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ORIGINAL ARTICLE

Latin America: the next region for haematopoietic transplant progress

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Haematopoietic cell transplant activity in the 28 countries comprising Latin America is poorly defined. We conducted a voluntary survey of members of the Latin American Bone Marrow Transplantation Group regarding transplant activity 2009–2012. Collated responses were compared with data of transplant rates from the Worldwide Network for Blood and Marrow Transplantation for other geographic regions. Several socio-economic variables were analysed to determine correlations with transplant rates. In total, 94 teams from 12 countries reported 11 519 transplants including 7033 autotransplants and 4486 allotransplants. Annual activity increased from 2517 transplants in 2009 to 3263 in 2012, a 30% increase. Median transplants rate (transplant per million inhabitants) in 2012 was 64 (autotransplants, median 40; allotransplants, median 24). This rate is substantially lower than that in North America and European regions (482 and 378) but higher than that in the Eastern Mediterranean and Asia Pacific regions (30 and 45). However, the Latin America transplant rate is 5–8-fold lower than that in America and Europe, suggesting a need to increase transplant availability. Transplant team density in Latin America (teams per million population; 1.8) is 3–4-fold lower than that in North America (6.2) or Europe (7.6). Within Latin America, there is substantial diversity in transplant rates by country partially explained by diverse socio-economic variables including *per capita* gross national income, health expenditure and physician density. These data should help inform future health-care policy in Latin America.

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INTRODUCTION

Haematopoietic cell transplant activity varies widely across world regions and between countries.[1] In 2012, >90% of transplants were done in three geographic regions, North America, Europe and Asia Pacific.[2,3] The first reported transplants in Latin America were in the 1980s with activity increasing continuously thereafter.[4] However, despite episodic reports there is no comprehensive survey of Latin American transplant activity.[5–8] The Latin American Bone Marrow Transplant Group (LABMT) was founded in 2011 under the auspices of the Worldwide Network for Blood and Marrow Transplantation (WBMT), a non-governmental organisation of the World Health Organization (WHO). The LABMT's aim is to foster cooperation and reporting amongst transplant centres in Latin America. This report focuses on estimating transplant activity and rates, identifying variables associated with these endpoints and detecting trends. Data from Latin America were compared with data from three geographic regions.

PATIENTS AND METHODS

Transplant teams were identified by a survey of Latin American haematology societies, transplant societies and transplant donor registries. Using this strategy, we identified 154 transplant centres that were invited to report transplants in 2009–2012. A total of 94 transplant teams accepted and sent data. We used a WBMT-developed questionnaire to collect data from responding centres (Supplementary Figure 1). There was no independent investigation of transplant activity in each Latin American country and no comprehensive review of biomedical publications in

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diverse languages to identify discordances between reporting to us and publications. Variables ascertained in the WBMT template included disease, disease state, relationship between donor and recipient and graft-type. There was no auditing of transplant centres. Reports were supplemented by data from the WBMT for 28 Latin America WHO member states (Table 1). Population data were obtained from the International Data Base Country Rankings of the US Census Bureau (https://www.census.gov/population/international/data/idb/rank.php). As subject-level identifiers were not used, Ethical Committee approval was judged unnecessary.

We defined transplant rate as numbers of transplants per million inhabitants *per* country *per* year. Transplant team density was defined as number of transplant teams *per* million inhabitants *per* country or region. We compared these metrics with other variables including *per capita* gross national income (GNI), infant mortality rate, life expectancy (unadjusted), *per capita* health-care expenditure (HCE), HCE as a function of GNI, percent public-funded HCE, physician and nurse densities (*per* 1000 population), human development index, education level, numbers of public health facilities, country surface area, population density, population density of the capital city and percent population living in rural areas. 2012 data were obtained from the World Bank (www.worldbank.org) and WHO (www.who.int). Reporting countries were ranked by population, surface area, *per capita* GNI and HCE and physician density. To assess economic efficiency, we quantified transplant rates by *per capita* GNI and HCE.

Statistical analyses

The relationship between the 2012 transplant rate and socio-economic variables was analysed by multiple linear regression. The confidence interval was set to 95%, and the result of the analysis (fit) was evaluated using the R2 software.

