



# Can we lower the cost and maintain quality?

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*BMT Late effects initiative*

*Chair, ASBMT survivorship SIG*

# Disclosures

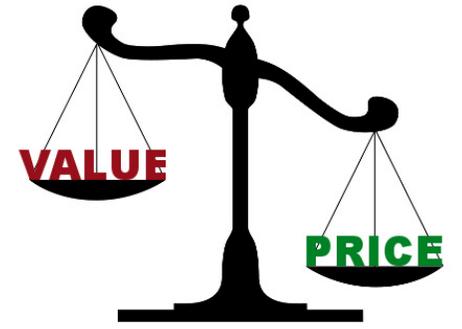
- No relevant disclosures

# Goals and Objectives

To understand

- Basics of costs in HCT
- Basics of quality in HCT
- Quality and costs together: Can you maintain both costs and high quality?
- Future directions

# Basics of Costs (Economic definitions)



- Value: How much usefulness or pleasure an individual gets from a commodity or service. Value is still stable and subjective (utility)
- Price/Cost: Cost and the (final) price are identical numbers (unless market trends are being studied). Real cost should be adjusted for inflation e.g. for 2015 US\$.
- Worth: In economics, worth is related to the theory of capital. We will sell something only when its worth in the market exceeds its value to us.
- Competitive market: Buyers and sellers are equally informed.

# Costs of Hematopoietic Cell Transplant (HCT)

Costs of autologous and allogeneic HCT in US: a study using a large National Private Claims Database – Majhail et al.

<i>Cost category</i>	<i>Transplant type</i>		
	<i>Autologous HCT</i>	<i>Allogeneic HCT</i>	<i>Not specified<sup>a</sup></i>
<b>Sample size</b>	<b>1678</b>	<b>1320</b>	<b>367</b>
<b>Number of hospitalizations, median (range)<sup>b</sup></b>	<b>1 (1–8)</b>	<b>1 (1–7)</b>	<b>1 (1–6)</b>
<b>Total days hospitalized, median (IQR)</b>	<b>19 (15–23)</b>	<b>31 (23–45)</b>	<b>20 (6–30)</b>
<b>Total costs, median (IQR)</b>	<b>\$99 899 (73 914–140 555)</b>	<b>\$203 026 (141 742–316 426)</b>	<b>\$106 782 (54 728–198 963)</b>
<b>Total outpatient costs, median (IQR)</b>	<b>\$7462 (3079–16 038)</b>	<b>\$20 767 (8898–41 271)</b>	<b>\$7829 (1771–22 756)</b>
<b>Total inpatient costs, median (IQR)</b>	<b>\$88 429 (62 828–123 328)</b>	<b>\$174 398 (116 996–269 129)</b>	<b>\$90 000 (51 994–170 553)</b>
<b>Costs for HCT hospitalization, median (IQR)</b>	<b>\$82 606 (59 165–110 881)</b>	<b>\$151 899 (106 438–233 282)</b>	<b>\$82 641 (46 377–145 326)</b>
<b>Costs for subsequent hospitalization, median (IQR)<sup>c</sup></b>	<b>\$0 (0–0)</b>	<b>\$0 (0–22 585)</b>	<b>\$0 (0–7940)</b>

# Costs of HCT as reported in literature

<b>Publication</b>	<b>Year of publication</b>	<b>Country</b>	<b>Cost of allogeneic HSCT (US\$)</b>	<b>Cost of autologous HSCT (US\$)</b>
Saito et al.	2008	United States	128,800	
Sharma et al.	2014	India	17, 914	12,500
Jaime-Perez et al.	2015	Mexico	12,504	
Saber et al.	2013	Brazil	31, 500 (related)  40,500 (unrelated)	

# Costs of HCT - Drivers

Direct costs vs indirect costs

- Drugs and other treatment modalities (e.g. ECP)
- Testing (including molecular, HLA, infectious panels)
- Inpatient hospitalization, hospital acquired infection & readmission costs
- Transfusion costs
- Complications: Infections, GVHD, death?
- Radiology
- Who bears the cost: Hospital, insurance company, federal budgets, individuals, city, state, country, world?
- Unaccountable: Work loss, caregiver work loss, OOP expenses.

# GVHD costs?

## Hashmi et al. ASBMT 2017

Table 1. Treatment protocols and costs

Active ingredient	Brand names	Dose/form	Price	Treatment protocol	6 months cost*
Tacrolimus		0.5 mg (100)	\$ 222	0.12 mg/kg/day, 6 months	\$ 6,823
		1 mg (100)	\$ 445		
		5 mg (100)	\$ 2,229		
Sirolimus		2 mg (100)	\$ 3,149	6mg loading, 2mg/day, 6 months	\$ 5,732
Rituximab	Rituxan	100 mg/10 mL (10mL)	\$ 963	375 mg/m <sup>2</sup> /week, 4 weeks	\$ 26,984
		500 mg/50 mL (50mL)	\$ 4,818		
Ruxolitinib	Jakafi	5 mg (60)	\$ 12,703	10-20 mg/day, 6 months	\$ 76,219
		10 mg (60)	\$ 12,703		
HCQ		200 mg (100)	\$ 408	800 mg/day, 6 months	\$ 2,943
Imatinib	Gleevec	100 mg (90)	\$ 10,112 \$ 12,146	100 mg/day, 6 months	\$ 20,225
Bortezomib	Velcade	3.5 mg (1)	\$ 1,923	0.2 mg/m <sup>2</sup> /week, 6 months	\$ 46,166
Ibrutinib	Imbruvica	140 mg (90)	\$ 12,291	420 mg/day, 6 months	\$ 73,746
ECP			\$ 7,000	**	\$ 217,000
Pomalidomide	Pomalyst	1 mg (21)	\$ 15,669	1-4 mg/day, 21 of 28 days per course 6 courses	\$ 94,018
		2 mg (21)	\$ 15,669		
		3 mg (21)	\$ 15,669		
		4 mg (21)	\$ 15,669		

Abbreviations: ECP=extracorporeal photopheresis; HCQ=hydroxychloroquine

\* Cost calculation based on 170 cm height and 70 kg weight and only includes direct costs calculated per described protocol

\*\* 3 times during week 1, and then twice weekly on consecutive days during weeks 2 through 12. Responding patients continue 2 ECP treatments every 4 weeks until week 24

