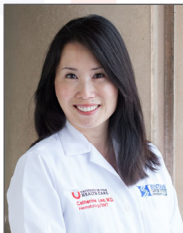



Late Effects after a Transplant Using Donor Cells (Allogeneic Transplant)

Celebrating a Second Chance at Life Survivorship Symposium

April 17-23, 2021




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Late Effects After A Transplant Using Donor Cells (Allogeneic Transplant)

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Overview

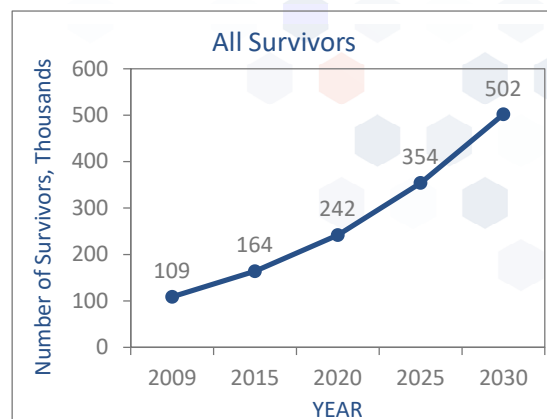
- Survivor Trends
- Why Survivorship?
- Medical Late Effects
 - Screening, Prevention, and Treatment
- Thriving After Allogeneic Transplant



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Survivor Trends

- In 2010: 110,000 HCT survivors in the United States
- In 2020: Increase by 2.5X to 250,000
- In 2030: Estimated increase by 5X to 500,000+
- Distribution: 60% autologous and 40% allogeneic HCT
- 60% of HCT survivors are age 18-59



Majhail NS et al. BBMT 2013; 19(10):1498-1501; Locke et al. The Lancet Oncology. 2019; 20(1):31-42

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Survivor Trends

- Long-term survival is increasingly possible, due to advances in HCT
- Survival may come with a price
 - **66% of BMT survivors** report at least one chronic health condition compared to 39% of healthy siblings
 - **79% of survivors** have a non-malignant late effect at 5 years after BMT
- ***Life expectancy among 5-year survivors remained 30% lower compared to the general population***

Sun C et al. Blood. 2010; 116 (17):3129-3139; Khera N et al. J Clin Oncol. 2012; 30(1):71-77;
Martin PJ et al. J Clin Oncol. 2010; 28(6):1011-1016.



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Medical Long-Term Effects

- **Symptoms that began while undergoing treatment and linger for months or even years**
- Fatigue
- Neuropathy and other pain syndromes
- Premature menopause
- Infertility
- Chemo Brain
- Cataracts
- Sexual dysfunction
- Anxiety, depression



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Medical Late Effects

- **Toxicities that were absent at the end of treatment but show after treatment has ended**
- Cardiovascular Disorders
 - Coronary Artery Disease
 - Congestive Heart Failure
- Secondary Cancers
- Bone Diseases
 - Osteopenia/Osteoporosis
- Endocrine Disorders
 - Diabetes, Thyroid
 - Low sex hormones
- Chronic GVHD
- Neurocognitive Impairments
- Infertility
- Lung
- Kidney
- Liver
- Infections



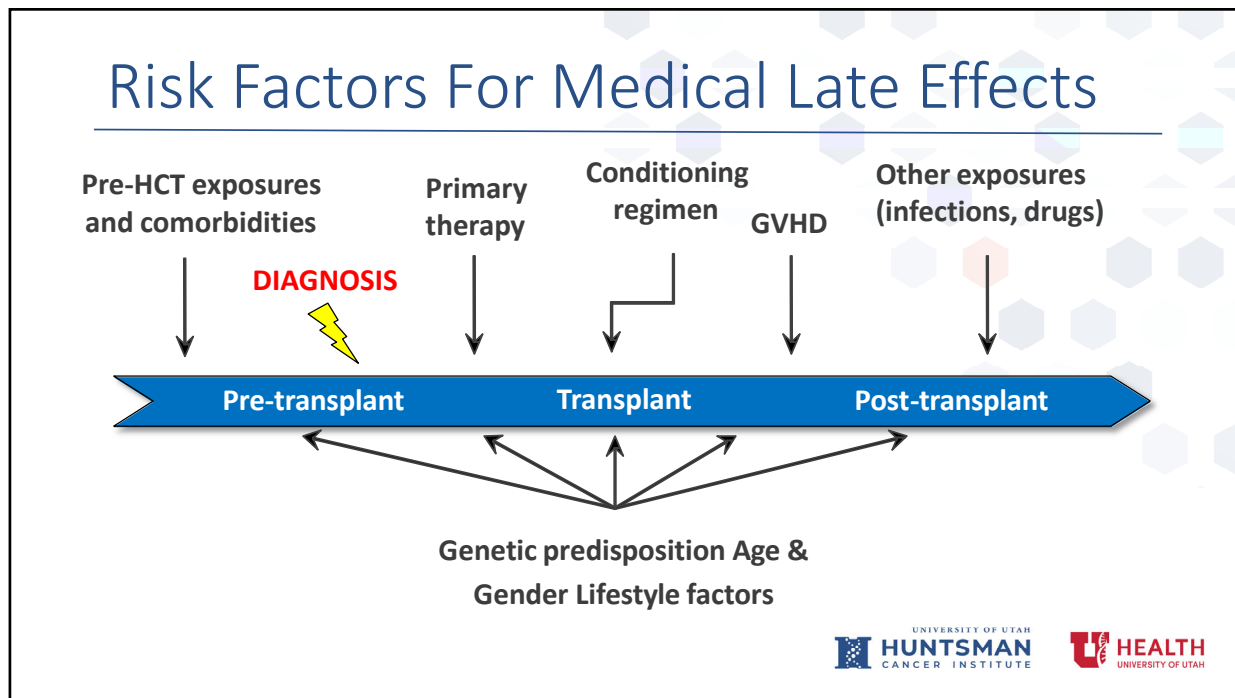
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Consequences of Medical Late Effects

