HSCT for Thalassemia Major

1. **Have Transfusion**

   or

2. **Half transplantation**

1. **Have transplantation**

   or

2. **Have transplantation**

Said Yousuf Mohamed,
Professor of Internal Medicine , H.O.T
Ain Shams University Hospital, Cairo, Egypt
SCA-Transplant program, KFSHRC, Riyadh, SA

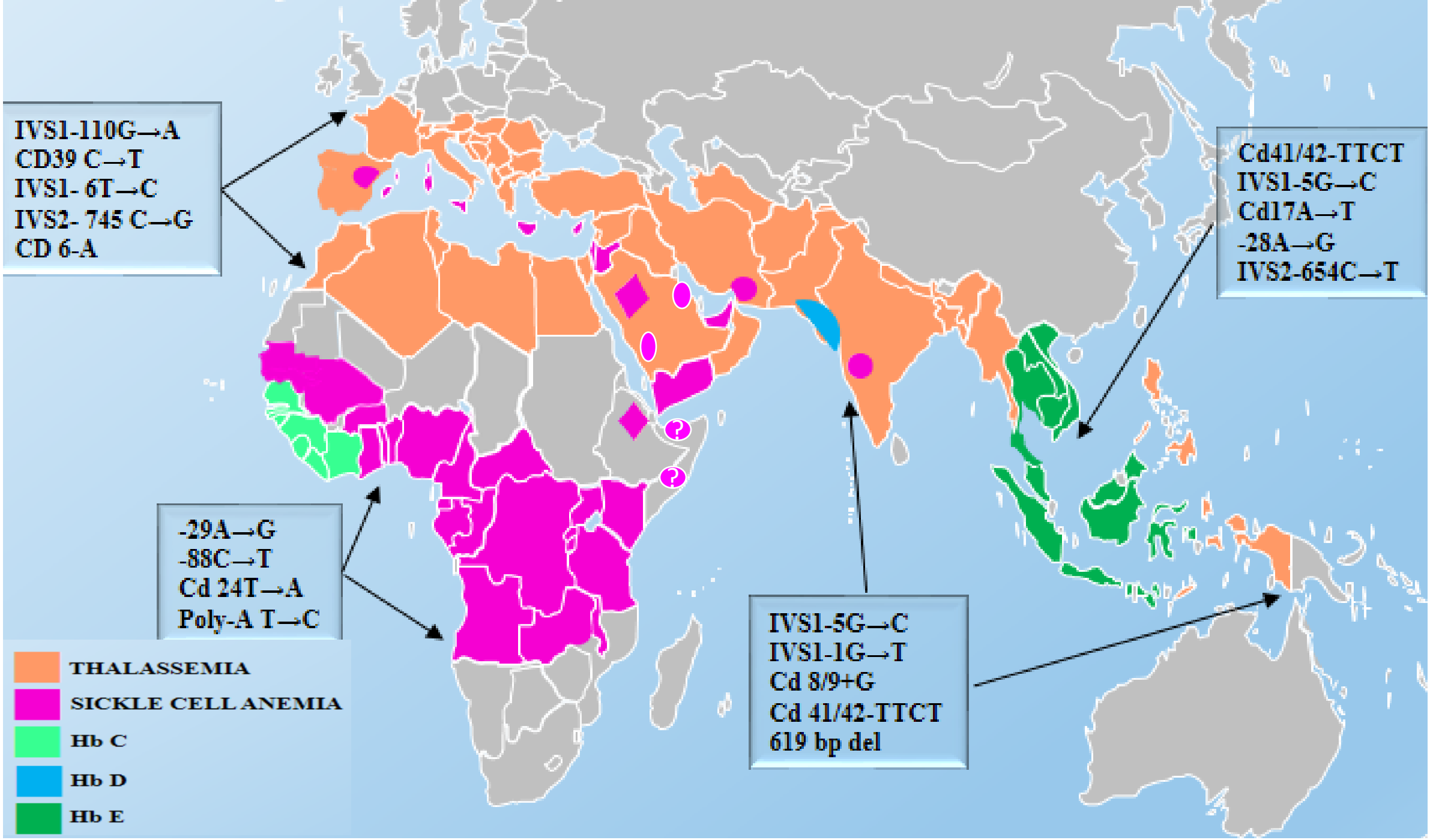
- No science.

T.M is 4-mos old **1st boy** for a 42 y/o mother and a 58y/o father.
He feels SOB and choking with breast feeding.
o/E: Pallor, jaundice, HSM.
CBC/DD & Hb EP: hypochr. Microcyt. anemia (7 gm), retic 11% ,
HbEP: A2 is 5.2%, Hb F: 7% , Hb
Well: he's like his cousin who required Transfusions but died at the age of 4

Mother:

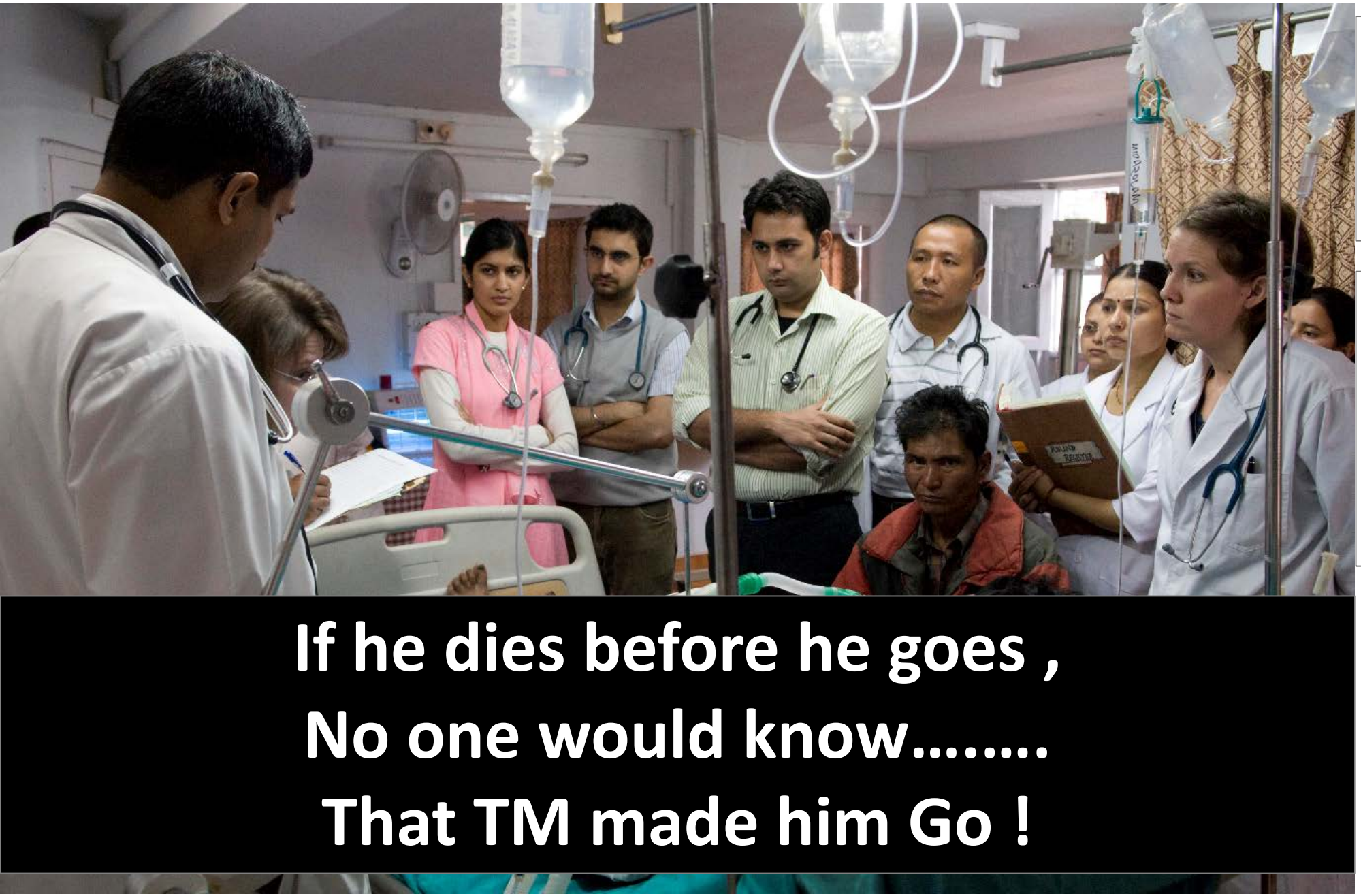
1. **Is it benign or malignant?**
2. **Does it kill like acute leukemia (ALL)?**
3. **I wished he will be a doctor! And ….Marry !**
4. **Is he going die like his cousin?**
5. **How can you us ?**

It depends !!!!!


IVS1-110G→A
CD39 C→T
IVS1- 6T→C
IVS2- 745 C→G
CD 6-A
Cd41/42-TTCT
IVS1-5G→C
Cd17A→T
-28A→G
IVS2-654C→T
-29A→G
-88C→T
Cd 24T→A
Poly-A T→C
IVS1-5G→C
IVS1-1G→T
Cd 8/9+G
Cd 41/42-TTCT
619 bp del
THALASSEMIA
SICKLE CELL ANEMIA
Hb C
Hb D
Hb E


Apollo Hospitals
GROUP
Apollo Hospitals

Academic center



If he dies before he goes ,
No one would know……..
That TM made him Go !

Do EBM (not EBMT)
Do Research
Do Publish

Believe what they publish &what similar others publish


We have to be realistic

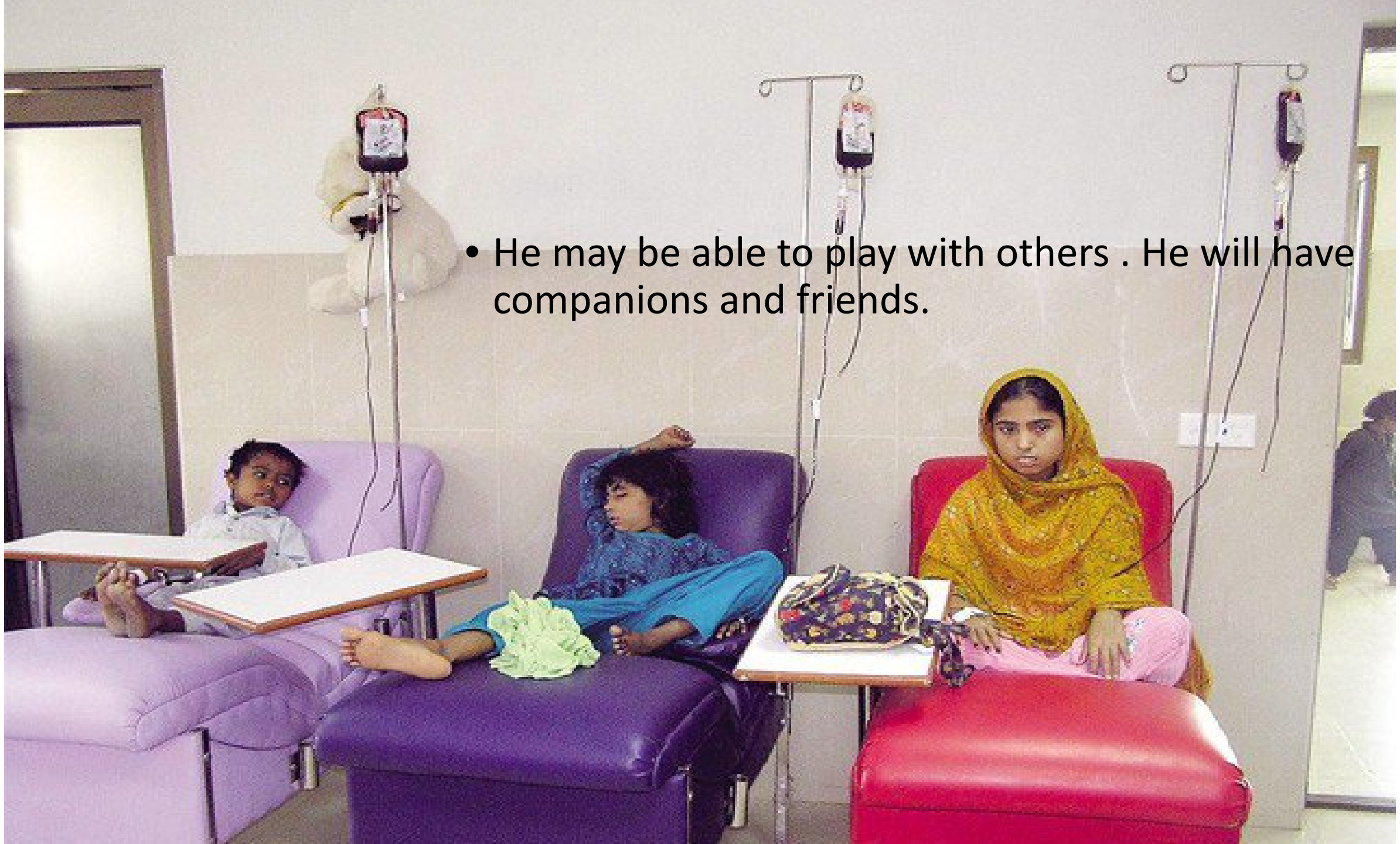
Can we make it better

Thalassemia major: what a disease

TM: How they live & die ?

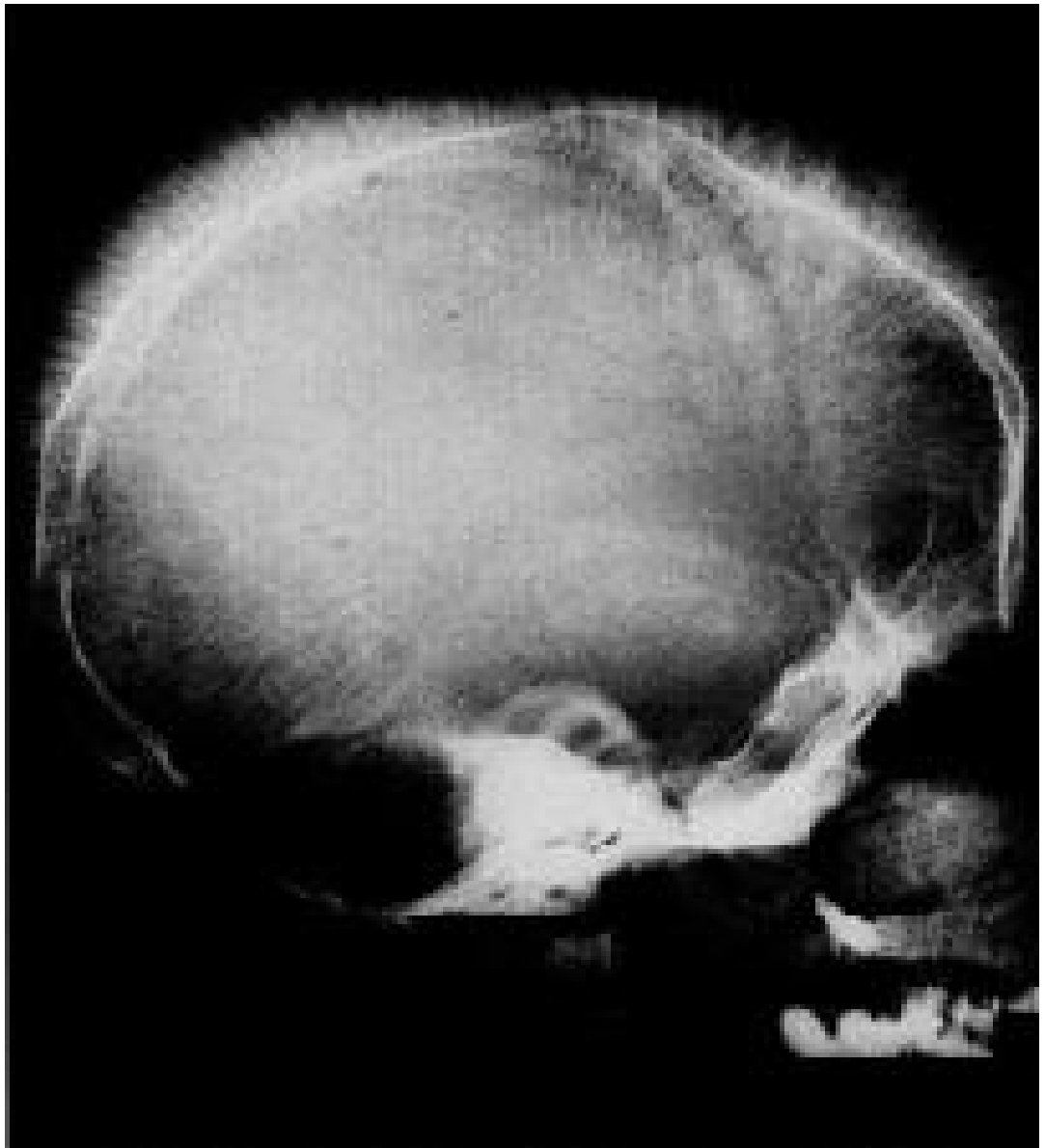
TM comprehensively Kills !

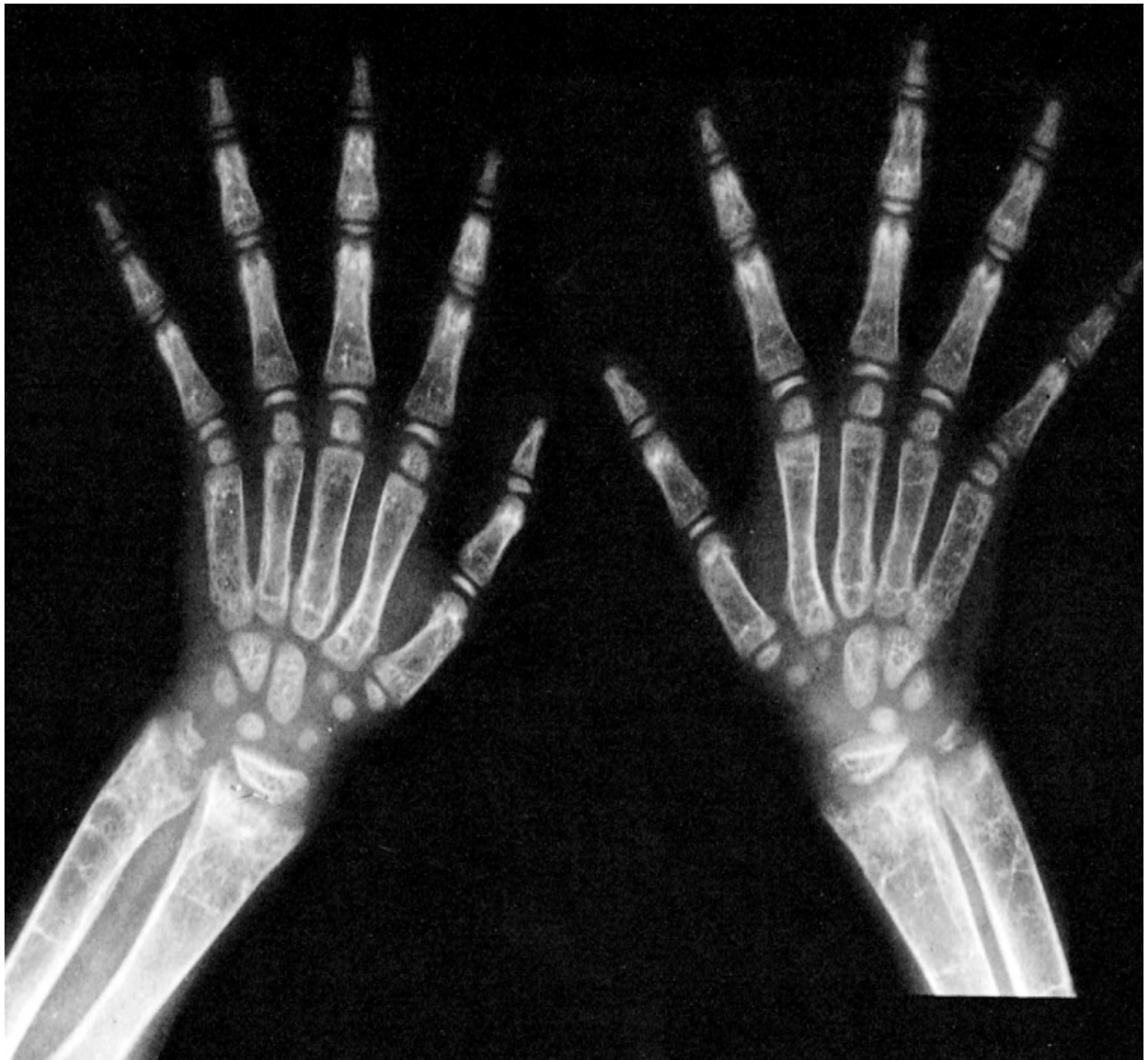
- No marriage
- No jobs
- Cardiomyopathies/ Arrythmia
- Liver cirrhosis
- HCV/HBV/other infections
- Transfusions-Chelation (insufficient)
- Poor growth, development, deformities



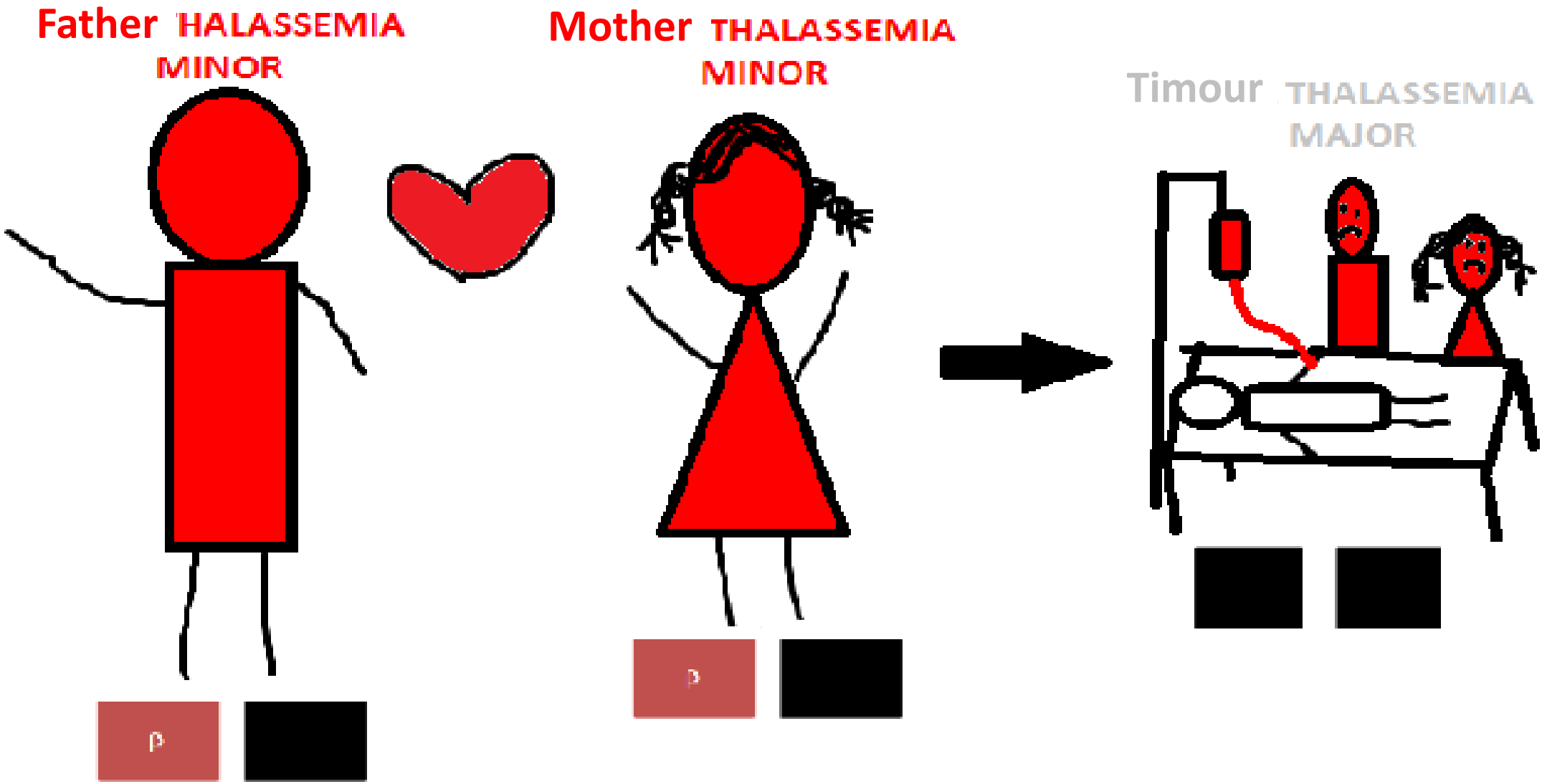
- He may be able to play with others . He will have companions and friends.

