Graft-versus-Host Disease: A Major complication After Hematopoietic Stem Cell Treatment

Betty Ky Hamilton MD
Blood and Marrow Transplant Program
Taussig Cancer Institute, Cleveland Clinic
Session 2- Late Effects of Hematopoietic Stem Cell Treatment
November 15, 2021

Overview

Chemo+/- radiation conditioning

HCT

Chronic GVHD

Acute GVHD

Chemo/drug toxicities

Infection: bacterial, viral, fungal

Infection: viral, fungal

LATE EFFECTS:

- **CV disease**
- **Subsequent malignancies**
- Bone Health
- Renal/Liver
- Sexual Health
- Neurocognitive health
- Psychosocial

Day 0 | Day 30 | Day 100 | Day 365

Pre-engraftment | Post-engraftment | Late phase

Overview

Chemo+/- radiation conditioning

HCT

Acute GVHD

Chronic GVHD

Chemo/drug toxicities

Infection: bacterial, viral, fungal

Infection: viral, fungal

LATE EFFECTS:

- **CV disease**
- **Subsequent malignancies**
- Bone Health
- Renal/Liver
- Sexual Health
- Neurocognitive health
- Psychosocial

Day 0 | Day 30 | Day 100 | Day 365

Pre-engraftment | Post-engraftment | Late phase

Graft-versus-Host Disease

- Graft-versus-host disease is a systemic inflammatory condition primarily mediated by the transplanted immune system that can lead to severe multi-organ damage.
- Graft-versus-host disease remains a major cause of morbidity and mortality following transplantation.
- Despite current prophylaxis, 30-70% of recipients will still have acute GVHD and 20-50% will develop chronic GVHD.
- GVHD and prolonged immunosuppression increases the risk of: infection, organ impairment, poor quality of life, and ultimately survival

GVHD

Classic acute GVHD:

- **Skin:** inflammatory maculopapular erythematous skin rash
- **Liver:** elevated bilirubin
- **GI tract:** anorexia with weight loss, nausea/vomiting, diarrhea, severe pain, GI bleeding and/or ileus

Overlap chronic GVHD

Classic chronic GVHD:
2014 NIH diagnostic criteria:

- Skin, nails, scalp, hair
- Mouth
- Eyes
- Esophagus
- Lungs
- Muscles, joints, fascia
- Genitalia

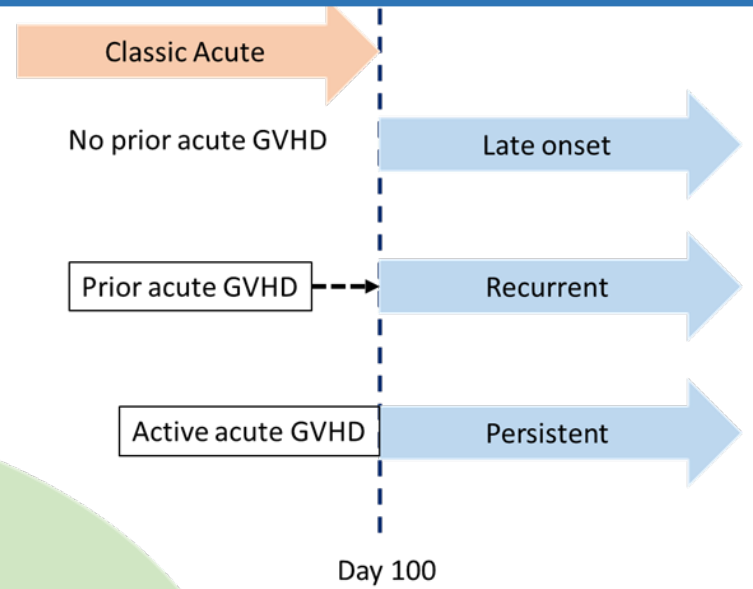


Figure adapted from Schoemans et al. BMT 2018, 53: 1401-1415

Acute GVHD

Classic acute GVHD:

- **Skin:** inflammatory maculopapular erythematous skin rash
- **Liver:** elevated bilirubin
- **GI tract:** anorexia with weight loss, nausea/vomiting, diarrhea, severe pain, GI bleeding and/or ileus

ASH image bank

Chronic GVHD

Classic Chronic GVHD

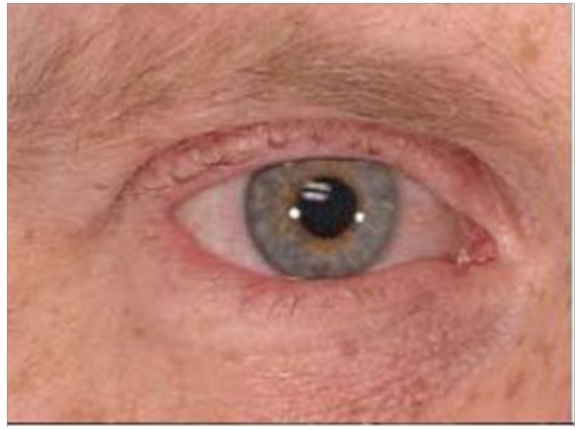
- Skin, scalp, nails, hair
- Mouth
- Eyes
- Esophagus
- Lungs
- Muscles, joints, fascia
- Genitalia

