



Dana-Farber
Cancer Institute

Survivorship After Allogeneic Stem Cell Transplantation

Corey Cutler, MD, MPH, FRCP(C)

Director, Stem Cell Transplantation Program,
Dana-Farber Cancer Institute

Professor of Medicine,
Harvard Medical School

Boston, MA

Disclosures

Consulting Fees/Honoraria: Sanofi, Incyte, Syndax, CSL Behring, GSK, CareDx

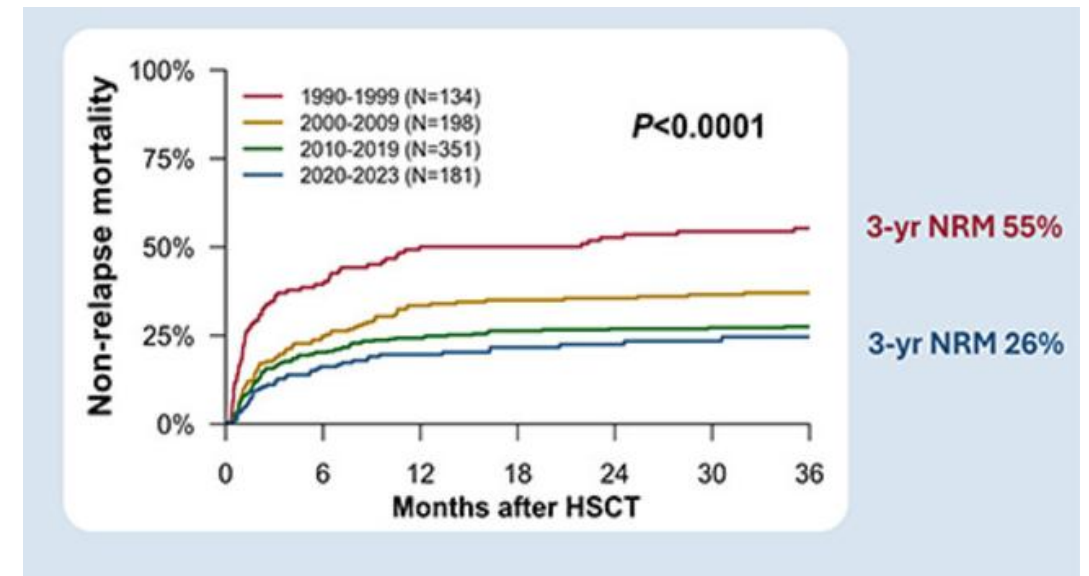
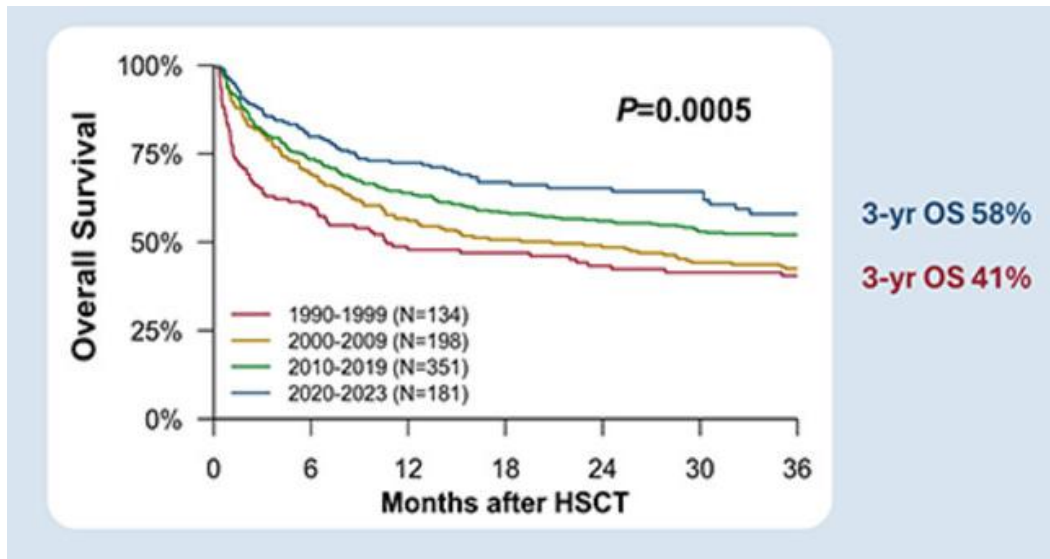
Consulting Fees/Equity: Cimeio, Oxford Immune Algorithmics, OrcaBio

None relevant to this discussion

Outcomes in Allogeneic Transplantation

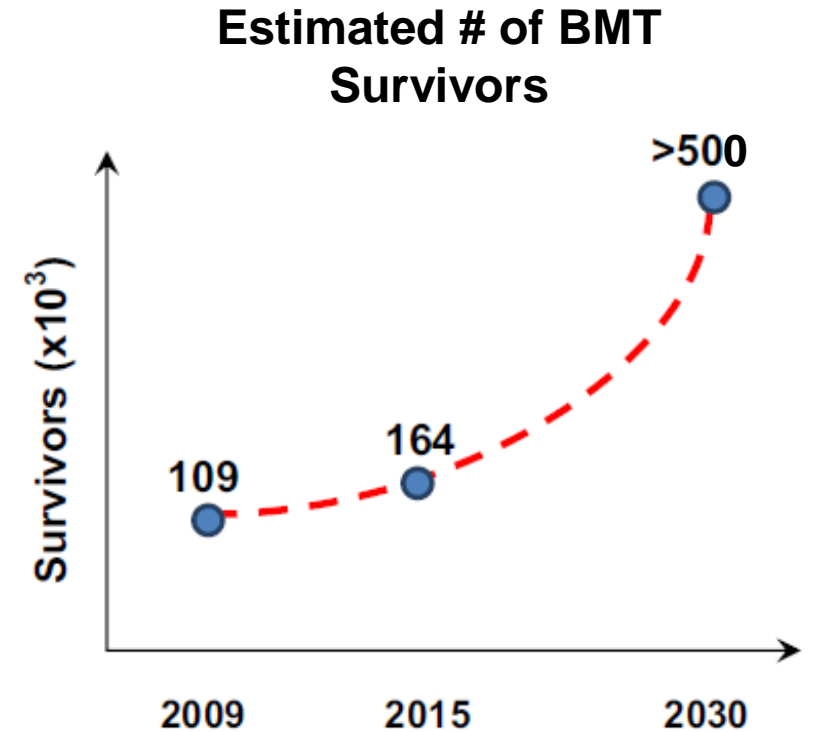
Transplant technology is improving

- ▶ Donor-recipient matching
- ▶ GVHD prophylaxis/therapy
- ▶ Treatment of complications
- ▶ Supportive care