RESULTS

Transplant centres in 12 of the 28 WHO Latin America region member states reported 11 519 first transplants in 2009–2012. Data were from 82 teams in 2009 increasing to 94 teams in 2012 (Tables 1 and 2). Ecuador started a transplant programme in this interval. No transplants were reported from countries with < 3.3 million inhabitants or with *per* capita GNI $<$ $3400 USD. Cuba and Dominican Republic did not report data, although we identified $\geqslant 1$ transplant centre in each country from the biomedical literature. Whether there are unreported transplant programmes and centres in other non-reporting countries is unknown. Median transplant team density was 1.8 in 2012 with the highest value in Uruguay (15.2) and lowest in Venezuela (0.7; Table 1). The Latin American transplant team density is substantially lower than that of North America (6.2) and Europe (7.6).[3]

Of the 11 519 first transplants, 7033 were autotransplants (61%) and 4486 were allotransplants (Table 2). Autotransplant graft types included blood cells ($N = 6854$; 97%) and bone marrow cells ($N = 178$; 3%; Table 2). Reason for autotransplants were lympho-proliferative neoplasms including plasma cell myeloma ($N = 6155$; 88%), solid cancers ($N = 490$; 7%), leukaemias ($N = 316$; 5%) and non-neoplastic diseases ($N = 150$; 1%; Supplementary Table 1). Donors for allotransplants included an HLA-identical sibling ($N = 3135$; 70%), a HLA-matched unrelated donor ($N = 1095$; 24%) or a HLA-haplotype-matched relative ($N = 229$; 5%; Table 2). Graft types from family donors included blood cells ($N = 1867$; 59%), bone marrow cells ($N = 1242$; 40%) and umbilical cord blood cells ($N = 53$; 1%). Most transplants from

Table 1. Demographics of Latin American countries and macroeconomic factors in 2010–2011

	Population Mio	*Surface km²*	*GNI/cap $*	*HCE/cap $*	*Physicians density*	*Team density*
Countries with HSCT						
Argentina	41.3	2 766 890		995	3.86	4.0
Brazil	195.8	8 511 965	11 630	1056	1.89	1.9
Chile	16.8	756 950	14 310	1103	1.02	2.9
Colombia	44.2	1 138 910	7020	530	1.47	1.1
Costa Rica	4.5	51 100	8820	951	1.11	4.3
Ecuador	14.7	283 560	5170	361	1.72	2.0
Mexico	114.1	1 972 550	9640	618	2.1	0.9
Panama	3.4	78 200	8510	76.3	1.65	8.6
Paraguay	6.4	406 750	3400	72.7	1.23	1.5
Peru	28.9	1 285 220	6060	74.2	1.13	1.4
Uruguay	3.3	176 000	13 580	1318	3.74	15.2
Venezuela	27.2	912 050	12 460	593	1.94	0.7
Countries without HSCT						
El Salvador	6.704	21 040	3590	254	0.25	—
Guatemala	14.655	108 890	3120	240	0.9	—
Haiti	8.121	27 750	760	53	0.37	—
Honduras	6.9752	112 090	2120	195	0.47	—
Jamaica	2.731	10 991	5130	318	0.93	—
Nicaragua	5.465	129 494	1650	144	1.6	—
Countries with missing/uncertain information						
Cuba	11.1	110 860	5890	684	NA	—
Dominica	0.07	754	6440	392	NA	—
Dominican Republic	9.8	48.730	5470	310	NA	—
Grenada	0.09	344	7220	478	NA	—
Guyana	0.77	214 970	3410	235	NA	—
Saint Kitts and Nevis	0.39	261	NA	73.3	NA	—
Saint Lucia	0.17	616	NA	74.8	NA	—
Saint Vincent and the Grenadines	0.12	389	NA	NA	NA	—
Suriname	0.44	163 270	8680	521	NA	—
Trinidad and Tobago	0.11	5128	14 710	972	NA	—

Abbreviations: GNI/capita $ = gross national income/capita F$; HCE/capita $ = health-care expenditure/capita $; HSCT = haematopoietic stem cell transplant; NA = not available/not applicable; physician density = number of physicians/10 million inhabitants; team density = number of teams/10 million inhabitants.

