ORIGINAL RESEARCH

The Cost of Hematopoietic Stem-Cell Transplantation in the United States

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BACKGROUND: Hematopoietic stem-cell transplantation (HSCT) requires highly specialized, resource-intensive care. Myeloablative conditioning regimens used before HSCT generally require inpatient stays and are more intensive than other preparative regimens, and may therefore be more costly.

OBJECTIVE: To estimate the costs associated with inpatient HSCT according to the type of the conditioning regimen used and other potential contributors to the overall cost of the procedure.

METHOD: We used data from the Truven Health MarketScan insurance claims database to analyze healthcare costs for pediatric (age <18 years) and adult (age ≥18 years) patients who had autologous or allogeneic inpatient HSCT between January 1, 2010, and September 23, 2013. We developed an algorithm to determine whether conditioning regimens were myeloablative or nonmyeloablative/reduced intensity.

RESULTS: We identified a sample of 1562 patients who had inpatient HSCT during the study period for whom the transplant type and the conditioning regimen were determinable: 398 patients had myeloablative allogeneic HSCT; 195 patients had nonmyeloablative/reduced-intensity allogeneic HSCT; and 969 patients had myeloablative autologous HSCT. The median total healthcare cost at 100 days was $289,283 for the myeloablative allogeneic regimen cohort compared with $253,467 for the nonmyeloablative/reduced-intensity allogeneic regimen cohort, and $140,792 for the myeloablative autologous regimen cohort. The mean hospital length of stay for the index (first claim of) HSCT was 35.6 days in the myeloablative allogeneic regimen cohort, 26.6 days in the nonmyeloablative/reduced-intensity allogeneic cohort, and 21.8 days in the myeloablative autologous regimen cohort.

CONCLUSION: Allogeneic HSCT was more expensive than autologous HSCT, regardless of the regimen used. Myeloablative conditioning regimens led to higher overall costs than nonmyeloablative/reduced-intensity regimens in the allogeneic HSCT cohort, indicating a greater cost burden associated with inpatient services for higher-intensity preparative conditioning regimens. Pediatric patients had higher costs than adult patients. Future research should involve validating the algorithm for identifying conditioning regimens using clinical data.

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KEY WORDS: allogeneic HSCT, autologous HSCT, healthcare costs, hospitalization, inpatient, myeloablative conditioning regimen, nonmyeloablative/reduced-intensity conditioning regimen

Cancer is costly. As new cancer therapies become available that extend survival, and as the US population ages and continues to grow, the cost of cancer care is estimated to reach almost $158 billion in 2020, according to the National Cancer Institute.[1] The costs of cancer care vary considerably by cancer type and stage of treatment. In the year after a cancer diagnosis, treatment costs can exceed $110,000 for cancers of the brain or pancreas, for example, whereas end-of-life costs are much higher for all cancers, approaching $200,000 in the last year of life for patients with leukemia or with brain cancer.[1]

The growing cost burden of cancer care to our healthcare system compels society to seek value in cancer treatments by maximizing cost benefits, and by finding ways to reduce costs. By exploring several significant drivers of cost, we want to identify ways in which to optimize these costs, particularly for addressable factors, such as long hospital stays that lack a clinical basis. Using the example of hematopoietic

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KEY POINTS

- Hematopoietic stem-cell transplantation (HSCT) is costly, and its use is steadily rising in the treatment of cancer.
- This retrospective study of claims data compared the costs of inpatient autologous or allogeneic HSCT, based on the use of a myeloablative or a nonmyeloablative/reduced-intensity conditioning regimen.
- The median total healthcare cost at 100 days was twice as high with a myeloablative regimen before allogeneic HSCT ($289,283) than before autologous HSCT ($140,792).
- The algorithm developed for this study showed that transplant type, conditioning regimen, and patient age affect the cost of HSCT.
- Overall, allogeneic HSCT was more expensive than autologous HSCT based on this algorithm.
- Myeloablative conditioning is costlier than nonmyeloablative/higher-intensity conditioning in patients with allogeneic transplant, likely because of added complications.
- Future research is needed to validate the algorithm for identifying conditioning regimens used with HSCT based on clinical data.

stem-cell transplantation (HSCT), a lifesaving, increasingly common, and expensive procedure for hematologic or bone marrow disorders, we evaluated the total cost of care and specific cost drivers for patients undergoing HSCT.

Stem-cell transplantation in the United States has risen steadily for more than 2 decades, with 340,000 cumulative HSCTs having been performed by 2014; the annual number of HSCTs performed in 2014 surpassed 8000 allogeneic and 10,000 autologous transplants.[2] The hospital costs associated with HSCT have also grown by approximately 85% to nearly $1.3 billion between 2004 and 2007, making it one of the hospital procedures with the largest increase over that period.[3]

Several previous studies have analyzed the costs of HSCT (which range from approximately $87,000 to $300,000), but few have examined the conditioning regimen as a determinant of the cost, and none used a population sample derived from all geographic regions of the United States.[4-11] For this study, we used health insurance claims covering 50 million individuals in the United States[12] to investigate potential drivers of HSCT costs in the oncology setting, including conditioning regimens, transplant type, and patient age.