Intelligent but this may be his skull





he will be an artist : draws picture about his life



When may he die?

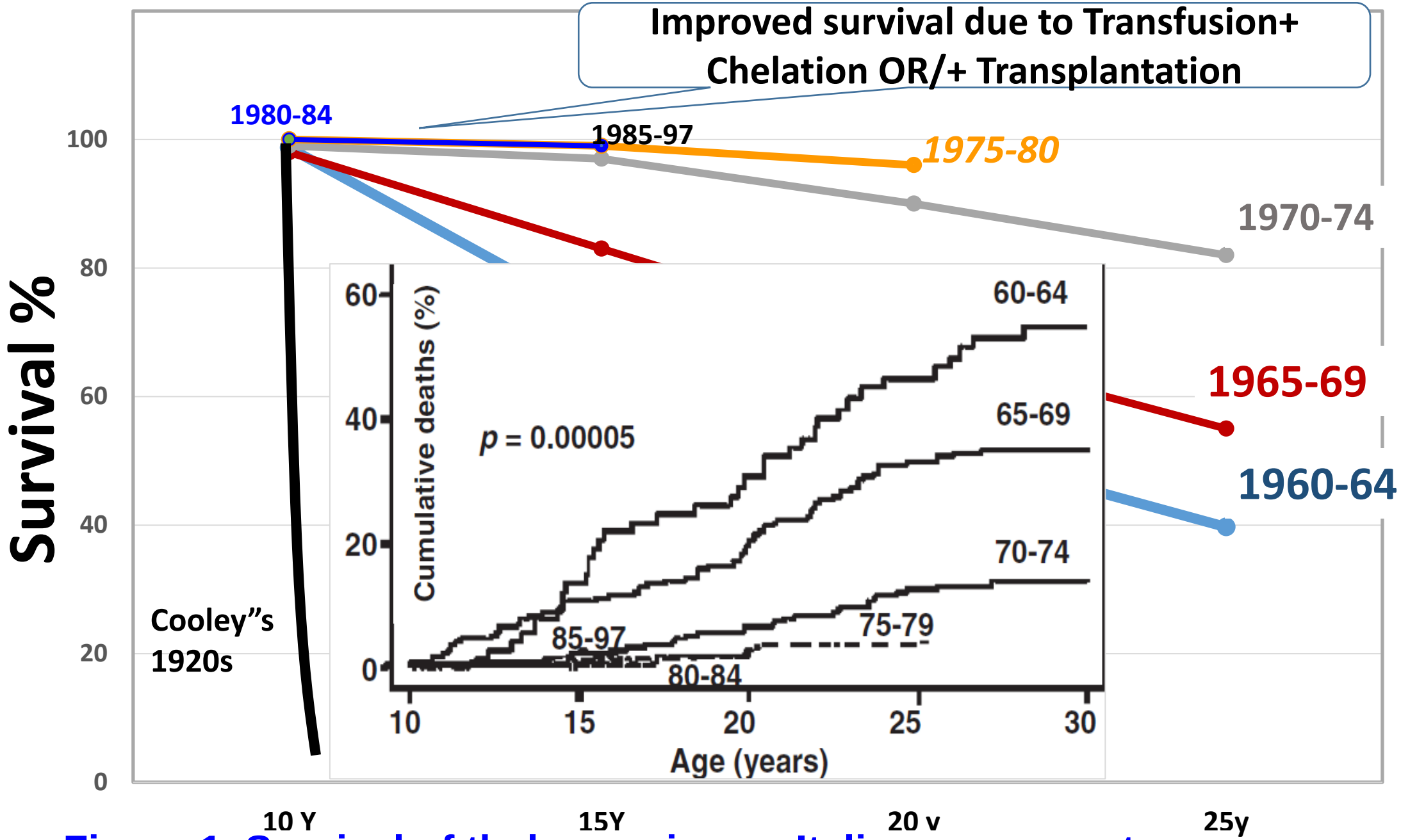


Figure 1. Survival of thalassemia : an Italian success story

Borgna-Pignatti C et al., ann NY acad SCI 2005

[haematologica]
2004;89:1179-1186

Clinical and histological characterization of liver disease in patients with transfusion-dependent β-thalassemia. A multicenter study of 117 cases

DANIELE PRATI

A B S T R A C T

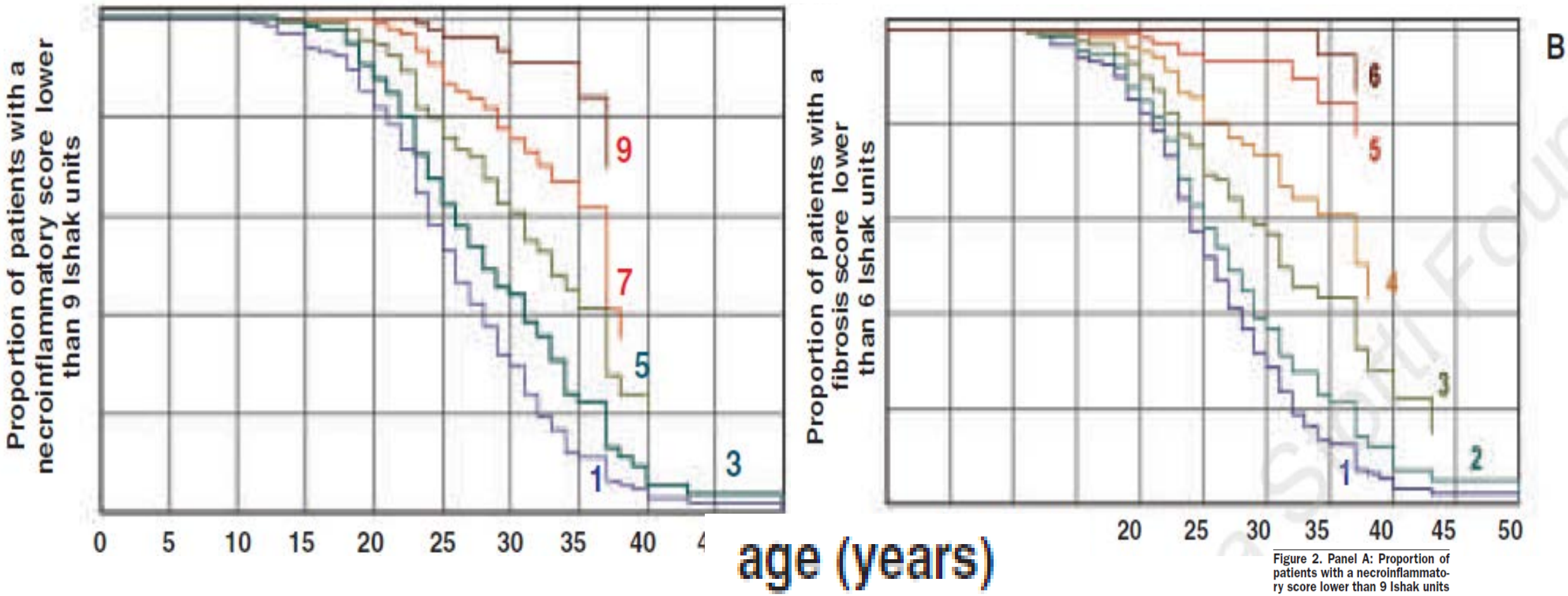
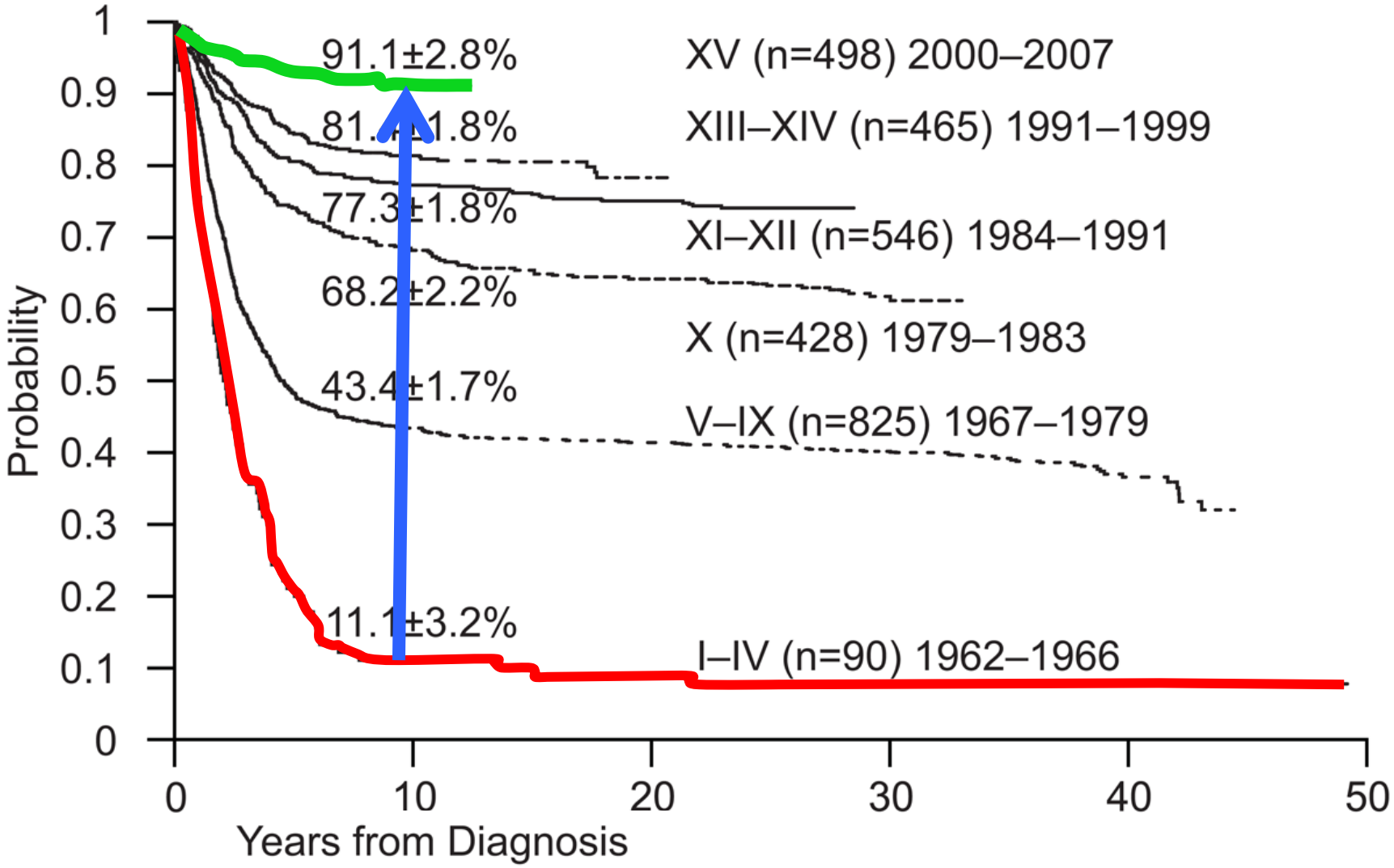


Figure 2. Panel A: Proportion of patients with a necroinflammatory score lower than 9 Ishak units as a function of age. Panel B: Proportion of patients with a fibrosis score lower than 6 Ishak units as a function of age.

Early endeavors focused on Transfusion

- **Transfusion + Chelation= life**
- **No transfusion: No life**

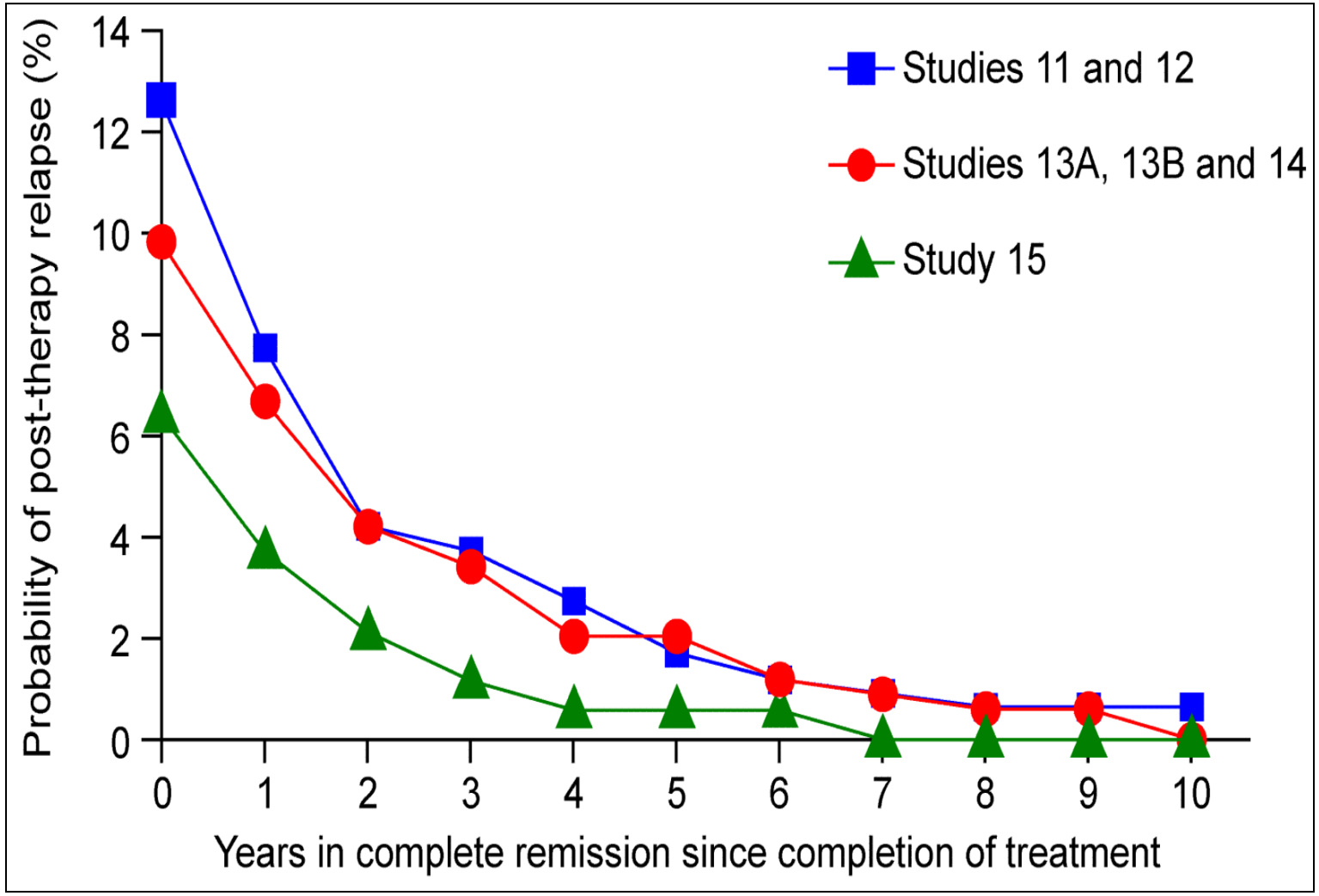
Is it benign or malignant?
An...emia or Leuk..emia?



10 Y OS for 2852 children with newly diagnosed ALL who were enrolled in 15 consecutive Total Therapy studies at SJCRH 1962-2007

Pui CH , Evans WE Semin Hematol. Semin Hematol. 2013 July; 50(3): 185–196

A Revised Definition for Cure of Childhood ALL



Pui CH et al., Leukemia. 2014 Dec; 28(12): 2336–2343

Medical Attitude Paradox:

➔Benign diseases kill

Acute Leukemia is less likely to kill

Even Farmers are Comprehensive

So be comprehensive
H.A.V.E Transfusion or Transplantation

Pediatric ALL specialists
Intense fight: “Face your enemy”& keep fighting
until we die or we kill the enemy!

SCA & TM specialists

Turning a back to an enemy: " It is benign"

No or PRN Transfusion for Adults in many areas

Challenges in the management of TM:

- **The size of the problem**
- **Political unrest**
- **Economic issues**
- **Rigidity issues**
- **Awareness (medical Professionals):** ***let it go let it go let it go***
- **WBMT mission is not clear: Sheikh to the audience.**
  - **The money of WBMT activity = 40 fellow x 6 months each at KFSHRC or 20 at UMN.**

The inherited diseases of hemoglobin are an emerging global health burden

Table 1. Breakdown of the annual number of births with the different hemoglobin disorders from data available[2]

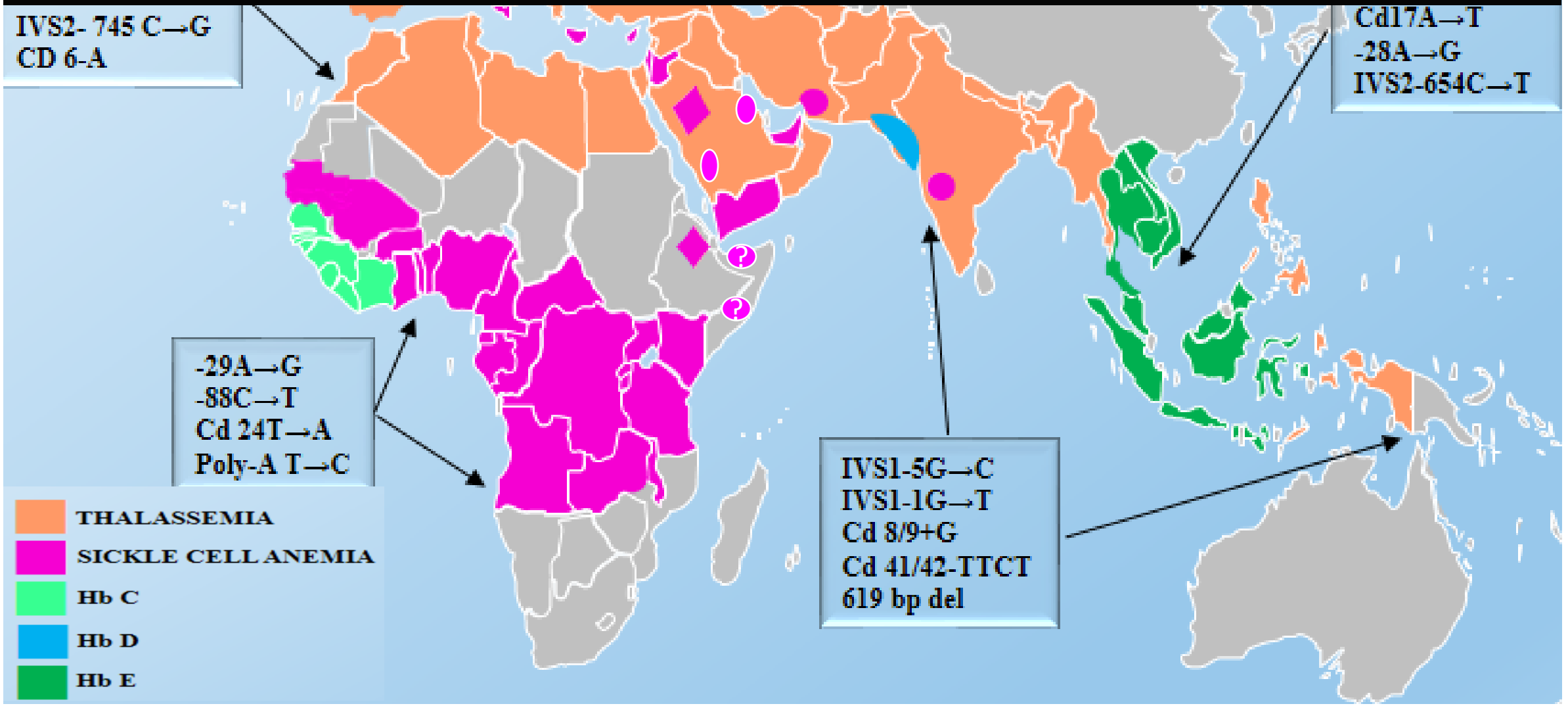
Major hemoglobin disorder	No. of annual births
β thalassemia major	22 989
HbE β thalassemia	19 128
HbH disease	9 568
Hb Bart hydrops ($\alpha^{\circ}/\alpha^{\circ}$)	5 183
SS disease	217 331
S β thalassemia	11 074
SC disease	54 736

Weatherall DJ, Blood. 2010;115(22):4331-4336

Global: 80-90 Millions carriers of Thalassemia genes

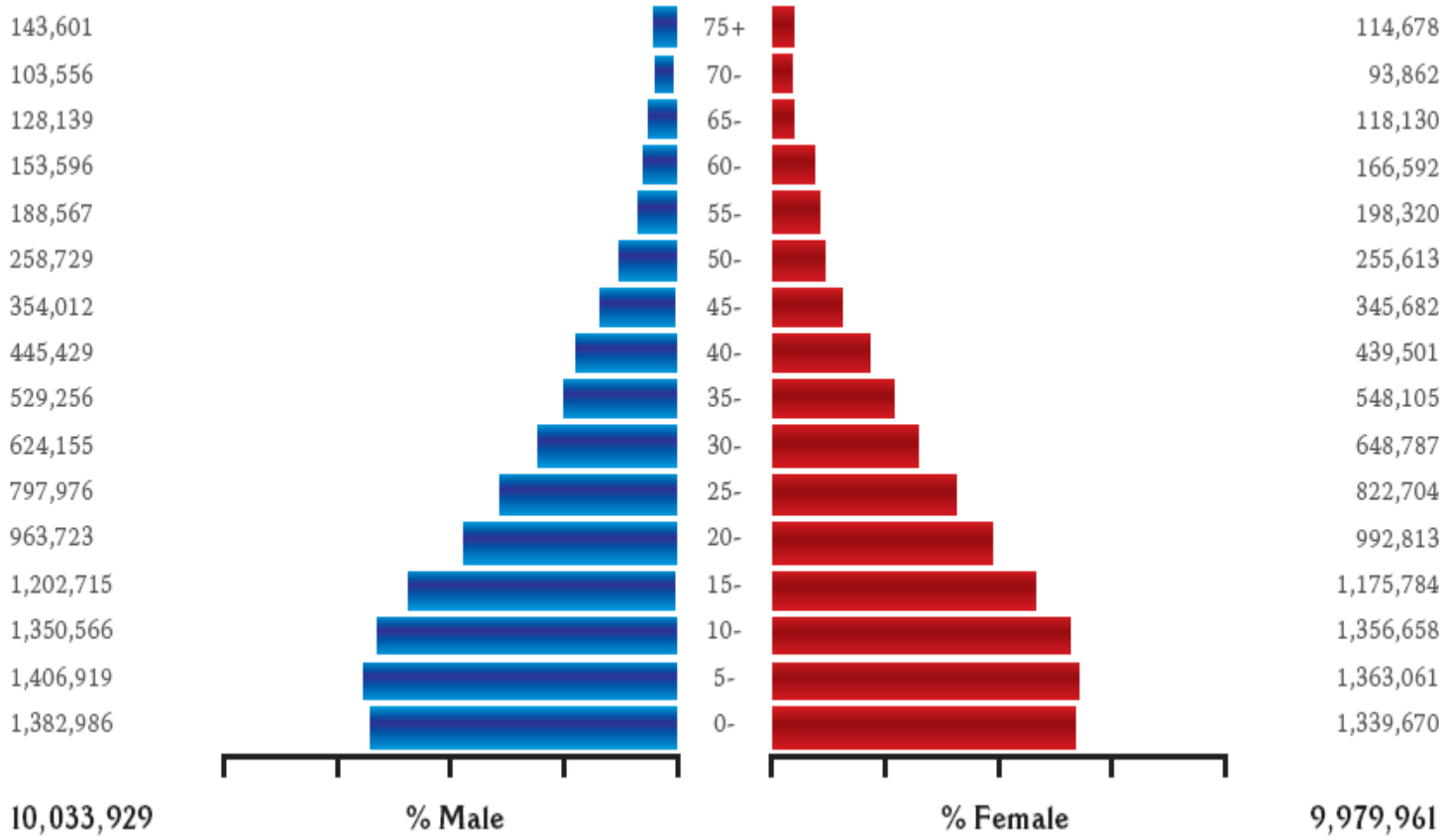
50,000–100,000 children with β-TM die /year in L/M-Income countries

Report of a Joint WHO–Geneva 17–19 May 2006.



