Transplantation and Cellular Therapy 30 (2024) 542.e1–542.e29

Transplantation and Cellular Therapy

journal homepage: www.astctjournal.org

ASTCT American Society for Transplantation and Cellular Therapy

Analysis

Healthcare Resource Utilization and Cost Associated with Allogeneic Hematopoietic Stem Cell Transplantation: A Scoping Review

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Article history:
Received 16 October 2023
Accepted 30 January 2024

Key words:
Allogeneic hematopoietic stem cell transplantation
Cost analysis
Health care resource utilization

A B S T R A C T

This scoping review summarizes the evidence regarding healthcare resource utilization (HRU) and costs associated with allogeneic hematopoietic stem cell transplantation (allo-HSCT). This study was conducted in accordance with the Joanne Briggs Institute methodology for scoping reviews. The PubMed, Embase, and Health Business Elite Electronic databases were searched, in addition to grey literature. The databases were searched from inception up to November 2022. Studies that reported HRU and/or costs associated with adult (≥18 years) allo-HSCT were eligible for inclusion. Two reviewers independently screened 20% of the sample at each of the 2 stages of screening (abstract and full text). Details of the HRU and costs extracted from the study data were summarized, based on the elements and timeframes reported. HRU measures and costs were combined across studies reporting results defined in a comparable manner. Monetary values were standardized to 2022 US Dollars (USD). We identified 43 studies that reported HRU, costs, or both for allo-HSCT. Of these studies, 93.0% reported on costs, 81.4% reported on HRU, and 74.4% reported on both. HRU measures and cost calculations, including the timeframe for which they were reported, were heterogeneous across the studies. Length of hospital stay was the most frequently reported HRU measure (76.7% of studies) and ranged from a median initial hospitalization of 10 days (reduced-intensity conditioning [RIC]) to 73 days (myeloablative conditioning). The total cost of an allo-HSCT ranged from $63,096 (RIC) to $782,190 (double umbilical cord blood transplantation) at 100 days and from $69,218 (RIC) to $637,193 at 1 year (not stratified). There is heterogeneity in the reporting of HRU and costs associated with allo-HSCT in the literature, making it difficult for clinicians, policymakers, and governments to draw definitive conclusions regarding the resources required for the delivery of these services.

Financial disclosure: See Acknowledgments on page 542.e26.

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https://doi.org/10.1016/j.jtct.2024.01.084

Nevertheless, to ensure that access to healthcare meets the necessary high cost and resource demands of allo-HSCT, it is imperative for clinicians, policymakers, and government officials to be aware of both the short- and long-term health resource requirements for this patient population. Further research is needed to understand the key determinants of HRU and costs associated with allo-HSCT to better inform the design and delivery of health care for HSCT recipients and ensure the quality, safety, and efficiency of care.

INTRODUCTION

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is an effective therapy for many malignant and nonmalignant diseases. However, allo-HSCT is a high-risk and complex procedure associated with potentially fatal complications and substantial long-term and late effects [1], which can affect patients' quality of life through physical and psychosocial sequelae [2]. The long-term follow-up of these patients is complex, requiring a collaborative interdisciplinary approach across multiple specialists and allied health services, including ophthalmology, dermatology, respiratory, physiotherapy, dietetics, and psychology [3]. Late effects of allo-HSCT and the requirements of long-term care result in increased patient and carer treatment burden, healthcare resource utilization (HRU), and costs [4].

HSCT is resource- and cost-intensive, with transplantation-associated hospital costs (excluding readmissions) estimated at $49.6 million AUD in Australia during the financial year 2014-15 [5]. In the United States, HSCT was identified as the procedure associated with the most rapid increase in hospital costs between 2004 and 2007, with an 84.9% growth over that period, resulting in costs totaling $1.3 billion USD in 2007 [6]. In 2018, the Center for International Blood and Marrow Transplant Research reported that transplantation activity was continuing to increase in the United States, particularly in age $\geq$70 years [7]. Thus, the use of HSCT continues to grow with expansions in the age of eligibility for transplantation (allowing HSCT in older patients) and advances in supportive therapy and donor options, such as unrelated and haploidentical donors [8], leading to an increasing pool of transplantation-eligible individuals.

But although the increasing demand for HSCT is known, the resource requirements to meet the healthcare needs for this patient population remain unclear. Understanding the HRU associated with HSCT is important for clinicians, policymakers, and government officials to assess the delivery of this procedure and forecast future healthcare expenditures and resource requirements [9].

Literature reviews previously undertaken to assess the cost of HSCT [10,11] included data on autologous and allo-HSCT populations and were published a decade ago. Since then, allo-HSCT has achieved notable milestones, such as the use of HLA-haploidentical donors [12] and novel advances in the management of graft-versus-host disease (GVHD) [13]. The present scoping review builds on those previous studies, with a focus on the overall costs of the HRU and costs associated with allo-HSCT, and encompasses a more expansive database search (allo-HSCT including other population databases and the grey literature).

Owing to the complexity and variability in the procedural aspects of allo-HSCT and the anticipated breadth of the literature captured through this scoping review, the exploration of that evidence has been divided into 2 parts. Part 1 provides evidence, taking a comprehensive approach to exploring the overall HRU and costs associated with allo-HSCT. Part 2 focuses on specific clinical outcomes associated with allo-HSCT, including GVHD and other allo-HSCT-associated complications. Here we report on the methods and results associated with Part 1 of the study, a comprehensive review of total HRU and costs of allo-HSCT. The methods and results for Part 2 will be reported in a separate article.

METHODS

The scoping review was conducted in accordance with the Joanne Briggs Institute methodology for scoping reviews [14]. Given the study objective of understanding the extent and type of extant evidence on HRU and costs for allo-HSCT, conducting a scoping review was considered appropriate. A prospective study protocol was published on Open Science Framework (https://osf.io/5tdsw/).

Data Sources and Search

The PubMed, Embase, and Health Business Elite databases were searched using key terms related to "allogeneic hematopoietic stem cell transplantation"

and "health care resource utilization" with Boolean operators. To capture the breadth and trajectory of allo-HSCT HRU and cost publications over the years, the search was not limited by publication date. The PubMed search strategy was developed in consultation with an Information Services Librarian at the University of Technology Sydney and reviewed by all members of the study team. The Embase search terms were built on the PubMed search strategy, with slight modifications to accommodate the replacement of Medical Subject Headings (MeSH) terms with Emtree terms.

A structured grey literature web search was conducted using the Health Technology Assessment Agencies and Health Economics sections from the Canadian Agency for Drugs and Technologies in Health Grey Matters checklist [15]. The search used the terms in the "International" subsection of the checklist rather than the country-specific sections, as the latter were considered to overrepresent specific countries (eg, Canada, Australia) and thus potentially could bias the study results.

Eligibility Criteria

Inclusion criteria were studies of primary research, written in English, with full-text availability. Specific population, concept, and context (PCC) [14] eligibility were as follows:

Population

Eligible studies included adult patients (age ≥18 years) who underwent allo-HSCT. When study population age eligibility was not reported, the baseline age range or standard deviation of the study population was reviewed to assess eligibility. Where the nature of the HSCT (ie, autologous or allogeneic) was unclear, the opinion of the HSCT physician (I.K.) was sought, and the study was excluded unless it was determined that the clinical context directly implied an allo-HSCT.

Studies that reported only the costs of an HSCT registry, only the pretransplantation phase (eg, donor screening), or a single complication of allo-HSCT (eg, GVHD, cytomegalovirus or fungal infection) did not meet the eligibility criteria.

Concept

Studies that reported direct HRU and costs from the health system perspective were included. Studies solely reporting indirect or nonmedical costs, such as costs associated with community care, productivity loss, or patient out-of-pocket costs, were excluded. For studies that presented both direct and indirect costs, results associated with the healthcare system perspective (if presented separately) were included.

Context

Studies from high-income countries as defined by the World Bank Country and Lending Groups [16] were included for comparability with respect to access and affordability [17].

In applying the PCC eligibility criteria, studies were not limited to those that assessed HRU and costs as a primary objective. Studies that reported HRU or costs in a manner that could be extracted from their results, such as subgroup analyses or a particular arm within a study, were also included to ensure broad capture of the literature. Literature review publications identified during the search were not included, but references were scanned for potential additional studies.

Data Extraction

The database literature search results were screened using Covidence [18] and Microsoft Excel. A pilot test of the eligibility criteria was conducted by 2 reviewers (N.V.K. and G.M.) based on a randomly selected 1% of the identified studies. No subsequent changes were made to the eligibility criteria.

Search results were screened in 2 stages, starting with selection based on both title and abstract using the inclusion criteria, followed by a full-text retrieval of potentially relevant evidence for further detailed review [14]. The principal investigator (N.V.K.) screened all the studies, and a 20% sample was reviewed at each stage by a second investigator (G.M.), with discussion among the reviewers after each 10% sample.

Interrater reliability (IRR), measured by the prevalence-adjusted bias-adjusted kappa (PABAK), was calculated at each stage, with >80% agreement set as the threshold for acceptability [19]. The PABAK was used because it was anticipated that a high-volume of citations would result from the search strategy, with a commensurate high proportion of those being excluded relative to inclusions. This difference potentially would adversely affect other measures of IRR, such as Cohen's kappa [20]. Expert opinion (I.K., R.D.A.L., S.Y.) was sought for studies where the PCC were not clearly described, or if there was uncertainty as to whether the study reflected current practice (ie, standard of care). The grey literature screening was conducted in a single stage with a 20% sample reviewed by the second reviewer.

Data extraction was standardized using a derivation of the Joanne Briggs Institute template

instrument for extraction of source evidence details, characteristics, and results. The data extraction form is presented in Appendix 1. A 20% sample of the extracted data was audited by the second reviewer (G.M.).

Data Analysis

In accordance with standard methods for scoping reviews, the methodologic limitations or risk of bias of the included studies were not critically appraised [21]. From the extracted data, details of the HRU and costs reported by the studies were summarized. This included, where possible, categorization of data by transplantation phase: pretransplantation (donor selection and collection) phase, initial transplantation phase, and postdischarge phase. For studies that did not report HRU and costs in this manner, results were summarized according to how they were reported within the studies, such as hospital length of stay (LOS), outpatient visits, readmission, drug use, laboratory, transfusion and acute care. The reported categories were organized according to the timeframes in which they were reported, and relevant metrics used in the respective studies (eg, for HRU - rates, duration, number of days). Where a study reported both the median and the mean as the measure of effect, the mean values are presented here.

HRU measures and cost were combined across studies reporting results defined in a comparable manner by combining the reported measure of central tendency used in the studies (ie, mean or median). For commonly reported results (eg, LOS, initial and total costs), HRU and costs were stratified according to donor selection, stem cell source, and choice of conditioning regimen: reduced-intensity conditioning (RIC)/nonmyeloablative or myeloablative conditioning (MAC). Where studies presented results according to other categories (eg, ethnicity, treating center, or further subdivision) a weighted average of the stratified groups was used. For studies that did not provide details on the donor, stem cell source, or conditioning regimen or where results were not extractable in this manner, the results of the entire eligible cohort are presented.

HRU and costs reported in aggregate only (eg, outpatient visits, hospital admission and readmission, total hospitalization and readmission costs, total outpatient and clinical visit costs) were summarized in tabular form. For each study reporting HRU and costs in this manner, a within-study weighted average was calculated to represent costs for the eligible cohort. Subsequently, a simple average and weighted average were presented at the 100-day and 1-year timepoints. Results that could not be combined across studies (ie, were reported by only 1 study), are described in narrative form.

Monetary values were standardized to 2022 US Dollars (USD). Results presented in currencies other than USD were converted to USD based on the exchange rate at the specified time period of the relevant study (according to the Board of Governors of the Federal Reserve System [22]) and inflated to 2022 prices using the US Bureau of Labor Statistics Consumer Price Index [23]. Where the time period or the currency of the reported costs was not specified in the study, the year of publication or the country of the primary author was used as reference.