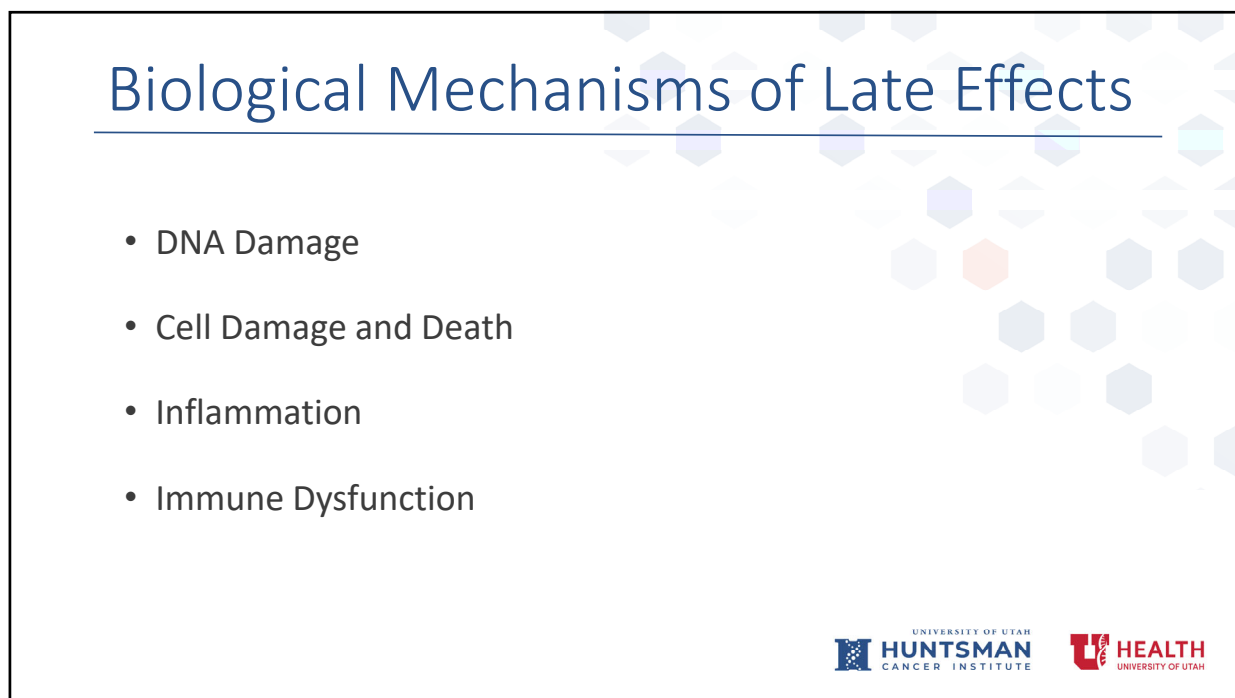
- Premature aging
- Cognitive issues
- Physical symptoms
- Disabilities
- Loss of job
- Financial problems
- Disabilities
- Separations/divorce
- Suicidal thoughts



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Individual Risk Factors

- **Past Medical History:**
 - Past and current medical problems
- **Family Medical History:**
 - Cancer syndromes, early heart disease, diabetes
- **Occupational Exposures:**
 - Chemicals, sun exposure, airway irritants
- **Lifestyle factors:**
 - Activity & exercise, diet, sleep, social supports, coping & resiliency
- **Habits:**
 - Smoking, alcohol, illicit drug use



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Key Medical Late Effects

- Heart Disease
- Secondary Cancers
- Bone Disorders
- Endocrine Disorders
- Lung Disorders
- Iron Overload
- Neurocognitive Changes
- Fatigue
- Sexual Dysfunction & Infertility
- Others!



