

Strive to Thrive: How to Protect Your Health after a Transplant Using Your Own Cells (Autologous Transplant)

Celebrating a Second Chance at Life
Survivorship Symposium

July 11-17, 2020



Peter McSweeney, MD
Colorado Blood Cancer Institute

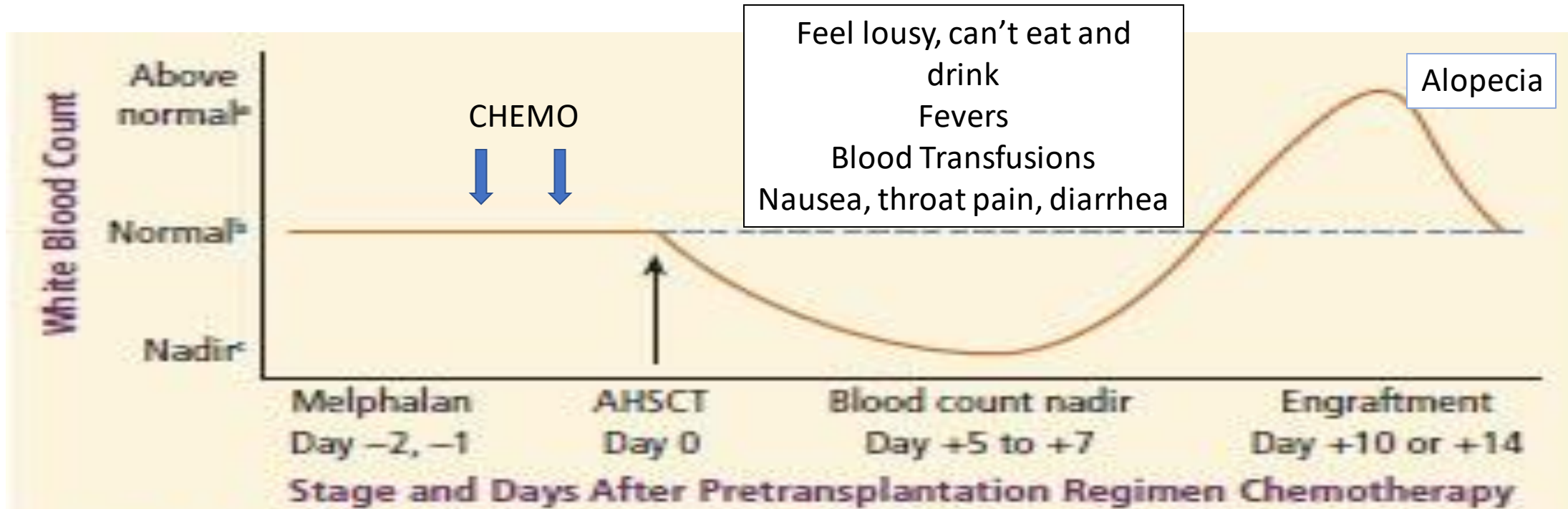
Autologous Transplant Procedure

Use of high dose chemotherapy (+/-radiotherapy) to treat underlying disease

Components:

- Pre-transplant treatment to lower disease burden
 - Collection and storage of own “stem cells”
 - chemo or growth factor “mobilization”
 - High dose therapy using single or multiagent therapy
 - Maintenance treatment may be given after the transplant
1. Body encounters cumulative toxicity from these treatments
 2. Older, less healthy patients being transplanted these days