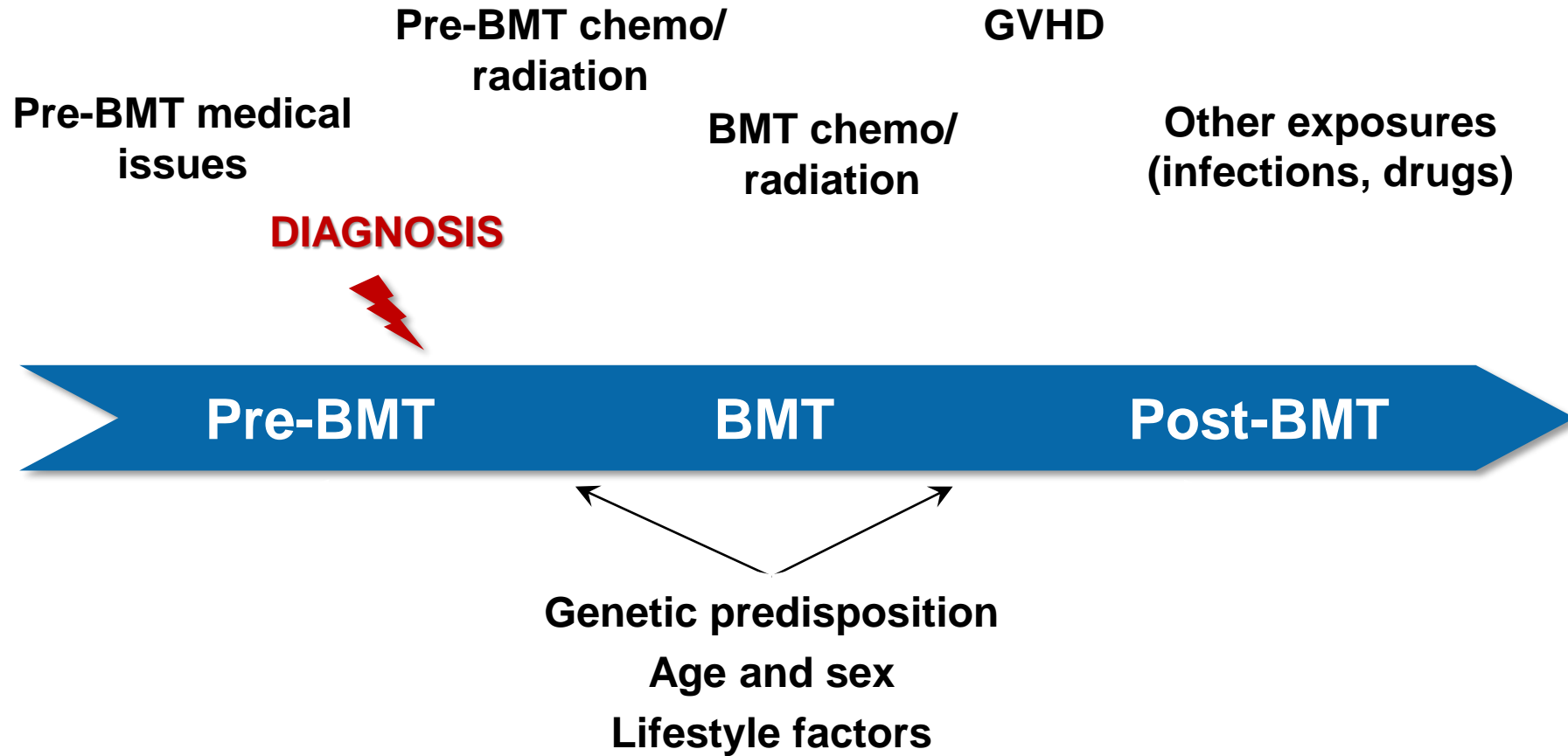


Stating The Obvious

- ▶ Transplantation might cure the hematologic malignancy, but it is not the panacea for the overall health of the transplant recipient
- ▶ Survivorship after transplantation is a “problem” we have been striving to intentionally create for years
- ▶ We are now obligated to deal with the consequences of our therapeutic success



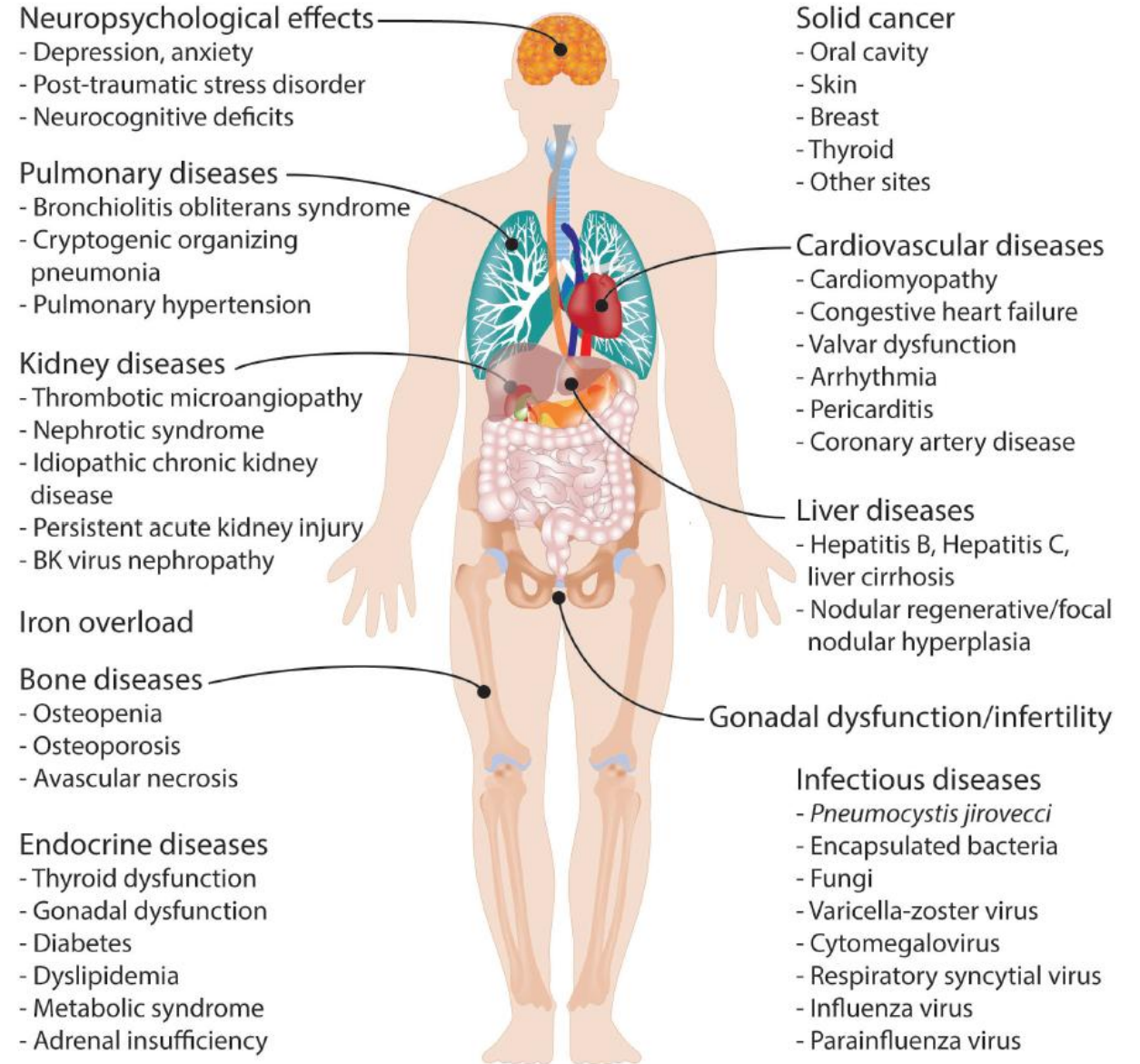
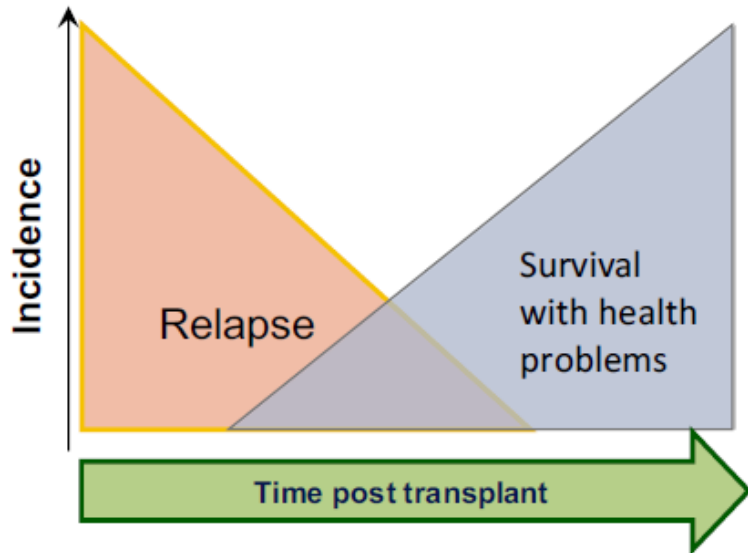
Why Is Survivorship in BMT Different?



