Ways to gain experience, training abroad, twinning with other institutes, internet, telemedicine, and others

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January 16, 2017
4th WBMT Workshop
Riyadh, Kingdom of Saudi Arabia

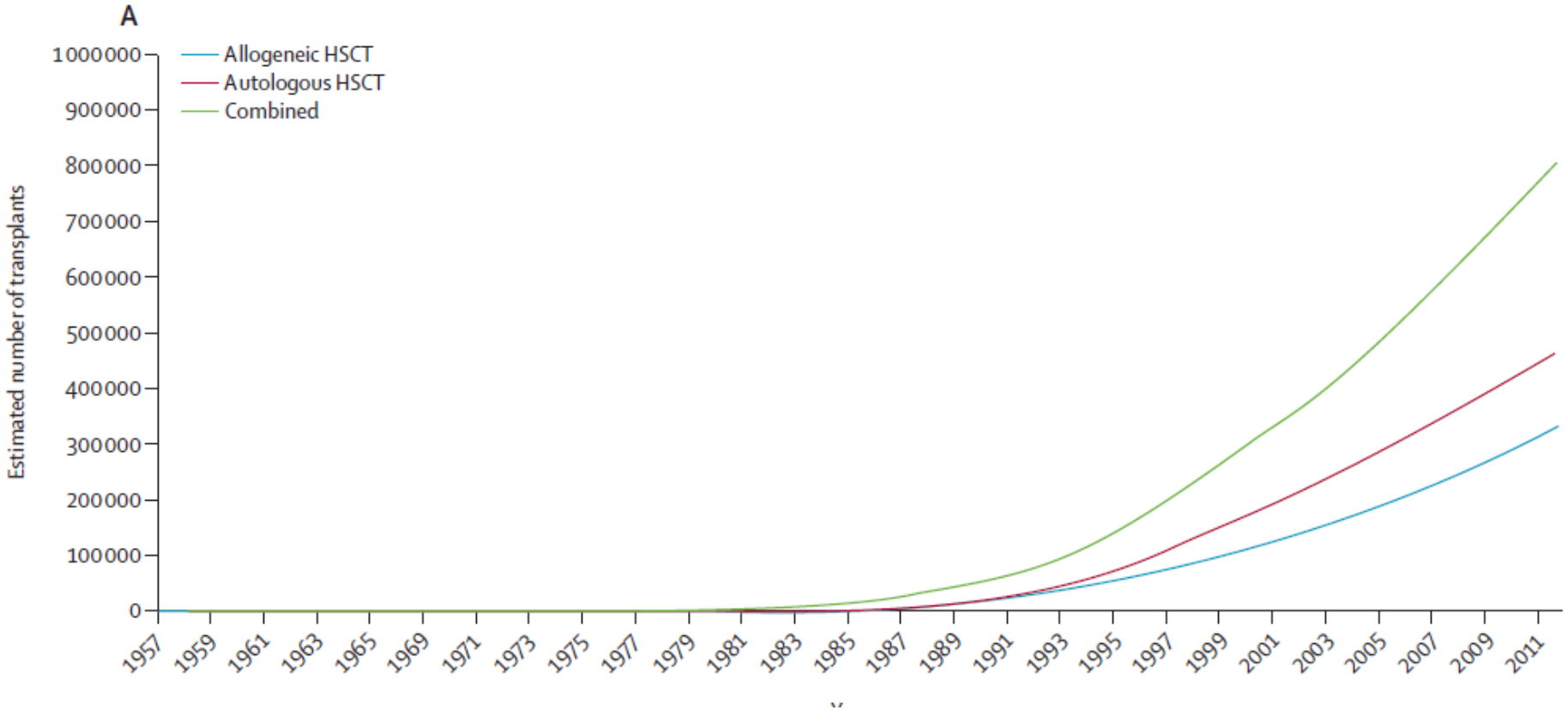
MOFFITT CANCER CENTER

Outline

- Hematopoietic cell transplantation activity
  - Here to stay
  - Becoming more complex
- Experience, training abroad
  - Focused based on needs
- Studies needed to develop national/regional data
  - Local-regional and international collaboration
- Twinning/networking
- Internet of things/telemedicine

