

# Transplant and CAR T-cell Therapy for Older Adults

## Celebrating a Second Chance at Life Survivorship Symposium

April 29 – May 5, 2023



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Memorial Sloan Kettering Cancer Center

## Financial Conflict of Interest

- Consultancy: Kite, A Gilead Company
- Independent Adjudication Committee: Priothera Ltd.

## Learning Objectives

- Age limit for HCT or CAR T-cell therapy as a treatment option
- Health issues (co-morbidities) that may preclude an older adult from undergoing these treatment
- Outcomes after HCT and CAR T-cell therapy for older adults as compared to less intensive therapies
- Outcomes after an allogeneic or autologous HCT and CAR T-cell therapy in older adults as compared to younger adults
- Strategies some transplant and CAR T-cell programs are using to attend to the needs of older adults

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## Presentation Overview

- The aging patient: scope of the problem
- Older patient outcomes
- Geriatrics principles of care
- Geriatric assessment (GA) in Transplantation and Cellular Therapy (TCT)
- GA-guided management in TCT
- Barriers and challenges

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## The Aging Patient with a Blood Cancer

Diagnosis	Median Age of Onset	Incidence per Year	Role of Hematopoietic Stem Cell Transplant (HCT)
Acute myeloid leukemia (AML)	63	10,500	Allogeneic HCT as consolidation of high risk CR1 patients or as salvage therapy for patients with advanced disease
Acute lymphoblastic leukemia (ALL)	12	6,950	Allogeneic HCT as consolidation of high risk CR1 patients or as salvage therapy for patients with advanced disease
Myelodysplastic syndromes (MDS)	70	16,000 estimate	Allogeneic HCT only curative therapy
Chronic lymphocytic leukemia (CLL)	70	16,000	Allogeneic HCT only curative therapy
Chronic myeloid leukemia (CML)	64	6,000	Allogeneic HCT as salvage therapy for patients who have failed tyrosine kinase inhibitors
Non-Hodgkin lymphoma (NHL)	66	72,000	Autologous HCT as consolidation of chemo-sensitive relapse of diffuse large B-cell lymphoma and follicular lymphoma. Consolidation of high-risk CCR1 patients (mantle cell lymphoma, double hit lymphoma, high IPI scores). Allogeneic HCT as salvage for patients who relapse after autologous HCT.
Multiple myeloma	73	18,000	Autologous HCT as consolidation of an initial remission considered standard of care. Allogeneic HCT as salvage for patients who relapse after autologous HCT.

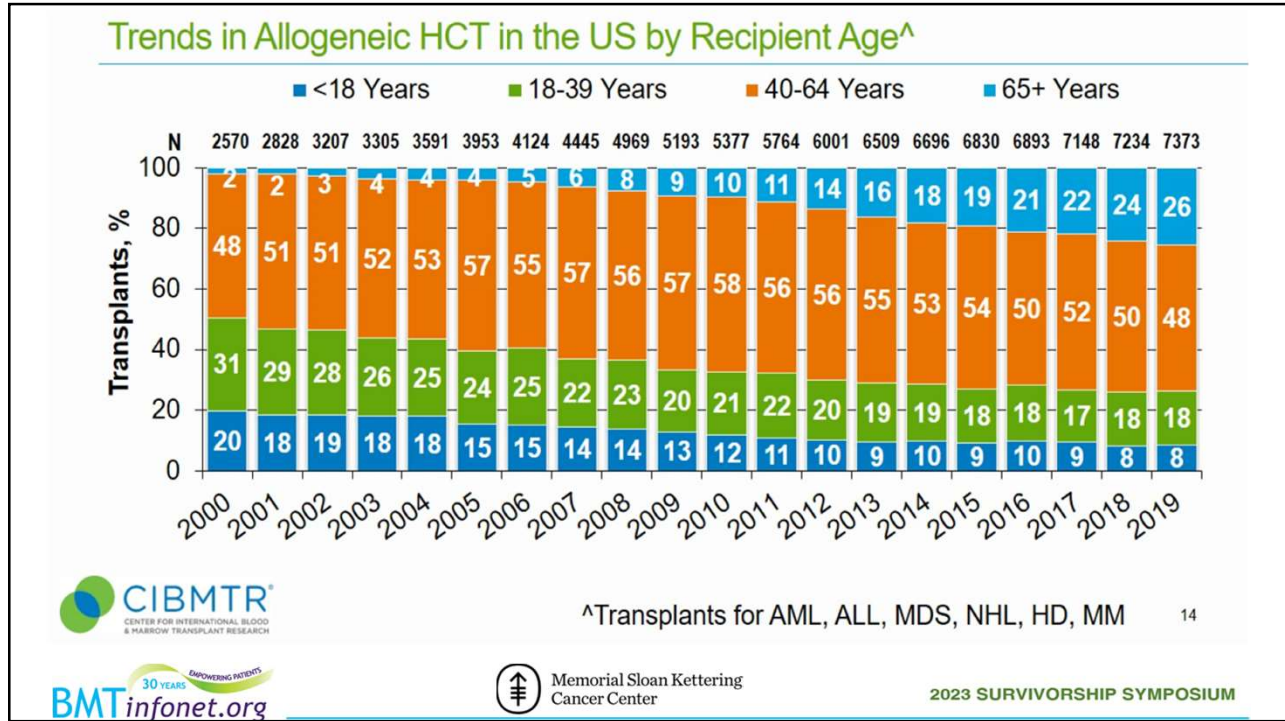
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### Trends in Autologous HCT in the US by Recipient Age<sup>^</sup>