Table 2. Total number of HSCT according to donor type and source of HSCT from 2009 to 2012

		2009	*2010*	*2011*	*2012*	*Total*
Total HSCT		**2517**	**2829**	**2910**	**3263**	**11 519**
Total autologous		**1513**	**1660**	**1803**	**2057**	**7033 (61%)**
Autologous	*PB*	*1475*	*1629*	*1745*	*2005*	*6854 (97%)*
	BM	*37*	*31*	*58*	*52*	*178 (3%)*
	CB	*1*	*0*	*0*	*0*	*1*
Total allogeneic		**1004**	**1169**	**1107**	**1206**	**4486 (39%)**
HSCT from related donors						
HLA identical	*PB*	*416*	*506*	*460*	*485*	*1867 (59%)*
	BM	*295*	*318*	*317*	*312*	*1242 (40%)*
	CB	*6*	*9*	*7*	*4*	*26(1%)*
	Total	*717*	*833*	*784*	*801 (+12%)*	*3135 (69.8%)*
Syngeneic	*BM/PB*	*0*	*5*	*6*	*5*	*16 (0.4%)*
HLAnonid	*PB*	*22*	*36*	*35*	*63*	*156 (65%)*
	BM	*17*	*18*	*7*	*31*	*73 (30%)*
	CB	*3*	*6*	*2*	*0*	*11 (5%)*
	Total	*42*	*60*	*44*	*94*	*240 (5.3%)*
Total related		**759**	**898**	**834**	**900 (+18.6%)**	***3391 (75.2%)***
HSCT from unrelated donors						
Unrelated	*PB*	*40*	*59*	*61*	*86 (+115%)*	*246 (22.4%)*
	BM	*88*	*95*	*106*	*113 (+28%)*	*402 (36.7%)*
	CB	*117*	*117*	*106*	*107*	*447 (40.8%)*
Total unrelated		**245**	**271**	**273**	**306 (25%)**	***1095 (24.4%)***

Abbreviations: BM = bone marrow; CB = cord blood; HSCT = haematopoietic stem cell transplant; PB = peripheral blood. Bold values indicate totals, and italics denote partial data.

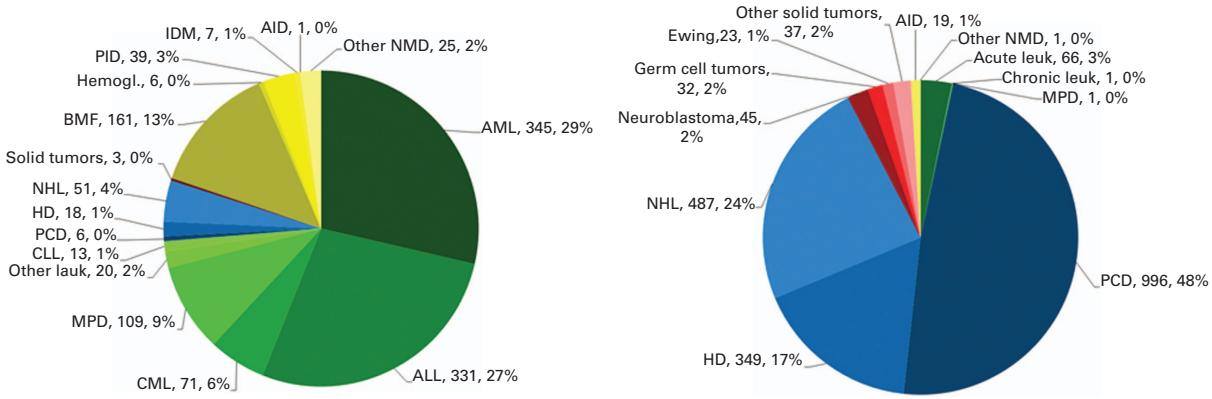

Figure 1. Reasons for auto (left) ($N = 2057$) and allotransplants (right) ($N = 1206$).

unrelated donors used umbilical cord blood cells ($N = 447$; 41%) followed by bone marrow cells ($N = 402$; 37%) and blood cells ($N = 246$; 22%). Reasons for allotransplants were leukaemias ($N = 3134$; 70%), non-neoplastic diseases ($N = 1027$; 23%) and lymphomas ($N = 301$; 7%; Supplementary Table 1). Amongst leukaemia transplants, acute leukaemias were more common than chronic leukaemias, and persons in first remission were more common than were persons in other disease states. In total, 144 of 232 (62%) transplants for AML were in persons with advanced disease from HLA-matched unrelated donors. Transplants for CML were uncommon ($N = 279$); only 116 CML were in persons in 1st chronic phase.