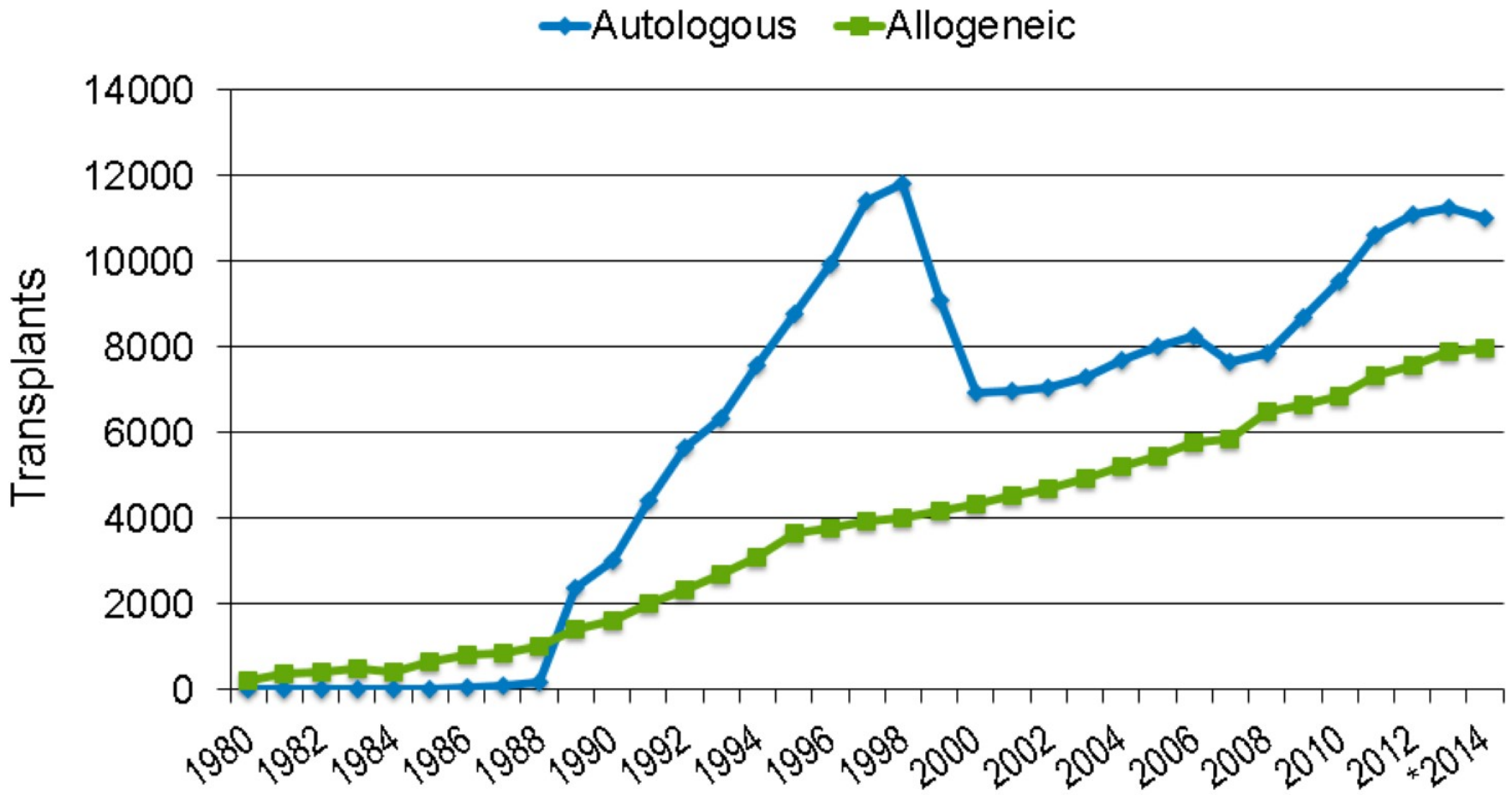
One million haemopoietic stem-cell transplants: a retrospective observational study

Alois Gratwohl, Marcelo C Pasquini, Mahmoud Aljurf, Yoshiko Atsuta, Helen Baldomero, Lydia Foeken, Michael Gratwohl, Luis Fernando Bouzas, Dennis Confer, Karl Frauendorfer, Eliane Gluckman, Hildegard Greinix, Mary Horowitz, Minako Iida, Jeff Lipton, Alejandro Madrigal, Mohamad Mohty, Luc Noel, Nicolas Novitzky, José Nunez, Machteld Oudshoorn, Jakob Passweg, Jon van Rood, Jeff Szer, Karl Blume†, Frederic R Appelbaum, Yoshihisa Kodera, Dietger Niederwieser, for the Worldwide Network for Blood and Marrow Transplantation (WBMT)



Gratwohl et al. Lancet Haematol. 2015 Mar;2(3):e91-100

Annual Number of Transplant Recipients in the US by Transplant Type



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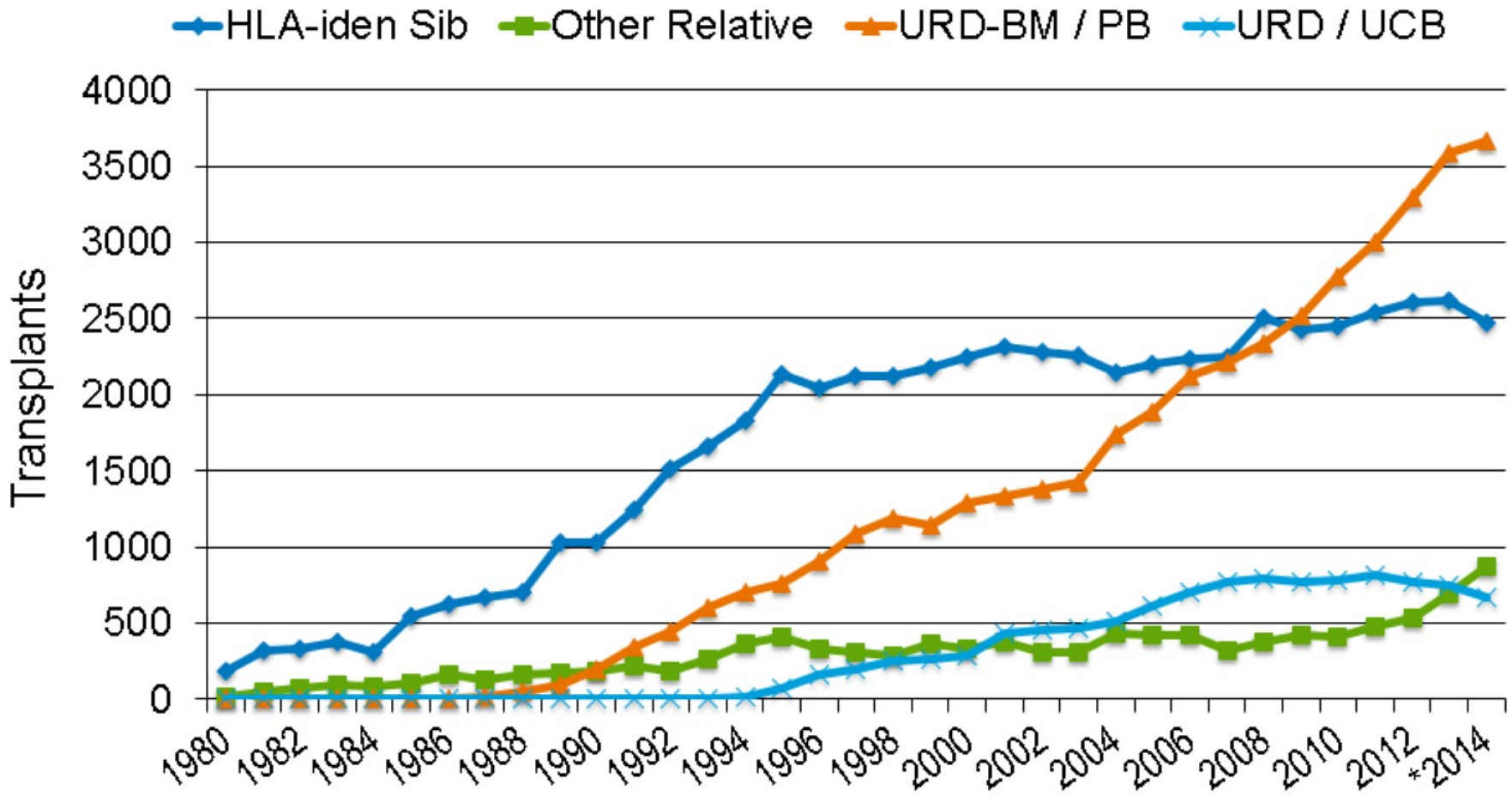
*2014 Data incomplete

