0137, Q0136, J0880; GPI: 82-40-10
Use of iron chelation therapy	Deferoxamine (GPI: 93-00-00-20-10) or deferasirox (GPI: 93-10-00-25-00)
Bone marrow biopsy	ICD-9-CM: 41.31, 41.38, 41.98; CPT: 38220, 38221
Neutropenia	
Neutropenia	ICD-9-CM: 288.00, 288.04, 288.09, 289.4
Febrile neutropenia diagnosis	ICD-9-CM: 780.61
Decreased white blood cell count	ICD-9-CM: 288.5x
Use of granulocyte colony-stimulating factors	HCPCS: J1440, J1441, J2505; GPI: 82-40-15
Pancytopenia	ICD-9-CM: 284.1
Potential complications of neutropenia	
Pneumonia	ICD-9-CM: 481, 482.xx, 485, 486
Unspecified fever	ICD-9-CM: 780.60
Thrombocytopenia	ICD-9-CM: 287.3x, 287.5
Transfusions	HCPCS: P9010, P9016, P9021, P9022, P9038, P9039, P9040, P9057, P9058, P9019, P9020, P9031, P9032, P9033, P9034, P9035, P9036, P9037, P9052, P9053, P9055; CPT: 36430; ICD-9-CM procedure code: 99.0x
CPT indicates <i>Current Procedural Terminology</i> ®; GPI, generic product identifier; HCPCS, Healthcare Common Procedure Coding System; ICD-9-CM, <i>International Classification of Diseases, Ninth Revision, Clinical Modification</i> .	

Study Population

This study included patients with a first diagnosis of MDS between February 1, 2007, and July 31, 2008 (ie, the identification period). MDS was identified using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* diagnosis codes of 238.72 through 238.75. The first date of a medical claim with an MDS diagnosis in any diagnosis field in the identification period was defined as the index date. Patients were followed for 1 year after the index date. To examine a more homogeneous group of patients with MDS in our final analytic cohort, we included newly diagnosed patients with MDS who received supportive care only; these patients had no claims for hypomethylating agents

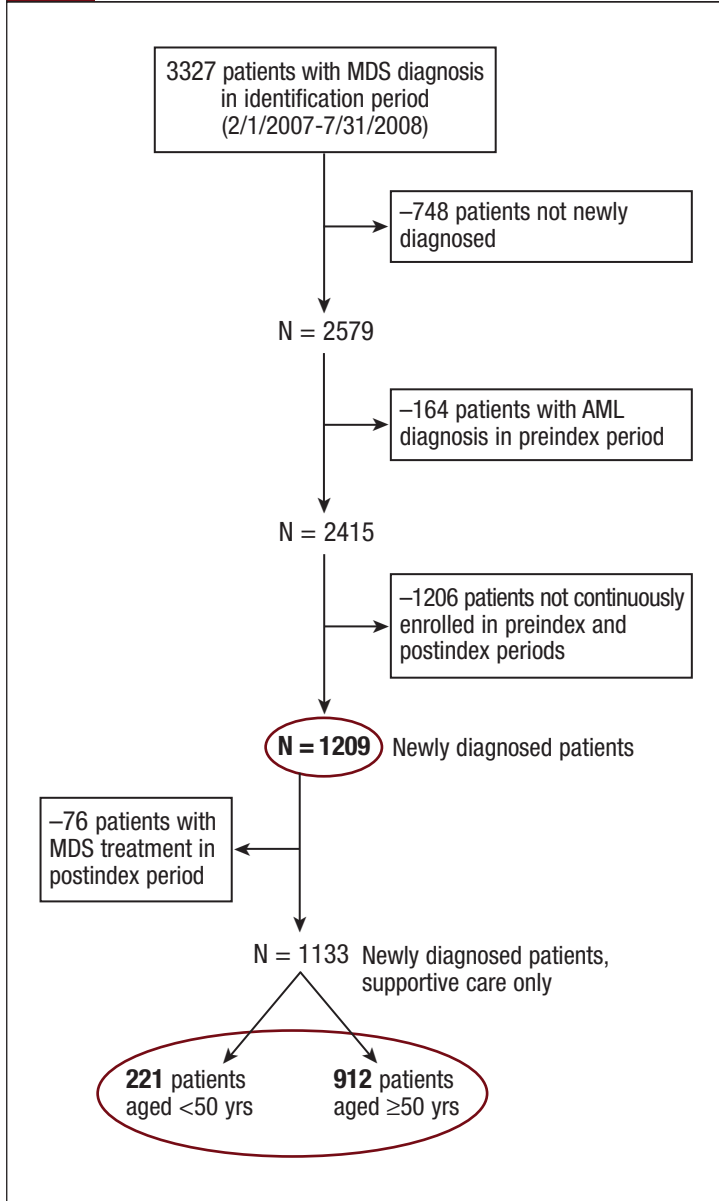
or for thalidomide analogues (ie, decitabine, 5-azacytidine, or lenalidomide) in the postindex period.