Martires et al. Blood 2011; 118: 4250-4257

Chronic GVHD

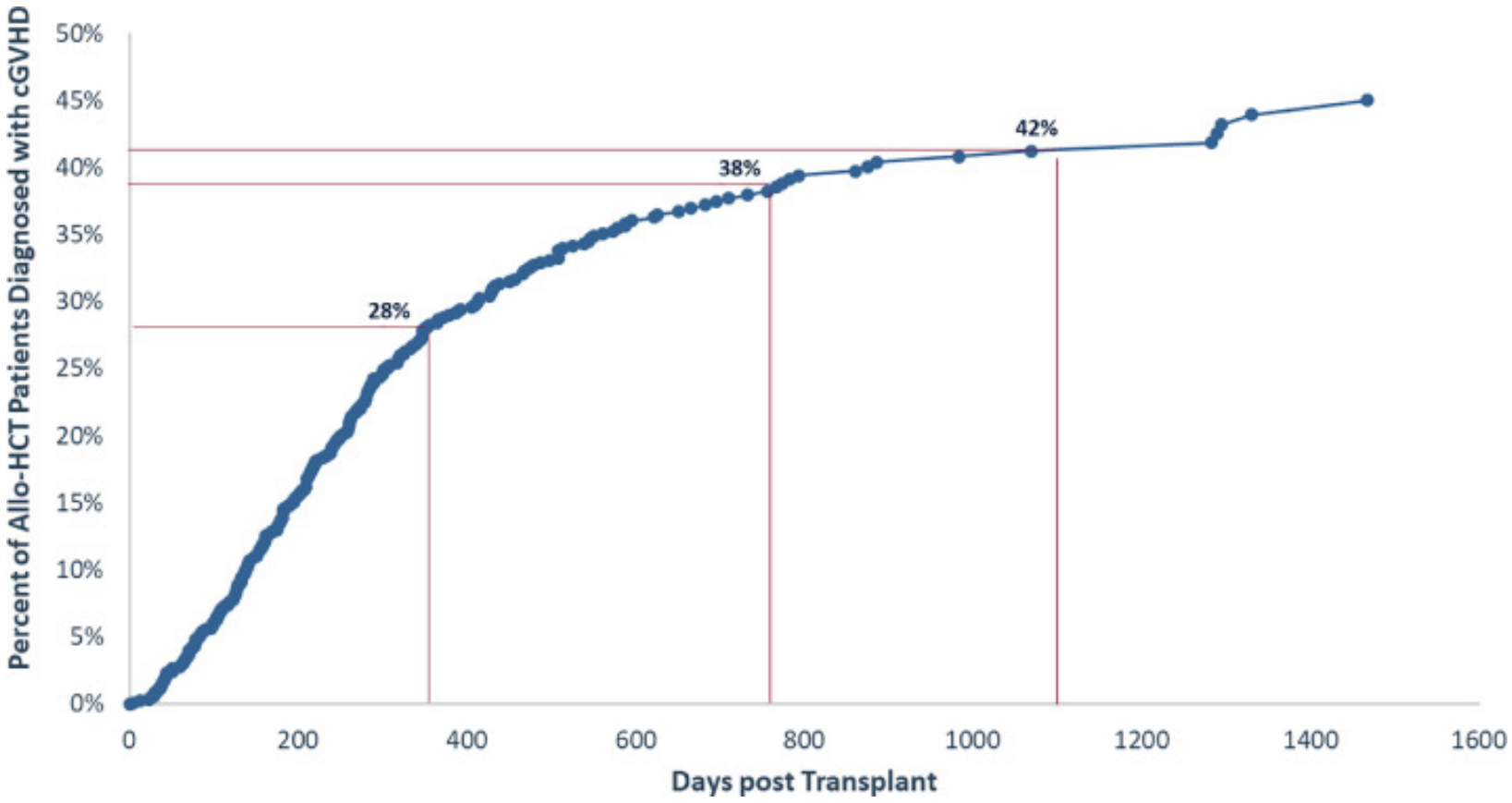
Classic Chronic GVHD

- Skin, scalp, nails, hair
- Mouth
- Eyes
- Esophagus
- Lungs
- Muscles, joints, fascia
- Genitalia



Treister N et al. Blood 2012; 120: 3407-3418

Increasing incidence of chronic GVHD



Bachier et al. Transplant Cell Ther 2021; 27:504.e1

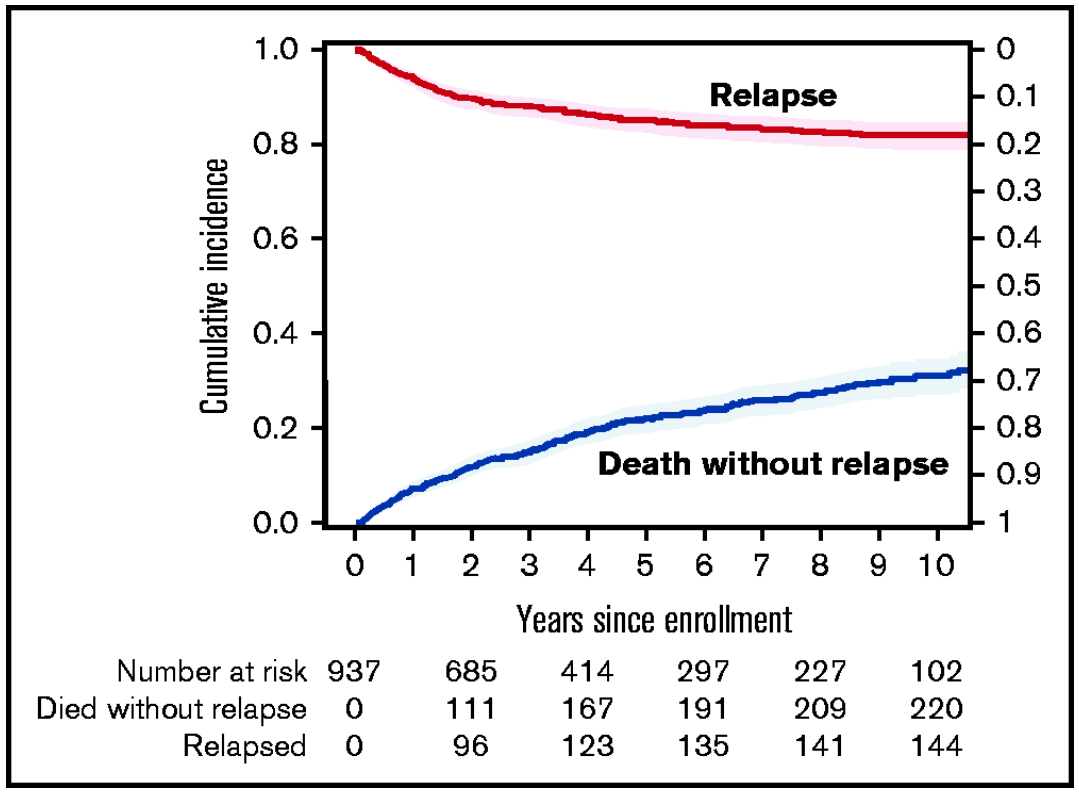
Chronic GVHD leading cause of non-relapse mortality