## Grubb et al. ASH 2016

Table 1. Unadjusted Mean (SD) Total LOS and Healthcare Costs During the Year Following Allogeneic HCT Among Patients With and Without Acute GvHD, by Evaluation Period (Student t-test)

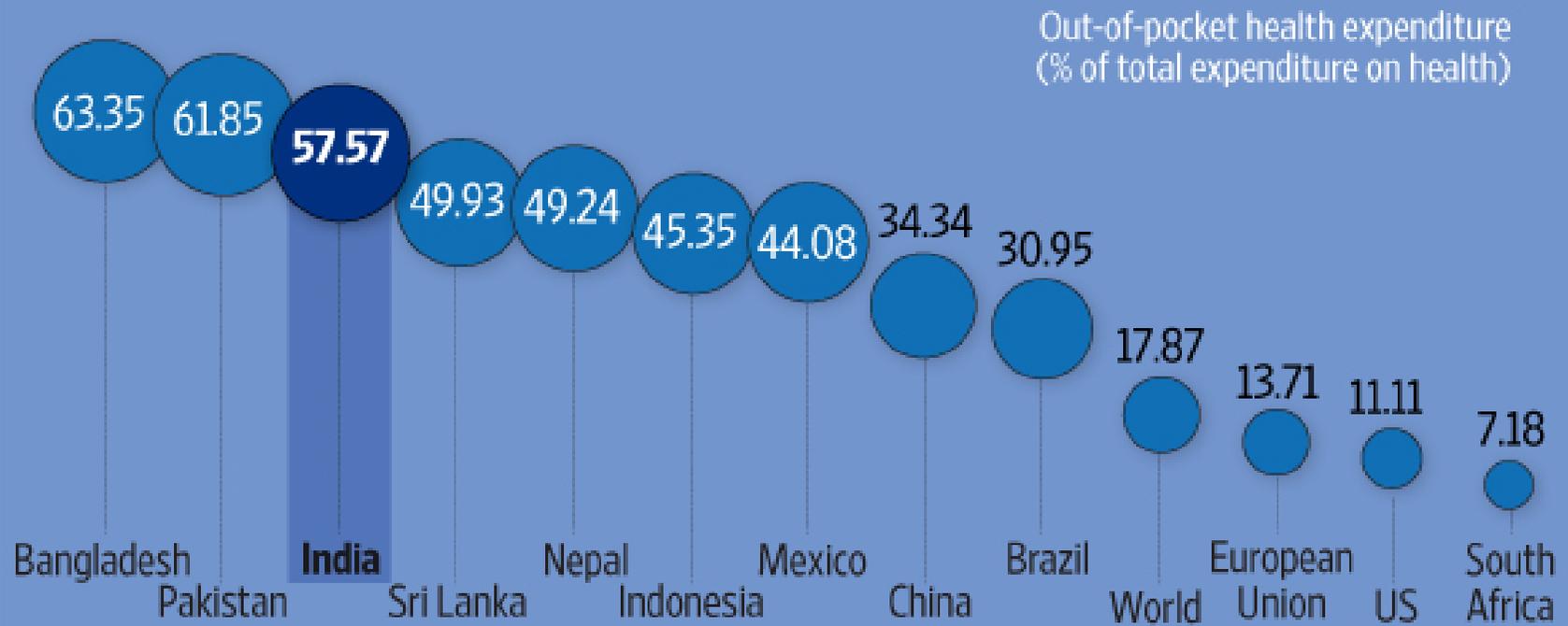
GvHD Cohort	Index Admission		100 Day Follow-Up		1-Year Follow-Up	
	Unadjusted Mean (SD)	p-value	Unadjusted Mean (SD)	p-value	Unadjusted Mean (SD)	p-value
<b>Total Length of Stay (LOS), days</b>						
No Acute GvHD	30.9 (19.0)		36.5 (22.7)		45.8 (32.0)	
Acute GvHD	36.6 (24.1)	<0.01	50.5 (35.2)	<0.01	63.2 (47.6)	<0.01
<b>Total Healthcare Costs, \$</b>						
No Acute GvHD	228,706 (192,234)		301,434 (224,770)		390,128 (299,692)	
Acute GvHD	264,357 (238,148)	<0.01	384,756 (301,406)	<0.01	513,348 (422,637)	<0.01

Table 2. Multivariate-Adjusted Mean (SE) Total LOS and Healthcare Costs During the Year Following Allogeneic HCT Among Patients With and Without Acute GvHD, by Evaluation Period (ANCOVA)

GvHD Cohort	Index Admission		100 Day Follow-Up		1-Year Follow-Up	
	Multivariate-Adjusted Mean (SE)	p-value	Multivariate-Adjusted Mean (SE)	p-value	Multivariate-Adjusted Mean (SE)	p-value
<b>Total Length of Stay (LOS), days</b>						
No Acute GvHD	31.1 (0.7)		36.5 (0.9)		45.6 (1.3)	
Acute GvHD	36.4 (0.8)	<0.01	50.6 (1.1)	<0.01	63.5 (1.5)	<0.01
<b>Total Healthcare Costs, \$</b>						
No Acute GvHD	233,451 (6,627)		305,486 (8,015)		393,688 (10,951)	
Acute GvHD	257,743 (7,857)	0.02	379,108 (9,503)	<0.01	508,386 (12,985)	<0.01

# OOP expenditures differ!

Another key reason for poor health of Indians is the high proportion of out-of-pocket expenditure on health because of low insurance coverage and weak public health systems, which forces even poor people to visit private medical practitioners, and drives up average health costs. High healthcare costs often lead people to delay treatment, aggravating health problems.