RESULTS

Literature Search

A total of 6487 titles and abstracts (database search, n = 3182; grey literature, n = 3305) and 500 full-text studies (database search, n = 269; grey literature, n = 231) were assessed for eligibility. Overall, 43 studies met the inclusion criteria with a comprehensive approach (ie, overall HRU and costs associated with allo-HSCT). Details of the exclusion criteria are provided in Figure 1. Grey literature details are presented in Appendix 2.

The PABAK for the second 10% sample at each stage of the database search was .96 and .71, respectively. Although the latter fell short of the acceptability threshold, the study team felt the results were acceptable given the small sample size (ie, 4 discrepancies out of 28 studies) and consensus between the 2 reviewers was achieved without the need for intervention by a third review [14]. Expert opinion was sought for 22 studies, of which 5 met the inclusion criteria. All 43 included studies were sourced via the search of the published literature. No grey literature results were eligible for inclusion.

Characteristics of Included Publications

The majority of the 43 studies (67.4%) were published in the last decade (ie, 2013 onward) and were country-specific, predominantly from countries in North America (55.8%), Europe (27.9%), and Asia (11.6%) (Table 1). Only 1 study [24] included data from more than 1 country (Germany, Sweden, and Canada) and presented the results separately for each of the countries. Two studies [25,26] may have derived results from the same data set. For the purpose of this

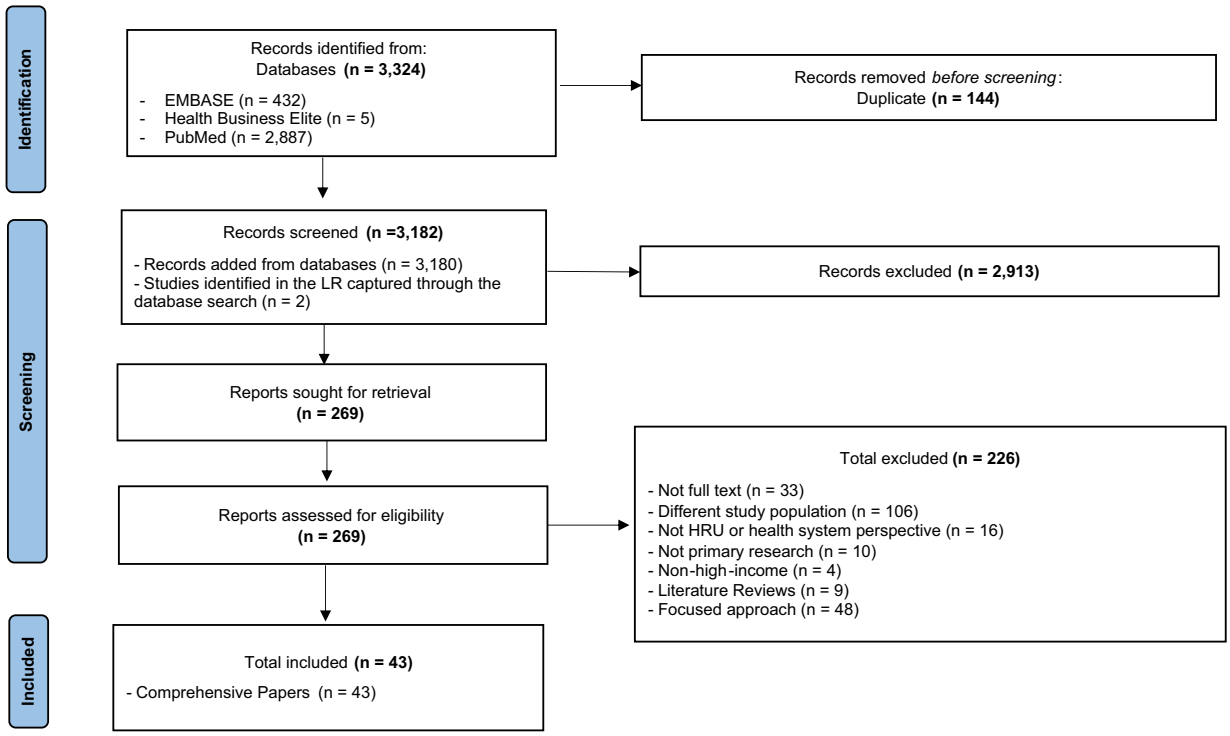

Figure 1. PRISMA for database search. Exclusion rationale according to the principal reviewer; conducted on April 11, 2022.

review, they were treated as separate studies (unless the same results were presented, these were noted) because they focused on different aspects of HRU and costs.

Nine studies (20.9%) [24,27-34] reported economic evaluations, and the remaining studies reported descriptive statistics. These descriptive studies were based predominantly on retrospective studies in the form of single-center (39.5%), multicenter (14.0%; range, 2 to 15 centers), and population-based (23.3%) studies, derived from various national and private healthcare claims databases. All but 2 of the studies [35,36] were retrospective; the study design of the 2 exceptions could not determined.

HRU and cost data extracted from 21 studies (48.8%) were derived from a specific arm within a study (n = 17) or a subgroup population (n = 4) (Table 1). Results from 4 studies (9.3%) [35,37-39] could not be combined with other studies owing to the nature of the HRU or cost measures (eg, monthly average costs), or timeframes (eg, aggregated results inclusive of the period prior to allo-HSCT) reported.

Thirty-two studies (74.4%) reported both HRU and costs associated with allo-HSCT (Table 1). The proportion of articles that presented results on HRU and costs were 81.4% and 93.0%, respectively.

HRU

LOS

LOS was reported in 33 of the 43 studies (76.7%) (Table 1). However, there were variations in both the timeframe in which these results were captured and how the results were framed. These included using such terms as "day of discharge after transplantation," or "total hematology inpatient days." The results of 3 studies [35,37,39], were not presented in a manner that could be combined with the other studies due to the expression of LOS, which included the proportion of patients based on categorical duration (eg, $\leq$10 days, >10 days), monthly hospital stays (in days), and/or timeframes used (eg, days 101 to 365, days 366 to 730, months 1, 2, and 3).

LOS for Initial Hospitalization. The LOS for initial hospitalization was the most consistently reported HRU measure across the studies (n = 17; 39.5%) (Table 1). It generally appeared to be shorter for RIC regimens (mean 34.72 days) [31-33,36,40-43] compared with MAC regimens (mean, 46.12 days) [31,32,36,41,44,45] (Figure 2A). Overall, cord blood (CB)-derived stem cells [32,46,47] resulted in a longer initial hospitalization LOS compared to peripheral blood (PB)-[36-40,42,44,46,48] and bone marrow (BM)-[46,48] derived stem cells. These results are

Table 1
Summary of HRU and Cost Study Characteristics

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost‡,§	Currency (yr)	Timeframe	Extraction
Barr et al., 1996	Other stratification: AML (2CR) ALL (1CR)	AML = 5, ALL = 5	Canada	Economic evaluation (single-center) Comparator: HSCT and control (patients assigned based on availability of donor)		Manual chart review	**Study period:** • Inpatient days (mean): 57¶	**Study period:** • Total cost (mean): $159,158¶	CAD (1992)	Minimum 18-mo follow-up	Partial, study arm
Faucher et al., 1998	PB, MAC	n = 17	France	Single-center, retrospective	Descriptive analysis	Medical records (April 1995-June 1997)	**Initial phase:** • Day of discharge after HSCT (NS): 28 **100 d:** • Readmission hospital days (NS): 15 • Drug use (NS, i.v. antibiotherapy), d: 15 • RBCs, units (NS): 12 • Platelets (NS, units): 5	**Initial phase:** • Collection (mean): $4650 • Hospitalization (mean):‖ $53,527 **100 d:** • Total cost (mean): $71,341 • Collection cost (mean): $4650 • Conditioning (mean): $2742 • Drug cost (mean): $6188 • Laboratory cost (mean): $5366	USD (1996)	100 d	Partial, study arm
Bennett et al., 1999	PB, BM	PB = 21, BM = 13	US	Single-center, retrospective	Descriptive analysis	NS (1995)	**Initial phase:** • Induction phase hospital bed, d (median): 9 (PB), 9 (BM) **HSCT recovery to 100 d:** • Hospital bed, d (median): 17 (PB), 22 (BM) •Physician/clinic visits (median): 36.04¶ • Drug use (NS, antibiotic days): 34.35¶ • RBCs (NS, units): 5.53¶ • Platelets (NS, units): 10.29¶	**Initial phase:** • Harvest cost (median): $11,118 (PB), $7085 (BM) **SCT recovery to 100 d:** • Total cost (median): $129,238 (PB) $159,667 (BM)	NS	100 d	Entire study cohort

(*continued*)

Table 1 (*Continued*)

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost†,§	Currency (yr)	Timeframe	Extraction
Cordonnier et al., 2005	MRD, MAC, non-MAC	MAC = 12, non-MAC = 11	France	Multicenter study (n = 2)	Descriptive analysis	Trial dates: MAC, February 1998-March 2000, non-MAC, August 2000-March 2003)	**Initial phase:** • LOS for initial hospitalization, d (mean): 22 (non-MAC, PB), 48 (MAC) **1 yr:** • LOS, d (mean): 56 (non-MAC, PB), 64 (MAC) • Readmission hospital days (mean): 24.61¶	**Day -8 to day 365:** • Total cost (median): $111,479 (non-MAC, PB), $106,096 (MAC)	Euro (2001)	1 yr	Entire study cohort
Skrepnek et al., 2005	MUD, BM	NA	US	Economic evaluation; comparator: imatinib and MUD-HSCT		Literature	•	**2 yr:** • Total cost: $ 242,963	Dollars (2004)	2 yr	Partial, study arm
van Agthoven et al., 2005		n = 7	Netherlands	Multicenter study (n =15), retrospective study	Descriptive analysis	Hospital database (1997-1998)	**Study period:** • Input days (mean): 43.1	**Study period:** • Total cost (mean): $78,197	Euro (2003)	NS, 3 yr; reflective of "treatment episode" ie, day 1 of conditioning regimen	Partial, subgroup
Svahn et al., 2006		n = 61	Sweden	Single-center, retrospective	Descriptive analysis	Institution database (January 1998-December 1999)	•	**5 yr:** • Total cost (median): $242,963	Euro (2005)	5 yr	Partial, subgroup
Saito et al., 2007	RIC, HDCT	HDCT = 185, RIC = 90	US	Single-center, retrospective	Descriptive analysis	Institution database (June 2000-September 2003)	**Initial phase:** • LOS for initial hospitalization, d (median): 10 (RIC), 32 (HDCT) **100 d:** • LOS, d (median): 13 (RIC), 36 (HDCT) • Outpatient clinical visits, n (median): 10.62¶ **1 yr** • LOS, d (median): 21 (RIC), 39 (MAC) • Outpatient clinical visits (median): 19¶	**Initial phase:** • Initial hospitalization (median): $32,444 (RIC), $133,782 (HDCT) **100 d:** • Total cost (median): $63,096 (RIC), $156,253 (HDCT) **1 yr:** • Total cost (median): $120,504 (RIC), $191,990 (HDCT)	USD (2004)	100 d, 1 yr	Entire study cohort

(*continued*)

Table 1 (*Continued*)