1st conclusion of the conclusion

- **TM kills at young age**
- **TM kills the future**



Estimated Mid-point 1998-2007 Population for GCC States' Nationals by Gender.

Ten-Year Cancer Incidence 1998-2007
GCCCP Report, 2011

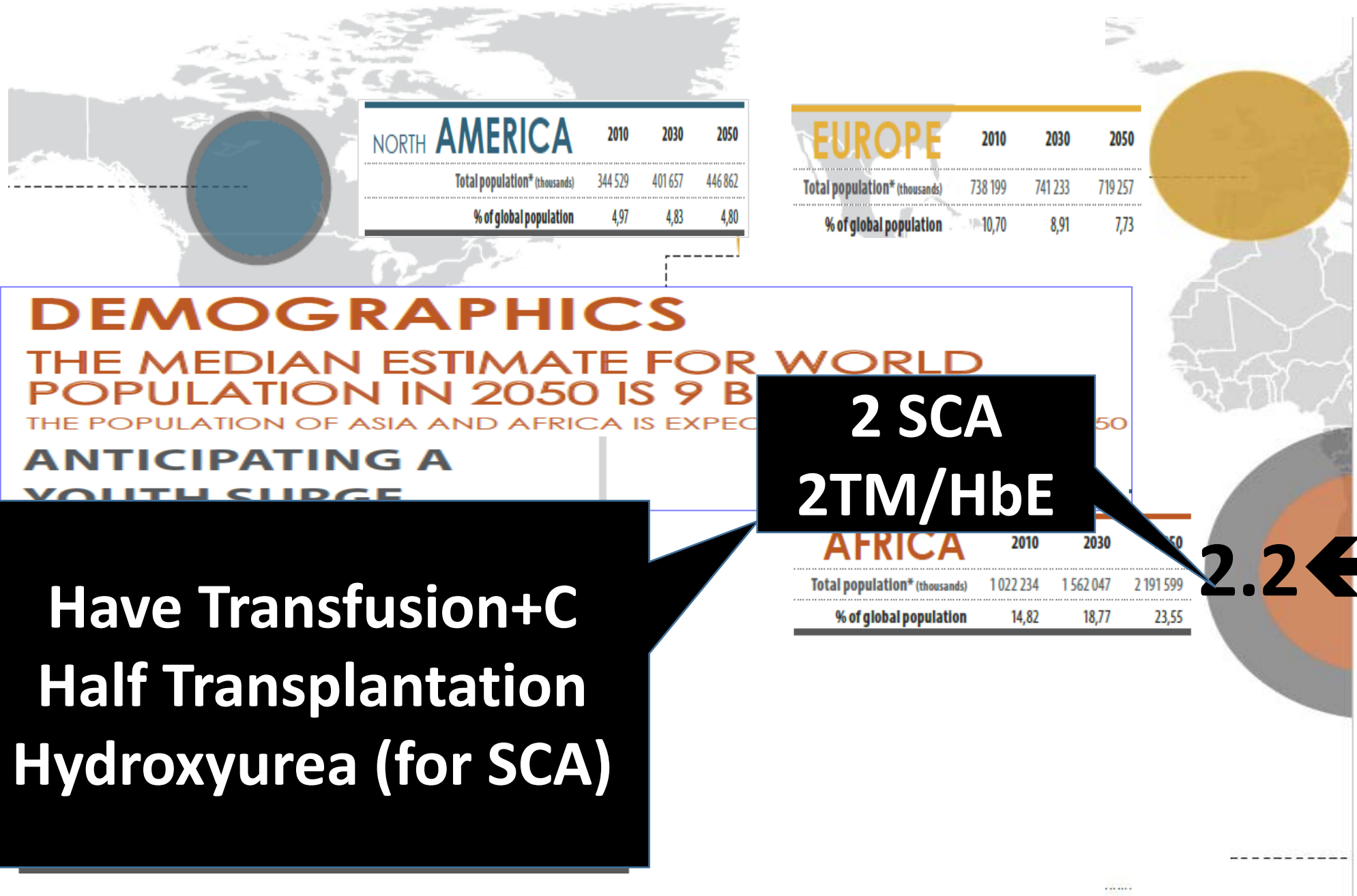
How much deaths due to Thal + SCA/year

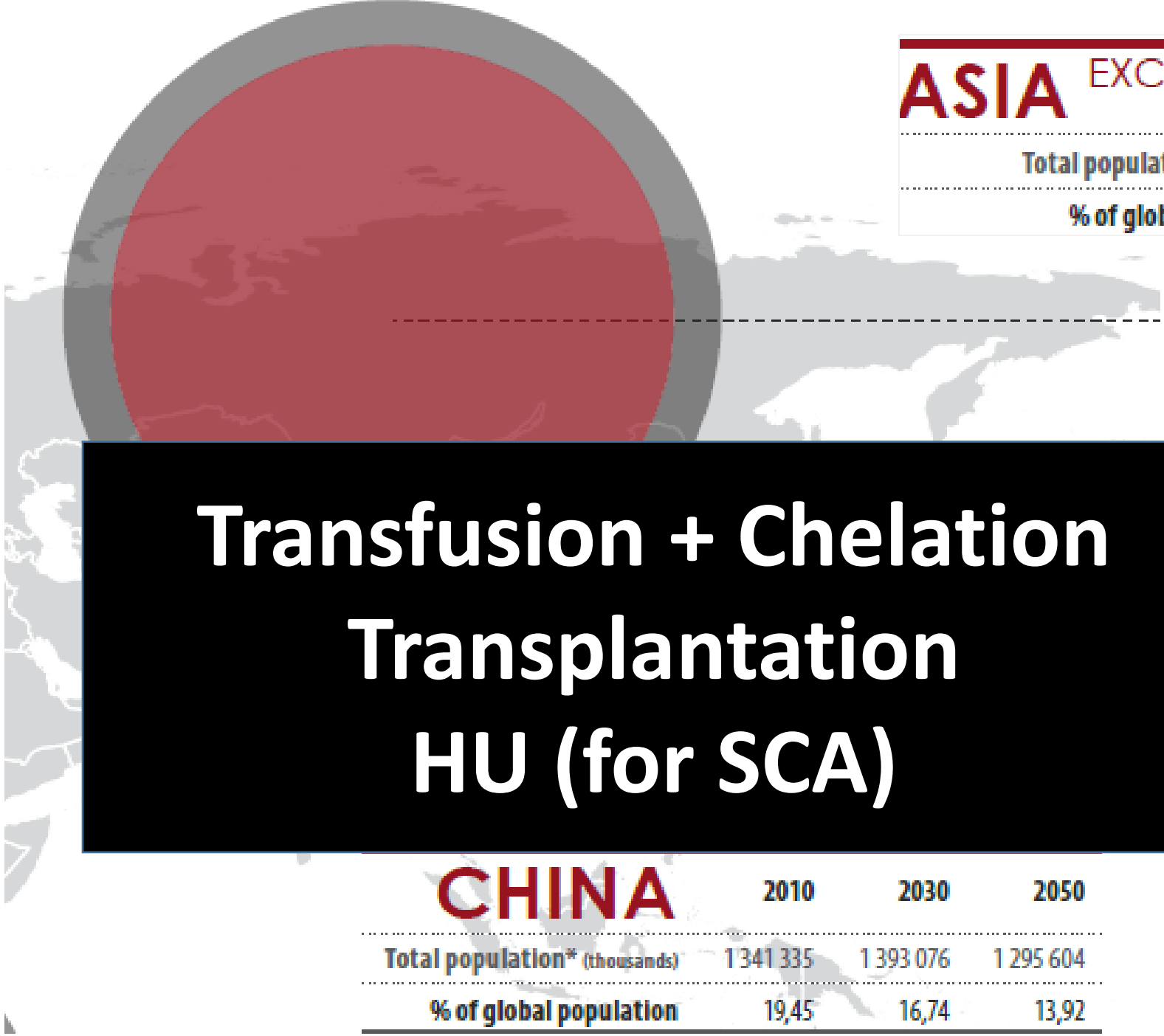
SCA in SA alone is 150,000

TM in SA: ?????

Minster of Health, Arab News 2015

GCCCP Report, 2011


NORTH AMERICA 2010 2030 2050
Total population* (thousands) 344 529 401 657 446 862
% of global population 4,97 4,83 4,80
EUROPE 2010 2030 2050
Total population* (thousands) 738 199 741 233 719 257
% of global population 10,70 8,91 7,73
DEMOGRAPHICS
THE MEDIAN ESTIMATE FOR WORLD POPULATION IN 2050 IS 9 B
THE POPULATION OF ASIA AND AFRICA IS EXPEC
50
ANTICIPATING A
AFRICA 2010 2030
Total population* (thousands) 1 022 234 1 562 047 2 191 599
% of global population 14,82 18,77 23,55
2 SCA
2TM/HbE
2.2←1 bn
Have Transfusion+C
Half Transplantation
Hydroxyurea (for SCA)



ASIA EXCLUDING CHINA	2010	2030	2050
Total population* (thousands)	2 822 917	3 474 665	3 846 616
% of global population	40,94	41,76	41,33

1.4 SCA
1.4TM/HbE

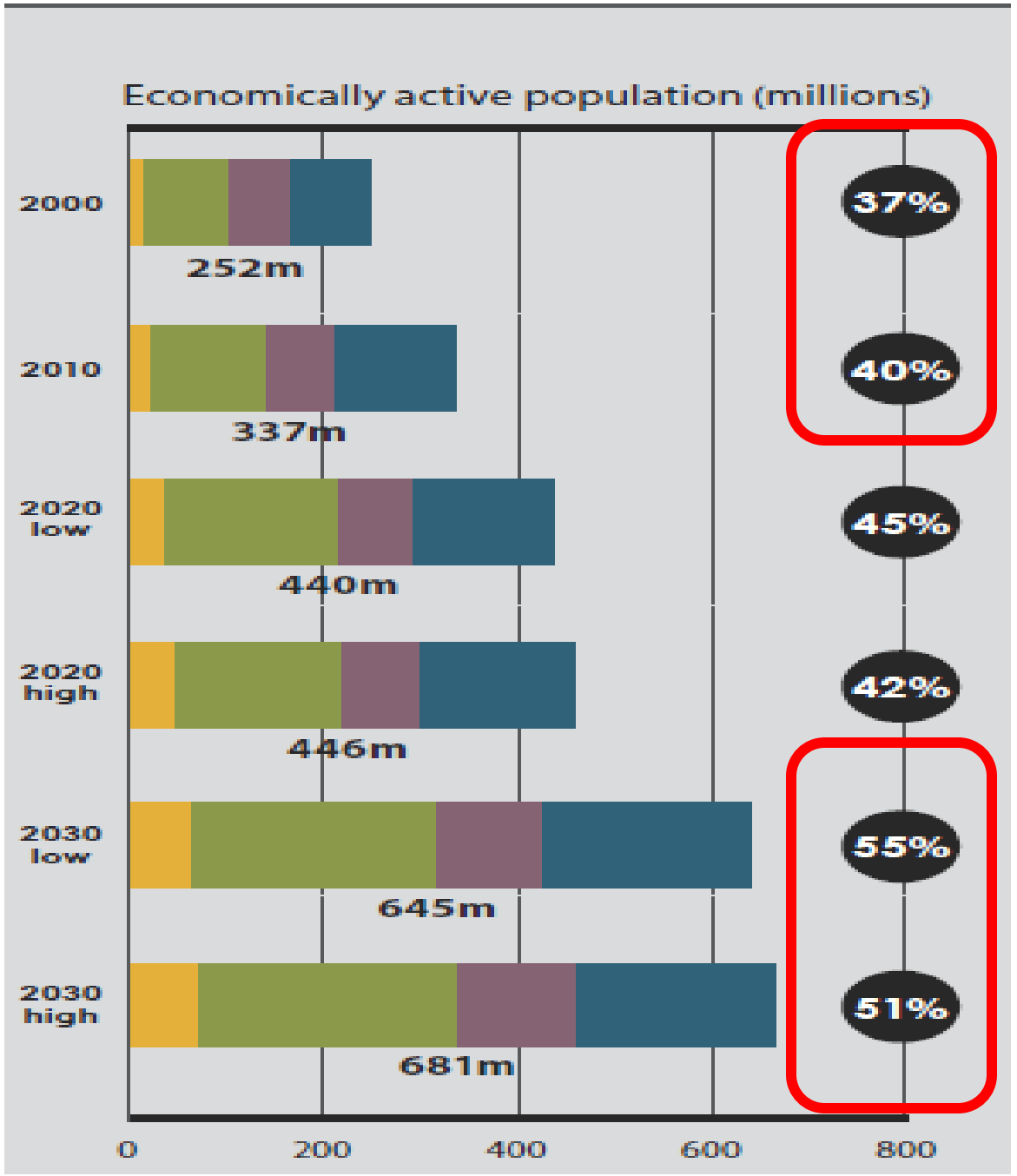
Transfusion + Chelation
Transplantation
HU (for SCA)

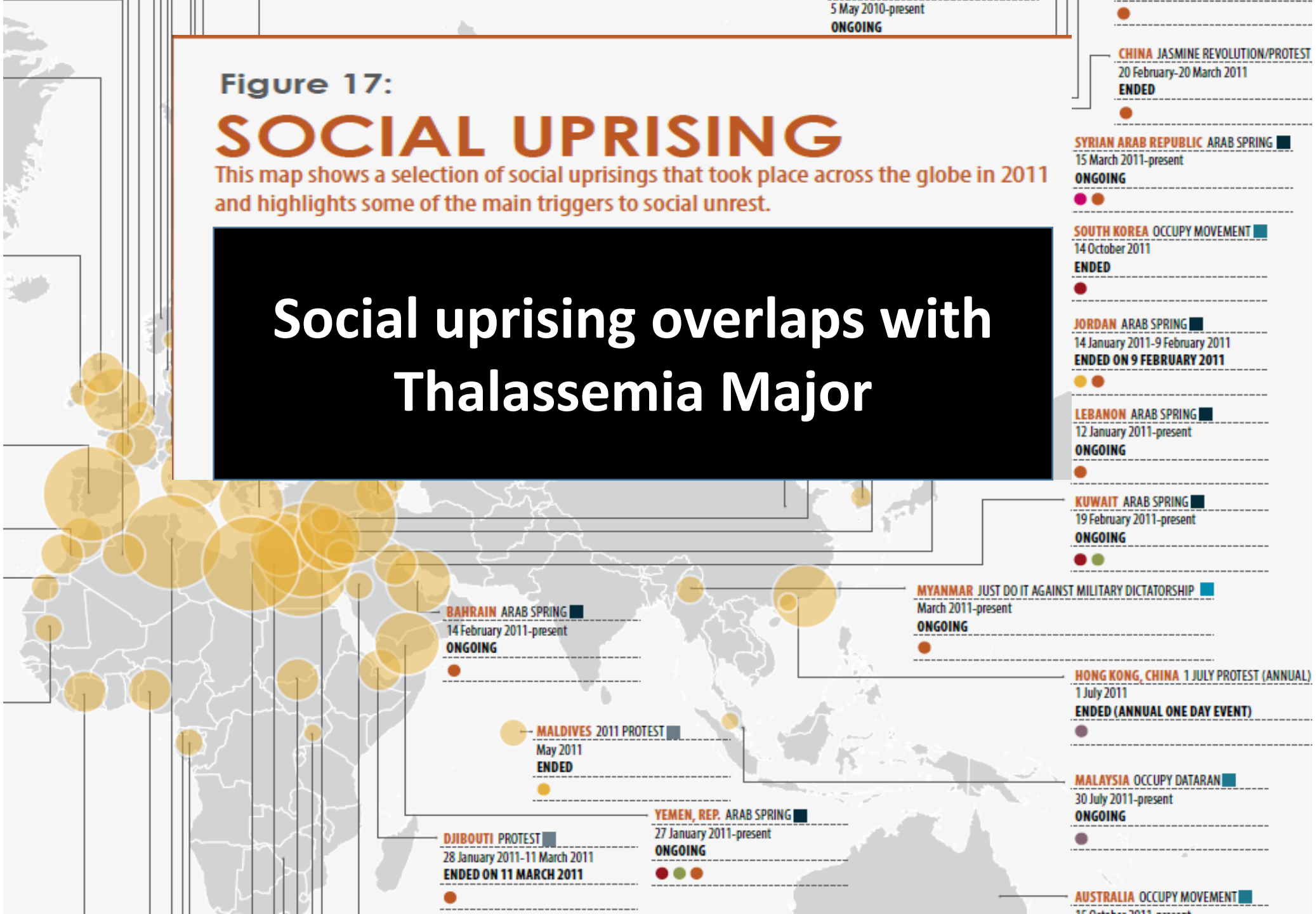
CHINA	2010	2030	2050
Total population* (thousands)	1 341 335	1 393 076	1 295 604
% of global population	19,45	16,74	13,92

Job and QOL will be a major goal of R/

THE JOB CREATION CHALLENGE

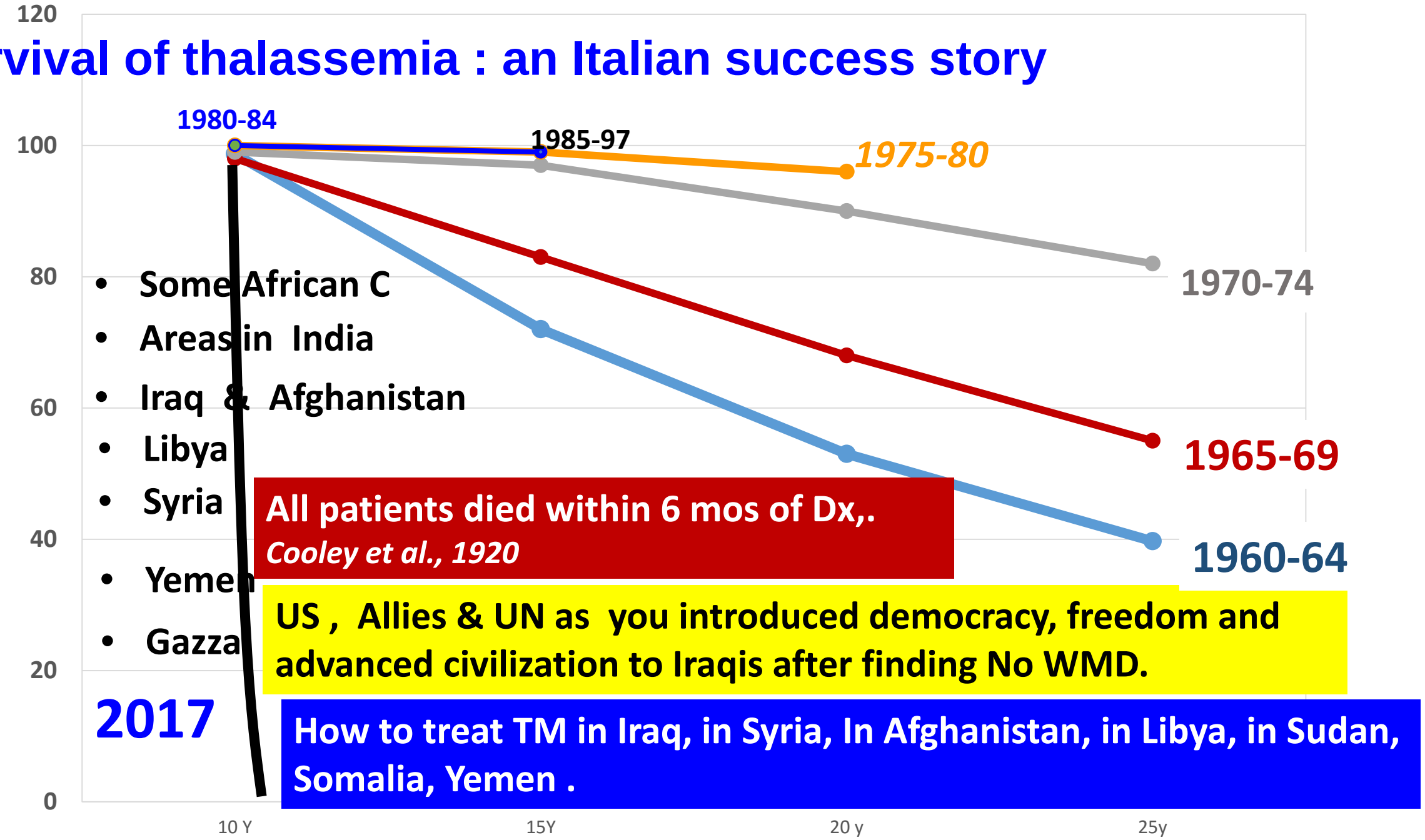
WITHIN SUB-SAHARAN AFRICA, THE ECONOMICALLY ACTIVE POPULATION IS EXPECTED TO CONTINUE TO INCREASE ACROSS ALL SUB-REGIONS, ESPECIALLY IN EASTERN AFRICA





Social uprising overlaps with Thalassemia Major

Survival of thalassemia : an Italian success story



All patients died within 6 mos of Dx,.
Cooley et al., 1920

US , Allies & UN as you introduced democracy, freedom and advanced civilization to Iraqis after finding No WMD.

How to treat TM in Iraq, in Syria, In Afghanistan, in Libya, in Sudan, Somalia, Yemen .

Borgna-Pignatti C et al., ann NY acad SCI 2005

Available transfusion service for Hb-pathies in the world:
17% only

WHO report 2015

Osman A slide

World Health Organization

Global epidemiology of hemoglobin disorders and derived service indicators

WHO region	Estimated annual births β thalassaemias		Transfusion	
	Total	Transfusion-dependent	% of Tx-dependent patients transfused	Annual deaths because not transfused
African	**1 386**	**1 278**	**2.7**	**97%**
American	341	255	52.4	121
EMRO	**9 914**	**9 053**	**17.8**	**75%**

[a] All figures are minimum estimates.