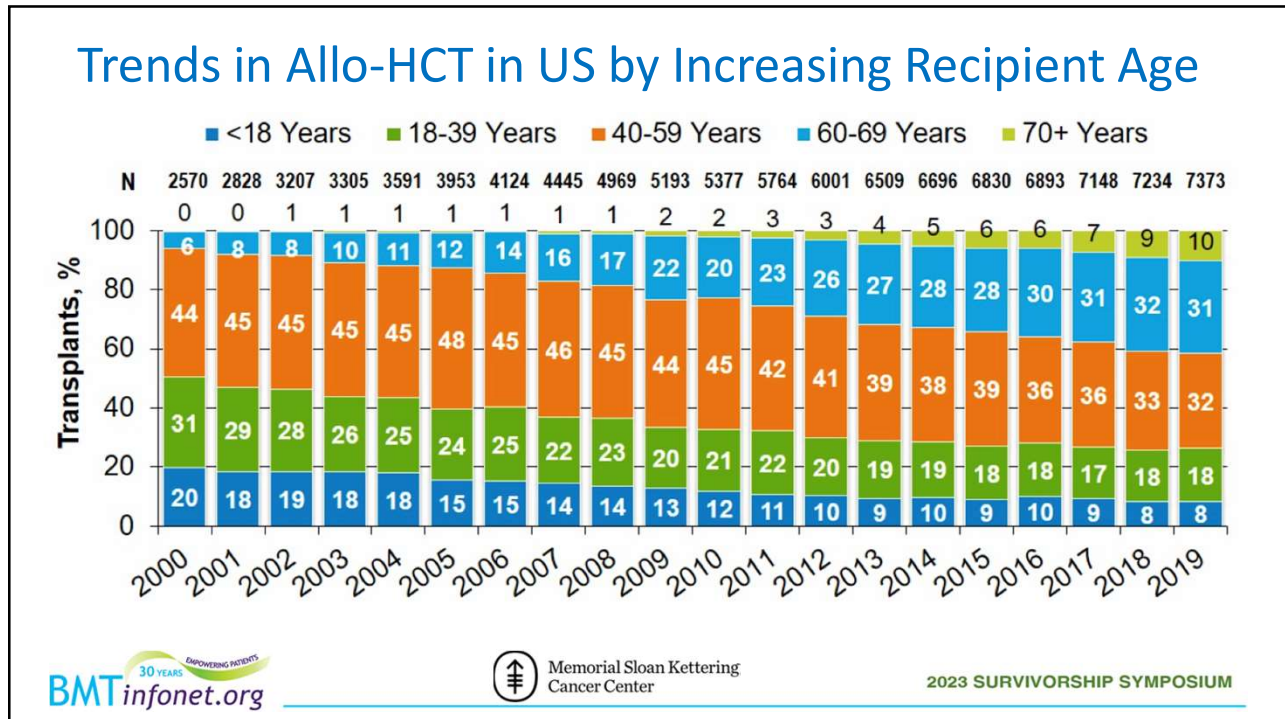


<sup>^</sup>Transplants for NHL, HD, MM 15

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# Challenges in Older Cancer Patients

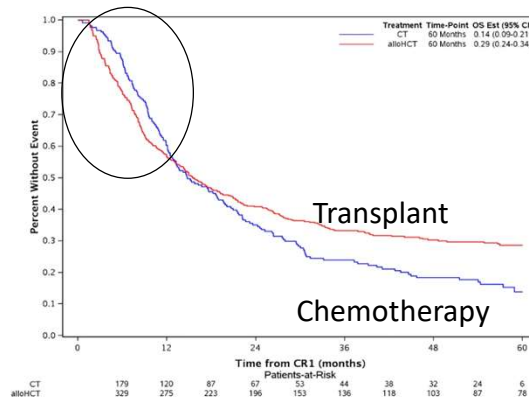
- Comorbidities
- Functional Impairment
- Cognitive Impairment
- Impaired mobility
- Malnutrition & sarcopenia (muscle loss)
- Polypharmacy PIM
- Frailty phenotype



- Access barriers
- Higher risk disease
- Increased regimen Toxicities
- Geriatric survivorship
- Geriatric syndromes (falls, sun-downing, incontinence, etc.)
- Older caregiver, social support
- End-of-Life care

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# Donor Transplant Compared to Chemotherapy in AML Patients Aged 60-75 years

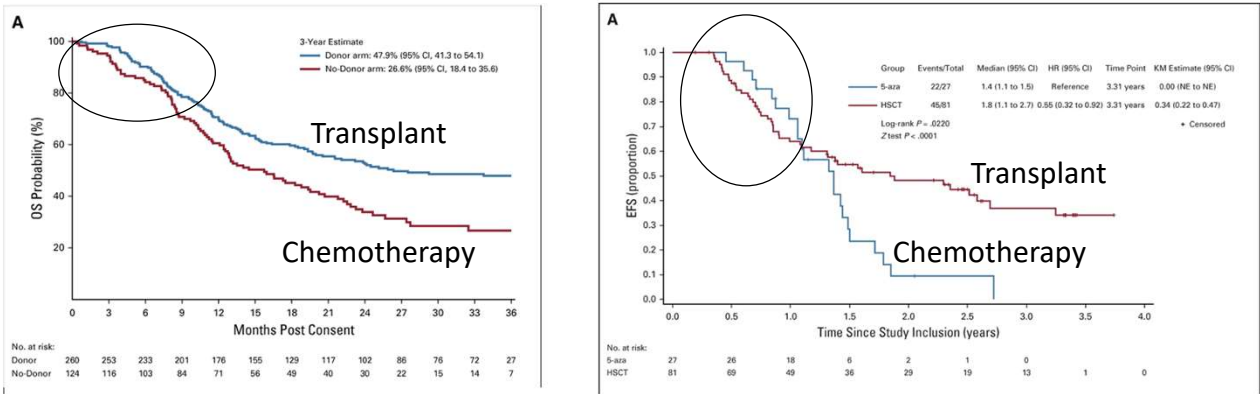


Time Point (years)	CT	AlloHCT
OS		
1	60.3% (53.9%-67.5%)	56.8% (51.6%-62.6%)
2	35.1% (29%-42.5%)	40.8% (36.2%-46.1%)
3	23.9% (18.6%-30.8%)	33.3% (28.9%-38.3%)
5	13.8% (9.2%-20.7%)	28.6% (24.4%-33.6%)

Utsun et al. 2019 Leukemia

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## Donor vs No-donor Biologic Assignment Trials for Older Patients with MDS



Nakamura R et al. 2021 ICO; Kroger N et al. 2021 ICO



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From: Comparison of Patient Age Groups in Transplantation for Myelodysplastic Syndrome: The Medicare Coverage With Evidence Development Study