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost‡,§	Currency (yr)	Timeframe	Extraction
Yu et al, 2007		18	Taiwan	Economic evaluation (single-center); comparator: HiDAC and Allo-HSCT		Administrative database (January 1994-Januart 2002)	**Follow-up period:** • In-hospital d (median): 48	**Allo-HSCT procedure alone:** • Total cost (mean): $44,510	USD (2003)	Median follow-up, 50 mo	Partial - subgroup
Breitscheidel et al, 2008	MUD	Hypothetical cohort = 1000	Germany	Economic evaluation Comparator: imatinib and MUD-HSCT		IRIS study, EBMT report	•	**5 yr:** • Total cost: $243,255	Euro (2005)	5 yr	Entire study cohort
Saito et al., 2008	HDCT	Early phase = 315, later phase = 252	US	Single-center, retrospective	Descriptive analysis	Institution database (June 2000-July 2004)	**100 d:** • Hospital stay, d (median): 36 **1 yr:** • Hospital stay, d (median): 39	**100 d:** • Total cost (median): $153,550 • Inpatient cost (median): $144,104 • Outpatient cost (median): $6,870 **1 yr:** • Total cost (median): $192,809 • Inpatient cost (median): $164,789 • Outpatient cost (median): $15,708	USD (2004)	100 d (early phase), 1 yr (later phase)	Entire study cohort
Majhail et al., 2009	CB, MRD, non-MAC, MAC	MRD (MAC = 67, non-MAC = 54), CB (MAC = 63, non-MAC=110)	US	Single-center, retrospective study	Descriptive analysis	Institution database and medical records (2004-2006)	**100 d:** • Hospital stay, d (median): 39 MA MRD, 48 MA CB, 23 non-MAC MRD, 38 non-MAC CB • Clinic visits, d (median): 26.53¶ • Dialysis (proportion): 11.04%¶ • Mechanical ventilation (proportion): 29.54%¶	**100 d:** • Total cost (median): $113,890 (non-MAC), $184,904 (MAC), $184,701 (CB), $ 112,223 (MRD)	Dollars (NS)	100 d	Entire study cohort

(*continued*)

Table 1 (*Continued*)

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost‡,§	Currency (yr)	Timeframe	Extraction
Imataki et al., 2010	RIC, MAC	MAC = 35, RIC = 15	Japan	Economic evaluation (single-center); comparator: MAC and RIC		Institution clinical records (January 2000-November 2002)	**Initial phase:** • Initial hospitalization, d (NS: 49 (RIC), 73 (MAC) **Up to 2 yr:** • Duration of total hospitalization, d (NS: 161 (MAC), 106 (RIC)	**Initial phase:** • Conditioning: $12,432 (RIC), $8,860 (MAC) **Up to 2 yr:** • Total cost (mean): $42,107 (RIC), $42,342 (MAC) up to 2 yr	USD (2006)	Up to 2 yr	Entire study cohort
Blommestein et al., 2012	MRD, MUD, CB	MRD = 59, MUD = 43, CB = 21	Netherlands	Multicenter study (n =3), retrospective study	Descriptive analysis	Institution database (2007-2009)	Initial phase: • Initial hospital admission for HSCT phase, d (mean): 19.6 (MRD), 19.1 (MUD), 42.4 (CB)	Initial phase: • Selection/ harvesting cost (mean): $107,664 (CB), $35,551 (MRD), $106,804 (MUD) 1 yr: • Total cost (mean): $419,292 (CB), $167,794 (MRD), $282,308 (MUD) • Inpatient cost (mean): $51,925 • Follow-up (mean): $118,262	Euro (NS)	1 yr	Partial, study arm
Khera et al., 2013	Other stratification: second HSCT, allo-allo and auto-allo	N = 245 (n = 55 allo-allo, n= 190 auto-allo)	US	Single-center, retrospective	Descriptive analysis	Institution database and medical records (2004-2010)	**100 d:** • LOS (median): 12.14¶	**100 d:** • Total cost (median): $157,435¶ • Inpatient cost (median): $50,136¶ • Outpatient cost (median): $94,520¶	USD (2010)	100 d	Entire study cohort

(*continued*)

Table 1 (*Continued*)

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost‡,§	Currency (yr)	Timeframe	Extraction
Majhail et al., 2013		N = 610	US	Population-based retrospective study	Descriptive analysis	Thomson Reuters MarketScan (January 2007- December 2009)	**100 d:** • Duration of hospitalization, d (median): 30 • Outpatient clinic visits (median): 22 • Hospitalizations (median): 1	**Initial phase:** • HSCT hospitalization (median): $182,789 **100 d:** • Total cost (median): $240,384 • Inpatient cost (median): $207,287 • Outpatient cost (median): $24,068	Dollars (NS)	100 d	Partial, study arm
Khera et al., 2014	RIC; other stratification: FHCRC, DF/ BWCC	N = 484	US	Multicenter study (n =2), retrospective study	Descriptive analysis	Institutional clinical and financial database (January 2008-June 2010)	**Day -7 to 100** • Inpatient days (median): 17.39¶ **Days 101-730** • Inpatient days (median): 14	**Days -7 to 100** • Total cost (median): $173,960¶ • Inpatient cost (mean): $125,117¶ • Outpatient cost (mean): $48,843¶ **Days 101-730** • Total cost (median): $118,313	USD (2010)	Beginning of conditioning (day -7) to day 100 (both centers), days 101-730 (DF/ BWCC only)	Entire study cohort
Labopin et al., 2014	sCB, dCB, RIC, MAC	sCB = 61, dCB = 73	France	Economic evaluation (multicenter; n = 26); comparators: sCB and dCB for RIC and MAC		NS	**Initial phase:** • LOS for initial hospitalization, d (mean): 61 (MAC, sCB), 68 (MAC, dCB), 48 (RIC, sCB), 53 (RIC, dCB) **1 yr:** • Outpatient visits, d (NS): 11.71¶ • Further hospitalization, d (mean): 32.13¶	**Initial phase:** • Initial hospitalization cost (mean): $180,293 (RIC)¶, $230,143 (MAC)¶, $189,98 (sCB)¶, $209,750 (dCB)¶ **1 yr:** • Total cost (mean): $316,818 (RIC)¶; $359,165 (MAC)¶; $311,053 (sCB)¶; $353,541 (dCB)¶ • Readmission (mean): $43,221¶ • Outpatient (mean): $17,968¶	Euro (2010)	1 yr	Entire study cohort

(*continued*)

Table 1 (*Continued*)

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost‡,§	Currency (yr)	Timeframe	Extraction
Rauenzahn et al., 2014	PB, RIC	n = 56	US	Single-center, retrospective	Descriptive analysis	Institutional department and medical records (2007-2012)	**Initial phase:** • LOS for index admission, d: 26	**After discharge from index admission to day 100:** • Total charge (median): $85,502 • Inpatient charge (median): $30,040 • Outpatient charge (median): $52,458	USD (NS)	100 d	Partial, study arm
Khera et al., 2015	Allo-BMT	n = 296	US	Single-center, retrospective	Descriptive analysis	Clinical research database (November 2003-October 2012)	**0-3 mo:** • LOS after HCT/ inpatient admission, d (median): 21.73 **3-12 mo:** • LOS after HCT/ inpatient admission, d (median): 8.27 **1 yr:** • Inpatient admissions/ person-yr (NS): 4.29 > **1 yr:** • LOS after HCT/ inpatient admission, d (median): 6	•	•	Median follow-up, 20 mo and 26 mo for the 2 study arms (based on ethnicity)	Entire study cohort
Suh et al., 2015	RIC	n = 79	S. Korea	Single-center, retrospective	Descriptive analysis	Institutional database (2005-2012)	**Initial phase:** • LOS for initial hospitalization, d (mean): 43 1 yr: • Outpatient visits (mean): 22 • Further hospitalizations, d, (mean): 28	**Initial phase:** • Initial hospitalization (mean): $39,416 **1 yr:** • Total cost (mean): $69,218 • Pharmacy cost (mean): $16,497 • Laboratory cost (mean): $6968 • Outpatient visits (mean): $7606 • Readmission (mean): $22,193	USD (2013)	1 yr	Partial, study arm

(*continued*)

Table 1 (*Continued*)

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost‡,§	Currency (yr)	Timeframe	Extraction
Bonafede et al., 2017		n = 972	US	Population-based retrospective study	Descriptive analysis	Truven Health MarketScan commercial and Medicare supplemental databases (January 2011-June 2014)	**1 yr:** • Hospital stay, d (NS): 23.2	**1 yr:** • Total cost (mean): $637,193 • Inpatient costs (mean): $484,650 • Pharmacy cost (mean): $26,773 • Laboratory cost (mean): $36,474 • Physician office visit (mean): $6461	USD (2015)	1 yr	Partial, study arm
Broder et al., 2017	MAC	n = 318	US	Population-based retrospective study	Descriptive analysis	Truven Health MarketScan claims database (January 2010- September 2013)	**Initial phase:** • LOS for index HSCT admission, d (mean): 30.9 **100 d:** • Subsequent hospitalization (proportion): 43.4% • Subsequent LOS, d (mean): 9.4	**Initial phase:** • Index hospitalization (mean): $326,665 **100 d:** • Total cost (mean): $446,888 • Inpatient cost (mean): $372,756 • Outpatient cost (mean): $63,077 • Pharmacy cost (mean): $6188	USD (2013)	100 d	Partial, study arm
Decook et al., 2017	First allo-BMT	n = 328	US	Single-center, retrospective	Descriptive analysis	Medical records (Jan 2010 - Jun 2014)	**Initial phase:** • LOS for initial hospitalization, d (median): 25 **100 d:** • LOS, d (median): 29 **1 yr:** • LOS, d (median): 36	•	•	1 yr	Entire study cohort
Kitazawa et al., 2017	BM, PB	BM = 91, PB = 51	Japan	Population-based retrospective study	Descriptive analysis	National Database of Health Insurance Claims and Specific Health Checkups of Japan (April 2009-March 2010)	Reported HRU (LOS) could not be combined with other studies	Reported costs could not be combined with other studies	JPY (NS)	Month before and up to 2 mo after HSCT	Partial, study arm

(*continued*)

Table 1 (*Continued*)

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost†,§	Currency (yr)	Timeframe	Extraction
Perales et al., 2017	Other stratification: with complications and without complications	With complications, n = 928, without complications, n = 44	US	Population-based retrospective study	Descriptive analysis	Truven Health MarketScan commercial and Medicare supplemental databases (January 2011-June 2014)	**1 yr:** • Readmission (mean, number): 2.2	**1 yr:** • Total cost (mean): $5637,193§	USD (2015)	1 yr	Partial, study arm
Debals-Gonthier et al., 2018	MUD, Haplo, RIC	Haplo = 29, MUD = 63	France	Economic evaluation (single-center); comparator: Haplo and MUD		Institution records (2011-2013), literature	**Initial phase:** • LOS for initial hospitalization, d (mean): 44 (MRD, RIC), 45 (HAPLO)	**Initial phase:** • Pretransplantation phase cost (mean): $71,330 (RIC, MUD), $8705 (HAPLO) • Initial hospitalization (mean): $75,398 (RIC, MUD), $90,710 (Haplo) **2 yr:** • Total cost (mean): $248,903 (RIC, MUD), $161,642 (Haplo)	Euro (2014)	2 yr	Entire study cohort
Maziarz et al., 2018		n = 86	US	Cross-sectional, retrospective study	Descriptive analysis	Two large administrative claims databases, names not specified (2008-2015)	**Initial phase:** • Duration of index hospitalization, d (mean): 27.9 **100 d:** • Inpatient, d (mean): 34.1 • Outpt services, d (mean): 35 • Inpatient admissions (mean): 1.7 1 yr: • Inpatient, d (mean): 38.5 • Outpatient services, d (mean): 100.5 • Inpatient admissions (mean): 2.5	**Initial phase:** • Index hospitalization (mean): $298,974 **100 d:** • Total cost (mean) $431,370 • Inpatient cost (mean): $353,606 • Prescription drug cost (mean): $9519 • Laboratory cost (mean): $ 27,135 **1 yr:** • Total cost (mean) $553,603 • Inpatient cost (mean): $321,981 • Prescription drug cost (mean): $25,417 • Laboratory cost (mean): $73,472	USD (2015)	3 yr	Entire study cohort

(*continued*)

Table 1 (*Continued*)