Sources: World Health Organization, OECD, World Bank, Credit Suisse AG

# Back to the basics

- What are the costs of HCT?
- What is the value of HCT?
- How to measure value in HCT? see quality next

# Are healthcare costs really rising?

## Premiums have soared

Average annual health insurance premiums for family coverage

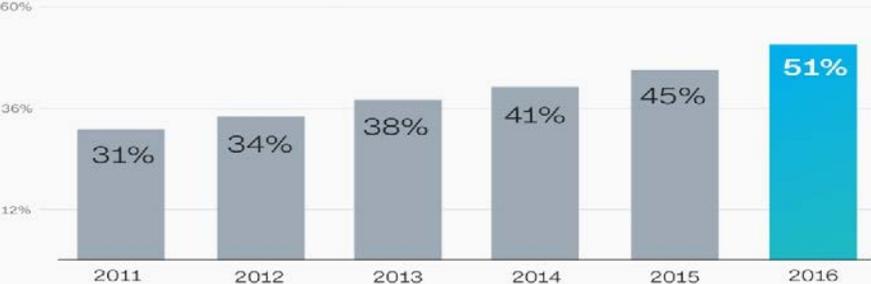


## Deductibles keep climbing



\*AVERAGE DEDUCTIBLE FOR SINGLE COVERAGE. SOURCE: KAISER/HRET EMPLOYER-SPONSORED HEALTH BENEFITS SURVEY, 2016

## More workers have \$1,000+ deductibles



\*SHARE OF WORKERS WITH AN ANNUAL DEDUCTIBLE OF \$1,000 OR MORE FOR SINGLE COVERAGE  
SOURCE: KAISER/HRET EMPLOYER-SPONSORED HEALTH BENEFITS SURVEY, 2016



# Quality of a HCT Program

- What should be the goal of a HCT program?
- Survival outcomes?
- QoL outcomes?
- Systems checklists?
- Research productivity?
- Staff satisfaction?
- Stem cell lab standards?
- Which societies can give guidance?

# Accreditation

- FACT
- JACIE
- ISCT standards
- AABB standards

# FACT-JACIE Standards (6<sup>th</sup> edition)

- **CLINICAL PROGRAM STANDARDS:** Clinical Unit, Personnel, QM, Policies and Procedures, Allogeneic and Autologous Donor Selection, Evaluation, and Management
- **MARROW COLLECTION FACILITY STANDARDS:** Marrow Collection Facility; Personnel, Quality Management, Policies and Procedures, Allogeneic and Autologous Donor Evaluation and Management, Coding and Labeling of Cellular Therapy Products, Process Controls, Cellular Therapy Product Storage, Cellular Therapy Product Transportation and Shipping, Records, Direct Distribution to Clinical Program
- **APHERESIS COLLECTION FACILITY STANDARDS:** Apheresis Facility, Personnel, Quality Management, Policies and Procedures, Allogeneic and Autologous Donor Evaluation and Management, Coding and Labeling of Cellular Therapy Products, Process Controls, Cellular Therapy Product Storage, Cellular Therapy Product Transportation and Shipping
- **PROCESSING FACILITY STANDARDS:** Processing Facility, Personnel, Quality Management, Policies and Procedures, Equipment, Supplies, and Reagents, Coding and Labeling of Cellular Therapy Products, Process Controls, Cellular Therapy Product Storage, Cellular Therapy Product Transportation and Shipping, Distribution and Receipt, Disposal

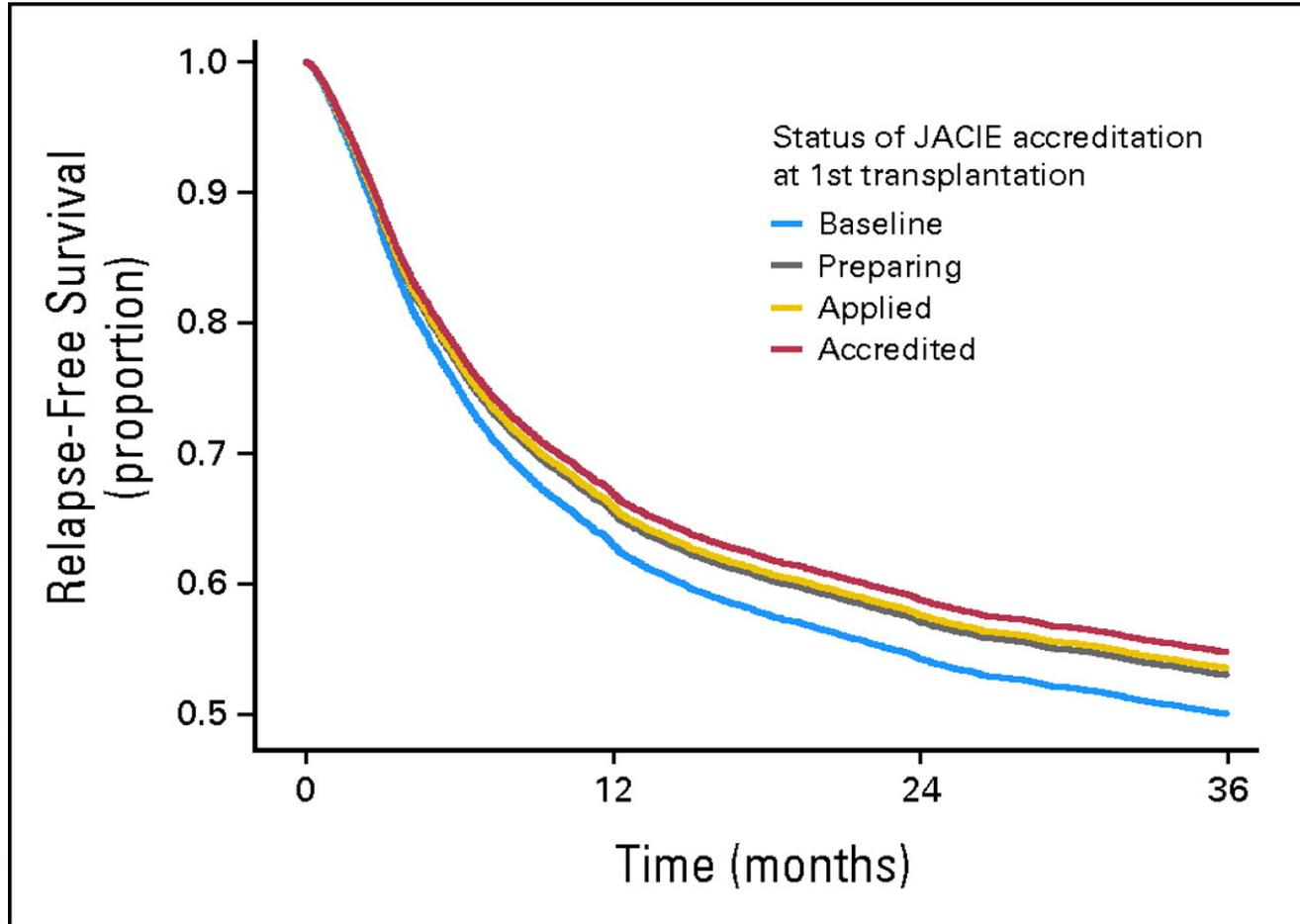
# What is required to get top quality?

