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ARTICLE

The paradox of haematopoietic cell transplant in Latin America

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Abstract

Hematopoietic cells transplants are technically complex and expensive imposing a huge burden on health care systems, especially those in developing countries and regions. In 2017 > 4500 transplants were done in 13 Latin American countries with established transplant programmes. We interrogated data on transplant rate, cost, funding source, hospital type, Gini coefficient and the United Nations Development Programme Inequality-Adjusted Human Development Index to determine co-variates associated with transplant development. Transplant rates varied almost 30-fold between the 13 countries from 345 in Uruguay to 12 in Venezuela with a regional transplant rate 7–8-fold lower compared with the US and EU. We found significant correlations between higher transplant cost, public funding, transplants in private hospitals with transplant rate. Low cost *per* transplant regardless of payor and transplants done in public hospitals were associated with low transplant rates. In contrast, high cost *per* transplant funded by the government and transplants done in private hospitals were associated with high transplant rates. Surprisingly, we found transplant rates were higher when transplants cost more, when they were done in private *for-profit* hospitals and payed for with public funds. These data give insights how to increase transplant rates in Latin America and other developing regions.

Introduction

Hematopoietic cells transplants started in Latin America since 1980 [1]. Because they are technically complex and expensive they have a huge impact on health care expenditures (HCEs) [2–4]. Despite these barriers, there has been a steady

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growth in annual numbers of transplants in Latin America over the last 40 years. In 2017, an estimated 4500 transplants were done (Latin America Bone Marrow Transplant Group or LABMT-World Bone Marrow Transplant Network [WBMT] unpublished data). Nevertheless, only 13 of 28 Latin American countries have stable transplant programmes [5]. Some of these countries share economic, political, social and cultural features, other not.

Transplant development needs support from health care systems. Transplant rates in Latin America (numbers of transplants *per* 10 million inhabitants *per* year) correlate with *per* capita gross domestic product (GDP), *per capita* HCE, with physician density (number of physicians *per* 1000 inhabitants) and with transplant team density (number of transplant teams *per* 10 million population) [5]. Surprisingly, there were no significant correlations between transplant rate and total population, population density, infant mortality rate, life expectancy, nurse densities (*per* 1000 population), human development index (HDI), education level, numbers of public health facilities, country surface area, population density, population density of the capital city or percentage population living in rural areas [5].

The US and EU have very high inequality-adjusted HDIs (IHDIs > 0.800 where 1.000 is the best IHDI) and are classified as very high human development, whereas only three Latin American countries, Argentina, Chile and Uruguay, have a similar IHDI. Most Latin American countries including Mexico have IHDIs of 0.700–0.799 and are classified as high human development save for Bolivia and Guiana with HDIs of <0.799, classified as medium human development according to United Nations Development Programme (http://hdr.undp.org/en/content/inequality-adjusted-human-development-index-ihdi).

Transplant rate is also influenced by socio-economic disparities [6, 7]. The Gini coefficient or index is a statistical measure of economic inequality and income dispersion within a country. A Gini coefficient of 0 (or 0%) means a countries' wealth is equally shared by its inhabitants, whereas a coefficient of 1 (or 100%) means one person has all a countries' wealth. Several Latin American countries such as Argentina, Chile, Bolivia and Peru have Gini coefficients of 40.0 to 44.9 like the USA (41.4), whereas others such as Brazil, Mexico, Paraguay and Venezuela have Gini coefficients of 45.0–49.9. Uruguay has a Gini coefficient of 39.7, lower than the USA. Large EU countries such as the UK, France, Germany and Spain have Gini coefficients, 30.0–34.9, whereas Nordic countries such as Sweden, Denmark, Norway and Finland have coefficients of 25.0–29.9. According to the United Nations Childrens' Fund (UNICEF) Latin America has the highest net income Gini coefficient globally at 48.3 [8]

Transplant rates are roughly equivalent in North America and the EU despite a much higher Gini coefficient in the USA indicating other co-variates operate to influence transplant rate. One important variable which is difficult to accurately quantify is health care access. However, we found no correlation between surrogates of health care access and transplant rate including health expenditure as a function of Gross national income (GNI), percentage public-funded HCE, nurse density, HDI or IHDI [5]. Interestingly, Latin American transplant rates are seven- to eightfold lower compared with North America (personal communication, Helen Baldomero; WBMT) despite a similar Gini coefficient even after adjusting for *per* capita GDP

There is also huge variation by funding source and hospital type. In some Latin American countries private health care organizations pay for transplants, for example, Colombia, Ecuador and Argentina, whereas in other countries there is no charge to recipients nor third party payors, for example, Cuba. Often there is a mixed funding system. There is also a mix of public, *not-for-profit* and private *for-profit* hospitals. These co-variates partly explain the wide range of transplant rates in Latin America.