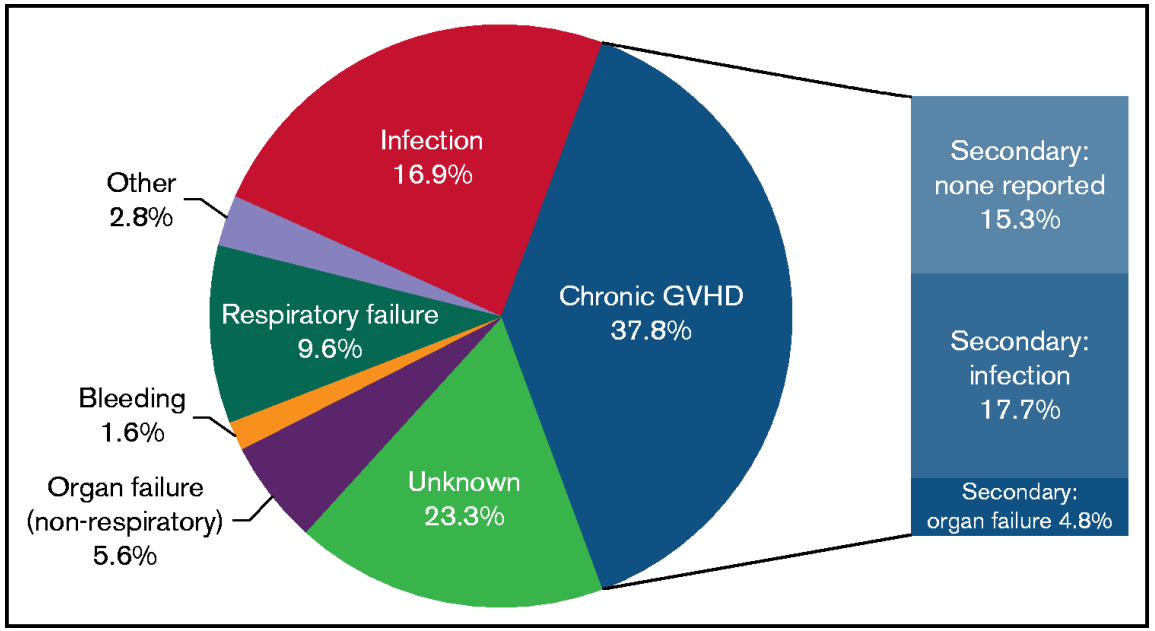
Table 2. Causes of Death of Patients Receiving Myeloablative Allogeneic Transplantations and Surviving at Least 2 Years in Remission Post Transplantation After Undergoing Transplantation Through 2003 As Reported to the CIBMTR

	Years After Transplantation by Disease																											
	AML						ALL						MDS						Lymphoma						SAA			
	2-4		5-9		≥ 10		2-4		5-9		≥ 10		2-4		5-9		≥ 10		2-4		5-9		≥ 10		2-4		5-9		≥ 10	
Cause of Death	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Recurrent or persistent disease	162	47	81	43	11	15	132	55	48	36	11	23	33	34	16	43	3	17	15	27	7	28	2	20	0		0		0	
GVHD	63	18	12	6	7	9	27	11	16	12	4	9	14	14	1	3	0		12	22	1	4	1	10	21	25	12	23	2	6
Infection	45	13	17	9	4	5	27	11	11	8	2	4	15	15	4	11	3	17	8	15	4	16	0		17	20	6	11	8	24
Organ failure	19	5	21	11	8	11	23	10	11	8	5	11	13	13	3	8	4	22	10	18	6	24	1	10	13	16	10	19	4	12
Interstitial pneumonitis	5	1	3	2	0		3	1	1	1	1	2	1	1	0		0		2	4	1	4	0		2	2	0		0	
Secondary malignancy	14	4	19	10	7	9	11	5	18	14	5	11	3	3	2	5	2	11	1	2	0		1	10	6	7	7	13	4	12
Hemorrhage	6	2	0		1	1	1	<1	0		2	4	2	2	1	3	0		0		0		1	10	4	5	5	9	0	
Graft rejection	1	<1	0		0		2	1	1	1	0		0		0		0		0		0		0		5	6	3	6	1	3
Other causes*	7	2	6	3	1	1	3	1	6	5	0		5	5	2	5	0		1	2	1	4	0		5	6	0		1	3
Unknown	25	7	28	15	35	47	12	5	20	15	17	36	11	11	8	22	6	33	6	11	5	20	4	40	10	12	10	19	14	41