Survivorship in BMT

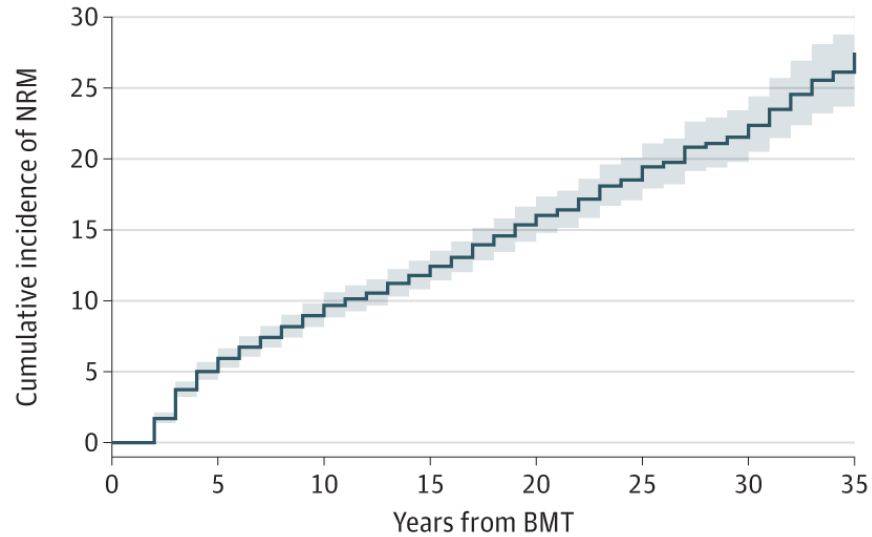
- ▶ 2 components:
 - ▶ Surviving Malignancy
 - ▶ Surviving Transplantation

- ▶ Different sets of risks and complications need to be considered



The Good News

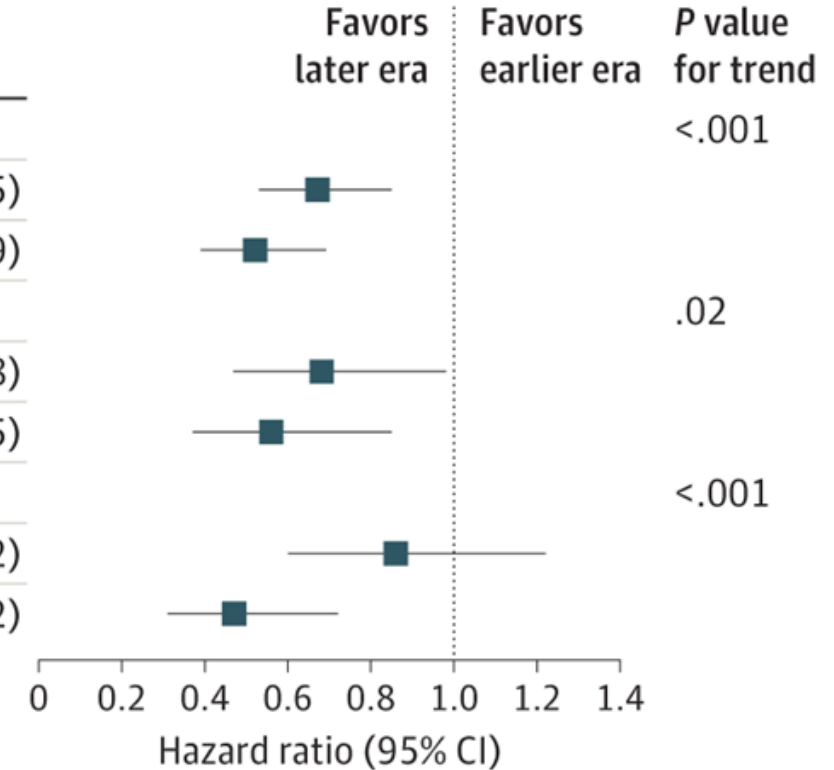
B Incidence of nonrecurrence-related mortality



No. at risk 4741 4191 2850 1934 1212 675 342 145

Death is unfortunately, inevitable

Source	Hazard ratio (95% CI)
All-cause mortality	
1990-2004	0.67 (0.53-0.85)
2005-2014	0.52 (0.39-0.69)
Recurrence-related mortality	
1990-2004	0.68 (0.47-0.98)
2005-2014	0.56 (0.37-0.85)
Nonrecurrence-related mortality	
1990-2004	0.86 (0.60-1.22)
2005-2014	0.47 (0.31-0.72)

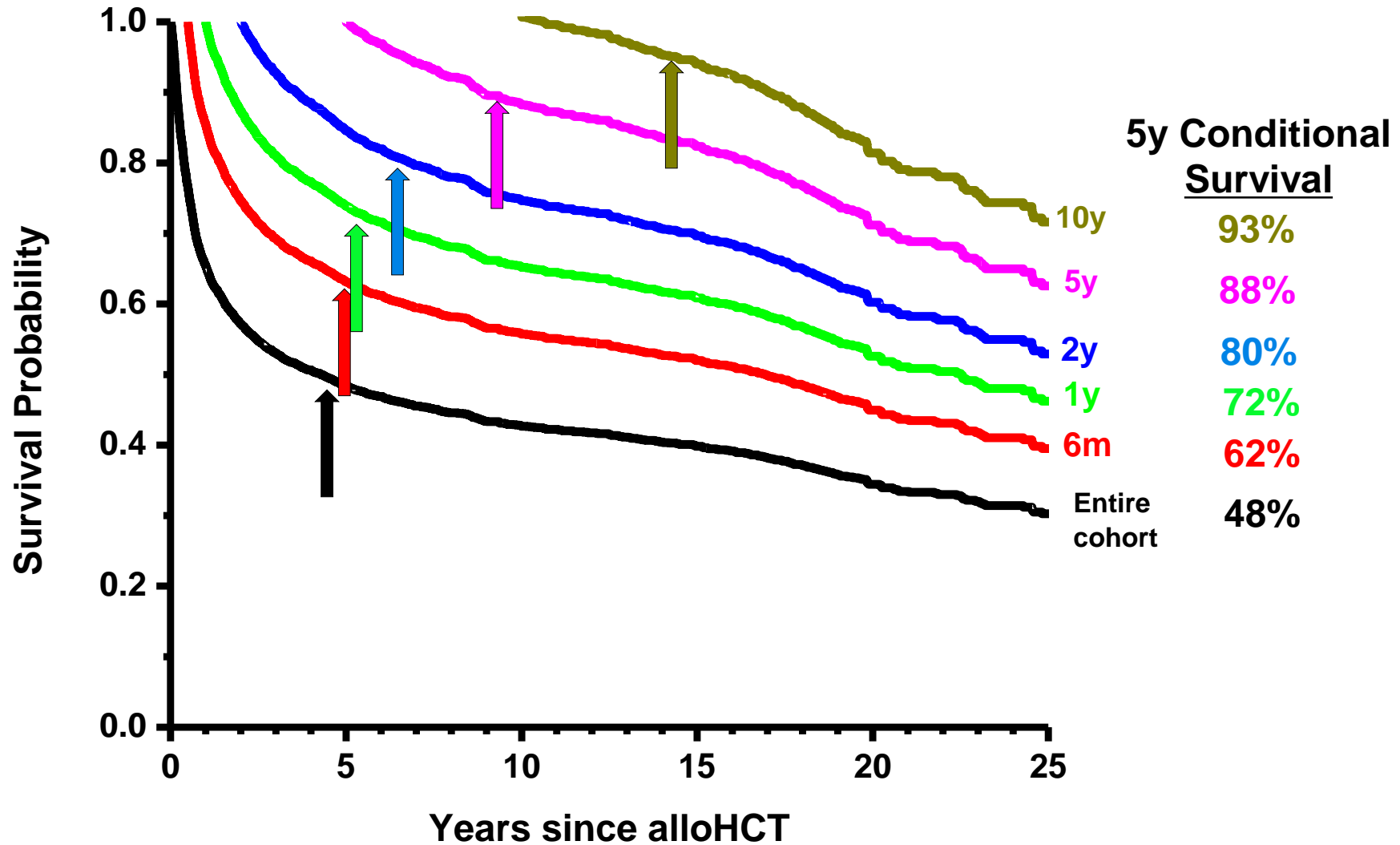


BMT Survivors Study (BMTSS):

