Workshop I: Patient Selection

Current indication for HCT in adults

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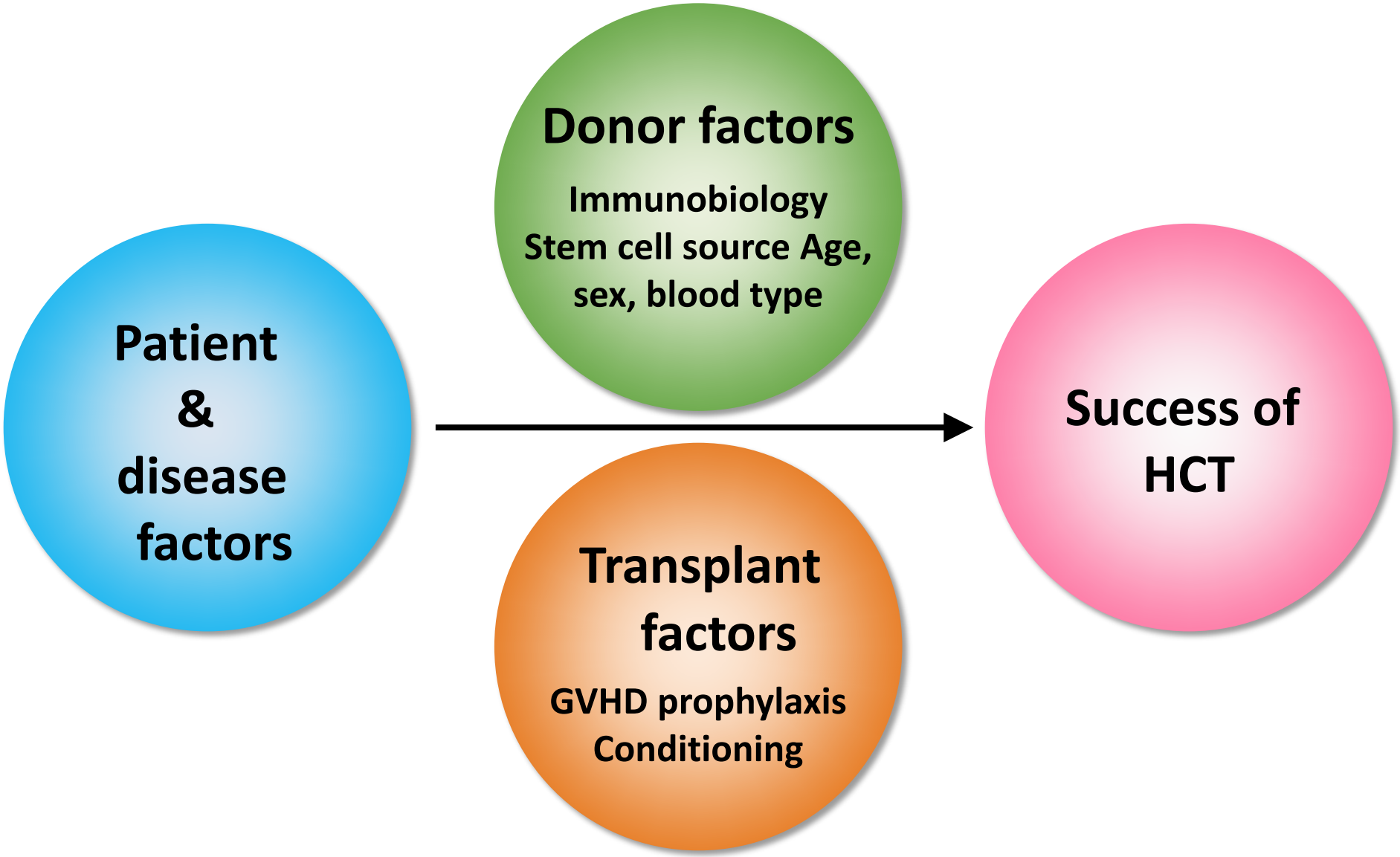
Factors to Take into Account with Recommending HCT



Disease factors

Disease
Prior therapies
Disease stage/risk
Tempo of progression
non-transplant Tx.

Indication of HCT according to disease/disease risk

Guideline

Indications for Autologous and Allogeneic Hematopoietic Cell Transplantation: Guidelines from the American Society for Blood and Marrow Transplantation

Biol Blood Marrow Transplant 21(2015): 1863-1869

SPECIAL REPORT

Indications for allo- and auto-SCT for haematological diseases, solid tumours and immune disorders: current practice in Europe, 2015

Bone Marrow Transplantation (2015) 50: 1037-1056

Guidelines for HCT in clinical practice

- The guidelines categorize target diseases/disease status into three levels according to currently available evidences.

- Standard of care (S) including clinical option (CO)and rare indication for rare disease
- Developmental (D)
- Not generally recommended (NGR)

CAN I LIVE TO BE 125?

BY JONATHAN WEINER

If you don't, your children may, thanks to scientists looking for longevity genes. But who will want to live that long?

number of Americans age 100 or older could approach 850,000 by 2050

Some scientists predict that by 2100, our descendants could live to be 200 years.

Indication of Allo-HCT for adult AML

	ASBMT	EBMT		
	All	MSD	MUD	Alternative
CR1 low risk	GNR	C	D	GNR
CR1 intermediate risk	S	S	C	D
CR1 high risk	S	S	S	C
CR2	S	S	S	C
Not in remission	C	C	C	D