Patients were excluded from the study if they (1) had a diagnosis of MDS in the 6-month preindex period, (2) had a diagnosis of AML (ICD-9-CM 205.0x, 205.2x-205.9x, 206.0x, 206.2x-206.9x, 207.0x, 207.2, 208.0x, 208.2x-208.9x) in the 6-month preindex period, or (3) were not continuously enrolled in the 6-month preindex and the 1-year postindex periods.

Measures

Baseline variables in the study were patient demographics, bone marrow biopsy, number of physician office visits, number of emergency department visits and hospi-

Figure Study Cohort Selection: Newly Diagnosed MDS Patients of All Ages Who Received Supportive Care Only



talizations, length of stay among patients with hospitalizations, and total healthcare charges. We also calculated the adapted Charlson comorbidity index at baseline, which is a clinical comorbidity index designed to be used with select ICD-9-CM diagnoses and procedure codes.^{14,15}

The primary outcomes were AML diagnosis and mean number of days to first AML diagnosis (among patients with AML diagnoses). Other outcomes included number of transfusions, number of anemia diagnoses, number of neutropenia diagnoses, potential complications of neutropenia, number of thrombocytopenia diagnoses, number of pancytopenia diagnoses, and number of

decreased white blood cell count diagnoses.² We also calculated the number of physician office visits, hospitalizations, and emergency department visits; the length of stay among patients with hospitalizations; and the total healthcare charges. The MDS-related charges were estimated by adding charges from medical claims with a primary diagnosis related to MDS or to AML and charges from pharmacy claims for the treatment of MDS. Table 1 lists the codes used to derive the study measures.

Analyses

All pharmacy and inpatient and outpatient medical claims were reviewed in the 6-month preindex period to derive the baseline variables and in the 1-year postindex period to derive the study outcomes (bone marrow biopsies were identified in the preindex and postindex periods). Preindex and postindex analyses were stratified by 2 age cohort groups: patients aged <50 years and patients aged ≥50 years.

We report means, medians, and standard deviations (SDs) for continuous variables, whereas patient counts and percentages are reported for categorical variables. Appropriate statistical tests (ie, *t*-tests for continuous variables and chi-square tests for categorical variables) were used to compare study measures across age cohorts. All statistical analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC).

Results

Cohort Selection

We identified 3327 patients with an MDS diagnosis in the identification period (between February 1, 2007, and July 31, 2008). Of these patients, 748 were not newly diagnosed, 164 had an AML diagnosis in the preindex period, and 1206 patients were not continuously enrolled in both the preindex and postindex periods. After exclusion of these 2118 patients, there were 1209 newly diagnosed patients. For our final cohort of newly diagnosed patients with supportive care only, 76 patients who were treated with hypomethylating agents and thalidomide analogue in the postindex period were removed from the data, resulting in the final analytic sample size of 1133 patients (Figure).

Among these 1133 patients with newly diagnosed MDS, 123 (10.9%) had a first diagnosis of low-grade MDS lesions (ICD-9-CM code 238.72), 36 (3.2%) had a diagnosis of high-grade MDS lesions (238.73), 18 (1.6%) had a diagnosis of MDS with 5q deletion (238.74), and 956 (84.4%) patients had a diagnosis of MDS unspecified (238.75). There were no differences in these distributions between the 2 age cohorts (*P* = .141).