- Accreditation?
- PROM?
- Survival statistics?
- Databases?
- Basic and clinical research?
- Integrated quality systems?
- Combination of above?
- Costs?
- Value? (if yes, then to whom)

## U.S. News Best Hospitals 2016-17

1	<b>Mayo Clinic</b> Rochester, Minn.
2	<b>Cleveland Clinic</b> Cleveland, Ohio
3	<b>Massachusetts General Hospital</b> Boston
4	<b>Johns Hopkins Hospital</b> Baltimore
5	<b>UCLA Medical Center</b> Los Angeles
6	<b>New York-Presbyterian University Hospital</b> New York
7	<b>UCSF Medical Center</b> San Francisco
8	<b>Northwestern Memorial Hospital</b> Chicago
9	<b>Hospitals of UPenn-Penn Presbyterian</b> Philadelphia
10	<b>NYU Langone Medical Center</b> New York

# Accreditation matters!



# Quality and costs together!



# Principles of maintaining quality with low cost!

- Feasibility (professional groups) – needs, logistics (rural vs urban) – Nigeria vs Bangladesh HCT program
- Quality systems (Lean 6 sigma, Swiss cheese model)
- Pilot projects – very specific outcome measure evaluations
- New is not always the best! Drug therapy costs
- Health Economic Analysis (CEA, CUA etc)
- Accreditation
- Defining Value

# HCT programs in developing countries

**Table 1** – Reported Transplantation Cohorts in Developing Countries

Study	Country	Study Date	Transplantations (No. Allo)	Indications
Chandy et al <sup>13</sup>	India	1986-1999	221 (221)	Thal (48%), CML (14%), AML (16%), ALL (5%), SAA (10%), MDS (3%), Others (3%)
Mahmoud et al <sup>14</sup>	Egypt	1989-2007	1,362 (1,090)	CML (31%), AML (25%), ALL (12%), AA (21%), Thal (7%), MDS (7%), Others (5%)
Ramzi et al <sup>15</sup>	Iran	1993-2008	423 (311)	Thal (37%), lymphoma (20%), AML (16%), ALL (7%), CML (7%), MM (6%), Others (2%)
Ullah et al <sup>16</sup>	Pakistan	2001-2007	48 (48)	Thal (100%)
van Be et al <sup>17</sup>	Vietnam	1993-2007	52 (19)	AML (53%), CML (19%), ALL (13%), Thal (12%), NHL (2%)

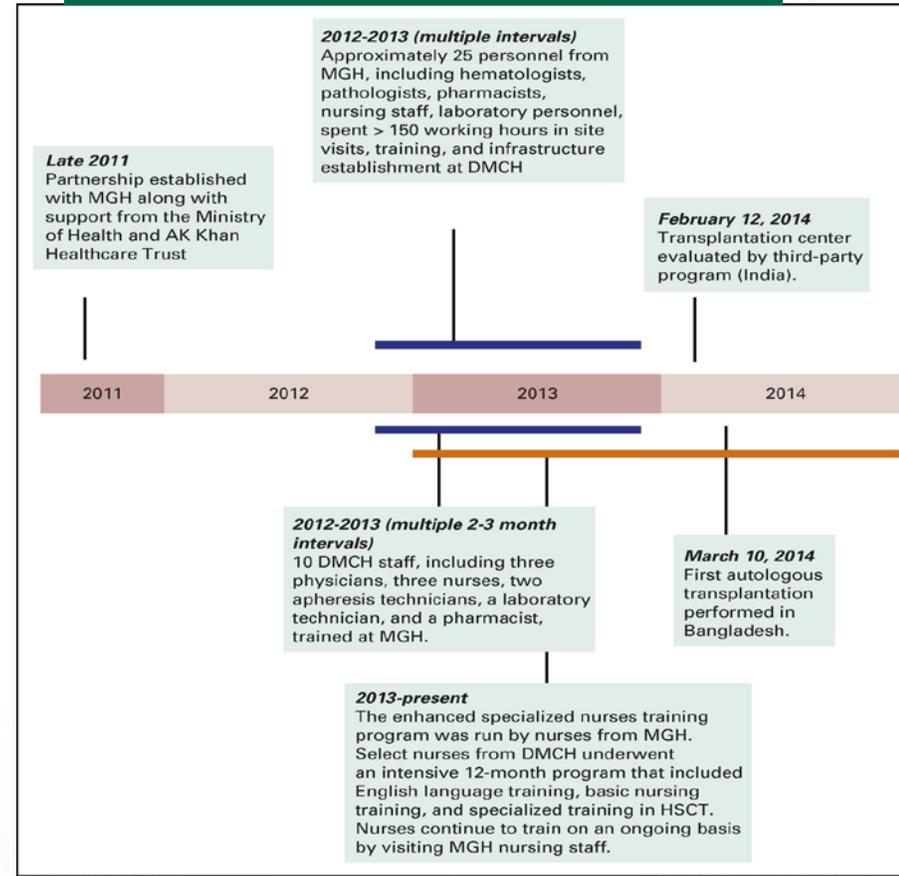
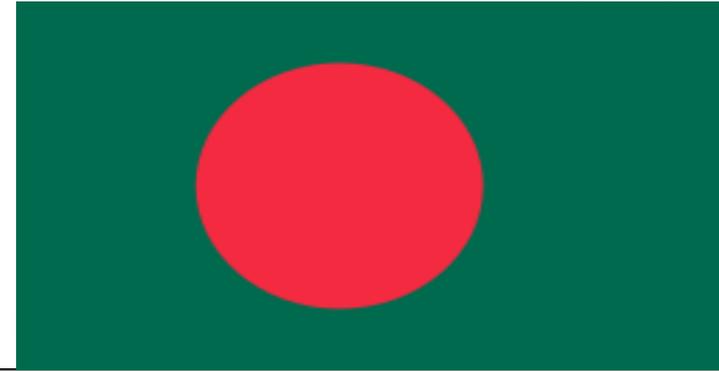
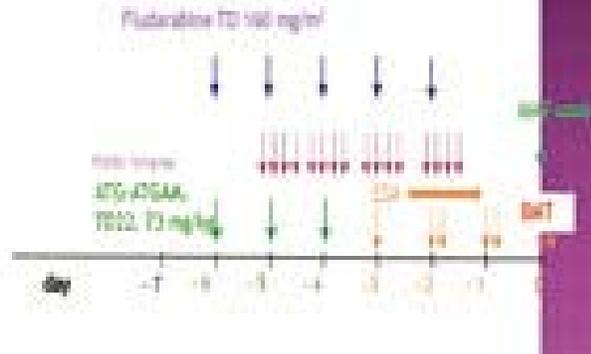
NOTE. Overview of transplantation programs reported in five developing countries with study date, volume of transplantation, and major indications shown.

