

## Out of the Frying Pan ..? Life After Transplant Using Donor Cells (Allogeneic Transplant)

**Celebrating a Second Chance at Life  
Survivorship Symposium**

April 29 – May 5, 2023



**Scott Rowley MD, FACP**  
MedStar Georgetown  
University Hospital



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## Cancer Survivorship: No Longer a Rare Event

**“From the moment of diagnosis  
and for the balance of life,  
a person with cancer is  
a survivor”**

***(Caregivers and family members are also cancer survivors)***

National Coalition of Cancer Survivors  
[www.canceradvocacy.org](http://www.canceradvocacy.org)



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## Late Effects after Allogeneic Transplant

At the conclusion of this presentation, you should be able to:

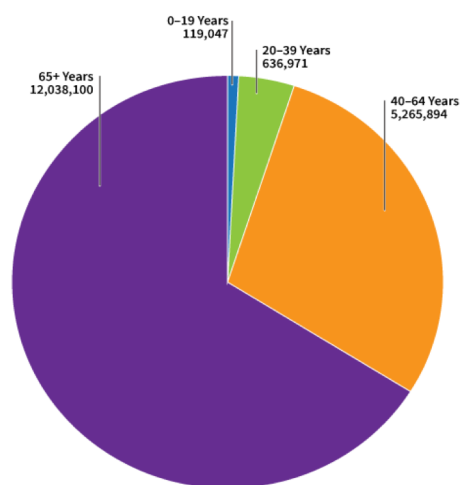
- Understand the long-term health risks after transplantation
- Establish a proper long-term care plan with your physician
- Care for your care-giver

## Cancer Survivorship: No Longer a Rare Event

- Over 18,000,000 cancer survivors in United States in 2022
- What are the care needs of survivors (and caregivers)?

### Estimated Number of Cancer Survivors in the U.S., by Current Age

JANUARY 1, 2022



REFERENCE: Cancer Treatment & Survivorship Facts & Figures 2022-2024. Atlanta: American Cancer Society; 2022.

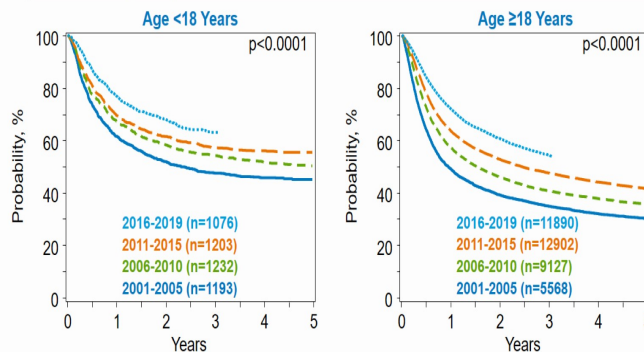
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## Survival by Year of Transplant

Improved survival over time:

- More cancer survivors
- AND
- More cancer caregivers

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



78

Auletta JJ, et al. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR US summary slides, 2021.

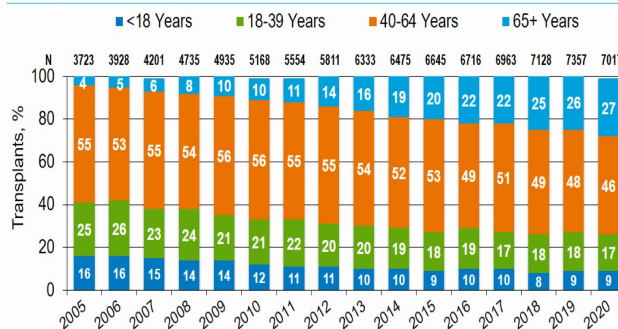
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## Increasing Age of Transplant Recipients

- The age of transplant recipients continues to increase
- Older patients are more likely to have co-morbid health issues, complicating transplant AND post-transplant care considerations

Relative Proportion of Allogeneic HCTs for Malignant Diseases\* in the US by Recipient Age



\*Includes Acute myelogenous leukemia, Acute lymphoblastic leukemia, Myelodysplastic syndromes/Myeloproliferative neoplasms, Non-Hodgkin lymphoma, Hodgkin lymphoma

32

Auletta JJ, et al. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR US summary slides, 2021.