Latin America countries have segmented health systems reflecting social and economic inequalities [9]. Unlike Cuba with a unified public health care model, most Latin American countries have a mixed health model with some features of the Bismarck model: an insurance system or *sickness funds* financed jointly by employers and employees through payroll deduction and the Beberidge model: Hospitals and clinics are owned by the government and doctors are public employees but there are also private clinics and doctors who collect fees from the government [10, 11]. There are private health care groups in some countries such as Argentina under state incentives. Another health care segment is supported by social security and workers' insurance. There are also public health care systems designed to help everyone regardless of financial resources [12]. The proportion of these potential fiscal resources to funding transplants varies widely between and within countries.

Methods

This study was based on two 2017 data surveys: (1) WBMT/LABMT annual survey; and (2) a transplant expert directed questionnaire to LABMT member countries (Mexico, Cuba, Panama, Costa Rica, Colombia, Peru, Brazil, Ecuador, Venezuela, Uruguay, Paraguay, Chile and Argentina). LABMT conducts an annual activity survey of data from responding centres. Ninety-five centres completed the WBMT/LABMT questionnaire including data on diagnosis, types of transplant and graft, donor type and other co-variates (Supplement Table 1). The LABMT questionnaire was completed by ≥1 transplant expert in each country. It queried

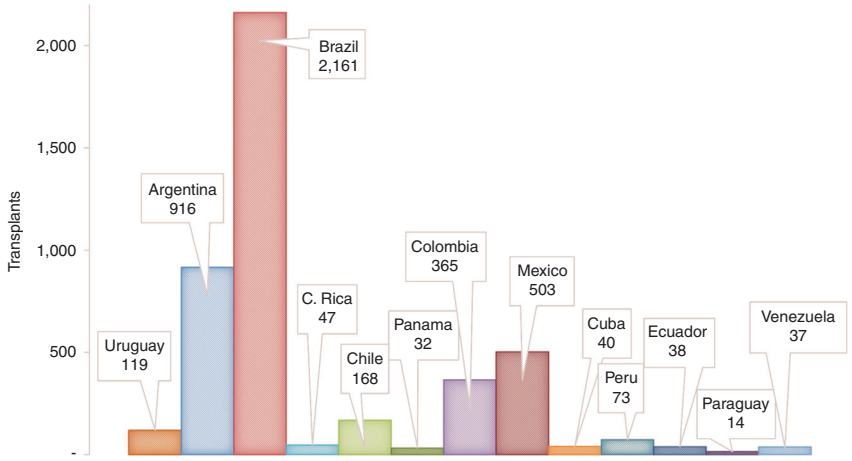

Fig. 1 Transplant number per country. Year 2017.

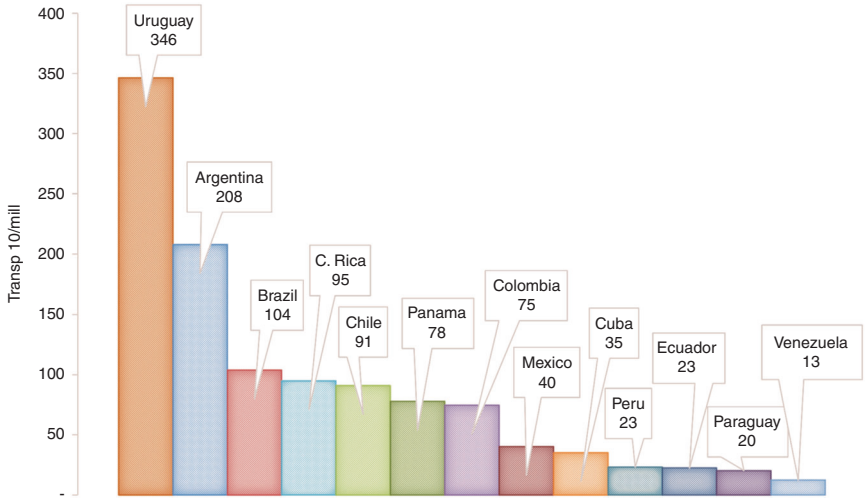

Fig. 2 Transplant rate (number of transplants per 10 million inhabitants). Year 2017.