Abbreviations: ALL, acute lymphoid leukemia; Allo, allogeneic; AML, acute myeloid leukemia; CML, chronic myeloid leukemia; MDS, myelodysplastic syndrome; MM, multiple myeloma; NHL, non-Hodgkin's lymphoma; SAA, sickle-cell anemia; Thal, thalassemia.

# Most optimum way to establish a new HCT program?



## UBTH Protocol: BU/Flu-RIC regimen For SCD and matched sibling donor



# What's the next step after HCT program establishment?

How do you assure quality?

Pilot programs?

Clinical outcomes?

Consultancy (internal or external)?

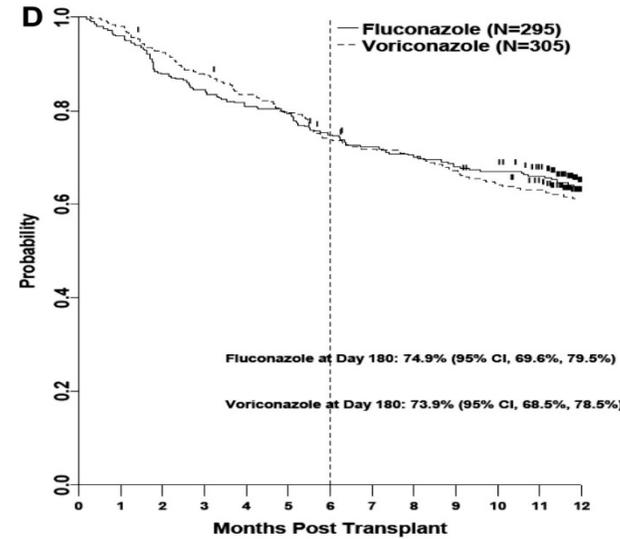
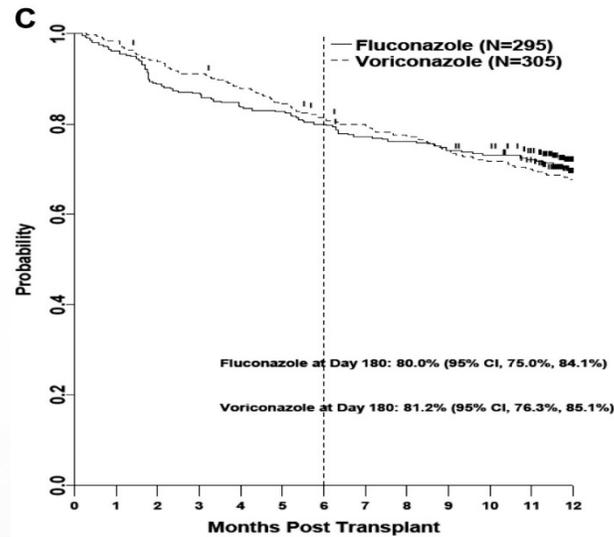
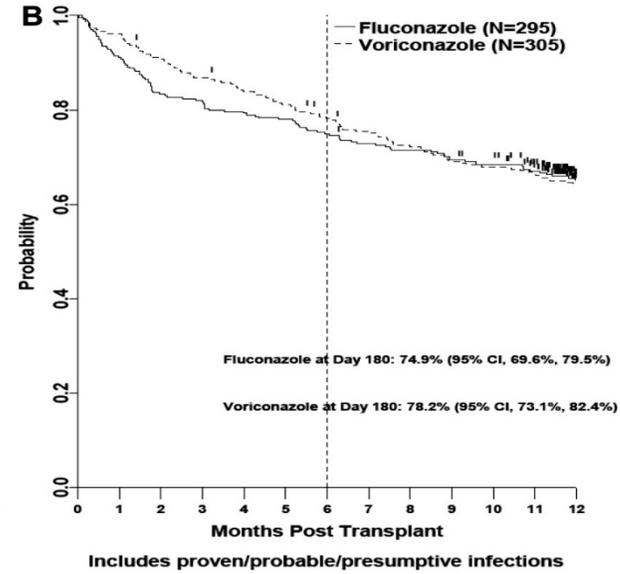
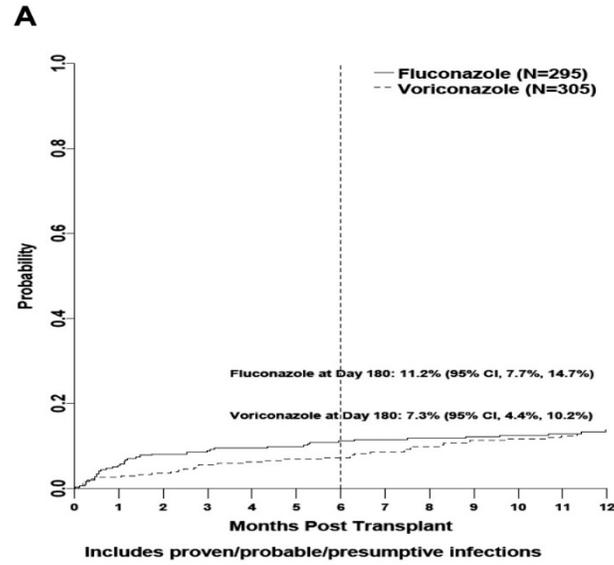
## Transplant Characteristics – Bangladesh Program