- Bernadette Modell, Matthew Darlison
Volume 86, Number 6, June 2008, 480-487
- Bulletin of the World Health Organization

Yearly Cost of BTIC of TM

Type of costs	Total
Blood	1118.0
Medical Visits	182.9
Nursing Services	303.7
Laboratory Services	136.6
Diagnostic Services	216.0
Medicine	5026.4
Deferoxamine pump and other consumer items in home	155.0
Hospitalization	103.4
Splenectomy	44.8
Going to the service providing centers	205.3
Transportation	69.8
Lost opportunities for patients	356.2
Lost opportunities for patients' families	217.4
Building rent and other costs related to buildings	186.3
Lost welfare	No data [b]
Total	8321.8

Esmaeilzadeh F et al JRHS 2016; 16(3):111-115

Asian Experience & Available services For TM

Country	Transfusion	Iron chelation				PND	National program
		DFO	L1	Exjade	BMT		
Bangladesh	[redacted]	(+)	–	[redacted]	[redacted]	–	[redacted]
Cambodia		(+)	–			–	
China							
Guangxi		(+)	(+)		(+)	+	
Hong Kong		+	+	(+)	+	+	+
Taiwan		+	+	(+)	+	+	+
India	Enough? Safe? For all ?	(+)	(+)	[redacted]	(+)	(+)	[redacted]
Indonesia		(+)	(+)		[redacted]	(+)	
Laos		(+)	–			–	
Malaysia		+	+	(+)	+	+	+
Maldives		+	+	[redacted]	(+)	–	+
Myanmar		(+)	–		[redacted]	–	[redacted]
Philippines		(+)	–	(+)		–	
Singapore		+	+	(+)	+	+	+
Sri Lanka		+	+	[redacted]	[redacted]	–	+
Thailand		+	+	(+)	+	+	+
Vietnam		(+)	(+)	[redacted]	(+)	–	[redacted]

Int J Health Policy Manag 2015, 4(11), 733–740

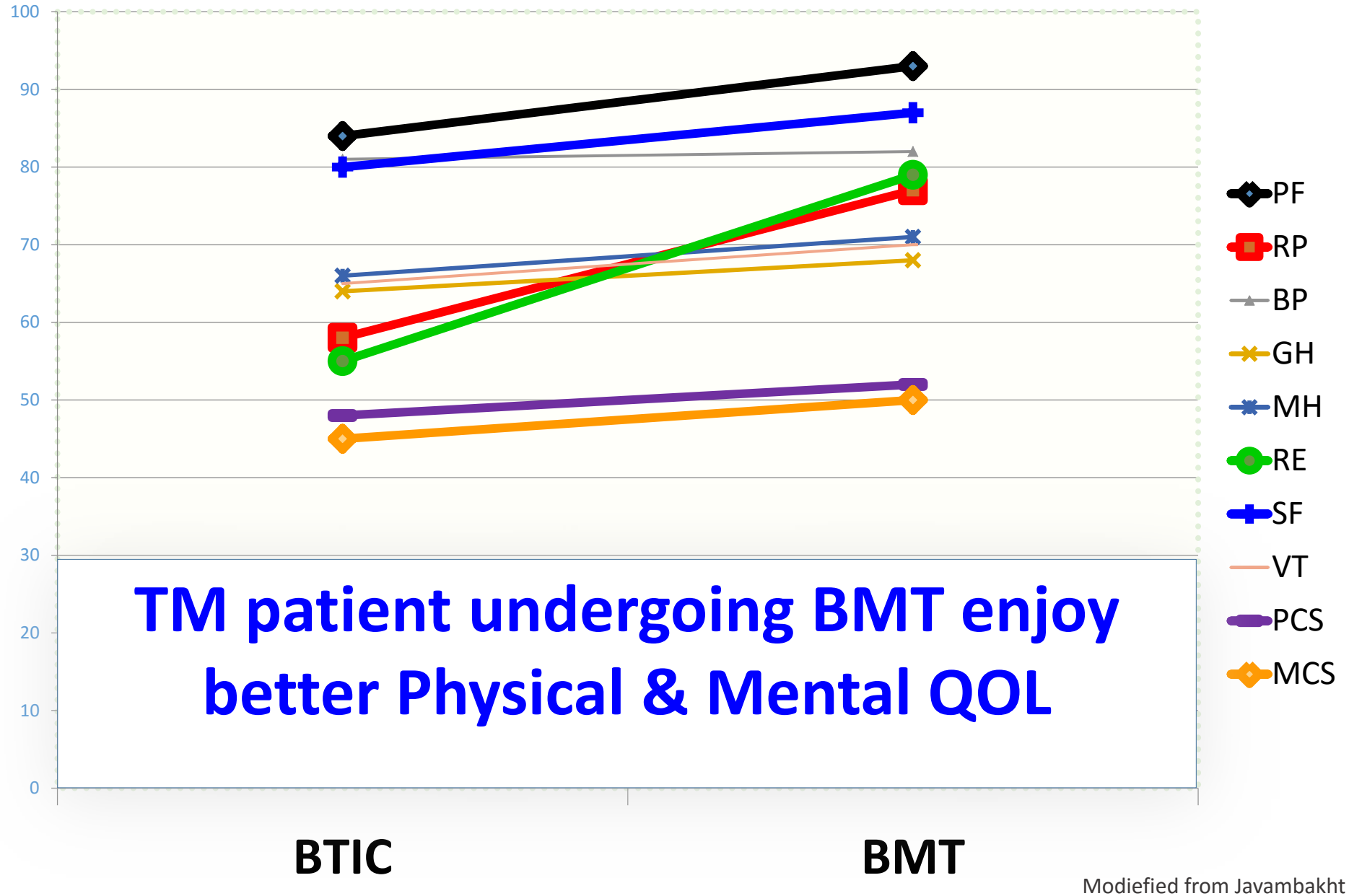
IJHPM International Journal of Health Policy and Management

Original Article

Comparison of Blood Transfusion Plus Chelation Therapy and Bone Marrow Transplantation in Patients with β-Thalassemia: Application of SF-36, EQ-5D, and Visual Analogue Scale Measures

Mehdi Javanbakht[1], Ali Keshtkaran[2], Hossien Shabaninejad[3,4], Hassan Karami[2*], Maryam Zakerinia[5], Sajad Delavari[6]

QOL Component	SF-36 Subscales	BTIC Mean	BTIC SD	BMT Mean	BMT SD	P
PHYSICAL FUNCTIONING	PF	84.93	17.60	93.07	10.90	.004[a]
ROLE LIMITATIONS	RP	58.88	38.32	77.84	29.14	.003[a]
Bodily pain	BP	81.68	20.09	81.36	20.82	.928
General health	GH	64.24	21.82	68.41	20.22	.259
Mental Health	MH	65.66	19.78	70.55	15.48	.133
ROLE LIMITATIONS	RE	55.92	40.35	78.79	39.43	.001[a]
Social functioning	SF	80.02	21.35	86.93	20.70	.058
Vitality	VT	65.89	18.24	69.89	16.96	.195
PHYSICAL COMPONENT SCALE	PCS	48.23	7.09	51.65	6.60	.005[a]
MENTAL COMPONENT SCALE	MCS	45.19	9.76	49.53	9.59	.010



Modiefied from Javambakht M et al., 2015

Better QOL after HSCT if done early & No cGVHD

Study	Tools used	Patients	Results and conclusions of the study
Cheuk et al, BMT 2008 (8)	WHOQOL-BREF(HK) PedsQLTM4.0 Cross-sectional analysis	74 TM on supportive care 24 TM > HCT	Adults >18 y: Overall health better after HCT – less medical aids, higher activity, better relationships and physical health. Children <18 y: Better physical function after HCT. Lower scores on school attendance restriction and hospital visits
Caocci et al, BBMT 2011(85)	PedsQLTM4.0 Before HCT, 3, 6, & 18 mos after HCT	28 TM-HCT patients	• Physical function declined until 3 mo> HCT then increased. • No significant DD in emotional, social or psychosocial domains
La Nasa et al, Blood 2013 (86)	SF36 , FACT- BMT Cross-sectional analysis	109 Ex-TM (HCT 1980 - 2000) vs124 TM on Supportive care	• Higher HRQol following HCT. • Older age & cGVHD affected HRQoL negatively
Javanbakht M et al., 2015 Int'l J health policy manag	SF-36 cross-sectional	Total 160 on BTIC vs. 50 after HSCT	Significant better physical function, Role limitation, mental component scale after HSCT. Other parameters favors HSCT .

- *WHOQOL-BREF(HK) – World Health Organization Quality of Life Measure Abbreviated*
- *PedsQLTM4.0 – Pediatric Quality of Life Version 4.0*
- *SF-36 – Short Form 36 version 1 ,*
- *FACT-BMT - Functional Assessment of Cancer Therapy – Bone Marrow Transplant*
- *HCT- Hematopoietic Cell Transplant;*
- *cGVHD - chronic graft-versus-host disease ,*
- *HRQoL – Health related quality of life*
- *BTIC= Blood transfusion and iron Chelation*

Not only Patients but also their parents are affected

Caocci et al. BMC Blood Disorders 2012, 12:6

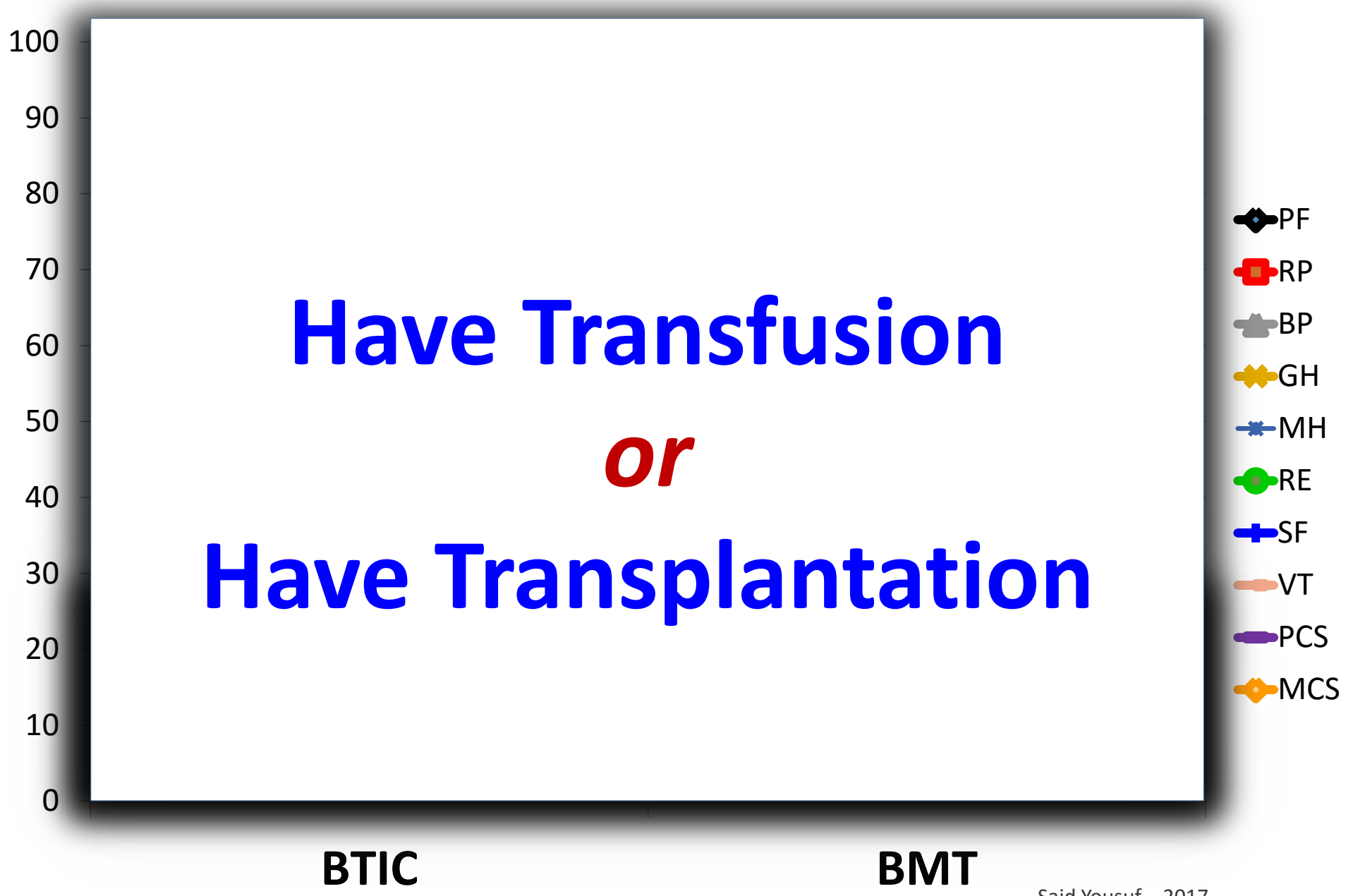
RESEARCH ARTICLE Open Access

BMC Blood Disorders

Health related quality of life in Middle Eastern children with beta-thalassemia

Differences in child and parent PedsQL domain scores, expressed as median and inter-quartile ranges

PEDsQL scale	Patients	Parents	Difference (95% CI)	P value
Physical Functioning	75 (56.3, 91.40)	75 (55.5, 85.18)	3.75 (−1.55, 7.8)	0.112
Emotional Functioning	85 (60, 100)	75 (50, 95)	10 (2.5, 15)	0.002*
Social Functioning	82.50 (60, 91.25)	75.8 (65, 90)	0.74 (−3.5, 7.5)	0.576
School Functioning	75.00 (50, 85)	70 (50, 80)	2.5 (−5, 7.5)	0.465
Psychosocial Health Summary	79.15 (61.88, 88.30)	70.3 (59.58, 83.72)	4.2 (0.85, 7.5)	0.015*
Total Summary Score	77.75 (61.45, 88.28)	74.35 (60.35, 82.77)	2.45 (4.62, 4.9)	0.047*



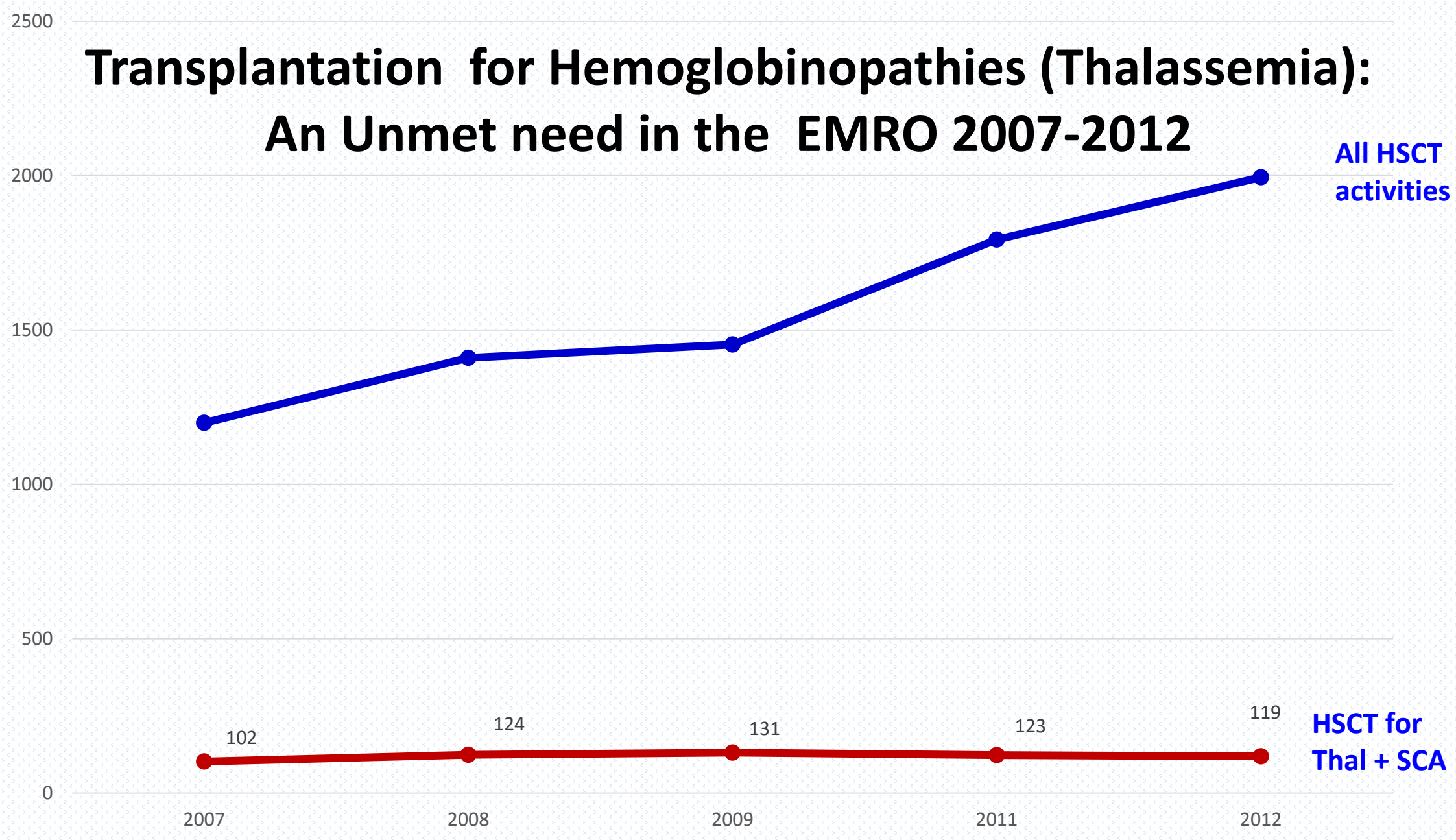
Have Transfusion

or

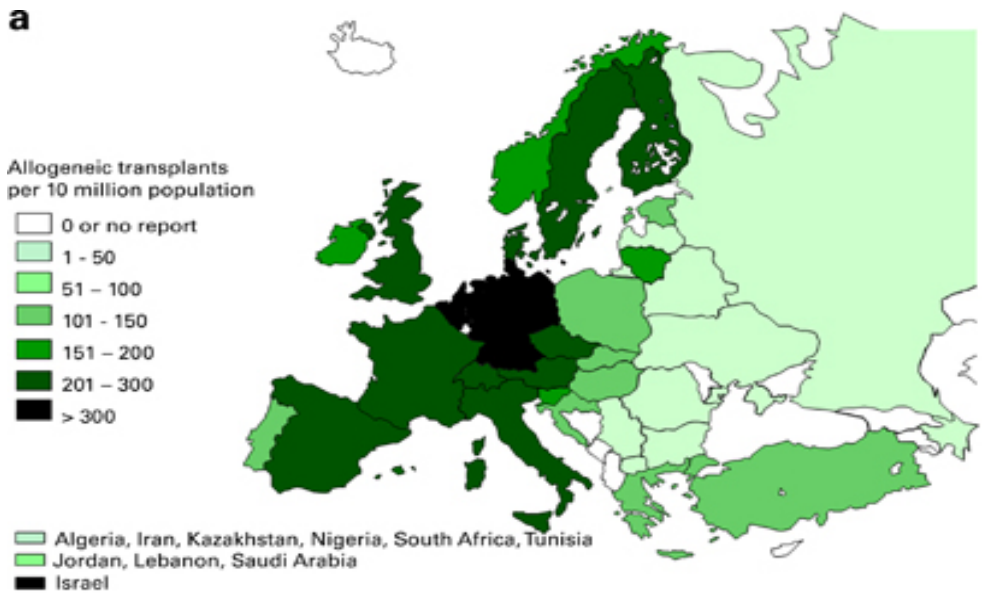
Have Transplantation

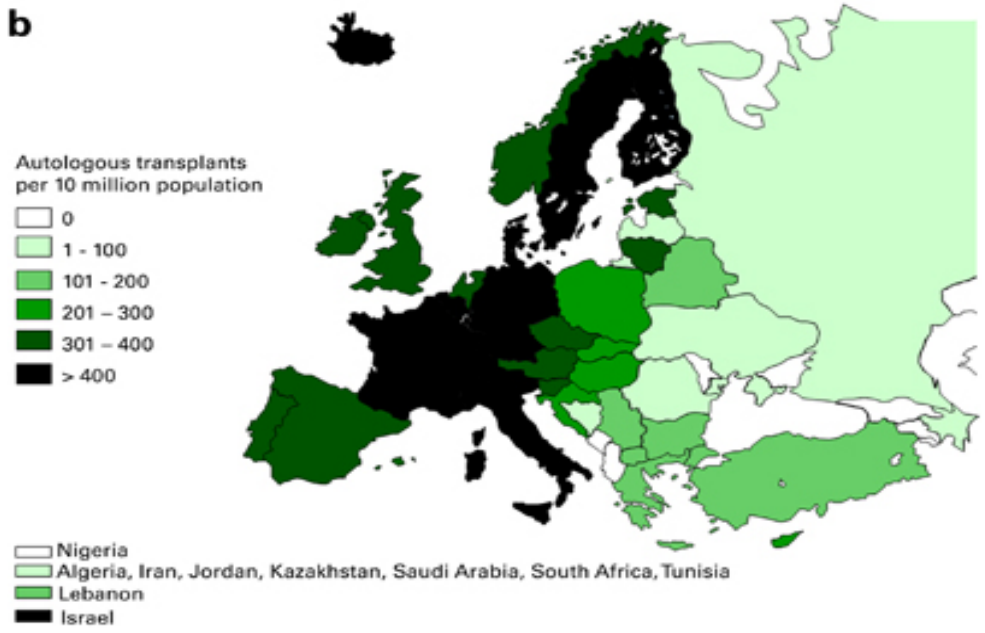
Said Yousuf , 2017

Transplantation for Hemoglobinopathies (Thalassemia): An Unmet need in the EMRO 2007-2012

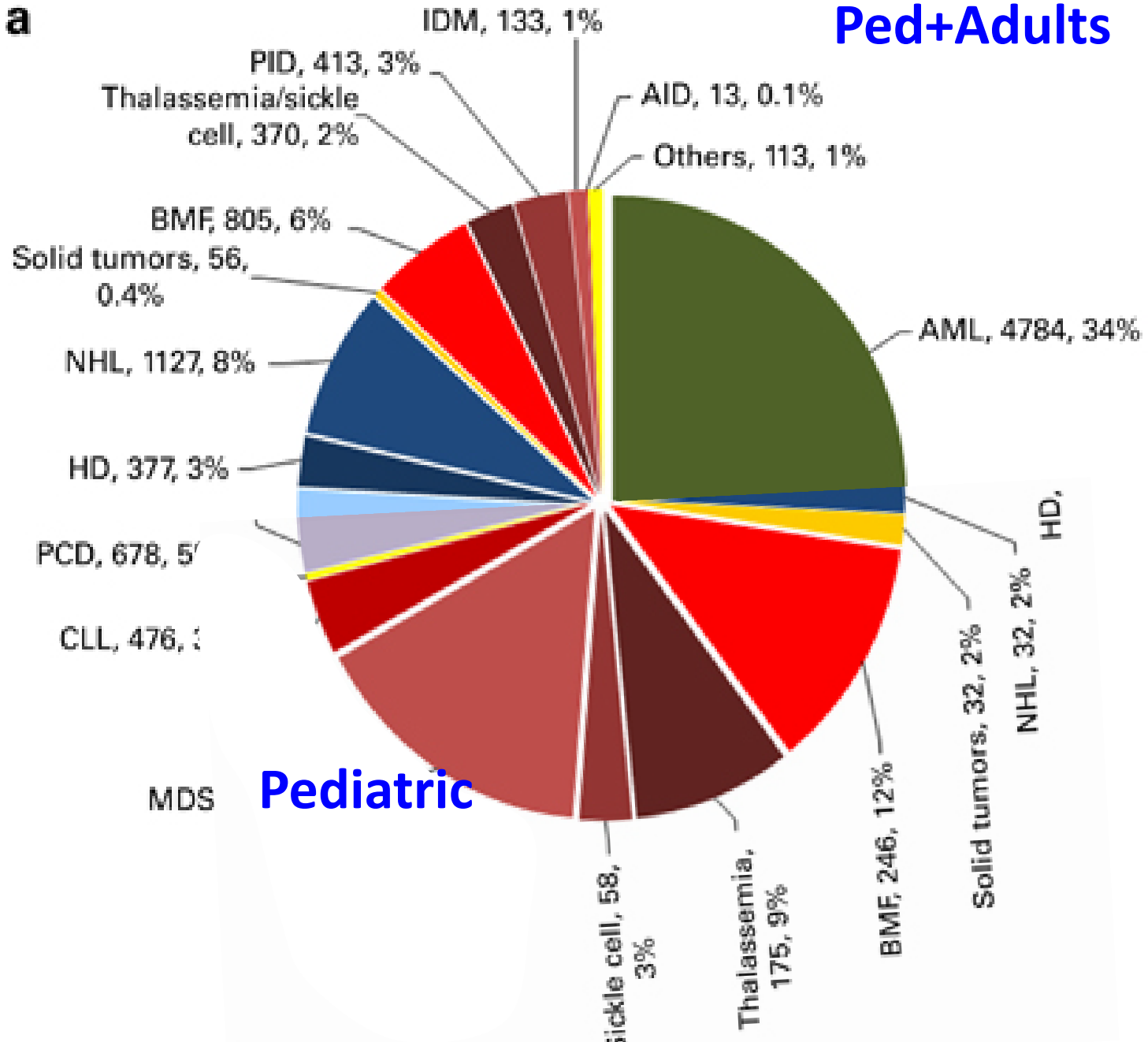


Mohamed S.Y, 2017.

