

BMT Survivorship:

The Need for Care Continues after Treatment Ends

12th Annual Controversies in Hematologic Malignancies Symposium

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knowledge changing life



Disclosures

- Bluebird bio: Advisory Board Participant
- Amgen: Research Funding

Objectives



Increase awareness of ongoing medical issues encountered by BMT survivors

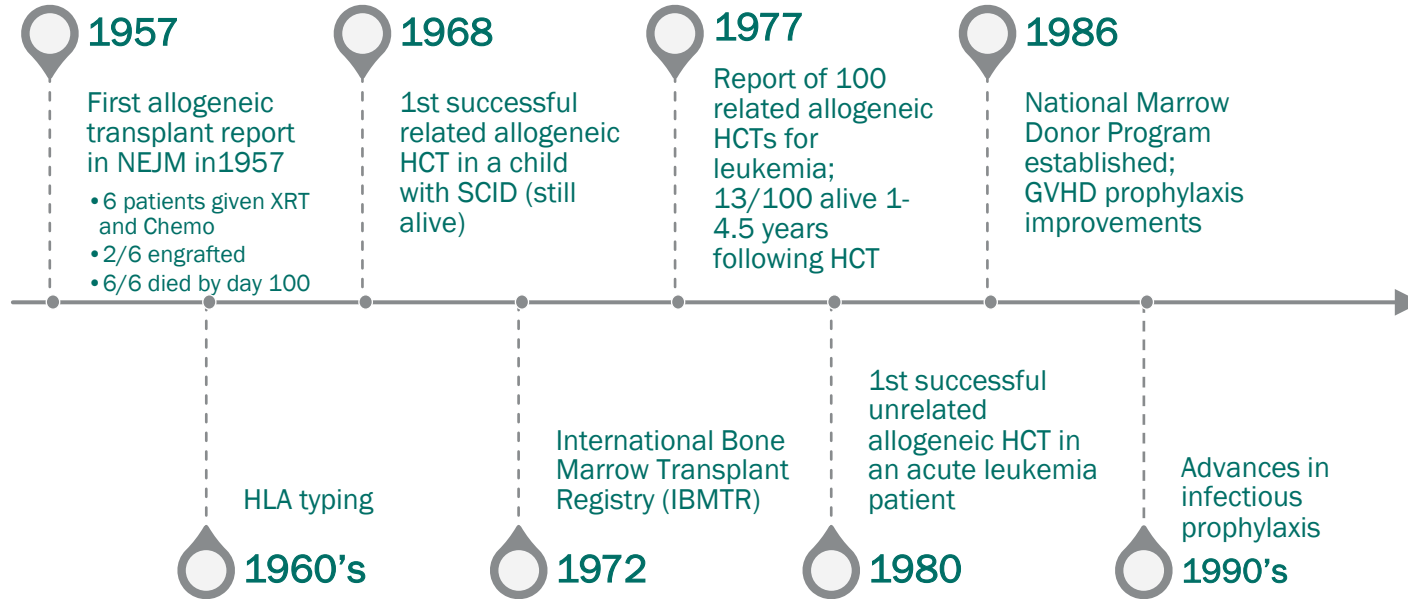


Review complex care needs for this patient population



Discuss emerging research in the field and how novel therapies and technology may impact the world of survivorship in the future

A Quick History Lesson

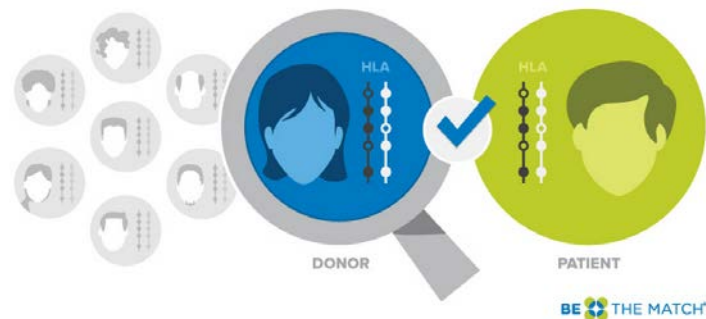


Changing landscape for HCT Outcomes

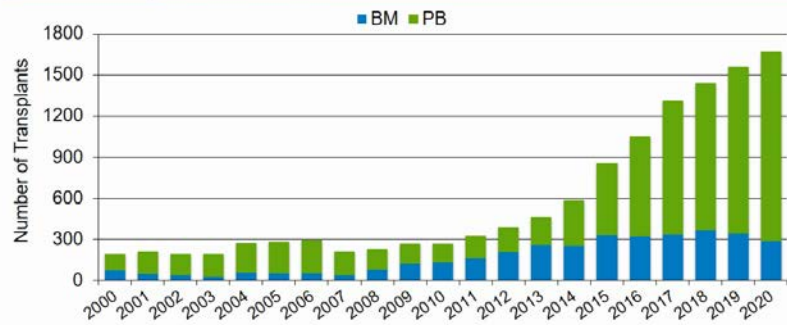
What is changing?

- ▶ Improvements in supportive cares (infection prophylaxis, GVHD prevention, etc.)
- ▶ Better HLA matching
- ▶ Increasing number of HCTs performed
 - ▶ Increasing indications for malignant and non-malignant diseases
 - ▶ Increasing age of eligible patients
 - ▶ Better availability of alternative donors (haploidentical donors, etc)
 - ▶ Better bridging and maintenance therapies to decrease disease burden and reduce relapse risk

Matching **donors** with **patients**.

