Estimating Demand and Unmet Need for Allogeneic Hematopoietic Cell Transplantation in the United States Using Geographic Information Systems

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Abstract

Purpose: Allogeneic hematopoietic cell transplantation (HCT) is an increasingly used therapy for many patients with hematologic malignancies and other marrow failure or immune system disorders. The purpose of this study was to quantify and visualize both the demand and unmet need for HCT.

Methods: HCT use for 2012 was described using the Center for International Blood and Marrow Transplant Research registry. Potential demand for HCT was calculated using 2012 SEER data and published literature for HCT-treatable conditions. Point locations of transplant centers were geocoded using geographic information system (GIS) software; Thiessen polygons were created to establish adult (age 20 to 74 years) and pediatric (age 0 to 19 years) market areas. Market-area population estimates were

calculated using 2012 population estimates by age aggregated by census block.

Results: US market areas for HCTs were identified separately for transplant centers treating adult ($n = 62$) and pediatric patients ($n = 52$). Overall HCT demand among adults was 16,096, with an unmet need for HCTs of 10,276 patients. For pediatric patients, the total demand was 4,561, with an unmet need of 3,213 potential recipients. Evaluation of adult and pediatric market areas indicated that the largest unmet needs tended to be in areas with large populations.

Conclusion: Market-area maps and statistics developed using GIS will help communicate the unmet need for HCT, inform policy, and assist transplant centers in planning for the anticipated growth in HCT use.

Introduction

Allogeneic hematopoietic cell transplantation (HCT) is a potentially curative therapy for many patients with life-threatening malignant and nonmalignant hematologic diseases. Allogeneic HCT occurs when a patient receives blood stem cells from a related or unrelated donor. An estimated 20,000 HCTs are performed annually in the United States,¹ and this number is expected to continue to increase over time.

To meet the need for this expected growth, strategies to increase transplant center capacity are required.² To examine the current system and assist in developing such strategies, the National Marrow Donor Program (NMDP) sponsored HCT in 2020: A System Capacity Initiative, a multiyear initiative aiming to increase access for all patients in need of HCT by understanding and addressing personnel, systems, and infrastructural barriers to HCT.^{3,4} This initiative brought together multiple stakeholders, including HCT providers (physicians, nurses, midlevel practitioners, pharmacists, and social workers), professional societies, the government, payers, and HCT program and hospital administrators to focus on the professional workforce, facility capacity and care delivery, and financial aspects of the HCT system. Workgroups provided innovative ideas to increase HCT system efficiency using current capacity, address the

needs for future capacity, and ensure adequate reimbursement of HCT programs.^{2,4}

One component of the System Capacity Initiative focused on assessment of the operational capacity of the US health care system to support the needs of patients undergoing HCT with respect to hospital and health care facility infrastructure and care delivery. To better inform this initiative, there was a need to describe current use of allogeneic HCT within geographic or market areas around transplant centers and assess the potential unmet need for allogeneic HCTs within those areas. Providing information by market would allow transplant centers to consider the potential for growth as they make capital allocation decisions. This article describes an innovative method for estimating allogeneic HCT demand and unmet need using several databases and geographic information system (GIS) technology.

The relationship between geography and health is well established. One of the most notable examples came from John Snow in the mid 1800s, when he identified city water pumps as the transmission source of cholera by overlaying place of residence of the diseased with a map of the city infrastructure.⁵ The role of geography and mapping in health research has since expanded with the development of and recent advances in GIS technologies. GIS can be used in health care research to analyze

need, measure access, and study variations in use and delivery of health care.⁶ It has also been used to perform spatial analysis aimed at examining access, demand, and use of cancer care.⁷⁻¹⁰ A common geographic approach to measuring health care access is with a distance-based measure. Travel-time estimates from patients' places of residence to treatment centers provide the most accurate information regarding distance-based access.⁵ Another way to estimate distance-based access is through use of Thiessen polygons.¹¹ All points or locations within the area of a Thiessen polygon can be described as being closest, by straight line or Euclidean distance, to the location of the polygon-associated entity being studied. This was the preferred method of estimating access for our study, because unlike travel-time or distance-based measures, Thiessen polygons ensure complete geographic coverage and therefore assignment of all individuals within census blocks to a market area. Transplant centers were used as the point locations, and market boundaries were drawn equidistant between two centers or a group of centers. Previous studies have used Thiessen polygons in this way to predict the catchment population of health care facilities.^{11,12} In our study, Thiessen polygons were used to calculate the HCT demand and estimate the unmet need of allogeneic HCT-eligible patients within US transplant center population catchments or market areas.