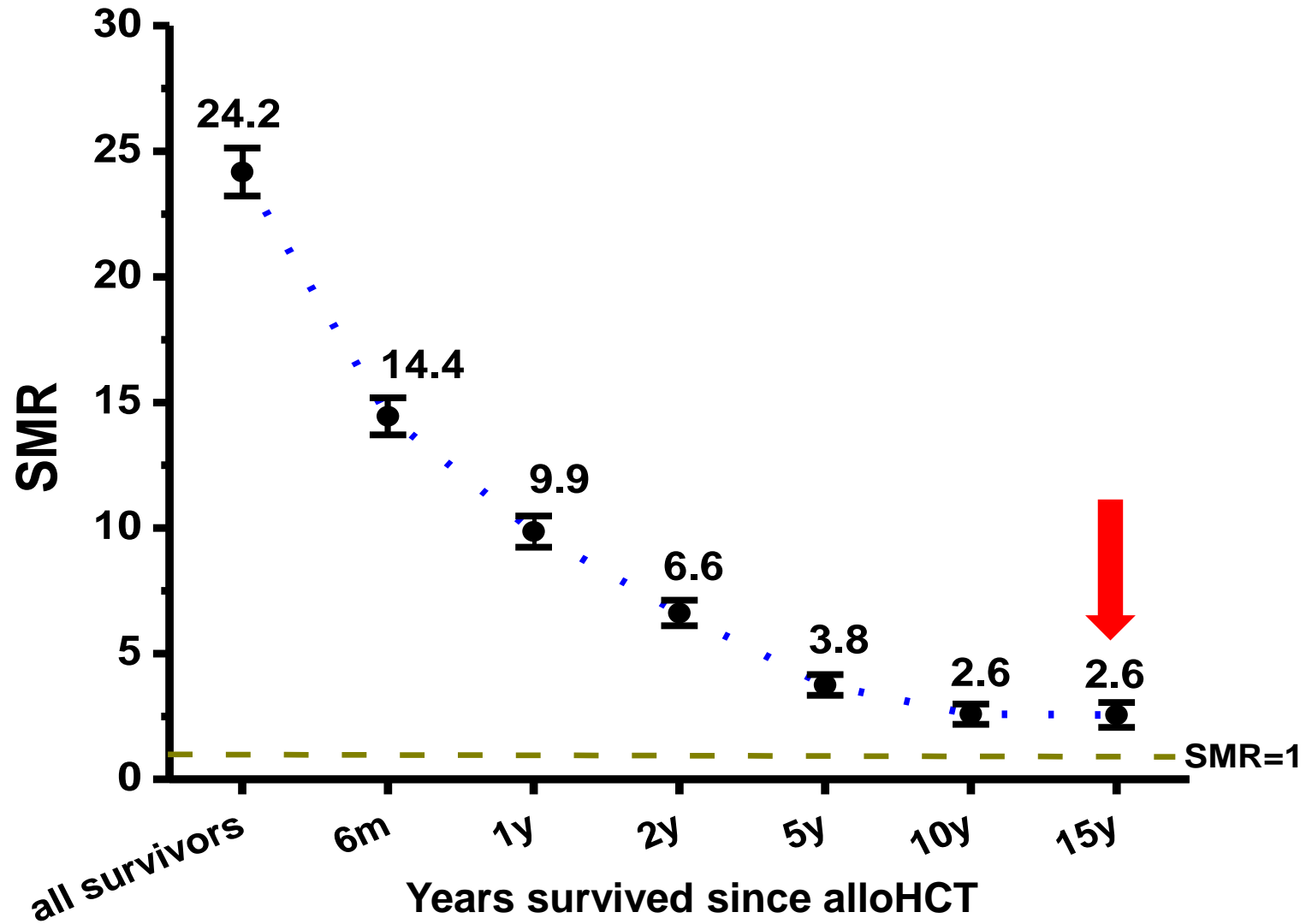
Conditional Survival and Mortality Risks After Allogeneic HSCT

	Number	Percent / range
Cohort size	4288	
Year of alloHCT	1976 – 2013	
Males	2421	56%
Age at HCT, avg	38 y	(0.4 – 75 y)
Race/ethnicity	2301	54%
White		
Hispanic	1272	30%
Asian	450	11%
African-American	147	3%
Other	92	2%
Length of survival		
> 1y	2796	65%
> 7y	1275	30%

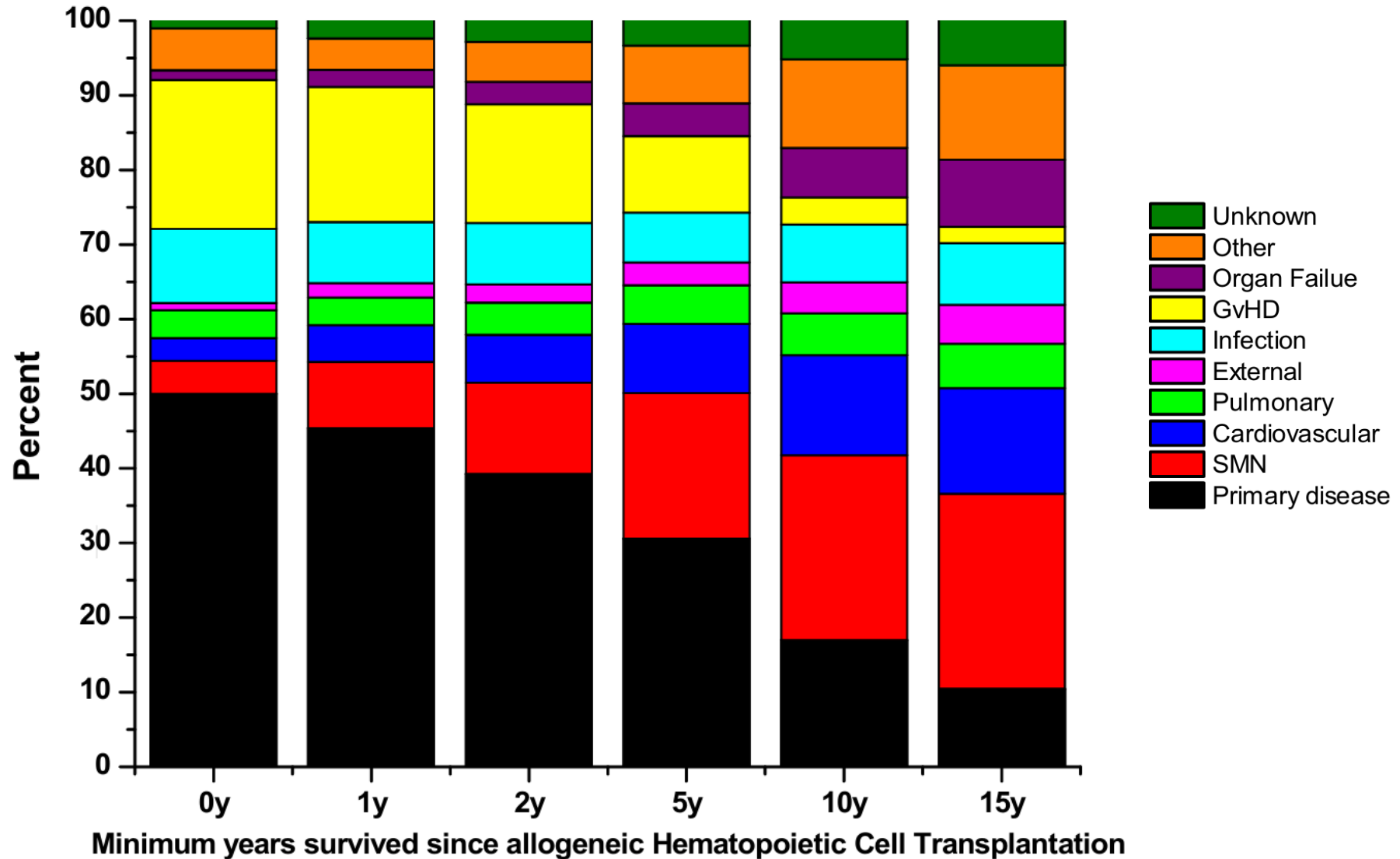
Survival Rates, Conditional on Years Survived