Guidelines for HCT in clinical practice

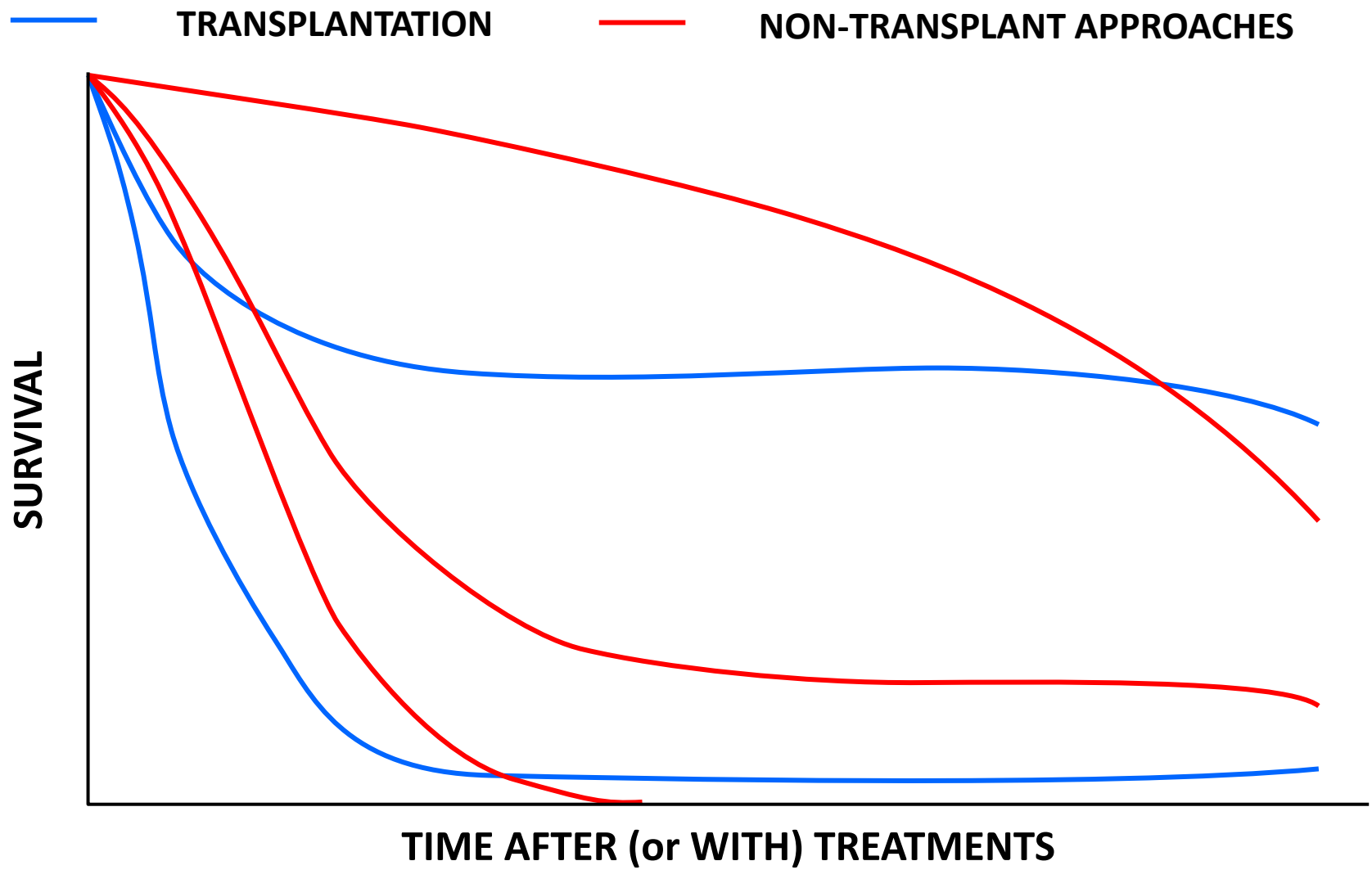
- The guidelines categorize target diseases/disease status into three levels according to currently available evidences.

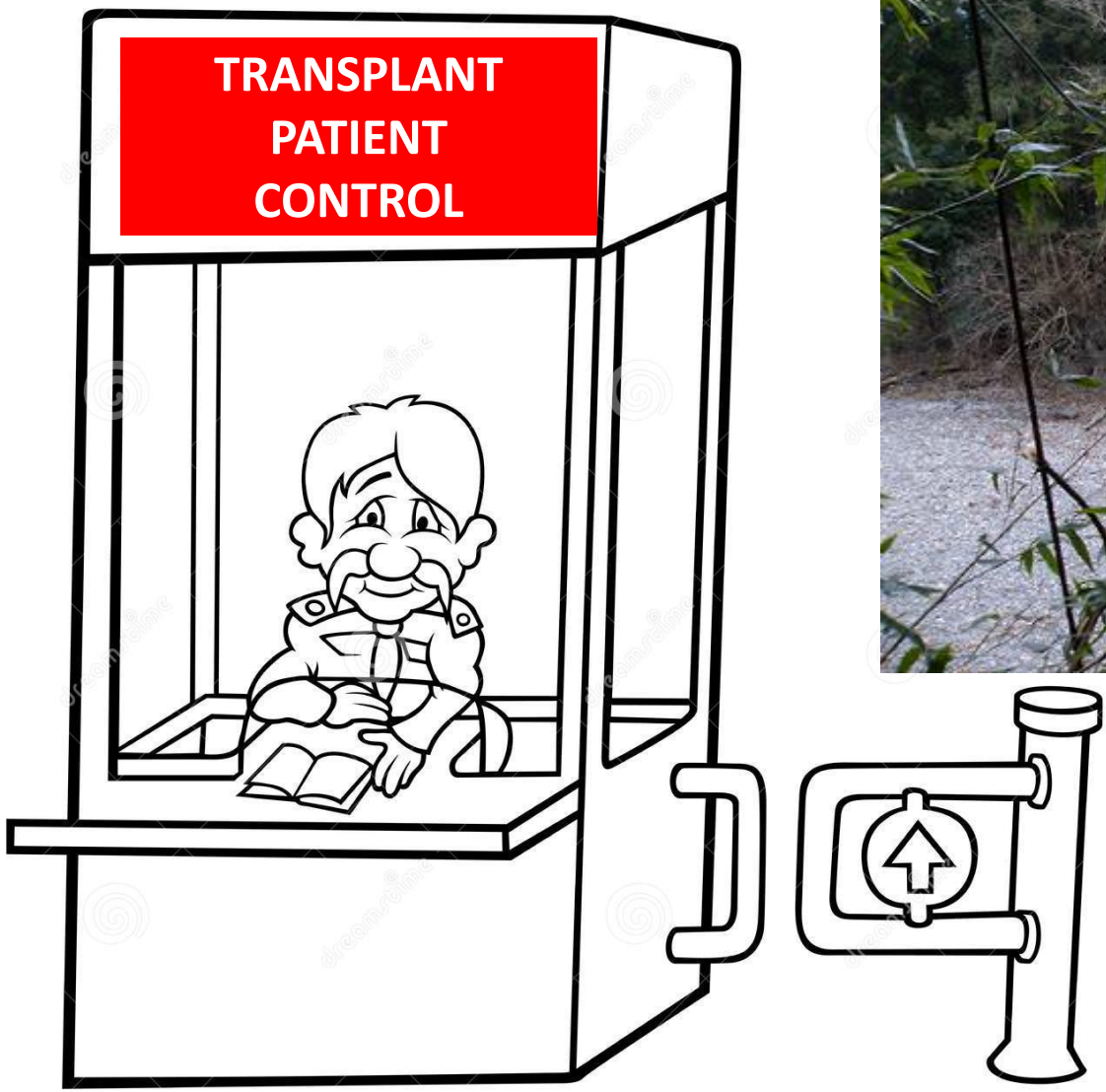
  - Standard of care including clinical option and rare indication for rare disease
  - Developmental
  - Not generally recommended

- These guidelines should not be used to determine whether HCT should be pursued as a treatment for an individual patient.