Methods

Measure of HCT Use

Data on patients who underwent allogeneic HCT at US transplant centers in 2012 were retrieved from the Center for International Blood and Marrow Transplant Research (CIBMTR). The CIBMTR comprises a voluntary working group of > 450 transplant centers worldwide that contribute detailed outcome data on HCT to the statistical center at the Medical College of Wisconsin and the NMDP. Participating centers are required to report all transplants consecutively, and patient follow-up occurs longitudinally. The CIBMTR also administers the Stem Cell Therapeutic Outcomes Database portion of the C.W. Bill Young Transplantation Program, under which transplant centers in the United States are required by law to report all allogeneic HCTs to the CIBMTR. Algorithm-based reviews for discrepancies, physician review of submitted data, and on-site audits of participating centers ensure data quality. This observational study was performed in compliance with all applicable federal regulations pertaining to the protection of human research participants. Protected health information used in the performance of such research is collected and maintained by the CIBMTR as a public health authority under the Health Insurance Portability and Accountability Act Privacy Rule. In our study, patients were categorized into two groups by age at time of transplantation: adult (age 20 to 74 years) and pediatric patients (age 0 to 19 years).

Measure of Transplant Demand

Several data sources were used to estimate HCT demand, defined as the total number of patients who could have potentially

benefitted from allogeneic transplantation in 2012. First, incidence of HCT-treatable malignant conditions was determined using SEER data. Scientific literature informed the estimated incidence of nonmalignant diseases that indicate transplantation.¹³⁻²³ By applying disease-specific incidence rates to detailed age population data from the US Census Bureau, the number of patients diagnosed with diseases that could be treated with HCT was determined (Appendix Table A1, online only, provides examples for acute myeloid leukemia). The proportion of patients with diseases eligible to proceed with allogeneic HCT was determined by conducting a literature review, including a review of the National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology²⁴⁻³⁰ and consultation with transplant and nontransplant subject matter experts (Appendix Table A2, online only). Methods used to integrate these data sources have been published previously³¹ (details on methods provided in Appendix, online only). The calculated demand for allogeneic HCT per 100,000 individuals was 7.4 for adults and 5.4 for the pediatric group.

Transplant Center–Derived Market Areas

Point locations of US centers that performed transplants in 2012 (for adults, $n = 118$; for pediatric patients, $n = 88$) were geocoded by their full address using ArcGIS software (version 10.1; Esri, Redlands, CA) with the US street addresses locator. Thiessen polygons were calculated using the ArcGIS (version 10.1) Create Thiessen Polygons tool, with transplant center point locations by category as the input layer. A Euclidean or straight-line distance measure was used as a parameter for establishing the geographic market areas containing $\geq$ one transplant center. This approach was used to ensure all locations and associated US Census blocks were assigned to a market area. Separate geographic market-area boundaries were established around transplant centers designated as either adult or pediatric. Transplant centers with both adult and pediatric programs were used to establish boundaries for each of the respective market-area categories. Geographic boundaries for each market area were initially drawn by calculating Thiessen polygons around each transplant center. Thiessen polygon boundaries were then combined in highly populated areas where transplant centers were located within 50 miles of one another and, in our opinion, represented a distinct geographic market. In the end, 62 adult and 52 pediatric market areas were identified to evaluate transplant use and demand.