fiscal support, hospital types, transplant costs and other covariates (Supplement Table 2). There was no auditing of the data. Population data were obtained from the World Bank database 2017. GNI was obtained from the World Bank database (https://databank.worldbank.org/reports.aspx). *per capita* GNI was calculated using with Atlas method, a World Bank method of computing exchange rates to reduce the impact of market fluctuations in the cross-country comparison of national incomes. Data were anonymized such that Ethical Committee approval was not required.

The transplant rate was defined as numbers of transplants *per* 10 million inhabitants *per* country *per* year and used as a surrogate of transplant activity. Funding was considered public when provided and administered by national, state or province taxes and private when provided by social health insurance, including employer and employees contributions, private medical insurance or *out-of-pocket*. Hospitals or health providers were considered public (organized and funded by the state) or private such as those belonging to communities, universities and any *for-profit* entity. Cost was defined as monies charged by providers to payors for the first 100 days posttransplant and expressed in USD. Most countries apply a bundled payment or fixed amount *per* transplant (unit cost) method which reimburses providers for a full range of care rather than itemized costs.

Statistics

The transplant rate was the unit of analysis. Correlations of the transplant rate, type of facility, funding source and cost used the R^2 test (Linear Regression Analysis with least squares) method [13]. Weighted average costs considering frequency of use for type and numbers of transplants were used to calculate unit cost.

Results

Four thousand five hundred and thirteen transplants were reported in 2017 by 95 teams from 13 countries including

Table 1 Number and type of transplant, cost of each procedure and weighted average cost.

Country	N Transplants			Cost USD				*Per capita* GNI[#]	
	Autologous	Allogeneic related	Allogeneic unrelated	Autologous	Allogeneic related	Allogeneic unrelated	Weighted average cost	current US$	Transplant rate[*]
Uruguay	109	8	2	60,000	86,000	86,000	62,080	15,150	354
Argentine	595	247	74	34,000	45,000	71,000	39,939	13,120	207
Brazil	1,383	527	251	10,000	25,000	35,000	16,562	8,700	104
Chile	67	57	44	41,000	83,000	1,74,000	89,777	13,270	94
	33	14	0	65,000	70,000	85,000	66,500	11,150	94
Panama	19	13	0	9,000	18,000	18,000	12,690	13,750	85
Colombia	234	121	11	32,000	40,000	60,000	35,463	5,930	77
Mexico	191	304	8	12,000	15,000	20,000	13,939	8,930	40
Cuba	26	14	0	NA	NA	NA	NA	7,480	35
Peru	61	12	0	18,000	70,000	80,000	26,320	6,060	22
Paraguay	13	1	0	25,000	40,000	60,000	26,050	5,390	20
Ecuador	22	12	4	30,000	60,000	60,000	42,600	5,860	18
Venezuela	31	6	0	15,000	20,000	20,000	15,800	13,080	12

The GNI per capita of Cuba is from 2016 and for Venezuela is from 2013.

[#]Per capita GNI and transplant rate.

[*]World Bank Atlas method.

2771 auto- and 1742 allotransplants (Fig. 1). Median transplant rate was 58 ranging from 354 in Uruguay, the country with the lowest Gini coefficient, to 12 in Venezuela, a country with a high Gini coefficient, a 28-fold difference in transplant rate (Fig. 2 and Table 1).

Costs of an autotransplant varied from US $9000 in Panama to US $65,000 in Costa Rica, a sevenfold difference. Costs of an HLA-matched related allotransplant ranged from US $15,000 in Mexico to US $86,000 in Uruguay, a sixfold difference. Costs of an HLA-matched unrelated donor transplant excluding donor costs ranged from US $18,000 in Panama to US $174,000 in Chile, a tenfold difference (Table 1).