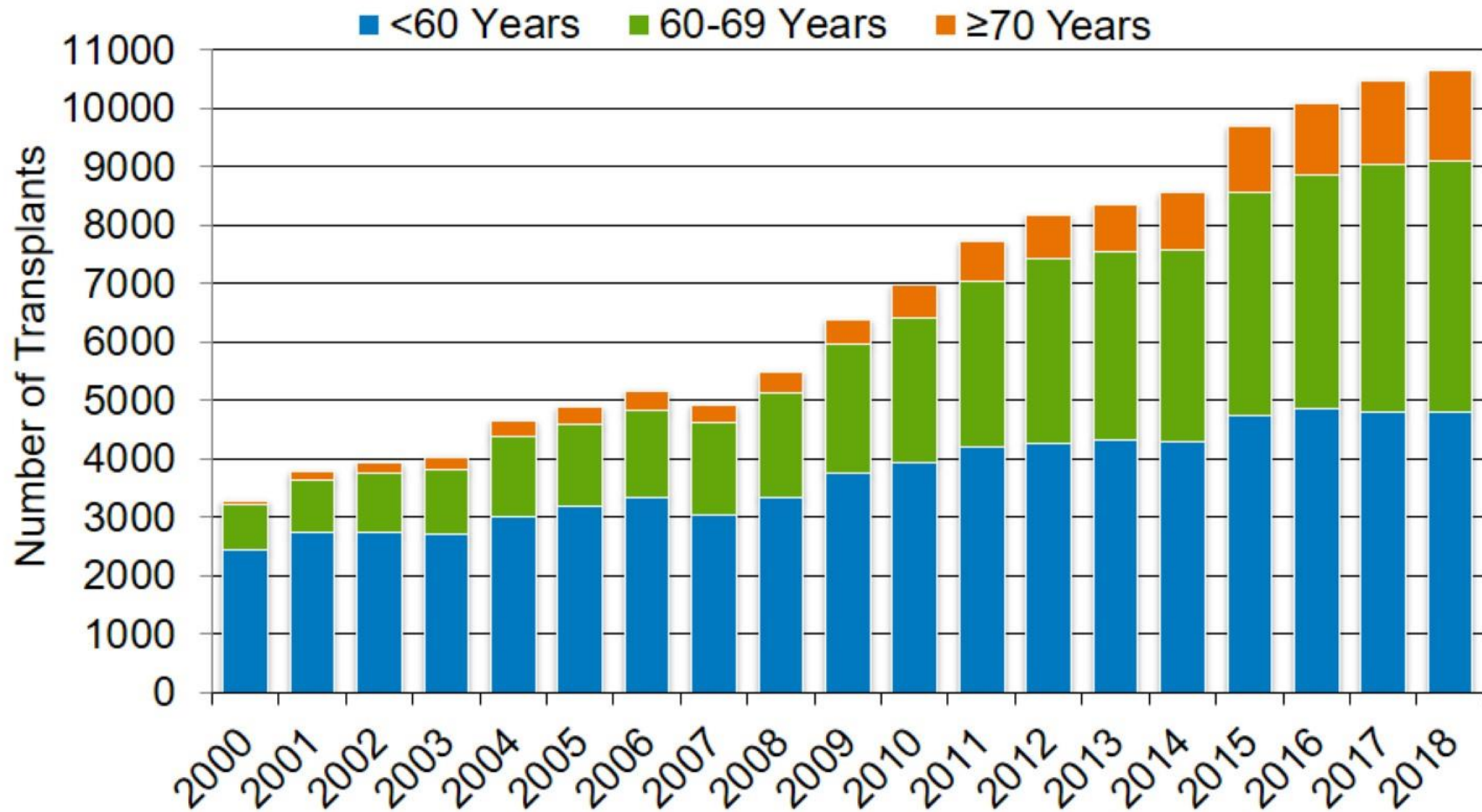
Autologous Transplant for Myeloma



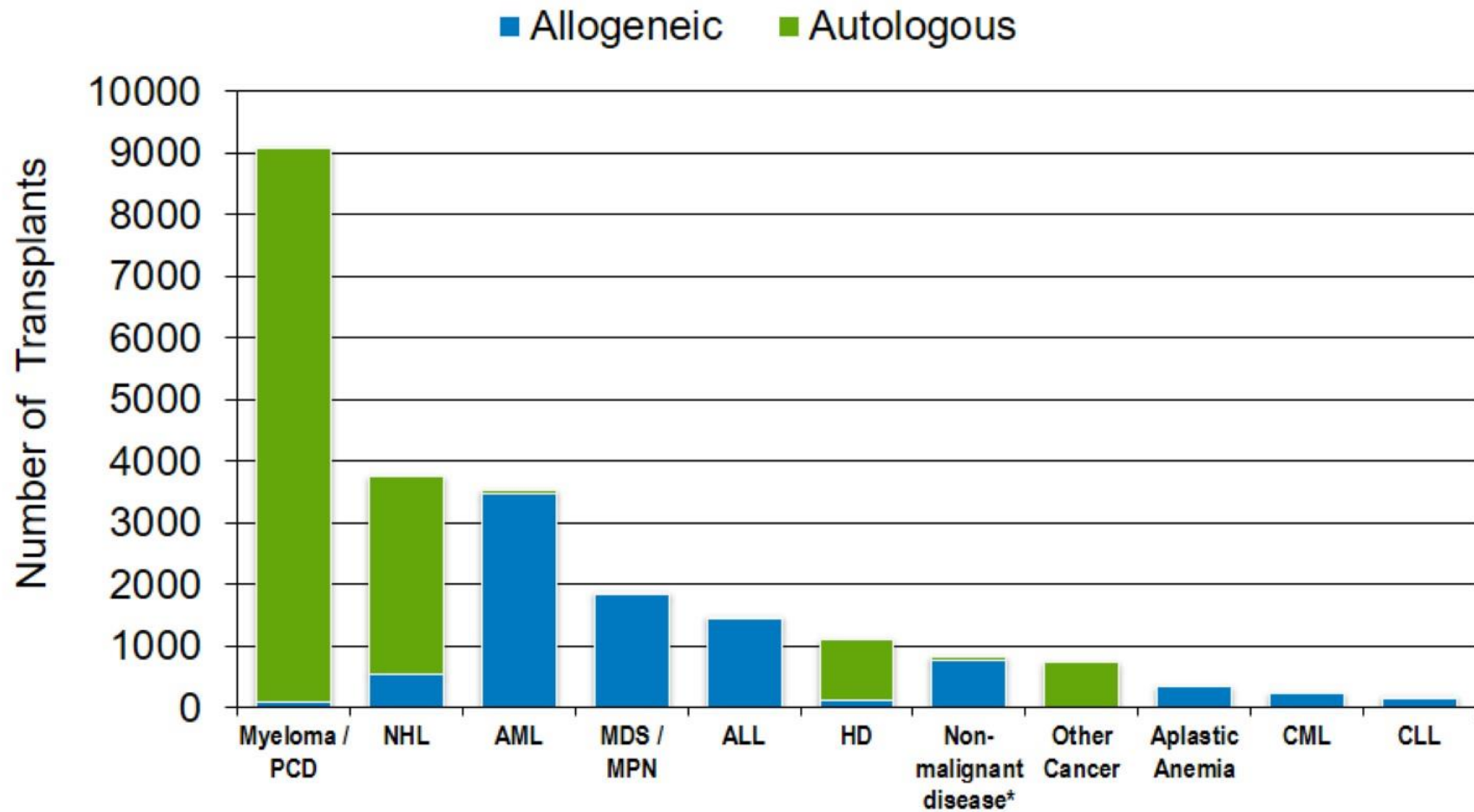
Diseases Treated with Autologous Transplant