Guidelines for HCT in clinical practice

Transplantation vs. non-transplant approach





TO SUCCESS of
(or BETTER LIFE AFTER)
TRANSPLANTATION

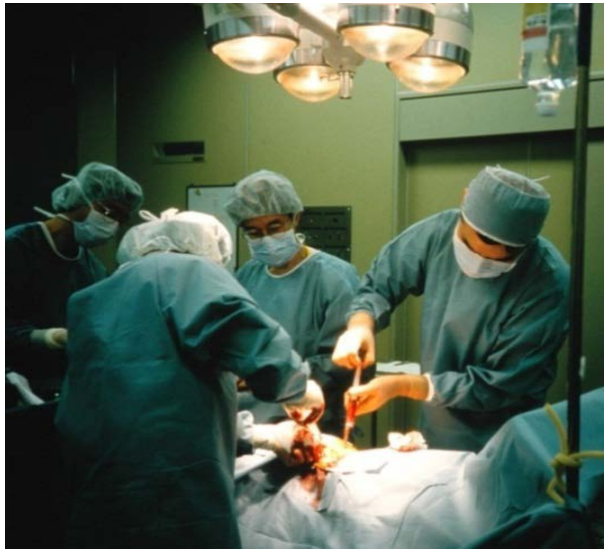
Ideal Eligibility Criteria for Adult Candidates for High-dose Therapy Followed by HCT

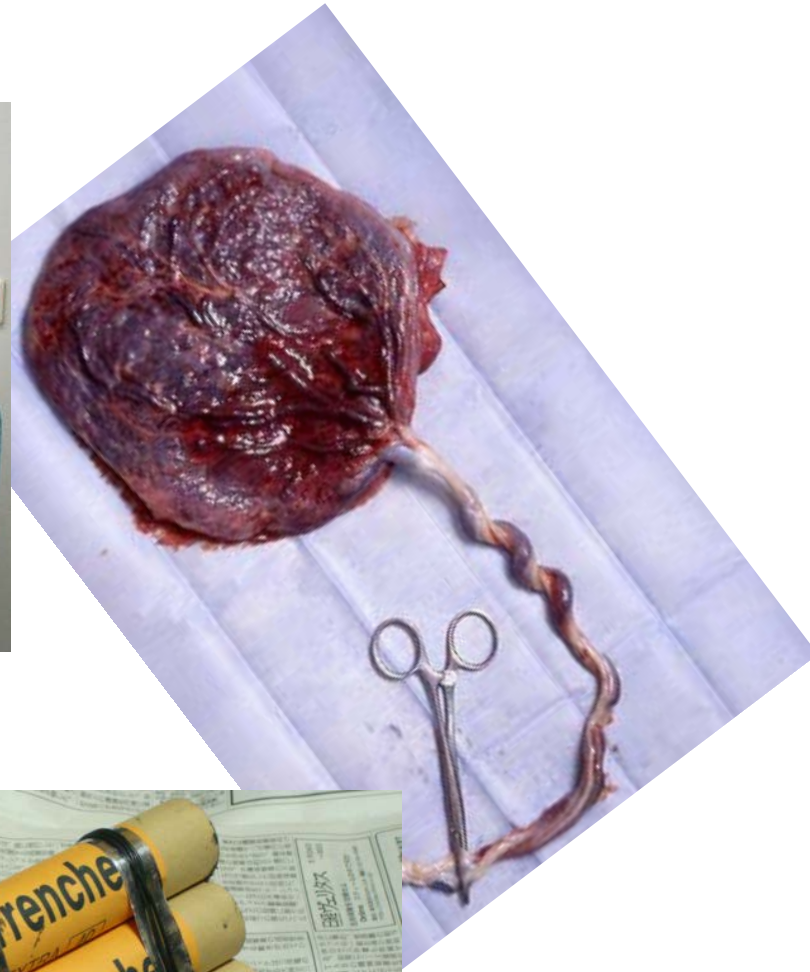
	Allogeneic HCT	Autologous HCT
Age	0 – 60	0 – 75
Karnofsky performance score	70 – 100	70 – 100
Left ventricular ejection fraction	≥45%	≥45%
Pulmonary function test; forced vital capacity	≥60%	≥60%
Diffusion capacity	≥60%	≥60%
Serum creatinine	≤1.5 mg/dL	≤1.5 mg/dL
Serum bilirubin	≤2 mg/dL	≤2 mg/dL
Alanine aminotransferase	1 – 2 × normal	1 – 2 × normal
Aspartate aminotransferase	1 – 2 × normal	1 – 2 × normal
Body weight	95 – 145% of IBW	95 – 145% of IBW

IBW, ideal body weight

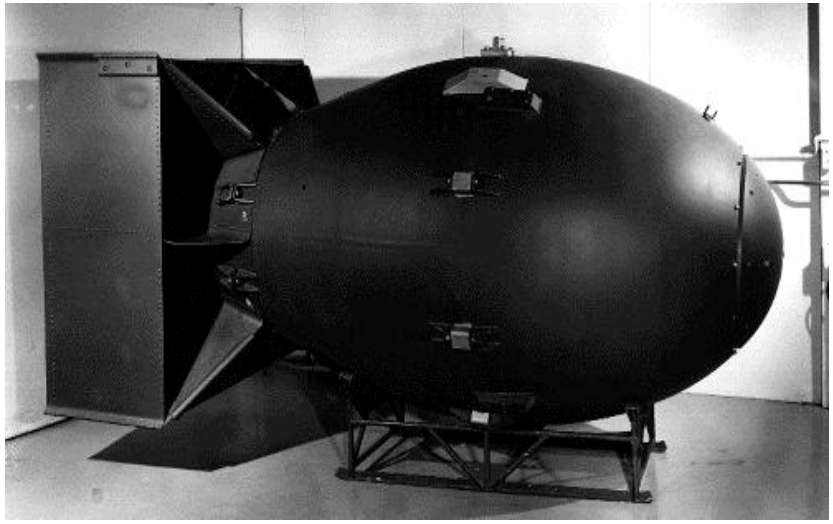
Thomas' Hematopoietic cell transplantation (4thed.) (pp.445-460)

Expanding Stem cell sources…





Less aggressive conditionings…..