In Costa Rica, Cuba, Panama and Paraguay transplants are done only in public facilities. In Ecuador transplants were only done in private hospitals. In the remaining countries, transplants were done in both. In Costa Rica, Cuba, Panama and Uruguay transplants are payed for with public funds only, whereas in the remaining countries payors were a mix of public or private funding (Table 2). In all countries save Paraguay and Venezuela, there is, in theory, universal access to transplants. Whether this operates effectively in practice is unlikely.

Transplant rate correlated with institution type in countries where transplants were done in private hospitals having higher rates ($R^2 = 0.1051$; Fig. 3). The transplant rate was also higher when the payor was public ($R^2 = 0.1659$; Fig. 4). Lower cost, regardless the payor, was associated with a low transplant rate ($R^2 = 0.1725$; Fig. 5). Private facilities, regardless of funding source, were associated with higher transplant rate ($R^2 = 0.1051$; Fig. 6).

Table 2 Haematopoietic cell transplant distribution per country according to type of hospitals and funding source.

	Transplants done in		Transplants payor %	
	Public facilities %	Private facilities %	Public	Private
Argentina	12	88	18	82
Brazil	43	57	76	24
Chile	22	78	65	35
Colombia	12	88	10	90
Costa Rica	100	0	100	0
Cuba	100	0	100	0
Ecuador	0	100	0	100
Mexico	78	22	80	20
Panama	100	0	100	0
Paraguay	100	0	16	84
Peru	66	34	30	70
Uruguay	40	60	100	0
Venezuela	50	50	17	83

Discussion

Transplant programmes in some Latin American countries such as Peru, Panama and Costa Rica predominantly reflect

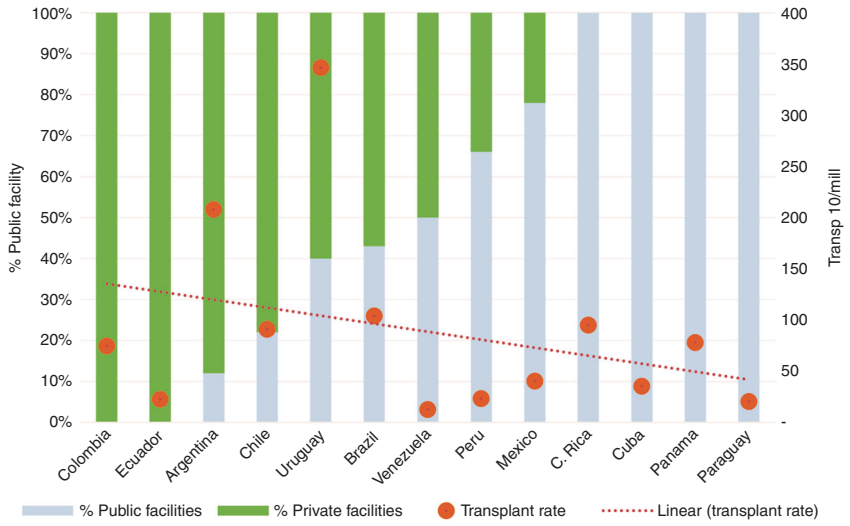

Fig. 3 Influence of hospitals type and transplant rate. In light blue, public hospitals. Mixed colour bars indicate both types of hospitals (colour figure online).