- Multiple Myeloma
- Non-Hodgkin Lymphoma
- Hodgkin Lymphoma
- Leukemia
- Solid Tumors
 - Germ cell
 - Neuroblastoma
- Autoimmune Disease
 - Scleroderma
 - Multiple Sclerosis

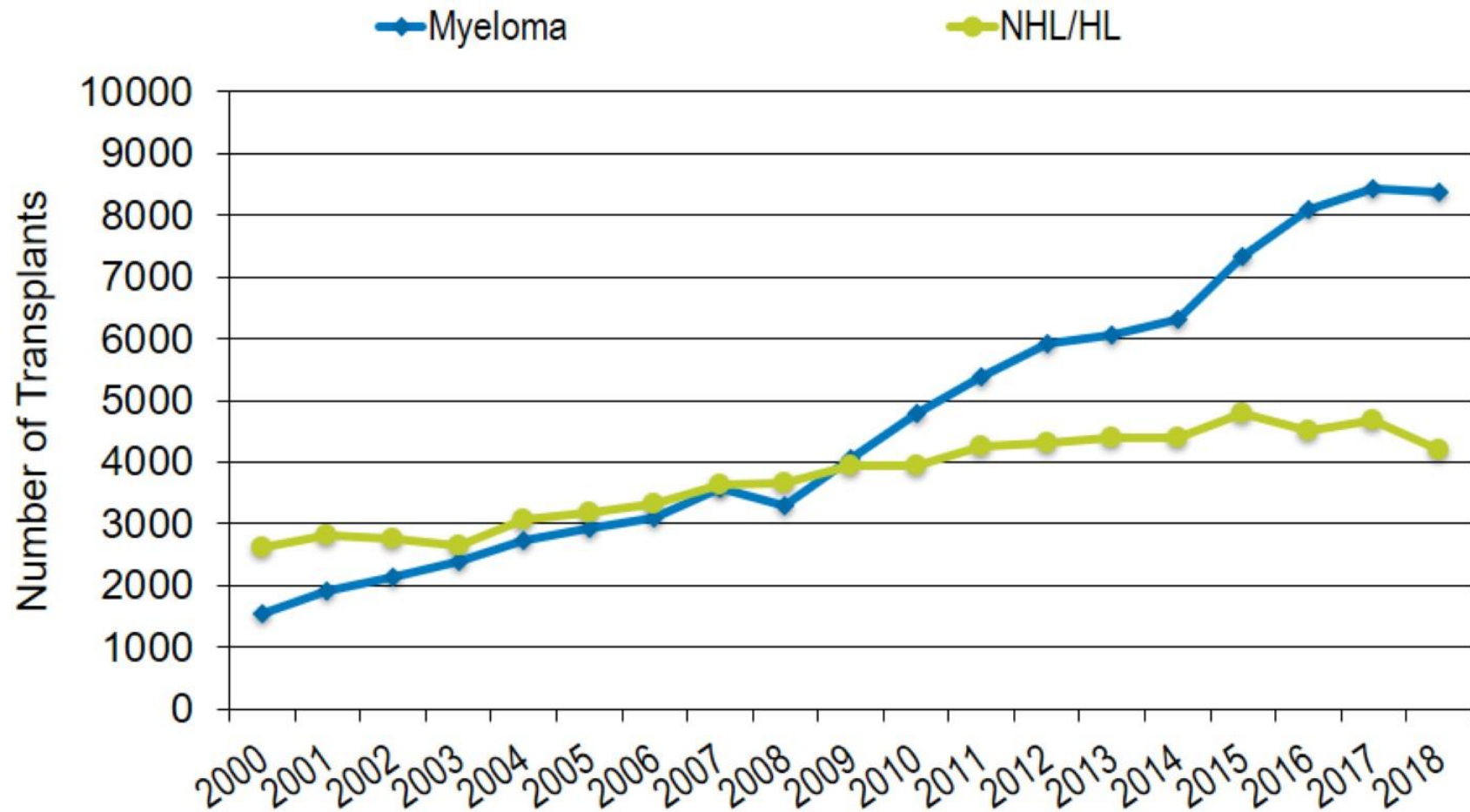
Trends in Autologous HCT in the US by Recipient Age[^]