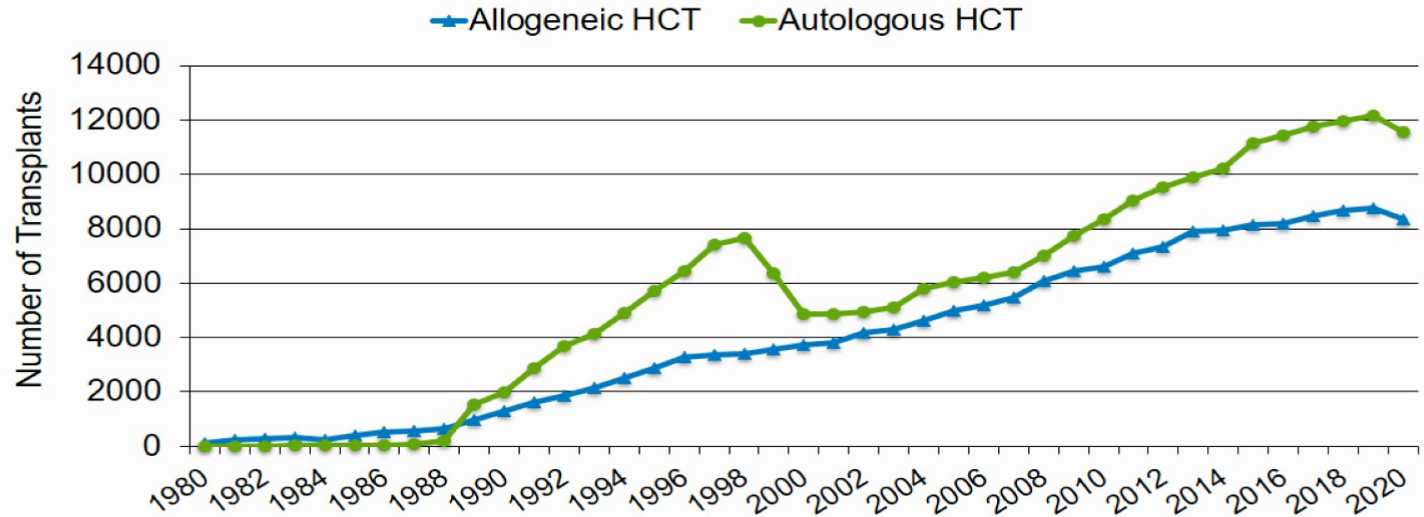


Number of Haploidentical Donor[#] HCTs in the US in Recipients Aged ≥18 Years by Graft Source



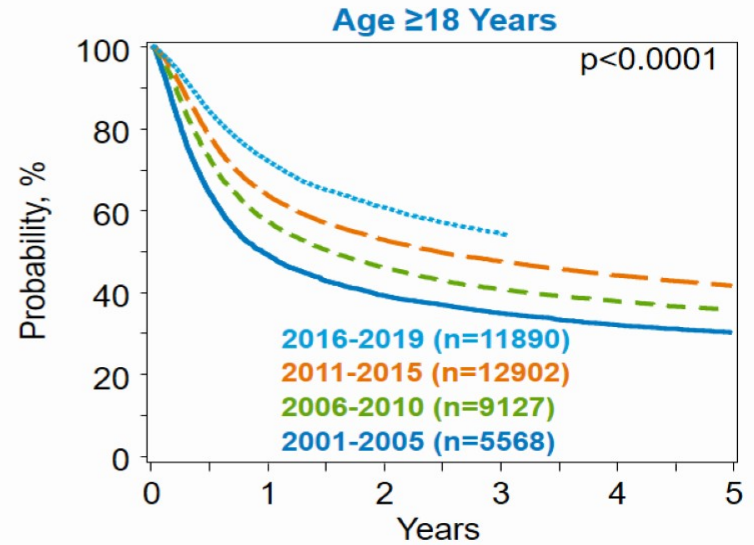
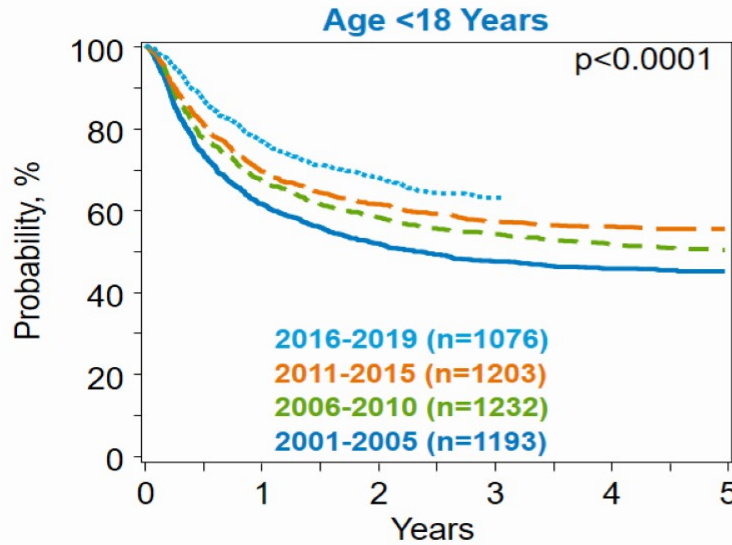
Auletta JJ, Kou J, Chen M, Shaw BE. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR US summary slides, 2021