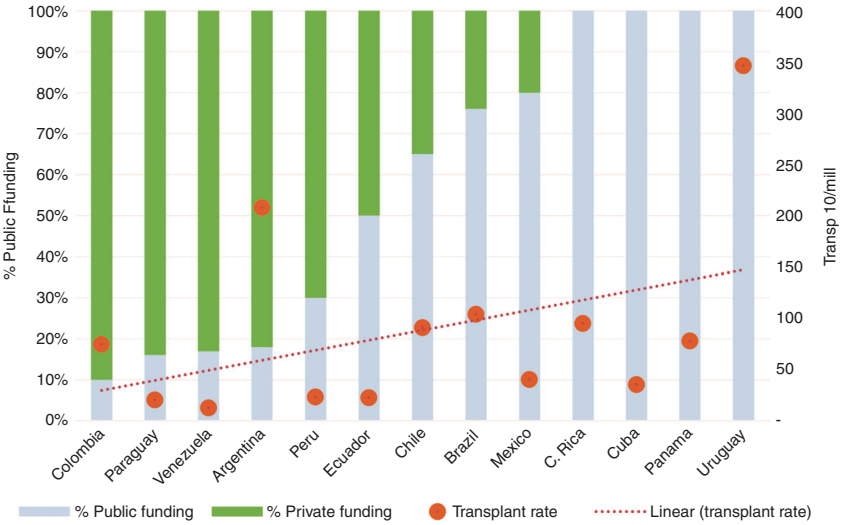

Fig. 4 Influence of funding type on transplant rate. In light blue are public funds. In green private origin funds (colour figure online).

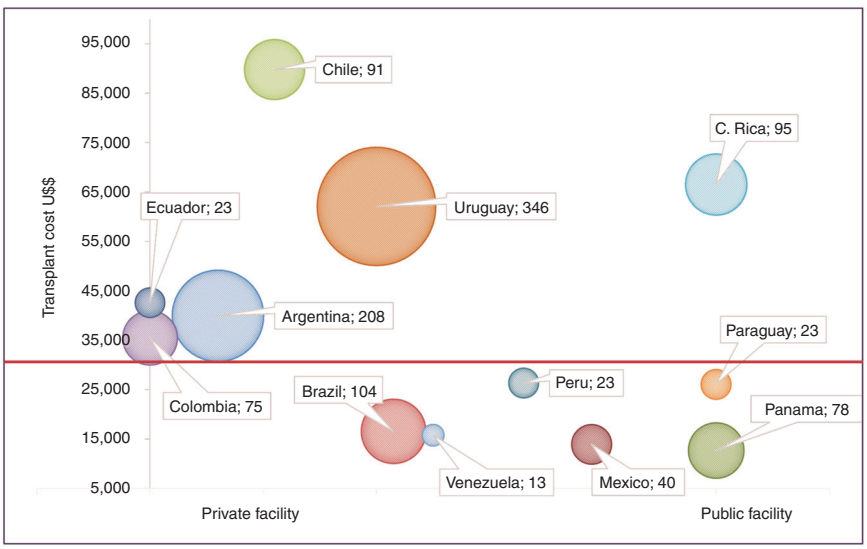

Fig. 5 Correlation among transplant cost, type of hospitals and transplant rate. Bubble size reflects transplant rate. Below the red line countries with lower TR and lower cost are situated (colour figure online).

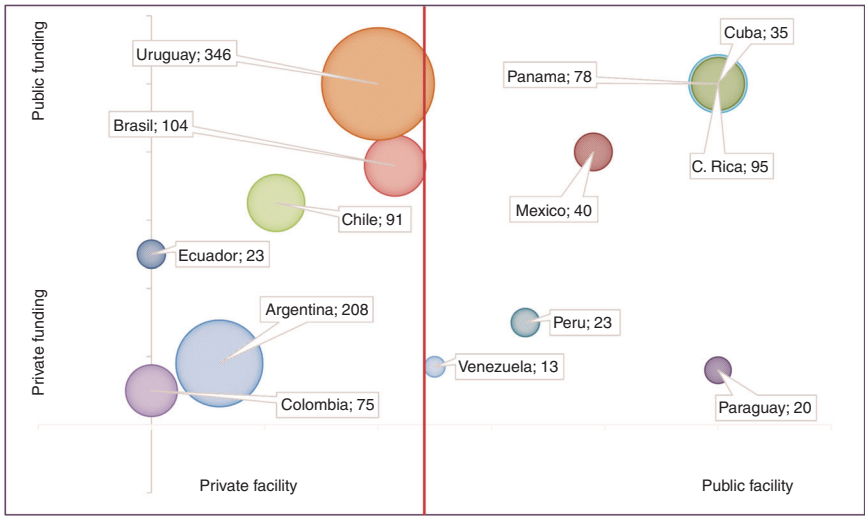

Fig. 6 Correlation among transplant rate, hospitals type and funding origin. On the left of the red line, private hospitals are situated. On the top, public funding (colour figure online).

government health care policies. In others, such as Argentina and Colombia, transplant programmes reflect initiatives of private physicians and hospitals with little government health care policy involvement. Transplant programmes in other countries such as Uruguay, Mexico and Brazil are a mix of these systems.