HCT-specific co-morbidity Index (HCT-CI)

Comorbidity	Score	Comorbidity	Score
Arrhythmia	1		
Cardiac	1	Rheumatologic	2
Inflammatory bowel disease	1	Peptic ulcer	2
Diabetes	1	Moderate/severe renal	2
Cerebrovascular disease	1	Moderate pulmonary	2
Psychiatric disturbance	1	Prior malignancy	3
Hepatic, mild	1	Heart valve disease	3
Obesity	1	Severe pulmonary	3
Infection	1	Moderate/severe hepatic	3

Augmented HCT-CI	Score
High ferritin	1
Mild hypoalbuminemia	1
Thrombocytopenia	1
Moderate hypoalbuminemia	2

Sorror ML, et al. blood 2005;106:2912-12919.

Augmentation of HCT-CI Predictability by combining with Other factors

Composite model	*Risk groups*		*Outcomes at 2 years*	
	HCT-CI	*KPS*	*NRM (%)*	*OS (%)*
Comorbidity / PS	0 – 2	>80%	16	68
	0 – 2	≤80%	17	58
	≥3	>80%	30	41
	≥3	≤80%	39	32
Comorbidity / age score (nonmyeloablative versus RIC)	HCTCI/age			
	0		5 – 12	81 – 87
	1 – 2		9 – 18	66 – 67
	3 – 4		17 – 36	47 – 54
	≥5		35 – 41	34 – 35

Sorror ML, Estey E. *Hematology Am Soc Hematol Educ Program* 2014; 2014: 21-33.

disease factors

Transplant factors

Donor factors

Patient factors

Combined patient & disease (and transplant) assessment model: EBMT risk score

RisK Factor		Score
Patient age (years)	>20	0
	20-40	1
	40<	2
Disease stage	Early	0
	Intermediate	1
	Late	2
Time from Dx. To HCT (months)	<12	0
	12<	1
Donor Type	HLA identical sibling	0
	Unrelated others	1
Donor/recipient Sex	All other s	0
	Female to Male	1

Augmentation of HCT-CI Predictability by Combining with Other Models

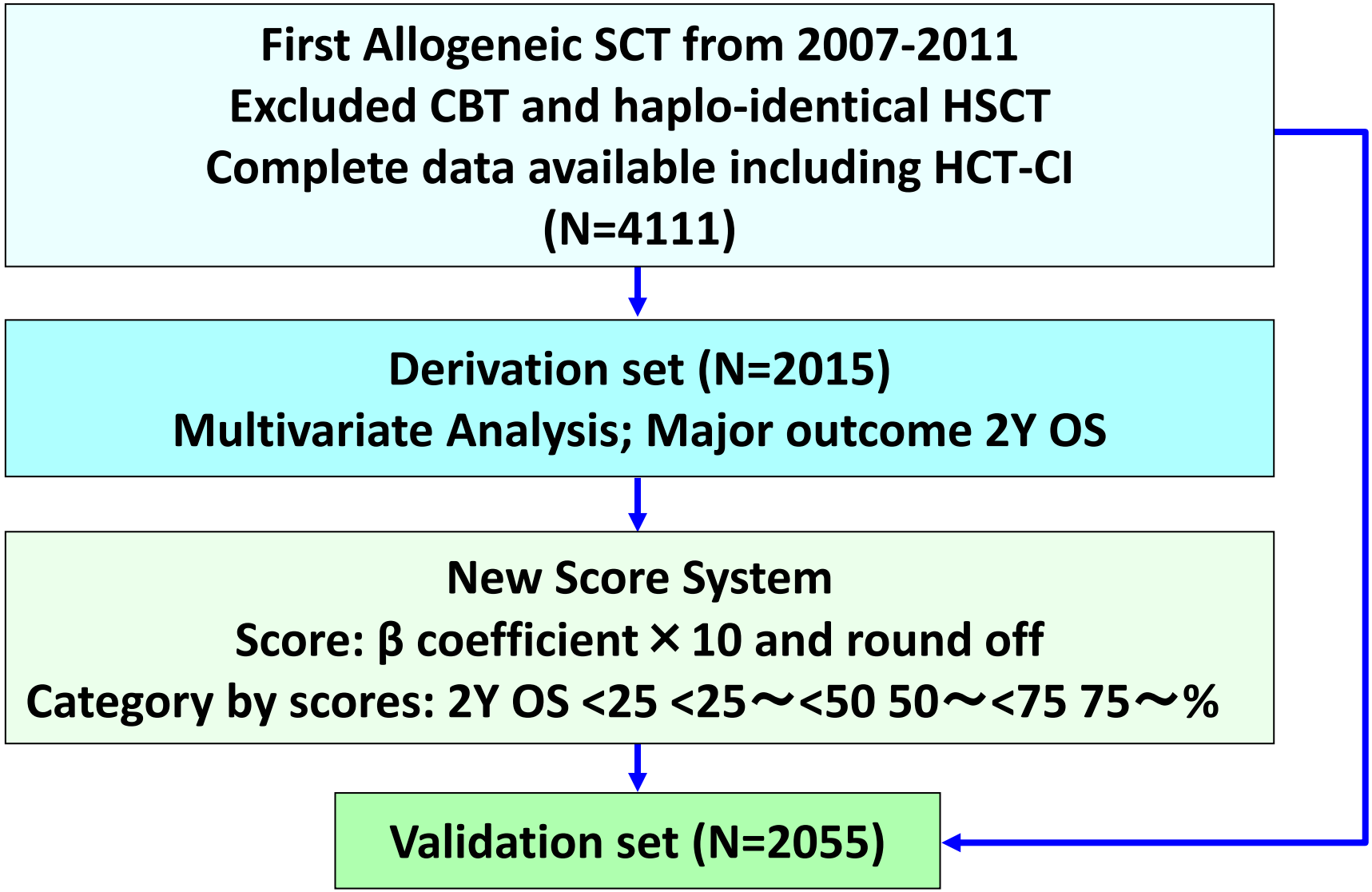
Composite model HCT-CI/EBMT

Risk groups		*Outcomes at 4 or 5 years*	
HCT-CI	*EBMT*	*NRM (%)*	*OS (%)*
0	<4	11	72
0	≥4	19	61
1 – 2	<4	16	63
1 – 2	≥4	28	48
≥3	<4	31	40
≥3	≥4	41	30

Sorror ML, Estey E, *Hematology Am Soc Hematol Educ Program* 2014; 2014: 21-33.