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## Examples of Health Issues

Pre-Diagnosis	Disease-Related	Treatment-Related
Hypertension Hyperlipidemia Diabetes Obesity	Bone damage Malnutrition Muscle loss Organ damage	Heart disease Second cancers Ovarian failure Osteoporosis Cataracts Skin damage Depression Fatigue

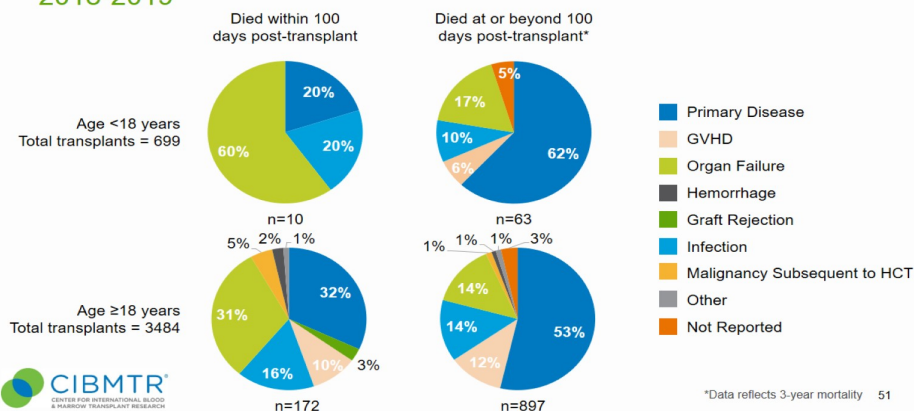
- Cancers are age-related, more common in older individuals
- Such individuals come to transplantation with pre-existing health issues
- Pre-existing health issues may be exacerbated by transplantation

## Causes of Death After Allogeneic HSC Transplant

- Relapse is primary cause of death for longer-term transplant survivors
  - But much less likely after 2 years
  - Transplant programs are actively exploring consolidation and/or maintenance therapies to reduce the risk of relapse and
- Chronic GvHD is associated with increased ongoing infection risk and organ damage
- The “holy grail” for transplant programs is **both** GvHD and relapse-free survival (aka “GRFS”)

## Causes of Death after Allogeneic HSC Transplant

### Causes of Death after Matched Related Donor HCTs in the US, 2018-2019



\*Data reflects 3-year mortality 51

Auletta JJ, et al. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR US summary slides, 2021.

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## The Range of Possible Health Issues after Transplantation

- Cardiovascular disease
- Second cancers
- Pulmonary disease
- Liver disease
- Renal dysfunction
- Bone and joints damage
- Oral health
- Infections
- Ocular complications
- Dermatologic complications
- Endocrine disorders
- Sexual functioning and fertility
- Neurocognitive health
- Fatigue
- Depression

Majhail NS, et al. Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. Biol Blood Marrow Transplant 2012;18:348-71

## Other Possible Health Issues after Transplant

- Psychological:
  - Depression
  - Anxiety
  - Uncertainty
  - Isolation
  - Altered body image
- Social:
  - Interpersonal relationships (including caregiver)
  - Health or life insurance
  - Job lock or loss
  - Financial burden

### Existential and Spiritual Issues:

- Sense of purpose or meaning
- Appreciation of life

## Not Just Transplant Recipients: Health Status Outcomes in Adult Survivors of Childhood Cancer

Cancer Dx	General Health	Functional Impairment	Activity Limitations	Mental Health
All Patients	2.5x	5.2x	2.7x	1.8x
Leukemia	2.2x	3.8x	1.8x	1.7x
Hodgkin Disease	2.7x	2.4x	2.1x	2.0x
Non-Hodgkin	2.3x	3.0x	2.0x	1.3x
Central Nervous	3.5x	18.0x	4.1x	2.0x
Wilms	1.8x	3.2x	2.0x	1.3x
Sarcoma	2.2x	4.2x	2.3x	1.7x

Shown are the odds ratio (patient “times” more likely to experience) of adverse health outcomes compared to a healthy sibling. N=9535 adult survivors of childhood cancer.