ID	Age/ Sex	Disease	Initial Staging	Disease Status d0	Prior therapies	Mobilization	Transplant Day	Conditioning	Engraft (d)	Notable Complications	Outcome
1	52M	MM	Not available	CR1	VAD, Thal/dex, VTD	Cy/G-CSF	3/10/14	Melphalan	11	PNA ( <i>Acinetobacter</i> )	CR
2	50M	MM	IIIA / ISS-I	CR2	VAD, Thal/dex, RVD	Cy/G-CSF	4/26/14	Melphalan	11	Sepsis ( <i>S.epi</i> )	CR
3	46M	MM	IIIA / ISS-I	VGPR	Thal/dex, MPT, VTD	Cy/G-CSF	6/8/14	Melphalan	12	Sepsis ( <i>S.epi</i> )	CR
4	49M	MM	IIIA / ISS-I	VGPR	RVD	Cy/G-CSF	8/24/14	Melphalan	9	Sepsis ( <i>PsA</i> )	CR
5	45F	MM	ISS-II	VGPR	VCD	Cy/G-CSF	9/18/14	Melphalan	10		CR
6	16M	AML	M2	Relapsed	DA (7+e), MA (7+2)	HiDAC/G-CSF	10/1/14	Bu/Cy	11		CR
7	19M	DLBCL	IV	CR2	CHOP, IFRT, R-ICE	R-ICE/G-CSF	10/2/14	BEAM	16		CR
8	49M	MM	IIIB / ISS-III	VGPR	VTD	Cy/G-CSF	11/13/14	Melphalan	9		Relapsed d214
9	31M	HD	NS IIIB	CR	ABVD, ICE, GND	GND/G-CSF	11/20/14	BEAM	14	Sepsis ( <i>PsA</i> )	CR
10	47M	MM	IIB / ISS-I	VGPR	Bor/dex, Len/dex, VCD	Cy/G-CSF	1/1/15	Melphalan	10		CR
11	49M	MM	IIIA / ISS-II	VGPR	VCD, IFRT, RVD	Cy/G-CSF	1/8/15	Melphalan	10	Sepsis ( <i>MRSA/ Klebs</i> ), CMV	CR
12	20M	DLBCL	IB	Refractory	CHOP, R-CHOP, R-ICE	R-ICE/G-CSF	2/8/15	BEAM	11	<i>C.Diff</i>	CR
13	29M	NHL (PTCL)	IIIB	CR	CHOP, CHOEP, ICE	ICD/G-CSF	3/10/15	BEAM	9	<i>C.Diff</i>	CR
14	43F	MM	IIIA / ISS-III	PR	VCD, Thal/dex	Cy/G-CSF	3/11/15	Melphalan	12		CR

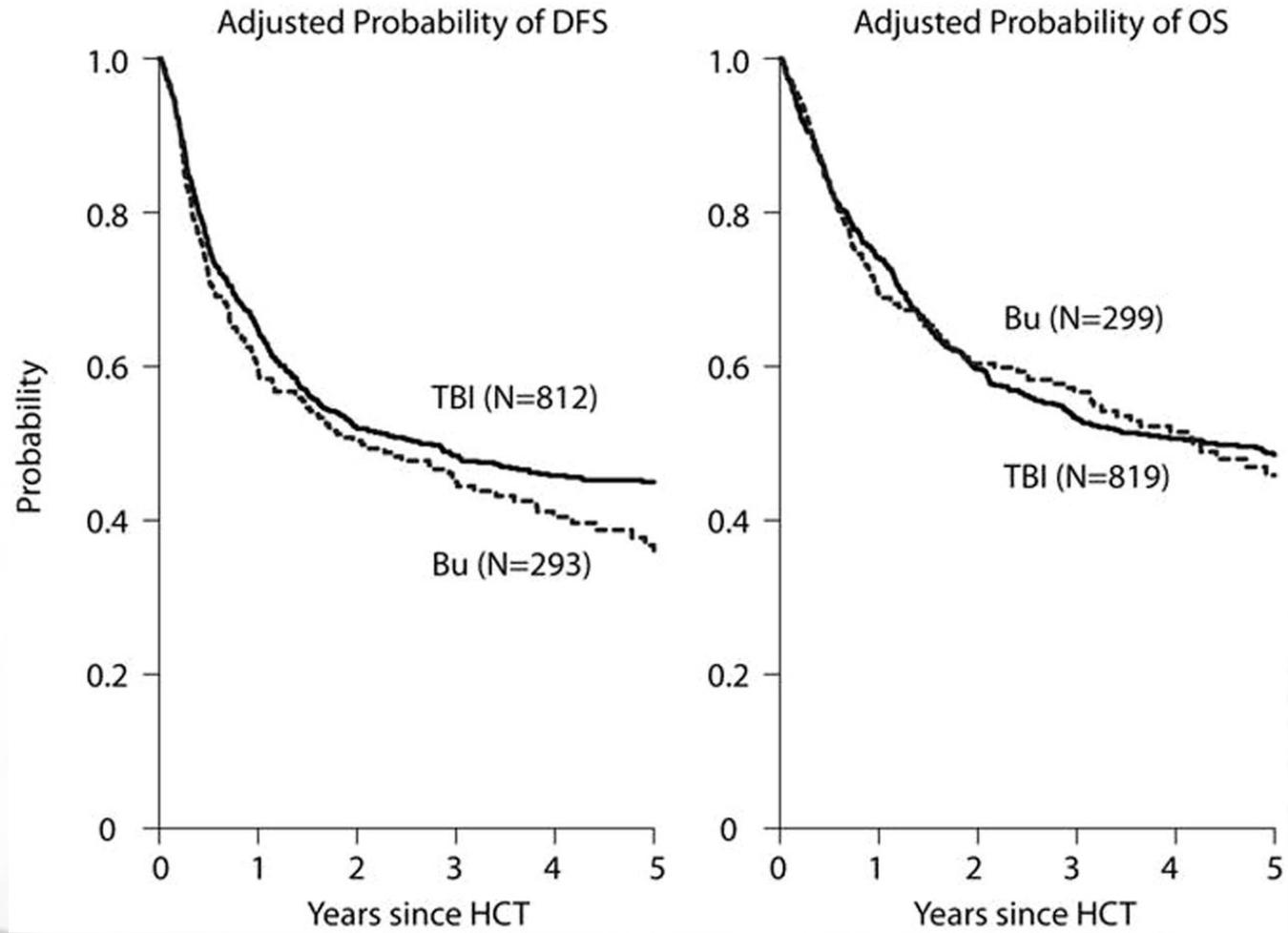
# Common questions for a new HCT program?