New Scoring System

- JSHCT -



New Scoring System -Multivariate Analysis / Scoring-

	HR	P value	β	Score	HCT-CI
Arrhythmia	1.70	0.031	0.53	5	1
Cardiac	1.51	0.025	0.41	4	1
Inflammatory bowel disease	0.85	0.743	-0.16	0	1
Diabetes mellitus	1.04	0.825	0.04	0	1
Cerebrovascular	0.87	0.673	-0.13	0	1
Psychiatric	1.39	0.104	0.33	3	1
Hepatic, mild	1.37	0.016	0.31	3	1
Obesity	1.34	0.172	0.29	3	1
Infection	1.81	<0.001	0.59	6	1
Rheumatologic	3.15	0.001	1.15	12	2
Peptic ulcer	1.10	0.825	0.10	1	2
Renal, moderate / severe	1.75	0.151	0.56	6	2
Pulmonary, moderate	1.00	0.984	0.00	0	2
Pulmonary, severe	1.08	0.72	0.08	0	3
Prior solid tumor	1.50	0.007	0.40	4	3
Heart valve disease	0.73	0.488	-0.32	0	3
Hepatic, moderate / severe	2.24	0.001	0.81	8	3

Fuji S, presented at JSH 2014

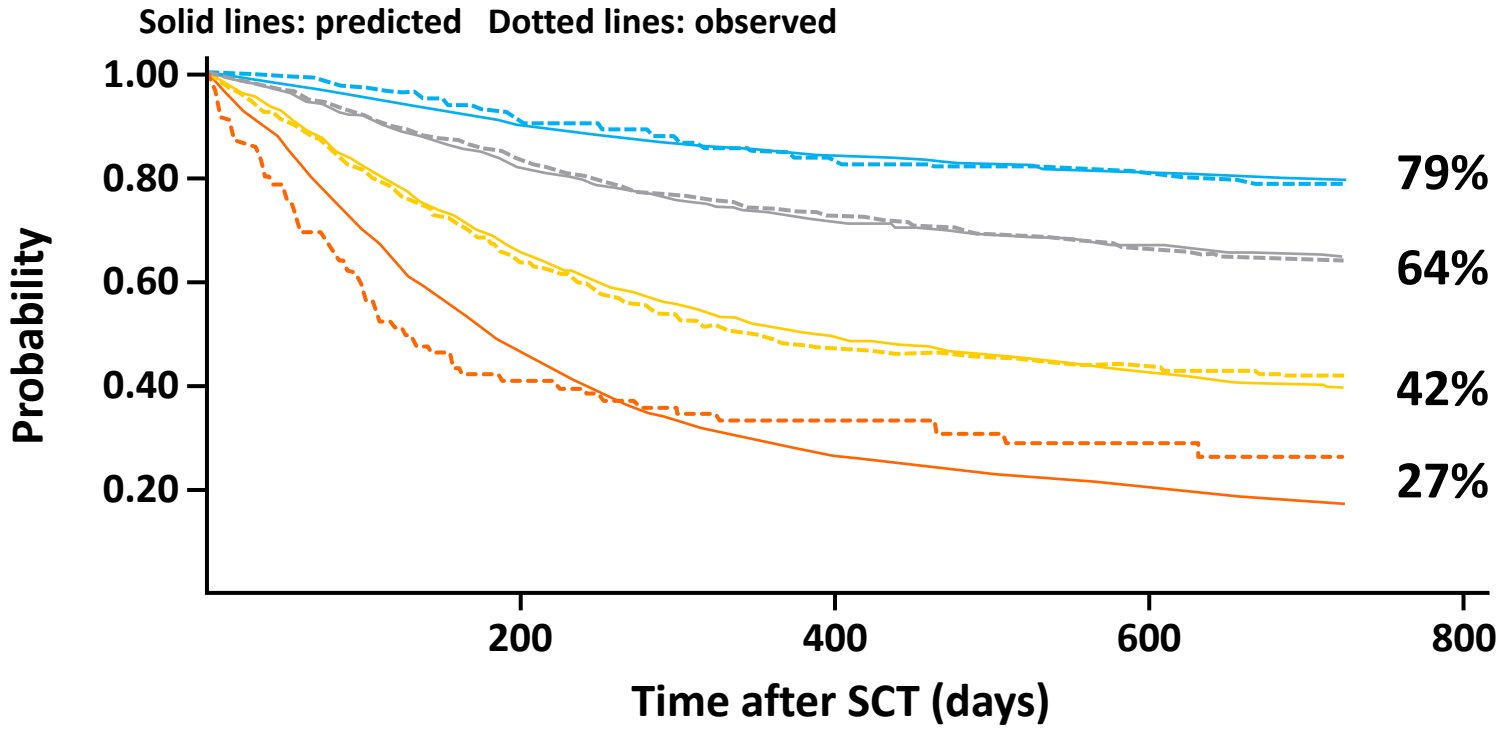
New Scoring System -Multivariate Analysis / Scoring-

	HR	P value	β	Score
Age				
18～29	1			
30～39	0.89	0.437	-0.11	0
40～49	1.28	0.066	0.25	2
50～59	1.22	0.013	0.20	2
≥60	1.49	0.005	0.40	4
Donor / HLA combination				
Related match	1			
Unrelated	1.17	0.087	0.16	2
Related mismatch	1.49	0.021	0.40	4
ECOG PS				
0	1			
1	1.29	0.002	0.26	3
≥2	1.82	<0.001	0.60	6
Disease risk				
Low	1			
Intermediate	1.30	0.106	0.26	3
High	2.07	<0.001	0.73	7