## Not Just Transplant Recipients: % of Adult Survivors of Childhood Cancer with Adverse Health Status

Cancer Dx	General Health	Functional Impairment	Activity Limitations	Mental Health
All Patients	10.9%	12.0%	12.5%	17.2%
Leukemia	9.6%	9.3%	8.6%	17.5%
Hodgkin Disease	12.7%	6.4%	17.8%	19.0%
Non-Hodgkin	9.6%	7.2%	9.0%	17.8%
Central Nervous	14.6%	31.7%	17.8%	19.0%
Wilms	8.2%	7.7%	8.8%	14.1%
Sarcoma	9.9%	9.8%	11.3%	16.1%

Shown are the percentage of patients who report limitations in health.



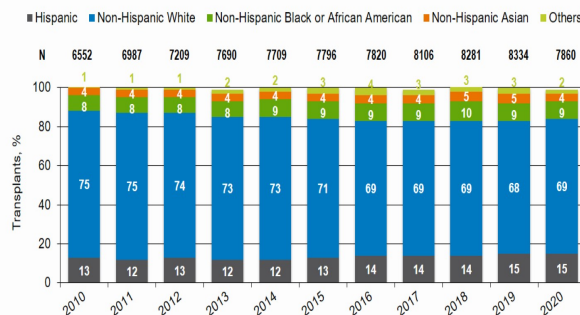
N=9535 adult survivors of childhood cancer.

Hudson et al. J Amer Med Soc 2003;290:1583-92  
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## Individual Patients May Have Special Needs

- Race, sex, ethnicity, and one’s “social determinants of health” will influence survivorship for both the patient and the caregiver
- Social determinants of health are:
  - Economic Stability
  - Education Access and Quality
  - Health Care Access and Quality
  - Neighborhood Environment
  - Social and Community Context

Relative Proportion of Allogeneic HCTs in the US by Race and Ethnicity



\*Includes non-Hispanic Native Hawaiian or other Pacific Islander (n=19), American Indian or Alaska Native (n=32), More than one race (n=51), and Non-resident of the US (n=75) in 2020

Auletta JJ, et al. Current use and outcome of hematopoietic stem cell transplantation: CIBMTR US summary slides, 2021.  
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## Possible Health Issues after Transplant (\* are specifically addressed at this symposium)

- Chronic GvHD\*
- Cardiovascular disease\*
- Second cancers\*
- Pulmonary disease\*
- Liver disease
- Renal dysfunction
- Bone and joints\*
- Oral health\*
- Infections\*
- Ocular complications\*
- Dermatologic complications\*
- Endocrine disorders\*
- Sexual functioning and fertility\*
- Neurocognitive health\*
- Fatigue\*
- Depression

Majhail NS, et al. Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. *Biol Blood Marrow Transplant* 2012;18:348-71

## Health Issues after HSCT: Life Expectancy

- Studied 4741 individuals, transplanted 1974-2014, alive >2 years after HSCT
- Compared to sex-specific US life-table data from CDC
- Findings:
  - Changing patient populations (age, regimens, diseases, donor type) over 30 yrs
  - 8.8-fold increased overall mortality compared to controls,
    - highest at 2-5 years after HSCT (34.3-fold) but still elevated at 30 years (5.4-fold)
  - 20.8% decrease in life expectancy (8.7 years of life lost)
  - Relapse-related mortality was 12.2%
  - Non-relapse mortality was 22.3% (infections 10.7%, second cancer 7.0%, heart disease 4.6%)

Bhatia S, et al. Trends in Late Mortality and Life Expectancy After Allogeneic Blood or Marrow Transplantation Over 4 Decades: A Blood or Marrow Transplant Survivor Study Report. *JAMA Oncol.* 2021;7:1626-34.