Wingard et al. J Clin Oncol 2011; 29:2230-2239

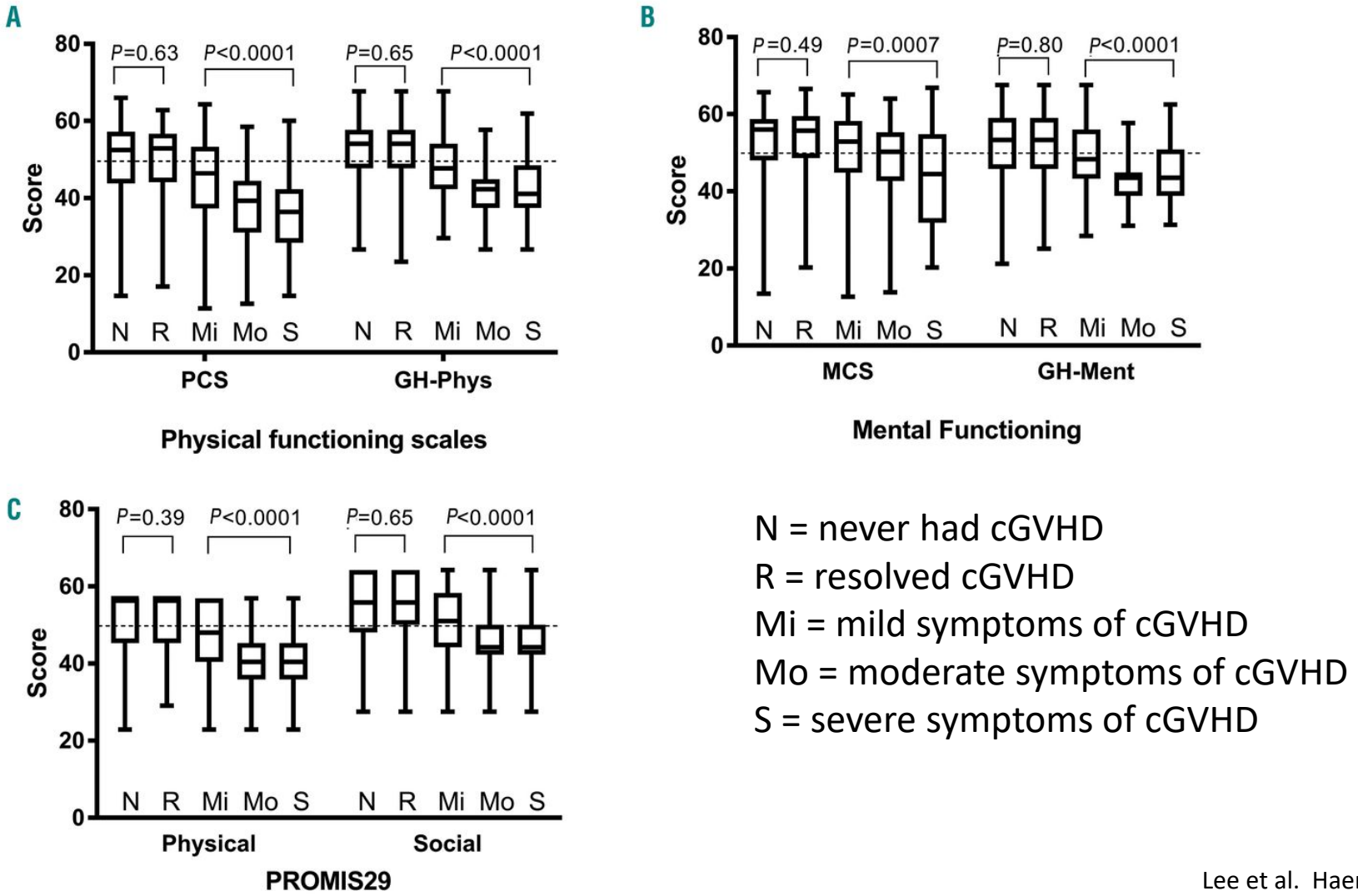
Non-Relapse Mortality in Chronic GVHD





DeFilipp Z, et al. Blood Adv. 2021; 5(20): 4278-4284

Patient reported health status in Chronic GVHD



N = never had cGVHD
R = resolved cGVHD
Mi = mild symptoms of cGVHD
Mo = moderate symptoms of cGVHD
S = severe symptoms of cGVHD

Lee et al. Haematologica 2018; 103 (9)

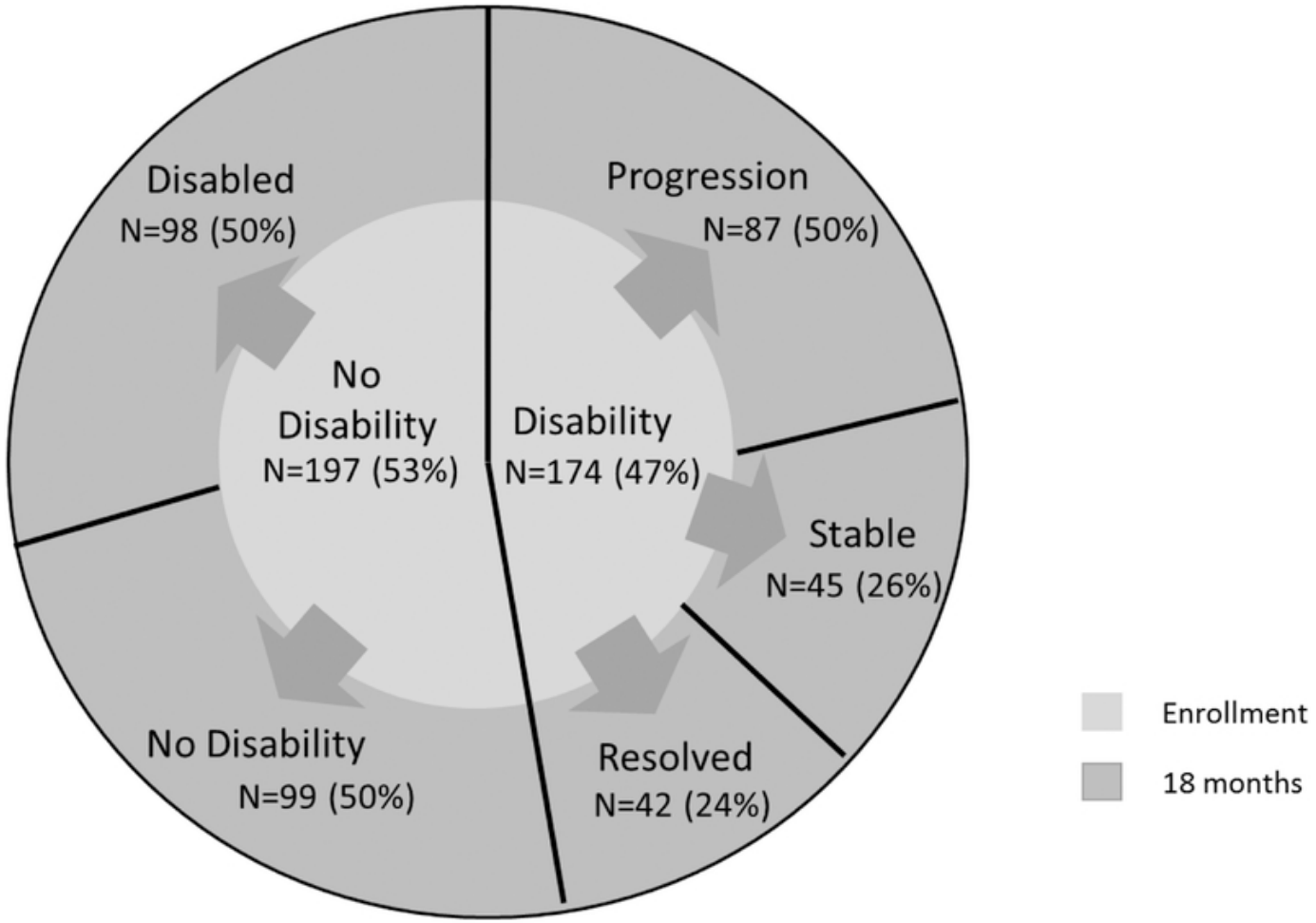
Disability in Chronic GVHD

- Disability is often associated with chronic medical conditions which can result in physical/mental impairments.
- Limited data on disability in chronic GVHD
- Chronic GVHD related disability (NIH moderate-severe eye involvement, scleroderma, joint/fascia involvement, severe esophageal stricture, and any lung involvement)→ longer duration of systemic treatment for chronic GHVD, less likely to return to work or school

Fatobene et al. Haematologica 2019; 104(4): 835-843

Chronic GVHD

Chronic GVHD related disability as a composite endpoint (GVHD criteria, decline in human activity profile (HAP), or decline in performance status over time).