Fuji S, presented at JSH 2014

2 Years of OS by New Score System in Validation Set

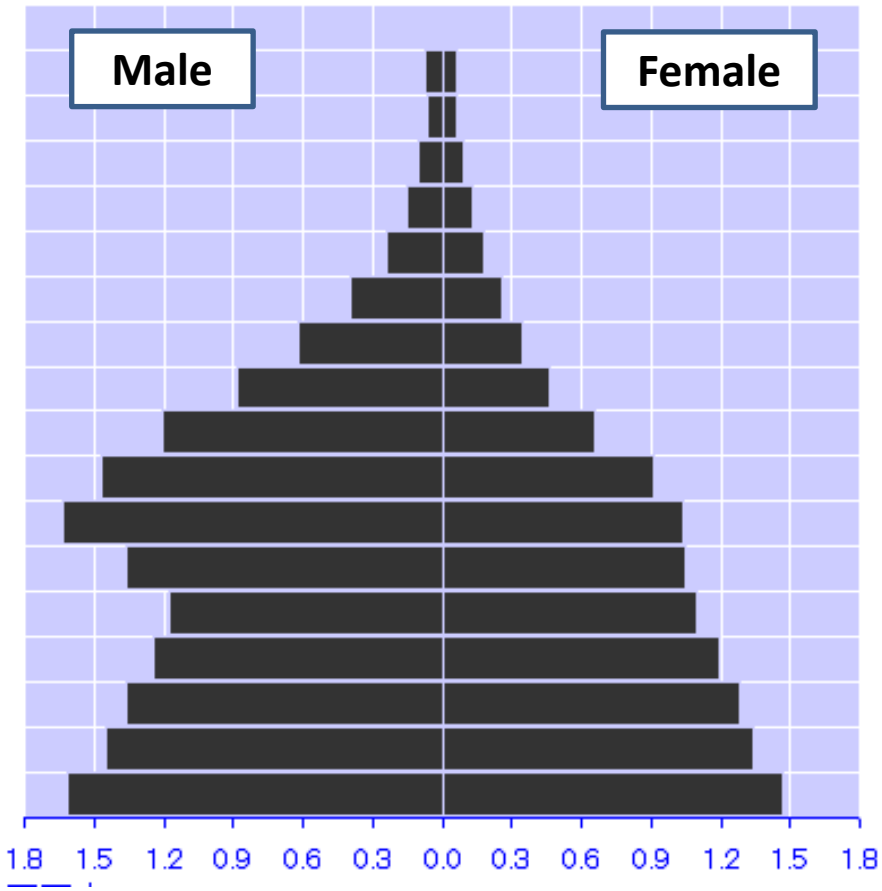
	N (%)	HR (95% CI)	P value
Group 1 (0～5)	410 (20.0)	Referent	
Group 2 (6～13)	1136 (55.3)	1.93 (1.49-2.48)	<0.001
Group 3 (14～20)	420 (20.4)	4.10 (3.14-5.35)	<0.001
Group 4 (21～)	89 (4.3)	7.67 (5.44-10.81)	<0.001