Number of HCTs in the US Reported to CIBMTR by Transplant Type



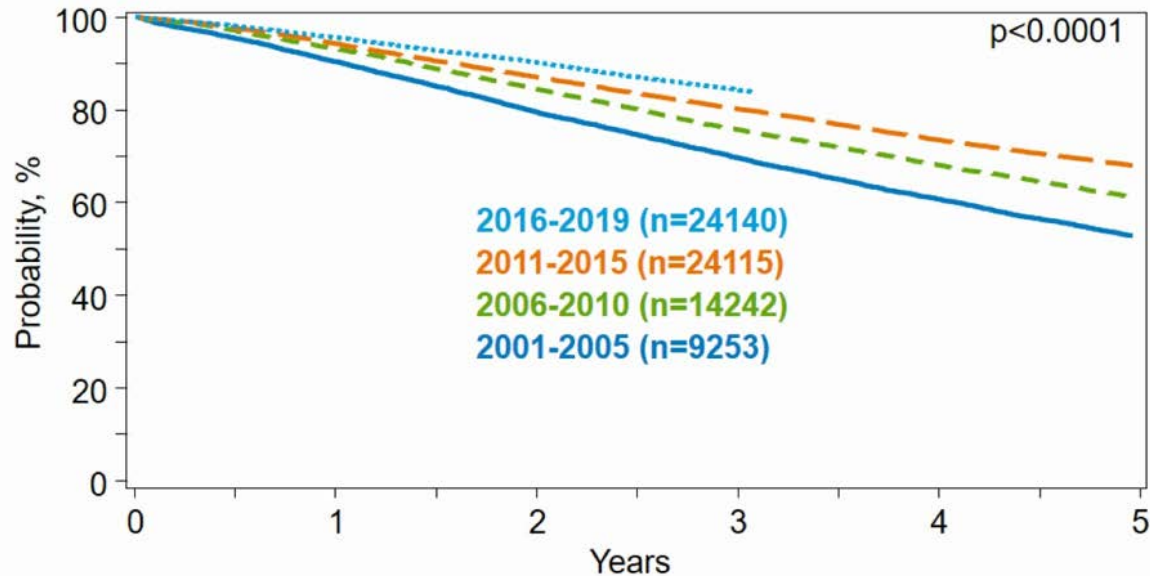
More Transplants...

Trends in Survival after Allogeneic HCTs for Acute Myelogenous Leukemia (AML), in the US, 2001-2019



With Better Outcomes...

Trends in Survival after Autologous HCTs for Multiple Myeloma (MM), in the US, 2001-2019

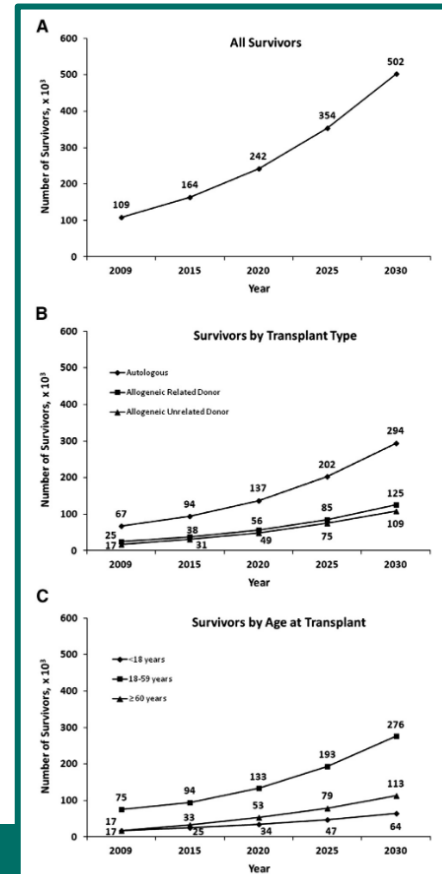


With Better Outcomes...