Baseline Patient Characteristics

At baseline, the mean age in this cohort was 62.9 years

Table 2 Demographics, Comorbidities, Bone Marrow Biopsy, and Healthcare Utilization and Charges in the 6-Month Preindex Period in Patients Receiving Supportive Care

	Patients aged <50 yrs (N = 221)	Patients aged ≥50 yrs (N = 912)	Total (N = 1133)	P value
Mean age, yrs (SD)	39.1 (9.4)	68.7 (10.8)	62.9 (15.8)	N/A
Female, N (%)	137 (62.0)	479 (52.5)	616 (54.4)	.011 ^a
Region, N (%)				.036 ^a
East	36 (16.3)	96 (10.5)	132 (11.7)	
Midwest	46 (20.8)	198 (21.7)	244 (21.5)	
South	114 (51.6)	465 (51.0)	579 (51.1)	
West	25 (11.3)	153 (16.8)	178 (15.7)	
Charlson comorbidity index, mean (SD)	1.2 (2.1)	2.4 (2.7)	2.1 (2.6)	<.001 ^a
Bone marrow biopsy, ^b N (%)	113 (51.1)	413 (45.3)	526 (46.4)	.118
Mean physician office visits, N (SD; median)	8.2 (7.8; 6)	10.5 (9.1; 9)	10.1 (9.0; 8)	<.001 ^a
Hospitalizations, N (%)				.52
0	164 (74.2)	646 (70.8)	810 (71.5)	
1	41 (18.6)	171 (18.8)	212 (18.7)	
2	9 (4.1)	48 (5.3)	57 (5.0)	
3+	7 (3.2)	47 (5.2)	54 (4.8)	
Length of stay among patients with hospitalizations, days (mean; SD)	57 (7.8; 7.9)	266 (9.0, 15.0)	323 (8.8; 14.0)	.417
Emergency department visits, N (%)				.264
0	208 (94.1)	870 (95.4)	1078 (95.1)	
1	7 (3.2)	14 (1.5)	21 (1.9)	
2+	6 (2.7)	28 (3.1)	34 (3.0)	
Mean total healthcare charges, \$ (SD; median)	30,177 (53,550; 9622)	31,832 (64,658; 12,248)	31,509 (62,627; 12,034)	.693
Mean medical charges, \$ (SD; median)	28,248 (52,264; 8413)	29,581 (63,660; 9790)	29,321 (61,584; 9616)	.745
Mean pharmacy charges, \$ (SD; median)	1929 (4451; 428)	2251 (4714; 1041)	2188 (4664; 895)	.358

^aP < .05.

^bIdentified in the preindex or postindex period.

N/A indicates not applicable; SD, standard deviation.

(SD, 15.8), with 19.5% (N = 221) of the sample aged <50 years and 80.5% (N = 912) of the sample aged ≥50 years (Table 2). Mean ages within the 2 cohorts were 39.1 years (SD, 9.4) and 68.7 years (SD, 10.8) in the younger and older age-groups, respectively. There was a significant dif-

ference between the 2 age cohorts in the proportion of females (62% vs 52.5% in the younger vs the older age-groups, respectively; P = .011) and in the distribution across US census regions (P = .036).

Based on the mean Charlson comorbidity index, the

group aged <50 years had fewer comorbid conditions than the group aged ≥50 years (1.2 vs 2.4, respectively; $P < .001$). There was no significant difference between the 2 age cohorts in the proportion of bone marrow biopsies (51.1% vs 45.3% in the younger and older age-groups, respectively).

Preindex Healthcare Utilization and Costs

In terms of baseline (preindex) healthcare utilization and costs (Table 2), no significant differences were seen between the 2 age cohorts, except for the mean number of physician office visits. There were fewer physician office visits in the younger age-group than in the older age-group (mean, 8.2 vs 10.5, respectively; $P < .001$). The younger and older groups had a similar proportion of hospitalizations (25.9% vs 29.3% for ≥1 hospitalizations; $P = .52$) and a similar mean length of hospital stay (7.8 vs 9.0 days; $P = .417$).

A similar proportion of younger and older patients had at least 1 emergency department visit (5.9% vs 4.6%; $P = .264$). The mean total 6-month preindex healthcare costs were \$30,177 (SD, \$53,550; median, \$9622) in the younger patients and \$31,832 (SD, \$64,658; median, \$12,248) in the older patients ($P = .693$).