Indications for Hematopoietic Cell Transplant in the US, 2018



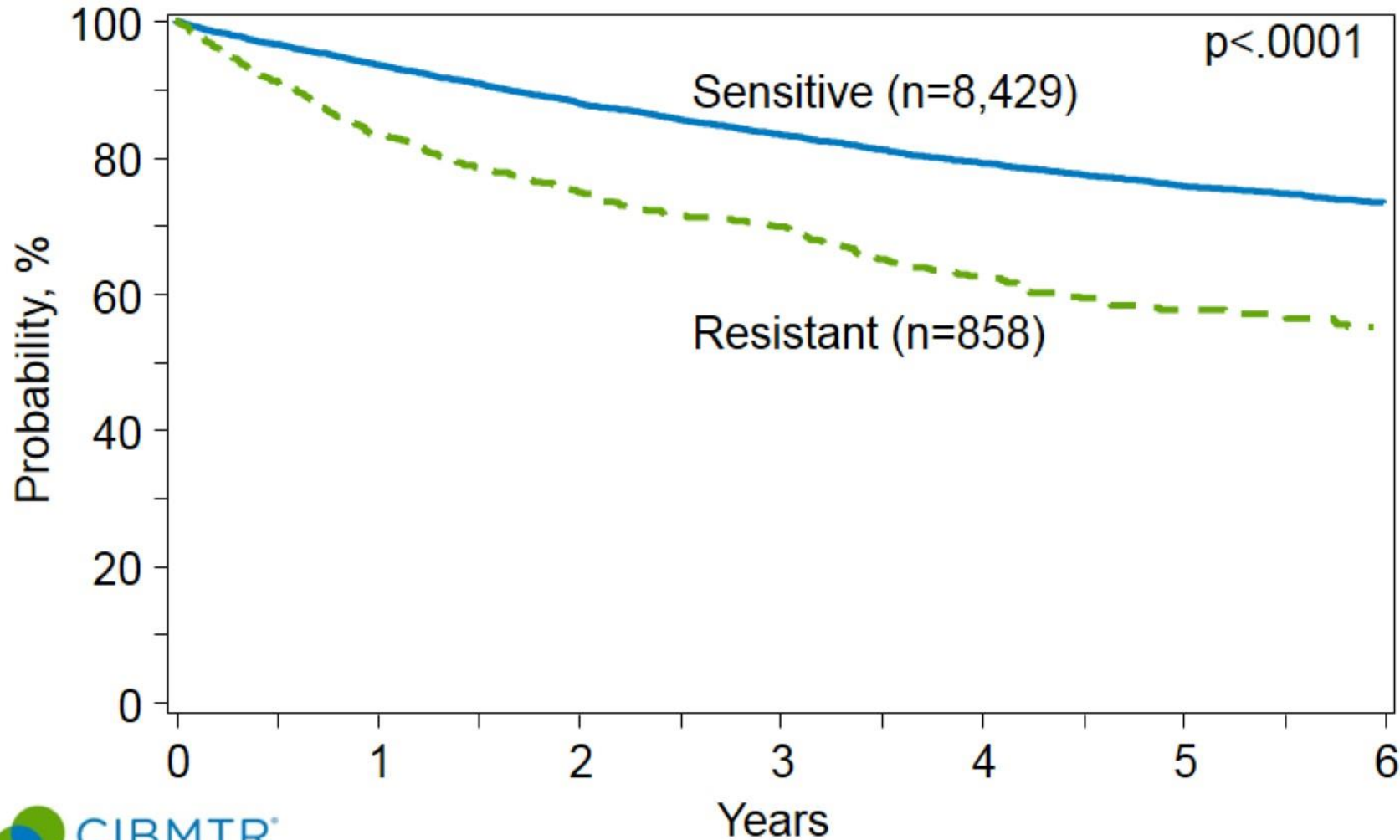
Selected Disease Trends for Autologous HCT in the US