Hamilton et al. Biol Blood Marrow Transplant 2020; 26(4): 772-777

Chronic GVHD Disability

- *Living with Chronic GVHD Patient Survey*
  - Cross sectional online survey administered May- August 2020 to adult patients who reported chronic GVHD within the previous 5 years
  - Respondents reported information pertaining to demographics, disease diagnosis, work status, chronic GVHD symptoms, and impact on activities of daily living

Hamilton et al. ASH 2021 abstract

Chronic GVHD Disability

Cognitive Disability (score 7-10 “severe”)

- Managing personal finances
- Using a computer
- Interacting socially with friends/family

47% respondents

Work Disability

- Ever taken disability leave because of chronic GVHD
- Ever left a job because of chronic GVHD

62.8% respondents

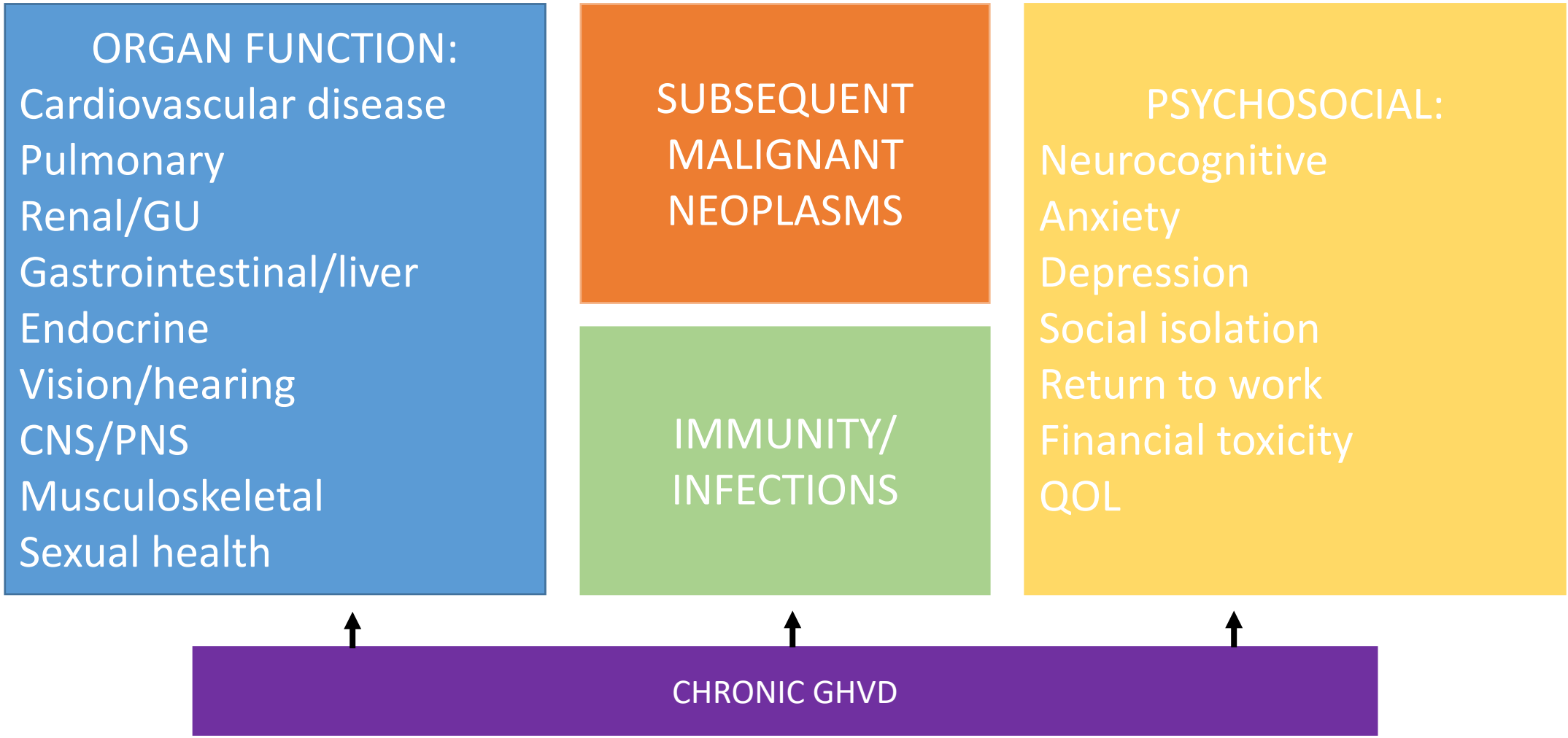
Physical Disability (score 7-10 “severe”)

- Personal hygiene
- Dressing
- Eating
- Ability to use restroom
- Ability to move around house
- Ability to get around outside of house
- Preparing meals
- Shopping
- Housework