Postindex MDS-Related Diagnoses, Healthcare Utilization, and Costs

As shown in Table 3, in the year after MDS diagnosis, the crude incidence of AML diagnosis was similar in the 2 age-groups—9% of patients aged <50 years versus 5.7% of patients aged ≥50 years ($P = .067$). There was no significant difference in the mean number of days to first AML diagnosis in patients who were diagnosed with AML between the 2 age-groups (43.8 vs 74.3 days; $P = .214$).

The younger patients aged <50 years had proportionally fewer transfusions than those aged ≥50 years (10.8% vs 14.9% had ≥1 transfusions; $P = .034$). The younger patients also had a significantly lower proportion of anemia diagnoses (46.6% vs 68.1%; $P < .001$) and significantly less erythropoietin use (10.9% vs 28.9%; $P < .001$) than the older patients. The proportion of patients with iron chelation therapy use was similar in the 2 groups (1.4% vs 0.8%, respectively; $P = .4$).

The proportion of neutropenia diagnoses was significantly higher in the younger group than in the older group (24.0% vs 17.1%, respectively; $P = .018$), but the difference in the use of granulocyte colony-stimulating factor was not significant (8.6% vs 6.5%, respectively; $P = .262$). Furthermore, fewer potential complications of neutropenia were seen in the younger age-group than in the older age-group (7.2% vs 14.1%, respectively; $P = .006$) and significantly fewer pneumonia diagnoses were

observed in the younger age-group (5.4% vs 12.4%, respectively; $P = .003$).

The number of unspecified fever diagnoses was similar between the 2 age-groups (2.7% for the younger group vs 3.4% for the older group; $P = .608$), and the use of outpatient pharmacy intravenous antibiotics was also similar (0.5% vs 0.3%, respectively; $P = .781$). The proportion of thrombocytopenia diagnoses was numerically but insignificantly higher in the younger group than in the older group—25.3% versus 22.3%, as was pancytopenia diagnoses (13.1% vs 12.6%, respectively); decreased white blood cell count diagnoses were the only significant difference, with 13.6% in the younger group and 6.5% in the older group ($P < .001$).

There were no significant differences in MDS-related costs between the 2 age cohorts, although the mean costs were higher in the younger age-group—\$35,888 (SD, \$139,081; median, \$2626) versus \$25,435 (SD, \$81,866; median, \$4717) for the older group ($P = .284$).

Overall, patients aged <50 years had significantly less erythropoietin use ($P < .001$) and significantly fewer transfusions ($P = .034$), anemia diagnoses ($P < .001$), complications of neutropenia ($P = .006$), and pneumonia diagnoses ($P = .003$) than patients aged ≥50 years; however, there was a higher percentage of neutropenia ($P = .018$) and decreased white blood cell count diagnoses in younger patients than in older patients ($P < .001$).

Postindex Overall Healthcare Utilization and Costs

A significant difference was seen in overall healthcare utilization in the 1-year postindex period (Table 4). Patients aged <50 years had a significantly lower mean number of physician office visits than patients aged ≥50 years (17.5 vs 24.2; $P < .001$), and a lower proportion of younger patients had at least 1 hospitalization (32.1% vs 44.6%; $P < .004$). However, the mean length of stay among patients with hospitalizations was longer in the younger age-group than in the older age-group (21 vs 14 days), although this difference was not statistically significant ($P = .131$). The proportion of patients that had at least 1 emergency department visit was similar in the 2 age-groups (8.6% vs 8.5%; $P = .74$).

As shown in Table 4, there was no significant difference in mean total healthcare costs in the postindex period between the 2 age cohorts ($P = .473$), but there was a numerical difference, with a mean cost of \$96,277 (SD, \$240,854; median, \$21,287) in younger patients compared with a mean cost of \$84,102 (SD, \$149,877; median, \$39,402) in older patients.