Allogeneic Transplant Recipients in the US, by Donor Type



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*2014 Data incomplete

COMMENTARY

Impending Challenges in the Hematopoietic Stem Cell Transplantation Physician Workforce

James L. Gajewski,[1] C. Frederick LeMaistre,[2] Samuel M. Silver,[3] Michael C. Lill,[4] George B. Selby,[5] Mary M. Horowitz,[6] J. Douglas Rizzo,[7] Helen E. Heslop,[8] Claudio Anasetti,[9] Richard T. Maziarz[1]

Table 2. Age of BMT Physicians

Age Range, Years	All BMT Physicians, %	Adult BMT Physicians, %	Pediatric BMT Physicians, %
70-78	1.6	1.8	0
65-69	3.1	3.5	0
60-64	10.2	11.7	2.4
55-59	13.6	14.8	6.5
50-54	21.2	21.5	18.7
45-49	18.6	20.0	12.2
40-44	17.1	15.1	28.5
34-39	14.6	11.6	31.7
All ages	100	100	100

Data derived, with permission (R. Krawisz, personal communication, June 2009), from the ASBMT membership records.

Table 3. Estimated Supply and Demand of BMT Physicians

	Adult BMT Physicians, n	Pediatric BMT Physicians, n	All BMT Physicians, n
BMT physician requirements in 2020	1991	235	2226
Current supply	959	156	1115
Projected retirements	232	15	247
New BMT physicians needed *	1264	94	1358

Data derived, with permission (R. Krawisz, personal communication, June 2009), from the ASBMT membership records.

Gajewski JL, et al. Biol Blood Marrow Transplant. 2009; 15: 1493-1501

Training & experience needed

- Access to allogeneic HCT has expanded with the advent of reduced-intensity/non-myeloablative allografting
  - Patients of more advanced age
  - With comorbidities

  } **A real challenge**

- Also,
  - ↑ Pool of HLA compatible unrelated donors
    - Not easily accessible to developing countries
  - Haploidentical transplantation
    - One child per family in China
    - Cost
  - Benign hematologic disorders (Sickle Cell Disease, Thalassemias, etc.)

Life expectancy at birth, male (years)

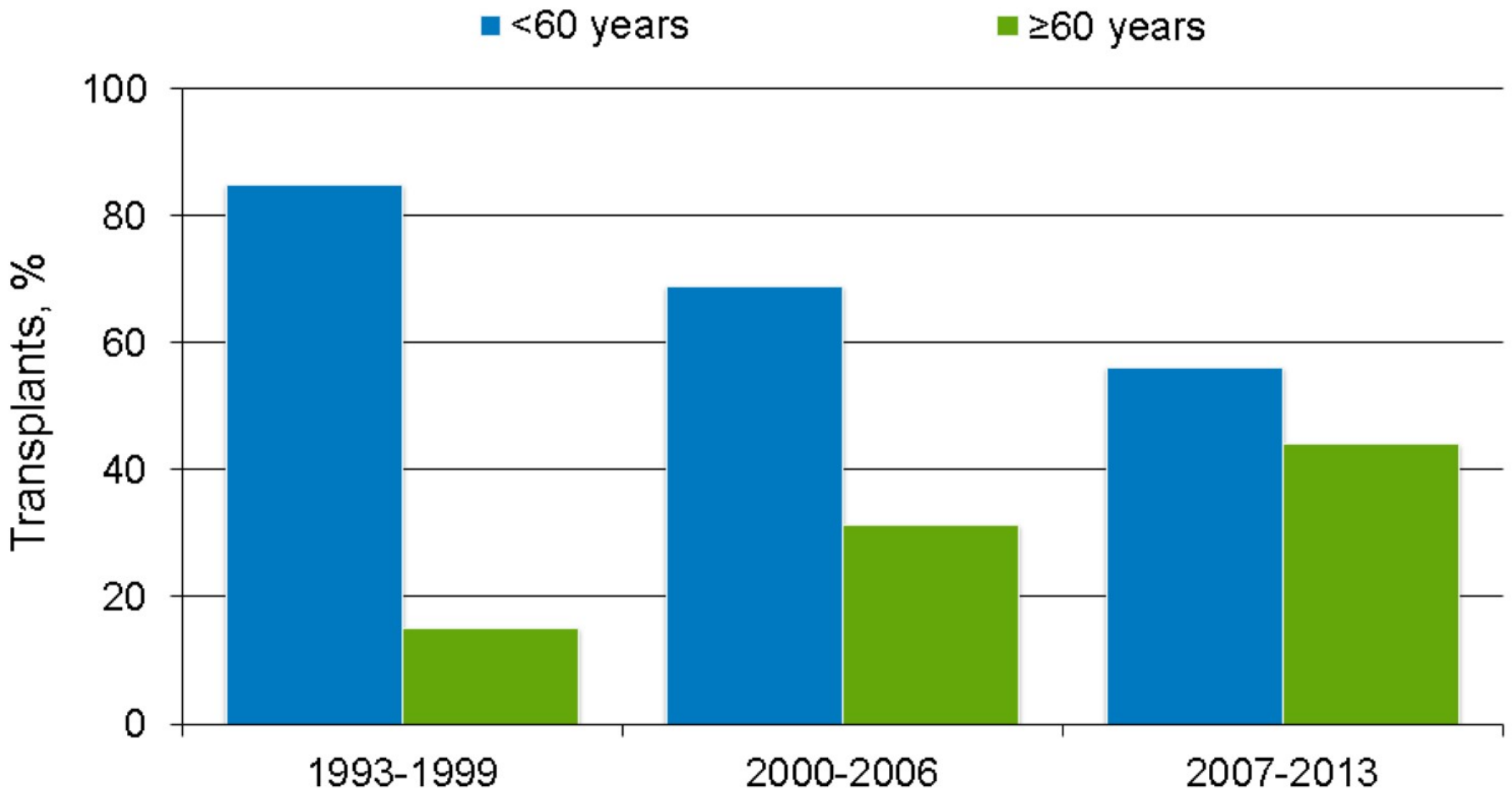
Source: data.worldbank.org (accessed Dec 27, 2016)