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Cardiac (Heart) Effects

BMT survivors have 1.4 - 3.5 X higher risk of heart disease compared to general population

Complications: Coronary Artery Disease (CAD) & Cardiomyopathy/Heart Failure

Risk Factors: Chemotherapy (Anthracyclines), chest radiation, total body irradiation, GVHD, steroids, high blood pressure, dyslipidemia, diabetes, obesity, alcohol, smoking, inactive lifestyle

Interventions: Optimize blood pressure, cholesterol, and diabetes; weight control/diet; exercise; smoking & alcohol cessation; health & wellness coach; support groups

Screening tests: EKG, Echocardiogram, cardiac stress test?



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Secondary Cancers

- BMT survivors have 3X higher risk of another cancer occurring after transplant
- Can be a solid tumor or blood cancer different from the cancer for which the transplant was performed
- Risk depends on exposure



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Risk Factors for Key Secondary Cancers

- **Skin:** Acute and chronic GVHD, immunosuppression, high doses of TBI, HCT at age < 18, fair skin
- **Thyroid:** TBI, female, chronic GHVD
- **Oropharyngeal:** Sustained chronic GVHD, prolonged immunosuppression, local radiation, male, tobacco use, HPV status
- **Breast:** TBI prior to age 30, chest radiation, family history
- **Cervical:** Chronic GVHD, HPV status, prolonged immunosuppression
- **Esophageal:** Chronic GVHD, prolonged immunosuppression
- **Therapy-related MDS/AML:** Prior chemotherapy or radiation



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Cancer Screening Recommendations

Site	Screening & Prevention Recommendations
Skin	Routine skin exam for all (at least annually), Broad spectrum sunscreen use (UVA/UVB) Avoid peak sun hours, sunglasses, hats, protective clothing, SunGuard
Thyroid	Annual physical exam



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Cancer Screening Recommendations

Site	Screening & Prevention Recommendations
Oropharyngeal	Exam every 6-12 months depending on risk factors Dental exam every 6 months Encourage cessation of tobacco use and alcohol HPV vaccination as indicated
Lung	Screening with low-dose CT considered for high risk groups only: <ul style="list-style-type: none"> - >55 years and ≥30 pack-year smoking history (excluding those who quit smoking >15 years ago) - ≥50 and ≥20 pack-year smoking history with additional risk factor(asbestos, family history, second hand smoke) Encourage stopping tobacco product use

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Cancer Screening Recommendations

Site	Screening & Prevention Recommendations
Breast	Age 20-40 years: clinical breast exam every 1-3 years Age > 40 years: annual clinical breast exam; annual mammogram Age 25 years or 8 years after radiation, whichever first, but no later than age 40 years: annual clinical breast exam, annual mammogram, annual breast MRI
Cervical	Annual Pap test and HPV DNA test HPV vaccination as indicated

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Cancer Screening Recommendations

Site	Screening & Prevention Recommendations
Esophageal	Symptom based screening: GI endoscopy for GERD symptoms or difficulty swallowing
Colorectal	<i>Starting at age 50</i> Fecal occult blood or fecal immunochemical test annually Sigmoidoscopy or CT Colonography every 5 years Colonoscopy every 10 years

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Bone Disorders

- **BMT survivors have a 20% incidence of osteoporosis by 2 years post-transplant**
- **Majority of bone loss occurs within 3-6 months after transplant**

Complications:

- Osteoporosis/osteopenia
- Compression/bone fractures
- Avascular necrosis

Risk Factors: Steroids, GVHD, hypogonadism, radiation, immunosuppression, vitamin D deficiency, sedentary lifestyle, age, race, smoking

Interventions: Increase physical activity, calcium/vitamin D repletion, bisphosphonates, hormone replacement therapy

Screening tests: Vitamin D levels, bone density scan, PTH level

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Endocrine Disorders

Complication: Low thyroid function (hypothyroidism)

Symptoms: Fatigue, feeling cold, dry skin, weight gain, depression

Risk Factors: Radiation, some chemotherapy

Interventions: Thyroid hormone replacement

Screening tests: Thyroid hormone levels (TSH, Free T4)



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Endocrine Disorders

Complication: Diabetes

Symptoms: Sometimes no symptoms, increased thirst, frequent urination, fatigue, blurry vision