The mean total healthcare costs were primarily driven by mean medical charges among younger and older patients: \$91,435 (SD, \$237,723; median, \$18,526) for younger patients versus \$78,612 (SD, \$146,631; median,

Table 3 MDS-Related Diagnoses, Healthcare Utilization and Charges in the 1-Year Postindex Period in Patients Receiving Supportive Care

	Patients aged <50 yrs (N = 221)	Patients aged ≥50 yrs (N = 912)	Total (N = 1133)	P value
AML diagnosis, N (%)	20 (9.0)	52 (5.7)	72 (6.4)	.067
Mean days to first AML diagnosis among patients with MDS diagnosis (SD; median)	43.8 (78.8; 4)	74.3 (96.9; 22)	65.8 (92.7; 16)	.214
Number of transfusions, N (%)				.034 ^a
0	197 (89.1)	776 (85.1)	973 (85.9)	
1	8 (3.6)	80 (8.8)	88 (7.8)	
2+	16 (7.2)	56 (6.1)	72 (6.4)	
Anemia diagnosis, N (%)	103 (46.6)	621 (68.1)	724 (63.9)	<.001 ^a
Erythropoietin use, N (%)	24 (10.9)	264 (28.9)	288 (25.4)	<.001 ^a
Iron chelation therapy use, N (%)	3 (1.4)	7 (0.8)	10 (0.9)	.4
Neutropenia diagnosis, N (%)	53 (24.0)	156 (17.1)	209 (18.4)	.018 ^a
Decreased white blood cell count diagnosis, N (%)	30 (13.6)	59 (6.5)	89 (7.9)	<.001 ^a
Use of granulocyte colony-stimulating factor, N (%)	19 (8.6)	59 (6.5)	78 (6.9)	.262
Potential complications of neutropenia, N (%)	16 (7.2)	129 (14.1)	145 (12.8)	.006 ^a
Pneumonia diagnosis, N (%)	12 (5.4)	113 (12.4)	125 (11.0)	.003 ^a
Unspecified fever diagnosis, N (%)	6 (2.7)	31 (3.4)	37 (3.3)	.608
Use of outpatient pharmacy intravenous antibiotics, N (%)	1 (0.5)	3 (0.3)	4 (0.4)	.781
Thrombocytopenia diagnosis, N (%)	56 (25.3)	203 (22.3)	259 (22.9)	.328
Pancytopenia diagnosis, N (%)	29 (13.1)	115 (12.6)	144 (12.7)	.837
Mean MDS-related charges, \$ ^b (SD; median)	35,888 (139,081; 2626)	25,435 (81,866; 4717)	27,474 (95,761; 4485)	.284

^aP <.05.
^bMDS-related costs include charges on medical claims with a primary diagnosis of conditions listed in this table and charges on pharmacy claims for medications listed in this table.
 AML indicates acute myeloid leukemia; MDS, myelodysplastic syndrome; SD, standard deviation.

\$32,782) for older patients. Although the mean postindex total healthcare charges and medical charges were higher in the younger group than in the older group, the medians of these charges were higher in the older group.

Discussion

Based on an analysis of a commercial claims database, our study indicates that MDS is associated with frequent and prolonged hospitalizations, frequent outpatient visits, and high charges in younger and in older patients who

are receiving supportive care. Although MDS is often referred to as a “disease of the elderly,”^{9,10} this study shows that a substantial percentage of patients with MDS are not elderly, with up to 20% of patients aged <50 years.

The greater representation of younger patients in our study allowed us to examine and demonstrate that younger patients may have higher healthcare utilization and higher costs on average. Although this study was not designed to examine the underuse of diagnostic tests or of treatments, we found evidence of low use of bone

Table 4 Overall Healthcare Utilization and Total Charges in the 1-Year Postindex Period in Patients Receiving Supportive Care

	Patients aged <50 yrs (N = 221)	Patients aged ≥50 yrs (N = 912)	Total (N = 1133)	P value
Mean physician office visits (SD; median)	17.5 (16.9; 12)	24.2 (16.3; 21)	22.9 (16.6; 20)	<.001 ^a
Hospitalizations, N (%)				.004 ^a
0	150 (67.9)	505 (55.4)	655 (57.8)	
1	37 (16.7)	188 (20.6)	225 (19.9)	
2	12 (5.4)	104 (11.4)	116 (10.2)	
3+	22 (10.0)	115 (12.6)	137 (12.1)	
Length of stay among patients with hospitalizations, days (mean; SD)	71 (21; 37.3)	407 (14; 21.9)	478 (15; 24.9)	.131
Emergency department visits, N (%)				.74
0	202 (91.4)	835 (91.6)	1037 (91.5)	
1	11 (5.0)	37 (4.1)	48 (4.2)	
2+	8 (3.6)	40 (4.4)	48 (4.2)	
Mean total healthcare charges, \$ (SD; median)	96,277 (240,854; 21,287)	84,102 (149,877; 39,402)	86,477 (171,391; 34,690)	.473
Mean medical charges, \$ (SD; median)	91,435 (237,723; 18,526)	78,612 (146,631; 32,782)	81,113 (168,261; 29,912)	.443
Mean pharmacy charges, \$ (SD; median)	4841 (8407; 1314)	5490 (8573; 3048)	5363 (8541; 2749)	.311