Life expectancy: selected countries

Country	1960 (years of age)	2014 (years of age)
Algeria	46	73
Central African Republic	35	49
China	42	74
Colombia	55	70
India	42	67
Japan	68	84
Lebanon	62	78
Saudi Arabia	44	73
United Arab Emirates	50	76
United Kingdom	68	79
United States of America	67	77

Source: data.worldbank.org (accessed Dec 27, 2016)

Trends in Autologous Transplants by Recipient Age*



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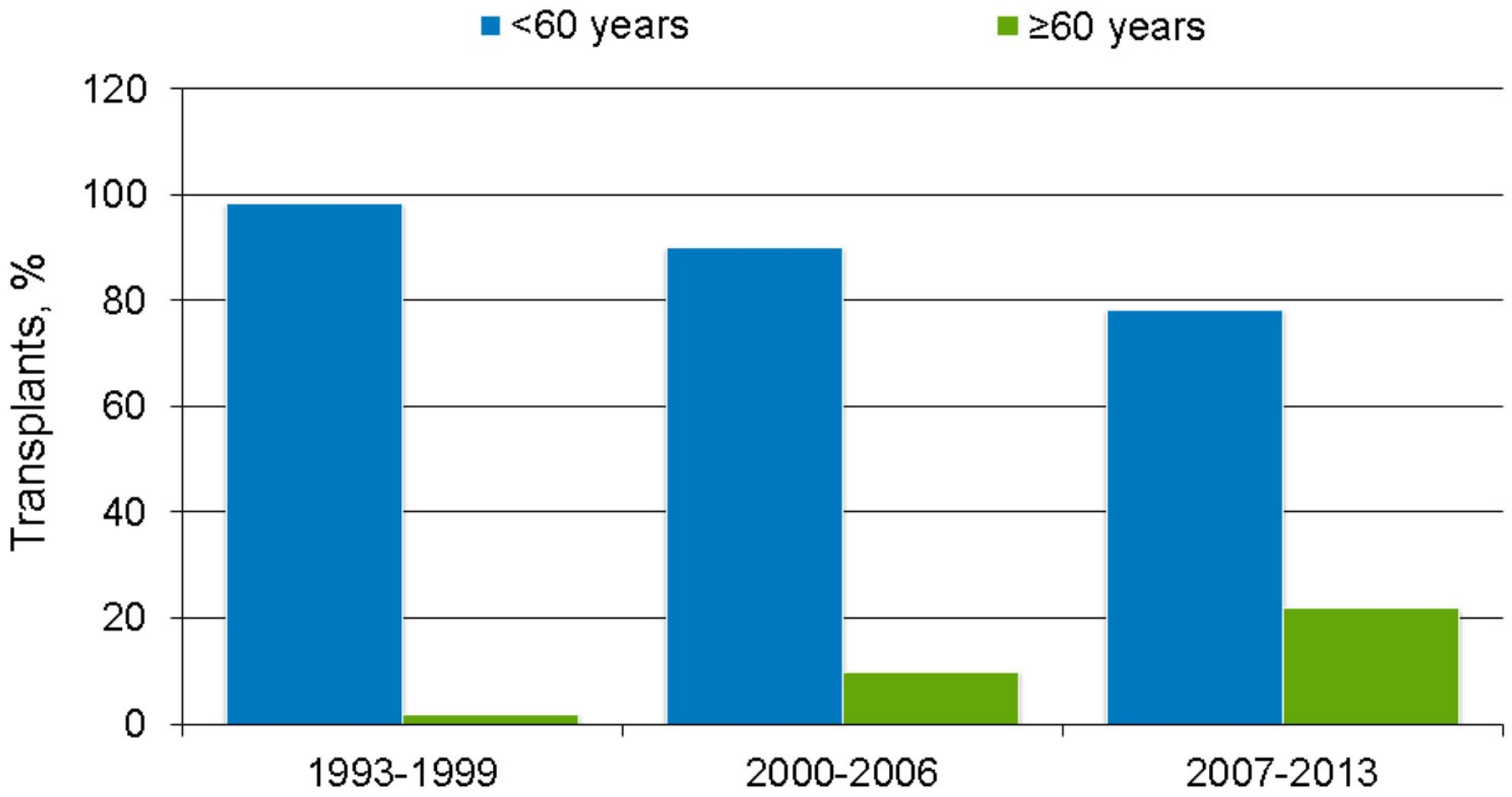
*Transplants for AML, ALL, NHL, Hodgkin Disease, Multiple Myeloma

Trends in Allogeneic Transplants by Recipient Age*



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*Transplants for AML, ALL, NHL, Hodgkin Disease, Multiple Myeloma

Bone Marrow Transplantation (2003) 31, 417–421

www.nature.com/bmt

Review

Transplant center characteristics and clinical outcomes after hematopoietic stem cell transplantation: what do we know

FR Loberiza Jr[1], DS Serna[1], MM Horowitz[1,2] and JD Rizzo[1,2]

