

## ARTICLE



# Increasing access to hematopoietic cell transplantation in Latin America: results of the 2018 LABMT activity survey and trends since 2012

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A total of 5642 hematopoietic cell transplants (HCT) in 5445 patients (2196—40% allogeneic and 3249—60% autologous) were reported by 127 teams in 14 Latin American countries that answered the 2018 LABMT/WBMT Global Transplant Activity survey. The transplant rate (defined as the number of first transplants per 10 million inhabitants per year) was 85 (51 autologous and 34 allogeneic) in 2018. The main indications for allogeneic HCT were acute leukemias (60%), while plasma cell disorders and lymphomas were the most common conditions warranting autologous HCT (50 and 36%, respectively). In the allogeneic HCT, HLA-identical siblings were the main type of donor (44%) followed by related mismatched/haploidentical donors (32%). Peripheral blood stem cells were used in 98% of the autologous and in 64% of the allogeneic transplants. From 2012 to 2018, there was a 64% increase of reported HCT (54% in autologous and 80% in allogeneic). In the allogeneic setting, the most pronounced increase in donor type was observed in haploidentical relatives (from 94 procedures in 2012 up to 710 in 2018), surpassing unrelated donors as of 2017. Significant trends detected in Latin America include rising numbers of the procedures reported, a faster increase in allogeneic HCT compared with autologous HCT and a significant increase in family mismatched/haploidentical donors. The LABMT/WBMT activity survey provides useful data to understand the HCT activity and trends in Latin America.

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## INTRODUCTION

Hematopoietic stem cell transplantation (HCT) is a well-established procedure for many inherited and acquired disorders of the hematopoietic system [1]. The Worldwide Network for Blood and Marrow Transplantation (WBMT) is a non-governmental organization in official relations with the World Health Organization (WHO) and promotes excellence in HCT, stem cell donation, cellular therapy, and accreditation, and fosters collaboration among existing international societies

through coordination, communication and advocacy [2]. The WBMT identifies differences in transplant rates (TRs) across the world's regions and between countries through the WBMT global transplant activity (GTA) survey. The WBMT GTA uses a standardized form to capture transplant center level data on volume of transplant activity, indications, disease status, donor types, and stem cell sources [3].

The Latin American Blood and Marrow Transplantation Group (LABMT) [4] is a WBMT member organization and promotes

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excellence in HCT, stem cell donation, cellular therapy, and accreditation in Latin America; it also participates in data collection for the WBMT GTA annual survey. The LABMT has reported data on demographics and macroeconomic factors of Latin American countries, as well as TRs and trends during the 2009–2012 period [5].

Based on the data obtained from the 2018 WBMT GTA for Latin America, this second LABMT report depicts the number of transplants, indications, type of donors and source of stem cells. It also describes the 2012–2018 transplant numbers, trends and rates, and contrasts the region's TRs to other geographic regions in the world.

## PATIENTS AND METHODS

### Study design and participants

This is a retrospective, observational study on the HCT procedures performed in Latin America during 2018. All HCT teams were invited by the LABMT to report their activity through the 2018 WBMT GTA survey. Two main regions were defined based on language. Spanish-speaking Latin America included thirteen countries with known HCT activity, namely Argentina, Bolivia, Chile, Colombia, Costa Rica, Cuba, Ecuador, Mexico, Panama, Paraguay, Peru, Uruguay, Venezuela, and Brazil as the only Portuguese-speaking country. Each country had one delegate that centralized data collection but Brazil had one delegate for each of the five sub-regions. Data were collected and analyzed with support from the WBMT GTA Survey Office. The WBMT GTA survey reporting sheet (available at [www.wbmt.org](http://www.wbmt.org)) captured information on the first transplants performed during 2018. They were divided into allogeneic or autologous ones. Allogeneic donors were separated into family members (subdivided into HLA-identical siblings, other mismatched/haploidentical relatives (haplo) or twins), and unrelated donors (URD). Stem cell source was specified into bone marrow (BM), peripheral blood stem cells (PBSC), and cord blood (CB), respectively. Indications for HCT were stratified according to disease and disease status at transplant. Disease definitions were according to the European Society for Blood and Marrow Transplantation (EBMT) List of Disease Classifications [6]. Finally, the total number of transplants performed in 2018 (1st, 2nd, 3rd, etc.) was also included. The primary study endpoint was numbers of patients treated for the first time with HCT reported according to disease, donor type and stem cell source as well as total number of transplants. Secondary endpoints were trends in relation to previous LABMT surveys (2012–2017) and a comparison to other regions of the world. No individual patient data were used; thus, no ethics committee approval was mandated. TR was calculated as the number of first HCTs per 10 million inhabitants, not normalized for the population age distribution. Population data for each country and the region were obtained from the United Nations' World Population Prospects [7]. World regions were defined in accordance with WBMT and WHO [8]. Other definitions and statistical analyses were as previously described [9, 10].