Fuji S, presented at JSH 2014

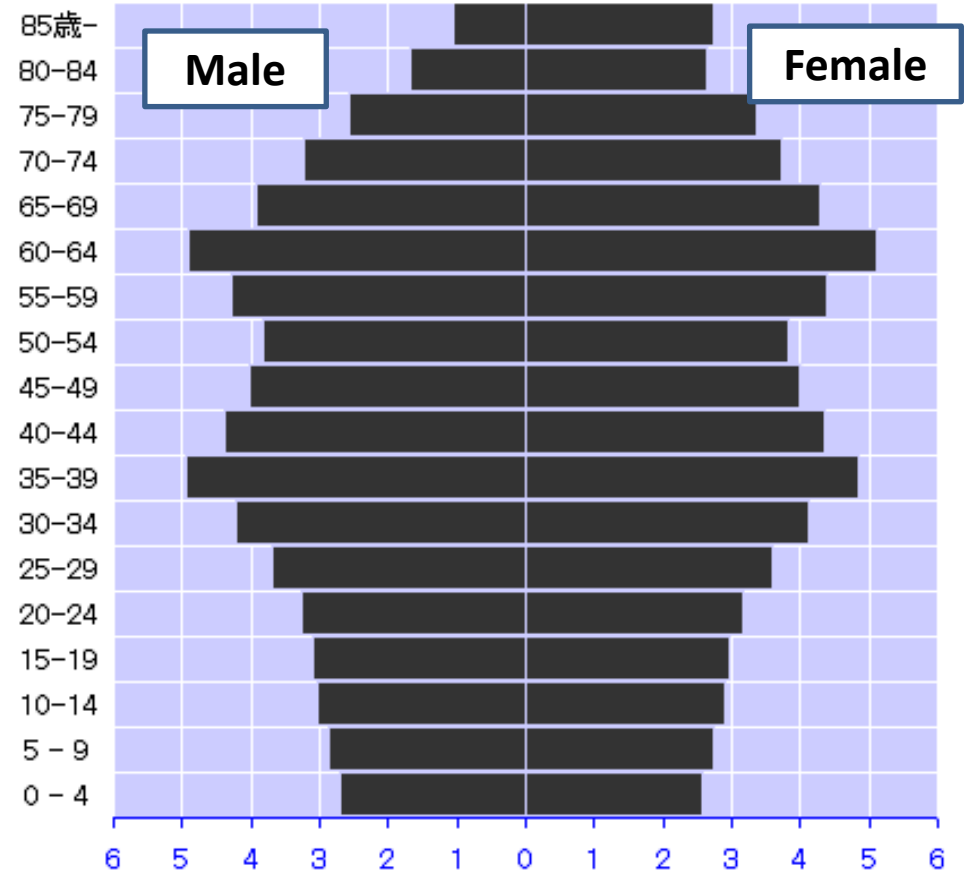
Population pyramid of KSA in 2009

KSA: age 65< 2.8%



x one million

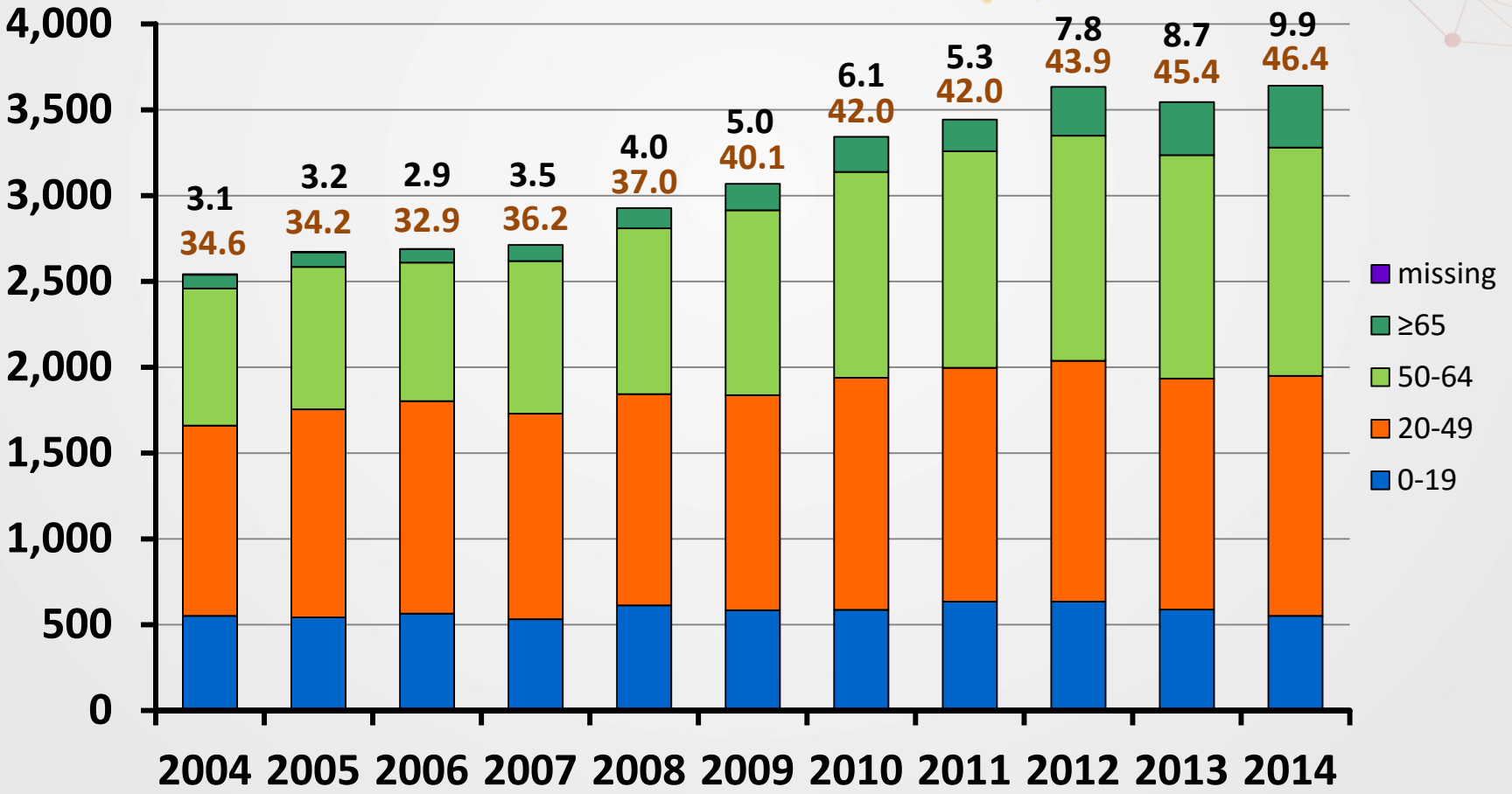
Japan age 65<23%



x one million

Transplant candidates are aging.....

Numbers of Allogeneic HSCT in Japan by recipient age



*% (Auto HSCT in patient ≥65 10.5% in 2004, 18.3% in 2014)

*% (Auto HSCT in patient ≥50 58.0% in 2004, 71.3% in 2014)

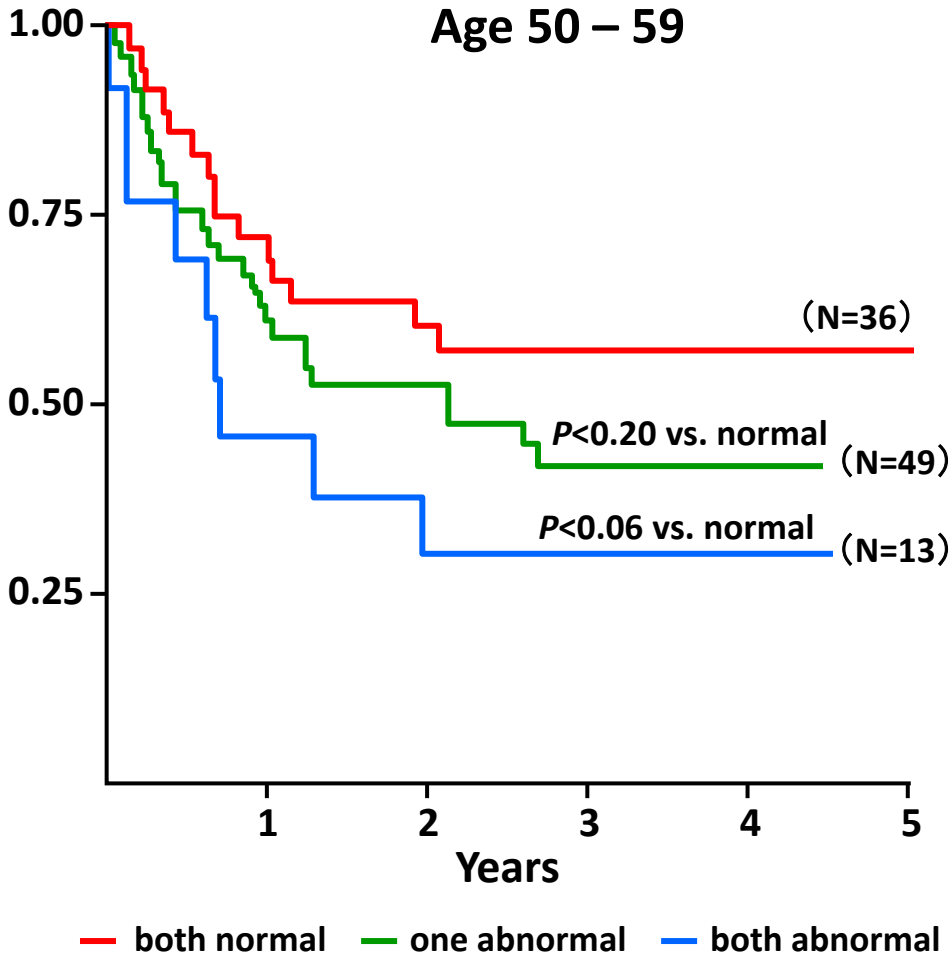
Geriatric Assessment to evaluate the fitness for HCT