JAMA Oncol. 2020;6(4):486-493. doi:10.1001/jamaoncol.2019.5140

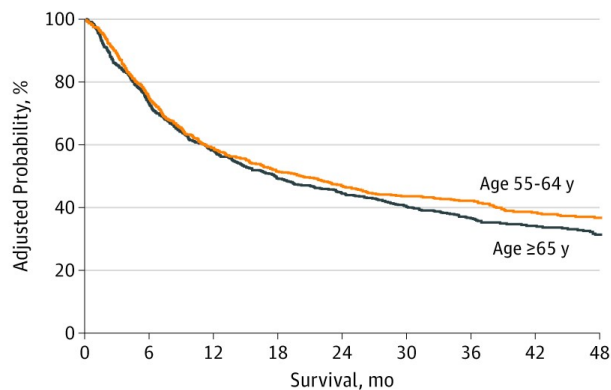
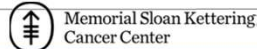


Figure Legend:  
 Overall Survival by Age



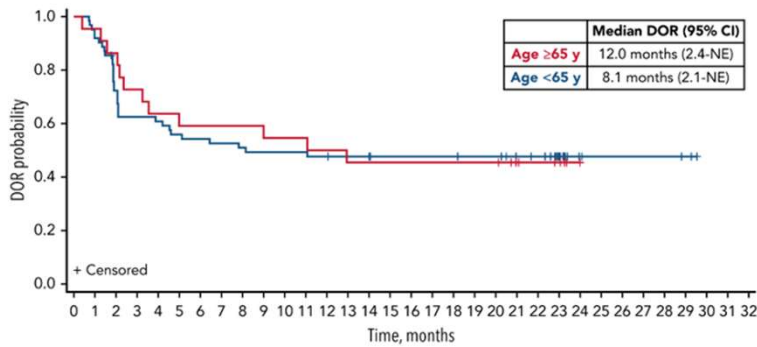
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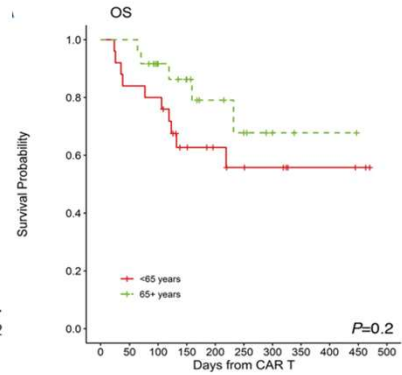


## CAR T-cell Therapy in Older Lymphoma Patients

### ZUMA-1 Study



### MSK Study



Neelapu SS, et al. 2020 Blood

Lin RJ, et al. 2020 Haematologica

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## Challenges in Older Cancer Patients

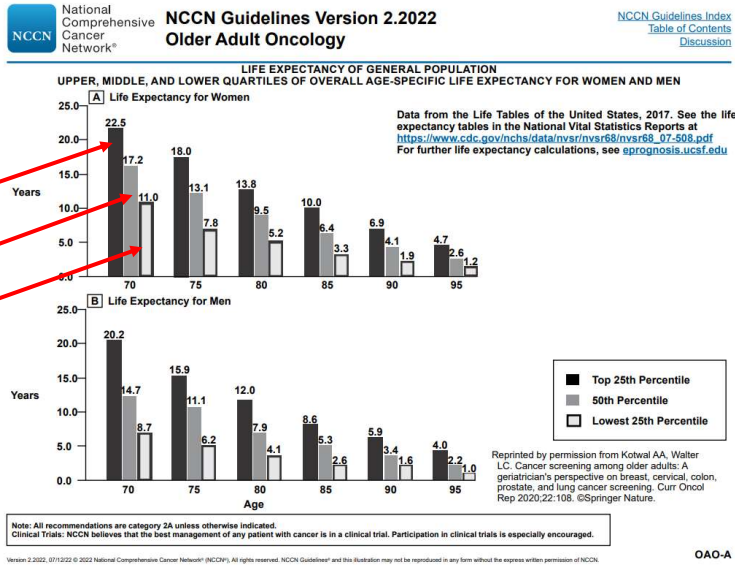
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- Access barriers
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# Geriatrics Principles of Care: Life Expectancy



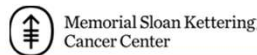
Fit/robust  
 Average/  
 vulnerable  
 Frail/sick



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# Geriatrics Principles of Care: Multidisciplinary Management

- Atypical disease presentation with many causes likely
- Quality of life/Independence preference
- Cognition impairment and other geriatric syndromes
- Complex medication management:
  - start low and go slow, active deprescribe



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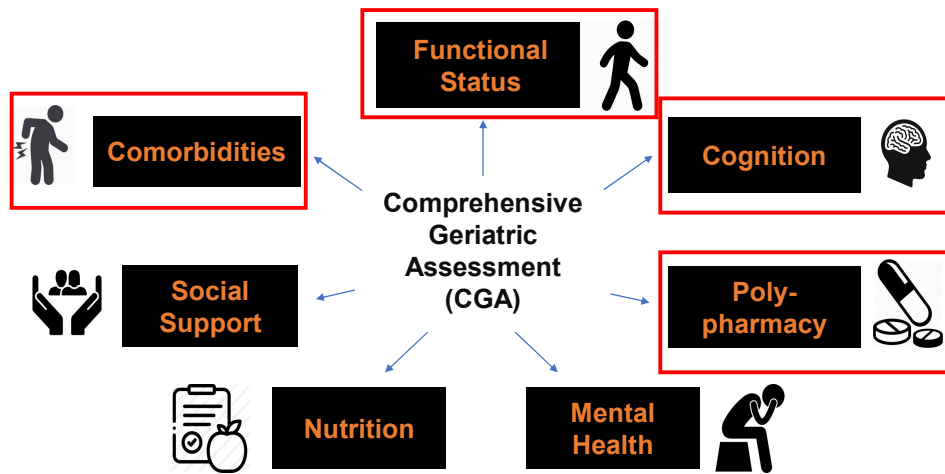