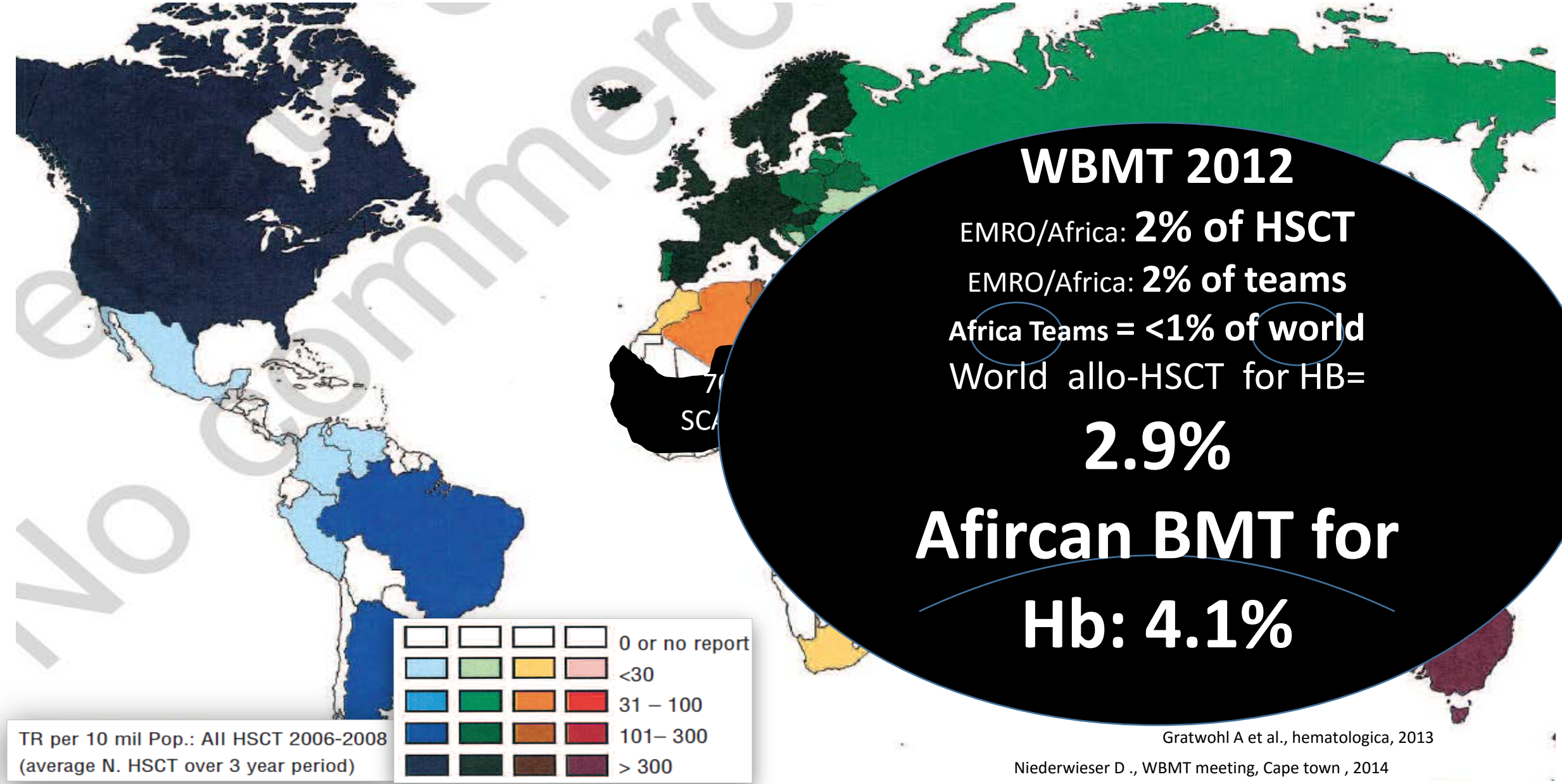




Passwig J et al., BMT 2014



Transplant rates for the total number of HSCT in participating countries by WHO regions 2006-2008. (n of HSCT, allo- & auto- combined, by 10 million inhabitants).



WBMT 2012

EMRO/Africa: **2% of HSCT**

EMRO/Africa: **2% of teams**

Africa Teams = <1% of world

World allo-HSCT for HB=

2.9%

Afircan BMT for Hb: 4.1%

Gratwohl A et al., hematologica, 2013

Niederwieser D ., WBMT meeting, Cape town , 2014

Why we are not offering TM transfusion or Transplantation?

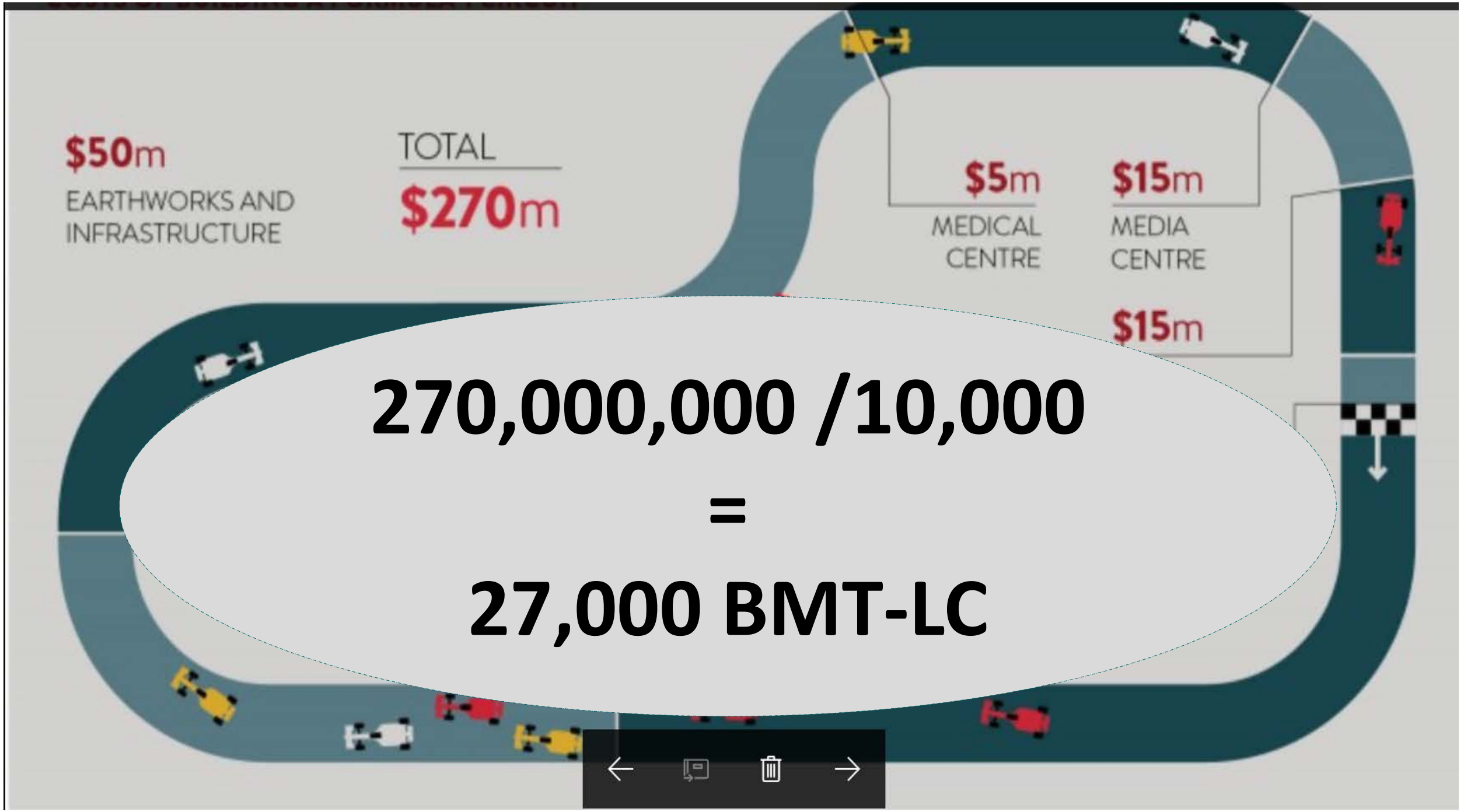
- Where the money goes?????

Each warplane costs $12,000 per hour to fly, and each helicopter $3,000 per hour, according to IHS.

Math of War and TM management

- **10 hours x100 planes = 12,000x10 h x 100 planes = 12,000,000 USD**
- **12,000,000 /10,000 = 1,200 LC-BMT per day**
- **Total LC-BMT in 1 mo= 36,000 BMT per month**
- **No criminal, no need for UN resolution but dissolution**

Replace pilots by Hematologist


$50m
EARTHWORKS AND INFRASTRUCTURE
TOTAL
$270m
$5m
MEDICAL CENTRE
$15m
MEDIA CENTRE
$15m
270,000,000 /10,000
=
27,000 BMT-LC

Who is responsible ?

- When will not remember the sword of our enemy, but the **silence** of our friends

An African preverb

Just start; we will reach there very soon

The development of the National Thalassaemia Centre, Kurunegala, Sri Lanka.

The building contains wards for both children and adults, counselling facilities and laboratories for screening and field-study research. (**A**) Early construction. (**B**) Completed building.

If they wanted to go they should have prepared ???

Real work
No image
No show !!


© UNICEF/NYHQ2012-0531/Asselin

Clinic Science

Challenges in Transplantation of Thalassemia

1. **Information-education-consenting**
2. **Cost**
3. **Prioritization (Paradox of Benign)**
4. **Donors**
    1. **MSD &MRD**
    2. **MUD, CBT**
    3. **HaploIdentical**
5. **Iron Overload & accumulated morbidit*ititititititititit*ies**
6. **Suppression of chronic inflammation pre-transplant**

1- Information/Awareness

7%

Low utility of curative strategies (BMT) for SCA is partly attributable to lack of information.

WBMT is the best venue for:

1- Awareness,

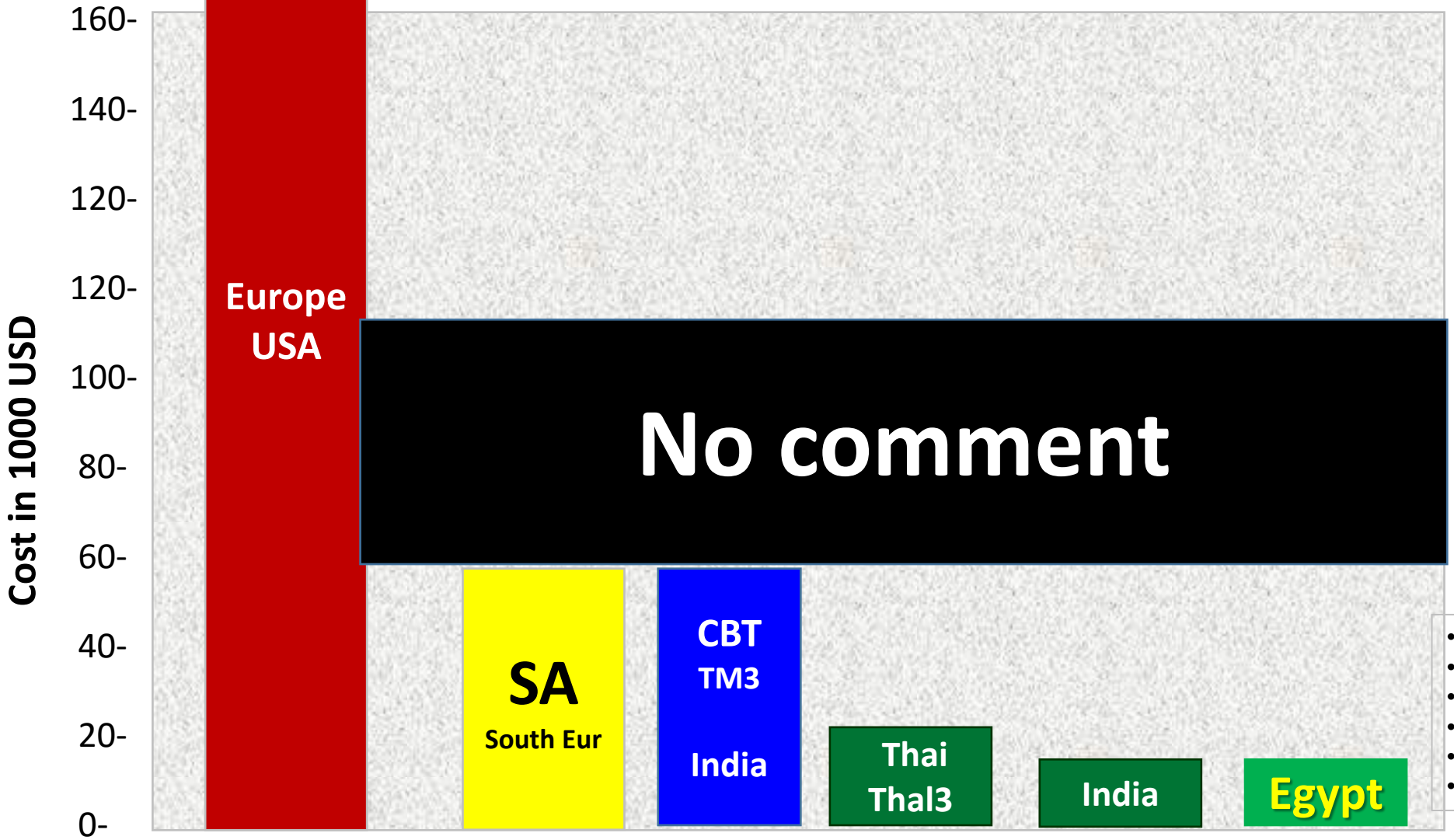
2- Registries

3- National centers

- Jae GA et al., Ethnicity and Health. 2011

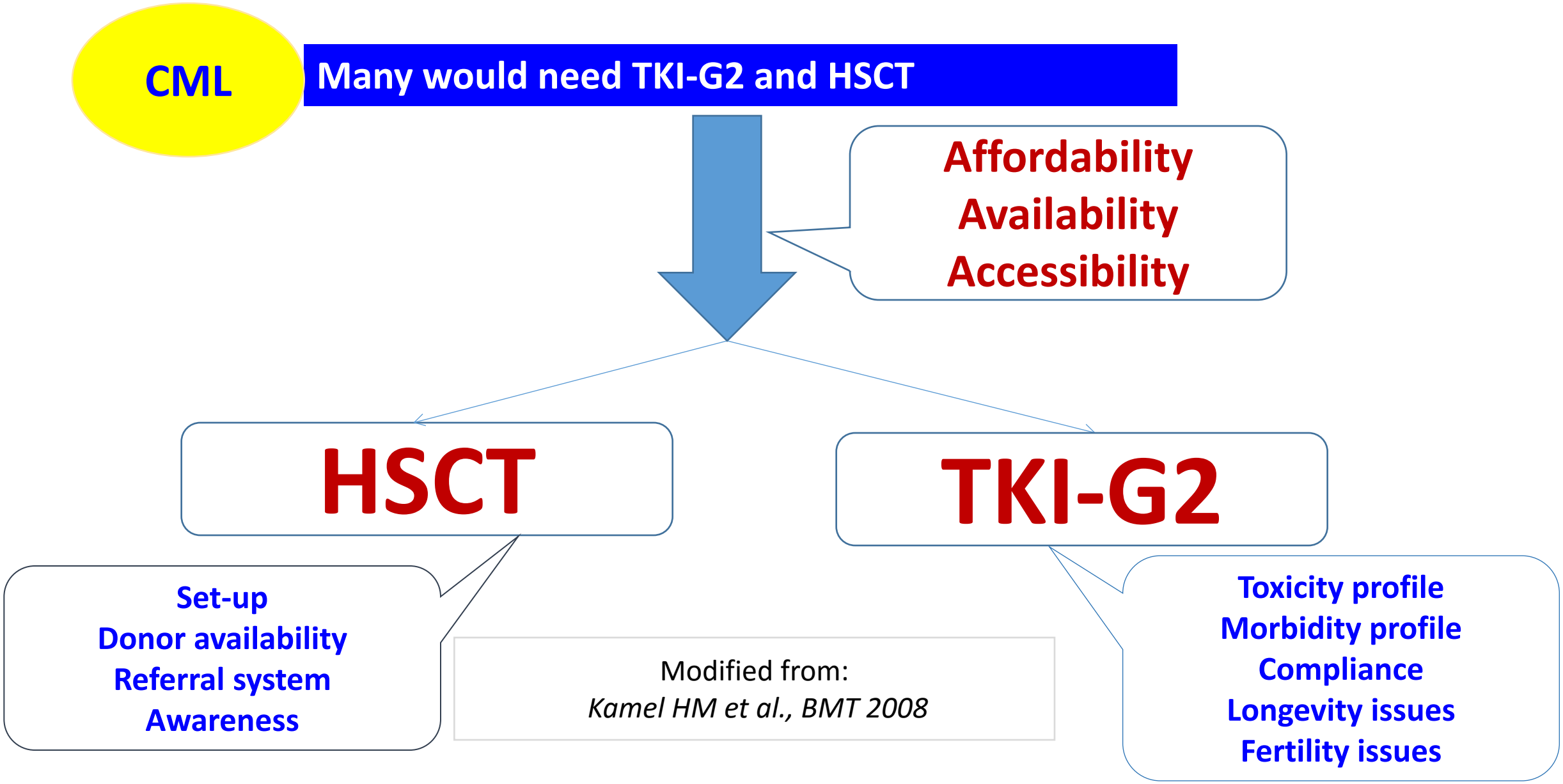
2. Cost

Claimed high cost of BMT?



- Krejci M et al., BMT 2006
- Jae GA et al., Ethinicity and Health. 2011
- Issaragrisil S et al., BMT 2008
- Sharma SK et al., Medit J of Hematol.
- & Infect Dis., 2014
- Kamel HM et al.,BMT 2008

The majority of cancers in Africa are diagnosed at an advanced stage

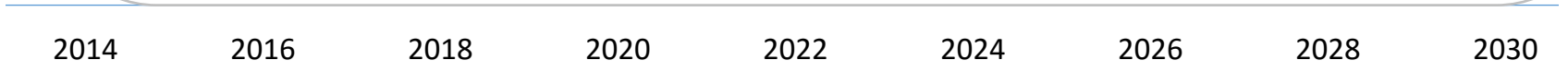


Phasing out the solution for TM

H.A.V.E. Transfusion

OR

TRANSPLANT



Donors

Results of BMT for β –Thalasemia .

Historical results from Pesaro experience during 1980s-1990s

Pesaro Class	Regimen	OS%	TFS%
1	Bu 14 – Cy 200	93	90
2	Bu 14 – Cy 200	87	84
3	Bu14-Cy120-160	66	62

Lucarelli G et al., 1992
Sodani P, 2004
Angelucci E et al.,2009

Recent results are better : EBMT report Hb-pathy registry:

	Patients	Overall Survival	Thalassemia Free Survival
<= 2 years	96	0.94 ± 0.03	0.90 ± 0.03
2-5 years	388	0.92 ± 0.02	0.82 ± 0.02
5-10 years	473	0.88 ± 0.02	0.81 ± 0.02
10-14 years	248	0.94 ± 0.02	0.83
14-18 years	154	0.78 ± 0.04	0.70
> 18 years	133	0.77 ± 0.04	0.74 ± 0.04

The earlier, the better

- N: 1493 ß-TM
- Transplanted after 2000
- From **MSD** , (MRD, MUD, CBT)
- Stratified by age
- Median age 7.2 y (0.3–45.1)
- Only 133 (9.8%) were adults ≥ 18 years
- Difference in outcome ➔ **p value of < 0.001**

MSD

OS: 91 ± 0.01% & TFS: 83 ± 0.01%

Adults: still an unmet needs

Centers Avoid Adults or Adults centers avoid or publishers avoid both

Baronciani D et al., ASH 2011

MSD or MRD transplantation for Thalassemia Major

Study	Number	Age	OS	TFS
Lucarelli G et al., NEJM 1990	222	Children	82	75
Lucarelli et al Blood 1996	107	Adults	66	63
Argiolu F et al., BMT, 1997	37	Children	88	88
Clift RA et al., BMT, 1997	68	Children	94	81
Dennison D et al., BMT 1997	50	Advanced , Older	76	68
Ghavamzadah A et al., BMT1997	60	Children	83	73
Issaragrisi S et al., BMT 1997	21	Advanced, Older	76	53
Lin HP et al., BMT 1997	28	Children	86	82
Li CK et al., BMT 2002	44	Children	86	82
Lawson SE et al., Brit J Hematol 2003	54	Children	95	82
Di Bartolomeo P et al., Blood 2004	111	Children	90	86
Sodani P et al., Blood 2004	33	Children	93	91
Hongeng S et al, BBMT 2006	28	Children	92	82
Isgro 2010	37class 1-2	Children	97	89
	35 class 3	Children	87	80
Sablof 2011	75 class 2	Children	91	88
	64 class 3	Adv/Old	64	63
Gaziev J et al., Transplantation 2016	37	Children	92	92