Methods

In this retrospective cohort study design we used commercial insurance data from the Truven Health MarketScan claims database to analyze the 100-day and 1-year costs for patients who received inpatient autologous or allogeneic HSCT between January 1, 2010, and September 23, 2013 (ie, the identification period), and stratified patients by the type of the conditioning regimen and age-group, including pediatric (age <18 years) and adult (age ≥18 years) patients.

Patients were required to have at least 1 claim with an appropriate *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) procedure code indicating the HSCT type. Allogeneic and autologous transplants were distinguished using *ICD-9-CM* and *Current Procedural Terminology* (*CPT*) 4 codes (see **Appendix Table 1** at **www.AHDBonline.com**). The MarketScan database of employer-sponsored health plans in the United States contained information on enrollment and demographics, in addition to the data reported on administrative claims, including inpatient and outpatient services and costs, diagnoses and procedures (*CPT* and *ICD-9-CM* procedure codes), and outpatient pharmacy medication dispensing information (eg, days of drug supply, fill dates, and National Drug Codes).

The study population comprised patients who underwent allogeneic or autologous HSCT and received myeloablative or nonmyeloablative/reduced-intensity conditioning regimens before transplantation. The first date of an HSCT claim (eg, with one of the codes listed in Appendix Table 1) during the identification period was defined as the index date. To qualify for study inclusion, patients were required to be continuously enrolled in a health plan for 1 year before the index date (ie, the baseline period) and for 100 days after this date. This 1-year baseline period was used to ensure that the inpatient HSCT was the first such transplant.

Allogeneic and autologous HSCT are billed using different *ICD-9-CM* codes, making it straightforward to distinguish between them. Distinguishing between different conditioning regimens is far more complicated, because the regimen types do not have their own codes and are billed by the individual chemotherapy or radiation components used. Furthermore, although chemotherapeutic agents administered in the outpatient setting are generally identifiable in claims, inpatient claims do not provide sufficient detail to distinguish one agent from another.

Finally, although differing doses of radiation are an important determinant of whether a conditioning regimen is myeloablative, radiation dosing is not easily determined in claims. Therefore, we relied on published literature and expert clinician input to develop an algo-

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rithm that distinguished myeloablative from nonmyeloablative/reduced-intensity conditioning regimens.[13,14] The expert clinical input came from a variety of sources, including experienced hematologist/oncologists who treat adults and children, coding specialists at the American Society for Radiation Oncology, and the Center for International Blood and Marrow Transplant Research. The algorithm included data on the underlying malignancy, type of treatment (ie, chemotherapy type, radiation, and total body irradiation procedures), location of service, and therapy timing (see **Appendix Table 2** at **www.AHDBonline.com**) to identify a subset of patients for whom we determined we could reliably define their conditioning regimen type.

We made several assumptions about capturing the costs of HSCT through claims data. First, we assumed that all HSCT-related care occurring in the oncology setting could be observed through claims. Second, we assumed that all conditioning regimen–related costs could be captured, which we believe was reasonable for outpatient regimen procedures, because outpatient claims provide sufficient detail about such services. However, any inpatient conditioning regimen costs were not isolated, because inpatient claims lack specific regimen information. Finally, based on expert clinical input, we used a 10-day look-back period from the date of the HSCT to fully capture any billing associated with the conditioning regimen, which is typically given 6 to 8 days before HSCT, but also to avoid including unrelated costs associated with earlier care.

We computed healthcare costs, our primary outcome, using the fee-for-service equivalent or amount paid field in the claims. The costs were calculated for the HSCT hospital admission and for services in the 10 days before transplantation; the latter was done to account for expenses related to the conditioning regimens administered before HSCT. We estimated the mean and median costs for total, inpatient (all services, including intensive care unit care), outpatient, and pharmacy services at 100 days and at 1 year (all calculated by summing the costs, regardless of diagnosis on the claims). The 100-day and 1-year costs included relevant services in the 10 days before transplantation.

Outpatient HSCT did not qualify patients for inclusion in the study; however, a small fraction (0.8%) of patients had outpatient HSCT before their qualifying inpatient HSCT. These outpatient costs had a negligible effect on the overall HSCT cost estimates. Hospitalization was measured by the mean length of stay (LOS) during the index HSCT admission (by definition, a single hospital stay). In addition, we examined subsequent hospitalization at 100 days and at 1 year of follow-up, which was defined by the proportion of patients hospitalized after HSCT and by mean LOS across all subsequent hospitalizations.