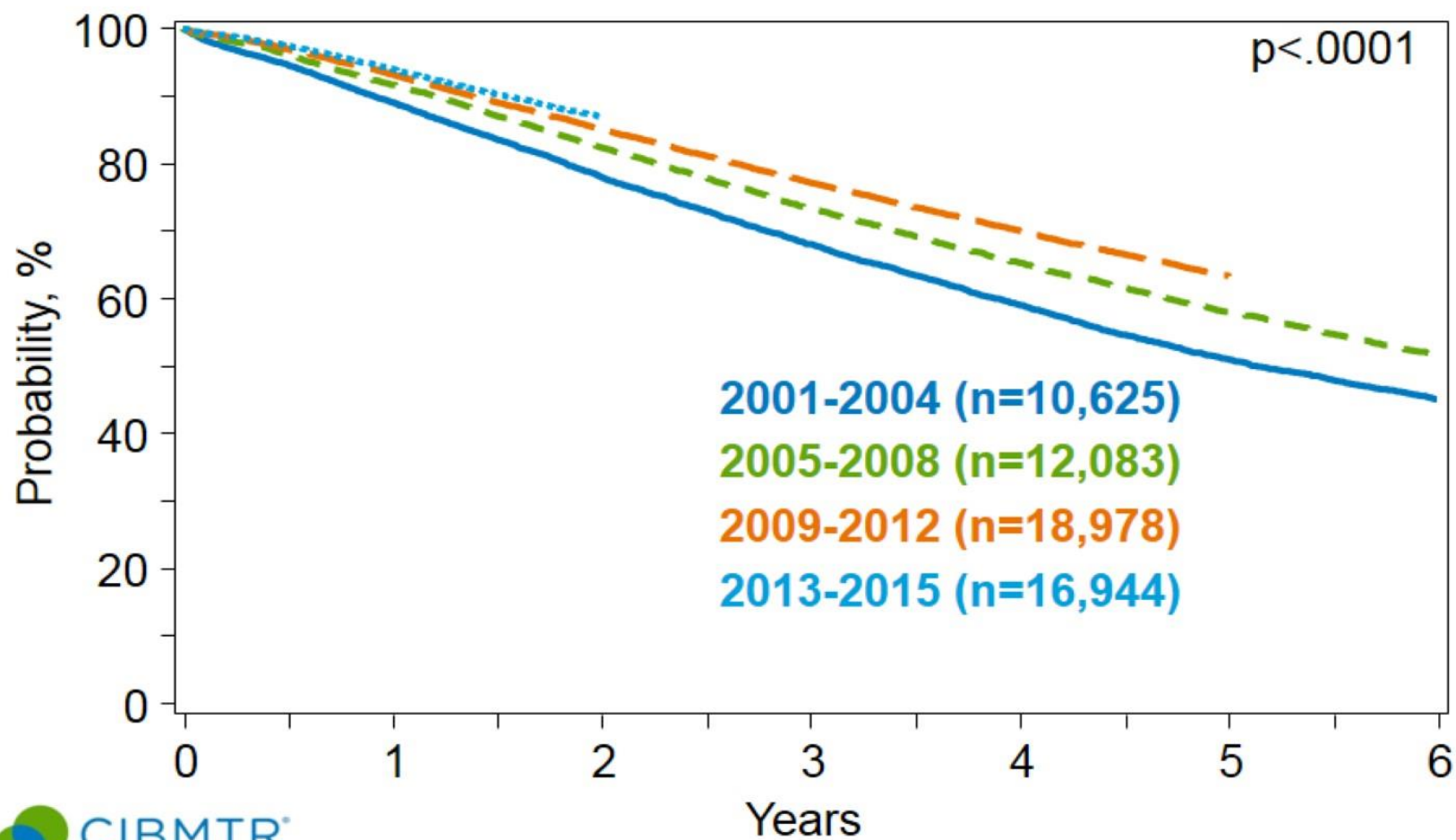
Goals of Autologous Transplant

- Cure of disease
- Extend survival
- Eliminate or reduce symptoms of disease

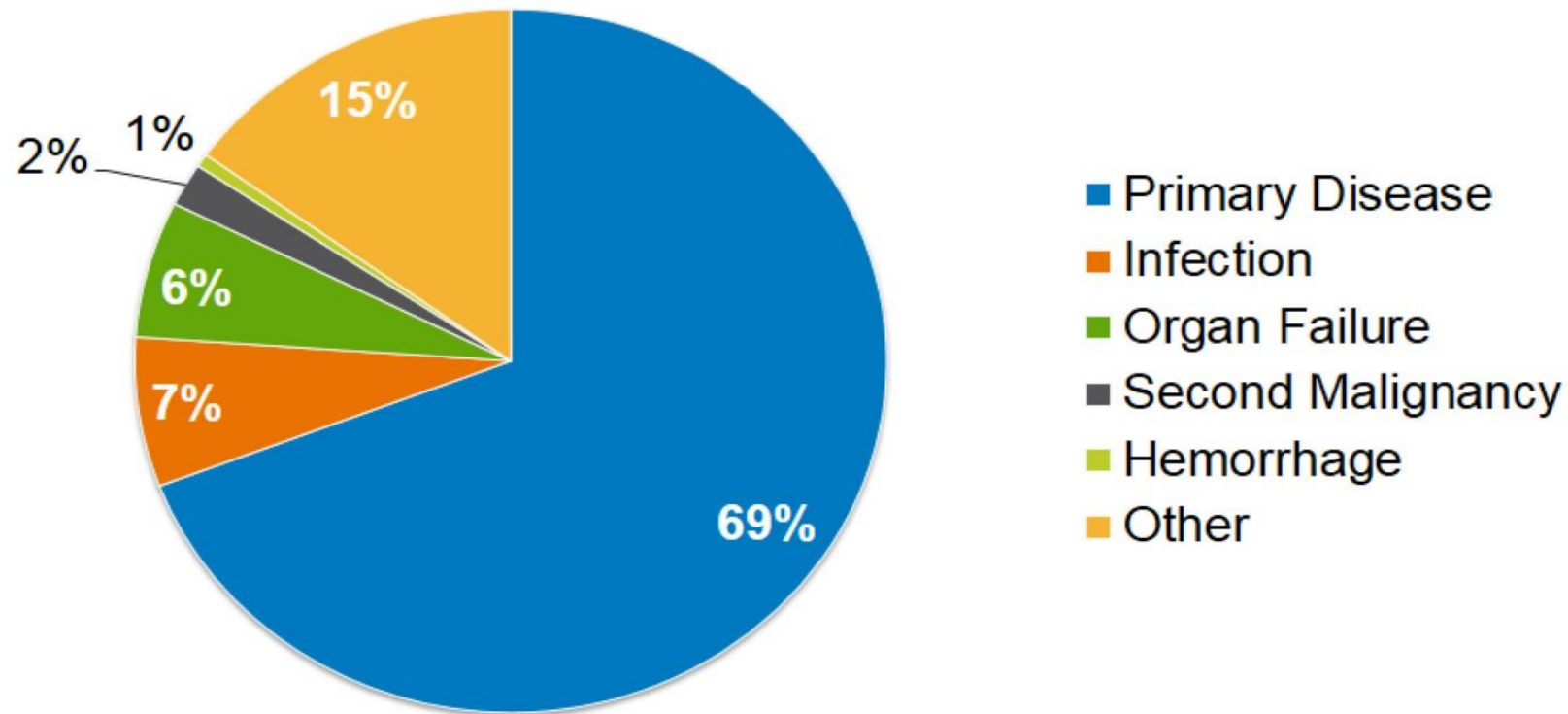
Survival after Autologous HCT for Hodgkin Lymphoma, 2005-2015