# Geriatric Principles of Care: Frailty and Resilience

"Frailty" Constructs	Examples	Frailty and Resilience from the Perspective of a Complex Structure (Golden Gate Bridge)	Potential Strengths
<b>A. Phenotypic Frailty (defined state)</b>	Fried CHS Study Sarcopenic Obesity		Capture existence of a clinically defined and measurable phenotypic state Define risk factors and mechanisms with some specificity for given phenotype Measure treatment effect when a degree of treatment specificity is involved
<b>B. Stochastic Frailty (accumulation of deficits)</b>	Rockwood FI Index (e.g. FIClin, Filab)		Perform prognostication Define cross-cutting risk factors Measure treatment effects when more pleiotropic interventions are studied Measure treatment effects when testing geroscience-guided therapeutics
<b>C. Resilience (Measure of homeostasis in face of stressor)</b>	Orthostasis Vaccine Responses Recovery from infection, surgery, anesthesia, dehydration, bedrest, chemotherapy, trauma or BM transplant		Identify "hidden" vulnerability Identify resilient mechanisms Obtain more individualized risk Design more precise interventions Design earlier interventions Design interventions targeting resilient mechanisms

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# Geriatric Assessment in TCT Biological versus Chronologic Age



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## Functional Status: ADL and IADL

### Katz Activities of Daily Living (ADL)

1 point for independence in each of 6 areas:

- Bathing
- Dressing
- Toileting
- Transferring
- Continence
- Feeding

### Lawton Instrumental Activities of Daily Living (IADL)

2 points for independence, 1 point for needing assistance, and 0 points for dependence in each of 8 areas:

- Using the telephone
- Shopping
- Food preparation
- Housekeeping
- Laundry
- Using transportation
- Managing medications
- Handling money



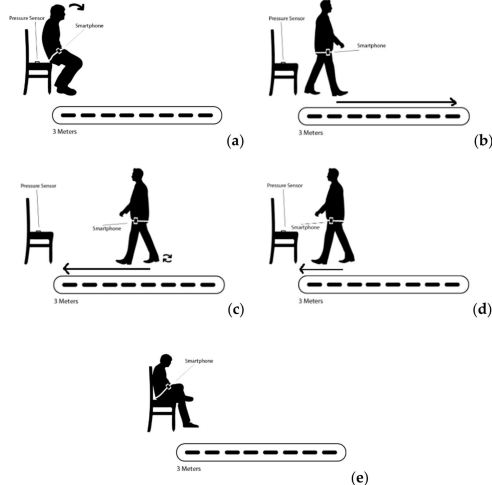
Slide courtesy: R. Olin UCSF

Katz, Gerontologist 1970; Lawton, Gerontologist 1969

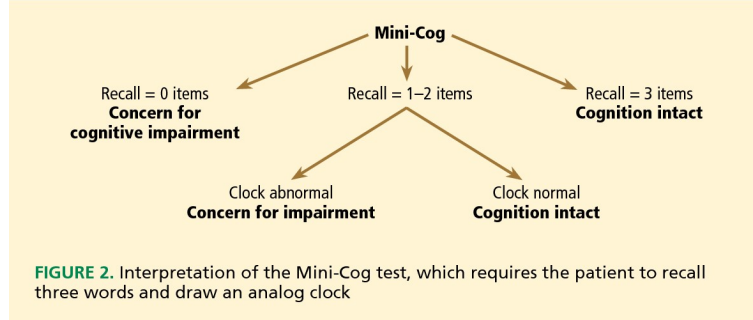
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## Timed Up and Go (TUG) Test

- Can be done in the clinic
- Easy assessment without a watch into 3 categories:
  - <10 secs (fit)
  - 10-20 secs (vulnerable)
  - >20 secs (frail)
- Can be followed overtime



# The MiniCog Test



- Can be done in the clinic (3 minutes)
- Easy assessment to establish the need for more in-depth evaluation: 3 points or less on a total of 5 points (3 points for recall, 2 points for clock)
- Not sensitive to follow overtime

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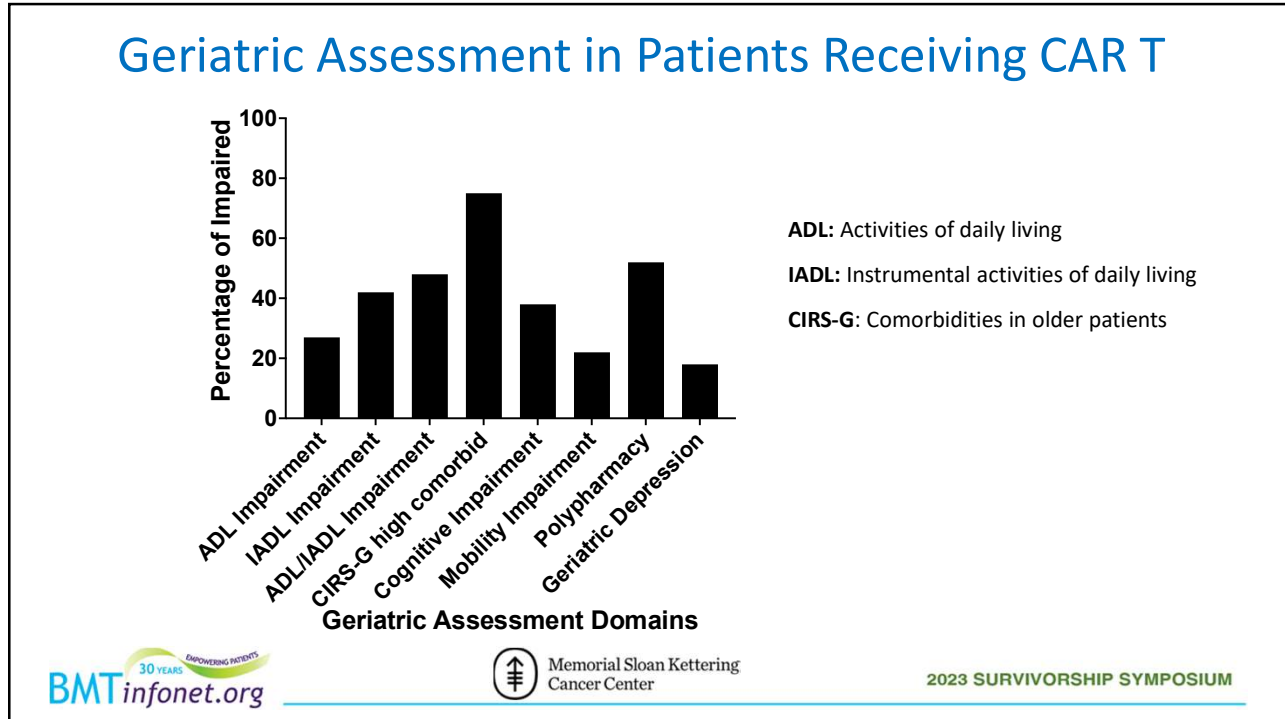
# Prognostically Important Geriatric Deficits in Donor Transplantation