## RESULTS

### 2018 LABMT/WBMT survey

One hundred ninety-seven HCT teams were detected in Latin America by LABMT in 2018 although some of them could not be active. One hundred twenty-seven teams from 14 countries fed their activity data into the 2018 WBMT GTA survey. Reporting teams are listed below the Acknowledgments section by country. Reporting rates differed between countries; in Argentina, Bolivia, Cuba, Ecuador, Peru, Uruguay, and Venezuela over 80% of the teams reported; in Costa Rica, Mexico, and Paraguay the percentages went from 50–80% of the teams, and in Brazil, Chile, Colombia, and Panama the teams that reported their activity were fewer than 50%. Figure 1 and Table 1 describe the TR and number of procedures per country in the Latin American region. As shown in Fig. 1, there are countries in Latin America with no reported HCT activity.

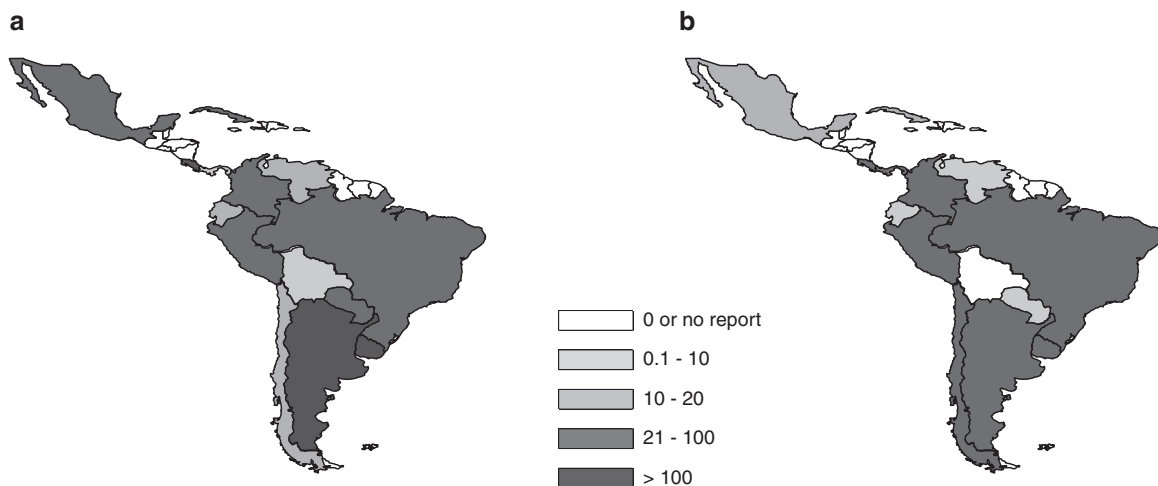
A total number of 5445 first transplants (3249—60% autologous and 2196—40% allogeneic) were reported in 2018, while the overall number of transplants (including, first, second, third, etc.) was 5642 (Table 2). The 2018 overall TR for the first transplants in Latin America was 85 including 34 for allogeneic and 51 for autologous HCT. The TR in active countries ranged from 4 to 338 (4 to 259 autologous HCT and 0 to 82 allogeneic HCT) and the number of HCT in active countries ranged from 4 to 2643 (4 to 1576 autologous and 0 to 1067 allogeneic HCT).