Transplant activity in 2012

We analysed the 3263 first transplants done in 2012 in greater detail (Figure 1). Transplants were for lympho-proliferative neoplasms ($N = 1907$; 59%), leukaemias ($N = 957$; 29%), non-neoplastic diseases ($N = 259$; 8%) and solid cancers ($N = 140$; 4%). Autotransplants ($N = 2057$; 63%) were more common than allotransplants ($N = 1206$; 37%). Most allotransplants ($N = 900$; 75%) were from relatives. In total, 107 of the unrelated donor transplants (35%) used umbilical cord blood cell grafts. Most countries reported doing auto- and allotransplants except Paraguay which reported only autotransplants (Table 3a). Seven countries (Argentina, Brazil, Chile, Colombia, Ecuador, Mexico and Uruguay; Table 3a) reported transplants from HLA-matched unrelated donors. There was an inverse relationship between numbers of HLA-matched unrelated donor transplants and HLA-haplotype-matched relative transplants (Supplementary Figure 1).

Trends

Numbers of transplants increased by 30% from 2009 to 2012 (2517 vs 3263) with a 36% increase in autotransplants and a 20% increase in allotransplants (Supplementary Table 1). Increased autotransplants were predominately for plasma cell myeloma (39%). Increased allotransplants were predominately for acute leukaemias (33%). There was a slight decline in transplants for non-neoplastic disorders (Supplementary Table 1). Transplants of blood and bone marrow cells from unrelated donors increased by 115% and 28%, respectively (Table 2). There were also

Table 3a. Transplant numbers and rates in 2012

	Allotransplant (related)				*Allotransplant (unrelated)*		*Allotransplant*		*Autotransplant*		*Total*	
	Total	*Sibling/twin*	*Other relative*	*TR*	*Total*	*TR*	*Total*	*TR*	*Total*	*TR*	*Total*	*TR*
Argentina	111	106	5	26	51	12	162	38	465	110	627	149
Brasil	449	416	33	23	182	9	631	32	1062	53	1693	85
Chile	28	23	5	16	30	18	58	34	47	28	105	61
Colombia	95	83	12	21	14	3	109	24	162	36	271	60
Costa Rica	14	9	5	30	0	0	14	30	33	70	47	102
Ecuador	10	10	0	7	4	3	14	9	14	9	28	18
Mexico	106	82	24	9	21	2	127	11	97	8	224	19
Panama	11	11	0	31	0	0	11	31	27	75	38	109
Paraguay	0	0	0	0	0	0	0	0.0	9	14	9	14
Peru	35	35	0	12	0	0	35	12	37	13	72	24
Uruguay	24	14	10	73	4	12	28	85	71	215	99	300
Venezuela	17	17	0	6	0	0	17	6	33	12	50	18
LABMT	900	806	94	18	306	6	1206	24	2057	40	3263	64
Europe	5776	4827	949	68	7495	89	13 271	157	18 836	223	32 107	379
North America	3174	2639	535	91	4396	126	7570	218	9220	2659	16 790	483
Asia Pacific	4557	3017	1540	15	4137	13	8694	28	5 232	17	13 926	45
Eastern Mediterranean	1086	1033	53	16	99	1	1185	17	875	13	2060	30
Global	15 493	12 322	3171	18	16 433	13	31 926	28	36 220	40	68 146	63

Abbreviation: LABMT = Latin American Bone Marrow Transplant Group; TR = transplant rate.