Impairment in GA domains with impact on outcomes

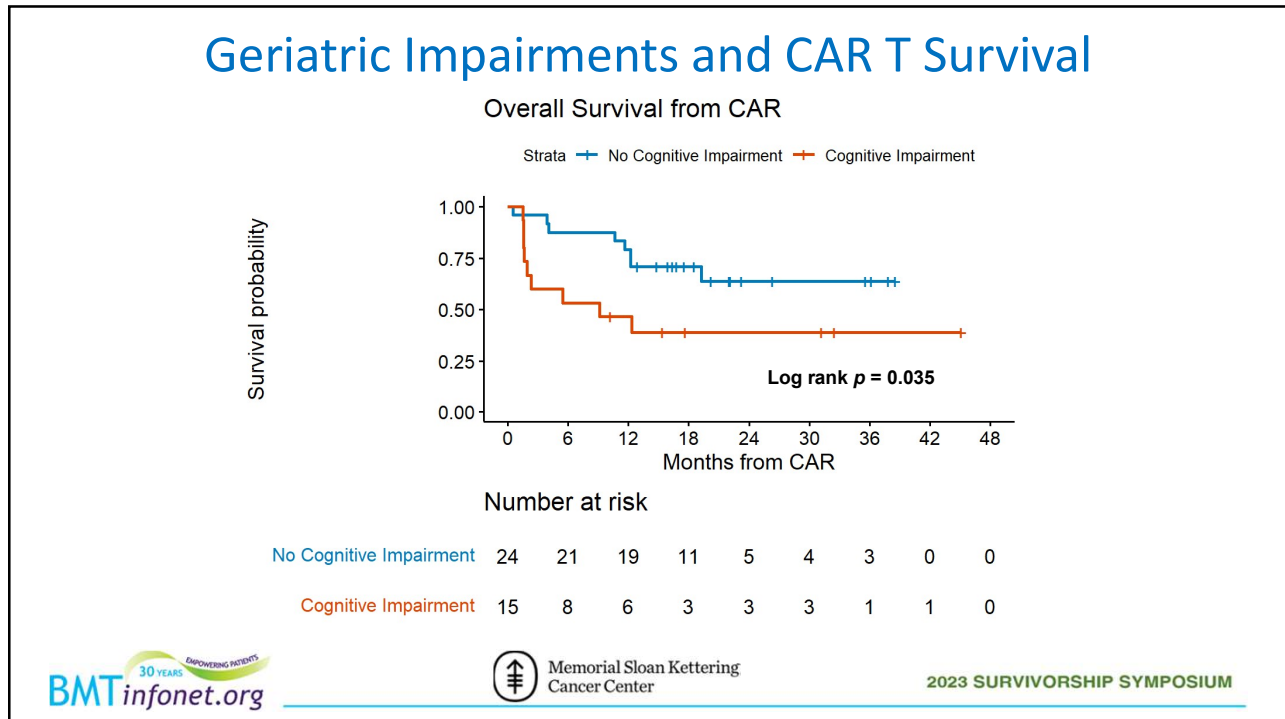
Comorbidity	Function	Mobility	Cognition	Medication	Frailty scale
NRM ↑ OS ↓	NRM ↑ OS ↓	OS ↓			
NRM ↑ PFS ↓	OS ↓ PFS ↓	OS ↓			
	OS ↓ PFS ↓ NRM ↑ Toxicities ↑				OS ↓ Toxicities ↑
		NRM ↑ OS ↓			NRM ↑
NRM ↑			NRM ↑ OS ↓		
NRM ↑	NRM ↑ OS ↓ PFS ↓				NRM ↑ OS ↓
				Toxicities ↑ OS ↓	