The Result: a Growing Population of HCT Survivors

By 2030, estimated to be ~500,000 HCT survivors in the US alone

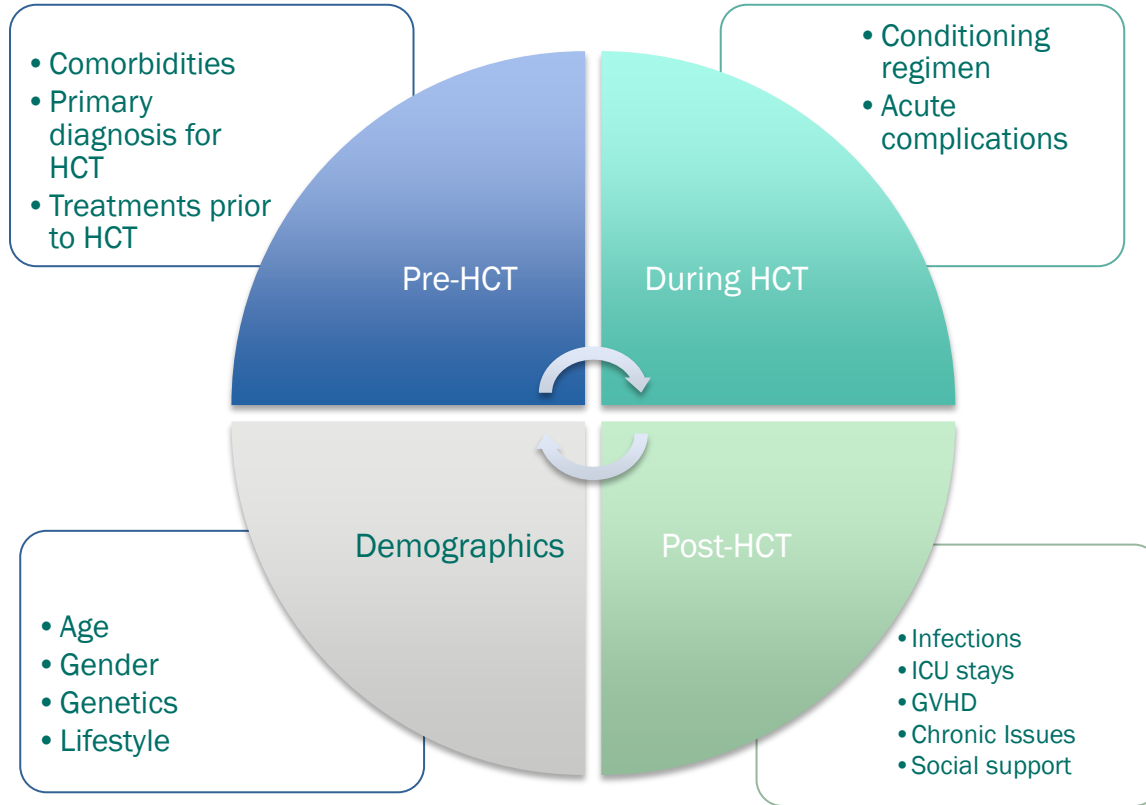
Of those, 14% expected to be survivors of childhood HCT → many years of follow-up care and multiple transitions



N.S. Majhail et al. / Biol Blood Marrow Transplant 19 (2013) 1498–1501

Figure 1. Projected number of hematopoietic cell transplant survivors in the US by year 2030 for (A) all survivors, (B) survivors by transplant type, and (C) survivors by age at transplant.

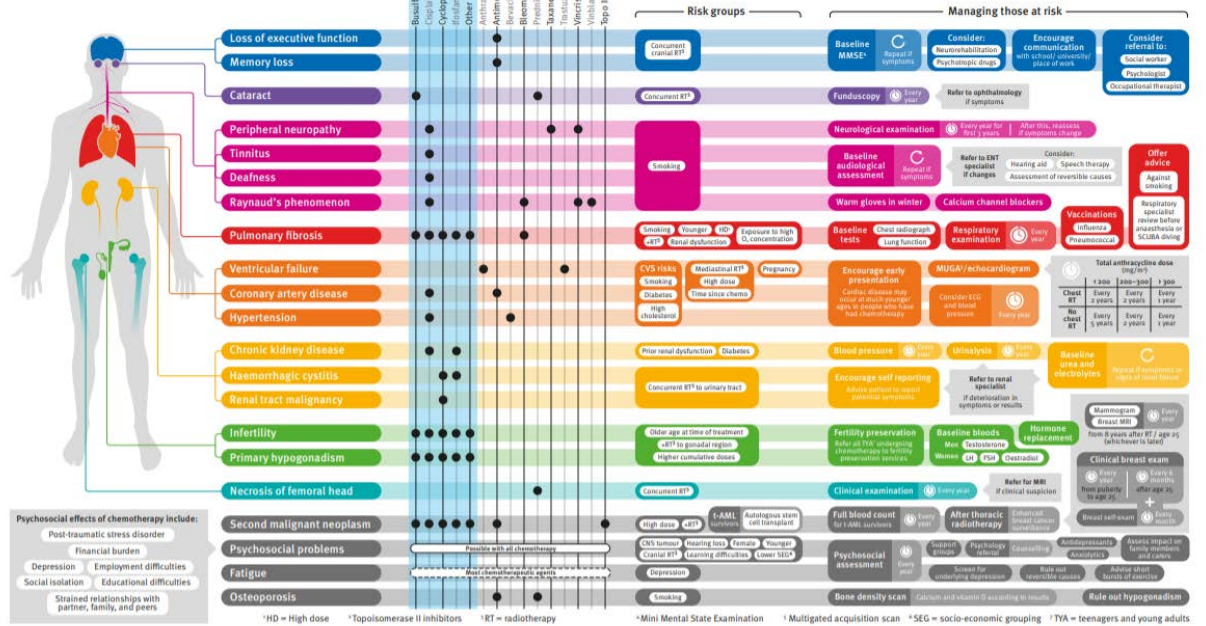
Risk Factors for Late Complications



Therapy and Disease Related Late Effects

Managing long term side effects of chemotherapy

Teenagers and young adults (TYA) who survive cancer treatment can have a range of side effects later in life. If it is known which chemotherapeutic agents were used, the "Principal causative drugs" column can guide monitoring and management. Factors that further increase the risk of complications from chemotherapy are listed in the "risk groups" section.