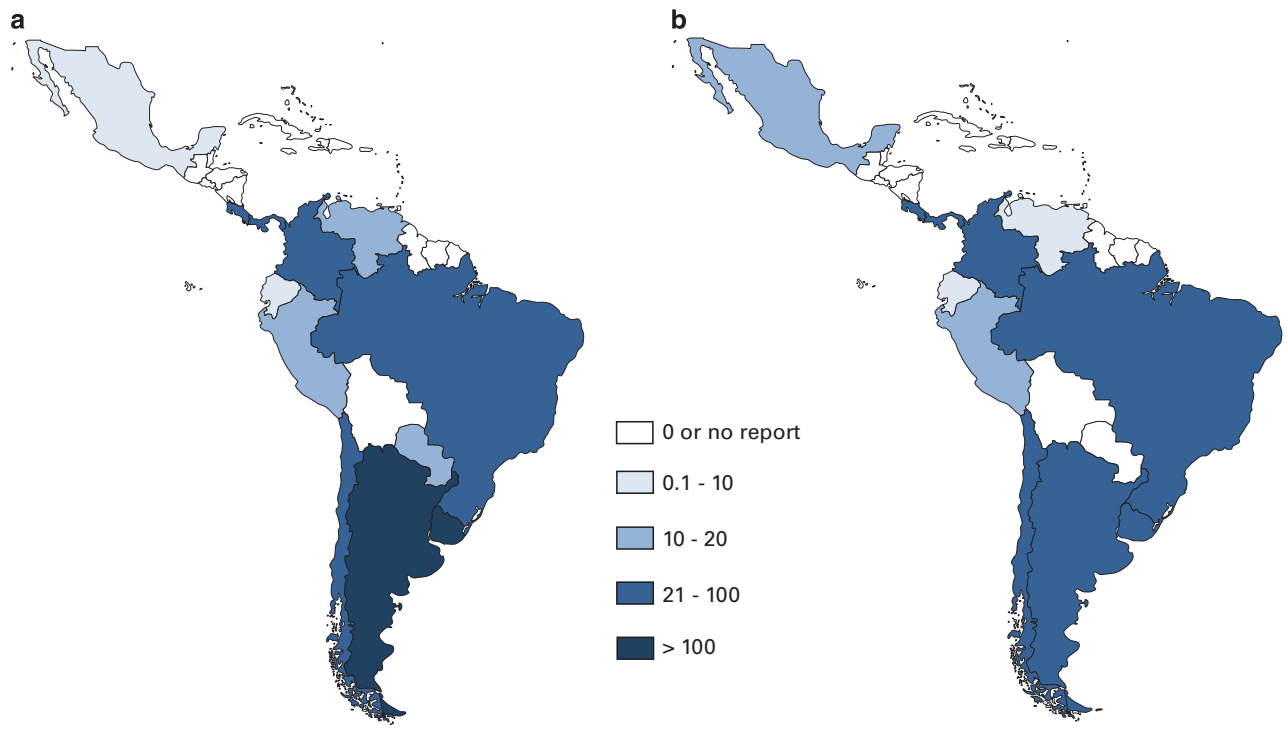

Figure 2. Transplant rate. Transplants per 10 (**a**), autotransplants; **b**, allotransplants.

small increases in transplants of blood and bone marrow cells from HLA-matched relatives and from HLA-haplotype-mismatched related donors, of 12% and 124%, respectively (Table 2).

Comparison with other regions

2012 transplant rates in Latin American countries are shown in Figure 2. The Latin American region median transplant rate was 64 ranging from 14 in Paraguay to 300 in Uruguay (Table 3b). Median transplant rates for auto and allotransplants were 40 (range, 8–215) and 24 (range, 0–88; Table 3a). Median rates for related and unrelated donor transplants were 18 (range, 0–73) and 6 (range, 0–18; Table 3a). Transplant rates in Latin America (median 60) were higher than in the Eastern Mediterranean (median 30) and Asia/Pacific (median 45) regions but lower than those in the American (median 482) and European (median 379) regions.

Transplant rates and socio-economic variables

No transplants were reported from countries with < 3.3 million population or with a *per capita* GNI $< \$3400$ USD (Table 1).

Table 3b. Transplant rates, donor types and economic efficiency

	Transplants		*Donor type (%)*			*Economic efficiency*	
	N	*Transplant rate*	*HLA-haplotype-matched*[a]	*HLA-matched unrelated*[b]	*Allo-/autotransplants*[c]	*Transplant rate/per capita GNI*	*Transplant rate/per capita HCE*
Argentina	627	149	5	31	0.35	NA	0.15
Brasil	1693	85	7	29	0.59	0.007	0.08
Chile	105	61	18	52	1.23	0.004	0.06
Colombia	271	60	13	13	0.67	0.009	0.11
Costa Rica	47	102	36	NA	0.42	0.012	0.11
Ecuador	28	18	NA	29	1.00	0.003	0.05
Mexico	224	19	23	17	1.31	0.002	0.03
Panama	38	109	NA	NA	0.41	0.013	1.42
Paraguay	9	14	NA	NA	0.00	0.004	0.18
Peru	72	24	NA	NA	0.95	0.004	0.32
Uruguay	99	300	42	14	0.39	0.022	0.23
Venezuela	50	18	NA	NA	0.52	0.001	0.03
Latin America	3263	61	10	25	0.59	NA	NA
Europe	32 107	379	16	56	0.70	NA	NA
North America	16 790	483	17	58	0.82	NA	NA
Asia/Pacific	13 926	45	34	48	1.66	NA	NA
East Mediterranean	2060	30	5	8	1.35	NA	NA
Worldwide	68 146	—	—	—	—	—	—

Abbreviations: GNI = gross national income; HCE = health-care expenditure; NA = not available/not applicable. [a]Percent related allotransplants from HLA-haplotype-matched relatives. [b]Percent allotransplants from HLA-matched unrelated donors. [c]Ratio of allotransplants to autotransplants.