Table 2 shows the transplant activity reported to LABMT by indications, type of HCT (autologous or allogeneic), stem cell source, and types of donors in the case of allogeneic HCT. Stem cell sources for first allogeneic HCT were PBSCs in 64%, BM in 33%, and CB in 3%. In first autologous HCT PBSCs were administered in 98%, and BM in 2%. Type of donor for allogeneic HCT were HLA identical siblings in 44%, haplo in 32%, URD in 21%, while unrelated CB was used in 3%.

The main indications for first allogeneic HCT were acute lymphoblastic leukemia (33%), acute myeloid leukemia (27%) and BM failure syndromes (12%), while the main indications for first autologous HCT were plasma cell disorders (50%) and lymphomas (36%) (Fig. 2).

### Trends in Latin American during the 2012–2018 period

A total of 27,124 first transplants (16,745 autologous and 10,379 allogeneic) were reported to the WBMT GTA survey in the Latin American region in the 2012–2018 period. The number of first and total HCTs captured per year in the LABMT database showed a continuous increase in the number of procedures



**Fig. 1** TR in Latin American countries. **a** TR for autologous HCT in 2018; **b** TR for allogeneic HCT in 2018. TR transplant rate (first HCT per 10 million population), HCT hematopoietic cell transplantation.

**Table 1.** Total number of HCT and rates per 10 million inhabitants according to donor type and country in 2018 as reported to LABMT.

2018 LABMT	Allotransplant (related)				Allotransplant (unrelated)		Allotransplant		Autotransplant		Total	
	Total	Sibling/twin	Other relative	TR	Total	TR	Total	TR	Total	TR	Total	TR
Argentina	249	139	110	57	110	25	359	82	551	125	910	207
Bolivia	0	0	0	0	0	0	0	0	4	4	4	4
Brazil	736	471	265	35	331	16	1067	51	1576	75	2643	126
Chile	88	32	56	46	20	11	108	57	104	55	212	112
Colombia	182	93	89	36	58	12	240	48	301	60	541	108
Costa Rica	11	6	5	22	0	0	11	22	64	128	75	150
Cuba	11	1	10	10	0	0	11	10	26	24	37	34
Ecuador	10	10	0	6	0	0	10	6	25	15	35	21
Mexico	186	81	105	15	1	0	187	15	272	22	459	36
Panama	11	5	6	28	0	0	11	28	3	8	14	35
Paraguay	3	2	1	4	0	0	3	4	16	23	19	27
Peru	157	103	54	49	0	0	157	49	191	60	348	109
Uruguay	23	15	8	68	4	12	27	79	88	259	115	338
Venezuela	5	4	1	2	0	0	5	2	28	10	33	11
LABMT	1672	962	710	26	524	8	2196	34	3249	51	5445	85

HCT hematopoietic cell transplantation, LABMT Latin American Bone and Marrow Transplantation Group, TR transplant rate (first HCT per 10 million population).

performed annually, as well as in the TRs for both autologous and allogeneic HCT. Figure 3 shows the number of first HCT, (allogeneic or autologous) reported per year in the 2012–2018 period. Latin America showed an overall 67% increase in the HCT activity reported from 2012 to 2018 ( $n = 3263$  to  $n = 5445$  first transplant/year respectively) with a mean annual increase of reported HCT of 11%.