- A single center study of HCT survivors found a 93% cumulative incidence of late effects, with 25% reporting severe or disabling effects
- Some of these take many years to develop



Some Late-Effects Take Years to Develop

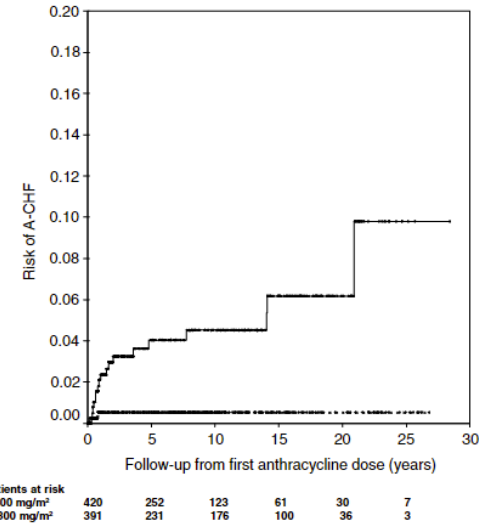
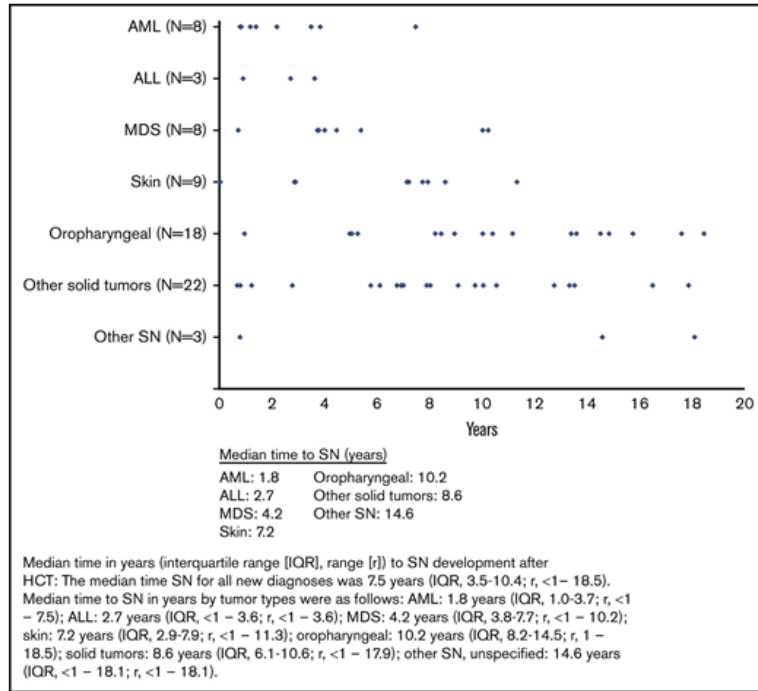


Fig. 3 – Kaplan–Meier plot of the estimated risk of anthracycline-induced clinical heart failure (A-CHF) as a function of the follow-up time after the first dose of anthracyclines for patients treated with a cumulative anthracycline dose of less than 300 mg/m² (lower line) or 300 mg/m² or more (upper line).

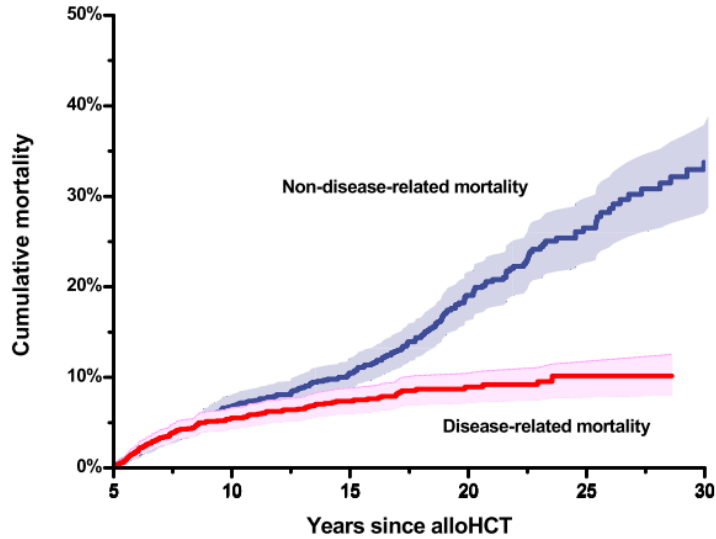


Figure 2. Cumulative cause-specific mortality (95% confidence bands) for 5-year survivors of allogeneic hematopoietic cell transplantation. alloHCT = allogeneic hematopoietic cell transplantation.

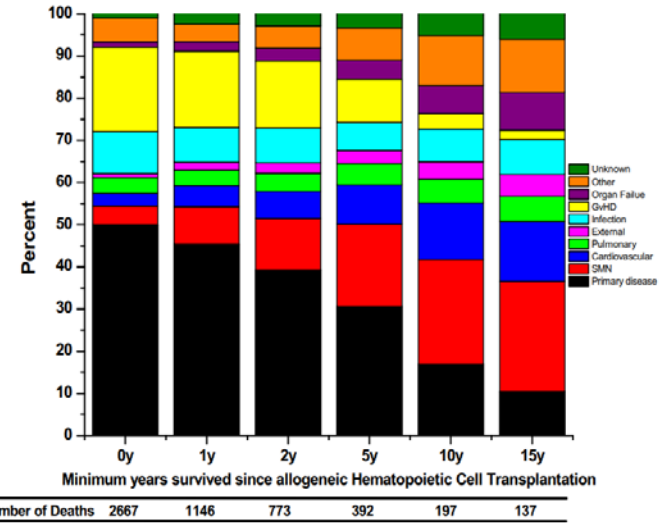


Figure 3. Distribution of causes of deaths by minimum years survived after allogeneic hematopoietic cell transplantation. GvHD = graft-versus-host disease; SMN = subsequent malignant neoplasms.