## Health Issues after HSCT

### Infectious Diseases: Late Fatal Infections

- CIBMTR analysis, 10,336 adults, 5088 pediatric HSCT survivors >2 yrs
- Infections were cause of death for 31% and 29% of deaths (adults, children)
- By 12 yrs, cumulative incidence of fatal infections: 6.4% and 1.8% (adults, children)

#### Risk Factors

- Older Age
- Mismatched or Unrelated Donor
- Chronic GvHD

#### Types of Infections (Adults)

- Bacterial (35%)
- Viral (9%)
- Fungal (11%)
- Unspecified (37%)

- Many infections are vaccine- or antibiotic-preventable illnesses
- No good test of robust immune recovery

## Health Issues after HSCT: Second Cancers

#### Incidence Ratio\*

- Any skin: 7.2x
- Thyroid: 5.8-6.6x
- Oral: 7-27x
- Lung: 0.7-2.6x
- Female breast: 0.3-2.0x
- Cervix: 0.7-2.3
- Colon: 0.5-2.2x
- Prostate: 0.5-0.7x

\*Compared to age-match control

#### Risk Factors

- Skin: GvHD, TBI, younger age, race
- Thyroid: Radiation, female, cGvHD, age
- Oral: Persistent GvHD, radiation therapy
- Lung: Tobacco use
- Breast: Radiation, younger age
- Cervix: cGvHD
- Colon: None reported
- Prostate: None reported

## Health Issues after HSCT: Heart Disease

Event	10-yr Cumulative Incidence <sup>1</sup>	Relative Risk (vs control) <sup>2</sup>	Relative Risk (3 risk factors*) <sup>2</sup>
Cardiovascular death	3.7%	2.7x	25.1x
Ischemic heart disease	3.8%	1.4x	68.0x
Heart failure	6.0%	2.5x	60.6x
Stroke	3.5%	1.3x	133.3x

- Cumulative incidence (total risk over time) for 509 pts without pre-transplant risk factors
- Relative risk for 1096 pts vs 4352 controls
- Survivors >2 yrs after transplantation, Washington residents
- \*Risk factors are: hypertension, high lipid levels, diabetes, renal disease

1. Chow EJ, et al. Late cardiovascular complications after hematopoietic cell transplantation. *Biol Blood Marrow Transpl.* 2014;20:794-800.
2. Chow EJ, et al. Cardiovascular hospitalizations and mortality among recipients of hematopoietic stem cell transplantation. *Ann Intern Med* 2011;155:21-32

## Health Issues after HSCT: Metabolic Syndrome

- Metabolic Syndrome: High lipids, high glucose, hypertension, abdominal fat
- Associated with: Heart disease, diabetes, and all-cause death
  - Obesity: Waist circumference more informative than BMI
    - Risk of sarcopenic obesity (normal weight, loss of muscle, increase in body fat)
  - High lipid levels: Relative risk 2.31-fold in transplant population
  - Hypertension: Relative risk 2.06-fold
  - Diabetes: Relative risk 3.65-fold
- Leading to a 12.4-fold relative risk of coronary artery disease if 2-4 factors

DeFilipp Z, et al. Metabolic Syndrome and Cardiovascular Disease after Hematopoietic Cell Transplantation: Screening and Preventive Practice Recommendations from the CIBMTR and EBMT. *Biol Blood Marrow Transplant.* 2016;22:1493-503.