67.4% respondents

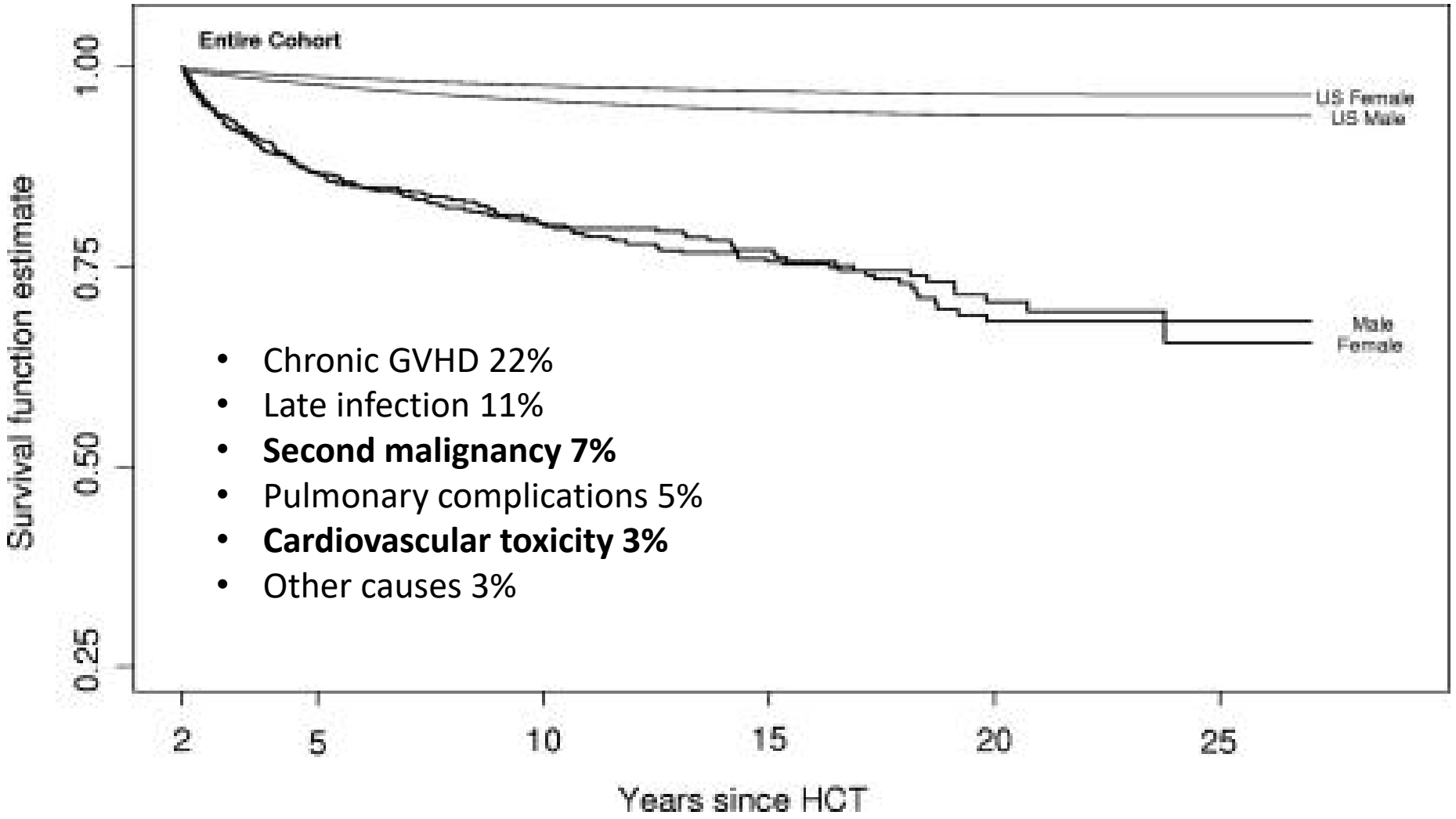
Hamilton et al. ASH 2021 abstract

Late Effects after Allogeneic HCT



Majhail et al. BBMT 2012: 18(30: 348-371

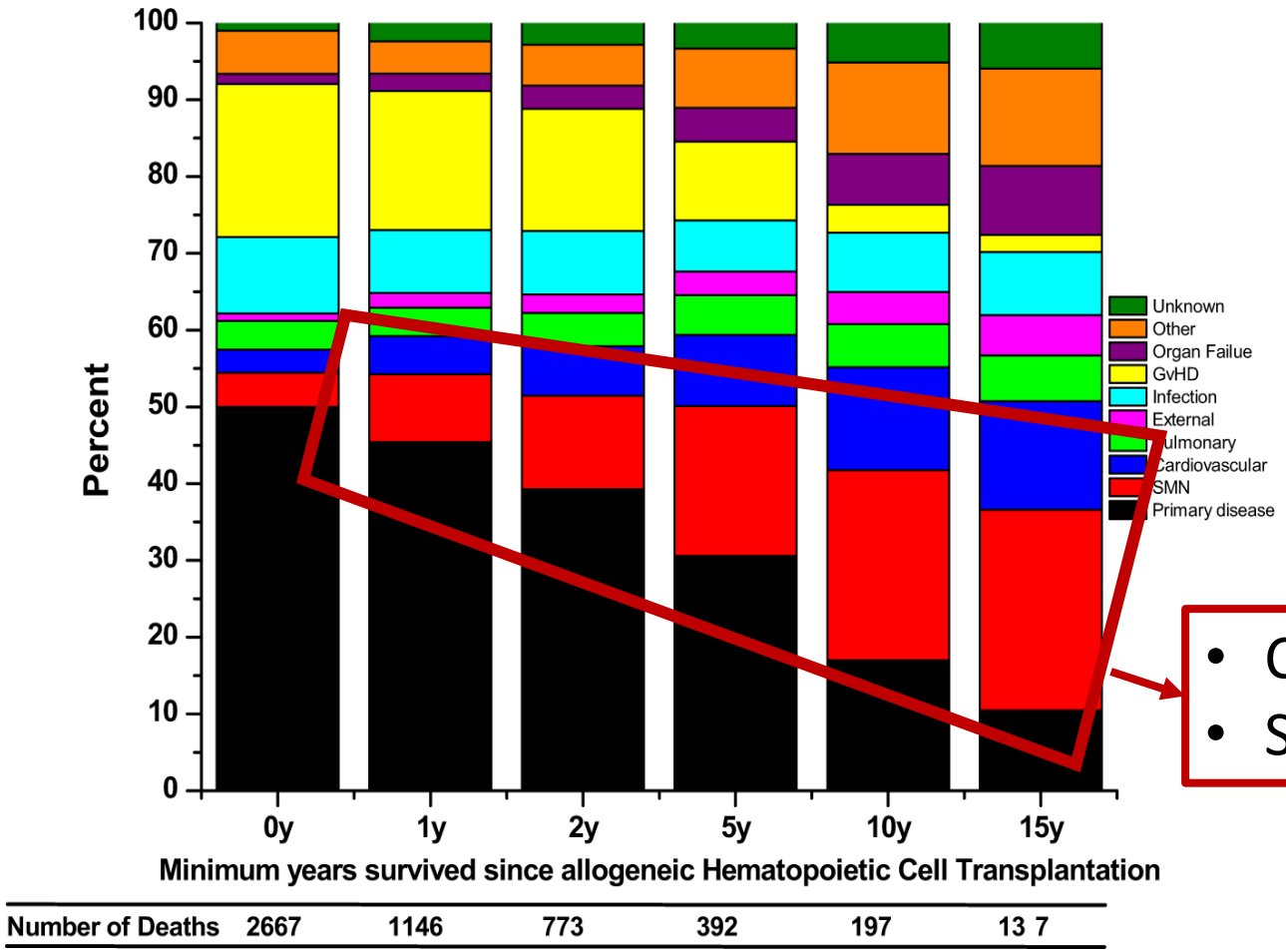
Late mortality after allogeneic HCT



- Chronic GVHD 22%
- Late infection 11%
- **Second malignancy 7%**
- Pulmonary complications 5%
- **Cardiovascular toxicity 3%**
- Other causes 3%