Research Article

Framingham Risk Score Is an Ineffective Screening Strategy for Coronary Heart Disease in Long-Term Allogeneic Hematopoietic Cell Transplant Survivors

Natasha A. Jain^{1,†,✉}, Marcus Y. Chen^{2,†}, Sujata Shanbhag², Prathima Anandi¹, Xin Tian³, Sawa Ito¹, Priyanka A. Pophali¹, Kimberly Doucette¹, Robert Q. Le¹, Upneet Chawla¹, Eleftheria Koklanaris¹, Richard W. Childs¹, A. John Barrett¹, Minoo Battiwalla^{1,4,*}

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TABLE 3. Colorectal Carcinoma Surveillance Recommendations for Adult Survivors of Childhood Cancer

Organization	Highest risk parameters	Surveillance recommendations
NCCN ⁴⁷	Radiation to abdomen, flank, pelvis, or total body irradiation ≥ 20 Gy	Colonoscopy every 5 y starting at age 30 or 5 y after radiation, whichever occurs later
Children's Oncology Group Long-Term Follow-Up Guidelines for ASCC (COG-LTFU), 2018 version ⁴⁸	Radiation to abdomen, pelvis, flank, or spine, or total body irradiation* Familial adenomatous polyposis (FAP) Hereditary Nonpolyposis Colon Cancer (HNPCC) Lynch syndrome Inflammatory bowel disease (IBD) Personal history of GI malignancy, adenomatous polyps, or hepatoblastoma Family history of colorectal cancer or polyps in first-degree relative	For patients with radiation history, gold standard: Colonoscopy starting at age 30 or 5 y after radiation, whichever occurs later Other options (also starting at the above time point): multi-target stool DNA test every three years Select surveillance type based on informed decision-making between patient and provider For patients at high risk due to personal or family history or hereditary colorectal cancer predisposition syndrome: screening should be performed based on current guidelines for their specific history or hereditary syndrome

*Additional factors to consider that may increase risk:

Patient factors: current age ≥ 45 .

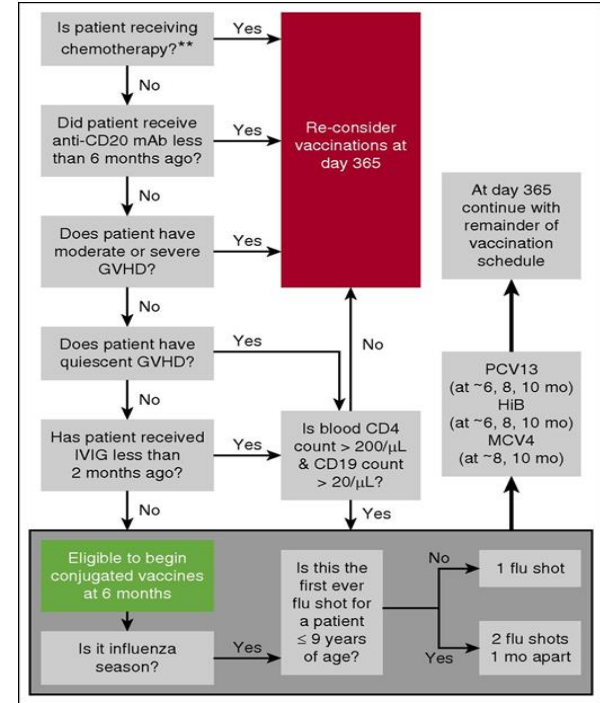
Cancer/treatment factors: Radiation dose ≥ 20 Gy, combination with chemotherapy (especially alkylators).

Comorbidities: obesity.

Health behaviors: high fat/low fiber diet.

Starting post BMT Immunization Process

- Need to assess patient's overall medical status
- Is their immune system ready to get vaccines?
 - Post BMT therapy
 - GVHD treatment
 - Adequate number and function of immune system to respond to immunizations



Multiple Critical Transitions

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graph LR; A[Active Therapy] --> B[Surveillance]; B --> C[Surveillance]; C --> D[PCP/Adult Care]; E[End of Therapy] --> B; F[Survivorship Program] --> C
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Active Therapy

Surveillance

Surveillance

**End
of
Therapy**

**Survivor-
ship
Program**

**PCP/
Adult
Care**

Optimizing Long-Term Care

Survivorship Guidelines

- Children's Oncology Group:

[Survivorshipguidelines.org](https://www.survivorshipguidelines.org)

- NMDP/BeTheMatch Long-term Care Guidelines:

<https://bethematchclinical.org/post-transplant-care/long-term-care-guidelines/>

- Updated, comprehensive guidelines being developed by international group of collaborators (anticipate publication in 2023)

Bone Marrow Transplant. 2012 March ; 47(3): 337-341. doi:10.1038/bmt.2012.5.