**OS:** Overall survival  
**PFS:** Relapse-free survival  
**NRM:** Death without relapse

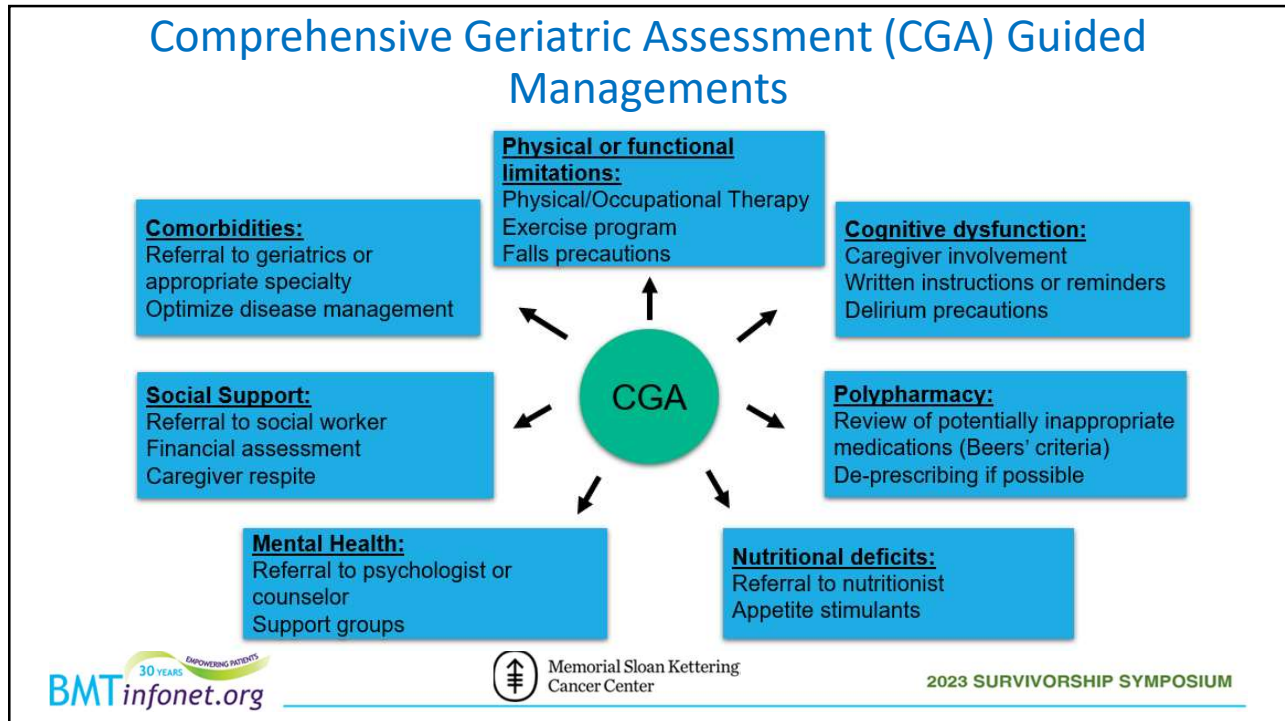
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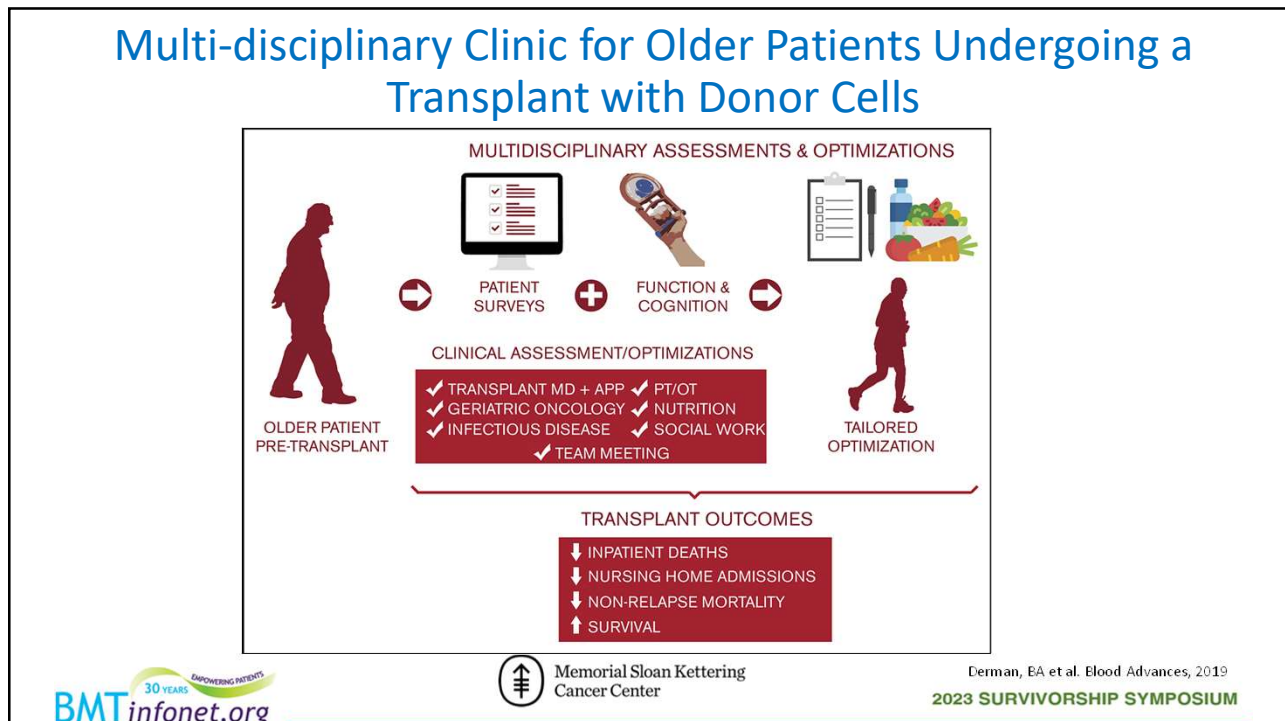
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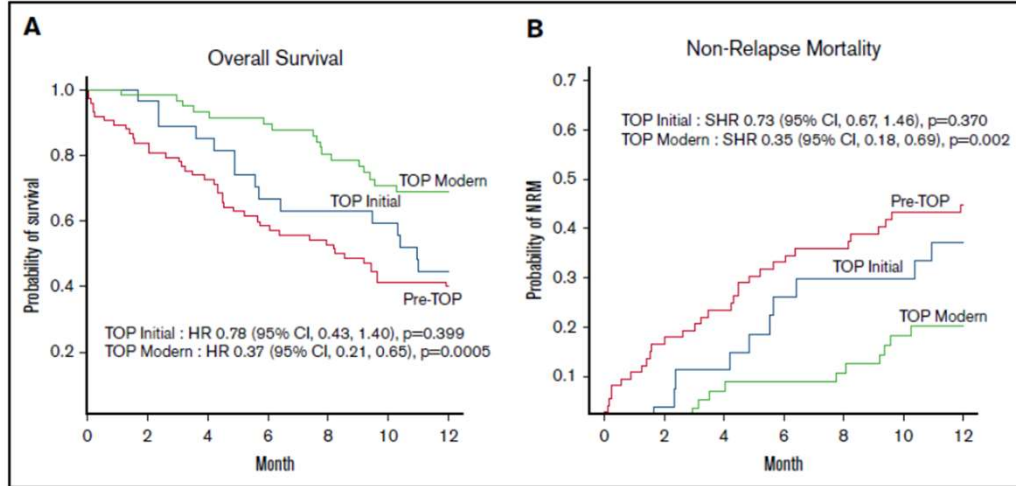