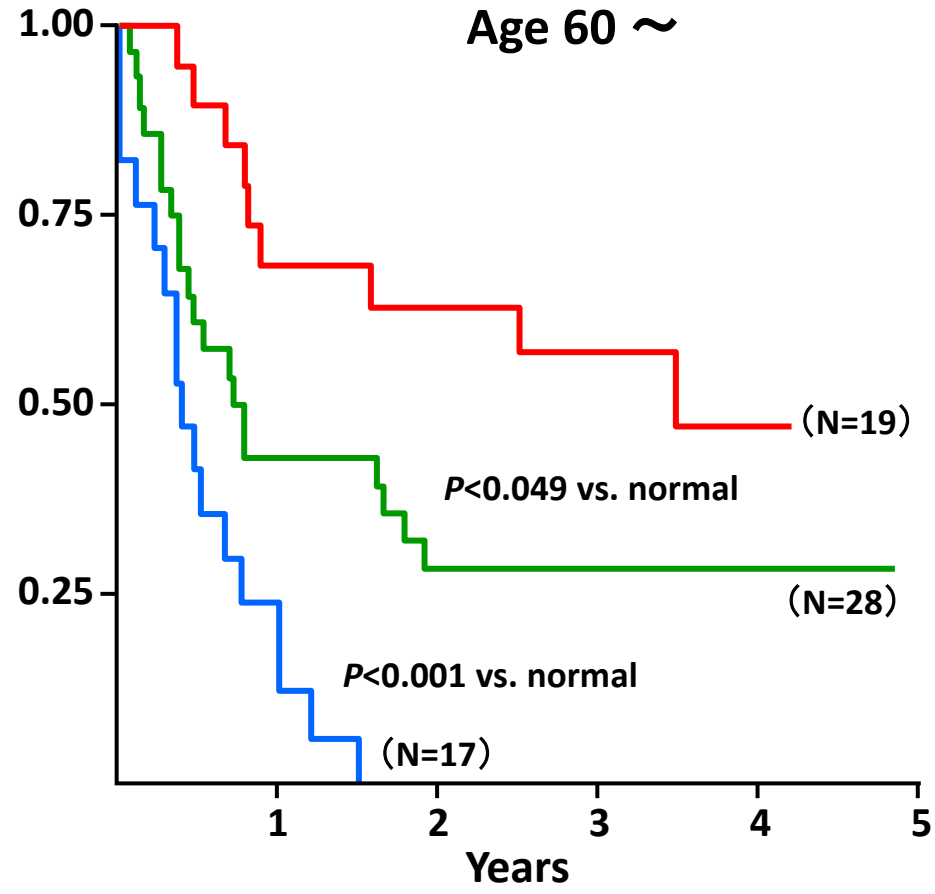
- Aging is heterogeneous process with changes across many domains…… Physiologic, Physical, functional, social, psychiatric, and cognitive.
- The comprehensive geriatric assessment may well to unmask those domains.

HCT-CI / IADL	Scores	OS (2 Y)
HCT-CI score of ≥3 or IADL score <14 acquire a score of 1. Both abnormalities get a score of 2	0	62
	1	44
	2	13

Muffly LS. et al, Haematologica, 2014; 99(8): 1373-1379

Geriatric Assessment (GA) to predict OS in Older Allogeneic HCT (N=203)

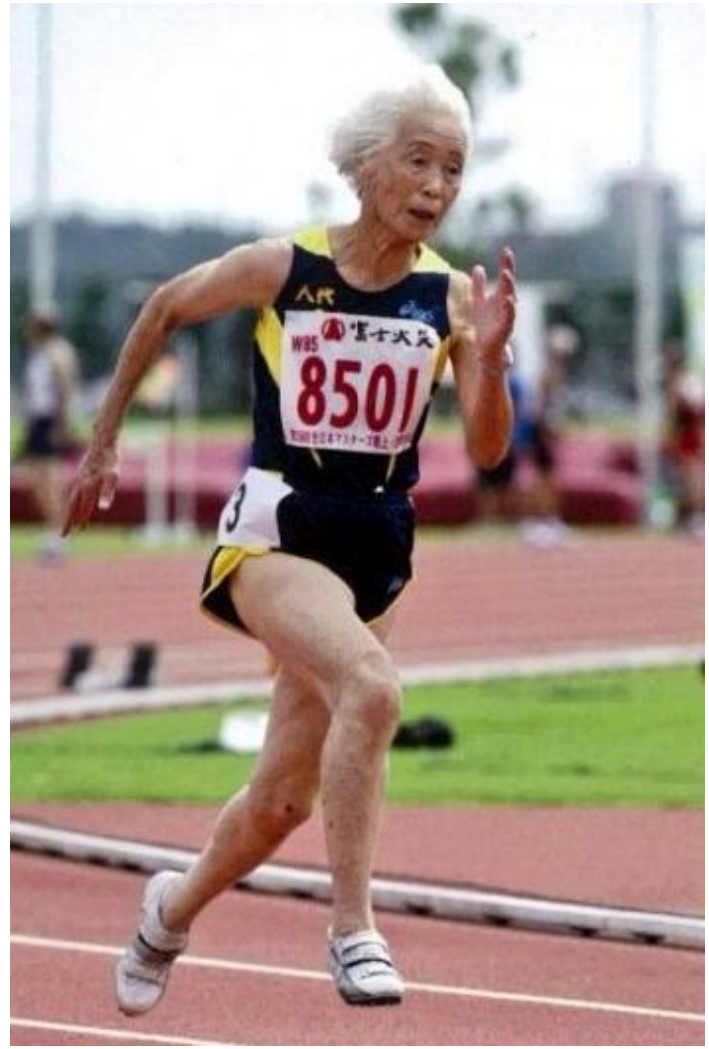




Muffly LS. et al, Haematologica, 2014; 99(8): 1373-1379

How can we choose the best candidates for transplants in the elderly ….

- *Co-morbidities*
- *Age*
- *Disease risks*
- *Geriatric assessment*
- *Availability of caregiver*
- *Financial status*
- *Patient's view of life*
- *Etc…..*



A woman without her man is nothing

Man's response

A woman, without her man, is nothing

Woman's response

A woman: without her, man is nothing

Survival is no longer sole measure of benefit for elderly undergoing HSCT

Life with good quality of life

Cost for HSCT
Cost for late complications
Limited recourses of our society

GVHD-free, relapse-free survival (GRFS)

Composite end point of transplant outcomes after Allo-HSCT

GRFS is defined as the absence of

- Grade Ⅲ-Ⅳ acute GVHD
- Systemically treated chronic GVHD
- Relapse
- Death

GRFS is a patient-centered definition of success that represents ideal recovery without significant GVHD-related morbidity.

Summary

- The indication of HCT should be decided on a case by case basis.
- Identifying adults patient who may benefit from HCT involves patients and disease factors.
- Advent of the tool assessing those factors may serve as assets for the decision-making process.
- Psychosocial assessment is also crucial to maximize participation in their own care, and successful return to life after HCT