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost‡,§	Currency (yr)	Timeframe	Extraction
Cho et al., 2019		n = 406	US	Population-based retrospective study	Descriptive analysis	National Inpatient Sample data (January 2012- December 2014)	**Study period:** • LOS, d (mean): 26.5	**Study period:** • Total cost (mean): $146,386	USD (2014)	NS (3-yr study period)	Partial, study arm
Guru Murthy et al., 2019	RIC; other stratification: inpatient and outpatient	Inpatient = 116, outpatient = 35	US	Single-center, retrospective	Descriptive analysis	Chart reviews of institutional transplantation database (January 2014- January 2017)	**100 d:** • Readmission (proportion): 37.59% • Renal replacement therapy (proportion): 3.95%¶ • Mechanical ventilation (proportion): 7.87%¶	**100 d:** • Total charge (median): $300,686¶	Dollars (NS)	100 d	Entire study cohort
Hirt et al., 2019	Other stratification: Germany, Sweden, Canada	NA	Germany, Sweden, and Canada	Economic evaluation; comparator: ponatinib		Literature, national tariffs	•	**Lifetime:** • Total cost: $513,273¶	USD (2014)	Lifetime	Partial, study arm
Kanate et al., 2019	dCB, Haplo	dCB = 37, Haplo = 49	US	Multicenter study (n = 2), retrospective study	Descriptive analysis	Institutional database (March 2009-March 2017)	•	**Initial phase:** • Graft acquisition (mean): $100,663 (CB), $40,042 (Haplo) **100 d:** • Total charge (mean): $782,190 (CB), $699,854 (Haplo) • Inpatient charge (mean): $585,073¶ • Outpatient charge (mean): $ 83,612¶	USD (2018)	100 d	Entire study cohort
Kim et al., 2019	Other stratification: domestic and international donors	n = 159	S. Korea	Multicenter study (n = 5), retrospective study	Descriptive analysis	National Health Insurance Service data (January 2005-April 2015)	•	**1 yr:** • Expense (mean): $48,627¶ **Study period:** • Total expense (mean): $72,848	USD (2017)	Total follow-up (87.4 mo for international donors and NS for domestic donors)	Entire study cohort

(*continued*)

Table 1 (*Continued*)

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost†,§	Currency (yr)	Timeframe	Extraction
Mau et al., 2019	PB, BM, CB, non-MAC, MAC	n = 250	US	Population-based retrospective study	Descriptive analysis	Merged dataset of CMS-Medicare claims data and CIBMTR datasets (March 2010-December 2011)	**1 yr:** • Inpatient service, d (mean): 50 • Outpatient service, visits (mean): 33 • Inpatient admissions (mean): 3	**Initial phase:** • Organ acquisition (mean): $19,011 **100 d:** • Reimbursement (mean): $193,854 **1 yr:** • Reimbursement (mean): $219,475 (non-MAC), $319,626 (MAC) $365,538 (CB), $196,086 (BM), $259,215 (PB), $269,492 (total)	Dollars (NS)	1 yr	Entire study cohort
Mayerhoff et al., 2019	Allo-BMT	Allo subgroup - ≥ 18 ALL (n = 45), DLBCL (n =10), FL (n = 9)	Germany	Population-based retrospective study	Descriptive analysis	German administrative claims data (January 2010-June 2014)	•	Reported costs could not be combined with other studies	Euro (NS)	2 quarters before and 8 quarters after HSCT	Partial, study arm
Gutiérrez-García et al., 2020		Inpatient = 39, outpatient (at home) = 41	Spain	Single-center, retrospective	Descriptive analysis	Department financial director (2015 -2018)	**Initial phase:** • Admission, b (median): 31 **100 d:** • Readmission rate: 24%	100 d: • Total cost (mean): $100,547	Euro (NS)	Time from start of conditioning treatment to engraftment	entire study cohort
Saraf et al., 2020	MRD, PB, non-MAC	n = 16	US	Single-center, retrospective	Descriptive analysis	Clinical data (Augusr 2011-April 2016)	**Initial phase:** • LOS for initial hospitalization, d (median): 33	**Initial phase:** • Inpatient HSCT cost (median): $101,954 **1 yr:** • Total cost (median): $149,156	Dollars (NS)	1 yr	Partial, study arm
Zhou et al., 2020	allo-BMT	n = 436	NS but author affiliation with US universities	Population-based retrospective study	Descriptive analysis	Truven MarketScan Health Databases (January 2009-December 2014)	Reported HRU (LOS) could not be combined with other studies	Reported costs could not be combined with other studies	USD (2014)	•	Partial,- study arm

(*continued*)

Table 1 (*Continued*)

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost‡,§	Currency (yr)	Timeframe	Extraction
Godara et al., 2021	PB, BM, CB	n = 68,296	US	Population-based retrospective study	Descriptive analysis	National Inpatient Sample (NIS) (2002-2015)	**Initial phase:** • LOS (median): 36.9 (CB), 27.2 (BM), 25.4 (PB)	**Initial phase:** • HSCT hospitalization charge (median): $282,596 (PB), $262,758 (BM), $507,532 (CB), $286,950 (total) • HSCT hospitalization cost (median): $ 95,840 (PB), $95,995 (BM), $169,902 (CB), $98,465 (total)	Dollars (NS)	Inpatient admission for HSCT	Entire study cohort
Herr et al., 2021	First allo-BMT	Training cohort, 2010-2016 (n = 349); replication cohort, 2016-2019 (n = 163)	US	Single center	Descriptive analysis	Institution database (training cohort = 2010-2016; replication cohort = 2016-2019)	Reported HRU (LOS) could not be combined with other studies	•	•	1 yr	Entire study cohort
Vijenthira et al., 2021		NA	Canada	Economic evaluation; comparator: ASCT, O-CHOP (3 arms)		Literature	•	**20 yr:** • Total cost: $292,735	CAD (2019)	20 yr	Partial, study arm

(*continued*)

Table 1 (*Continued*)

Study	Allo-HSCT Population*	Sample Size†	Country	Design	Analysis Summary	Data Source	HRU‡	Cost‡,§	Currency (yr)	Timeframe	Extraction
Solana-Altabella et al., 2022		n = 10	Spain	Single-center, retrospective	Descriptive analysis	Institution records (2010-2019)	**Study period:** • LOS, d (mean): 87	**Study period:** • Reimbursement (mean): $104,858	Euro (NS)	NS "period after allo-HSCT"	Partial, subgroup
van Gorkom et al., 2022	MRD, MUD, Haplo	MRD = 29, MUD = 56, Haplo = 24	Netherlands	Single-center, retrospective	Descriptive analysis	Institution records (January 2016-Sept 2018)	**Initial phase:** • LOS for transplantation phase, d (mean): 23.44 (MRD), 22.37 (MUD), 33.83 (HAPLO) **post-transplantation phase to 1 yr:** • LOS, d (mean): 28.21 (MRD); 24.89 (MUD); 19 (Haplo) • Readmissions (mean): 1.73¶	**Initial phase:** • Pretransplantation phase cost (mean): $19,277 (MRD), $44,216 (MUD), $20,208 (Haplo) • Transplantation phase cost (mean): $45,035 (MRD), $52,919 (MUD), $74,780 (Haplo) • Post-transplantation cost (mean): $54,081¶ **1 yr:** • Total cost (NS): $105,350 (MRD), $132,041 (MUD), $129,289 (Haplo)	Euro (2020)	1 yr	Entire study cohort

AML indicates acute myeloid leukemia; ALL, acute lymphoblastic leukemia; ASCT, autologous stem cell transplantation; auto, autologous; CAD, Canadian dollar; dCB, double cord blood; DF/BWCC, Dana-Farber/Brigham and Women's Cancer Center; EBMT, European Society for Blood and Marrow Transplantation; FHCRC, Fred Hutchinson Cancer Research Center; Haplo, haploidentical; HDCT, high-dose chemotherapy; HiDAC, high dose cytarabine; JPY, Japanese yen; MRD, matched related donor; MUD, matched unrelated donor; NS, not specified; O-CHOP, chemo-immunotherapy; sCB, single cord blood.

* Characteristics of the study population eligible for this scoping review.

† Sample size of study population eligible for this scoping review.

‡ Results that could be combined with other studies for the purpose of this scoping review.

§ Monetary values were standardized to 2022 USD.

¶ Weighted average.

‖ Considered initial hospitalization cost, as readmission costs are presented separately.

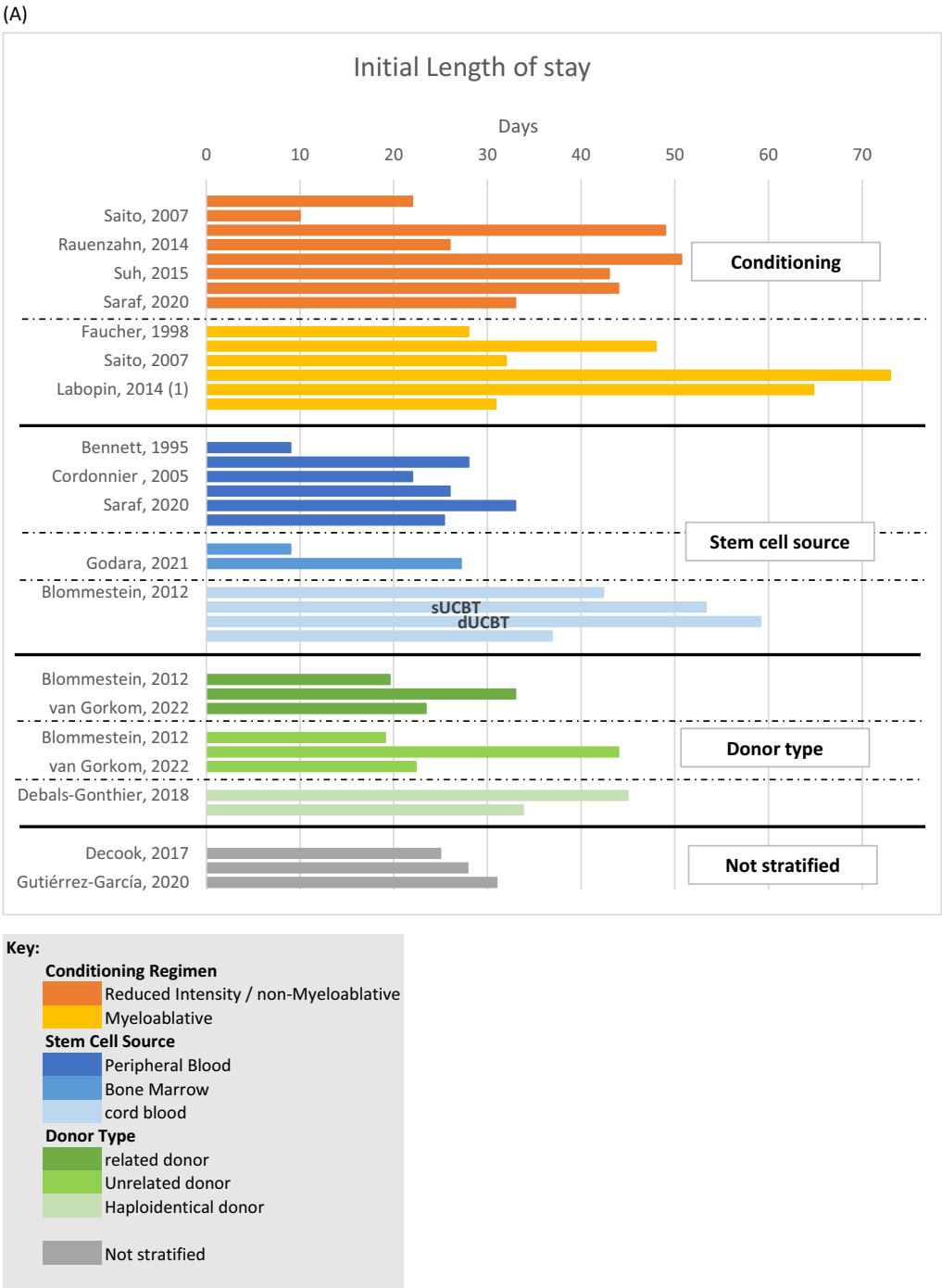

Figure 2. (A) Initial Length of stay

consistent with those presented in one study [46] that reported a direct comparison of LOS according to stem cell source (median LOS: PB, 25.4 days; BM, 27.2 days; CB, 36.9 days). One single-center study [49] presented a direct comparison of mean LOS by donor type, with a longer LOS for haploidentical HSCT (33.83 days) compared to those sources from matched unrelated or related donors (22.37 and 23.44 days, respectively).