## Health Issues after HSCT: Neurocognitive Disorders

### Domains of Concern:

- Attention/Concentration
- Perceptual processing
- Learning and working memory
- Abstract thinking/executive functioning
- Information processing speed
- Motor function
- Emotions

### Issues:

- Up to 58% of adult patients report
- Limited data for older patients
- Most patients recover to baseline in most domains, but...
  - 41.5% with at least mild symptoms at 5 years
- Interventions:
  - Reduce use of neurotoxins
  - Manage acute toxicities
  - Non-pharmacologic interventions
  - Pharmacologic interventions

## Health Issues after HSCT Vaccine Preventable Diseases

Time/Vaccine	3 mo	6 mo	12 mo	14 mo	18 mo	24 mo	Annually
Pneumonia	Prev 13	Prev 13	Prev 13			PPSV23	
Human Papilloma Virus			X (<26 yrs)		X (<26 yrs)		
Hepatitis B			X		X		
Polio			X	X	X		
Tetanus/diphtheria			X (Tdap)	X	X		
Haemophilus			X	X	X		
Meningococcus			X	X			
Recomb Shingles			X (if ab pos)	X (if ab pos)			
MMR						X*	
Varivax						X*	
Influenza							X

## Health Issues after HSCT Recommended Cancer Screening

CANCER	AGE			
	20-39	40-49	50-64	65 or older
Colon	If High Risk	Start age 45 yrs	Routine	Up to 75 yrs
Lung	None	None	Low-dose CT*	Low-dose CT*
Breast	Talk with PCP	Annual at 45 yrs	Annual to 54 yrs, then every 2 yrs	Every 2 yrs
Cervical	HPV every 5 yrs or PAP every 3 yrs	HPV every 5 yrs or PAP every 3 yrs	HPV every 5 yrs or PAP every 3 yrs	No test if normal for 10+ yrs
Prostate	None	Talk with PCP at 45 yrs	Talk with PCP	Talk with PCP

American Cancer Society Guidelines. Adapted from: <https://www.cancer.org/healthy/find-cancer-early/screening-recommendations-by-age.html#21-29>

\* History of tobacco use



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## Health Issues after HSCT Recommended Cardiovascular Health

Topic	Recommendation
Risk Score	Variety of tools to assess 10 yr risk ( <a href="#">ASCVD Risk Estimator Plus</a> )
Nutrition	Discuss dietary patterns that increase risk of heart disease
Obesity	Overweight (BMI >25) increases risk
Physical activity	Aerobic physical activity lowers risk
Diabetes	Type 2: Influenced strongly by dietary pattern, physical activity, obesity
Lipids	Age and risk guidance provided for use of statin drugs
Hypertension	Target is now <120/80
Tobacco	No tobacco use is ever beneficial to health
Aspirin	Consider for patients 40-70 yrs of age

Adapted from: Arnett D, et al. 2019 ACC/AHA Guideline on the Primary Prevention of Cardiovascular Disease. *J Am Coll Cardiol.* 2019;74e177-e232.

<https://doi.org/10.1016/j.jacc.2019.03.010>

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## Health Issues after HSCT: Transition to General Medical Care

- Is the transplant center the primary care team? Long-term clinic?
- Issues:
  - Distance from transplant center
  - Convenience
  - Medical expertise
- No Primary Care Physician (PCP) visit by year (data from University of Ottawa):
  - Pre-transplant: 17.6%
  - 2<sup>nd</sup> yr post-HSCT: 24.8%
  - 5<sup>th</sup> yr post-HSCT: 36.4%

## Health Issues after HSCT: Transition to General Medical Care

- Lipid screen:
  - 2<sup>nd</sup> year: 20.9%
  - by 4<sup>th</sup> year: 25%
- Diabetes screen:
  - 2<sup>nd</sup> year: 17.8%
  - by 4<sup>th</sup> year: 20.9%
- Breast cancer screen:
  - Pre-HSCT: 30%
  - by 4<sup>th</sup> yr: 31.1%
- Cervical cancer screen:
  - pre-HSCT 16.4%,
  - after HSCT: 17.9%
- Colon cancer screen:
  - pre-HSCT 22.5%,
  - after HSCT 17.9%

## Post-Treatment Survivorship

People may want to ask these questions about follow-up care:

- How often should I have a routine visit?
- What follow-up tests, if any, should I have?
- How often will I need these tests?
- What symptoms should I watch for?
- If I develop any of these symptoms, whom should I call?