Per capita GNI and physician density were significantly associated whether there was reported transplant activity. Except for El Salvador, countries with >1 physician per 1000 inhabitants reported transplants. *Per capita* GNI (coefficient − 0.001; SE, 0.0004; $P = 0.01$), *per capita* HCE (coefficient 0.016; SE, 0.0056; $P < 0.01$) and physician density (coefficient 3.447; SE, 1.4474; $P = 0.03$) were significantly associated with transplant rate. These three variables explained 90% of variations in transplant rates in reporting countries. There were no significant correlations between total population, population density, infant mortality rate, life expectancy, health expenditure as a function of GNI, percent public-funded HCE, physician and nurse densities (*per* 1000 population), human development index, education level, numbers of public health facilities, country surface area, population density, population density of the capital city and percent population living in rural areas.

Per capita GNI and HCE and transplant rates varied substantially between reporting countries (see Supplementary Figure 2). Consequently, the 12 reporting countries were ranked for descriptive analysis. Some countries had high economic indices and high transplant rates (Uruguay, Argentina), whereas others reported low-transplant rates despite high economic indices (Chile, Venezuela). Others had high transplant rates despite low-economic indices (Panama; Tables 3a, Table 3b). Some countries had higher transplant rates as a function of *per capita* GNI (Uruguay, Panama and Costa Rica) and as a function of *per capita* HCE expenditures (Panama, Peru) than others had (Mexico, Venezuela; Table 3b).

DISCUSSION

We report an analysis of haematopoietic cell transplant activity in Latin America. We found a 30% increase in transplant rate from 2009 to 2012, an increase greater than that reported in other geographic regions.[1] Nevertheless, the Latin America transplant rate is 5–8-fold lower than that in the North America and European regions, suggesting substantial growth potential.[1] Also, the proportion of allotransplants from HLA-matched unrelated donors was substantially less in Latin America compared with that in North America and European regions (25% vs 54%). This disparity likely results from smaller unrelated donor registries and less efficient search and sharing logistics in Latin America. Only four countries had unrelated donor registries (Brazil, Argentina, Mexico and Uruguay), and five countries reported no HLA-matched unrelated transplants. Also, median search time to transplant was long (for example, 6 months in Argentina) compromising use in persons with acute leukaemias.[9] Also, the proportion of bone marrow grafts was higher than in the North America and European regions.[1] This likely reflects economic considerations such as costs of apheresis devices and granulocyte-CSF (G-CSF). The higher proportion of transplants for bone marrow failure syndromes in Latin America (13%), a setting where use of bone marrow is preferred to blood cells, may also contribute to this disparity.

Several socio-economic factors are associated with transplant rates including *per capita* GNI, HCE and physician density. Similar data are reported for other geographic regions.[1,2,10] Other variables such as infant mortality rate, life expectancy or human development index were not reported. We estimate three variables, *per capita* GNI, *per capita* HCE and physician density, explain about 90% of the variance in transplant rates between reporting countries. The density of transplant teams in Latin America (1.8 per million population) is also substantially lower than in North America (6.2) and Europe (7.6).[3] This disparity correlates with fewer transplants in Latin America. For example, Uruguay has the highest team transplant density and transplant rate, whereas Venezuela has the lowest of both. However, it is not possible to know whether less transplant team density causes fewer transplants, fewer transplants cause less transplant team density or an interaction.[10]

Worldwide there is decreasing use of umbilical cord blood cell donors, especially in adults and increasing use of HLA-haplotype-matched relatives. There is a similar trend in our 2009–2013 data. We plan our next analysis in 2017 and will focus on this issue.

There are several important caveats to our conclusions. First, incompleteness. Not all invited transplant centres responded

to the survey and two countries with known transplant activity did not respond. Other transplant centres may be unknown to us. Consequently, there may be under-reporting. Accuracy is another issue. We did not audit reporting centres for accuracy, consecutive reporting, data completeness or other variables. This could result in under-, over- and/or incorrect-reporting. Finally, we did not query transplant outcomes nor did we request subject-level data. These issues are targets of future LABMT reports. Despite these caveats, our analyses are an important starting point for developing transplant activities in Latin America.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Supplementary Information accompanies this paper on Bone Marrow Transplantation website (http://www.nature.com/bmt)