In the case of allogeneic HCT, acute leukemias were the main indication and showed a 96% increase from 2012 ( $n = 676$ ) to 2018 ( $n = 1324$ ). In autologous transplants, plasma cell disorders were the most frequent indication and they showed a 62% increase ( $n = 996$  to  $n = 1614$ ), followed by lymphomas, with a 40% increase ( $n = 836$  to  $n = 1170$ ) in the same period. Percentages of each indication for autologous and allogeneic transplants in 2018 remained without major changes in comparison to the 2012 report; the only exception was autoimmune diseases, for which the percentage for autologous HCT went from 1 to 5% (Fig. 2).

As shown in Fig. 4, in the allogeneic HCT category, there was an increase in HLA identical siblings, URD, and haplo donors, with a reduction of CB donors (not shown). The increase was more pronounced among haplo HCT (from 94 in 2012 to 710 in 2018), surpassing URD as of 2017.

The number of teams reporting to the LABMT/WBMT GTA survey increased over time (from 94 in 2012 to 127 in 2018), as did the median number of transplants per team (from 22 in 2012 to 31 in 2018) (Table 3).

#### Transplant rates in Latin America and worldwide

The global HCT activity continues to increase in all the WHO regions as reported by the WBMT, with significant variations across different countries and world regions. The frequency of autologous HCT is slightly higher than that of allogeneic HCT. A total of 82 718 transplants (38425 - 47% allogeneic and 44293 - 53% autologous) were reported to the WBMT in 2016. The TR for all HCTs in 2016 worldwide was 136: 9 in Africa, 54 in the Asia-Pacific region, 36 in the East-Mediterranean region, 439 in Europe, 561 in the USA and Canada, and 77 in Latin America, as shown in Table 4 [11].

#### DISCUSSION

The LABMT/WBMT activity survey and the development of the LABMT have produced data on HCT activity from the Latin American region on an annual basis. Our results show that transplant numbers and rates have a constant increase both in autologous and allogeneic HCTs. Similar to what is observed in USA/Canada and Europe and contrary of what happens in East-Mediterranean, Africa, and Asia-Pacific regions [10–12], Latin American countries reported more autologous (60%) than allogeneic HCTs. Relative proportions of the main indications are very similar to what is observed worldwide in autologous HCT with a predominance of plasma cell disorders, followed by lymphomas [11]. In allogeneic HCT, Latin America shows some differences compared to the 2016 WBMT world report, such as predominance of acute lymphoblastic leukemia over acute myeloid leukemia, a higher proportion in nonmalignant disorders (17.5% vs 14%) and BM as a source of stem cells (33% vs 20%) [11]. The causes of these differences should be evaluated in future surveys, particularly if they could be attributed to a higher percentage of pediatric HCT in our region.

With an annual increase of 11% in reported total number of HCTs in the recent years, Latin America is increasing faster than the median worldwide (5.9%) [11], as it was previously described for autologous HCT in multiple myeloma [13]. The relative proportions of the indications for HCT in the region did not differ significantly over time, except for autologous transplant due to autoimmune disease, which showed an increase in the 2012–2018 period, an observation also described in Europe [14].