LOS by reported timeframe. Nine studies (20.9%) [41,48,50-57] reported the LOS at 100 days, and 8 studies (18.6%) [25,36,41,49,50,52,55,58] reported LOS at 1 year (Figure 2B). Consistent with the LOS for initial hospitalization, RIC was associated with a shorter LOS compared to MAC at 100 days (mean, 21.15 days [41,51,54] and 38.45 days [41,52,54], respectively) and at 1 year (mean, 38.50 days [36,41] and 47.33 days [36,41,52], respectively).

(B)

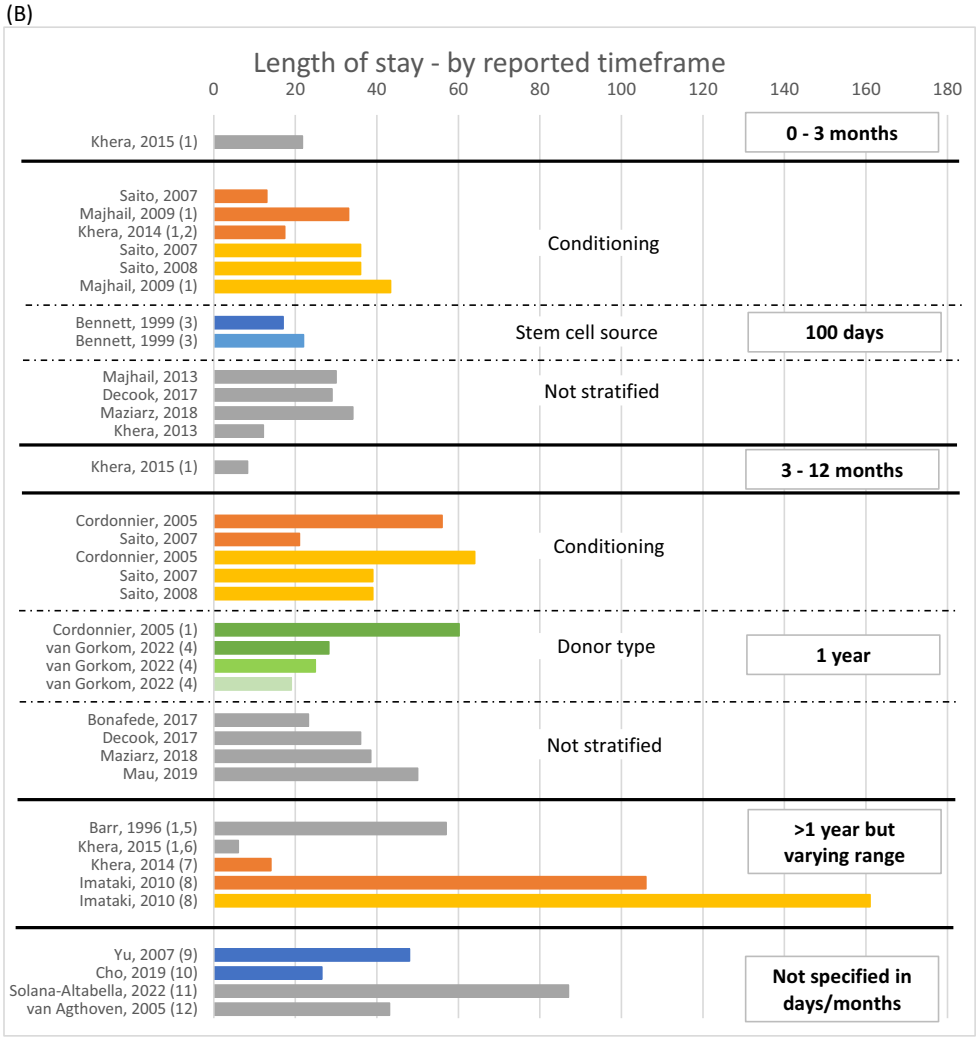

Figure 2. Continued.

(B) Length of stay by reported timeframe.
Notes:
(1) Weighted average was calculated.
(2) Timeframe: days -7 to 100
(3) HSCT recovery (to 100 days post-transplantation)
(4) Post-transplantation phase (defined as discharge to 1 year)
(5) Timeframe: minimum 18 months
(6) Timeframe: > 1 year, median follow-up was 20 months for the minority arm and 26 months for the non-Hispanic arm.
(7) Timeframe: days 101-730
(8) Timeframe: up to 2 years
(9) Timeframe: median follow-up, 50 months (from diagnosis)
(10) Timeframe: 3-year study period
(11) Timeframe: diagnosis to death or last follow-up

One study [48] reported LOS with respect to stem cell source. The timeframe in which these results were reported was "stem cell transplant recovery to 100 days post," thus potentially resulting in an overall shorter LOS (PB, 17 days; BM, 22 days) compared to other definitions of 100 day outcomes.

Results for studies that reported LOS beyond 1 year were not able to be combined due to the diversity in timeframe and the categorization of how the results were presented (eg, by ethnicity, underlying condition, stem cell source and conditions regimen). Fourstudies [59–61,62] did not report a specific timeframe; 1 study reported a minimum of 18-months, 1 reported the study period (3 years), and the other 2 studies reported the phase of follow-up (eg, "period after allo-HSCT," "treatment episode," where day 1 was the start of conditioning regimen).

Studies varied in reporting mean or median results, with few studies reporting both. Two studies presented both the median and the mean initial LOS [43,55], with medians approximately 14% lower than the reported means (mean, 43 and 27.9 days; median, 37 and 24 days, respectively). Another 3 studies [51,55,60] presented both means and medians at varying timeframes, and in all cases the mean was greater than the median; for example, 1 study [51] reported a mean LOS (days 101 to 730) of 14 days; however, the median was 0 days (range, 0 to 146 days).

Other HRU measures

Other HRU measures, which were combined across 2 or more studies at 100 days and 1 year timepoints, are presented in Table 2.

Outpatient Visit. Outpatient visits were reported in 10 studies (23.3%), including 5 studies at 100 days [41,48,53-55] and 5 studies at 1 year [32,41,43,55,58], but could be combined for 8 studies, which reported them at a consistent timepoint. The timeframes presented in the studies not combined [56–61] included "induction period," "treatment episode," or median follow-up. For the purpose of this review, studies that reported outpatient visits in terms of either the number or days of visits were considered to be the same (ie, 1 visit per day). The average number of outpatient visits across the studies was 26.04 visits at 100 days and 37.23 visits at 1 year. The study that reported the largest number of outpatient visits (36.04 visits) at 100 days [48] had a relatively shorter observation period of "stem cell transplant recovery to 100-days post"; however, this shorter period of recovery was considered unlikely to significantly influence results, as patients are likely to be hospitalized during the stem cell recovery period.

Hospital admission and readmission. Five studies (11.6%) presented the number of hospital admissions, at 100 days in 2 of these studies [53,55] and at 1 year in 3 studies [55,56,58], with 1 study [55] presented data at both timepoints. The average number of hospital admissions across the studies was 1.35 at 100 days and 3.26 at 1 year. These data excluded results for 1 study [60], for which the timeframe for reporting was based on "period after allo-HSCT," with a median follow-up of 328 days.

Hospital readmissions were variously reported across the studies as number of readmissions in 2 studies (4.7%) [26,49] at 1 year, readmission rates in 3 studies (7.0%) [45,63,64] at 100 days, and number of readmission hospital days in 5 studies (11.6%), including 2 studies [44,45] at 100 days and 3 studies [32,36,43] at 1 year. The average readmission rate and number of hospital days across the studies at 100 days was 35.0% and 12.2 days, respectively. No studies presented the number of readmissions at 100 days. The average number of readmissions and number of readmission hospital days across the studies at 1 year was 1.96 and 28.25 days, respectively.

Other. Other HRU measures that were combined included 2 studies [54,62] that reported the proportion of patients requiring dialysis/renal replacement therapy (mean, 7.5%) and mechanical ventilation (mean, 18.71%) at 100 days.

The use of other health care resources during the pretransplantation phase, including laboratory testing, acute care (emergency and intensive care), parenteral nutrition/hyperalimentation, drug utilization, and blood transfusions, was variously reported across several studies but has not been summarized owing to a lack of comparability in reporting across the studies. Reporting of these measures varied based on allo-HSCT phase (eg, potential donor HLA typing, HRU associated with workup), categorization of HRU (eg, number of laboratory tests compared to laboratory/imaging services), and variations in HRU measures (eg, number of emergency department visits, proportion of patients with emergency department visits, and days with emergency department service).

Costs Associated with Allo-HSCT

Seven studies (16.3%) [42,46,58,60,63,65,66] reported monetary values in terms of charges (n = 5), reimbursement (n = 1), and expenses (n = 1), whereas all other studies expressed results as costs. One of these studies [46] presented results both in terms of charges and costs. The results of 3 studies [37–39] could not be combined owing to expression of costs as monthly averages and presentation of aggregated costs which included the period prior to transplant.

Initial Phase Costs

Initial phase costs were combined across 17 studies (39.5%) (Table 1). These costs were associated with pretransplantation (n = 9; 20.9%), conditioning regimen (n = 2; 4.7%), and initial hospitalization (n = 12; 27.9%) (Figure 3A).

Studies differed in the reporting of pretransplantation phase costs, using such terms as cost of "harvesting," "collection," "selection/harvesting,"

Table 2
Other HRU and Costs Reported in Studies (presented in ≥2 or more papers)

Parameter	100 Days						1 Year					
			Average						Average			
	No. of Studies	Size	Weighted	Per Study	Minimum	Maximum	No. of Studies	Size	Weighted	Per Study	Minimum	Maximum
Health resource utilization												
Outpatient visits	5	1313	22.00	26.04	10.62	36.04*	5	838	32.09	37.23	11.71	100.5
Admission number	2	696	1.09	1.35	1	1.7	3	632	3.54	3.26	2.50	4.29
Readmission												
Number of readmissions							2	1081	2.15	1.96	1.73†	2.2
Readmission rate, %	3	549	38.98	35.00	24	43.40						
Number of hospital days	2	335	9.68	12.20	9.4	15	3	236	30.02	28.25	24.61	32.13
Other												
Dialysis/renal replacement therapy, %	2	445	8.64	7.50	3.95	11.04						
Mechanical ventilation, %	2	445	22.19	18.71	7.87	29.54						
Cost (2022 USD)												
Hospitalization	7‡	2144	207,062	262,583	50,136	585,073	4	1390	383,337	255,836	51,925	484,650
Readmission							2	213	35,422	32,707	22,193	43,221
Outpatient												
Total cost	7§	2108	44,362	53,350	6870	94,520	2	386	16,492	16,838	15,708	17,968
Clinic visit							2	1051	6547	7034	6461	7606
Follow-up cost							2	232	88,108	86,172	54,081	118,262
Drug cost	3	421	10,544	8920	6188	11,054	3	1094	25,977	22,896	16,497	26,773
Laboratory cost							2	1051	34,256	21,721	6968	36,474

* Study timeframe: HSCT recovery (to 100 days post-transplantation.
† Study timeframe: post-transplantation phase (discharge to 1 year).
‡ Consisted of 1 study with a varied time frame: day -7 to day 100.
§ Consisted of 2 studies with varied time frames: day -7 to day 100 and d discharge up to day 100.