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

Navneet S Majhail^{1,2}, J Douglas Rizzo³, Stephanie J Lee⁴, Mahmoud Aljurf⁵, Yoshiko Atsuta⁶, Carmem Bonfim⁷, Linda J Burns⁸, Naeem Chaudhri⁵, Stella Davies⁹, Shinichiro Okamoto¹⁰, Adriana Seber¹¹, Gerard Socie¹², Jeff Szer¹³, Maria Teresa Van Lint¹⁴, John R Wingard¹⁵, and Andre Tichelli¹⁶

Biol Blood Marrow Transplant 22 (2016) 782–795



ELSEVIER

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

ASBMT
American Society for Blood and Marrow Transplantation

Report

Late Effects Surveillance Recommendations among Survivors of Childhood Hematopoietic Cell Transplantation: A Children's Oncology Group Report



Eric J. Chow^{1,*}, Lynnette Anderson², K. Scott Baker¹, Smita Bhatia³, Gregory M.T. Guilcher⁴, Jennifer T. Huang⁵, Wendy Pelletier⁴, Joanna L. Perkins⁶, Linda S. Rivard⁷, Tal Schechter⁸, Ami J. Shah⁹, Karla D. Wilson¹⁰, Kenneth Wong¹¹, Satkiran S. Grewal¹², Saro H. Armenian¹⁰, Lillian R. Meacham¹³, Daniel A. Mulrooney¹⁴, Sharon M. Castellino¹³

Survivorship Care Plans

- Survivorship Care Plans
 - Best format?
 - What to include?
 - When to give and who to give to?
 - How can we increase the use?
- INSPIRE Trial
 - Online Cancer Survivorship Program
 - Less likely to enroll if male, <40 years, and African American
- Are we improving knowledge and compliance?
 - Study of 1549 survivors >2 years from HCT
 - Median adherence to recommendations of 75% (ranged from 42-96%)
 - Despite 98% of respondents having insurance, 26% still reported concerns about medical costs

Table 3. Data regarding use of SHP in facilitation of cancer survivorship care using Likert scale 0-10

Variable	Patient Survey (median, IQR)	Parent Survey (median, IQR)
Confidence in sharing SHP?	6 (4-8)	7 (3-9)
Confidence in understanding SHP?	7.5 (7-9)	9 (7-10)
Confidence in asking for health care needs based on SHP?	6 (4-9)	8 (5-10)
Has it taught you about a medical problem you did not know?	6 (3-8)	3 (1-8)
Has it helped to coordinate care?	8 (4-9)	5 (3-8)
Does it remind you to schedule care appointments?	5 (2-8)	3 (1-7)

Table 2. General descriptive statistics of use and feedback regarding SHP

Variable	Patient responses	Parent responses
Do you carry your passport?	63% carry in their wallet 6% carry in their bag 3% puts in their pocket 29% does not carry it at all	67% carry in their wallet 3% carry in their bag 1.5% placed in the car 1.5% placed in the medicine kit 26% does not carry it at all
Regularly see a primary care provider (PCP)?	89% see a PCP	98% see a PCP
Who else comprises your care team (other than your PCP)?	50% +1 other specialist 21% +2 other specialists 29% +3 or more specialists	44% +1 other specialist 35% +2 other specialists 21% +3 or more specialists
Other formatting may be useful?	91% smartphone application	64% smartphone application

***Manuscript in Press**

Patient: DOB: Updated: February, 2017
 Providers: Dr. J, APNP/Deb Schmidt, APNP 414-266-2420

System	Exam	Time Frame
<i>All Survivors: History and Physical Exam Yearly, Dental Exam Every 6 Months</i>		
Secondary Cancer	Routine cancer screening for secondary malignancies Inspection and palpation of skin and soft tissues in irradiated fields CBC with manual differential	Yearly/Ongoing Yearly dermatology follow-up recommended As clinically indicated
Cardiology	Echocardiogram	Yearly, Every X years
Ophthalmology	Eye exam, screen for cataract development	Yearly
Renal	Blood pressure and Urinalysis BUN, Creatinine and Electrolytes	Yearly Baseline, then as clinically indicated
Hearing	Audiological evaluation	Yearly
Endocrine	TSH, Free T4 FSH, LH, Estradiol, Testosterone Monitor for signs and symptoms of early menopause MRI/Mammogram Monitor growth and pubertal development	Yearly Baseline at age 13,14, then ass clinically indicated Ongoing Age 25 (year) or 8 years post end of therapy Ongoing
Pulmonary	Pulmonary Function Testing (PFT'S)	As clinically indicated
Musculoskeletal	Monitor for scoliosis/kyphosis	As clinically indicated
Neuro-cognitive	Neuro-psychological testing	As needed if school problems develop
Reproductive	Referral to a reproductive medicine physician	As clinically indicated

Abbreviated Treatment History

Diagnosis:
 Protocol:
 Start date:
 End of therapy date:

Chemotherapy	Dosage			
Total anthracycline dose: . Age at first dose: .				
Doxorubicin	mg/m2			
Cyclophosphamide	1 gm/m2			
Cytarabine	600 mg/m2			
Methotrexate	1 gm/m2			
Vincristine, PEG-Asparaginase Mercaptopurine, Thioguanine, Dexamethasone and Prednisone				
Significant Surgery	Date			
Radiation Treatment	Start	End	Fractions	Dose