Patients were divided into 3 groups, based on the conditioning regimen and the type of transplant: (1) patients receiving a myeloablative regimen before an allogeneic transplant (henceforth labeled "allogeneic MA"); (2) patients receiving a nonmyeloablative/reduced-intensity regimen before an allogeneic transplant ("allogeneic NMA"); and (3) those receiving a myeloablative regimen before an autologous transplant ("autologous MA"). We did not include patients (N = 2) who received a nonmyeloablative/reduced-intensity regimen and underwent an autologous transplant because of their infrequency.

To compare the study groups, we measured several baseline variables available in the claims data, including age, sex, and geographic region. We also considered the cancer diagnosis(es) reported at the index HSCT hospitalization, which was based on the presence of *ICD-9-CM* codes in any diagnosis field for acute myeloid leukemia (*ICD-9-CM*: 205.0x, 205.3x, 206.0x, 207.0x, 207.2x), acute lymphocytic leukemia (*ICD-9-CM*: 204.0x), chronic myeloid leukemia (*ICD-9-CM*: 205.10), myelodysplastic syndrome (*ICD-9-CM*: 238.72, 238.73, 238.75), lymphoma (*ICD-9-CM*: 196.xx, 200.xx, 201.xx, 202.xx), multiple myeloma and plasma-cell neoplasms (*ICD-9-CM*: 203.xx, 277.3x), chronic lymphocytic leukemia (*ICD-9-CM*: 204.1x), aplastic anemia (*ICD-9-CM*: 284.xx), and sarcoma (*ICD-9-CM*: 171.xx).

All analyses were stratified according to transplant type, conditioning regimen, and age-group. Descriptive statistics, including means, medians, standard deviations, and percentages, were reported for all study measures as appropriate. The costs were updated to 2013 US dollars using the healthcare component of the Consumer Price Index.[15] All data transformations and analyses were performed using SAS version 9.4 (SAS Institute, Inc; Cary, NC).

Results

We identified 6671 patients who had an HSCT during the identification period, 4474 of whom were continuously enrolled in a health plan during the 1 year before and 100 days after the index date. From this population, we derived our final study cohort of 1562 patients who had inpatient HSCT and for whom the transplant type and the conditioning regimen were determinable and were divided into the 3 cohorts—allogeneic MA cohort (N = 398); allogeneic NMA cohort (N = 195); and autologous MA cohort (N = 969).

Figure 1 (see **AHDBonline.com**) describes the patient identification process for the study. **Table 1** outlines the patients' baseline characteristics. The majority (87.5%) of patients had myeloablative conditioning. Our

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sample included 61% males, and 92.9% of the patients were aged ≥18 years (mean age, 48.6 years; standard deviation, 16.4 years). Overall, the most common malignancy diagnoses reported during admission for HSCT were lymphoma (62.5%), aplastic anemia (46.3%), acute lymphocytic leukemia (21.5%), and acute myeloid leukemia (11.2%; not mutually exclusive; Table 1).

100-Day Costs and Hospitalization

The descriptive findings on the first 100 days after transplantation are presented in **Table 2**. The median total healthcare cost was $289,283 for patients in the allogeneic MA cohort versus $253,467 for the allogeneic NMA cohort and $140,792 for the autologous MA cohort. The median inpatient cost, which made up the largest share of the total costs, was $239,959 for the allogeneic MA cohort compared with $182,256 for the allogeneic NMA cohort and $113,272 for the autologous MA cohort.

The cost of HSCT hospitalization made up 73% to 76% of the 100-day costs for those receiving a myeloablative conditioning regimen and 66% for patients receiving a nonmyeloablative/reduced-intensity conditioning regimen (**Figure 2**). The highest median costs for HSCT hospitalization were for the allogeneic MA cohort, at $208,857, followed by $161,241 and $110,209 for the allogeneic NMA and autologous MA cohorts, respectively.

The median outpatient costs and pharmacy costs were similar between the allogeneic NMA cohort ($41,349 and $6551, respectively) and the allogeneic MA cohort ($40,655 and $6451); these costs were higher than the costs for the autologous MA cohort ($18,400 and $673; Table 2). The mean LOS for the index HSCT hospitalization was 35.6 days for the allogeneic MA cohort, 26.6 days for the allogeneic NMA cohort, and 21.8 days for the autologous MA cohort. Subsequent hospitalization occurred for 42.5% of the allogeneic MA cohort, with a mean LOS of 9 days, compared with 43.6% for the allogeneic NMA cohort, with a mean LOS of 11 days, and 20.8% for the autologous MA cohort, with a mean LOS of 6.5 days (Table 2).