## Post-Treatment Survivorship

Patients should be given a written (ideally) follow-up plan:

- Likely course of recovery from acute toxicities
- Description of recommended cancer screening and other periodic testing and examinations
- Information regarding possible late and long-term effects of treatment
- Information on the potential insurance, employment, and financial consequences of cancer and the treatment received
- Need for ongoing health maintenance
- Recommended chemopreventive therapies (e.g., maintenance therapy)
- A listing of cancer-related resources and information

Earle CC: Failing to plan is planning to fail: improving the quality of care with survivorship care plans. J Clin Oncol 2006;24:5112-6

## Survivorship: The Care Giver

What do we know about the caregiver before and after transplantation?

- Anxiety and depression are present before transplantation, may be higher than for patient
- Anxiety (46.6% caregivers) and depression (16.1%) are correlated with:
  - Social support
  - Physical well-being
  - Self-efficacy
  - Coping
  - Care-giving burden
  - Leisure time
  - Financial stability
  - Intimate connection

## Survivorship: The Care Giver

What do we know about the caregiver before and after transplantation?

- We now recognize symptom “clusters”
- These clusters often occur as a group
  - Fatigue
  - Sleep Disturbance
  - Depression
  - Anxiety
  - Cognitive difficulty
- Loneliness associated with greater symptoms
- Self-efficacy associated with lesser symptoms

## Caregiver Support: Two Intervention Models

### BMT-CARE:

- 6-session caregiver-directed coping skills intervention through day +60
- Integrates HCT-related education with cognitive-behavioral strategies
- Improved:
  - Caregiving burden
  - Anxiety symptoms
  - Depression symptoms
  - Self-efficacy
  - Coping skills

El-Jawahri A, et al. Cancer 2020;126:1758065



### PsychoEducation, Paced Respiration and Relaxation (PEPRR):

- 8-session caregiver-directed coping skills intervention through day +100
- Improved:
  - Perceived stress
  - Anxiety
  - Depression
  - Total mood disturbance

Laudenslager ML, et al. Bone Marrow Transplant 2015;50:1110-18

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## CareGiver: “Fit for Duty”

Guidelines for supporting and preparing HCT caregivers to effectively care for their loved ones at home have not yet been established. Suggestions:

1. Comprehensive family caregiver screening pre-HCT.
2. Identification of a “family caregiver champion” on the HCT team
3. Education delivered to family caregivers pre-transplantation.
4. Repeated screening for family caregivers’ unmet needs at critical points along the HCT trajectory.
5. Ongoing, open communication between family caregivers and the HCT treatment teams.
6. Delivery of targeted psychosocial interventions for family caregivers.

Applebaum AJ, et al. Fit for Duty: Lessons Learned from Outpatient and Homebound Hematopoietic Cell Transplantation to Prepare Family Caregivers for Home-Based Care. Transplant Cell Ther. 2023;29:143-50.



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## Survivorship: Quality of Life, Recipients and Caregivers

- Female > male partners reported worse mental health, depression, cognitive dysfunction, social functioning
- Partners were similar to controls in reported general health (but better than patients)
- Partners (and patients) reported:
  - Worse sleep and sexual problems than controls,
  - Worse fatigue and cognitive dysfunction, and
  - Worse impairments in mental health and depressive symptoms
- Partners (not patients) reported:
  - Lower social support, higher loneliness, less satisfaction in partnership than controls

Bishop MM, et al. Late effects of cancer and hematopoietic stem-cell transplantation on spouses or partners compared with survivors and survivor-matched controls. *J Clin Oncol.* 2007;25:1403-11.

## CareGiver: “Bill of Rights”

### I HAVE THE RIGHT

- To take care of myself.
- To seek help from others even though my loved ones may object.
- To maintain facets of my own life that do not include the person I care for, just as I would if he or she were healthy.
- To get angry, be depressed, and express other difficult feelings occasionally.
- To reject any attempts by my loved one (either conscious or unconscious) to manipulate me through guilt, and/or depression.