Wait & Lose

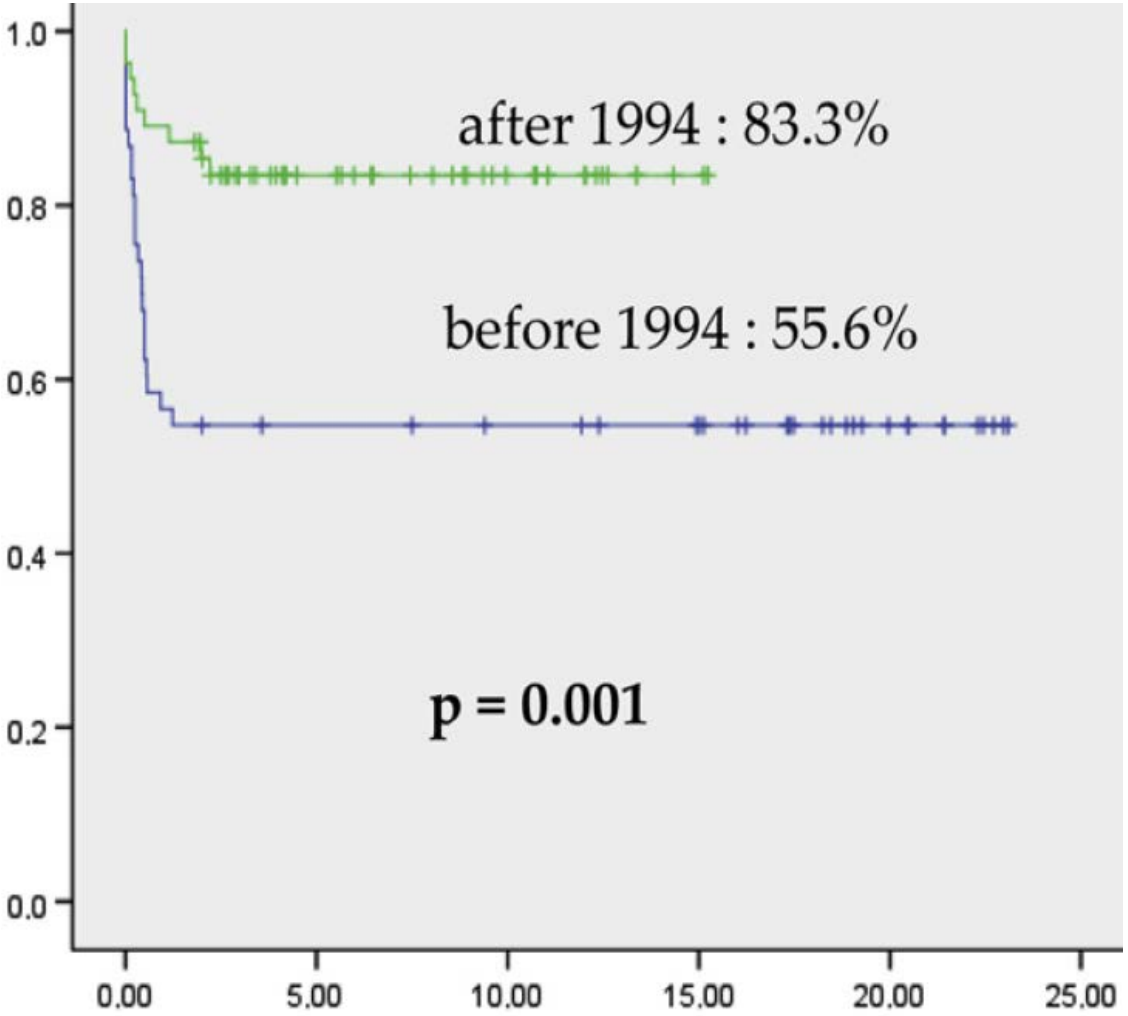
Wait & lose

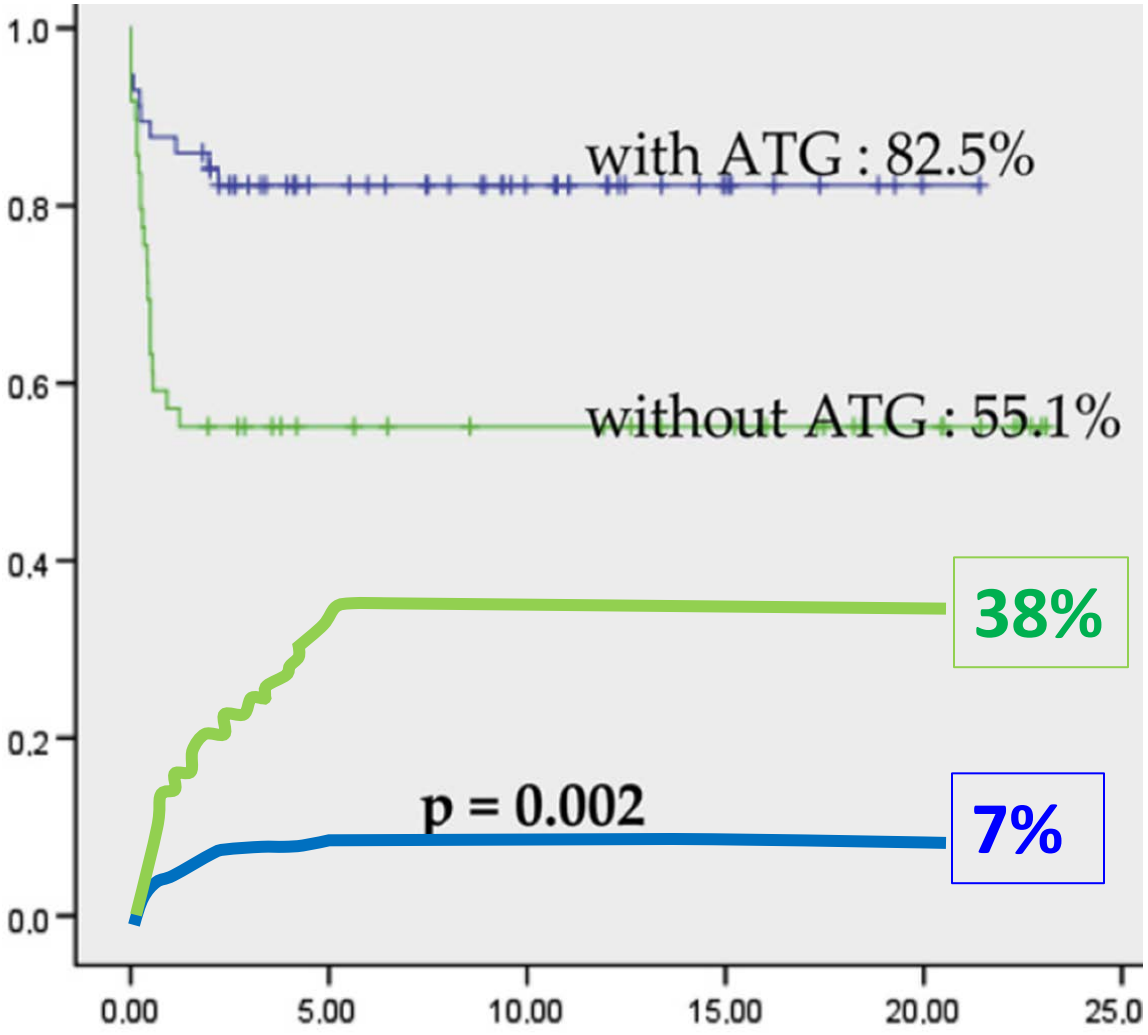
Mohamed S. 2017

The French experience: 6 risk “YAACSS”

1. **Year of transplant </> 1994: multiple factors**
2. **Age of patient 14 or above**
3. **ATG use**
4. **Class 1-2 vs 3**
5. **Splenectomy (*)**
6. **Sib vs. others**

French experience



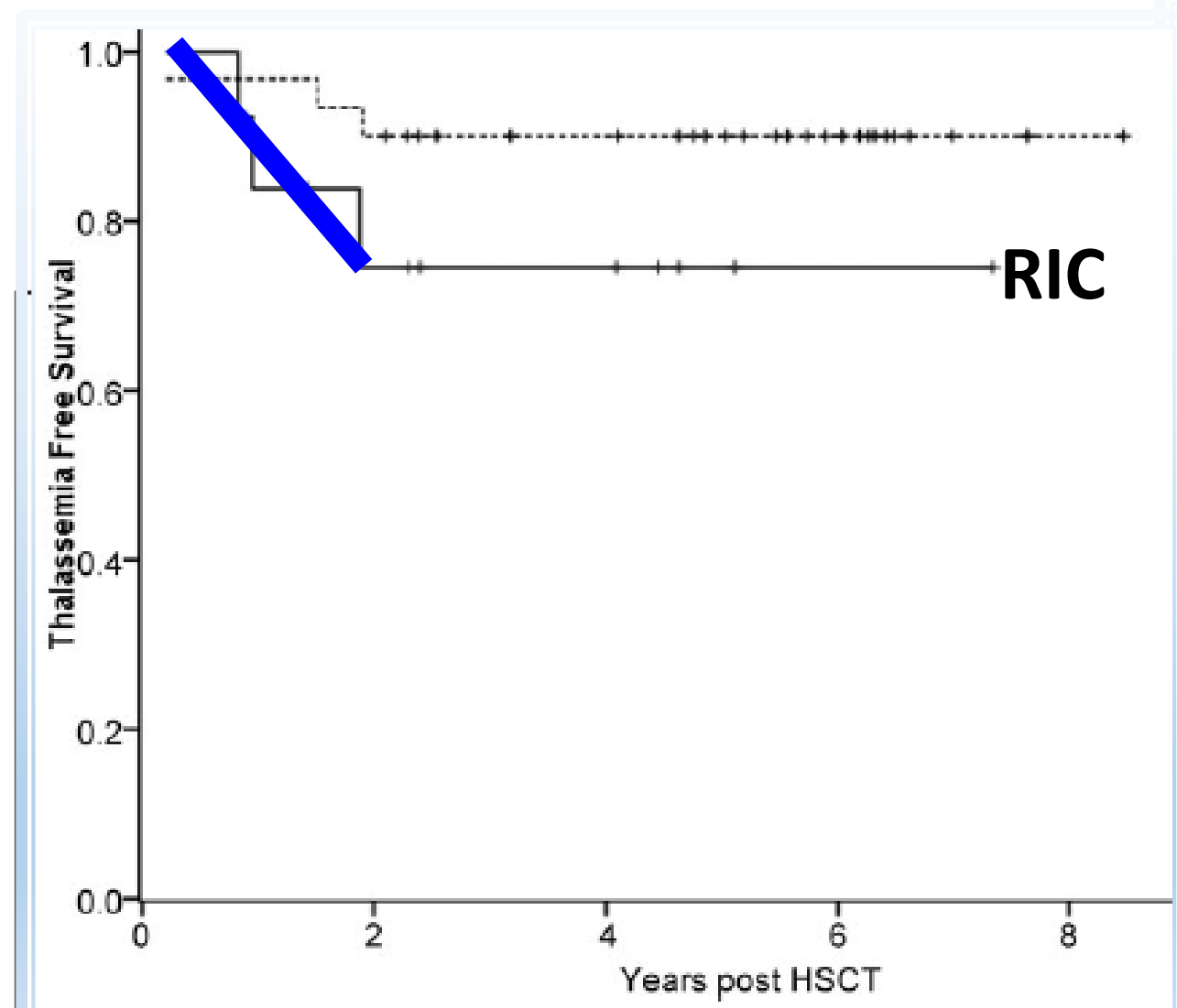


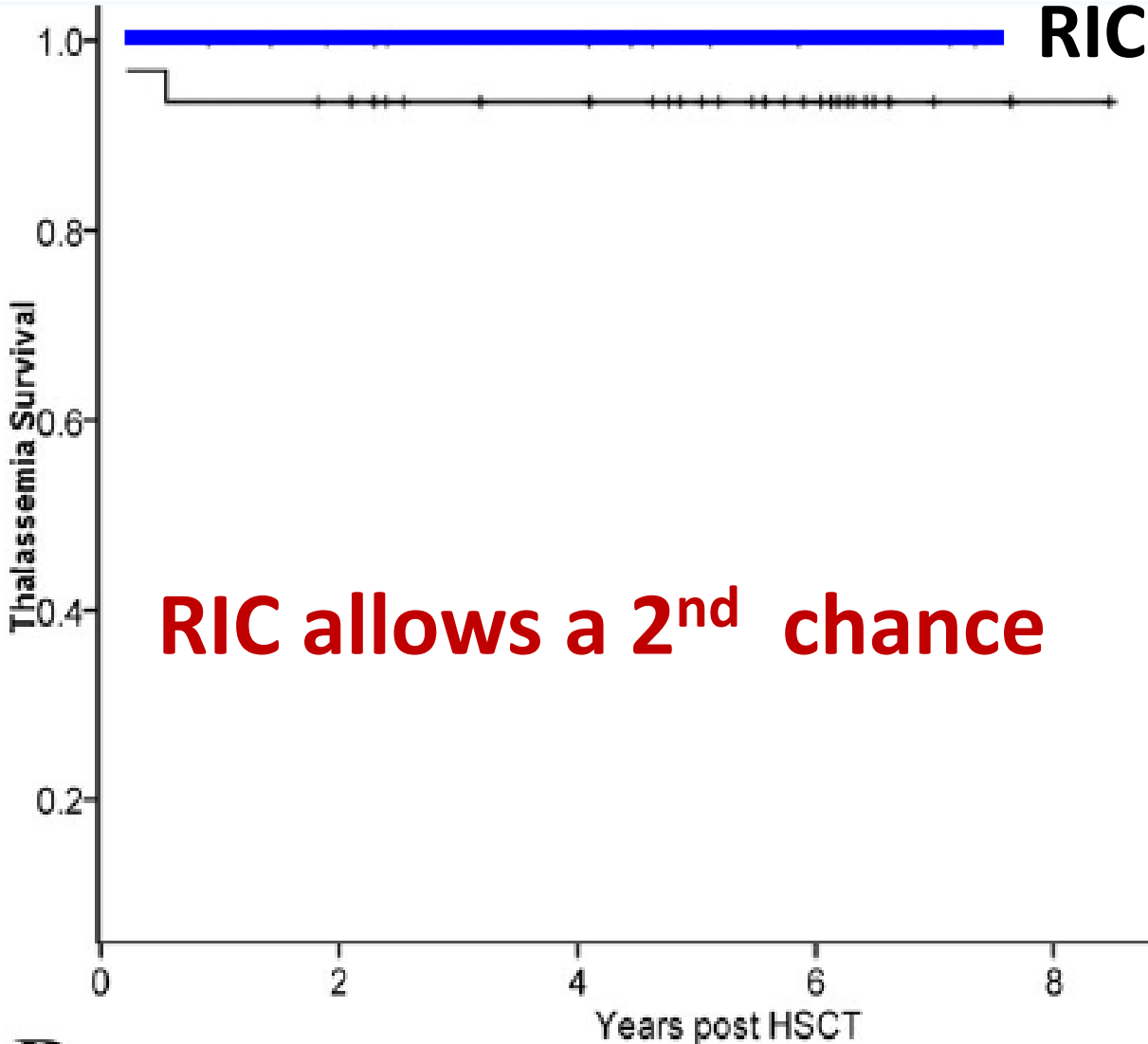
Actuarial survival and TFS at 15 years

Galambrun C et al., BBMT 2013

Pediatr Blood Cancer 2013;60:1345–134

Risk Adopted Allogeneic Hematopoietic Stem Cell Transplantation Using a Reduced Intensity Regimen for Children with Thalassemia Major

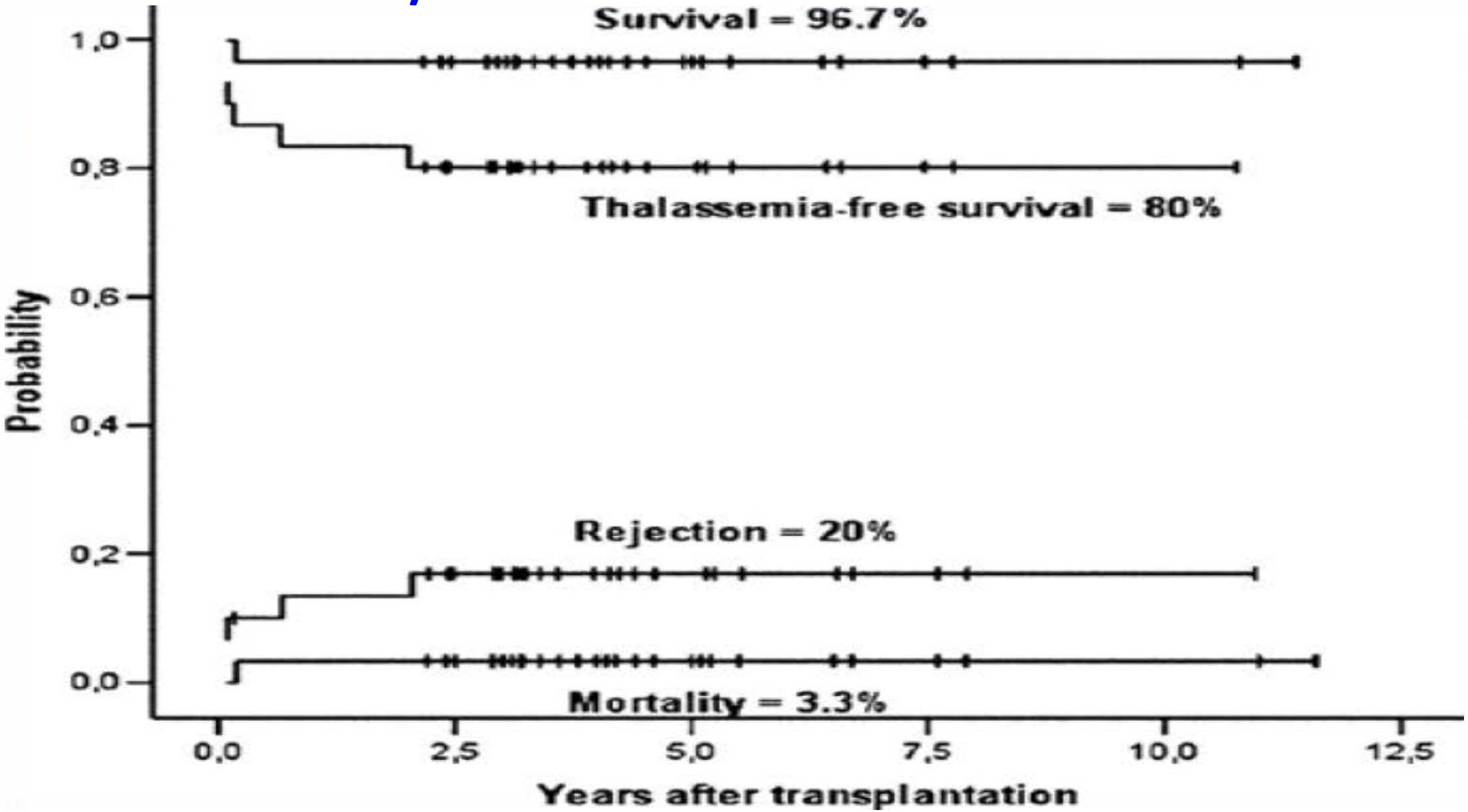




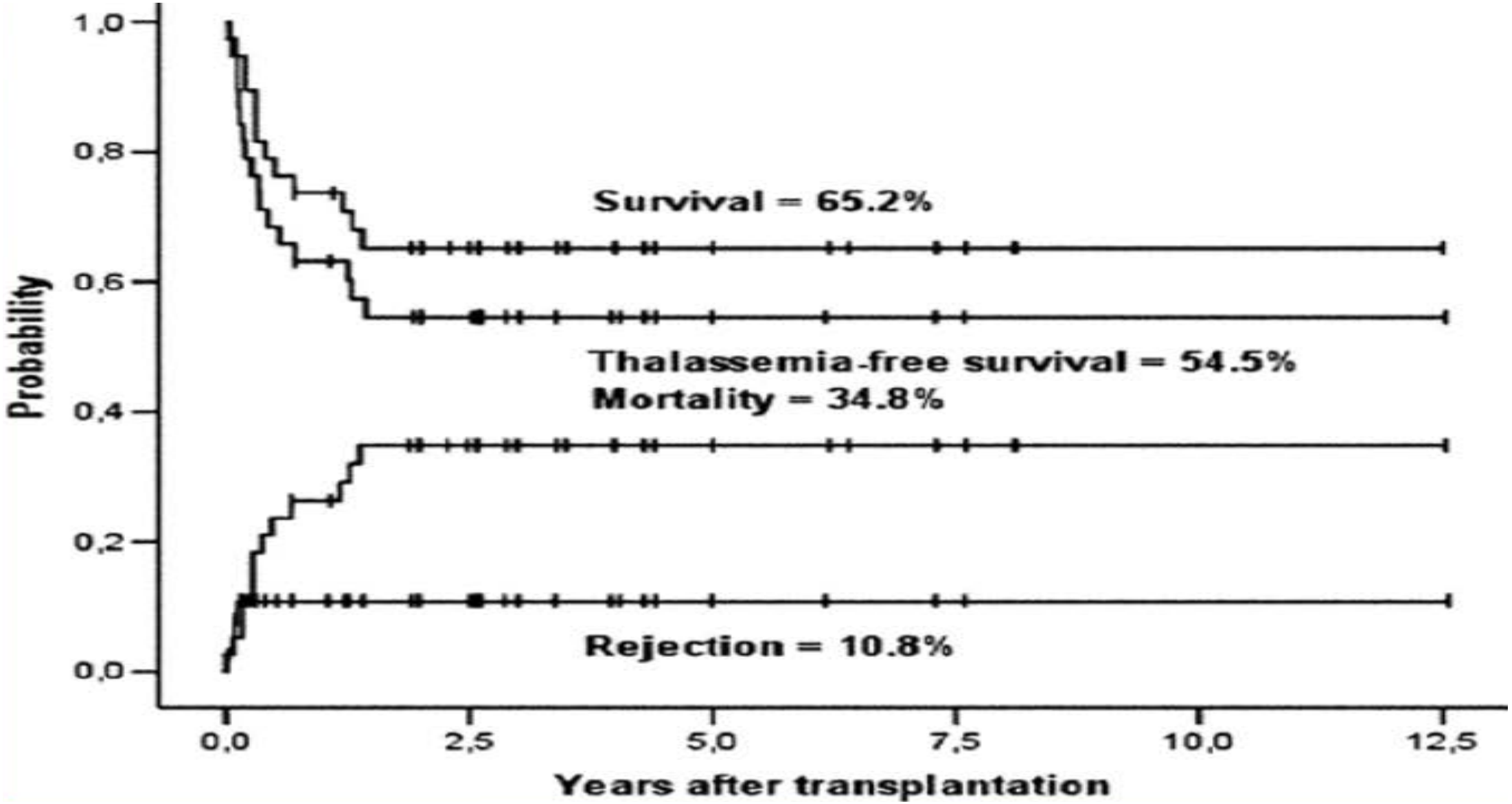
RIC allows a 2nd chance

Close your eyes

MUD-Class 1/2


Survival = 96.7%
Thalassemia-free survival = 80%
Rejection = 20%
Mortality = 3.3%
Probability
1,0
0,8
0,6
0,4
0,2
0,0
0,0
2,5
5,0
7,5
10,0
12,5
Years after transplantation