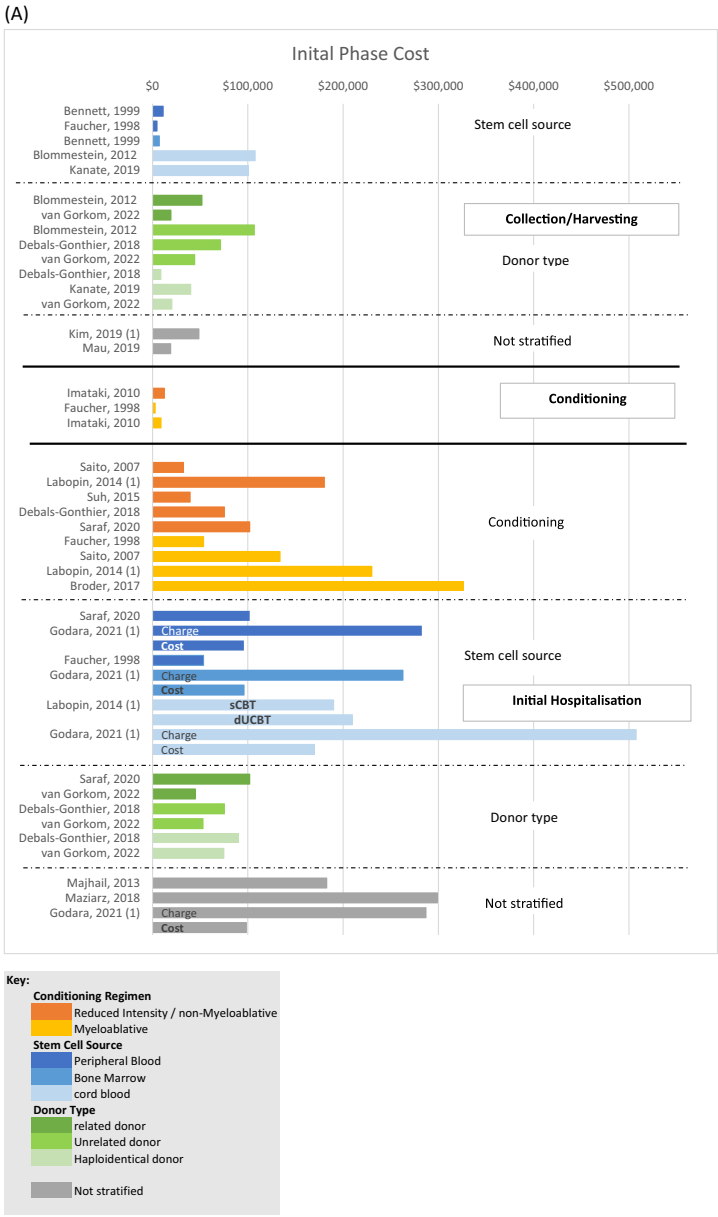

Figure 3. (A) Initial phase costs.

"graft acquisition," "donor search and graft acquisition," and "pretransplant." The results presented here assume these terms to be synonymous. Pretransplantation costs were much higher (approximately 10-fold) for CB-derived stem cells [47,65] compared with PB- [44,48] and BM- [48] derived stem cells (Figure 3A). Pretransplantation costs for matched unrelated donors [33,47,49] (mean, $74,117) were higher than those for related donors [47,49] (mean $35,551) and haploidentical donors [33,49,65] (mean, $22,979). Conditioning regimen costs were presented in 2 studies (4.7%) [31,44], of which 1 [31] presented a direct comparison between conditioning approaches and noted a higher cost for RIC compared to MAC ($12,732 versus $8,860).

Eleven studies (25.6%) [32,33,40,41,43-46,49,53,55] presented costs for initial hospitalization (Table 1), which ranged from $32,444 to $507,532. Overall, the use of RIC regimens [32,33,40,41,43] was associated with a lower initial hospitalization cost compared to MAC regimens [32,41,44,45] (mean, $85,901 and $186,029, respectively). These findings were consistent with those from 2 studies [32,41] that presented a direct comparison of these factors (RIC, $32,444 and $180,293, respectively; MAC, $133,782 and $230,143, respectively). When considering costs

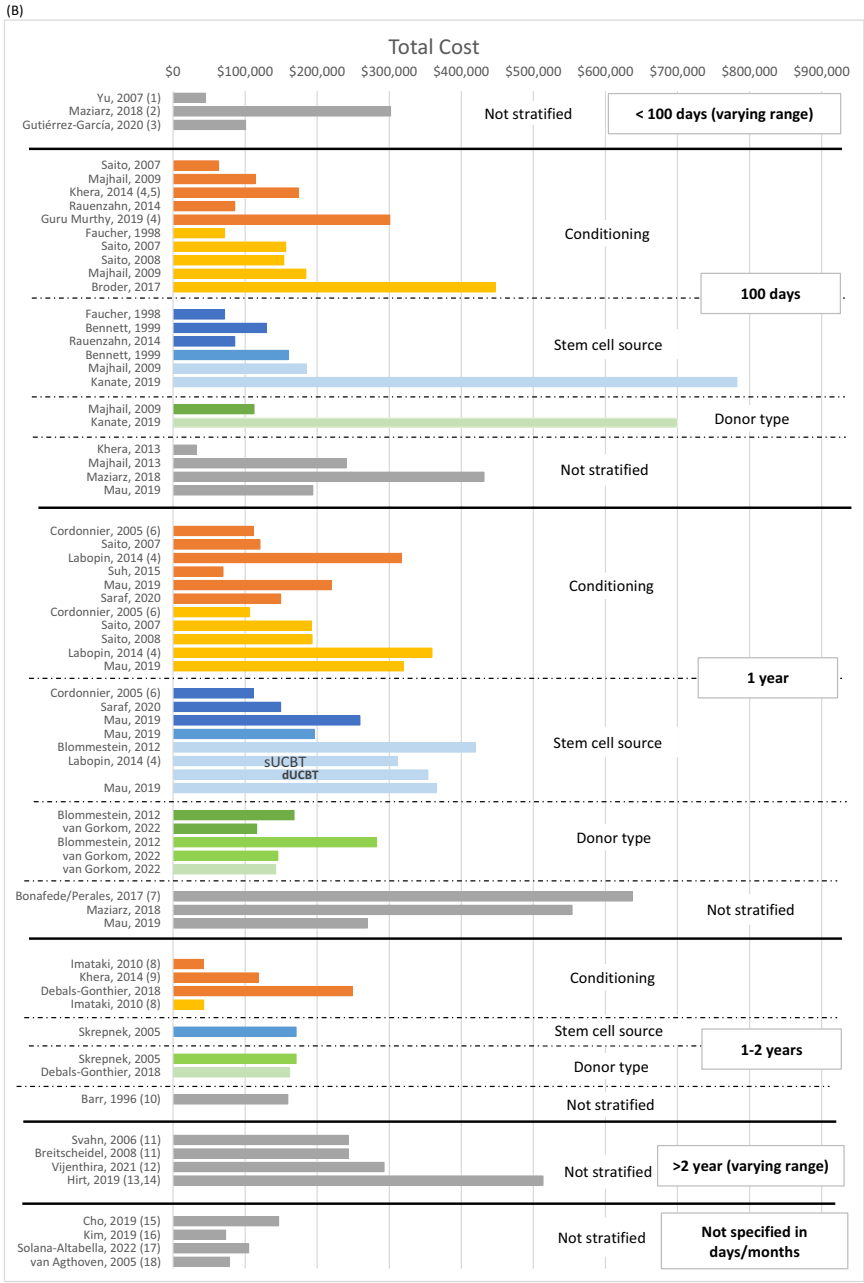

Figure 3. Continued.

(B) Total cost by reported timeframe.
Notes:
(1) Timeframe: allo-HSCT procedure alone
(2) Timeframe: index hospitalization
(3) Timeframe: time from start of conditioning treatment to engraftment
(4) Weighted average was calculated.
(5) Timeframe: days -7 to 100
(6) Timeframe: days -8 to 365
(7) Bonafede et al. (2017) and Perales et al. (2017) appeared to be based on the same dataset and presented the same results.
(8) Timeframe: up to 2 years
(9) Timeframe: Day 101-730
(10) Timeframe: minimum 18 months
(11) Timeframe: 5 years
(12) Timeframe: 20 years
(13) Timeframe: lifetime
(14) Average across the 3 countries reported (Germany, Sweden and Canada)
(15) Not specified (3-year study period)
(16) Total follow-up (87.4 months for international donors; domestic, not specified).
(17) Not specified, period after allo-HSCT
(18) Not specified, 3 years. Reflective of "treatment episode," ie, day 1 of conditioning regimen

(over charges) reported by Godara et al. 2021 [46], initial hospitalization costs with CB stem cells as the donor source [32,46] (mean, $185,328) were higher than those associated with BM [46] ($90,391) and PB [40,44,46] (mean $83,774) stem cells as the donor source.

Total Cost – by reported timeframe

Thirty-six studies (83.7%) reported on the total cost of allo-HSCT over different timeframes (Table 1), including 15 (34.9%) at 100 days, 13 (30.2%) at 1 year, and 8 at various timeframes beyond 1 year (with the maximum being a lifetime time horizon as part of an economic model [24]; Figure 3B).

The overall total cost reported at 100 days ranged from $63,096 to $782,190, and that at 1 year ranged from $69,218 to $637,193. Total costs associated with RIC were lower than those associated with MAC at 100 days (mean, $147,427 [41,42,51,54,62] and $202,425 [41,44,45,52,54], respectively), and at 1 year (mean, $164,442 [32,36,40,41,43,58] and $233,937 [32,36,41,52,58], respectively). Consistent with initial hospitalization, costs associated with CB stem cells [32,47,54,58,64] were higher at 100 days and 1 year compared to stem cells sourced from BM [48,58] and PB [36,40,42,44,48,58], respectively (Figure 3B).

Other Costs

Other costs that were combined across 2 or more studies at 100 days and 1 year timepoints are presented in Table 2.

Total hospitalization and readmission cost. Total hospitalization costs at 100 days and 1 year were reported in 8 (18.6%) [42,45,51-53,55,57,65] and 4 (9.3%) [25,47,52,55] studies, respectively. Costs reported across the studies differed by approximately 12-fold (minimum to maximum) at 100 days (range, $50,136 to $585,073) and by and 9-fold at 1 year (range, $51,925 to $484,650). The average cost of hospitalization was $262,583 across the studies reporting total hospitalization costs at 100 days and $255,836 for studies reporting total hospitalization costs at 1 year. The average readmission cost at 1 year was $32,707 across 2 studies [32,43].

One study [42] presented hospitalization costs from discharge to up to 100 days ($30,040); however, these results could not be combined with results of other studies, as the cost calculation did not include hospital charges during the index transplantation admission.

Total outpatient and clinic visit costs. Total outpatient costs were reported at 100 days in 7 studies (16.3%) [42,45,51-53,57,64] and at 1 year in 2 studies (4.7%) [32,52]. One of the studies [42] had a slightly varied timeframe (ie, discharge from index transplant admission up to day 100); however, this was considered to have a minimal impact on total outpatient costs. The average total outpatient cost across the studies was $53,350 at 100 days and $16,838 at 1 year. The average outpatient costs appeared to be higher at 100 days than at 1 year. Two studies (4.7%) [25,43] presented clinic visit costs at 1 year (which averaged $7,034).

Postdischarge costs. Two studies (4.7%) [47,49] presented costs associated with the postdischarge period. One study referred to this as "post-transplantation," and the other called it the "follow-up" phase. The timeframe between these studies differed; the former study defined it as the period from discharge to 1 year after allo-HSCT, whereas the latter calculated costs at the 1 year follow-up. The average postdischarge cost at 1 year was $86,172 across the studies.

Drug and laboratory costs. Across 3 studies (7.0%), the average drug costs were $8,920 at 100 days [44,45,55] and $22,896 at 1 year [25,43,55]. Laboratory costs at 1 year were presented in 2 studies (4.7%) [25,43], with a mean cost of $21,721.

DISCUSSION

This review summarizes the evidence in relation to HRU and costs associated with allo-HSCT. LOS was the most widely reported HRU measure, with 39.5% of studies reporting the initial LOS and 46.5% reporting LOS at various timeframes. The duration of initial hospitalization ranged from 9 days (PB/BM) to 73 days (MAC) and from 13 days (RIC) to 43.36 days (MRD, MAC) at 100 days, and from 19 days (haploidentical) to 64 days (MRD, MAC) at 1 year. The total cost of an allo-HSCT, reported in 83.7% of studies, ranged from $63,096 (RIC) to $782,190 (double CB transplantation) at 100 days, and from $69,218 (RIC) to $637,193 at 1 year (not stratified).