- Is voriconazole/posaconazole better than fluconazole for prophylaxis of fungal infections?
- Is TBI necessary for start up program for adult ALLs?
- Absence of fully matched sibling next donor source? CBT, Haplo, 10/10 MUD
- Can we use RIC for middle-aged AML's rather than MAC?
- Is it possible to abolish the use of CNIs in allografts?
- Is cryopreservation necessary for autologous HCTs?
- Plerixafor necessary for mobilization?
- Are HCT trained professionals necessary for a start-up program?
- HEPA filtered rooms necessary?
- Negative pressure vs positive pressure rooms?
- Many other questions

# Kaplan-Meier estimates. Antifungal Prophylaxis CTN 0101



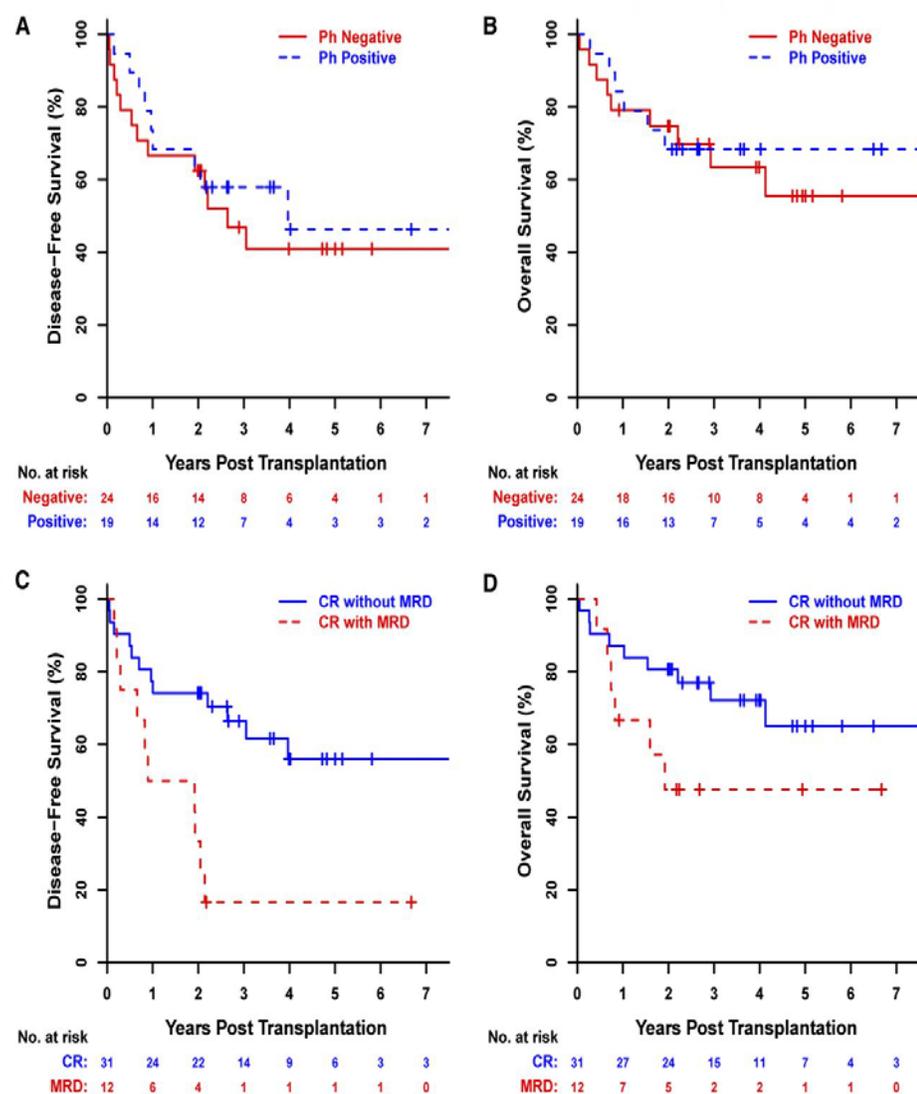
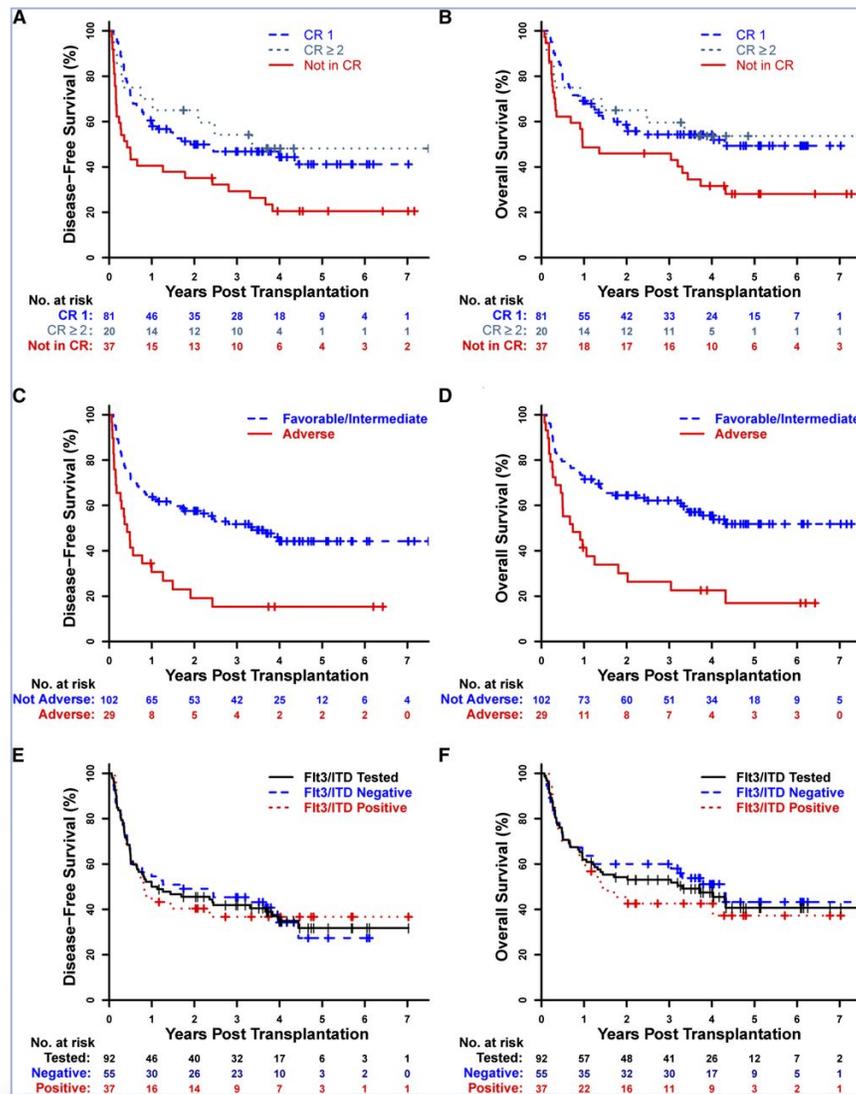
# TBI vs Busulfan based regimens in adult B-ALL – CIBMTR study