Table 1 Characteristics of Patients with Allogeneic and Autologous Transplants, by Conditioning Regimen

Characteristic	Allogeneic transplant		Autologous transplant	
	Myeloablative regimen (N = 398)	Nonmyeloablative/ reduced-intensity regimen (N = 195)	Myeloablative regimen (N = 969)	Total (N = 1562)[a]
Age, yrs, mean (SD)	37.5 (18.4)	54.8 (11.6)	51.9 (14.0)	48.6 (16.4)
<18 yrs, N (%)	80 (20.1)	4 (2.1)	27 (2.8)	111 (7.1)
18-40 yrs, N (%)	125 (31.4)	12 (6.2)	150 (15.5)	287 (18.4)
41-60 yrs, N (%)	157 (39.4)	116 (59.5)	513 (52.9)	786 (50.3)
≥61 yrs, N (%)	36 (9.0)	63 (32.3)	279 (28.8)	378 (24.2)
Female, N (%)	166 (41.7)	82 (42.1)	361 (37.3)	609 (39.0)
Male, N (%)	232 (58.3)	113 (58.0)	608 (62.8)	953 (61.0)
Region, N (%)				
Midwest	84 (21.1)	58 (29.7)	285 (29.4)	427 (27.3)
Northeast	102 (25.6)	56 (28.7)	195 (20.1)	353 (22.6)
South	129 (32.4)	54 (27.7)	313 (32.3)	496 (31.8)
West	83 (20.9)	27 (13.8)	176 (18.2)	286 (18.3)
Diagnosis of cancer type at index HSCT, N (%)[b]	398 (100.0)	192 (98.5)	968 (99.9)	1558 (99.7)
Acute myeloid leukemia	114 (28.6)	54 (27.7)	7 (0.7)	175 (11.2)
Acute lymphocytic leukemia	312 (78.4)	18 (9.2)	6 (0.6)	336 (21.5)
Chronic myeloid leukemia	12 (3.0)	8 (4.1)	0 (0.0)	20 (1.3)
Myelodysplastic syndrome	21 (5.3)	23 (11.8)	2 (0.2)	46 (2.9)
Lymphoma	47 (11.8)	38 (19.5)	891 (92.0)	976 (62.5)
Multiple myeloma and plasma-cell neoplasms	8 (2.0)	4 (2.1)	99 (10.2)	111 (7.1)
Chronic lymphocytic leukemia	7 (1.8)	96 (49.2)	9 (0.9)	112 (7.2)
Aplastic anemia	184 (46.2)	87 (44.6)	452 (46.6)	723 (46.3)
Sarcoma	0 (0.0)	0 (0.0)	2 (0.2)	2 (0.1)

[a]Patients (N = 2) who received autologous nonmyeloablative/reduced-intensity HSCT were not included in the study because of the low frequency.

[b]Including 4 patients who underwent transplant but did not have evidence of a selected malignancy at the index HSCT.

HSCT indicates hematopoietic stem-cell transplantation; SD, standard deviation.

1-Year Costs and Hospitalization

The 100-day costs were more than 66% of the total median costs at 1 year, which were $408,876, $374,065, and $181,933 for the allogeneic MA, allogeneic NMA, and autologous MA groups, respectively (Table 2). The median inpatient costs at 1 year were $276,620 for the allogeneic MA cohort compared with $235,620 for the allogeneic NMA cohort and $121,277 for the autologous MA cohort (Table 2).

The 1-year median outpatient and pharmacy costs were similar among the allogeneic NMA cohort ($83,435 and $15,487, respectively) and the allogeneic MA cohort ($81,575 and $14,429), but these were higher than the costs for the autologous MA cohort ($42,294 and $2043).

Subsequent hospitalization at 1 year occurred at a similar rate for the allogeneic transplant groups (allogeneic MA, 67.3% with a mean LOS of 26.6 days vs allogeneic NMA, 69.2% with 30.3 days) but occurred less frequently for the autologous MA cohort (37.9% with 18 days; Table 2).

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Table 2 Healthcare Costs and Hospitalization at 100-Day and 1-Year Follow-Up for Patients Receiving Myeloablative or Nonmyeloablative/Reduced-Intensity Conditioning Regimen