Risk Factors: Long-use of steroids for cancer treatment or GVHD

Interventions: Diet & exercise modifications, insulin or oral medications

Screening tests: HgbA1c, glucose level



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Endocrine Disorders

Complication: Hypogonadism (low sex hormones) and sexual dysfunction

Symptoms: Low sex drive, fatigue, vaginal changes and pain, ovarian failure, erectile dysfunction

Risk Factors: Radiation to pelvis/testes/spine/brain, TBI, high dose chemotherapy

Interventions: Hormone replacement when safe, testosterone replacement for symptoms (check PSA level), refer to Endocrine, GYN, Urology as needed

Screening tests: Estradiol, FSH, LH, morning testosterone, free testosterone



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Lung Disorders

Complications: Bronchiolitis obliterans syndrome (BOS), recurrent lung infection, fibrosis

Risk Factors: Chest radiation, TBI, chemotherapy, smoking, history of lung disease, cGVHD

Interventions: Exercise, pulmonary rehabilitation, smoking cessation, vaccinations, intravenous immunoglobulin

Screening tests: Interval pulmonary function tests, CT imaging of chest



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Iron Overload

Symptoms: Fatigue, muscle and joint pain, abdominal pain

- Can cause damage to the liver, pancreas, heart, and endocrine system with subsequent organ specific symptoms

Risk Factors: Frequent blood transfusions, genetics

Interventions: Remove iron (phlebotomy or medications)

Screening tests: Ferritin and transferrin saturation level, T2* MRI



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Neurocognitive Changes

Symptoms: Short-term memory loss, slow thinking, word finding difficulty, learning impairment, executive function

- Declines at 80 days after BMT
 - May return to pre-transplant levels at 1 year
 - May improve 1 to 5 years after BMT



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Neurocognitive Changes cont'd

Risk Factors:

- Brain radiation, chemotherapy (systemic and intrathecal)
- Immune dysfunction
- Drug toxicity, steroids
- Infections
- Critical illness

Interventions: Cognitive rehabilitation, methylphenidate/modafinil

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Fatigue – Risk Factors

Most common concern among survivors

Risk Factors:

- Stress
- Anxiety
- Depression
- Pain
- Treatment-related
- Poor sleep
- Deconditioning
- Poor nutrition
- Dehydration
- Other causes

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Fatigue – Interventions

- Treat any medical cause
- Exercise
- Sleep
- Relaxation techniques
- Treat pain
- Cognitive & behavioral therapy
- Refer to supportive oncology/palliative care

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Other late effects

- **Ocular: Premature cataracts, dry eye syndrome**
 - Protect eye from the sun, annual eye exam
- **Oral: Dry mouth, cavities**
 - Routine dental exam, cleaning & Xray, fluoride treatments
- **Chronic kidney dysfunction**
 - Check urine protein
- **Liver: Fatty liver, cirrhosis, chronic hepatitis**
 - Avoid alcohol, improve diet & exercise
- **Peripheral Neuropathy**
 - Foot exam

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Your Survivorship Team

- **A multidisciplinary team approach considers a provider's expertise and aims to meet each survivor's unique physical, social, psychosocial and spiritual needs**
- Cardiology
- Pulmonary
- Endocrinology
- Mental Health Professionals
- Physical/Occupational Therapy
- Neurology/Neuro-psychology
- Sexual Health/Fertility
- Supportive Oncology
- Social Work
- Primary Care



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Summary

- Medical late effects commonly occur after a donor transplant
- Know your treatment and risks
- Be informed and ask questions
- Actively own your health
- Follow recommendations for prevention and intervention
- Commit to lifelong follow-up


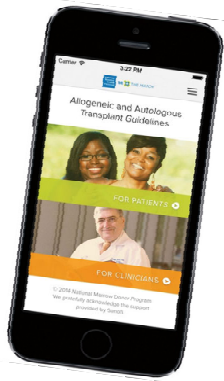




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After Transplant Guidelines for Patients

- Transplant guidelines mobile app
 - Customizable 6-month and yearly **checkup guidelines**
 - Chronic **GVHD symptom checker**
 - **Set reminders** (appointments, medicines, etc.)
 - Search “**transplant guidelines**” in app stores to download
- 6-month and yearly guidelines also available online and print:

[BeTheMatch.org/CareGuide](https://www.bethematch.org/CareGuide)







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LaShonda, transplant recipient

Be The Match Survivorship Program

Our Goal:
To improve quality of life for BMT patients who do not have access to comprehensive survivorship care.

Our Plan:
Be The Match will conduct research studies examining the effectiveness of a virtual survivorship program including:

- Individualized survivorship care plans
- Scheduled follow-up appointments with a nurse practitioner
- Clinical consultation Services
- Care coordination
- Access to critical resources
- Evaluation of the program's impact on patient QOL

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Questions?



Celebrating a Second Chance at Life Survivorship Symposium 2021

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