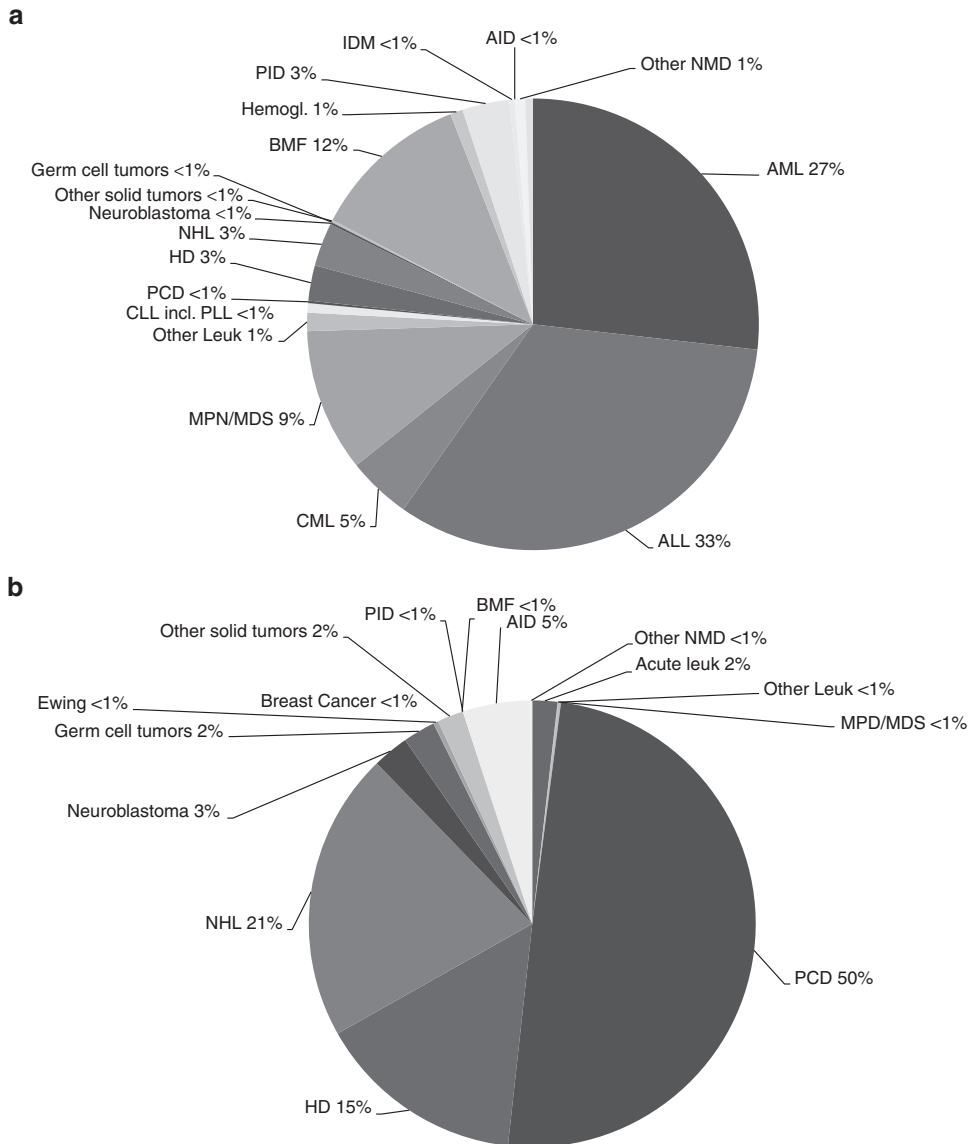
Overall, TRs are lower than the median worldwide as described in Table 4 and these values reveal a significant gap when compared against more developed regions, as Latin America's TRs are from 6 to 8 fold lower than Europe's and those of USA/Canada [11].

It is also to be noted that there is a significant heterogeneity in the number of transplants reported per country (from 4 to 2643 in 2018) as well as in the TR per country (from 4 to 338 in 2018) (Table 1) and that there are countries with no reported HCT activity (Fig. 1). There may be multiple causes for these disparities, with a strong impact of socio-economic parameters that have been previously described [15, 16].

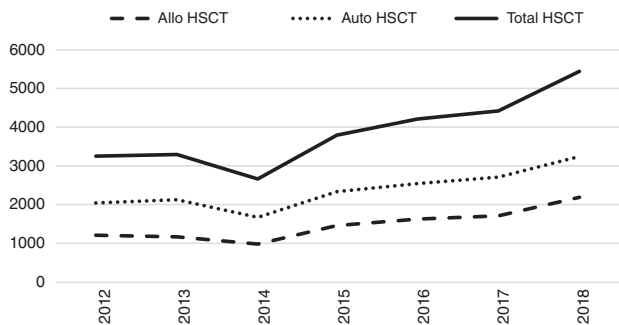
**Table 2.** Number of HCT in Latin America reported to the LABMT in 2018 according to indication, donor type, and stem cell source.