^aP <.05.
SD indicates standard deviation.

marrow biopsy (Table 2) and potential undertreatment with hypomethylating agents or with thalidomide analogues (Figure).

We estimated that almost 20% of patients in this commercial plan population were aged <50 years, which is almost twice the previously reported prevalence of MDS in that age-group.^{11,12} In a recent study, Cogle and colleagues demonstrated that cancer registries may have a high number of uncaptured cases of MDS, possibly because of misdiagnoses and/or underreporting of the disease, and that the annual incidence of MDS may be as high as 75 per 100,000 persons aged ≥65 years.⁷ Hence, our findings indicate that the incidence of MDS in the younger age-group (ie, <50 years) may be higher than expected, which highlights the importance of continuing to examine the impact of MDS in this age-group.

One possible reason for underreporting of MDS is the low use of diagnostic tests. Our study indicates that cases

of MDS may be insufficiently diagnosed, because only approximately half (46.4%) of patients newly diagnosed with MDS who are receiving supportive care have a claim for a bone marrow biopsy (Table 2), an estimate that could be considered low, given that the NCCN guidelines recommend using this procedure.³ In addition, our results show that physicians may not follow other aspects of treatment guidelines, which is evidenced by the relatively low use of thalidomide analogues and hypomethylating agents in our study sample (Figure).

Although the NCCN guidelines support the treatment of MDS with thalidomide analogues and hypomethylating agents,³ most newly diagnosed MDS patients in our study received supportive care only (1133 of 1209 total patients = 93.7%). Only 76 (6.2%) of newly diagnosed MDS patients in our study received treatment with decitabine, 5-azacytidine, or lenalidomide in the postindex period. We also found only 12 (1.1%) patients who were receiving allogeneic stem-cell

transplant treatment in our study (ICD-9-CM codes 41.05 and 41.08; results not shown).

These findings support the results previously reported by Van Bennekom and colleagues on the patterns of treatment among patients with recently diagnosed MDS in a national, disease-based, observational registry between 2006 and 2008.¹⁶ Van Bennekom and colleagues reported that only 24% of patients who were recently diagnosed with MDS had received disease-modifying treatments since diagnosis, including 5-azacytidine (9%), decitabine (7%), lenalidomide (6%), or multiple agents (2%), compared with 58% of patients who received supportive therapy.¹⁶ Consistent with previous studies,^{16,17} our results emphasize that most newly diagnosed commercially insured patients with MDS in the United States receive supportive therapy after their initial diagnosis, whereas relatively few receive other therapies. More appropriate treatment for MDS may therefore reduce the burden associated with this condition, such as progression to transfusion dependence that often occurs with supportive care.¹⁸

Despite receiving supportive care only, the average total annual healthcare charges for patients in our study were high (>\$86,000), with higher mean costs for younger patients (\$96,277 vs \$84,102; $P = .473$). There was no evidence that the higher total healthcare costs in younger patients were associated with age-related differences in baseline comorbidity; the mean Charlson comorbidity index was 1.2 in patients aged <50 years compared with 2.4 in patients aged ≥ 50 years ($P < .001$). Similarly, this postindex difference in the charges between the 2 age-groups was not associated with baseline mean total healthcare charges (\$30,177 in the group aged <50 years vs \$31,832 in the group aged ≥ 50 years; $P = .693$) or with healthcare utilization, because both were numerically higher in the group of older patients.