Market-Area Population and Socioeconomic Estimates

The adult and pediatric populations as well as socioeconomic variables (including percent minority population, average health care expenditure, and income per household) were calculated for each market area by aggregating census blocks within the geographic boundaries of the market area and summing the values. Market-area boundaries that intersected census blocks were assigned the population proportion equal to the census block within the respective market area. Estimates by

census block were obtained from the 2012 Business Analyst data set (Esri).

Market-Area Unmet Need

Calculated demand for allogeneic HCT by adult and pediatric categories was then applied to the market-area population respectively to determine the number of expected transplants in 2012. The number of allogeneic transplants (from the CIBMTR database) actually performed by the transplant center assigned to the respective market area during 2012 was subtracted from the expected number of transplants. This difference—the estimated unmet need—represents the number of potential allogeneic transplant-eligible patients within the market area who did not undergo transplantation in 2012.

Pearson's correlation coefficient was used to test for differences between market-area populations and unmet need. All calculations were performed using SAS EG software (version 4.3; SAS Institute, Cary, NC). All geographic analyses and maps were produced using ArcGIS software (version 10.1).

Results

The total 2012 demand for allogeneic HCT among adults across the United States was 16,096, with a median of 209 per market area (range, 66 to 1,248). The unmet need for the same population was 10,276, with a median of 133 by market area (range, -17 to 769), as shown in [Figure 1](#). The New York market area (southern New York state, western Connecticut, northern New Jersey, and northeastern corner of Pennsylvania) had the highest HCT demand and unmet need (1,248 and 769, respectively). The Rochester, Minnesota, market area (covering southeastern corner of Minnesota, north-central Wisconsin, and northeastern Iowa) had the lowest demand (66 HCTs) and unmet need (-17; 17 more transplants than expected were performed in 2012).

In the pediatric population, the total allogeneic HCT demand in the United States was 4,561, with a median of 70 by market area (range, 18 to 337); total unmet need was 3,213, with a median of 48 by market area (range, -5 to 254), as depicted in [Figure 2](#). The Los Angeles market area (south-central portion of California extending to southern tip of Nevada) had the highest demand and unmet need of 337 and 254 transplants, respectively. The Hawaii market area (state boundaries) had the lowest demand (18 HCTs), whereas the Cincinnati market area (northeastern Kentucky, parts of southern Ohio, and small portions of eastern Indiana and southwestern West Virginia) had the lowest pediatric unmet need of -5, indicating more HCTs were performed than expected.

Individual reports were compiled for each market area. Each report included adult and pediatric maps to display the geographic boundaries of the market area, the locations and names of the contributing transplant centers, and the locations of other hospitals within the market area. Data were also compiled for individual market areas to highlight the unmet need by age category. As an example, [Figure 3](#) shows the Chicago market area. Percentage of the population that is of minority race and

ethnicity, average household income, and average health care expenditure per household for the market area are included.

Evaluation results of the 62 adult and 52 pediatric market areas indicate that the largest unmet needs for HCT tended to be in areas with large populations. The correlation between unmet need and market area population was highly significant for both adult ($r = .92$; $P < .001$) and pediatric groups ($r = .95$; $P < .001$).

Discussion

GISs can be used to help inform health services research and policy as well as business decision making. GIS technology has been used to estimate access to cancer care across the United States⁸ and estimate local demand by major cancer care facilities in the United States.⁹ Our study is the first to our knowledge to use GIS technology to estimate the unmet need for HCT.

Reasons for the present unmet need are varied and complex. If patients have malignant or nonmalignant diseases, appropriate referral and timing of referral by hematologists and oncologists can play important roles in determining whether patients proceed to HCT,³² contributing to unmet need. Lack of access to HCT can also influence unmet need and can include donor availability, age, health care disparities, and economic and health care systemic barriers.³³ Other barriers that can contribute to unmet need include variability in insurance status,³³ insurance coverage of HCT,³⁴ and availability of a caregiver.