Overall, RIC conditioning was associated with lower cost and LOS compared to MAC, both in the initial phases of allo-HSCT and at 1 year. The use of CB-derived stem cells was associated with higher total costs, potentially driven by the higher costs of collecting and harvesting CB stem cells compared to stem cells sourced from PB or BM.

Whereas overall trends in HRU and costs, based on donor, stem cell source, and conditioning regimen were evident, quantifying these trends to inform the design and delivery of health care for HSCT is challenging because of the heterogeneity in how these results have been reported.

Heterogeneity in the costs associated with HSCT has been reported in previous reviews. Khera et al. [10] noted variations in study population, diagnoses, perspectives of analyses, time horizons, and study methods. According to Preussler et al. 2012 [11], the economic aspects of HSCT require further evaluation, and costs need to be better described. This scoping review has shown that the variation in reporting remains, particularly with respect to the time periods for which HRU and costs are reported, the HRU measures used, and the methods used to quantify costs.

There were inconsistencies among the studies reviewed in how measures of HRU and costs were expressed—as either means or medians, with a very small proportion reporting both. In the studies that reported both, the mean was greater than the median. Using the median to report costs disregards the distribution of the results, such as skewness of the data, and thus potentially underestimates the effects of extreme cases of total HRU and costs [67]. However, budgetary and resource requirement decisions need to account for costs and HRU for extreme outlier patients. Thus, the use of means may be more informative for assessment and policy analysis, as it incorporates the impact of these outlier patients while reflecting the overall average cost, thereby providing a more accurate basis for estimating allo-HSCT-associated costs and HRU as they are incurred.

The level of costing details provided in the studies with respect to cost inputs and how costs were calculated varied greatly across the studies. Studies ranged from not specifying this information to presenting detailed disaggregated assessment of cost inputs, their definition, and the contribution of these cost inputs to the overall costs. Some studies reported monetary values in terms of healthcare costs (usually incurred by the provider), others in terms of charges (commonly reimbursed by the payer), whereas others did not clearly articulate the perspective taken. Rationalization for the preference of reporting cost or charges differed among the studies. One US study [42] rationalized the use of hospital charges to circumvent variations in reimbursement across different payers and jurisdictions. Another US study [59] converted charges from the National Inpatient Sample (NIS) database to costs, as this was more reflective of the actual expenses (rather than charges billed by the institution) of the resource requirements. Although often used interchangeably, costs and charges differ, as highlighted in one study [46] that reported a 3-fold difference in the median cost and charge of transplantation hospitalization ($92,717 cost versus $270,198 charge). It is not uncommon for healthcare costing literature to use charges as a proxy for economics costs; however, this may lead to unwarranted conclusions regarding economic efficiency [68].

The extent of costs presented are as reported by the included studies. There may be aspects of real-world patient care (eg, transfer of patient care across institutions) that are not covered in this review because they were not stated in the studies. There are differences in allo-HSCT funding structures (eg, government or private payers), which vary across countries. Understanding that those differences can affect the context and basis of costing (eg, fees, charges, government-based funding allocations or resource-based costing) is critical for interpreting the evidence. For policymakers and government to make informed decisions, the actual HRU and the direct costs associated with the utilization of these services directly, are considered to provide a more accurate measure of cost.

Similar to the findings reported by Preussler et al. [11], many of the presented studies (39.6%) were derived from single-center projects often reflective of institutional practice [11]. Variations in allo-HSCT procedural practice among institutions include patient eligibility for transplantation, choice of conditioning regimen (RIC or MAC), donor selection, supportive care practices, and management of transplantation-associated adverse events [69,70]. Differences in allo-HSCT practice across centers have implications for HRU and cost; for example, one study [51] reported the impact of cost distribution at 2 centers based on preference for inpatient and outpatient conditioning, with the total outpatient costs inversely correlated to hospitalization costs at 100 days. The total outpatient costs at these 2 centers were $22,599 and $109,008, whereas the inpatient costs were $144,901 and $79,762 respectively. The study noted that successful interventions to reduce cost are heavily dependent on the local (institutional) environment. It is understood that there are challenges associated with the conduct of multicenter costing studies, attributed to the

complexity and decentralization of the healthcare system in many countries, due to the sharing of the health system initiatives, funds and governance across national and state governments [71,72]. However, further studies are needed to understand the HRU and costs of allo-HSCT from a health system perspective.

None of the identified published studies originate from Australia. However, there is a known study undertaken by the Centre for Health Service Development, University of Wollongong which was not identified through the literature search because it was published through the University's website. This costing study was commissioned by the New South Wales Department of Health in 2009 to provide a costing of HSCT services in New South Wales, Australia's most populous state [73]. The study examined the cost of both allogeneic HSCT and autologous HSCT in adult and pediatric hospitals. The study dataset was defined as data from 8 centers (of the 15 HSCT hospitals) that operated clinical costing systems. The window of service costed by the study commenced at 60 days pretransplantation and ended at 365 days post-transplantation (longer than the 1-year timeframe reported in this review). The total cost per allo-HSCT at an adult hospital was calculated as $121,669 USD, which falls within the range of total costs at 1 year identified in this study. Consistent with the findings of our scoping review, the study also noted that models of care and treatment pathways varied among hospitals and potentially resulted in variations in cost across the centers.

There are several limitations to this scoping review. First, HRU and costs were stratified by potential variables associated with allo-HSCT; HRU and cost differences arising due to underlying clinical diagnosis were not explored. Although some studies were specific to the underlying disease, others presented the proportion of patients with the underlying diseases. Furthermore, because the scoping review consisted of partial extraction of study arms and subgroups, the clinical characteristics of the specific cohort of interest often were not presented by a study. Second, although it is likely that differences for lower-intensity conditioning regimens (RIC or nonmyeloablative) may be associated with different outcomes and thus HRU and costs, it was not possible to further differentiate beyond the current presentation of data, as the studies included did not separate results based on the reporting of these regimens. Where a study reported nonmyeloablative regimens, this was highlighted in Table 1. Third, the studies varied in their use of reporting the mean or median measures of HRU and costs. Consequently, in some instances we combined those measures of central tendency. However, we recognize that this has the potential to underestimate HRU and cost; that is, in the few studies that reported both means and medians, the medians were lower than the means. Fourth, the costing inputs for the individual studies were not evaluated. Studies varied in the calculation of allo-HSCT associated costs, and thus comparisons across studies in the methods used to derive costs was not possible. Finally, cost calculation to present value may be confounded by the choice of pricing index and the year in which it was applied.

This review included studies focused on the overall cost of care of allo-HSCT to obtain a better understanding of the contemporary estimate of costs. It is understood that recent advances (eg, in the management of GVHD) might have cost and HRU implications. Preparation of a separate focused review is underway that addresses the literature as it pertains to specific therapies or aspects of allo-HSCT.

Further research is needed to understand the key determinants of HRU and costs associated with allo-HSCT to inform standards for the conduct of HRU and cost analyses. This would enable consistency in reporting and comparability across studies to accurately reflect the resource requirements for the design and delivery of allo-HSCT care.

CONCLUSION

There is heterogeneity in the reporting of HRU and costs associated with allo-HSCT in the literature making it difficult for clinicians, policymakers, and government officials to draw definitive conclusions regarding the resources required for the delivery of these services. Nevertheless, to ensure that access to healthcare meets the necessary high cost and resource demands of allo-HSCT, it is imperative that clinicians, policymakers, and government officials be aware of both the short- and long-term health resource requirements for this patient population. Further research is needed to understand the key determinants of HRU and costs associated with allo-HSCT, to better inform the design and delivery of health care for HSCT recipients and ensure the quality, safety, and efficiency of care.

ACKNOWLEDGMENTS

Financial disclosure: This project is supported by an Australian Government Research Training Program Scholarship (to N.V.K.).

Conflict of interest statement: There are no conflicts of interest to report.

Authorship statement: N.V.K., S.Y., I.K., and R.D.A.L. designed the study; N.V.K. acquired the data; N.V.K. and G.M. extracted the data; N.V.K., S.Y., I.K., and R.D.A.L. analyzed the data; and N.V.K., G.M., I.K., M.G., and R.D.A.L. drafted, reviewed, and approved the final manuscript.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.jtct.2024.01.084.

REFERENCES

1. Mohty B, Mohty M. Long-term complications and side effects after allogeneic hematopoietic stem cell transplantation: an update. *Blood Cancer J*. 2011;1:e16.
2. Gifford G, Gilroy N, Dyer G, et al. The experience of survival following allogeneic haematopoietic stem cell transplantation in New South Wales. *Australia.* Bone Marrow Transplant. 2016;51:1361–1368.
3. McErlean G, Brice L, Gilroy N, et al. Long-term treatment burden following allogeneic blood and marrow transplantation in NSW, Australia: a cross-sectional survey. *J Cancer Surviv*. 2022;16:432–444.
4. Eton DT, Ramalho de Oliveira D, Egginton JS, et al. Building a measurement framework of burden of treatment in complex patients with chronic conditions: a qualitative study. *Patient Relat Outcome Meas*. 2012;3:39–49.
5. Australian Government Department of Health and Aged Care. Review of the HPC sector—final report 2018. Available at: https://www.health.gov.au/resources/publications/review-of-the-hpc-sector-final-report-2018?language=en. Accessed August 1, 2023.
6. Stranges E, Russo CA, Friedman B. Procedures with the most rapidly increasing hospital costs, 2004–2007. *Healthcare Cost and Utilization Project (HCUP) Statistical Briefs [Internet]*. Rockville, MD: Agency for Healthcare Research and Quality (US). Statistical Brief #82; December 2009.
7. D'Souza A, Fretham C, Lee SJ, et al. Current use of and trends in hematopoietic cell transplantation in the United States. *Biol Blood Marrow Transplant*. 2020;26:e177–e182.
8. Rocha V, Fatobene G, Niederwieser D, et al. Increasing access to allogeneic hematopoietic cell transplant: an international perspective. *Hematology Am Soc Hematol Educ Program*. 2021;2021:264–274.
9. Carrasquillo O. Health care utilization. In: Gellman MD, Turner JR, eds. *Encyclopedia of Behavioral Medicine*. New York, NY: Springer; 2013:909–910.
10. Khera N, Zeliadt SB, Lee SJ. Economics of hematopoietic cell transplantation. *Blood*. 2012;120:1545–1551.
11. Preussler JM, Denzen EM, Majhail NS. Costs and cost-effectiveness of hematopoietic cell transplantation. *Biol Blood Marrow Transplant*. 2012;18:1620–1628.
12. Bashey A, Zhang X, Sizemore CA, et al. T-cell-replete HLA-haploidentical hematopoietic transplantation for hematologic malignancies using post-transplantation cyclophosphamide results in outcomes equivalent to those of contemporaneous HLA-matched related and unrelated donor transplantation. *J Clin Oncol*. 2013;31:1310–1316.
13. Gooptu M, Koreth J. Translational and clinical advances in acute graft-versus-host disease. *Haematologica*. 2020;105:2550–2560.
14. Peters MDJ, Marnie C, Tricco AC, et al. Updated methodological guidance for the conduct of scoping reviews. *JBI Evid Synth*. 2020;18:2119–2126.
15. Canadian Agency for Drugs and Technologies in Health (CADTH). Grey Matters: a practical tool for searching health-related grey literature. 2019. Available at: https://greymatters.cadth.ca/. Accessed November 1, 2022.
16. The World Bank. World Bank Country and Lending Groups. 2021. Available at: https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups. Accessed June 1, 2022.
17. Rivera Franco MM, Leon Rodriguez E. Importance of nongovernmental organizations for the establishment of a successful hematopoietic stem-cell transplantation program in a developing country. *J Glob Oncol*. 2018;4:1–8.
18. Veritas Health Innovation. *Covidence systematic review software*. Australia: Melbourne; 2022
19. Belur J, Tompson L, Thornton A, Simon M. Interrater reliability in systematic review methodology: exploring variation in coder decision-making. *Sociol Methods Res*. 2021;50:837–865.
20. Mak HK, Yau KK, Chan BP. Prevalence-adjusted bias-adjusted kappa values as additional indicators to measure observer agreement. *Radiology*. 2004;232:302–303.
21. Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. *BMC Med Res Methodol*. 2018;18:143.
22. Board of Governors of the Federal Reserve System. Federal Reserve Board: Data Download Program - Home. Available at: https://www.federalreserve.gov/datadownload/. Accessed July 3, 2023.
23. U.S. Bureau of Labor Statistics Databases, tables and calculators by subject. Available at: https://data.bls.gov/timeseries/CUUR0000SA0L1E?output_view=pct_12mths. Accessed July 3, 2023.
24. Hirt C, Iannazzo S, Chiroli S, et al. Cost effectiveness of the third-generation tyrosine kinase inhibitor (TKI) ponatinib, vs. second-generation TKIs or stem cell transplant, as third-line treatment for chronic-phase chronic myeloid leukemia. *Appl Health Econ Health Policy*. 2019;17:555–567.
25. Bonafede M, Richhariya A, Cai Q, et al. Real-world economic burden of hematopoietic cell transplantation among a large US commercially insured population with hematologic malignancies. *J Med Econ*. 2017;20:1244–1251.
26. Perales MA, Bonafede M, Cai Q, et al. Real-world economic burden associated with transplantation-related complications. *Biol Blood Marrow Transplant*. 2017;23:1788–1794.
27. Barr R, Furlong W, Henwood J, et al. Economic evaluation of allogeneic bone marrow transplantation: a rudimentary model to generate estimates for the timely formulation of clinical policy. *J Clin Oncol*. 1996;14:1413–1420.
28. Skrepnek GH, Ballard EE. Cost-efficacy of imatinib versus allogeneic bone marrow transplantation with a matched unrelated donor in the treatment of chronic myelogenous leukemia: a decision-analytic approach. *Pharmacotherapy*. 2005;25:325–334.