Similarly, the higher total annual healthcare charges in the younger patient cohort are likely not to be primarily driven by differences in MDS-related diagnoses and healthcare utilization, because anemia was more common in the older patients (aged ≥ 50 years) than in the younger patients (aged <50 years), as were erythropoietin use, blood transfusions, complications of neutropenia, and diagnoses of pneumonia (all significant differences), whereas diagnoses of neutropenia and decreased white blood cell count were more common in the younger patients than in the older patients.

MDS-related costs made up approximately 32% of total healthcare charges, with numerically higher mean costs in the younger age-group. This study included only claims with specific primary diagnoses as MDS-related charges; a more expansive definition would likely have resulted in a greater proportion of costs being related to MDS.

Our study shows that although the mean healthcare costs are greater in the younger age-group, the median MDS-related and the total healthcare costs show an opposite trend, with median healthcare costs being lower in younger patients than in older patients. That is, 50% of younger patients have total healthcare costs of $\geq \$21,287$ (and medical costs of $\geq \$18,526$), and 50% of the older patients have costs of $\geq \$39,402$ (and medical costs of $\geq \$32,782$).

One explanation for this finding may be the skewness of the total healthcare costs distribution. These results indicate that the distribution of healthcare costs in the 2 cohorts are skewed toward lower charges, especially in the younger age-group, with a few patients in this group accumulating the highest costs. Neutropenia, a complication strongly associated with increased hospitalization,¹⁹ was significantly more prevalent in patients aged <50 years (24%) than in patients aged ≥ 50 years (17.1%; $P = .018$).

It may be that the younger patients are using more expensive services than older patients, given the longer mean length of stay among younger hospitalized patients (21 days) compared with older patients (14 days; $P = .131$). Hence, a small group of very expensive younger patients may be considerably increasing the mean MDS-related costs and therefore the total healthcare costs.

Supportive care of MDS typically includes red blood cell transfusions, a treatment that most patients with MDS become dependent on given the noncurative nature of the disease.^{9,18,20,21} Studies have shown that transfusion dependence not only negatively affects morbidity and mortality, but also significantly increases costs in patients with MDS compared with patients with transfusion independence.^{18,21} For instance, Frytak and colleagues compared the economic burden of patients with MDS who are aged ≥ 55 years and with either transfusion independence or dependence, and found that the MDS transfusion-dependent cohort had significantly higher mean annual costs (pharmacy, \$4457 vs \$2926; medical, \$50,663 vs \$17,469; total, \$51,066 vs \$19,811 per patient annually).²¹ Studies have shown that transfusion requirements may be greater in elderly patients than in younger patients.^{20,21} Although Frytak and colleagues examined only patients aged ≥ 55 years, the MDS transfusion-dependent patients were significantly older than the MDS transfusion-independent patients.²¹

We found that a significantly smaller proportion of younger patients than older ones had ≥ 1 transfusions, and this difference may have contributed to the lower median healthcare charges in the younger patients. The younger cohort in our study also had a higher proportion of females, a population that, in general, may have less transfusion dependence²¹; this sex differential in our

study cohorts may be another factor associated with the lower median healthcare charges in the younger group.

Limitations

The use of insurance claims data for research presents unique challenges.²² Healthcare claims are collected for billing purposes, and they lack detail on measures of disease severity, such as the International Prognostic Scoring System, which is designed for evaluating prognosis in MDS.^{3,23}

In addition, our study included patients with commercial insurance, so patients with Medicare were underrepresented. Therefore, we could not further stratify the age-group of those ≥ 50 years in our study to perform additional age-group comparisons. Our results may therefore not be representative of the general MDS population, because different populations may have various outcomes.

We were also unable to examine other subgroups, because of the small sample sizes (eg, patients receiving allogeneic stem-cell transplant, and those receiving pharmacologic therapy with hypomethylating agents or with thalidomide analogues). In our previous study of 1209 patients newly diagnosed with MDS—a sample that included all treatment groups—we found that mean total healthcare costs were \$100,809 (SD, \$188,311; median, \$40,975), only \$14,332 greater than the total healthcare costs reported in the current study of supportive care patients (\$86,477; Table 4).²⁴

We also did not examine whether the newly diagnosed patients with MDS in our study could have had AML before MDS in the postindex period, or whether some patients had other clonal or nonclonal diagnoses that are common in a hematologic practice, such as autoimmune disease or toxic injury to the marrow.