Cost parameter		100-day follow-up: Allogeneic transplant: Myeloablative regimen (N = 398)	100-day follow-up: Allogeneic transplant: Nonmyeloablative/reduced-intensity regimen (N = 195)	100-day follow-up: Autologous transplant: Myeloablative regimen (N = 969)	1-year follow-up: Allogeneic transplant: Myeloablative regimen (N = 398)	1-year follow-up: Allogeneic transplant: Nonmyeloablative/reduced-intensity regimen (N = 195)	1-year follow-up: Autologous transplant: Myeloablative regimen (N = 969)
Total healthcare costs, $[a]	Mean	401,566	300,871	164,049	549,208	432,157	231,259
	SD	397,479	238,034	137,214	508,350	297,707	191,665
	Median	289,283	253,467	140,792	408,876	374,065	181,933
Inpatient costs, $[a]	Mean	343,352	231,463	134,268	422,973	295,749	160,581
	SD	396,217	238,505	129,394	480,513	272,290	163,290
	Median	239,959	182,256	113,272	276,620	235,620	121,277
Outpatient costs, $[a]	Mean	50,235	60,805	27,698	104,923	117,248	63,081
	SD	42,093	59,245	28,331	93,951	104,741	68,919
	Median	40,655	41,349	18,400	81,575	83,435	42,294
Pharmacy costs, $[a]	Mean	7979	8603	2083	21,312	19,159	7597
	SD	7217	7629	3847	21,124	16,814	15,462
	Median	6451	6551	673	14,429	15,487	2043
Costs of index HSCT hospitalization, $[b]	Mean	306,959	198,676	119,678	N/A	N/A	N/A
	SD	366,665	223,887	68,462	N/A	N/A	N/A
	Median	208,857	161,241	110,209	N/A	N/A	N/A
Length of stay for HSCT admission, days	Mean (SD)	35.6 (26.4)	26.6 (22.1)	21.8 (12.8)	N/A	N/A	N/A
Any subsequent hospitalization[c]	N (%)	169 (42.5)	85 (43.6)	202 (20.8)	268 (67.3)	135 (69.2)	367 (37.9)
Total length of stay, days[d]	Mean (SD)	9.0 (15.0)	11.0 (16.8)	6.5 (12.8)	26.6 (32.5)	30.3 (31.9)	18.0 (21.4)

[a]All costs include the claims from 10 days before through 100 days (or 1 year) after the transplant.

[b]Represents the costs of index transplant, including conditioning regimen; inpatient transplants include the costs from 10 days before admission through discharge from index admission; outpatient transplants includes the costs from 10 days before day of first outpatient *ICD-9* diagnosis code for HSCT.

[c]Within 100 days (or 1 year) of follow-up.

[d]Among patients with hospitalization subsequent to the HSCT admission and within 100 days (or 1 year) of follow-up. Total represents hospital days across all admissions subsequent to HSCT admission.

HSCT indicates hematopoietic stem-cell transplantation; *ICD-9, International Classification of Diseases, Ninth Revision*; N/A, not applicable; SD, standard deviation.

Pediatric Patients versus Adults

Table 3 shows the cost and hospitalization results according to age. The costs for the index HSCT hospitalization and for 100-day inpatient and outpatient healthcare services were greater for pediatric patients than for adult patients for the 2 transplant types. The median costs of the index HSCT hospitalization for myeloablative allogeneic and autologous transplants (we had insufficient numbers of pediatric patients receiving a nonmyeloablative/reduced-intensity regimen before transplant for comparison) were $363,379 and $154,266, respectively, in pediatric patients versus $191,541 and $109,113, respectively, in adults. The median inpatient costs for myeloablative allogeneic and autologous transplants were $406,195 and $194,125, respectively, for pediatric patients versus $212,332 and $111,419, respectively, for adults.

The median outpatient costs for myeloablative allogeneic and autologous transplants were $43,814 and $44,929, respectively, for pediatric patients versus $40,424 and $17,893, respectively, for adults. However, the median 100-day pharmacy costs were higher for adults than for pediatric patients in the allogeneic transplant groups, but not in the autologous groups. The median pharmacy costs for myeloablative allogeneic and autologous transplants were $2865 and $916, respectively, for pediatric patients versus $7174 and $662, respectively, for adults (Table 3).

The mean LOS for the index HSCT hospitalization was higher for pediatric patients than for adults in the allogeneic MA and autologous MA cohorts—54.1 days and 25.6 days for pediatric patients versus 30.9 and 21.6 days for adults. Subsequent hospitalization and LOS were not substantially different across the pediatric and adult allogeneic MA and autologous MA groups—38.8% (mean LOS, 7.1 days) and 40.7% (mean LOS, 10.4 days)

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versus 43.4% (mean LOS, 9.4 days) and 20.3% (mean LOS, 6.3 days; Table 3).

Discussion

This real-world study of administrative claims data provides evidence that in a selected sample of transplant recipients, conditioning regimens given before HSCT, transplant type, and age are all important determinants of the associated costs. In the sample of predominantly adults undergoing inpatient HSCT between 2010 and 2013, the highest overall 100-day and 1-year costs were for patients in the allogeneic MA cohort, followed by the allogeneic NMA and autologous MA cohorts. The majority of healthcare spending associated with HSCT occurred in the first 100 days, mainly as a result of the inpatient costs associated with the index HSCT hospitalization and the subsequent hospitalization. After 100 days, the inpatient costs declined, whereas the outpatient and pharmacy costs grew as a proportion of the total cost.