Trends in survival after Autologous HCT for Multiple Myeloma, 2001-2015



Causes of Death after Autologous HCT done in 2014-2015



Risk of Relapse after Auto Transplant

- Autologous transplant's major limitation is relapse of underlying disease
- Risk of relapse and length of remission are related to disease type, disease characteristics and remission status
- Post-transplant “maintenance” or “consolidation” therapies have been adopted to improve outcomes
 - Revlimid, Velcade, additional cycles of chemo, and second transplants in myeloma
 - Rituximab in mantle cell lymphoma
 - Brentuximab in Hodgkin lymphoma

Treatment of Relapse

GOALS

- Extend survival
- Alleviate symptoms
- Cure disease

TREATMENT OPTIONS

- Chemotherapy
- Clinical trials
 - Novel drugs
 - Immunotherapies
- Second Transplant
 - Autologous
 - Allogeneic
- CAR T cell therapy

CAR T Cell after Transplant

1. Now commercially available for aggressive B-cell NHL
 - Effective and likely curative in about 1/3 patients treated for relapsed or resistant disease
2. In relapsed and refractory myeloma high percent of responses in some studies
 - May provide benefit by extended responses
 - Use at earlier stages in disease being studied
 - Commercial product may be available in next year
3. Strategies for other diseases such as Hodgkin lymphoma and T-cell NHL under development

Late Side Effects of Autologous Transplant

- Specific type of chemotherapy, radiation
- Metabolic and Endocrine Health
- Immune System/Infections
- Fertility
- Cardiac/Pulmonary
- Neurological
- Fatigue
- Ocular
- Secondary Cancers
- Social and Work Functioning

Bone Loss

- Avascular necrosis (5-10% of patients)
 - Use of steroids- chronic or high dose
 - Hips > ankles and shoulders
- Bone thinning in 50-60%
 - 20% progress to osteoporosis
 - Symptomatic fractures in 1-5%
- Additional risk factors
 - Family history may increase chances/severity
 - Low testicular/ovarian function
 - Prolonged G-CSF therapy
 - Impaired kidney function

Prevention of Bone Loss

- Periodic Bone Density Testing (at risk)
- Bisphosphonates- osteoporosis
- Calcium/Vitamin D- based on levels
- Hormone replacement therapy (male and female)
 - Risk/benefit must be individualized
- Exercise
 - Before, during, after chemo and transplant
 - Core and cardiovascular focus
 - Time focused - scaled to energy levels
- Endocrinologist evaluation

Problems with Immunity/Infection

- Low immunoglobulins common
 - Splenic function reduced
- May need long term antibiotics for pneumococcus
- Shingles reactivation in 20-50%
- Pneumocystis carinii
 - Can occur >1 year post transplant
 - Can occur after use of fludarabine, 2-CDA, clofarabine
- Post-transplant patients require revaccinations after one year
- Post-transplant vaccination guidelines available in the CIBMTR Post-Transplant Guidelines

Vaccinations after Autologous Transplant

- Timing to start vaccinations often varies from transplant center to transplant center
 - Usually started 6-12 months post transplant
- Vaccines are scheduled as time 0, +2mo, +4mo, +12mo
 - Live vaccines may not be given if on maintenance chemo post transplant
- Shingles vaccine recommended after transplant
 - 2 and 4 months post transplant
- Flu vaccine effective after 6 months, more so after 12 months post transplant



Fertility after Transplant

- Infertility is not a certainty and recovery may occur
- Don't rely on transplant as contraception!
- High dose cytoxan, TBI associated with >80% loss fertility
 - Women >> Men
- Discussion of sperm, egg banking pre-treatment

Sexual Function after Transplant

- Therapy-related male and female menopause frequent
 - Regimen and age dependent
- Sexual function impairment by hormonal changes
 - Loss of lubrication, vaginal mucosal thinning
 - Low testosterone levels associated with lower libido
- Discussing sexual health with your doctors
 - Multidisciplinary approach

Pulmonary Problems after Transplant

- Pulmonary scarring associated with certain chemos
 - 5-10% incidence with bleomycin (testicular)
 - May occur years after prolonged carmustine (CNS)
 - Brentuximab - in combination with chemo
 - Radiation scatter from nearby chest, neck targets
- Post-surgical changes from loss of lung capacity
 - Lobectomy to remove sites of fungal infection
 - Effective loss from radiation
 - Pleural effusions, thickening or adhesions

Pulmonary Risks: What Can I Do?

- Report any changes in exercise tolerance
 - Think of exercise as a benefit and a “vital sign”
- Screening serial pulmonary function tests (PFTs) and high resolution chest CTs done post-transplant for at risk patients
 - Pulmonary BMT service
 - Early intervention against post-transplant inflammatory pneumonitis
- Don't start or restart smoking
- Vapor control in your workplace
 - Welding, solvents, corrosive chemicals

Heart Health after Transplant

- Heart attack risk seen after chest radiation, not total body irradiation (TBI)
- After treatment, increased risk of heart attack from:
 - Hormonal changes
 - Metabolic Syndrome:
 - Insulin resistance, hypertension, high lipids, abdominal obesity
 - 2.8 fold risk for chemo vs surgery treated testicular cancer
- Congestive heart failure risk with some chemotherapies
 - Higher anthracycline doses
 - May occur with high dose cytoxan, melphalan (<5%)

Heart Health after Transplant – What You Can Do

- Cardiac oncology services are emerging to work with these unique issues and needs