Furthermore, because of our study's relatively short follow-up period, we were unable to establish causal relationships. A small sample size could have limited our detection of significant differences (eg, differences in healthcare charges by age).

Other limitations that are particular to claims data analyses could have impacted the utilization and the cost results in this study. We were unable to estimate inpatient antibiotic use, because inpatient claims data only contain diagnoses and procedure codes and not information on medication use. Although we reviewed all inpatient and outpatient claims to identify transfusions, inpatient claims in the i3/Ingenix LabRx database include a maximum of 3 procedure codes; thus, inpatient transfusions may have been missed.

Similarly, we examined healthcare charges in the newly diagnosed MDS population, and therefore our results may differ from other studies that examined costs or paid amounts for claims associated with MDS. Additional suf-

ficiently powered longitudinal studies that account for severity of disease, that are conducted in various MDS populations, and that use various data sources are warranted.

Conclusions

Our study indicates that MDS is associated with frequent and prolonged hospitalizations, frequent outpatient visits, and high healthcare charges in both younger and older patients receiving supportive care. Although MDS is considered a disease of the elderly, the results of this study suggest that a small proportion of patients aged < 50 years may have this disease and may have a much higher healthcare utilization and cost-related burden of MDS than patients aged ≥ 50 years, possibly because of the longer length of stay among hospitalized younger patients. This study highlights the importance of conducting further studies to better elucidate the characteristics of patients with early-onset MDS. ■

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Author Disclosure Statement

Dr Powers and Dr Faria are employees of Eisai, and Dr Broder, Dr Chang, and Dr Cherepanov are employees of Partnership for Health Analytic Research.

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STAKEHOLDER PERSPECTIVE

Reconsidering the Management of Younger Patients with Myelodysplastic Syndrome

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PAYERS: Myelodysplastic syndrome (MDS) encompasses a heterogeneous group of myeloid disorders that increase the risk for progression to acute myelogenous leukemia (AML), which is associated with significant morbidity and mortality. MDS is more prevalent in older than in younger persons and in those who had been exposed to chemotherapy. Therapy is based on patient risks, needs for transfusion, and bone marrow biopsies; increasingly, genetic profiling has been used to assess risk. The goals of therapy vary with the risk profile. Reductions in transfusions and slowing the progression to high-risk disease or to AML are the goals in low-risk patients. Prolonging survival is the goal in high-risk patients. Treatments include growth factors, aggressive chemotherapy, stem-cell transplantation, lenalidomide, and the hypomethylating agents.¹ Research has shown that patients respond to specific treatments based on their risk profile with lenalidomide, demonstrating effectiveness in patients with lower-risk disease, anemia, and genetic alterations, as well as in high-risk patients who respond to 5-azacitidine and to decitabine. Supportive care with iron chelation therapy and prophylactic antibiotics is extensively used.¹

The small patient population, multiple treatment options, and recent research demonstrating different effectiveness of treatments for MDS based on risk warrant database analyses such as described in the present article by Powers and colleagues to help payers better understand the complications, healthcare utilization, and costs of treatment in their members with MDS. This study generates insights on the younger, lower-risk patient population, providing evidence to suggest opportunities to

improve compliance with the National Comprehensive Cancer Network (NCCN) guidelines for MDS² and advancements in MDS treatment based on latest research that indicate a need for more than supportive care in low-risk patients.

PATIENTS: This article highlights the important differences in disease complications and risk-based treatments for MDS and the goals of reducing transfusion dependence and progression to AML in younger, lower-risk patients. The data suggest potential underuse of bone marrow biopsies in the diagnosis of MDS, as well as underuse of lenalidomide and hypomethylating agents in low-risk patients as described in the NCCN guidelines² in favor of supportive care only.

PROVIDERS: The approach to treatment of MDS has changed over the years, focusing on therapy based on patient risk for disease progression and the use of genetics for the diagnosis. Diagnostic bone marrow biopsies are critical for treatment decisions, yet data presented by Powers and colleagues suggest suboptimal use. This analysis reflects the potential overuse of supportive care only in younger patients, overlooking the NCCN's recommendations for lenalidomide and hypomethylating agents for MDS management²; however, because the database used in this research lacks the detailed laboratory tests routinely used in clinical practice to make treatment-based decisions, further study is warranted to arrive at firm conclusions.

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