We recently reported a countries' transplant rate is highly correlated with *per capita* GDP, *per capita* HCE and physician and transplant team densities [5]. Public funding for hematopoietic cell transplants differs greatly between Latin American countries. The same applies to private funding. Often there is a mixture of funding from the public and private sectors. However, most support for skilled personal and specialized equipment comes from the private sector [14]. This is reflected by the association between high transplant rates in countries where most transplants supported by public sector funding are performed in private hospitals.

There are few other studies of transplant costs and/or reimbursement in Latin America [15, 16]. In one study, government reimbursement for autotransplants was US $13,000, for sibling donor allotransplants, US $31,500 and from an unrelated donor, US $40,500. The author mentioned hospitals were reluctant to perform these because of likely cost overruns. In a study from Mexico average allotransplant cost was about US $12,500. Interestingly, the authors suggested this low cost makes allotransplants doable in developing countries. This contrasts with our finding of higher transplant rates in countries with higher transplant costs. A possible explanation is our finding of a preference for private hospitals, whereas the Mexico report is from a public hospital.

Interestingly, and seemingly paradoxically, countries with the lowest transplant cost have the lowest transplant rates. This is likely because transplants are done in public facilities by publicly employed physicians on fixed salaries with little incentive to perform transplants because of considerable effort, limited resources and no fiscal benefit.

In socialized health care systems with predominately public hospitals, it is difficult to accurately estimate costs of complex medical procedures like transplants. Personnel cost such as doctors and nurses salaries are typically not considered nor are costs of many widely used drugs such as antibiotics, intravenous fluids, disposables, etc. In contrast, these costs are typically considered in private hospitals. When reimbursement for transplants is low there is little fiscal incentive for physicians and hospitals to perform them resulting in lower transplants rates. A low transplant team density is another confounding co-variate.

There are incentives other than fiscal which could explain diverse transplant rates and transplant team densities. The most altruistic is physicians wanting to provide what they deem a safe and effective therapy. Other incentives include academic promotion, national and international recognition, publications and interactions with and honoraria from drug companies. We discuss these interactions elsewhere [17] but because of the nature of our survey, we were unable to quantify these co-variates.

Our data show transplant rates in Latin America vary 30-fold, whereas costs of transplants vary 6–7-fold. Our most interesting finding is higher transplant rates are found in countries where physicians in private practice do transplants in private hospitals reimbursed by public funds. Although this may seem paradoxical we think it reflects greater efficiency of private hospitals which are driven by for-profit considerations.

Interestingly, co-variates associated with transplant rate in Latin America contrast with those in the USA and EU. These regions have similar transplant rates but different structures, socialized medicine in most European countries

versus predominately private insurance in the USA. Most transplants in the USA and in some EU countries are done in non-profit academic medical centres or university-affiliated hospitals. Moreover, physicians performing transplants typically do not benefit fiscally from doing more transplants. The major motivation in the USA and EU seems providing what is perceived to be *best* therapy, local, national and global recognition, securing hospital resources such as beds, nurses and assistants. Our data indicate some of these motivations are of a lesser magnitude in physicians doing transplants in Latin American countries.

Our study has important limitations. First, data were obtained from 1–2 transplant experts in each country. To check accuracy we queried several experts in three countries and found few discordances. Second, data reported to the WBMT/LABMT are not audited. Third, several correlations we report are modest. The correlation coefficients we report are weak, 0.10 to 0.16. As such, our conclusions need validation. We also determined <2% of persons left their country of residence and received a transplant elsewhere. Lastly, relationships we describe may not operate in other geographic regions, health care system and cultures. Regardless, our conclusions are actionable and can inform policies of how to improve transplant rates in Latin America and in other developing countries and regions.

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Compliance with ethical standards

Conflict of interest RPG is a Consultant to BeiGene Ltd., CStone Pharmaceuticals and Kite Pharmma; a Consultant toFusion Pharma LLC, LaJolla NanoMedical Inc. and Mingsight Parmaceuticals Inc.; an Advisory Board member for Antegene Biotech LLC and StemRad Ltd; Medical Director at FFF Enterprises Inc; Partner in AZACA Inc; and a member of the Board of Directorsof the Russian Foundation for Cancer Research Support.

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