- Ensure you manage risk factors well



- Blood pressure, diabetes, cholesterol

- Exercise

- Engage in regular recommended health maintenance checkups

- Report any changes in your overall health

Neurological Side Effects of Transplant

- Cognitive (chemobrain)
 - Affects memory, attention, verbal fluency, executive functioning and visuospatial functioning
 - Prior to transplant cognitive impairment may be present due to prior treatment
- Peripheral neuropathy
 - Fairly common side effect of chemo; may be worse after transplant
 - Treatment is symptomatic
- Causes
 - Chemotherapy toxicity
 - Radiation
 - Infections
 - Other drugs

Ocular Side Effects

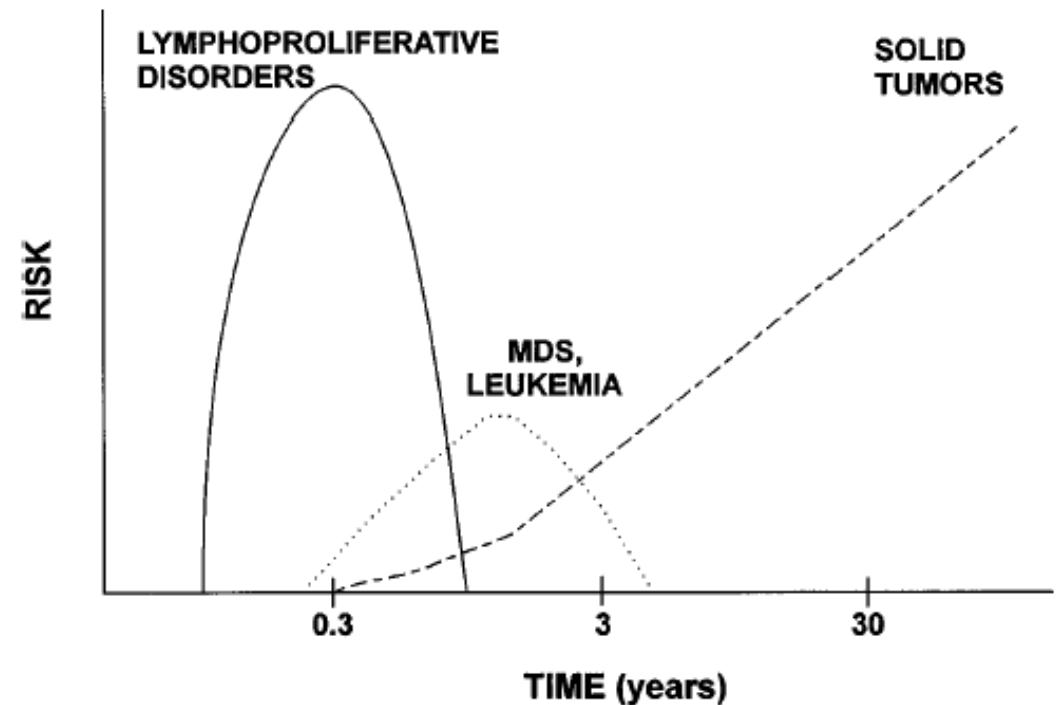
- Hemorrhages
- Cataracts
- Dry eyes
- Blood vessel damage in the ocular fundus
- Symptoms often fairly mild

Factors:

- Conditioning therapy especially total body irradiation
- Steroid exposure

Secondary Cancers

- Relative risk is 4-11 fold over general population
 - Cumulative incidence 10-12% at 15 years
- Risks related to:
 - Intensive cytotoxic chemotherapy conditioning
 - Previous chemo/radiotherapy
 - Infections
 - EBV- lymphomas
 - HPV- cervical cancer
 - HCV- liver cancer



Secondary Cancers

- Acute myelogenous leukemia (AML)/Myelodysplasia (MDS)
 - 4-5% incidence, generally occur 1-4 years post transplant
 - Use of some chemotherapies, focused radiation therapy
 - Transplant with <1 million stem cells
 - Total body radiation
- Solid tumors (skin cancer, breast cancer, oral, CNS)
 - Cumulative incidence 6-11% at 15 years
 - Highest risk in BMT patients under age 10
 - Related to immunosuppression, radiation, GVHD, viral infections

Secondary Cancers: What You Can Do

- Health maintenance
- Regular surveillance
- Health summary from transplant

Fatigue after Autologous Transplant

Common problem that is poorly studied in long term survivors.

Multiple factors contribute including:

- deconditioning
- neuropathy
- hormonal changes – thyroid, adrenal, sex hormones
- medications
- insomnia
- stress – financial, personal
- nutrition
- inflammation
- steroid myopathy
- unresolved toxicity of transplant procedure
- maintenance therapies
- depression and anxiety
- exacerbation of pre-existing medical problems
- persistent or relapsed disease

Fatigue after Autologous Transplant

Management includes:

- Assessment of nature and effects of fatigue
- Investigation of contributing factors
- Physical rehabilitation and exercise
- Addressing contributing medical and psychological issues
- Nutrition
- Cognitive Behavioral Therapy
- Match activities to energy

Sleep Disturbance

- Studies report disrupted sleep especially early after transplant
- May be persistent long term problem – reduced QOL, increased fatigue
- Contributing factors
 - Pain
 - Worry
 - Drugs - especially corticosteroids
 - Neuropathy
 - Depression
 - Anxiety
- Management
 - Treat exacerbating factors
 - Good sleep habits
 - Drug therapy
 - Cognitive behavioral therapy