29. Yu YB, Gau JP, You JY, et al. Cost-effectiveness of postremission intensive therapy in patients with acute leukemia. *Ann Oncol*. 2007;18:529–534.
30. Breitscheidel L. Cost utility of allogeneic stem cell transplantation with matched unrelated donor versus treatment with imatinib for adult patients with newly diagnosed chronic myeloid leukaemia. *J Med Econ*. 2008;11:571–584.
31. Imataki O, Kamioka T, Fukuda T, Tanosaki R, Takaue Y. Cost and effectiveness of reduced-intensity and conventional allogeneic hematopoietic stem cell transplantation for acute myelogenous leukemia and myelodysplastic syndrome. *Support Care Cancer*. 2010;18:1565–1569.
32. Labopin M, Ruggeri A, Gorin NC, et al. Cost-effectiveness and clinical outcomes of double versus single cord blood transplantation in adults with acute leukemia in France. *Haematologica*. 2014;99:535–540.
33. Debals-Gonthier M, Siani C, Faucher C, et al. Cost-effectiveness analysis of haploidentical vs matched unrelated allogeneic hematopoietic stem cells transplantation in patients older than 55 years. *Bone Marrow Transplant*. 2018;53:1096–1104.
34. Vijenthira A, Kuruvilla J, Prica A. Cost-effectiveness analysis of allogeneic versus autologous stem cell transplant versus chemo-immunotherapy for early relapse of follicular lymphoma within 2 years of initial therapy. *Bone Marrow Transplant*. 2021;56:2400–2409.
35. Herr MM, Rehman S, Zhang Y, et al. Replicated risk index of patient functional status prior to allogeneic hematopoietic cell transplantation predicts healthcare utilization and survival. *Transplant Cell Ther*. 2021;27:875.e1–875.e9.
36. Cordonnier C, Maury S, Esperou H, et al. Do minitransplants have minicosts? A cost comparison between myeloablative and nonmyeloablative allogeneic stem cell transplant in patients with acute myeloid leukemia. *Bone Marrow Transplant*. 2005;36:649–654.
37. Kitazawa T, Matsumoto K, Fujita S, Seto K, Hasegawa T. Cost analysis of transplantation in Japan, performed with the use of the national database. *Transplant Proc*. 2017;49:4–9.
38. Mayerhoff L, Lehne M, Hickstein L, et al. Cost associated with hematopoietic stem cell transplantation: a retrospective claims data analysis in Germany. *J Comp Eff Res*. 2019;8:121–131.
39. Zhou J, Nutescu EA, Han J, Calip GS. Clinical trajectories, healthcare resource use, and costs of long-term hematopoietic stem cell transplantation survivors: a latent class analysis. *J Cancer Surviv*. 2020;14:294–304.
40. Saraf SL, Ghimire K, Patel P, et al. Improved health care utilization and costs in transplanted versus non-transplanted adults with sickle cell disease. *PLoS One*. 2020;15: e0229710.
41. Saito AM, Zahrieh D, Cutler C, et al. Lower costs associated with hematopoietic cell transplantation using reduced intensity vs high-dose regimens for hematological malignancy. *Bone Marrow Transplant*. 2007;40:209–217.
42. Rauenzahn S, Truong Q, Cumpston A, et al. Predictors and impact of thirty-day readmission on patient outcomes and health care costs after reduced-toxicity conditioning allogeneic hematopoietic cell transplantation. *Biol Blood Marrow Transplant*. 2014;20:415–420.
43. Suh KJ, Kim I, Lim J, et al. Total costs and clinical outcome of hematopoietic stem cell transplantation in adults with leukemia: comparison between reduced-intensity and myeloablative conditioning. *Clin Transplant*. 2015;29:124–133.
44. Faucher C, Fortanier C, Viens P, et al. Clinical and economic comparison of lenograstim-primed blood cells (BC) and bone marrow (BM) allogeneic transplantation. *Bone Marrow Transplant*. 1998;21(suppl 3):S92–S98.
45. Broder MS, Quock TP, Chang E, et al. The cost of hematopoietic stem-cell transplantation in the United States. *Am Health Drug Benefits*. 2017;10:366–374.
46. Godara A, Siddiqui NS, Munigala S, et al. Length of stay and hospital costs for patients undergoing allogeneic stem-cell transplantation. *JCO Oncol Pract*. 2021;17:e355–e368.
47. Blommestein HM, Verelst SG, Huijgens PC, Blijlevens NM, Cornelissen JJ, Uyl-de Groot CA. Real-world costs of autologous and allogeneic stem cell transplantations for haematological diseases: a multicentre study. *Ann Hematol*. 2012;91:1945–1952.
48. Bennett C, Waters T, Stinson T, et al. Valuing clinical strategies early in development: a cost analysis of allogeneic peripheral blood stem cell transplantation. *Bone Marrow Transplant*. 1999;24:555–560.
49. van Gorkom G, Van Elssen C, Janssen I, Groothuis S, Evers S, Bos G. The impact of donor type on resource utilisation and costs in allogeneic haematopoietic stem cell transplantation in the Netherlands. *Eur J Haematol*. 2022;108:327–335.
50. Decook L, Chang YH, Slack J, et al. Association of hematopoietic cell transplantation-specific comorbidity index with resource utilization after allogeneic transplantation. *Bone Marrow Transplant*. 2017;52:998–1002.
51. Khera N, Emmert A, Storer BE, Sandmaier BM, Alyea EP, Lee SJ. Costs of allogeneic hematopoietic cell transplantation using reduced intensity conditioning regimens. *Oncologist*. 2014;19:639–644.
52. Saito AM, Cutler C, Zahrieh D, et al. Costs of allogeneic hematopoietic cell transplantation with high-dose regimens. *Biol Blood Marrow Transplant*. 2008;14:197–207.
53. Majhail NS, Mau LW, Denzen EM, Arneson TJ. Costs of autologous and allogeneic hematopoietic cell transplantation in the United States: a study using a large national private claims database. *Bone Marrow Transplant*. 2013;48:294–300.
54. Majhail NS, Mothukuri JM, Brunstein CG, Weisdorf DJ. Costs of hematopoietic cell transplantation: comparison of umbilical cord blood and matched related donor transplantation and the impact of posttransplant complications. *Biol Blood Marrow Transplant*. 2009;15:564–573.
55. Maziarz RT, Hao Y, Guerin A, et al., et al. Economic burden following allogeneic hematopoietic stem cell transplant in patients with diffuse large B-cell lymphoma. *Leuk Lymphoma*. 2018;59:1133–1142.
56. Khera N, Chang YH, Slack J, et al. Impact of race and ethnicity on outcomes and health care utilization after allogeneic hematopoietic cell transplantation. *Leuk Lymphoma*. 2015;56:987–992.
57. Khera N, Storer B, Sandmaier BM, Chapko MK, Lee SK. Costs of second allogeneic hematopoietic cell transplantation. *Transplantation*. 2013;96:108–115.
58. Mau LW, Meyer C, Burns LJ, et al. Reimbursement, utilization, and 1-year survival post-allogeneic transplantation for Medicare beneficiaries with acute myeloid leukemia. *JNCI Cancer Spectr*. 2019;3:pkz048.
59. Cho SK, McCombs J, Punwani N, Lam J. Complications and hospital costs during hematopoietic stem cell transplantation for non-Hodgkin lymphoma in the United States. *Leuk Lymphoma*. 2019;60:2464–2470.
60. Solana-Altabella A, Megías-Vericat JE, Ballesta-López O, et al. Healthcare resource utilization among patients between 60-75 years with secondary acute myeloid

leukemia receiving intensive chemotherapy induction: a Spanish retrospective observational study. *Cancers (Basel)*. 2022;14:1921.
61. van Agthoven M, Kramer MH, Sonneveld P, et al. Cost analysis of common treatment options for indolent follicular non-Hodgkin's lymphoma. *Haematologica*. 2005;90:1422–1432.
62. Svahn BM, Alvin O, Ringdén O, Gardulf A, Remberger M. Costs of allogeneic hematopoietic stem cell transplantation. *Transplantation*. 2006;82:147–153.
63. Guru Murthy GS, Hari PN, Szabo A, et al. Outcomes of reduced-intensity conditioning allogeneic hematopoietic cell transplantation performed in the inpatient versus outpatient setting. *Biol Blood Marrow Transplant*. 2019;25:827–833.
64. Gutiérrez-García G, Rovira M, Arab N, et al. A reproducible and safe at-home allogeneic haematopoietic cell transplant program: first experience in Central and Southern Europe. *Bone Marrow Transplant*. 2020;55:965–973.
65. Kanate AS, Szabo A, Raj RV, et al. Comparison of graft acquisition and early direct charges of haploidentical related donor transplantation versus umbilical cord blood transplantation. *Biol Blood Marrow Transplant*. 2019;25:1456–1464.
66. Kim SA, Lee J, Moon JH, et al. Utility of allogeneic hematopoietic stem cell transplantation using international donors in a homogenous ethnic population: question in the era of various alternative donors. *Ann Hematol*. 2019;98:501–510.
67. Mani K, Lundkvist J, Holmberg L, Wanhainen A. Challenges in analysis and interpretation of cost data in vascular surgery. *J Vasc Surg*. 2010;51:148–154.
68. Finkler SA. The distinction between cost and charges. *Ann Intern Med*. 1982;96:102–109.
69. Bevans M, Tierney DK, Bruch C, et al. Hematopoietic stem cell transplantation nursing: a practice variation study. *Oncol Nurs Forum*. 2009;36:E317–E325.
70. Majhail NS, Mau LW, Chitphakdithai P, et al. Transplant center characteristics and survival after allogeneic hematopoietic cell transplantation in adults. *Bone Marrow Transplant*. 2020;55:906–917.
71. Australian Government Department of Health and Aged Care. The Australian Health System. 2019. Available at: https://www.health.gov.au/about-us/the-australian-health-system. Accessed March 1, 2022.
72. Brown LD. Comparing health systems in four countries: lessons for the United States. *Am J Public Health*. 2003;93:52–56.
73. Gordon R, Thompson C, Carolan J, Eckstein G, Rostron C. *A costing study of blood and marrow transplantation services in NSW: Final report*, Wollongong, Australia: University of Wollongong Centre for Health Service Development; 2009.