Transplant activity 2018																				
	No. of patients																			
	Allogeneic						Autologous						Total							
	Family			Unrelated			Autologous			Total										
HLA - id	Other relative (mismatched or haplo)			Twin			Unrelated			Total										
	BM	PBSC	CB	BM	PBSC	CB	BM	PBSC	CB	BM	PBSC	CB	BM	PBSC	CB	BM	PBSC	CB	Auto	Total
Myeloid malignancies																				
Acute myeloid leukemia	74	199	1	38	157	0	0	0	35	70	20	0	46	0	594	46	640			
1st complete remission	59	128	0	20	76	0	0	0	21	34	17	0	28	0	355	28	383			
Not 1st complete remission	15	71	1	18	81	0	0	0	14	36	3	0	18	0	239	18	257			
Chronic myeloid leukemia	19	38	0	7	14	0	0	0	10	13	0	0	0	0	101	0	101			
Chronic phase	16	14	0	3	3	0	0	0	4	3	0	0	0	0	43	0	43			
Not chronic phase	3	24	0	4	11	0	0	0	6	10	0	0	0	0	58	0	58			
MDS or MD/MPN	23	58	0	12	31	0	0	0	16	25	4	0	1	0	169	1	170			
MPN (old MPS)	5	14	0	2	7	0	0	0	2	7	1	0	0	0	38	0	38			
Lymphoid malignancies																				
Acute lymphatic leukemia	81	213	3	52	211	0	0	0	58	86	26	0	13	0	730	13	743			
1st complete remission	52	129	1	16	96	0	0	0	32	51	13	0	11	0	390	11	401			
Not 1st complete remission	29	84	2	36	115	0	0	0	26	35	13	0	2	0	340	2	342			
Chronic lymphocytic leukemia (incl. CLL)	4	7	0	0	1	0	0	0	0	3	0	0	0	0	15	0	15			
Other Leukemia	3	9	0	0	4	0	0	0	2	3	1	0	7	0	22	7	29			
Plasma cell disorders—MM	0	0	0	0	4	0	0	0	0	0	0	0	27	1562	0	4	1589			
Plasma cell disorders—other	0	0	0	0	0	0	0	0	0	0	0	0	2	23	0	25	25			
Hodgkin lymphoma	6	21	0	2	23	0	0	0	2	2	0	0	20	470	0	56	490			
Non Hodgkin lymphoma	5	35	0	6	15	0	0	0	2	6	0	0	9	650	0	69	659			
Other LPD	1	2	0	0	2	0	0	0	1	0	0	0	0	21	0	6	21			
Solid tumors																				
Neuroblastoma	2	1	0	0	0	0	0	0	0	0	0	0	6	79	0	3	85			
Germ cell tumor	1	0	0	0	0	0	0	0	0	0	0	0	2	74	0	1	76			
Breast Cancer	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1			
Ewing	0	0	0	0	0	0	0	0	0	0	0	0	1	10	0	0	11			
Other solid tumor	1	2	0	0	0	0	0	0	0	0	0	0	2	57	0	3	59			
Nonmalignant disorders																				
Bone marrow failure—SAA	55	28	0	29	21	0	1	0	35	15	0	2	0	0	184	2	186			
Bone marrow failure—other	12	7	0	15	8	1	0	0	20	1	5	0	0	0	69	0	69			
Hemoglobinopathy	8	1	0	1	7	0	0	0	2	0	1	0	0	0	20	0	20			
Primary Immune Deficiency	7	4	1	17	12	1	0	0	20	6	7	0	1	0	75	1	76			
Inherited Dis of Metabolism	2	0	0	1	1	0	0	0	2	0	2	0	0	0	8	0	8			
Autoimmune Disease	1	0	0	0	0	0	0	0	0	0	0	0	0	159	0	1	159			
Other NonMalignant Disease	4	0	0	2	3	0	0	0	5	0	2	0	4	0	16	4	20			
Other (incl Histiocytosis)	2	1	0	0	3	0	0	0	5	1	0	0	0	0	12	0	12			
Total patients (1st. HSCT)	316	640	5	184	524	2	1	0	217	238	69	71	3178	0	2196	3249	5445			
Total transplants															2325	3317	5642			