MUD-Class-3 TM

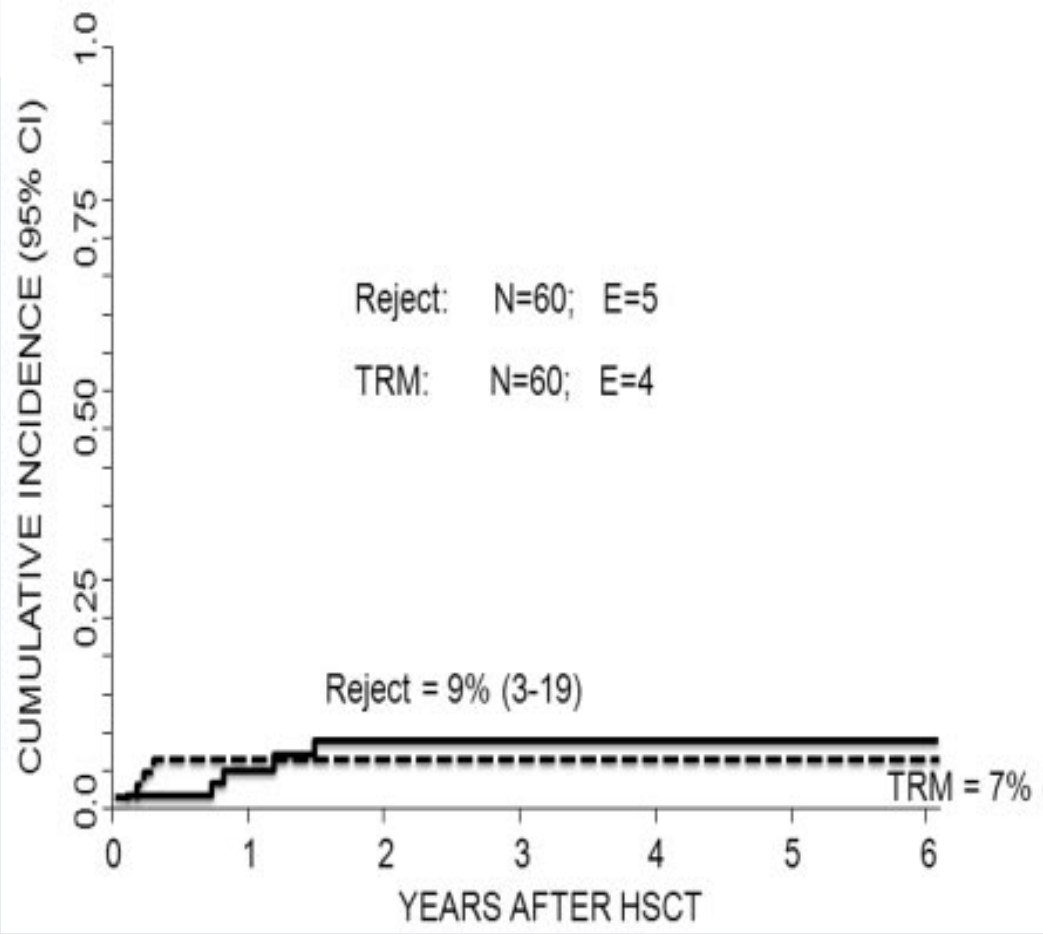


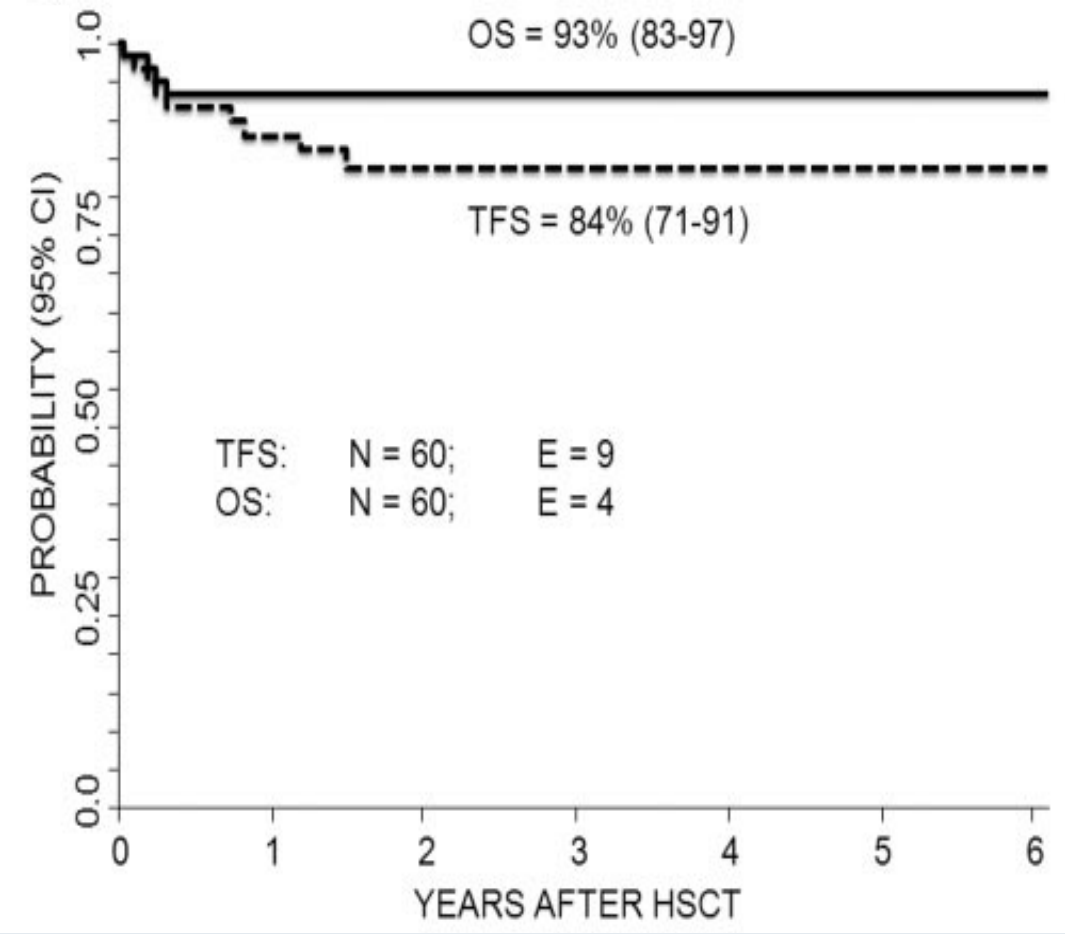
Outcomes of URD & CBT in Children & AYA with TM

First author	N° pts	Source	Age median years (range)	OS 90s	TFS 80s	TRM 10	Rejection 10s	aGvHD 25	cGvHD 15
La Nasa (2002)[12]	32	BM	14 (2-28)	79	66	19	12.5	41	25
La Nasa (2005)[13]	68	BM	15 (2-37)	79.3	65.8	20	13	40	18
Hongeng (2006)[51]	21	BM	4 (0.7-12)	85.7	71	14.3	14.3	42	14
Locatelli (2011)[9]	122	BM	10.5 (1-35)	84	75	16.4	13.1	28	13
Ruggeri (2011)[17]	35	CB	4 (0.5-14)	62	21	34	57	23	16
Jaing (2012)[16]	35	CB	5.5 (1.2-14)	88.5	88.5	11.4	0	47	35
Li (2012)[15]	52	BM/PB	6 (2-15)	92.3	90.4	7.7	1.9	9.6	0
Anurathapan (2014)[52]	26	BM/PB	8 (2-10)	94	82	7	0	28	15
Shah (2015)[18]	9	CB	3.8 (1.5-7)	100	56%	0	44%	33%	11%

from:. La Nasa G et al., Med J Hemat Inf Dis 2016

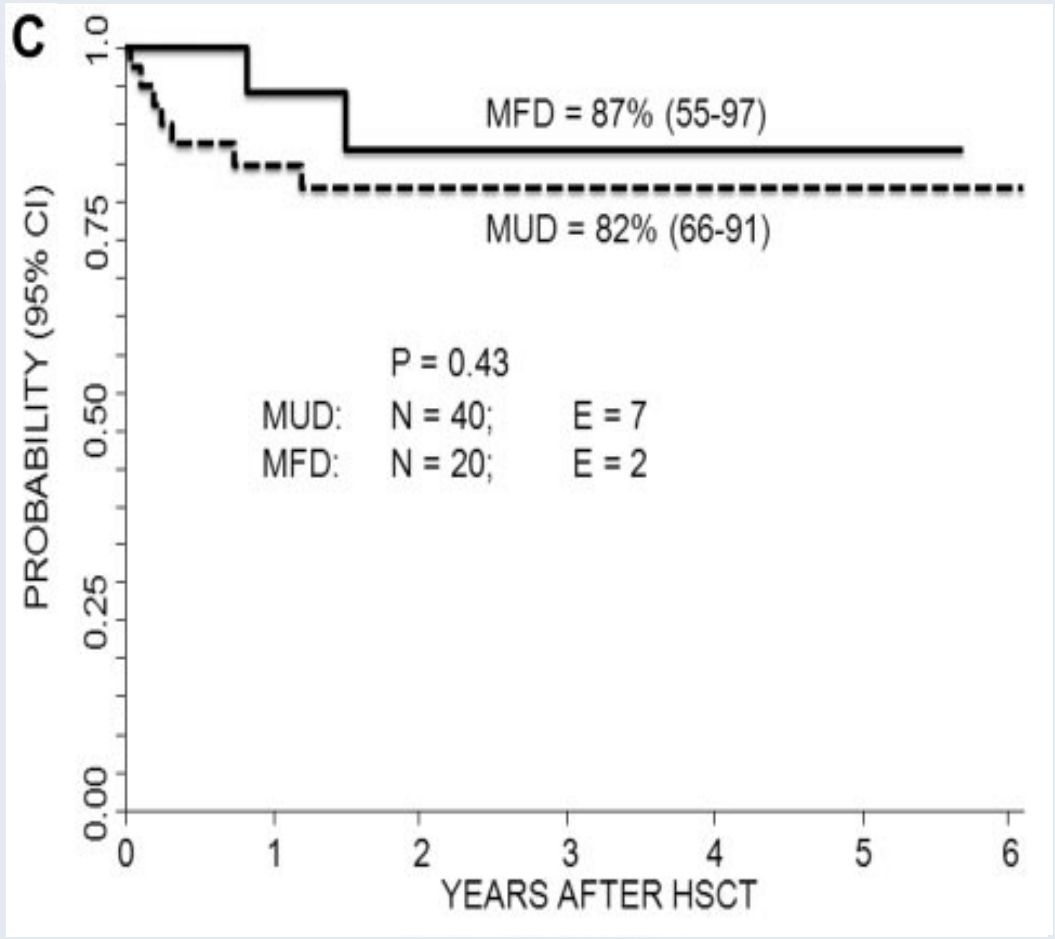
URD & CBT

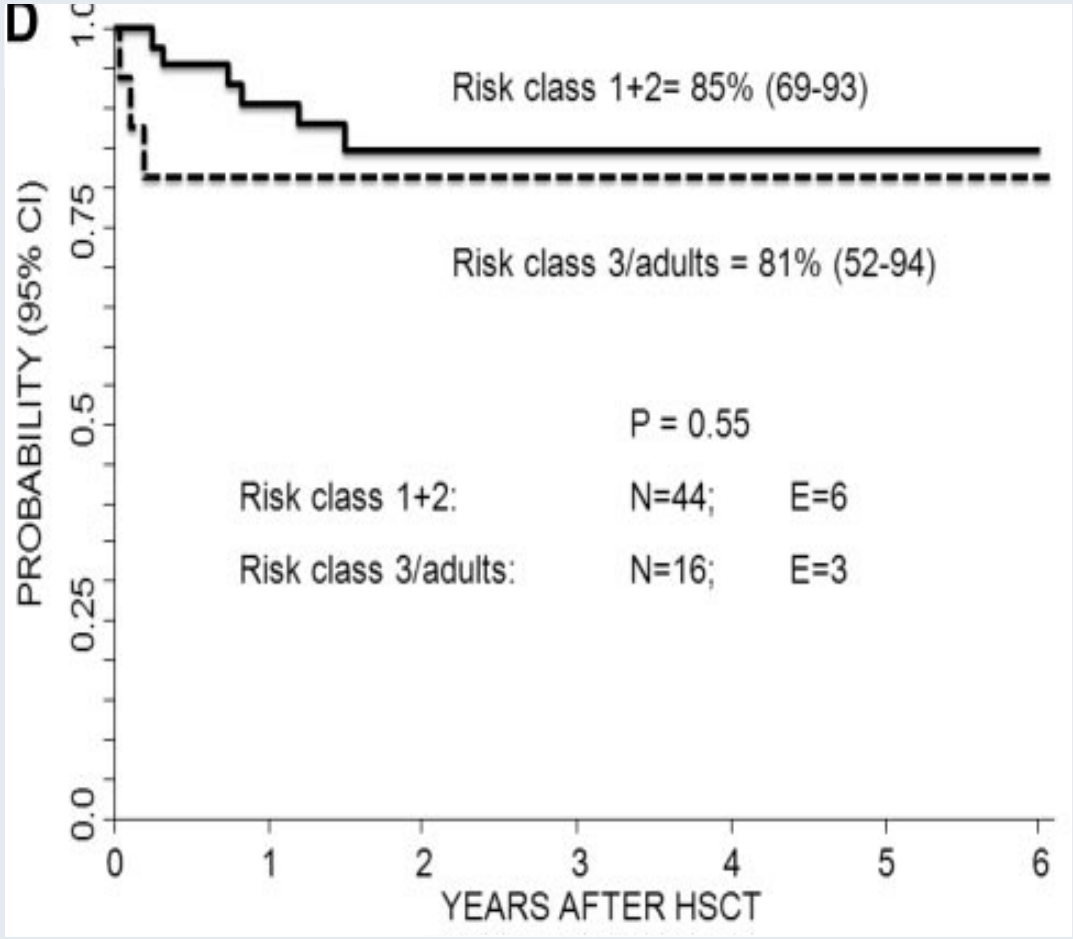




Bernardo, MEet al., Blood, 2012.

URD & CBT: TFS by Donor source and recipient Class/Age





Bernardo, MEet al., Blood, 2012.

RIC for Thalassemia using: FLU-ATG-Treosulfan

Number of patients	39 (100%)
Gender	
Males	24 (62%)
Females	15 (38%)
Age at HSCT (years, median, range)	8 (1–29)
Pesaro class at time of HSCT	
Class 1	16 (41%)
Class 2	11 (28%)
Class 3/adults	12 (31%)
Type of donor employed	
Matched family donor	8 (21%)
Matched unrelated donor	31 (79%)
Stem cell source	
Bone marrow	35 (90%)
Cord blood	2 (5%)
Peripheral blood	2 (5%)

Number of BM cells infused (nucleated cells $\times 10^8$/kg; median, range)	5 (2–13)
Conditioning regimen	
Thiotepa + Treo + Flu	8 (21%)
Thiotepa + Treo + Flu + ATG	31 (79%)
GvHD prophylaxis	
CsA + MTX[a]	8 (21%)
CsA + MTX + ATG[b]	31 (79%)
Number of days to PMN recovery[c] (median, range)	21 (14–30)
Number of days to PLT recovery[d] (median, range)	22 (11–32)
Graft failure[e]	3 (8%)
Chimerism[f] (median, range)	100% (60–100)

HSCT, haematopoietic stem cell transplantation; Treo, Treosulfan; Flu, Fludarabine; ATG, anti-thymocyte globulin; GvHD, graft-versus-host disease; CsA, cyclosporine; MTX, Methotrexate; PMN, polymorphonuclear neutrophils; PLT, platelets.

Bertaina A et al., Ann. N.Y. Acad. Sci. 1202 (2010) 141–148

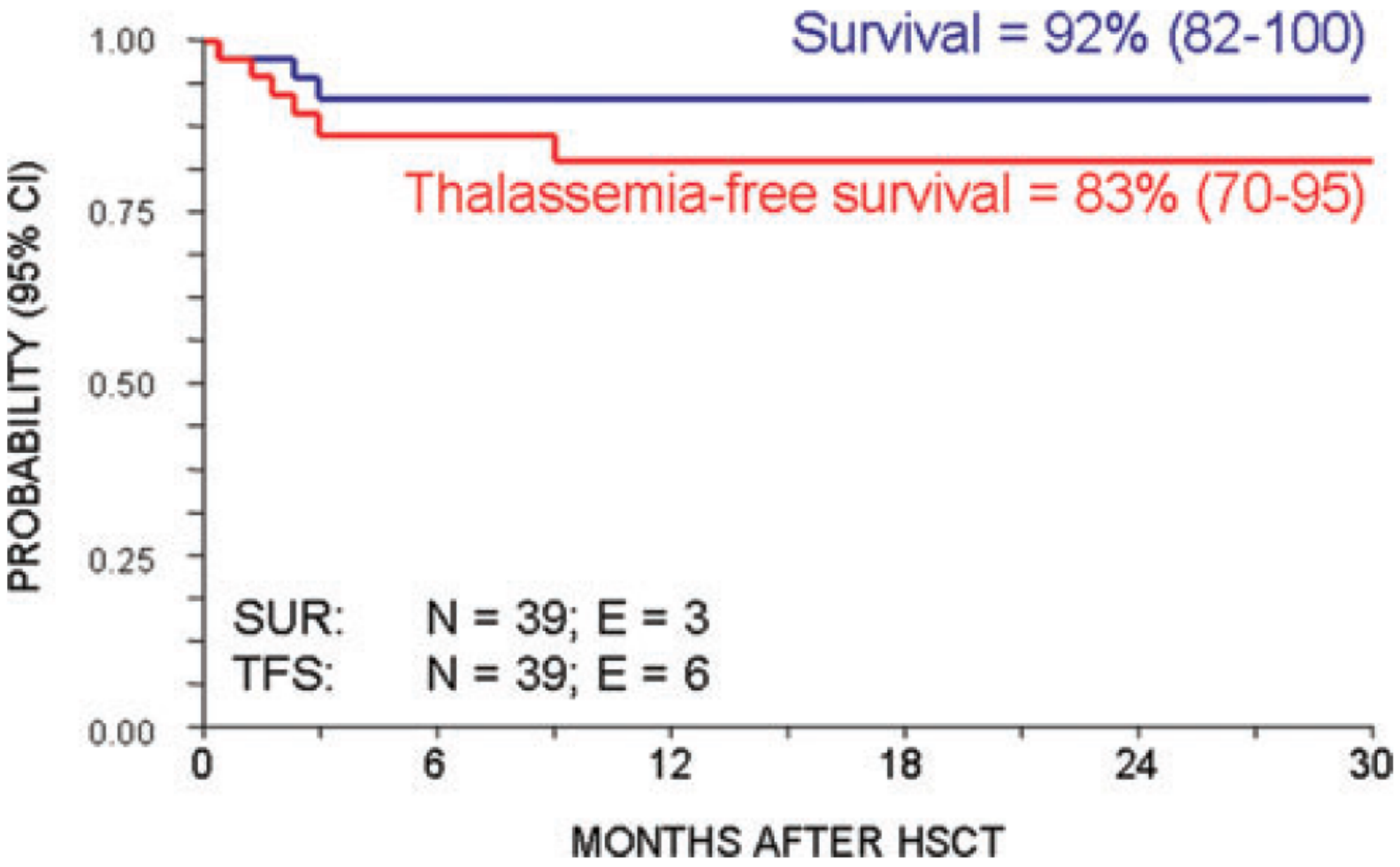
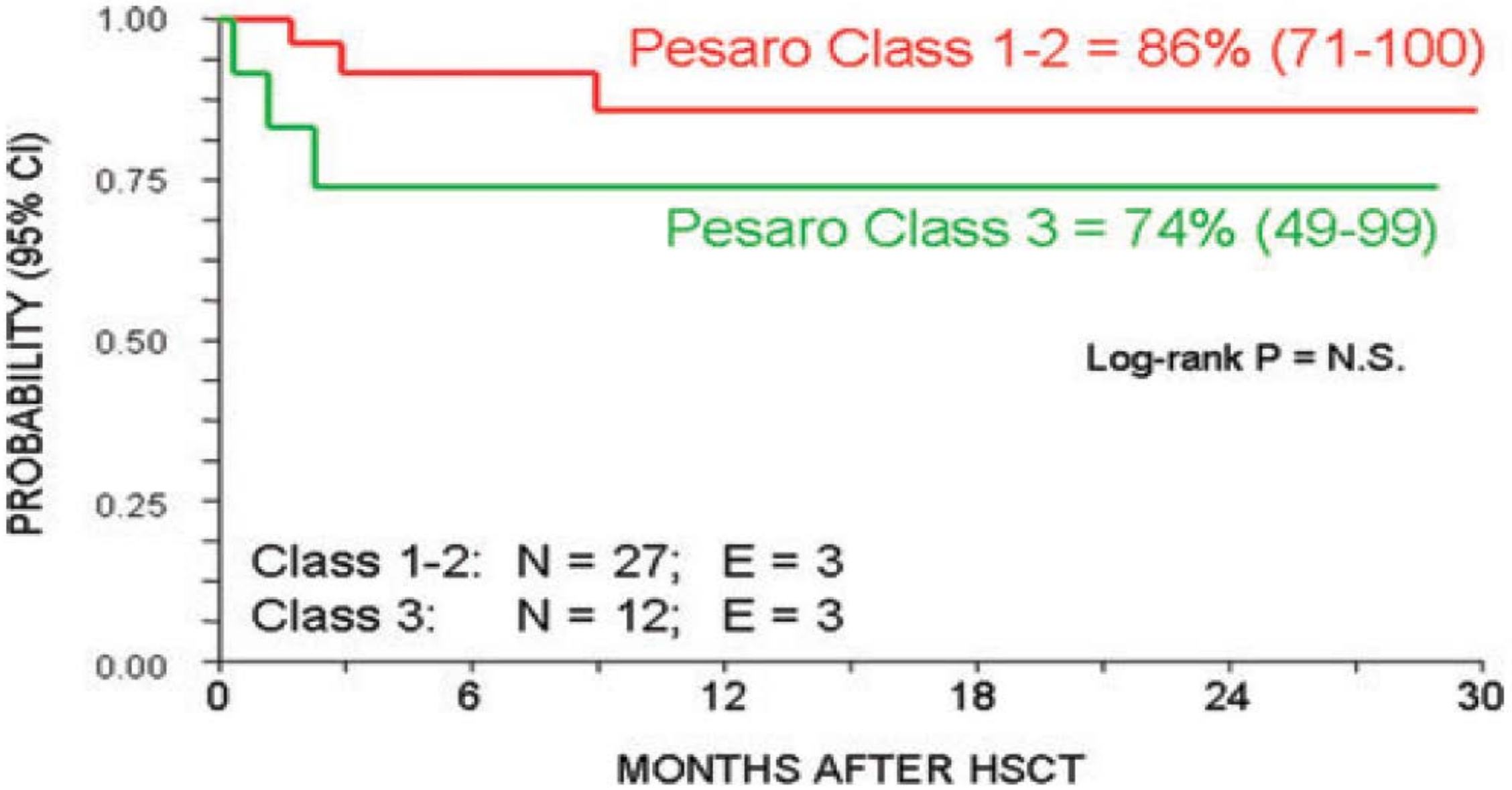


Figure 2. Kaplan-Meier estimate of survival and survival with transfusion independence in patients given the combination of thiotepa, treosulfan, and fludarabine in preparation to the allograft.