Adapted from Family Caregiver Alliance, Copyright © 1996-2023  
Original: Jo Horne *Caregiving: Helping an Aging Loved One*

## CareGiver: “Bill of Rights” (continued)

### I HAVE THE RIGHT

- To receive consideration, affection, forgiveness, and acceptance for what I do, from my loved ones, for as long as I offer these qualities in return.
- To take pride in what I am accomplishing and to applaud the courage it has sometimes taken to meet the needs of my loved one.
- To protect my individuality and my right to make a life for myself that will sustain me in the time when my loved one no longer need my full-time help.
- To expect and demand that as new strides are made in finding resources to aid physically and mentally impaired persons in our country, similar strides will be made towards aiding and supporting caregivers.

Adapted from Family Caregiver Alliance, Copyright © 1996-2023  
Original: Jo Horne *Caregiving: Helping an Aging Loved One*

## Late Effects after Allogeneic Transplant

### In summary:

- Long-term health consequences of cancer and treatment are real
- It is possible to establish a proper care plan to offset the risks of
  - Heart disease
  - Infections
  - Second cancers
- Your care-giver also requires long-term support in recovering from the psychological, social, and financial losses of being a care-giver



## Questions?

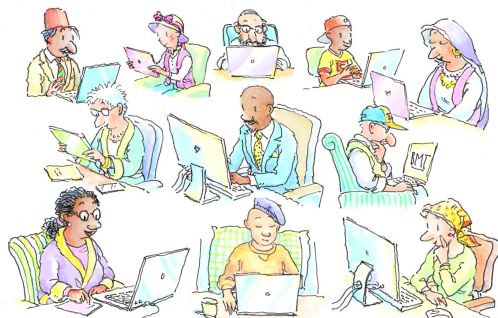


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## LET US KNOW HOW WE CAN HELP YOU



Visit our website: [bmtinfonet.org](http://bmtinfonet.org)

Email us: [help@bmtinfonet.org](mailto:help@bmtinfonet.org)

Phone: 888-597-7674 or 847-433-3313

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Twitter, [twitter.com/BMTInfoNet](https://twitter.com/BMTInfoNet)



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## Selected Resources (partial listing)

Cancer Survivors:

- BMT Infonet (<https://www.bmtinfonet.org>)
- National Marrow Donor Program (<https://www.bethematch.org/survivorship>)
- National Coalition of Cancer Survivors ([www.canceradvocacy.org](http://www.canceradvocacy.org))
- American Cancer Society ([www.cancer.org](http://www.cancer.org))
- Association of Cancer Online Resources ([www.acor.org](http://www.acor.org))
- Cancer Survivors Projects ([www.cancersurvivorsproject.org](http://www.cancersurvivorsproject.org))
- National Cancer Institute Office of Cancer Survivorship ([dccps.nci.nih.gov/ocs](http://dccps.nci.nih.gov/ocs))

## Selected Resources (partial listing)

Care-giver Support:

- BMT InfoNet (<https://www.bmtinfonet.org>)
- National Cancer Institute (<https://www.cancer.gov/about-cancer/coping/caregiver-support>)
- Health and Human Services (<https://www.hhs.gov/programs/providers-and-facilities/resources-for-caregivers/index.html>)
- National Alliance for Caregiving (<https://www.caregiving.org/resources>)
- Family Caregiver Alliance (<https://www.caregiver.org>)

## Selected Resources (partial listing)

### Legal and Financial Support:

- Triage Cancer: Provides free education on the legal and practical issues of patients and care-givers including employment and workplace issues (<https://www.triagecancer.org>)
- Cancer Legal Resource Center: Addresses the legal issues faced by people with cancer (<https://www.thedrlc.org>)
- American Cancer Society (<https://www.cancer.net/navigating-cancer-care/financial-considerations/financial-resources>)
- Cancer Financial Assistance Coalition: A coalition of 14 organizations helping cancer patients manage their financial challenges (<https://www.cancerfac.org>)
- National Cancer Institute: A database of over 100 organizations providing services including financial help (<https://www.supportorgs.cancer.gov>)