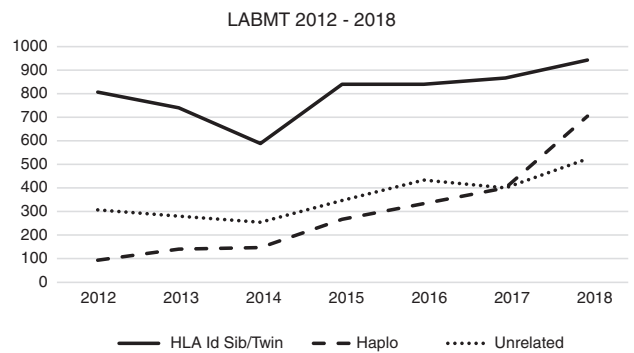
Bold values represent the sum of values for the different disease stages for acute myeloid leukemia, chronic myeloid leukemia and acute lymphoblastic leukemia. HCT hematopoietic cell transplantation, LABMT Latin American Bone and Marrow Transplantation Group, MDS myelodysplastic syndrome, MPN myeloproliferative neoplasm, MM multiple myeloma, LPD lymphoproliferative disease, HLA id HLA-identical, BM bone marrow, PBSC peripheral blood stem cells, CB cord blood.



**Fig. 2** Disease indications for hematopoietic cell transplantation (HCT) in 2018. **a** Relative proportion of allogeneic HCT; **b** relative proportion of autologous HCT.



**Fig. 3** Numbers of allogeneic, autologous, and total HCT reported to LABMT in 2012–2018. HCT hematopoietic cell transplantation, LABMT Latin American Bone and Marrow Transplantation Group.



**Fig. 4** Donor sources for first allogeneic HCT in the period 2012–2018. HCT hematopoietic cell transplantation, HLA Id Sib/Twin human leukocyte antigen identical sibling or twin donor, Haplo family mismatched/haploidentical donor; unrelated unrelated donor.

**Table 3.** Number of reporting teams and median number of transplants reported per team/year in the period 2012–2018.

Year	Total number of HCT	No. teams	HCT per team/year (median)
2012	3263	94	22
2013	3314	91	23
2014	2669	69	24
2015	3811	92	26
2016	4196	87	30
2017	4426	87	33
2018	5445	127	31

No. teams number of teams reporting to LABMT, HCT per team median number of transplants reported per team per year.

**Table 4.** TR reported to WBMT by world region and type of HCT in 2016.

World region (2016)	Allogeneic HCT TR	Autologous HCT TR	Total TR
USA/Canada	227	334	561
Europe	181	258	439
Latin America	30	47	77
Asia-Pacific	34	20	54
East-Mediterranean	22	14	36
Africa	5	5	9
Worldwide	63	73	136

HCT hematopoietic cell transplantation, WBMT Worldwide Network for Blood and Marrow Transplantation, TR transplant rate (first HCT per 10 million population).

Allogeneic HCT with all donor types are increasing in Latin America (HLA-identical siblings, haplo, URDs) except for CB. HLA identical siblings ranked first as type of donor from 2012 to 2018. During the same period, the fastest increase was observed in haplo HCT donors, who have become the second donor type after surpassing URDs in 2017. This observation is related in our region to the use of post-transplant cyclophosphamide for graft-versus-host disease prophylaxis in haplo HCT. Although with less experience than URDs [17] it has facilitated access for patients lacking an HLA-identical sibling due to outcomes, simplicity and costs associated with the procedure and can overcome some of the obstacles posed by URDs in our region [18]. Several reports from Latin American centers have described the experience in different diseases in both pediatric and adult populations with this modality [19–26].