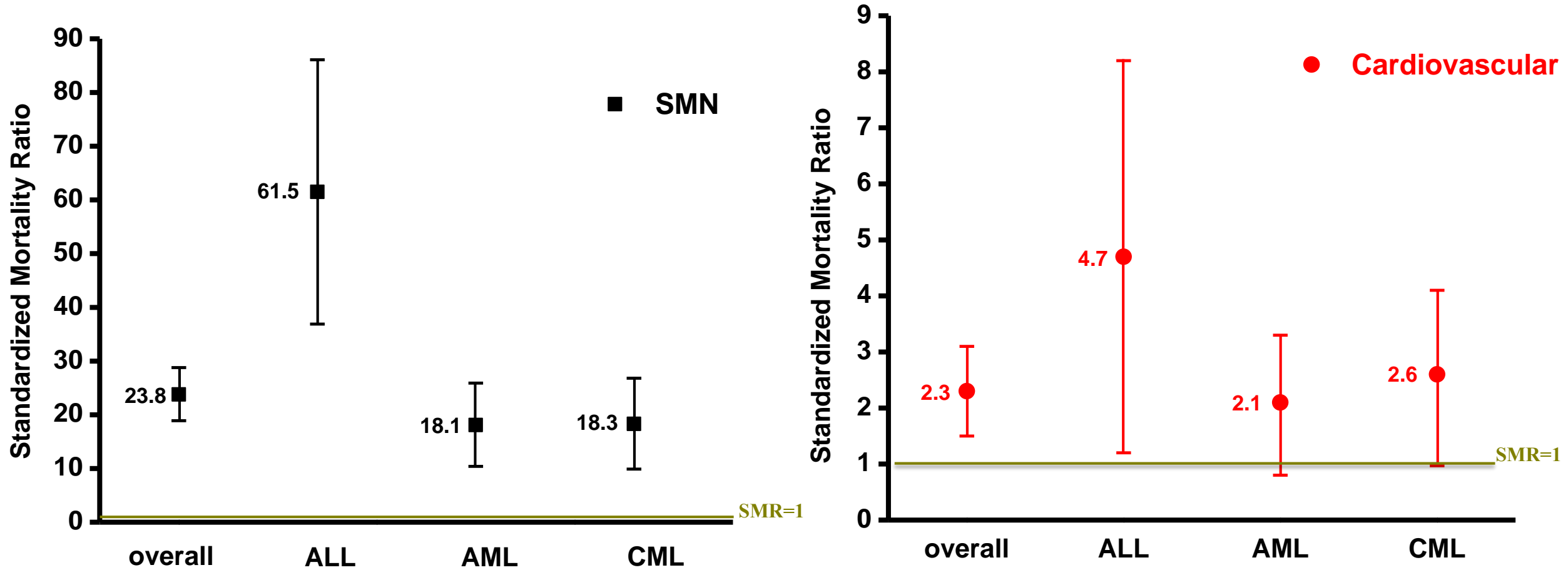
Standardized Mortality Ratio (SMR)



Causes of Death



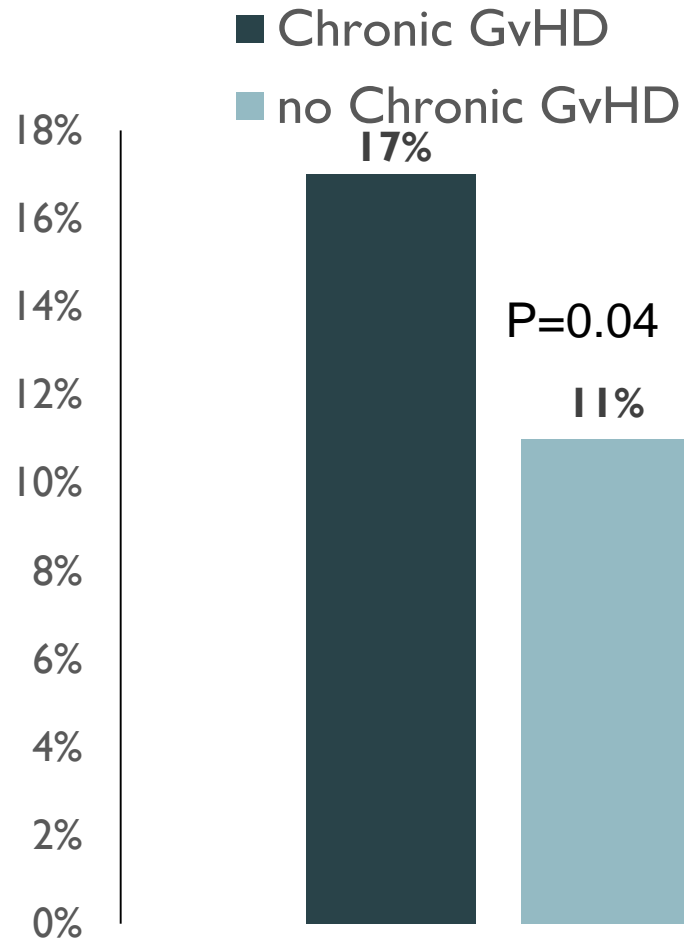
Cause-Specific Standardized Mortality Ratio



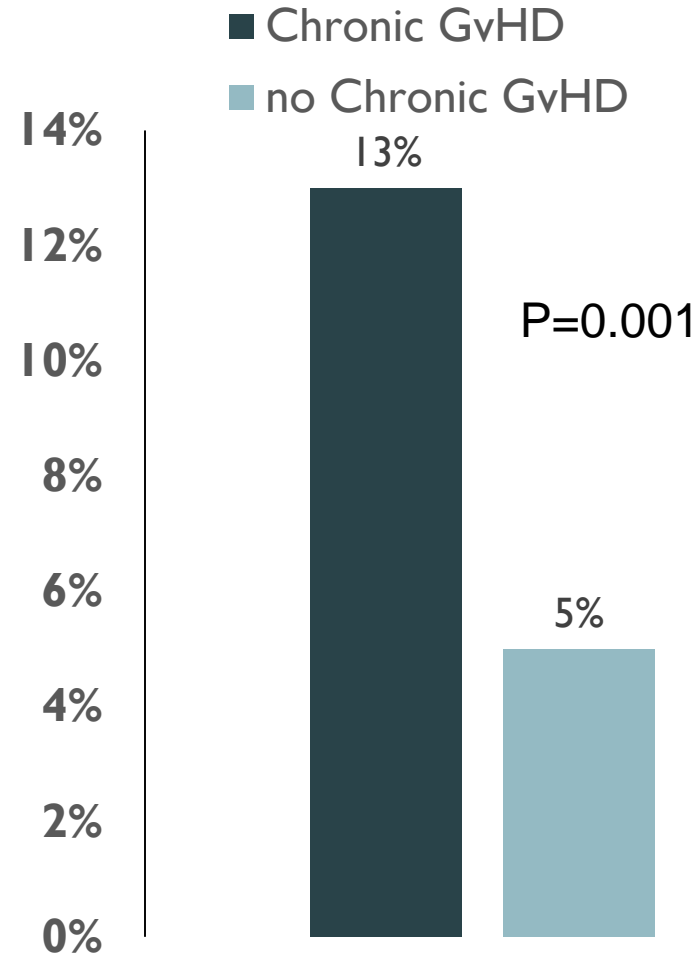
Late Effects with/without Chronic GvHD

Condition	No cGvHD (%)	cGvHD (%)	P
Ocular	52.4	63.5	0.007
Oral	17	30.9	<0.0001
Pulmonary	11.9	23	0.0005
GI	7.6	12.5	0.05
Neurology	23.1	33.2	0.007
Frailty	6.1	17.1	<0.0001
Endocrine	42.6	48	0.19
Cardiac	7.2	9.9	0.26
Renal	1.8	0.3	0.08
Second malignancy	26.7	26.3	0.91

Diabetes



Osteonecrosis



Analysis adjusted for age at BMT, sex, race/ethnicity, primary cancer diagnosis, graft source, risk of relapse, BMI, smoking status, comorbidities and exposure to TBI