Bhatia et al. Blood 2007; 110 (10): 3784-92

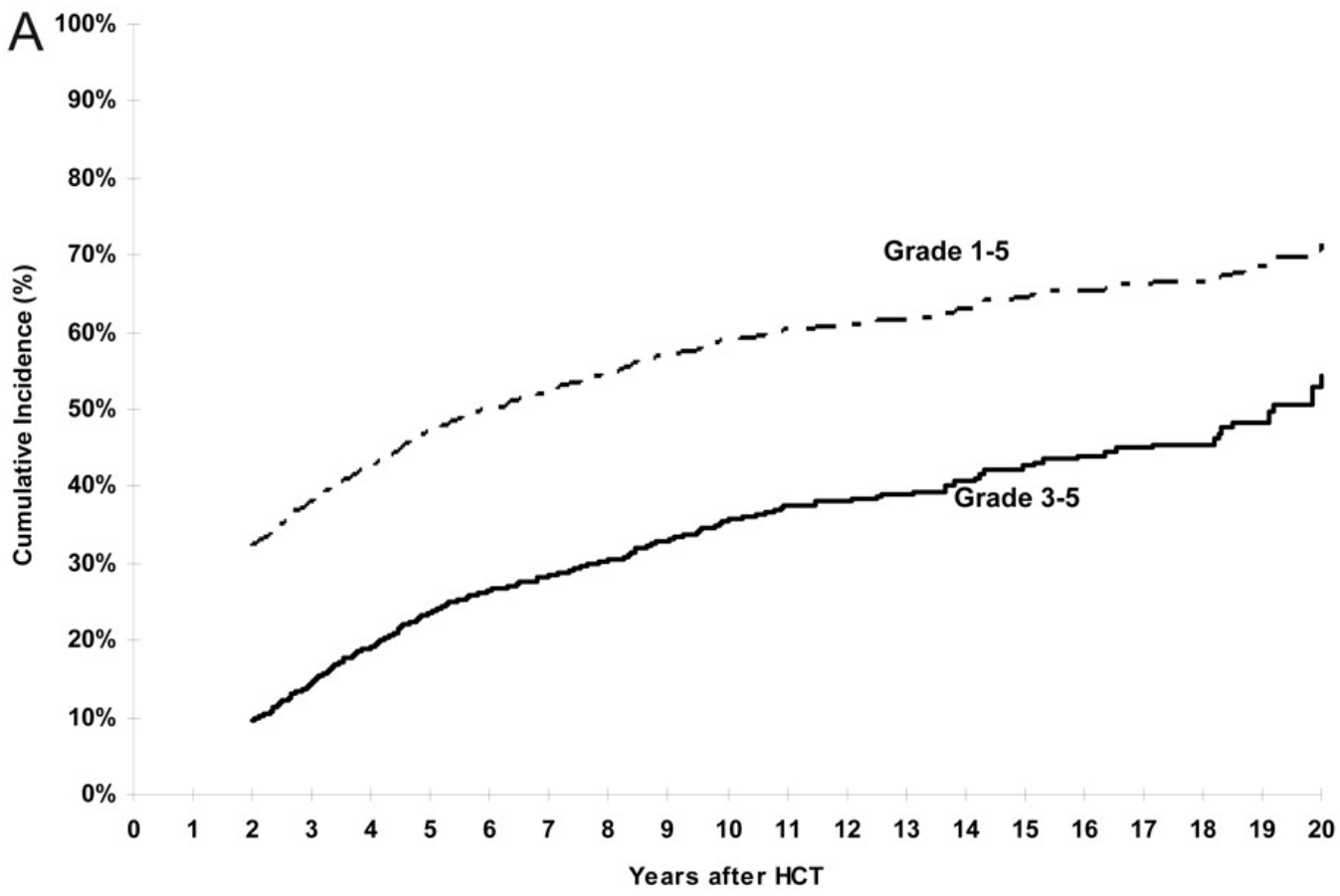
Causes of death



- Cardiopulmonary
- Subsequent malignancies

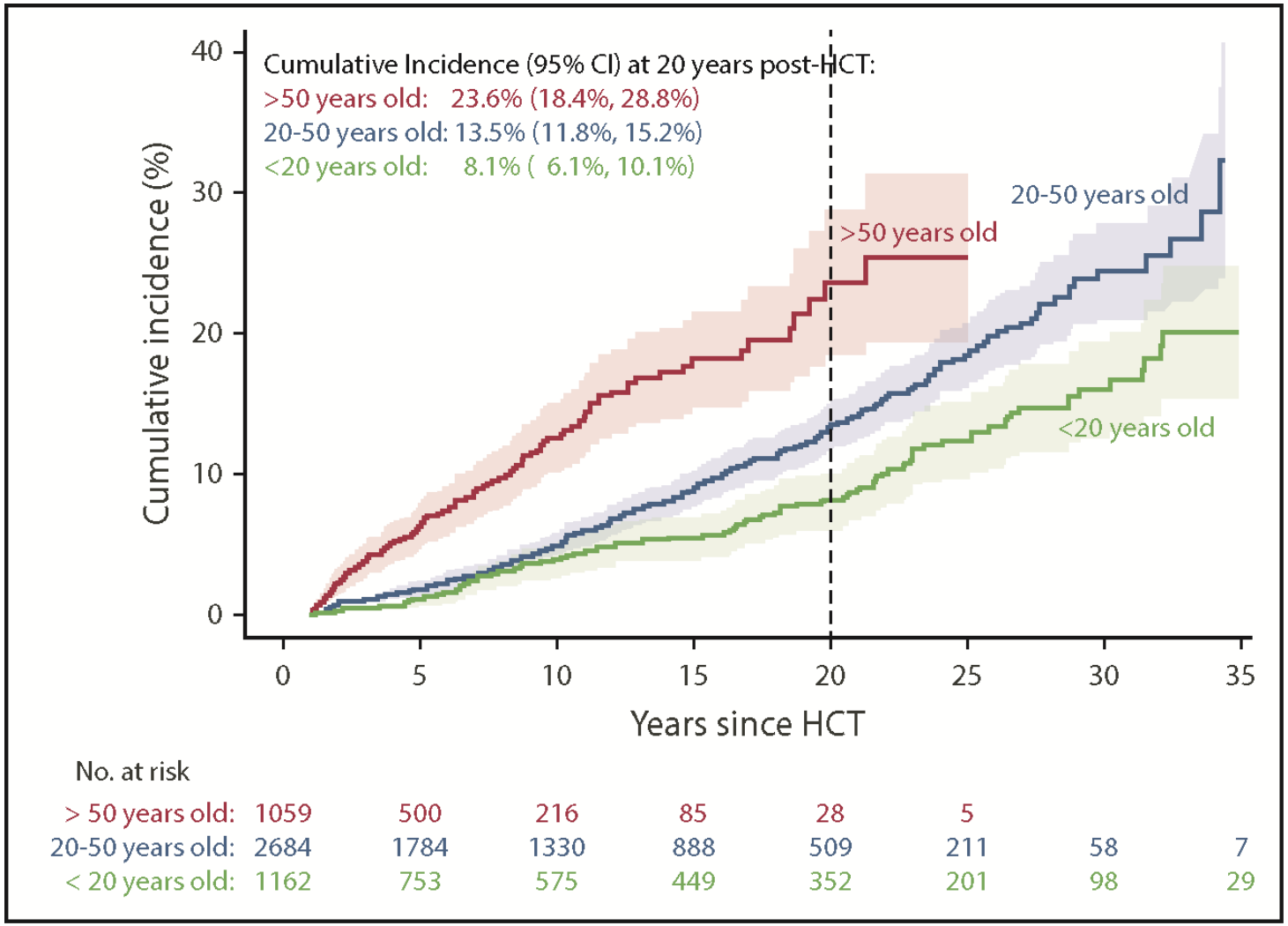
Wong et al. J Natl Cancer Inst 2020; 112 (11): 1153-1161