The national unmet need for HCT in 2012 was 10,276 for adults and 3,213 for children. Furthermore, our study found that unmet need for HCT tends to exist in areas with large populations. The need for HCT in the United States is expected to grow as a result of increases in overall population, the number of older individuals (among whom incidence of hematologic malignancies is highest), and increased access to HCT treatment because of improvements in treatment protocols. Transplant centers vary in their ability to expand HCT programs to meet this demand. Individual market-area maps and associated statistics are part of an ongoing effort by the NMDP to communicate the unmet need for HCT to transplant centers. These data will inform transplant centers as they make decisions for resource allocation and program expansion. The results of our study show that establishment or expansion of HCT centers may be most justified in markets where the population is highly correlated with unmet need for HCT.

The limitations of our study must be considered. The analysis did not take into account where patients actually reside or where they travel to for transplant care. Because of the limited number of transplant centers in the United States, some patients must travel to receive care. In addition, many patients may not go to their nearest transplant center (by geographic straight-line distance). Patients may travel outside their market area for care based on personal preference, physician referral, or payer recommendation. Transplant centers also have their own local and national referral patterns, and they may draw patients from outside their market areas. Thiessen polygons were used in an attempt to quantify the geographic pattern of transplant center use. This approach was intended to provide a reasonable

Figure 1. 2012 estimate of unmet need for hematopoietic cell transplantation by adult market area.

estimation of the need for HCT service. Incidence rates of many diseases treatable with transplant vary by race and/or ethnicity. This variation and the unequal distribution by racial and ethnic groups across the United States were not taken into account in our analysis. A standard rate was applied across each geographic region despite the race or ethnic composition of the underlying population. Finally, our analysis did not consider autologous HCT; autologous transplantation frequently comprises a substantial proportion of all transplant activity for centers, and policy decisions regarding center growth and expansion will need to take into account both autologous and allogeneic HCTs.

Results of our study indicate several additional aspects that can be considered for future research. Market areas of high unmet need were found to be highly correlated with the population density within each market area. Additional studies should be aimed at further assessment of patient access by analyzing transplant center characteristics, including assessment of the average drive time of US residents to their nearest transplant center. For example, a study by Abou-Nassar et al³⁵ showed that patients residing > 160 minutes drive time from a transplant center led to decreased HCT overall survival at 1 year after transplant. Combining data from the areas of high unmet need with geographic areas outside of center drive-time thresholds

Figure 2. 2012 estimate of unmet need for hematopoietic cell transplantation by pediatric market area.

Figure 3. Example of unmet need for hematopoietic cell transplantation (HCT) in individual market area for 2012: Chicago market area for adults. NMDP, National Marrow Donor Program.

would better inform decision makers of the locations with greatest need for transplant center expansion. Efforts are under way to collect patient ZIP code data so that the frequency of patients receiving care within designated market areas can be more accurately assessed. Other approaches, such as the two-step floating catchment area method,⁹ where both patient travel time and facility capacity are used to estimate access and local demand for cancer facilities, should be considered. Lastly, the NMDP is in the process of reviewing market analysis data with individual transplant centers to assess accuracy and utility.

Decisions about resource allocation and investment in program expansion are complex. Our data summarizing HCT demand and unmet need will inform transplant centers as they consider these complex policy decisions. This analysis lays the foundation for future work in this area and will support continued efforts to assist hospital and HCT administrations in systems thinking to address the unmet patient transplant needs in the United States. As we improve our methods and estimates,

for example, by incorporating patient ZIP codes, our findings will better inform policy makers about the gaps and opportunities in the transplant system network.

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- NCCN Clinical Practice Guidelines in Oncology: Hodgkin Lymphoma (version 1.2014). www.nccn.org/professionals/physician_gls/pdf/hodgkins.pdf
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- NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia (version 2.2013). www.nccn.org/professionals/physician_gls/pdf/aml.pdf
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Appendix

Methods for Estimating Hematopoietic Cell Transplantation Demand

The total patient population estimate was based on review of published literature, technical publications, government statistics, and expert opinions. An extensive literature review was performed to establish incidence rates of the primary diseases treated with hematopoietic cell transplantation (HCT) and understand established treatment protocols and response to treatment.