For detailed Long-Term Follow-Up Guidelines (V4.0):

www-survivorshipguidelines.org

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Return to Work and School

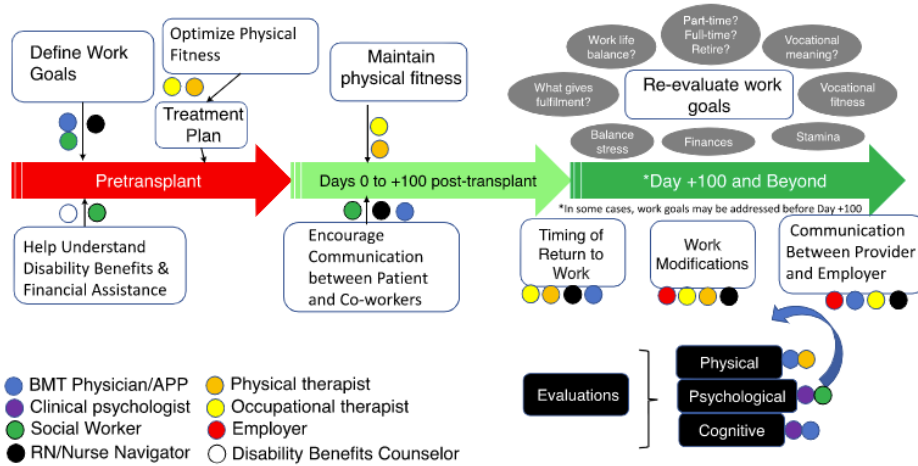


Figure 1. Pictorial of timepoints and personnel providing return to work assistance designated by colored dots.

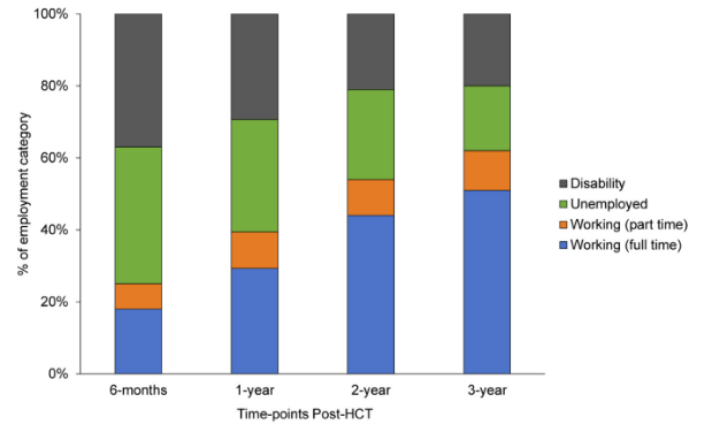


Figure 1. Work status of young adult (18 to 39 years) survivors of allogeneic HCT at 6 months and 1, 2, and 3 years post-HCT.

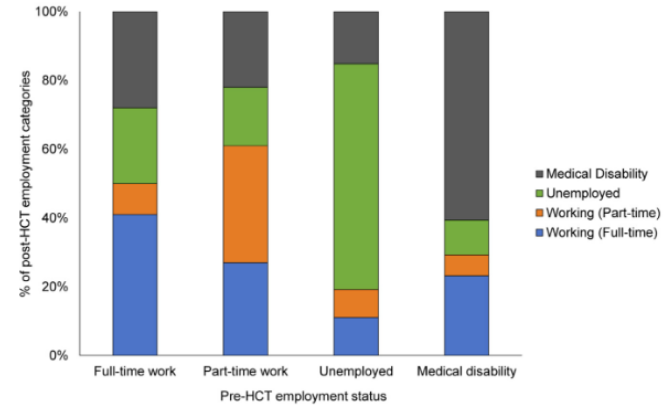


Figure 2. Work status of young adult (18 to 39 years) survivors of allogeneic HCT at 1 year post-HCT by pre-HCT work status category.

MACC Fund Center

- Oncology/BMT Specialists
- Psychology
- Social Work
- Dietician
- School teachers/advocates
- Nurse Clinician
- Community Navigator
- Physical Therapy
- Fertility Navigator
- Dermatology
- Cardiology
- Endocrinology
- PCP

How is Care Changing for Survivors?

knowledge changing life



Attempts to reduce risks upfront

- Total body radiation elimination → ALL undergoing HCT
- Radiation reduction in patients with Hodgkins Lymphoma
- Reduced intensity HCT for older patients/those with co-morbidities (higher HCT-CI)
- Dexrazoxane for cardioprotection for patients receiving high doses of anthracyclines
- Genome Wide Association Studies (GWAS)

Emerging Therapies...Unknown Late Effects



Chimeric antigen receptor (CAR)T cells



Bi-specific T-cell engagers



Checkpoint inhibitors



Other targeted molecular therapies...

Utilizing Technology to Reach our Patients and Intervene



Internet-based cognitive therapies



Mobile apps and/or games to help promote healthy eating/exercise



Texting reminders for follow-ups or medical advice



Telemedicine*

Conclusions



- Patients undergoing HCT are at risk for several long-term complications, regardless of age, gender or diagnosis
- Each patient's risk for complications is variable and screening plans must be tailored
- Lifelong follow-up, ideally in conjunction with a PCP and HCT specialist, is critical
- New therapies may decrease the risk of late-effects, but long-term studies of patients receiving these therapies is essential

Next Steps Survivorship Team

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Jodi Jacobson

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*Our patients and families



**The Everyday
Good Foundation**