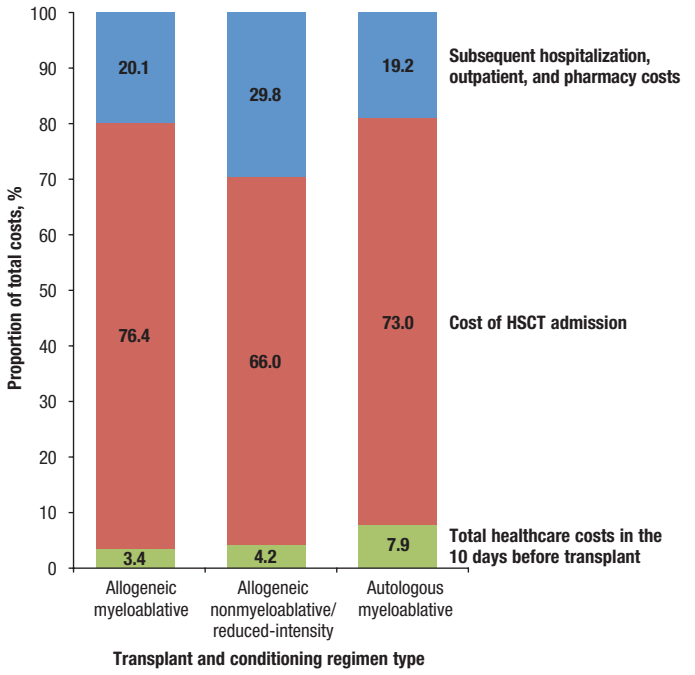
This study included a selected group of patients. Data limitations, in particular the lack of detailed information on inpatient chemotherapy regimens and total body irradiation, made it impossible to identify the conditioning regimens for a representative sample of patients undergoing transplant.[2] Therefore, we developed an algorithm that could identify the conditioning regimen in a select group of patients. Despite the use of this nonrepresentative sample, our findings are consistent with previous studies.[4,16,17]

For example, in our sample, allogeneic HSCT was nearly twice as costly as autologous HSCT for total, inpatient, outpatient, and pharmacy costs; this difference is similar to the findings by Majhail and colleagues who studied a larger group.[4] This cost difference, which we observed at 100 days and at 1 year, may be primarily a result of the greater complexity of allogeneic HSCT than of autologous HSCT, in addition to allogeneic transplant–associated graft-versus-host disease and other complications linked to prolonged hospital admission and rates of readmission.[16,17] In fact, we found that patients receiving myeloablative conditioning before allogeneic HSCT had longer index HSCT hospitalization and higher rates of subsequent hospitalization than patients undergoing autologous HSCT. Of course, the cost differences between patients undergoing allogeneic and autologous transplants are also undoubtedly influenced by the underlying clinical differences that guide the selection of HSCT grafting approach.

Our study also highlights the importance of the conditioning regimen with regard to 100-day and 1-year costs. The inpatient and total costs were higher for patients undergoing the allogeneic MA transplant who received myeloablative conditioning than those receiving nonmyeloablative/reduced-intensity conditioning, which is consistent with findings from single-institution studies.[8,9] In our sample, patients in the allogeneic MA cohort had longer LOS in the index HSCT hospitalization than patients in the allogeneic NMA group. Despite the difference in cost according to the conditioning regimen, the inpatient costs for the allogeneic NMA cohort (the lower-cost group) were still substantial.

We observed considerable cost differences between the pediatric patients and adults who had HSCT, which is consistent with past research.[18] Pediatric patients receiving myeloablative allogeneic or autologous HSCT had much higher 100-day inpatient, outpatient, and total costs than adults. These findings, particularly related to inpatient costs, likely reflect the different approaches to caring for pediatric patients and adults who have had HSCT. Children and adolescents tend to

Figure 2 Relative Contribution of Cost of Total Healthcare in the 10 Days Leading Up to Transplantation, the Cost of HSCT Admission, and Subsequent Hospitalization, Outpatient, and Pharmacy Costs in the First 100 Days After Transplantation



NOTE: For each of the 3 categories of patients shown (allogenic transplant with myeloablative conditioning, allogeneic transplant with nonmyeloablative/reduced-intensity conditioning, and autologous transplant with myeloablative conditioning), the bar segments indicate the proportion of the total cost accounted for in each of these 3 time periods: the 10 days before transplant, the transplant admission (<1% of patients in our sample had a transplant in the outpatient setting), and the remainder of the 100-day follow-up.

HSCT indicates hematopoietic stem-cell transplantation.