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Frailty

Responses from BMTSS questionnaire used to construct frailty phenotype

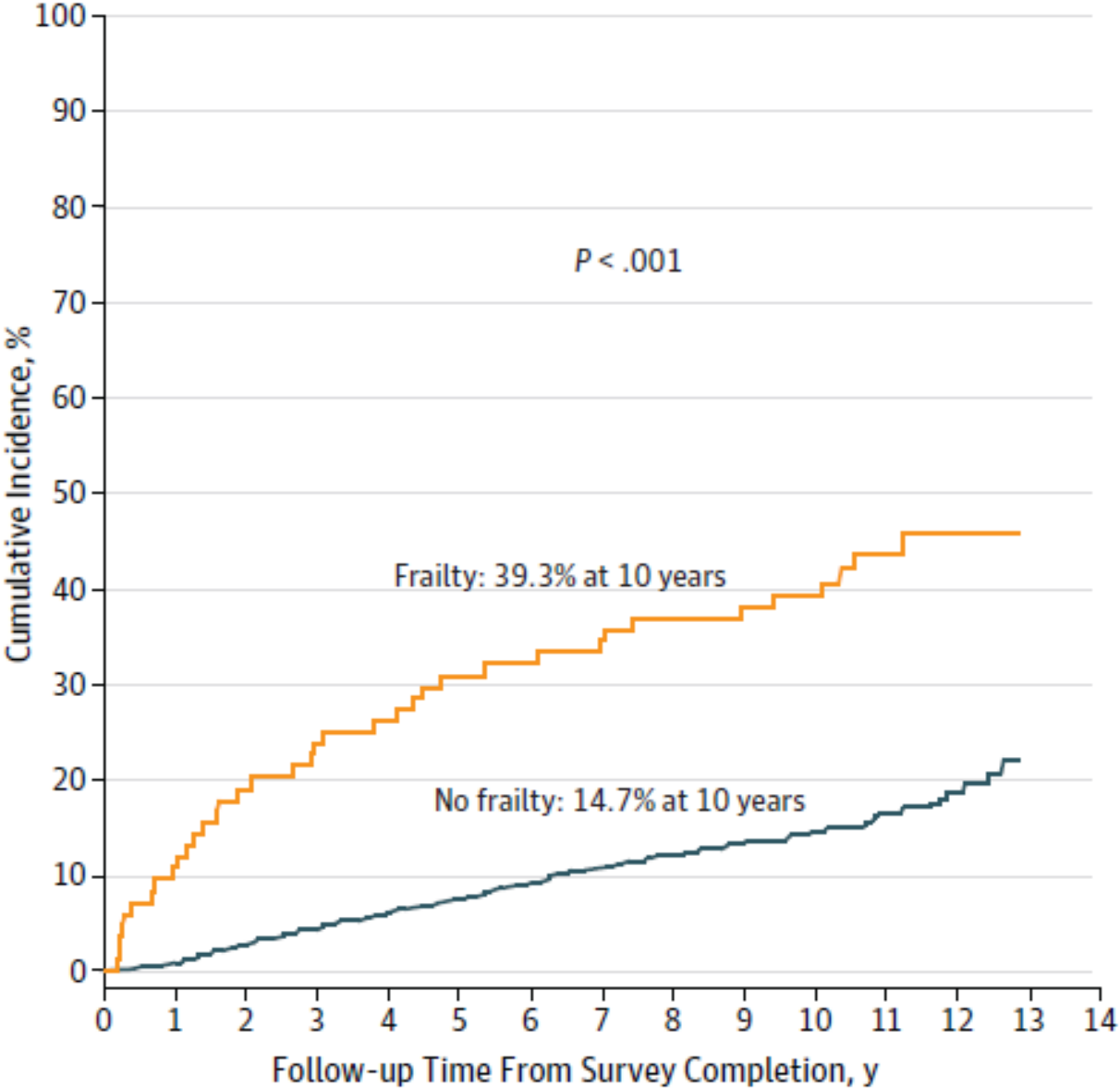


Domains	
1	Low lean muscle mass
2	Exhaustion
3	Low Energy Expenditure
4	Slowness
5	Weakness



Frailty = presence of ≥ 3 conditions

Frailty Matters



Medical Monitoring after BMT

GUIDELINES



Recommended Screening and Preventive Practices for Long-Term Survivors after Hematopoietic Cell Transplantation

Navneet S. Majhail,^{1,2} J. Douglas Rizzo,³ Stephanie J. Lee,⁴ Mahmoud Aljurf,⁵ Yoshiko Atsuta,⁶ Carmem Bonfim,⁷ Linda J. Burns,⁸ Naeem Chaudhri,⁵ Stella Davies,⁹ Shinichiro Okamoto,¹⁰ Adriana Seber,¹¹ Gerard Socie,¹² Jeff Szer,¹³ Maria Teresa Van Lint,¹⁴ John R. Wingard,¹⁵ Andre Tichelli¹⁶ for the Center for International Blood and Marrow Transplant Research (CIBMTR), American Society for Blood and Marrow Transplantation (ASBMT), European Group for Blood and Marrow Transplantation (EBMT), Asia-Pacific Blood and Marrow Transplantation Group (APBMT), Bone Marrow Transplant Society of Australia and New Zealand (BMTSANZ), East Mediterranean Blood and Marrow Transplantation Group (EMBT), and Sociedade Brasileira de Transplante de Medula Ossea (SBTMO)

Bone Marrow Transplantation (2015) 50, 3–9
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www.nature.com/bmt



How I Treat

How I monitor long-term and late effects after blood or marrow transplantation

Smita Bhatia,¹ Saro H. Armenian,² and Wendy Landier¹

¹Institute for Cancer Outcomes and Survivorship, University of Alabama at Birmingham, Birmingham, AL; and ²City of Hope, Duarte, CA

The New England Journal of Medicine

Clinical Practice

LONG-TERM CARE AFTER HEMATOPOIETIC-CELL TRANSPLANTATION IN ADULTS

JOSEPH H. ANTIN, M.D.



ELSEVIER

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org



Metabolic Syndrome and Cardiovascular Disease after Hematopoietic Cell Transplantation: Screening and Preventive Practice Recommendations from the CIBMTR and EBMT

Zachariah DeFilipp¹, Rafael F. Duarte², John A. Snowden³, Navneet S. Majhail⁴, Diana M. Greenfield⁵, José López Miranda⁶, Mutlu Arat⁷, K. Scott Baker⁸, Linda J. Burns⁹, Christine N. Duncan¹⁰, Maria Gillece¹¹, Gregory A. Hale¹², Mehdi Hamadani¹³, Betty K. Hamilton⁴, William J. Hogan¹⁴, Jack W. Hsu¹⁵, Yoshihiro Inamoto¹⁶, Rammurti T. Kamble¹⁷, Maria Teresa Lupo-Stanghellini¹⁸, Adriana K. Malone¹⁹, Philip McCarthy²⁰, Mohamad Mohty^{21,22,23}, Maxim Norkin¹⁵, Pamela Paplham²⁰, Muthalagu Ramanathan²⁴, John M. Richart²⁵, Nina Salooja²⁶, Harry C. Schouten²⁷, Helene Schoemans²⁸, Adriana Seber^{29,30}, Amir Steinberg¹⁹, Baldeep M. Wirk³¹, William A. Wood³², Minoo Battiwalla³³, Mary E.D. Flowers⁸, Bipin N. Savani³⁴, Bronwen E. Shaw^{13,*} on behalf of the CIBMTR Late Effects and Quality of Life Working Committee and the EBMT Complications and Quality of Life Working Party



blood

REVIEW

Clinical guidelines for gynecologic care after hematopoietic SCT. Report from the international consensus project on clinical practice in chronic GVHD

B Frey Tirri¹, P Häusermann², H Bertz³, H Greinix⁴, A Lawitschka⁵, C-P Schwarze⁶, D Wolff⁷, JP Halter⁸, D Dörfler⁹ and R Moffat^{10,11}

THE Definitive Guidelines for Post-Transplant Survivorship Care

Transplantation and Cellular Therapy 30 (2024) 349–385



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Transplantation and
Cellular Therapy

journal homepage: www.astctjournal.org

ASTCT

American Society for
Transplantation and Cellular Therapy

Guideline

International Recommendations for Screening and Preventative Practices for Long-Term Survivors of Transplantation and Cellular Therapy: A 2023 Update