Incidence of HCT-Treatable Conditions

Incidence was defined as the number of new cases of patients with an HCT-treatable condition diagnosed each year. Malignant disease incidence was based on SEER data published by the National Cancer Institute. Incidence of nonmalignant diseases was based on rates published in scientific literature or by organizations focused on specific diseases. The most conservative published rate was used. The incidence rate (number of cases per 100,000 people) was then multiplied by the total population to calculate the total number of people diagnosed in any given year. Population estimates were based on US Census Bureau data for 2012.

Allogeneic HCT–Treatment Candidates

The proportion of HCT-eligible patients was determined through examination of treatment guidelines (eg, American Society for Blood and Marrow Transplantation, Center for International Blood and Marrow Transplant Research, National Comprehensive Cancer Network guidelines), scientific literature, and expert opinions (Appendix Table A2). This review established an estimate of the proportion of patients who would need an allogeneic HCT. The need for allogeneic HCTs was further reduced to account for the presence of comorbid conditions that may make patients unsuitable for undergoing transplantation and for patient preference (eg, elderly patients may not want aggressive treatment such as transplantation; Appendix Table A1). The disease-specific need for allogeneic HCT was calculated by multiplying the annual incidence by the number of patients who would potentially be candidates for HCT. The total HCT need was calculated by adding the need for each disease indication.

Appendix Table A1 summarizes the methodology for calculating the HCT demand for acute myeloid leukemia. The HCT demand in each market was determined based on the market population, and the market potential was calculated by subtracting the actual number of HCTs performed in that market from the need.

Table A1. Estimating HCT Need Among Patients With AML

Age (years)	2012 US Population	AML Incidence per 100,000	Estimated Annual New Diagnoses*	Proportion Eligible for HCT	AlloHCT Demand
Pediatric, 0 to 19	82,504,800	0.7	609	0.45	274
Adult, 20 to 54	149,677,682	1.7	2,552	0.70	1,786
Adult, 55 to 64	38,586,202	5.2	2,016	0.55	1,109
Adult, 65 to 74	23,985,392	11.5	2,770	0.25	692
Total	294,754,076		7,947		3,861

Abbreviations: AlloHCT, allogeneic hematopoietic cell transplantation; AML, acute myeloid leukemia; HCT, hematopoietic cell transplantation.

* Estimated annual new diagnoses may not be direct product of US population and AML incidence rate presented in table because of rounding.

Table A2. Key Information Sources

Source
Population estimates www.census.gov/popest/data/national/asrh/2012/index.html http://seer.cancer.gov
Chronic myelogenous leukemia Applebaum FR: Semin Hematol 38:35-42, 2001 (suppl 8) www.cancer.gov/cancertopics/pdq/treatment/CML/HealthProfessional Goldman JM, Marin D: Semin Hematol 40:97-103, 2003 Goldman J: Semin Hematol 38:28-34, 2001 (suppl 8) Melo JV, Hughes TP, Apperley JF: Hematology Am Soc Hematol Educ Program 2003:132-52, 2003 www.nccn.org/professionals/physician_gls/f_guidelines.aspml

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Table A2. (continued)

Source
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Table A2. (continued)

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Key opinion leaders consulted
David Buchbinder (Children's Hospital of Orange County, Orange, CA)
Michael Burke (University of Minnesota, Minneapolis, MN)
Dennis Confer (National Marrow Donor Program, Minneapolis, MN)
Stella Davies (Cincinnati Children's Hospital, Cincinnati, OH)
Christine Duncan (Dana-Farber Cancer Institute, Boston, MA)
Mary Eapen (Center for International Blood and Marrow Transplant, Milwaukee, WI)
Mary Horowitz (Center for International Blood and Marrow Transplant, Milwaukee, WI)
Stephen Hunger (Children's Hospital Colorado, Aurora, CO)
David Jacobsohn (Children's National Medical Center, Washington, DC)
John Levine (Mott's Children's Hospital, Ann Arbor, MI)
Willis Navarro (National Marrow Donor Program, Minneapolis, MN)