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Table 3 Healthcare Costs and Hospitalization at 100-Day Follow-Up for Those Receiving a Myeloablative Conditioning Regimen: Adults versus Pediatric Patients

Parameter		Pediatric patients		Adults	
		Allogeneic transplant (N = 80)	Autologous transplant (N = 27)	Allogeneic transplant (N = 318)	Autologous transplant (N = 942)
Total healthcare costs, $[a]	Mean	585,300	244,337	355,344	161,747
	SD	441,427	74,986	372,341	137,921
	Median	445,916	243,257	264,632	138,966
Inpatient costs, $[a]	Mean	529,994	191,320	296,398	132,633
	SD	445,287	60,464	369,038	130,484
	Median	406,195	194,125	212,332	111,419
Outpatient costs, $[a]	Mean	50,552	51,883	50,156	27,005
	SD	32,916	40,436	44,147	27,627
	Median	43,814	44,929	40,424	17,893
Pharmacy costs, $[a]	Mean	4754	1134	8790	2110
	SD	5121	1305	7443	3893
	Median	2865	916	7174	662
Cost of index HSCT hospitalization, $[b]	Mean	494,621	162,439	259,749	118,453
	SD	432,533	65,081	332,603	68,195
	Median	363,379	154,266	191,541	109,113
Length of stay of HSCT hospitalization, days	Mean (SD)	54.1 (37.2)	25.6 (14.5)	30.9 (20.6)	21.6 (12.7)
Any subsequent hospitalization[c]	Days, N (%)	31 (38.8)	11 (40.7)	138 (43.4)	191 (20.3)
Total length of stay, days[d]	Mean (SD)	7.1 (9.7)	10.4 (11.7)	9.4 (16.0)	6.3 (12.8)

[a]All costs include the claims from 10 days before through 100 days (or 1 year) after the transplant.

[b]Represents the costs of the index transplant, including conditioning regimen; inpatient transplants include the costs from 10 days before admission through discharge from index admission; outpatient transplants include the costs from 10 days before the day of first outpatient *ICD-9* diagnosis code for HSCT.

[c]Within 100 days (or 1 year) of follow-up.

[d]Among patients with hospitalization subsequent to the HSCT admission and within 100 days (or 1 year) of follow-up. Total represents hospital days across all admissions subsequent to HSCT admission.

HSCT indicates hematopoietic stem-cell transplantation; *ICD-9, International Classification of Diseases, Ninth Revision*; SD, standard deviation.

stay in the hospital or intensive care unit for longer periods after HSCT than adults, despite comparable rates of major complications[18]; this difference may reflect the special clinical needs of pediatric patients or the additional time needed to prepare parents for home-based caregiving.

Our analysis shows that pediatric HSCT hospital stays were nearly twice as long as adult hospitalizations. Such prolonged hospital stays can account for large increases in HSCT costs. For 100-day pharmacy costs, adults who had myeloablative allogeneic transplant, but not autologous transplant, had higher costs than pediatric patients, which could be caused by the greater use of age-related chronic medications among adults.

To our knowledge, this methodologic approach of identifying conditioning regimens to calculate their contribution to HSCT costs has not been used previously and therefore adds to the existing research.

Limitations

The approach we took has significant limitations and should be considered only a first step in a process that will, if validated, allow the use of large, administrative data sets to examine more detailed questions than was previously possible.

Although our algorithm for identifying conditioning regimens was developed through multiple rounds of clinical input from a variety of sources, as noted before, it has not been validated. The algorithm could have misclassified regimens in ways that would have biased our findings, and validation would therefore be crucial to strengthening our findings. Specifically, we excluded many patients whose conditioning regimens were undeterminable, making our results sample-specific and thus not generalizable to all patients undergoing HSCT.

Our analysis includes a very small number (ie, 54) of patients who had an outpatient HSCT before their inpatient transplant (their index event); therefore our conclusions may not be generalizable to the broader group of such patients. In addition, few patients in the autologous NMA group were identified, because such patients are typically managed in the outpatient setting. We therefore limited the analysis of adults to the 3 remaining groups.

Our examination of costs by age-group focused only on myeloablative conditioning, because we identified few pediatric patients who received nonmyeloablative/reduced-intensity conditioning, reflecting real-world patterns.[19] Still, the costs for pediatric patients in our study may not be generalizable, because we focused on HSCT performed in the oncology setting, whereas the indications for pediatric transplants vary and include oncologic conditions, immunodeficiencies, and other genetic conditions.

We calculated the costs in the 10 days before HSCT as part of pretransplant conditioning. Some true conditioning-related costs might have occurred more than 10 days before HSCT, and some costs not related to conditioning might have occurred within the 10-day window, which may have led to overestimating or underestimating the conditioning regimen–related costs.