Seth J. Rotz^{1,2,*,#}, Neel S. Bhatt^{3,*}, Betty K. Hamilton², Christine Duncan⁴, Mahmoud Aljurf⁵, Yoshiko Atsuta⁶, Kristen Beebe⁷, David Buchbinder⁸, Peggy Burkhard⁹, Paul A. Carpenter³, Naeem Chaudhri¹⁰, Mohamed Elemary¹¹, Mahmoud Elsayw¹², Gregory MT Guilcher¹³, Nada Hamad¹⁴, Amado Karduss¹⁵, Zinaida Peric¹⁶, Duncan Purtill¹⁷, Douglas Rizzo^{18,19}, Morgani Rodrigues²⁰, Maria Belén Rosales Ostriz²¹, Nina Salooja²², Helene Schoemans²³, Adriana Seber²⁴, Akshay Sharma²⁵, Alok Srivastava²⁶, Susan K Stewart²⁷, K. Scott Baker³, Navneet S. Majhail²⁸, Rachel Phelan^{19,29}

[https://www.astctjournal.org/article/S2666-6367\(23\)01713-X/fulltext](https://www.astctjournal.org/article/S2666-6367(23)01713-X/fulltext)

ASTCT Clinical Practice Guidelines



checkup 12 months

Post-transplant care guide

1.888.999.6743 | BeTheMatch.org/patient



Congratulations—on the upcoming one-year anniversary of your transplant! To help you understand and prepare for your follow-up care, this guide includes an easy-to-understand list of tests and evaluations for your twelve-month appointments. This guide is the second in the series of three (6 month and 24+ month also available), based on recommendations from experts in post-transplant care¹, and brought to you by Be The Match®.

Why your twelve-month checkup matters

As a transplant recipient, your health needs monitoring and protection. Your health care team needs to regularly check how you are improving and look for potential issues. When issues are caught early, there may be more options for treatment, and those treatments can be more effective.

Even if you are feeling well, post-transplant checkups are very important to managing your health and staying healthy.

About this guide

This guide is based on a publication of post-transplant care recommendations¹ developed by doctors and researchers from around the world. This information is not intended to replace the recommendations of your transplant doctor. You may need different tests or evaluations based on your unique situation. Your transplant doctor knows you best, so follow his or her recommendations carefully.



Free mobile app

Use our free mobile app to:

- Access these guidelines anytime, anyplace
- Generate a list of tests and evaluations customized to your unique situation
- E-mail information to yourself, or your health care team

Available on iPhone®, iPad®, Android™, and BlackBerry®

Online at m.marrow.org/HCT



Scan QR Code
to download app

Medical Monitoring

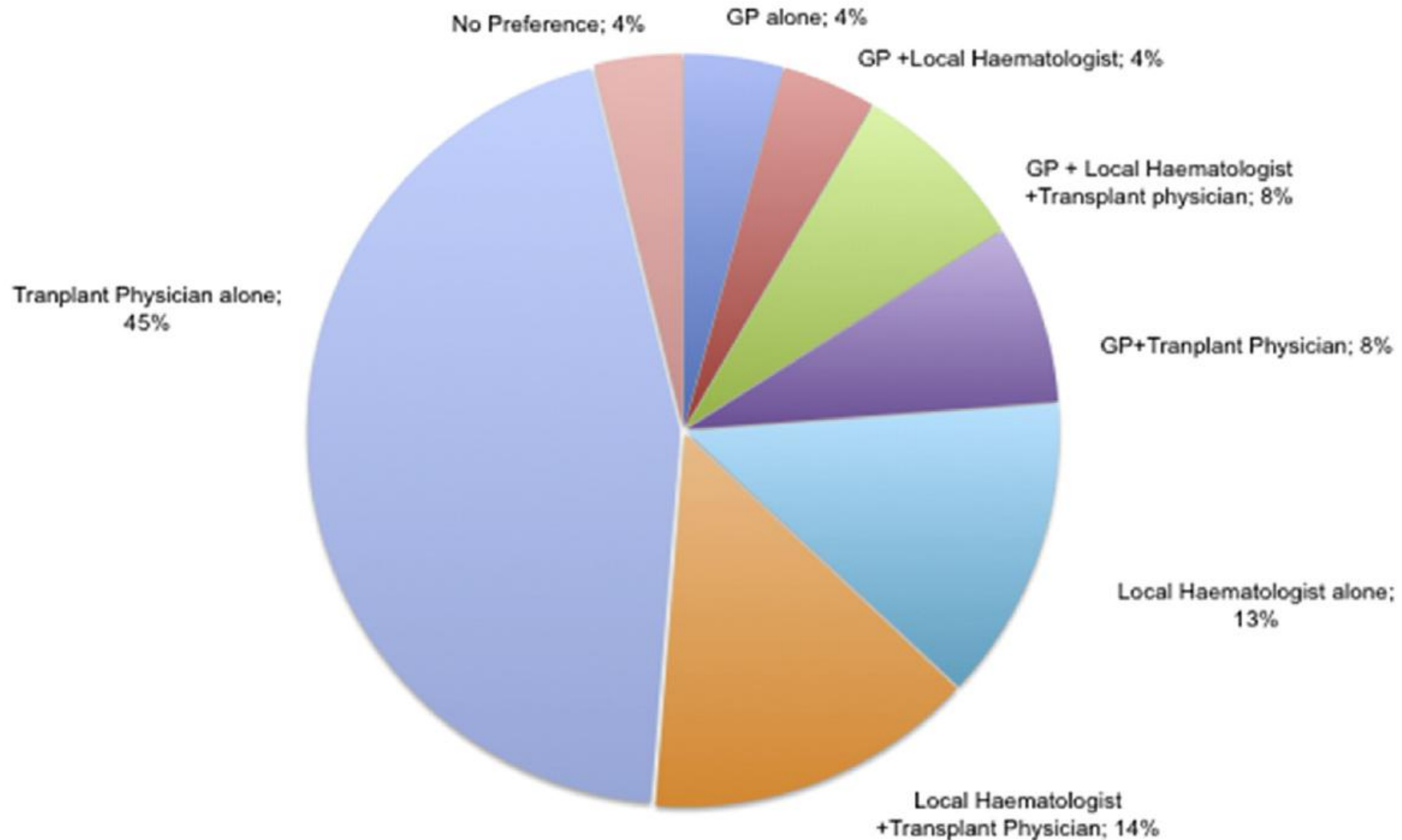
Late complications	Frequency	Risk-adapted screening
Cardiovascular	Up to 15%	<ul style="list-style-type: none">● BMI assessments● Lipid profile assessments● Echo/EKG
Metabolic syndrome	31 to 49%	<ul style="list-style-type: none">● BMI assessments● Lipid profile assessments● Blood pressure assessments
Kidney disease	4 to 80%	<ul style="list-style-type: none">● Blood pressure assessments● Renal function/urinalysis
Endocrine and gonadal dysfunction	5 to 40%	<ul style="list-style-type: none">● Thyroid function tests● LH/FSH/testosterone and estrogen levels
Infection	Variable depending on the type of infection	<ul style="list-style-type: none">● Lymphocyte subsets● Immunoglobulin levels● Hepatitis and HIV tests● CMV/EBV monitoring● Fungal tests if high suspicion
Liver complications	4 to 80%	<ul style="list-style-type: none">● Liver function tests● Viral testing● Liver biopsy in those at risk

Medical Monitoring

Late complications	Frequency	Risk-adapted screening
Iron overload	25 to 50%	<ul style="list-style-type: none">• Serum ferritin• MRI liver
Pulmonary complications	30 to 60%	<ul style="list-style-type: none">• Pulmonary function tests• Radiologic evaluation as needed
Bone disease	Up to 50%	<ul style="list-style-type: none">• DEXA scan• MRI for avascular necrosis
Secondary cancers	2 to 11%	<ul style="list-style-type: none">• History and physical• Breast MRI/mammogram• Skin exam• Colonoscopy
Ocular problems	4 to 50%	<ul style="list-style-type: none">• Ophthalmologic testing including Schirmer's
Oral complications	Up to 80%	<ul style="list-style-type: none">• Dental examination
Neuropsychological	10 to 40%	<ul style="list-style-type: none">• Neuropsychological testing• MRI brain as indicated
Psychological problems	12 to 40%	<ul style="list-style-type: none">• Clinical assessment/distress testing
Sexual dysfunction	Up to 70%	<ul style="list-style-type: none">• Genital exam• Questionnaires for sexual dysfunction
Sleep problems	14 to 50%	<ul style="list-style-type: none">• Screen for sleep disorders

Where Do Survivors Want to Receive Care?