[1]*International Bone Marrow Transplant Registry, Health Policy Institute, Medical College of Wisconsin, Milwaukee, WI, USA; and* [2]*Division of Neoplastic Diseases and Related Disorders, Department of Internal Medicine, Medical College of Wisconsin, Milwaukee, WI, USA*

- Outcomes may vary among patients with similar disease biology and treatment

- Center effect entails differences in outcome among centers presumed to be due to differences in the way health care is delivered:
  - Training and experience of personnel
  - Resources available
  - Organization

Table 2 Studies primarily looking at the center effects in hematopoietic stem cell transplantation setting

Studies	*Year*	*Selection*	*Center effect variable studied*	*Outcome studied*	*Results*
Horowitz *et al*	1992	Leukemia Early stage HLA-identical sibling	Procedure Volume ≤5/yr	Relapse 1.5X TRM TRM DFS	Not significant Significant Significant
Hows *et al*	1993	Leukemia MDS SAA All stages Unrelated donor	Procedure Volume <2/yr URD	Engraftment Acute GVHD Survival ↓ OS	Not significant Not significant Significant
Frassoni *et al*	2000	Leukemia Early stage HLA-identical sibling	Procedure Volume Center Experience	Relapse TRM DFS	Not significant Significant Significant
Matsuo *et al*	2000	Leukemia All disease stage All donors	Procedure Volume <25/7yr URD	100-day survival DFS Survival ↑ death risk	Significant Significant Significant
Matsuo *et al*	2000	MDS Lymphoma SAA All disease stage All donors	Procedure Volume	100-day survival Survival	Not significant Not significant

Modified from Loberiza et al. Bone Marrow Transplant. 2003; 31: 417-21

Focused training: assess your needs

- What is the expertise needed?
  - Clinical (BMT, Pathology, Radiation Oncology, ID, ICU)?
  - Pharmacy?
  - Nursing?
  - Stem cell processing/procurement?
  - Database management and maintenance?
  - Others?
- Where is it available?
  - For example, allo-HCT for Thalassemia (Italy, India, etc.)
- Are the imported algorithms applicable to your current practice setting?
  - Adjustment/tuning
  - Establishing new standards of care (late effects/survivorship)
  - Updating is constantly needed
- Resources needed/Cost (sustainability)

Define training needs

- Disease specific?
  - Thalassemia, Sickle Cell, BM failure syndromes
- Procedure-specific?
  - Develop a haploidentical transplant program
  - Cord blood program
- High-risk population?
  - Septuagenarians?
- Cell processing specific?
- LTFU/survivorship clinic?
- Others

Focused training: i.e. Thalassemia

- Understanding specific risks of the procedure to particular diseases
  - Age of the patient
  - Is there liver fibrosis? How bad?
  - Is hepatomegaly present? How bad?
  - Other organs: heart? Lungs?

- Allogeneic HCT can be successful in over 80% of low-risk cases

Focused training: Thalassemia

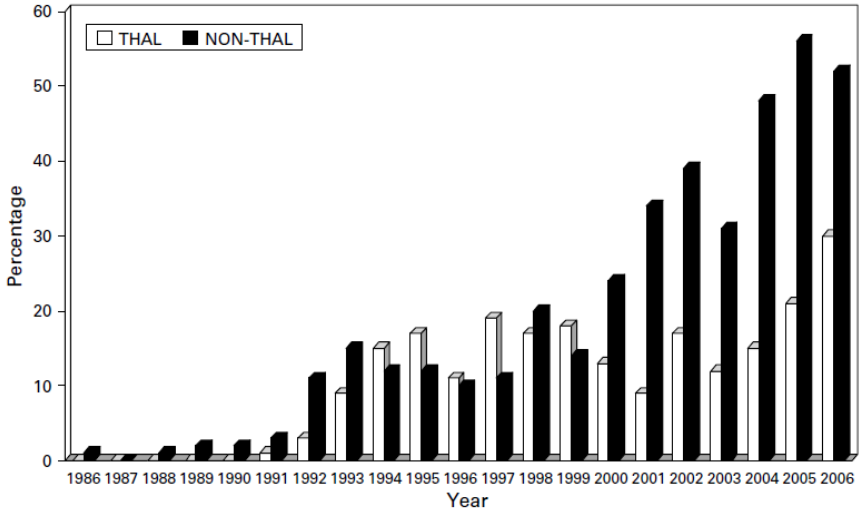

Figure 3 BMT at for thalassemia, compared with other indications. Christian Medical College Hospital, Vellore (October 1986–December 2006).

Table 3 Outcome of allogenic BMT for thalassemia Christian Medical College Hospital, Vellore (5-year Kaplan–Meier estimate of overall survival and EFS)

Class	*Number*	*Survival (%)*	*EFS (%)*	*Rejection (%)*
All patients	218	72.3 ± 3.1	65.3 ± 3.3	14.6
Class I	15	71.8 ± 11.98	71.8 ± 11.98	0
Class II	89	82.6 ± 4.1	78.3 ± 4.4	12.4
Class III	114	64.5 ± 4.6	54.6 ± 4.8	18.4

Risk groups	OS	DFS
Class 1 &2	96.7%	80%
Class 3	65.2%	54.5%
All	79.3%	65.8%

Unrelated BMT transplantation for beta-thalassemia: the experience of the Italian Bone Marrow Transplant Group

Chandy et al. Bone Marrow Transplantation. 2008; 42:S81-84
La Nasa et al. Ann NY Acad Sci. 2005; 1054: 186-95