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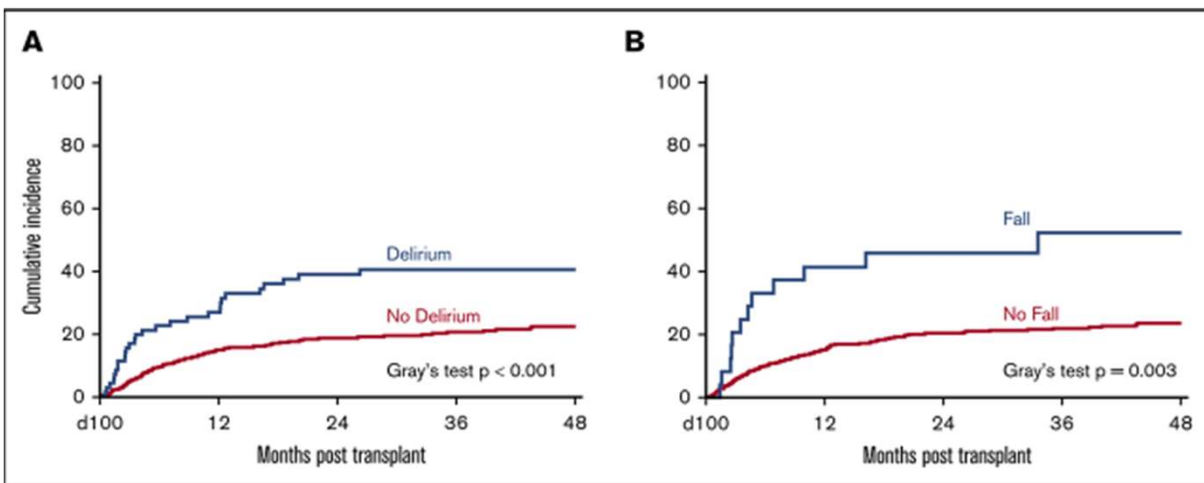
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## GA-Guided Multi-disciplinary Clinic for Older Patients Prior to Donor Transplant



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## Impact of Post-Transplant Geriatric Syndromes



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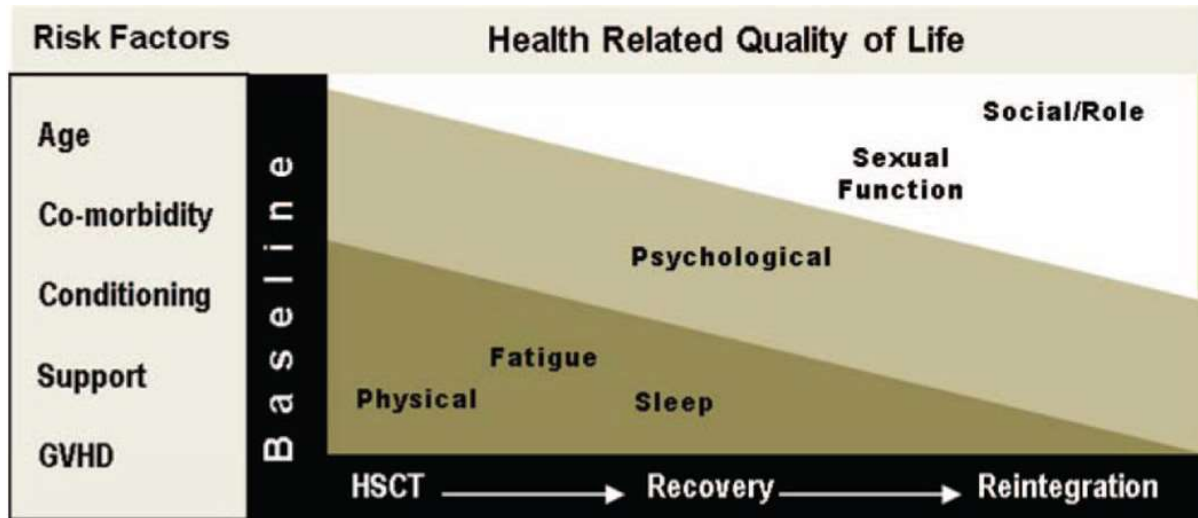


## Why Geriatric Assessment is Not Used at Some Transplant Centers

Why Geriatric Assessment Not Used	
Uncertainty about which assessment tools to use	59%
Lack of training, knowledge, understanding or experience about geriatric assessment	53%
Lack of clinical support staff	45%
Not aware of available assessment tools	41%
Lack of time	38%
Lack of available resources for referrals	41%
Limited evidence to support geriatric assessment	34%
Limited or available space to conduct the assessment	28%
No or limited provider reimbursement	26%

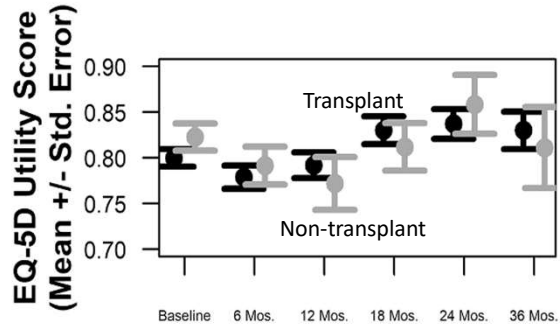
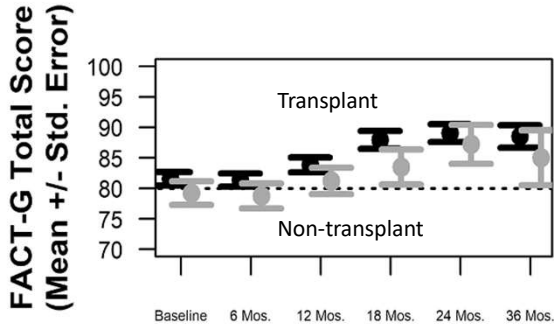
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## Quality of Life Following Transplant with Donor Cells



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## Similar Quality of life in MDS patients aged 50–75 with or without transplant with donor cells



N Responders	Assessment Time					
	Baseline	6 Mos.	12 Mos.	18 Mos.	24 Mos.	36 Mos.
Donor Arm	204	174	135	107	93	77
No Donor Arm	85	69	45	35	27	18