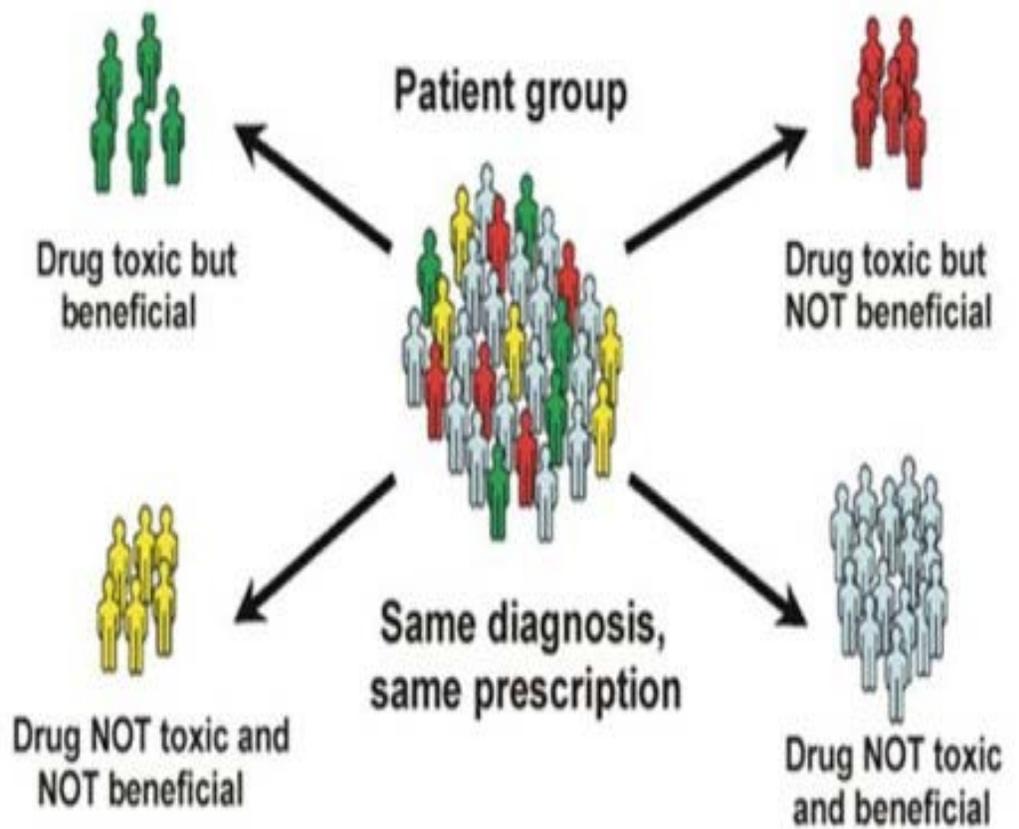
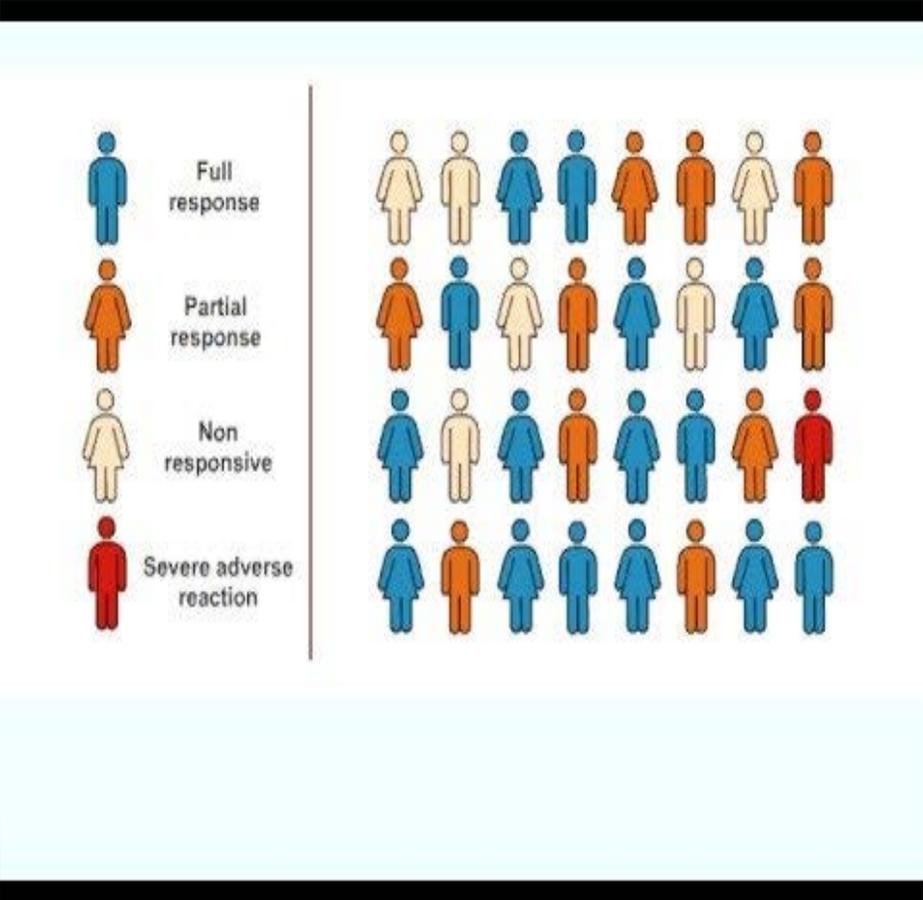
# CNI free GVHD prophylaxis

- Is there a study with PTCy as sole prophylaxis in MRD and MUD?

# Survival outcomes for AML and ALL patients post MAC with PTCy



# Do the results of trials in the developed world apply to the developing countries?



# Summary & Future Directions

- Feasibility and sustainability of a new program should be well documented
- Quality maintenance efforts have to be a part of a new start up HCT program
- Cost-reduction measures should be evidence based
- Pharmacogenomics studies are necessary to see the true impact of drugs on outcomes in specific populations
- Countries helping each other is the key to global success of HCT



# One world united for the same mission



You may say I'm a dreamer, But I'm not the only one; I hope some day you'll join us,  
And the world will be as one  
Imagine no possessions, I wonder if you can. No need for greed or hunger, A  
brotherhood of man. Imagine all the people sharing all the world, you