Because of small sample sizes and a lack of clinical detail in claims, our analysis did not adjust for other possible confounders that might have contributed to the HSCT costs, such as disease severity. For example, more fit patients are generally considered better candidates for the myeloablative conditioning regimen. However, we accounted for the factors of the transplant type, conditioning regimen, and age using a stratified analysis. We did not conduct multivariate analyses, because the goal

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of the study was to compare the actual costs for different types of conditioning regimens. The groups differed significantly, and these differences were related to or were drivers of the choice of the conditioning regimen.

We analyzed the costs at 1 year, but not all patients were alive or enrolled in a health plan at the end of the year. The costs generally increase in the months just before death, and because our intent was to examine the actual costs, limiting the analysis to patients who were still alive would have biased the results.

Finally, our analysis excluded donor-related costs, which, if added, would raise our estimates of the total costs associated with HSCT. Furthermore, our findings may not be representative of HSCT costs for patients with public or noncommercial insurance.

Conclusion

Our findings indicate that among patients who receive myeloablative conditioning regimens before a transplant, allogeneic HSCT is more expensive than autologous HSCT. Among patients undergoing allogeneic transplant, a myeloablative conditioning regimen is costlier than a nonmyeloablative/higher-intensity conditioning regimen, likely because of additional complications associated with more complex grafting procedures and regimens. Overall, pediatric HSCT is more expensive than HSCT in adults, which may be attributable to precautions used for pediatric patients, such as longer hospital stays. A crucial step for future research is to validate the accuracy of the algorithm in this study through clinical records, such as patient charts. ■

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STAKEHOLDER PERSPECTIVE

More Data Analysis Is Needed to Improve Outcomes, Lower Costs, and Maximize Appropriate Resource Use

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Analyzing the cost of various medical treatment options can be challenging and complex as health plans try to unbundle claims to get at the core elements that ultimately make up the charges for any service. The article by Broder and colleagues in this issue of the journal highlights the need to explore detailed claims data more efficiently to appreciate the differences in costs that do not appear to be directly identified when evaluating the finite finances of specific treatment options.[1]

PAYERS: Health plans certainly look at the cost of procedures from a variety of providers across the network and compare and contrast them to identify the most efficient or cost-effective procedures or to assess the quality of care by evaluating clinical outcomes among different providers.

The concept of looking at the total cost of care "all-in" encourages a broader look at the patient experience and, in this case, highlights the significant differences between myeloablative and nonmyeloablative conditioning regimens for hematopoietic stem-cell transplantation (HSCT). The approach to analyze a total episode of care or to measure the total cost of care for patients over a 1-year period can identify distinct differences in overall costs for patients with chronic diseases. As discussed by Broder and colleagues, inpatient claims lack the granularity to parse out the specific drugs used in the conditioning regimens for patients who have had HSCT.[1] This requires the creative use of published data and suggests that better collection methods or coding would help to advance our knowledge of the true cost of various protocols in oncology.

The data analysis presented in this study demonstrates the differences in the types of HSCT, with autologous HSCT costing significantly less than allogeneic HSCT, and requires an average of 2 weeks fewer hospitalization days.[1] The analysis focuses on 2 core parts of a treatment algorithm developed for this study, including the type of HSCT and the choice of conditioning regimen to be used in the protocol. The use of *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) coding allowed for an accurate assessment of the potential patient populations for the study. The recent update to *ICD-10* can only lead to more complete data being available for analysis by health plan actuaries, underwriters, and analysts.

The population of more than 1500 patients in this study enhances the validity of the output, and the investigators appropriately point out that further validation of the algorithms is needed to accurately assess the real differences between the various HSCT options and conditioning regimens.[1] Because HSCT has increased in cost and frequency over the past decade, health plans find this to be a reasonable target for a review of the costs associated with this procedure. The findings that the transplant type, conditioning regimen, and patient age affect the cost of HSCT[1] suggest that health plans should consider developing treatment algorithms or pathways to maximize outcomes while minimizing costs.

RESEARCHERS: The large data warehouses at hospitals, integrated delivery systems, physician practices, and health plans provide a treasure trove of claims activity that can be analyzed to truly understand the use of resources and to assess the ultimate value of various treatments. More work is needed in exploring and comparing utilization from various participants in the healthcare system, with the potential to improve outcomes, lower cost, and maximize the appropriate use of scarce resources.

It is tempting to focus on the largest cost areas; however, it is possible that great savings exist in smaller disease areas that would require significantly less effort to encourage practice change because of the small numbers of patients and providers.

We should challenge all of those who have control over the data sets to analyze, evaluate, and publish their findings in an effort to encourage the rest of us to validate the results and maximize our return on investment in healthcare resources. ■

1. Broder MS, Quock TP, Chang E, et al. The cost of hematopoietic stem-cell transplantation in the United States. *Am Health Drug Benefits*. 2017;10(7):366-374.

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