N Responders	Assessment Time					
	Baseline	6 Mos.	12 Mos.	18 Mos.	24 Mos.	36 Mos.
Donor Arm	203	170	134	108	93	78
No Donor Arm	85	71	46	36	27	19

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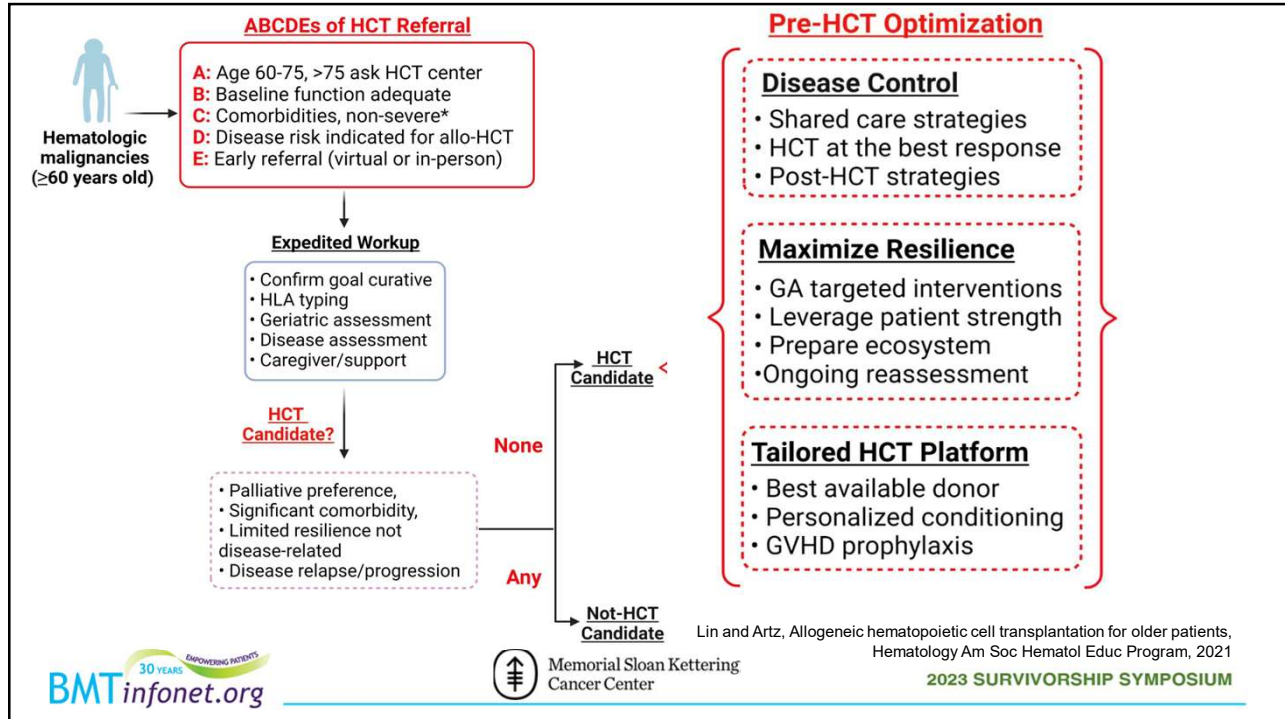
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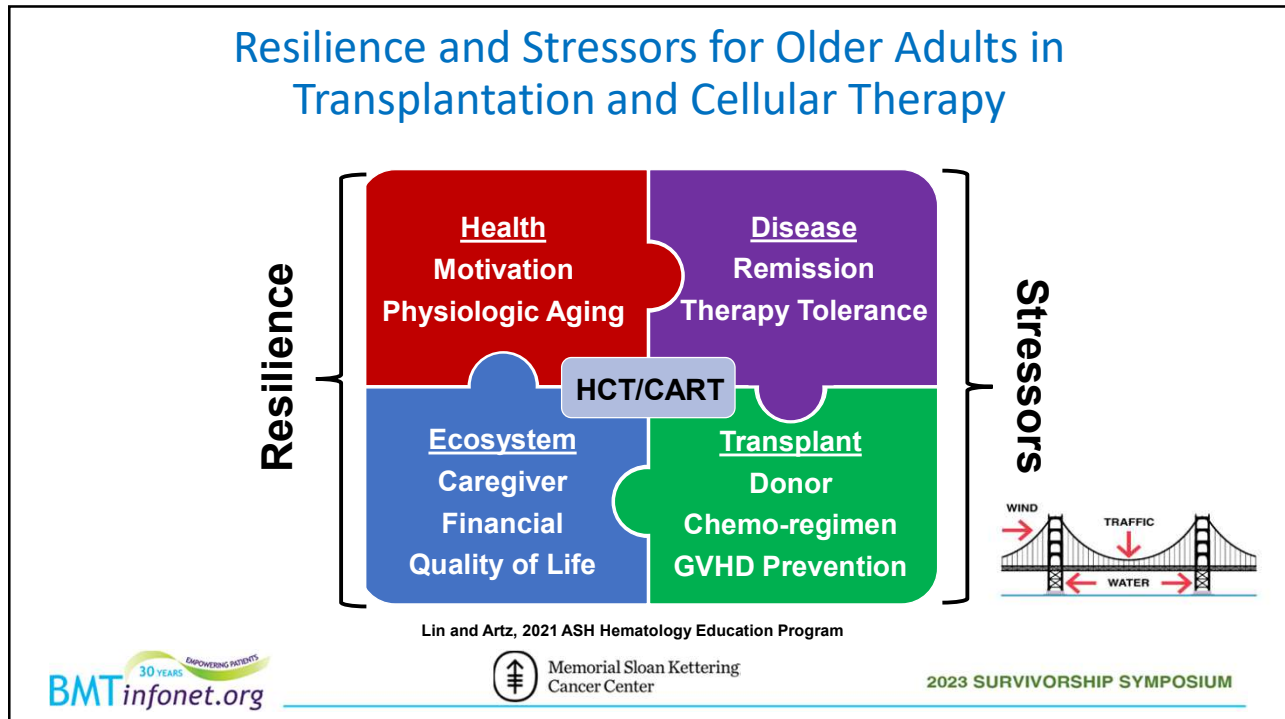


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# QUESTIONS?



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