Quality of Life after Transplant

- Many patients find limitations after transplant
 - 35% showed high levels of anxiety
 - 60% felt vulnerable
 - 35% showed unfulfilled needs in their love lives
- Physical functioning returns to pre-BMT level in >75% at 1 year
- 85% return to work or school
- Majority have good psychological health

Quality of Life after Transplant: What You Can Do

- You have accomplished a very difficult task
- Your body and psyche have experienced severe stress
- You are stronger than you think
- Live as healthy as possible
- Ask for help from family, physicians and counselors

Ability to Work after Transplant

- Ability of autologous transplant survivors to work little different from non-transplant patients
- Physical limitations to work in 26% after treatment; cognitive limits in 19%
 - More common after chemotherapy
 - More common if other health issues exist
 - Less likely if strong commitment to work
 - Less likely if good social climate at work
- Prevention of “chemobrain” through physical and mental activity in treatment and afterwards

Family Stressors

- Enhanced “white coat syndrome” at restaging visit
 - Anxiety, high blood pressure in the doc’s office, but not home
- Younger parents with unresolved anxiety or depression at time of BMT need more support
 - Higher incidence of PTSD and depression in parents
 - Families more active in care and recovery do better
- Anticipating these “anniversaries” as a family helps “own it”
 - Find ways to celebrate the win vs. reinforcing the fears
 - Your diagnosis and treatment is a part of you - move it from “theme song” to a “harmony line”

So Tell Me Some Good News....

- Make your remission count!
 - Open horizons, rather than be limited by what might occur
 - You are much more than your diagnosis and transplant
 - Don't focus on the cancer that was, focus on a healthy future
 - Empower yourself with knowledge

So Tell Me Some Good News....

- Take charge of your health and well-being
 - Preventative care and early intervention = better quality of life
 - Insist on communication between your health care providers and transplant team
- Seek help when and where you need it to thrive
 - Social connections rule!
- Always remember- YOU ARE A HERO!

Conclusions

- The number of long-term transplant survivors is increasing
 - More older patients with other medical issues
- Post-transplant therapies improve outcomes for some diseases
- Preventative health maintenance is key to post-transplant health
 - Multidisciplinary concern, not just the oncologist's worry
- Regular monitoring and health maintenance = prevention and more effective management of potential complications
- Patients and families who take an active role in treatment promote the best outcomes after transplant

Post-Transplant Care Guidelines - Resources

- More and more transplant centers are setting up long term/survivor follow-up clinics
- Individualized post-transplant follow-up for each patient for at least 10 years
 - Disease status monitoring
 - Disease relapse prevention
 - Prevention, diagnosis, monitoring and treatment of GVHD and immune reconstitution
 - Health maintenance for post BMT patients
- This should be a partnership with your local physicians
- <https://bethematchclinical.org/resources-and-education/materials-catalog/after-transplant-guidelines-for-patients/>
- <https://www.cibmtr.org/ReferenceCenter/Patient/Guidelines/Pages/index.aspx>



New tool to help manage post-transplant care

Even if you feel well, post-transplant checkups are important to managing your health. Our free guidelines can help you manage your posttransplant care.

Free mobile app

Features:

- Know what to expect after post-transplant checkups
- Get a list of tests and evaluations customized to your unique situation
- Email information to yourself or your health care team

Download now

Search for "transplant" on your phone's marketplace or scan this QR code

Access online or print versions: TheMatch.org/eaaguide

Screenshot of the CIBMTR website. The page title is "Post-Transplant Guidelines". The content includes a paragraph stating that in 2012, CIBMTR, in partnership with leading transplant organizations, published post-transplant care recommendations for adult and pediatric autologous and allogeneic bone marrow transplant recipients. It also mentions that these recommendations have been adapted into easy-to-understand guidelines and are now available through the National Marrow Donor Program (NMDP) The Match. There are two versions of the guidelines (patient and clinician) offered in multiple formats (print, online, mobile app). A "Learn more and access guidelines" section lists "Patient version" and "Clinician version". A "Reference" section lists a citation: "Majhar NL, Rizzo JD, Lee SJ, et al. Recommended screening and preventive practices for long-term survivors after hematopoietic cell transplantation. 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 (BM-TSAND), East Mediterranean Blood and Marrow Transplantation Group (EMBMTR), and Societe Brasileira de Transplante de Medula Óssea (SBTMO). Co-published in *Biol Blood Marrow Transplant*. 2012; 18(3): 348-371. *Bone Marrow Transplant*. 2012; 4(3): 331-341. and *Hematol Oncol Stem Cell Ther*. 2012; 5(1): 1-20." There is a "To view PDF documents you will need Adobe Reader." link and a "Last Updated: 4/13/2015 7:47 AM" timestamp. The footer contains the CIBMTR logo and a "Terms of Use / Privacy Statement" link.

Survivorship Information at bmtinfonet.org

- Late effects on organs and tissues
- Nutrition after transplant
- Infection control Antoniads
- Emotional challenges
- Employment/Financial health
- Health insurance
- Cognitive challenges
- Chronic fatigue
- Sleep difficulties
- Peripheral neuropathy
- Sexual health
- Building a family after transplant
- Caregiver challenges
- Secondary cancers



Questions?



Celebrating a Second Chance at Life Survivorship Symposium|

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