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Resources

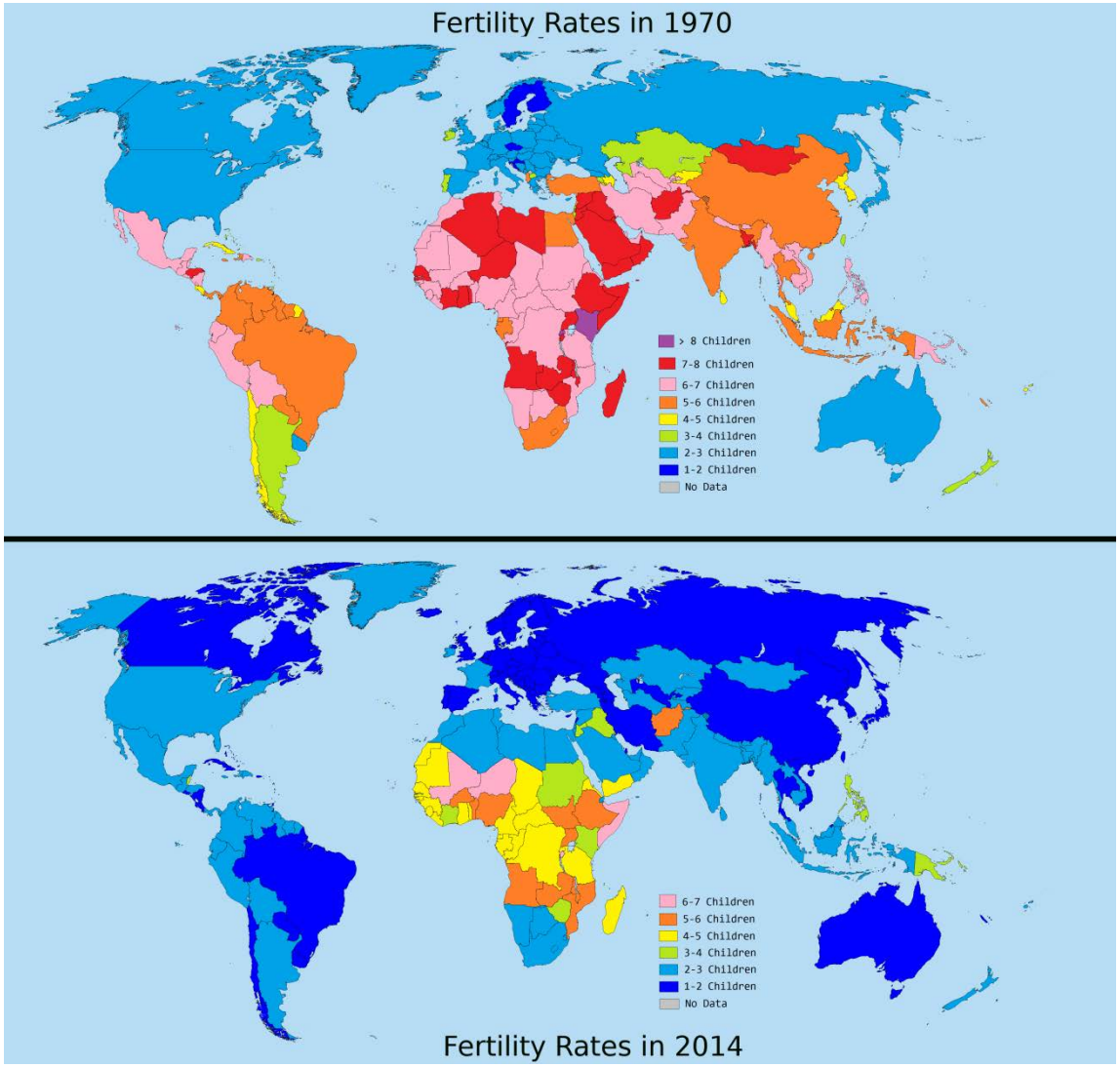
India (Jaipur)

A STOP Thalassemia project

- Cure2Children's (C2C) team of 6 volunteer doctors and 4 specialist nurses on rotation, worked "hands-on" with the local medical team for 6weeks, while simultaneously preparing the facility itselff
- In February of 2012, the local medical team conducted its 1st BMT
- All of the center's first transplanted children are doing well

http://www.cure2children.org/project/jaipur-india

Haploidentical transplantation: why?



- Declining fertility rates
- Smaller families
- Cost (?)

Source: http://brilliantmaps.com/fertility-rates/

Haploidentical transplantation: why?