Chronic health conditions



Sun et al. Blood 2010; 116 (17): 3129-3139

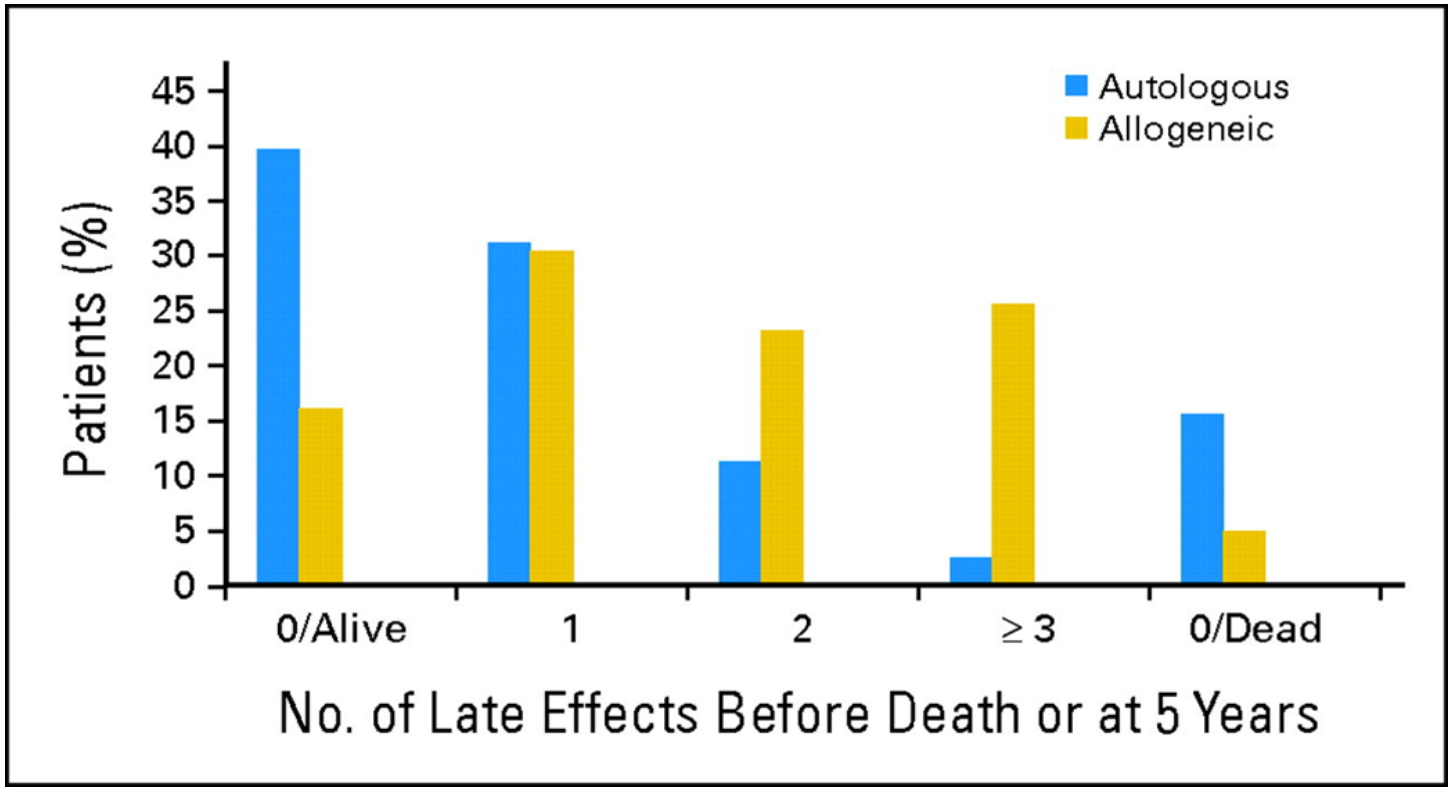
Subsequent malignant neoplasms



Baker et al. Blood 2019; 133(26): 2790-2799

Impact of Late Effects on the patient?

- Despite positive perception of HRQOL recovery in HCT, many long-term survivors report residual deficits



Survivors with ≥ 3 late effects had lower physical functioning, lower likelihood of full-time work or study, and higher likelihood of limitations on usual activities

Khera et al. J Clin Oncology 2012; 30: 71-77

Summary

- GVHD is a leading cause of non-relapse mortality after hematopoietic cell transplantation
- GVHD has a significant impact on health-related quality of life
- Hematopoietic cell transplant recipients have an increased risk of late effects and chronic health conditions
- Early studies in chronic GVHD populations demonstrate significant patient-reported disability

Thank you