Bertaina A et al., Ann. N.Y. Acad. Sci. 1202 (2010) 141–148



Bertaina A et al., Ann. N.Y. Acad. Sci. 1202 (2010) 141–148

Haplo HSCT for TM 2017

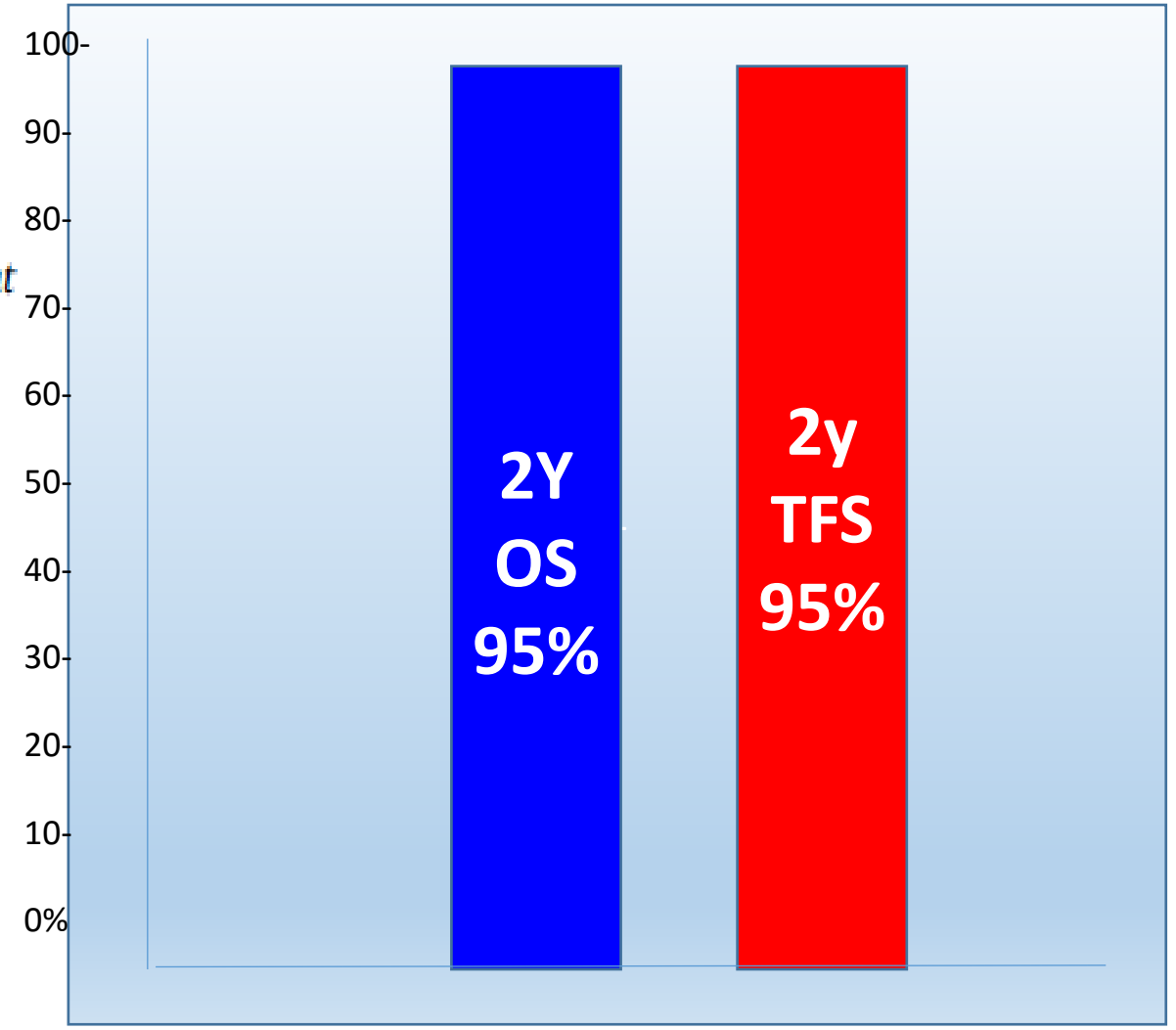
- **The majority of EMRO** countries did it
- **Results** : **promising**
- **Role of ATG** and **Risks of PTCy:**
  - HCV
  - Bilharziasis
  - **NecroInflammatory Liver with TM**

550

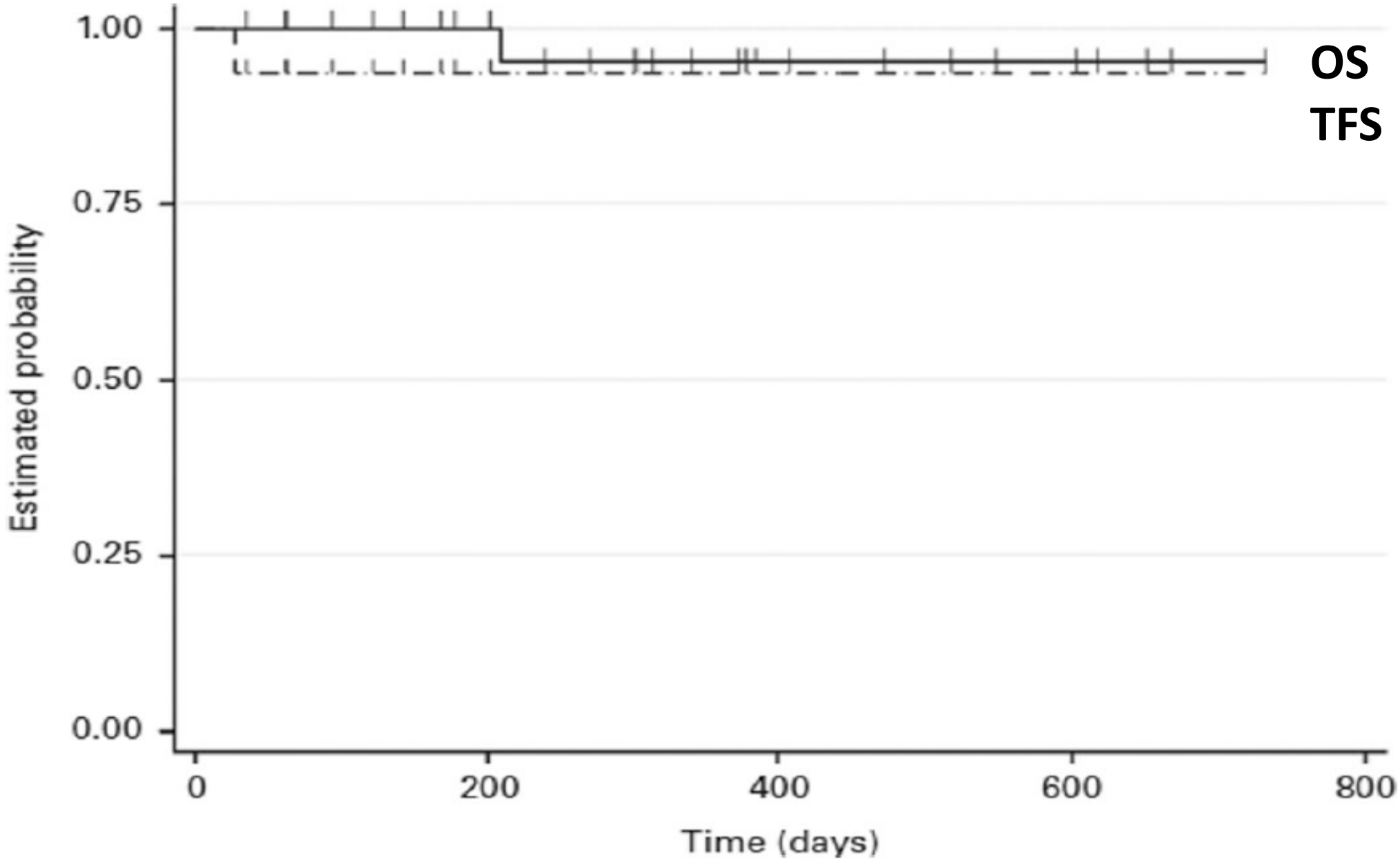
A Novel Approach of Hematopoietic Stem Cell Transplantation for Severe Thalassemia from Haploidentical Donors with Favorable Outcomes

Usanarat Anurathapan[1], *Suradej Hongeng*[1], *Samart Pakakasama*[1], *Nongnuch Sirachainan*[1], *Duantida Songdej*[1], *Ampaiwan Chuansumrit*[1], *Borje S. Andersson*[2]. [1] *Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand;* [2] *Department*

- **N:31**
- **Age: 10 (2-20)**
- **TCR-PBSC graft**
- **GF: 2/31; 29 ➔100% DC**
- **A-GVHD:9/31 (Grade II only)**
- **C-GVHD: 5/31 (limited only)**
- **Projected OS/TFS @ 2y=95%**



Abstracts / Biol Blood Marrow Transplant 22 (2016) S19–S481

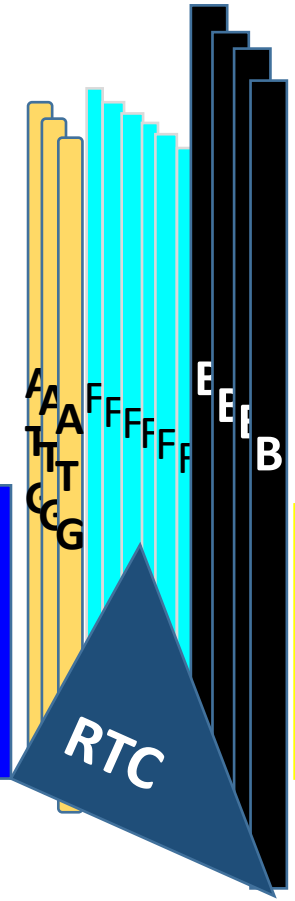

1.00
0.75
0.50
0.25
0.00
Estimated probability
0
200
400
600
800
Time (days)
OS
TFS

Principles, Themes and Promising conditioning

TM =
- chronic Inflammation
- Allo-immunization
- Immune Disturbance
- Germ line mutation
- High Disease Burden
- Iron-Overload
- 2 HLH

TM=
- **Comorbidities**
- **Less tissue reserve**

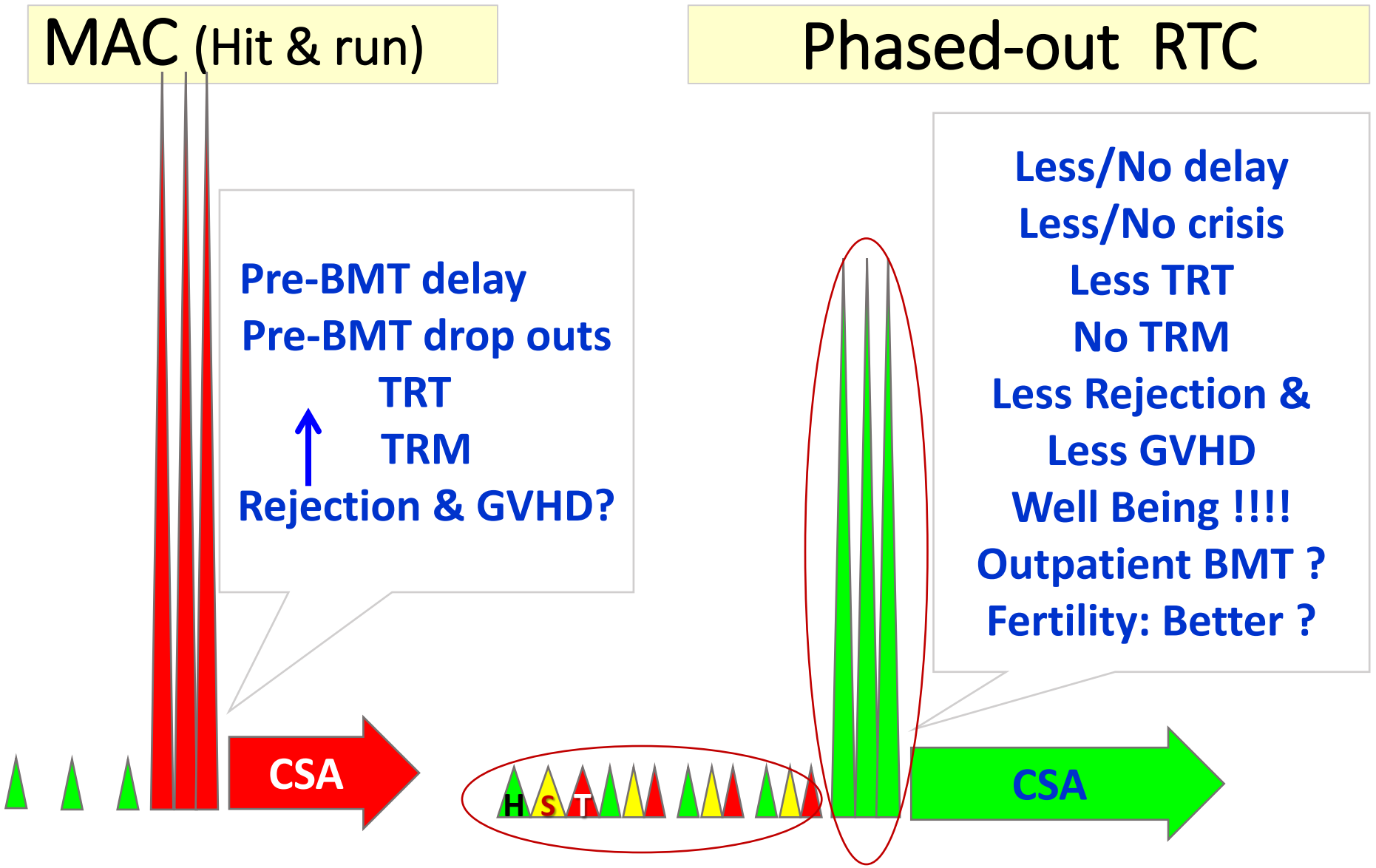
TM=
- **HLA-disparity Reject & react (GVHD)**

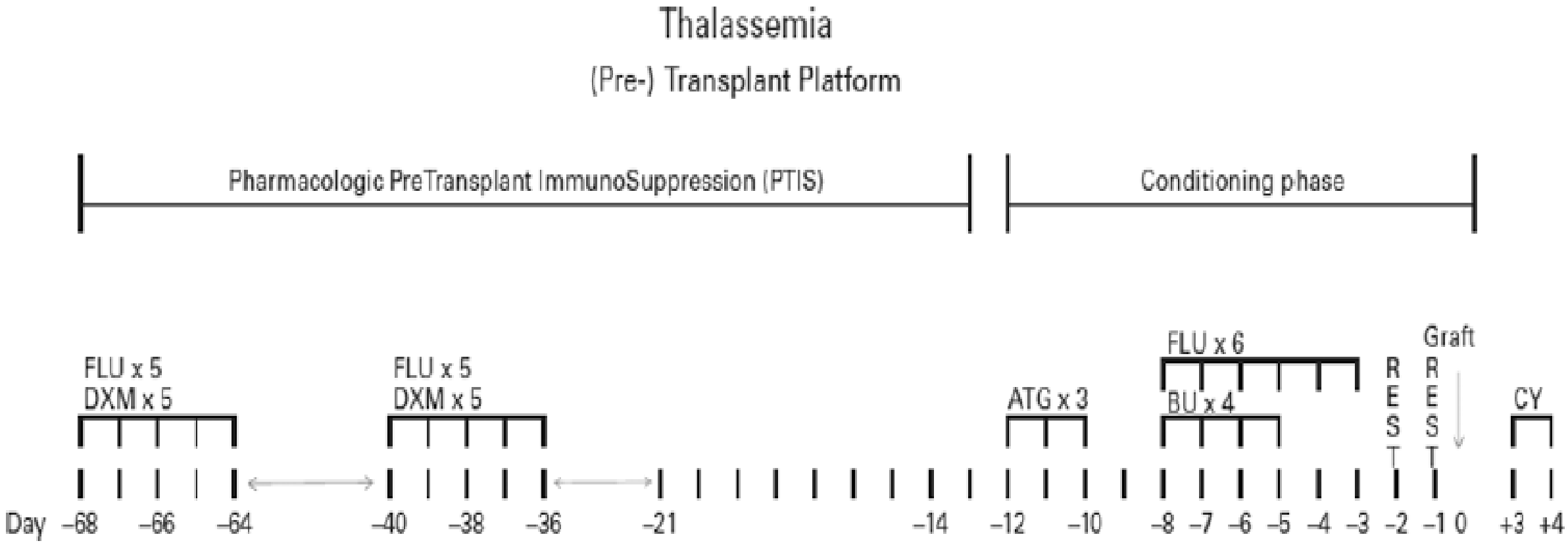


PTIS

Hydroxyurea
Hypertransfusion
(FLU + Dex) x5 d x 2 courses
Intense chelation

Change of paradigm of Conditioning



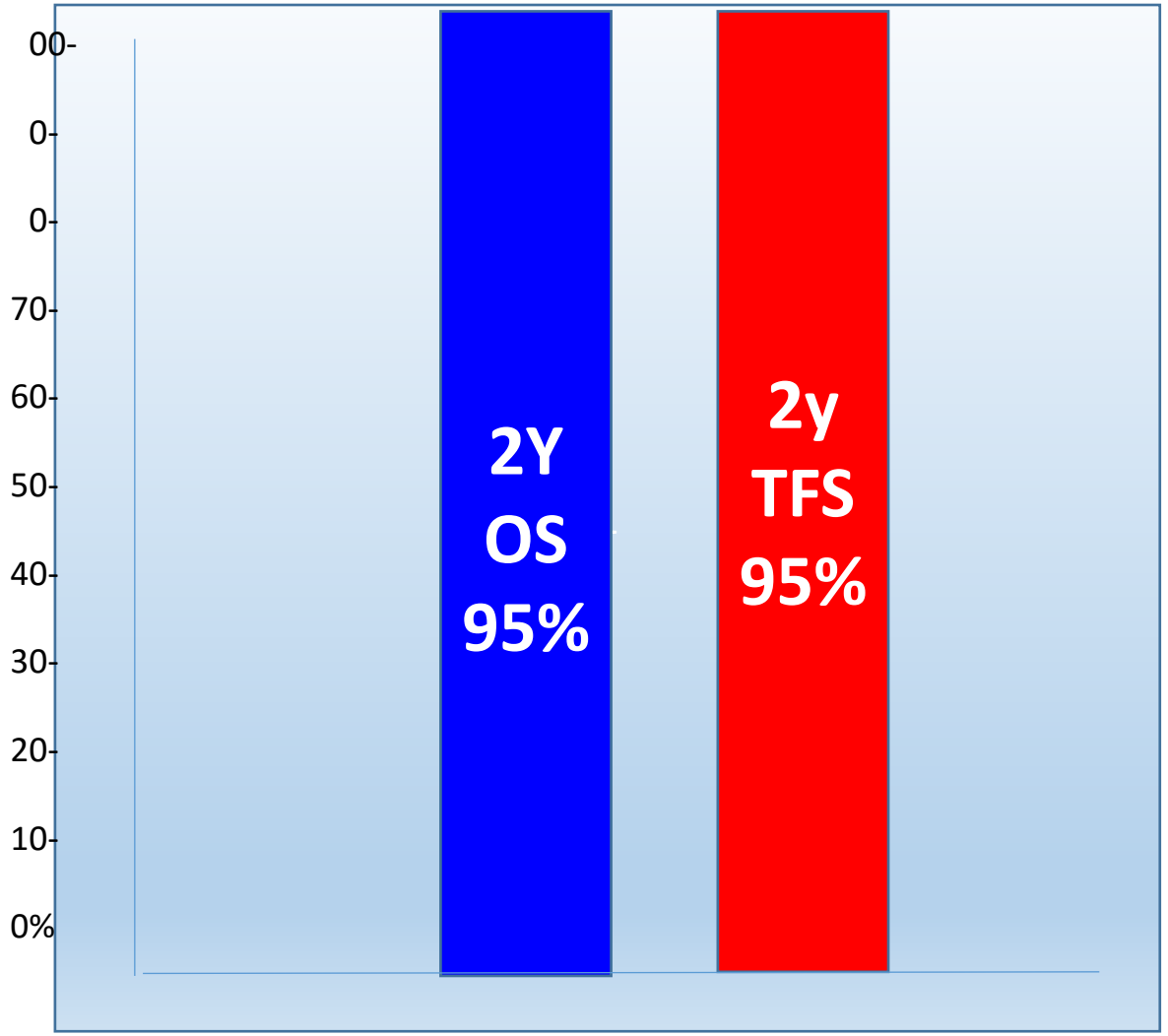

Thalassemia
(Pre-) Transplant Platform
Pharmacologic PreTransplant ImmunoSuppression (PTIS)
Conditioning phase
FLU x 5
DXM x 5
FLU x 5
DXM x 5
ATG x 3
FLU x 6
BU x 4
REST
REST
Graft
CY
Day −68 −66 −64 −40 −38 −36 −21 −14 −12 −10 −8 −7 −6 −5 −4 −3 −2 −1 0 +3 +4

11

Haploidentical Hematopoietic Stem Cell Transplantation (Haplo-SCT) with Pre-Transplant Immunosuppression and Post-Transplant Cyclophosphamide (Post-Cy) in Severe Thalassemia: A Novel Approach Transplant for Nonmalignant Diseases

Suradej Hongeng[1], *Samart Pakakasama*[1], *Usanarat Anurathapan*[1], *Borje S. Andersson*[2]. [1]*Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok, Thailand;* [2]*Stem Cell Transplantation and Cellular Therapy, UT M.D. Anderson Cancer Center, Houston, TX*

- Donors **11 Mothers 4 fathers**
- **12/15 class3**
- N:15 ➔14/15 (93% FDC)
- 1/15 needed 2nd BMT
- Age: 16 (2-20)
- **TCR-PBSC graft**
- GF: 1/15; 14➔100% DC
- A-GVHD: 6/15 (Grade I-III only)
- **C-GVHD: 1/15 (limited only)**
- Projected **OS/TFS @ 2y=100%**



Abstracts / Biol Blood Marrow Transplant 22 (2016) S19–S481

To “”TRANSFUSE””:

1. Safety is a major problem with C
2. Blood banking infra-structure
3. Life-long commitment
4. Chelation
5. Procurement
6. Cost , cost, and cost
7. Effectiveness compared to Transp
8. Let’s be practical and go to WHO

For “”TRANSPLANTation”” :

1. Safe now: well tested
2. Transfusion-free Survival
3. Once in life time for >90%
4. No Chelation
5. No Procurement
6. & 7. Cost: very cost effective if you do it the Egyptian/Indian way (15 K USD)

- **Bernadette Modell, Matthew Darlison**Volume 86, n.6, June 2008, 480-487 - ***Bulletin of the World Health Organization*** ***Kamel MH, BMT 2008***

Recommendation summary of HSCT in Thalassemia Major

Indication	Transfusion dependency
When? How? Where?	• ASAP • Better prepared with BTIC • At experienced Centers • Centers in high prevalence areas should get the necessary experience to perform alternate donor SCT • If comprehensive BTIC is not available, all sources of Stem cells should be entertained. • Not all TM are equal: do necessary modifications • WBMT should have a more active role……..

Said Yousuf. WBMT. Riaydh 2017

Just do it: start from scratch- Allah will help start Thalassemia National Centers until TM is gone or we are gone


Don’t worry, one day I will be great
© UNICEF/NYHQ2012-0531/Asselin


How much the cost of this house

UCBT in India: Breaking the Cost Barrier: *Abstract 4768*

- Pediatric Hematology Oncology & BMT Unit, Department of Pediatrics, Sir Ganga Ram Hospital, New Delhi, India,
- **Background** UCBT) is the only feasible option for patients who need to undergo unrelated HSCT in India but lack of experience and huge costs are perceived barriers. Data from USA showed mean cost of graft for pediatric UCBT was $58,910 and mean cost per day survived in first 100 days (excluding graft cost) was $4522 ((Majhail NS et al. Pediatr Blood Cancer 2010;54:138–143). The costs of UCBT among children in India have not been described previously.
- **Method -**We calculated the costs of **UCBT** within the first 100-days among four **children** who received UCBT at **Sir Ganga Ram hospital** from **April 2008 to Dec 2010.** We also analyzed costs of transplantation in relation to patient age, weight, single vs.double cord, conditioning, Graft vs. Host Disease (GVHD) and mean duration of stay before day 100.
- **Results -**The 100-day probability of OS was 100%. The mean cost per day survived (excluding costs of graft acquisition) was $402 (range $360-460)) for UCBT recipients. Average total cost of each UCBT was $43500 (Range $32000-52000). Average duration of **stay in hospital in first 100 days was 89 days** (range 75–100). All grafts were procured from a **public cord bank** in **India**. Average **cost of graft per cord unit was $5000**. Diagnosis was thalassemia major-2, Familial Hemophagocytic Lympho Histiocytosis (HLH)-1 and AML-1.
  - **Lowest cost: AML ($32,000) & highest: TM-Pesaro class III ($52,000).**
    - *Mean age was 2.75 years (range 1–5 year).*
    - *Mean weight was 12.25 kg (range 10–16 kg).*
    - *Mean cell dose infused was 7 × 10^7 nucleated cells/kg weight of recipient (range 3–10 × 10^7nucleated cells/kg). Conditioning was Busulfan and Cyclophosphamide (BuCY) and Rabbit Anti-Thymoglobulin (ATG) for two patients (1 Thalassemia, 1 AML) costing $1500 per patient, Fludarabine & Melphalan and Campath for HLH costing $2500 and*
  - **Treosulfan, Thiotepa, Fludarabine and ATG for class III TM cost: $7,500.**
    - *Mean cost per day for single cord was $385 and for double cord UCBT was $420. One patient rejected the graft. Three engrafted at median of 32 days (range 28 –39 days). GVHD was seen in two patients (both with double cord). CMV reactivation was seen in all cases. Invasive aspergillosis was seen in one patient who had thalassemia and it lead to highest expenditure. Campath based conditioning was associated with maximum hospital stay in child with HLH. All had Lansky score >90 pre-transplant No one needed dialysis, mechanical ventilation or hepatic veno-occlusive disease.*
- **Conclusions**
  - Total cost of UCBT in India is less than the cost of the UCBT graft in USA and
  - **Mean cost /day in India is almost 1/10^{th} of cost in USA.**
  - Low cost of UCBT in India would make this treatment feasible for many more patients who need to undergo unrelated HSCT.

Satya Prakash Yadav and Anupam Sachdeva Blood 2011 118:4768;