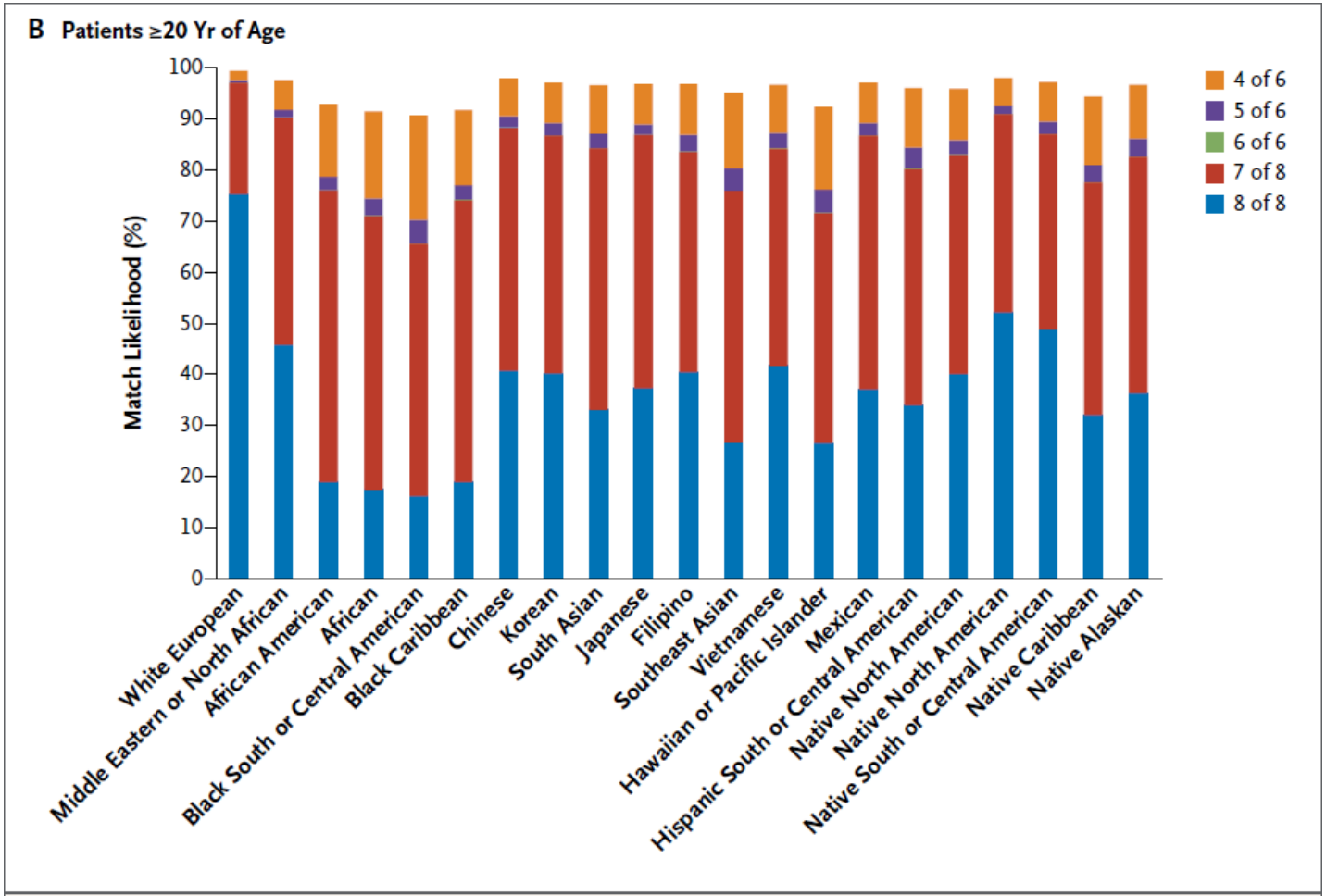


Figure 1. Match Likelihoods According to Racial and Ethnic Group and Age.

The likelihood of finding a match with the use of a search strategy in which an 8/8 HLA-matched donor is sought first, then a 7/8 HLA-matched donor, and thereafter a cord-blood unit with an adequate cell dose is shown.

Graget et al. N Engl J Med 2014;371:339-48.

Importance of registries

Bone Marrow Transplantation (2008) 42, S1–S2

www.nature.com/bmt

REVIEW

The role of registries in facilitating clinical research in BMT: examples from the Center for International Blood and Marrow Transplant Research

MM Horowitz

Department of Medicine, Medical College of Wisconsin, Milwaukee, WI, USA

- Observational databases facilitate research into HCT outcomes (CIBMTR, EBMT, others)
  - Address questions difficult to answer through clinical trials
    - Analyze trends
    - Vast volume
  - Platform to design and develop prospective clinical trials

Develop own databases / registries

- Allows to analyze outcome trends in own population
  - Identify gaps where new strategies are needed
    - Disease related
    - Supportive care
    - Center specific
    - Others
  - Use as benchmark for developing future prospective studies
    - Attract large pharma-sponsored studies to your part of the world
- Compare your outcomes to those of other transplant registries
  - Collaboration
  - Potential to improve publication output (quality and quantity)

Networking and twinning

St. Jude Children's Research Hospital

- **International networks**
  - Fosters development of regional networks among international partners and collaborators
  - Moves beyond one-on-one partnership approach
    - Promotes self-sufficiency and sharing of expertise among international sites
    - Accelerate global improvements in clinical care of children with cancer and other life-threatening diseases

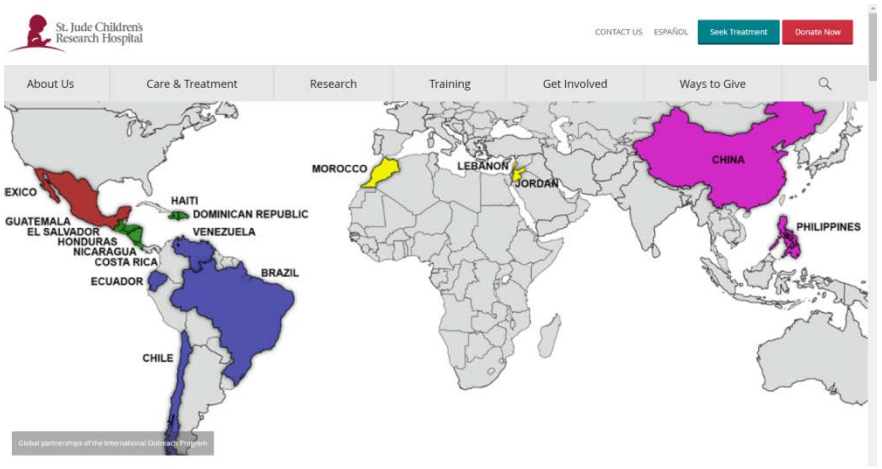
www.stjude.org/global/international-outreach/international-networks.html

St. Jude Children's Research Hospital

- International networks
  - **AHOPCA:** The Asociación de Hemato-Oncología Pediátrica de Centro América
    - Guatemala, Honduras, El Salvador, Nicaragua, Costa Rica, Dominican Republic and Panama
  - **POEM:** Pediatric Oncology East and Mediterranean Group
    - Armenia, Bahrain, Egypt, India, Iraq, Iran, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Palestine, Saudi Arabia, Syria, Tunis, Turkey, United Arab Emirates and Yemen
  - **National Childhood ALL Study Group in China**
    - 20 major centers in China are participating

www.stjude.org/global/international-outreach/international-networks.html

International partnership



Eastern Mediterranean		
JORDAN (Amman)	**Medical Facility**	**King Hussein Cancer Center Year Program Initiated: 1996**
	Foundation	King Hussein Cancer Center Foundation
LEBANON (Beirut)	Medical Facility	American University of Beirut Year Program Initiated: 2000
	Foundation	Children's Cancer Center of Lebanon
MOROCCO (Casablanca)	Medical Facility	Hôpital 20 Aout 1953 Year Program Initiated: 2000
	Foundation	Agir, Association Marocaine de Soutien Aux Malades du Sang
MOROCCO (Rabat)	Medical Facility	Hôpital d'Enfants Year Program Initiated: 2000
	Foundation	L'Avenir, Association des Parents et Amis de Enfants

ww.stjude.org/global/international-outreach/international-partnerships.html


Case report

OPEN ACCESS

A prospective international cooperative information technology platform built using open-source tools for improving the access to and safety of bone marrow transplantation in low- and middle-income countries