This picture is different from what happens in Europe or North America, where URDs take the lead, over HLA identical siblings or haplo HCT donors as described in the EBMT and CIBMTR reports although familial haplo HCT is also rapidly increasing in these regions [27, 28]. A rapid increase in haplos is also observed in the East-Mediterranean/Africa [10] and Asia-Pacific [12] regions, where there is a significant impact from China with the utilization of a mixture of BM and PBSC and G-CSF/ATG based “Beijing protocol” instead of post-transplant cyclophosphamide [29].

The different percentage in the utilization of URDs compared to high-income countries is probably multifactorial and associated with the lower odds of finding a matched donor in international registries for the Latin American population [30], HLA genetic diversity and differential admixture across sub-regions [31], limited

donor recruitment and the absence of URD programs in several countries (even when four of them have well-established national registries with the largest in Brazil-REDOME and Argentina-INCUCAL and currently eight Latin American countries have organizations that facilitate donations or store CB units according to the World Marrow Donor Association [32]) as well as economic, technical and logistical difficulties intrinsic to the procedure [33]. Development of national URD programs and a greater recruitment and representation of the Latin American population in international registries might help to further expand the number of URD HCT in the region.

Latin America should also increase the team density and the number of transplants per team to continue to close the gap with more developed regions. Policies should be implemented to achieve a better geographic distribution of the transplant teams with the aim of increasing accessibility to HCT in countries and regions with low TRs.

The region needs to improve not only the number of transplants, but also ensure progress in terms of quality. National health authorities have implemented HCT quality management requirements in most of the countries and LABMT is cooperating with FACT and JACIE to facilitate access to accreditation with the “FACT-JACIE International Stepwise Program” in Spanish-speaking Latin America and the “SBTMO-FACT” Program in Brazil. Improvement in quality management and access to international accreditation will have a positive impact on data collection, analysis and quality control, not only to ensure team compliance with standards of practice, but also to share this information with regional and international registries and outcomes databases [34, 35].

Despite the constraints due to underreporting and the limited number of variables collected, the survey contributes to a better understanding of the situation of HCT in Latin America. A key issue is to identify if the increase in the reported transplants is due to a real increase in the transplant activity in Latin America, or it merely reflects better reporting of transplant teams that were already operational. We think both aspects account for the increase in reported transplants observed in the period of 2012–2018. A better reporting rate is evidenced by a greater number of teams that are reporting for the LABMT/WBMT GTA survey, and a real increase in the number of procedures is evidenced by a growing trend in the number of transplants performed per team in the period 2012–2018 (Table 3).

LABMT and WBMT are establishing various strategies to improve data collection and analysis, including the development of a web-based reporting sheet, highlighting the importance of engaging the greatest number of transplant teams as possible in this voluntary survey. Additional information is planned to be captured in future surveys including discrimination between pediatric and adult HCTs, more data on disease status before transplant, characteristics of the conditioning regimen, information on graft-versus-host disease prophylaxis, and the possibility to include outcome measures.

In summary, HCT numbers and rates are increasing particularly fast in Latin America. TRs are in an intermediate zone compared to the other world regions, but are still 6–8 fold lower than in most developed areas. Furthermore, HCT rates have a wide inter-country variability, and some countries do not have an active HCT program yet. The LABMT/WBMT activity survey is a useful tool to detect trends and gaps in our region. The information it provides should be factored in when designing strategies to reduce inequalities and improve accessibility to HCT in Latin America.

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CC, OGR, and SG conceived the analysis and drafted the manuscript. CC, OGR, and HB were responsible for the data collection and assembly. ALB, RB, LA, BP, CR, MCH., CH, BM, AGD, NM, CF, LA, LD, MH, AS, AK, GJ, JMR, CB, HG, MK, MA, MI, WS, DN, and YA were responsible for the integrity of the data and gave scientific input.

#### COMPETING INTERESTS

The authors declare no competing interests.

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