Preferred Medical Providers nominated by HSCT survivors for their LTFU care
n=441



Challenges to BMT Survivorship Care

Transplant center and community healthcare provider level barriers

- Lack of resources for survivorship care
- Lack of interest and competing priorities
- Lack of awareness of clinical and psychosocial needs of survivors
- Lack of awareness of screening and prevention guidelines
- Lack of tools to facilitate care of survivors
- Insufficient reimbursement for providing care for survivors
- Inadequate communication (transplant center and community health care providers)

Patient-level barriers

- Lack of awareness of risks of late complications
- Lack of awareness of screening and prevention guidelines
- Socio-demographic barriers (for example, socioeconomic status, distance)
- Economic barriers (insurance coverage, out-of-pocket costs)

Healthcare system level barriers

- Lack of/inadequate reimbursement for survivorship care
- Lack of resources and specialists
- Competing priorities
- Existing models of care inadequate for care of survivors
- Insufficient prospective randomized trials to guide care of survivors

Ways to Improve Survivorship Care

1. Survivorship Care Plan / Treatment Summary

Critical Information in a Treatment Summary

- **Demographics**
- **Background Information:** Family History, Genetics, Tobacco use
- **Diagnostic Tests:** When performed and results
- **Malignant Tumor Characteristics:** Site, stage, grade, markers
- **Dates of treatment:** initiation and completion
 - Surgery, radiotherapy, chemotherapy
- **Treatment Regimen:** Total dosage, clinical trials (if any), and toxicities experienced during treatment
- **Support Services Accessed:** Psychosocial, nutritional, other
- **Care Team Contact Information:** Identification of a key coordinator of continuing care

Survivorship Plans

A personalized, comprehensive document outlining a patient's treatment history and follow-up care strategy

Clearly delineates timing, frequency of testing and follow-up visits

Clearly ascribes responsibility for follow-up to the patient, the primary hematologist/primary care or transplant physician.

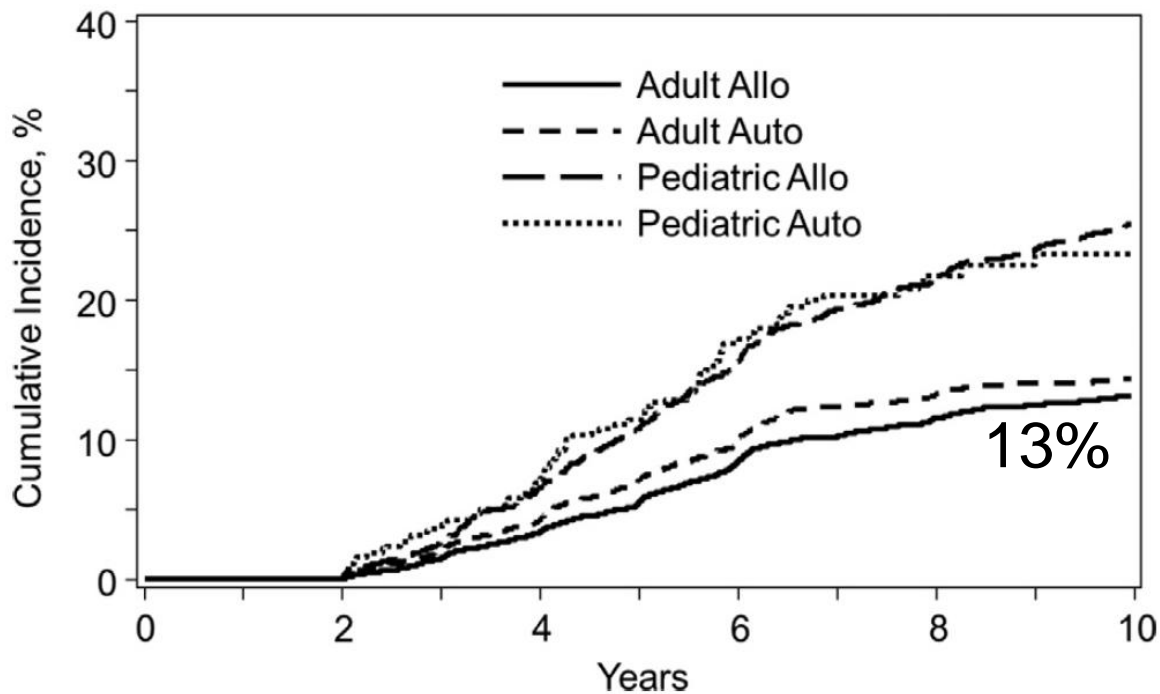
BMTInfoNet and nBMTLink offer Survivorship Plan assistance

Ways to Improve Survivorship Care

1. Survivorship Care Plan / Treatment Summary
2. Prevent Loss to Follow-Up

Preventing Loss to Follow-Up

Characteristics	N	HR (95% CI)	P-Value
Age at transplant (years)			<0.0001
51+	4665	Reference	
41-50	2307	1.38 (1.14-1.67)	0.0009
18-40	3395	2.19 (1.80-2.66)	<0.0001
Insurance			<0.0001
Private	6584	Reference	
None	70	2.33 (1.30-4.17)	0.004
Public	2394	1.29 (1.13-1.48)	0.0002
Other/Unspecified	449	1.41 (1.04-1.92)	0.03
Missing	870	1.22 (0.85-1.74)	0.29
Distance to center (miles)			0.0008
0-99	6056	Reference	
100+	2438	1.39 (1.11-1.72)	0.004
Unknown	1873	1.23 (1.00-1.53)	0.05
Marital status			0.008
Married	6644	Reference	
Single/Divorced/Widowed	3034	1.26 (1.09-1.46)	0.002
Missing	689	0.99 (0.75-1.31)	0.93
Disease			0.0008
Malignant/except CLL	9389	Reference	
CLL	525	0.61 (0.43-0.88)	0.007
Non-malignant	453	1.52 (1.18-1.94)	0.001



Ways to Improve Survivorship Care

1. Survivorship Care Plan / Treatment Summary
2. Prevent Loss to Follow-Up
3. Listen to the Patient!

Unmet Needs In Survivorship

Rank	Unmet Need	No. of Respondents (%)*
Male (N = 62)		
1	Paying household bills or other payments	10 (23)
2	Worry about earning money	10 (16)
3	Dealing with not feeling able to set future goals or make long-term plans	10 (16)
4	Dealing with changes in how my body appears	10 (17)
5	Adapting to living on a pension or disability allowance	09 (14)
Female (N = 48)		
1	Coping with having a bad memory or lack of focus	13 (28)
2	Dealing with losing confidence in my own abilities	11 (23)
3	Dealing with not feeling able to set future goals or make long-term plans	11 (23)
4	Being told I have cancer	10 (20)
5†	Knowing how to relax	10 (21)
5†	Dealing with changes in how my body appears	10 (21)

BMT Survivors – Psychosocial effects

Complication	Prevalence	Risk factors
Depression/anxiety	5 to 40%	<ul style="list-style-type: none"> • Younger age • Female sex • Lower household income • Poor health status • Use of steroids • Poor social support
Post-traumatic stress disorder	3 to 19%	<ul style="list-style-type: none"> • History of depression or anxiety at HCT • Younger age • Marital status-single • Low social support
Psychologic distress	3 to 40%	<ul style="list-style-type: none"> • Active chronic GVHD • Use of steroids • Lower household income • Low social support
Financial burden	20 to 70%	<ul style="list-style-type: none"> • Younger age • Low household income • Poor physical and mental functioning • Chronic GVHD
Inability to return to work	15 to 40%	<ul style="list-style-type: none"> • Lower physical function • Multimorbidity • Female sex • Use of peripheral blood as stem cell source • Pre-HCT unemployment/disability • Active GVHD

“HSCT has a profound and pervasive impact on the life of survivors-reducing their horizons and shrinking various parts of their worlds. While HSCT survivors can describe the ways in which their life has changed, many of their fears, anxieties, regrets and concerns are existential in nature and are ill-defined-making it exceedingly unlikely that they would be adequately captured by standard psychometric measures of QoL post HSCT”