Rajat Kumar Agarwal,[1] Amit Sedai,[1] Sunil Dhimal,[1] Kumari Ankita,[1] Luigi Clemente,[2] Sulman Siddique,[2] Naila Yaqub,[3] Sadaf Khalid,[3] Fatima Itrat,[3] Anwar Khan,[3] Sarah Khan Gilani,[3] Priya Marwah,[4] Rajpreet Soni,[4] Mohamed El Missiry,[2] Mohamed Hamed Hussain,[2] Cornelio Uderzo,[2] Lawrence Faulkner[2]

- **Jagriti innovations** (Bengaluru, Karnataka, India)
  - Tailored solutions for complex workflows and business applications
  - Developed a collaboration tool in partnership with the Cure2Children Foundation
  - Used by health professionals in Italy, Pakistan, and India for the collaborative management of BMT patients who received the procedure for Thalassemia major since Aug. 2008
  - Online open access database covers data recording, analyzing, and reporting besides enabling knowledge exchange, telemedicine, capacity building, and quality assurance

Agarwal RK, et al. J Am Med Inform Assoc 2014;21:1125–1128
www.jagriti.co.in

“Change is the law of life. And those who look only to the past or the present are certain to miss the future”

President John F. Kennedy

May 29, 1917-Nov 22, 1963

Telemedicine

Doctors are linking up with patients by phone, email and webcam. But some critics question whether the quality of care is keeping up with the rapid expansion of telemedicine. Illustration: C.J. Burton for The Wall Street Journal

By MELINDA BECK

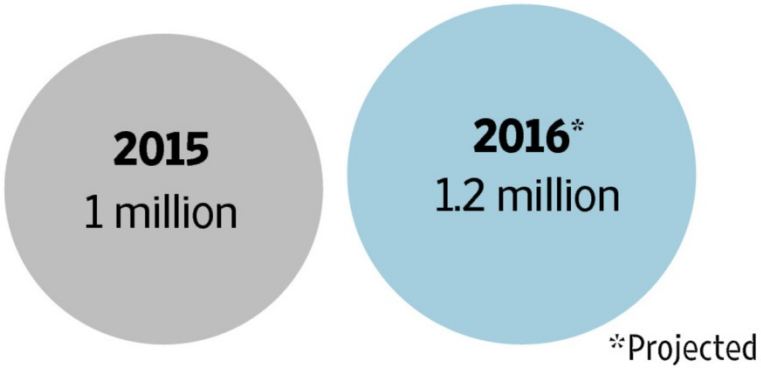
June 26, 2016 10:10 p.m. ET

THE WALL STREET JOURNAL.

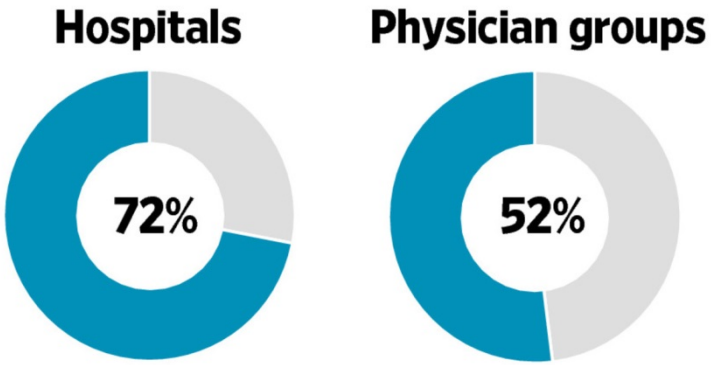
THE WALL STREET JOURNAL.

- Telemedicine is transforming healthcare
  - It is already here
  - It is facilitating
    - Physician ↔ Patient communication
    - Physician ↔ Physician communication
  - Allows better care where medical expertise is unavailable

The number of virtual doctor visits in the U.S.



Percentage of providers that have telemedicine programs



Beck M. Wall Street Journal. June 26, 2016

Telemedicine

- Telemedicine is spreading rapidly
  - >15 million Americans received some kind of medical care remotely in 2015, according to the American Telemedicine Association. Numbers expected to grow by 30% in 2016

- Challenges remain
  - Is quality being sacrificed for convenience?
  - Consulting random doctors
    - Continuity of care?
  - Licensing and regulations across state/provincial/country/continent lines
  - Privacy rules (not clearly defined doctor-patient relationship)

Beck M. Wall Street Journal. June 26, 2016

Telemedicine in Hematopoietic Cell Transplantation

- **Institution-to-institution**
  - Virtual meetings
    - Tumor board: discuss indications/eligibility for procedure
    - Review of Radiology/EKG
    - Pathology/Cytology: GVHD diagnosis, challenging diagnoses
- **Patient-to-physician**
  - Real time access to information regarding changes in clinical condition
  - Potential to improve compliance with prescribed therapies
  - Surveillance

Telemedicine in HCT: Institution-to-institution

- Ultimate goal is to share knowledge to:
  - Improve patient care
    - By developing modern treatment algorithms
    - Optimizing SOPs
  - Foster research collaborations
    - Enhance access to new therapies as part of clinical trials
    - Develop databases
      - Assess outcomes periodically
      - Identify gaps where change/improvement is needed
  - Enhance operational efficacy
    - Cost containment

Closing remarks

- Effective training requires clear understanding of the center needs
  - Focused
  - Continuous self-assessment
  - Twinning and networking
- Eventually move from
  passive learning → knowledge sharing
- Technology has made the world flat
  - Universal and easy access to available knowledge
  - Integrate technology to enhance and expand all aspects of care

شكرا

Thank you

Gracias

Grazie

Obrigado

Danke

ありがとうございました

Merci