After Transplant: Finding Qualified Health Care Providers

Celebrating a Second Chance at Life Survivorship Symposium

May 3-9, 2025

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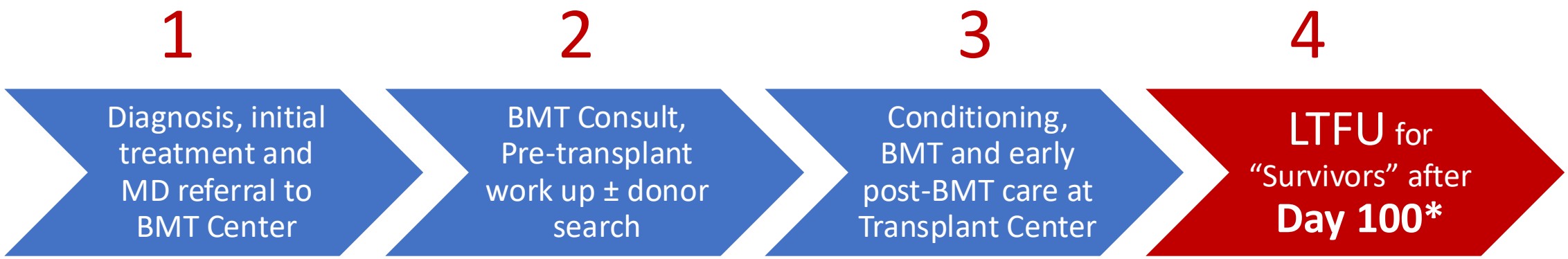
Learning Objectives

- The “When”, “Why”, “What” and “How” of BMT Survivorship or Long-Term Follow-Up (LTFU) Care
  - Care Models and their feasibility
- Goals of BMT Long-Term Follow-Up care:
  - Dr. Carpenter’s “Core to the Outer Spheres” for comprehensive Long-Term Follow-Up
- Role of Survivorship Care Plans
- What makes an ideal BMT LTFU healthcare provider?

When does Long-term Follow-Up care begin after BMT?

Phases of the BMT Care Continuum



quicker recovery if transplant is with own cells ("autologous") vs. donor cells ("allo")

*Long-term survivors often considered ≥2 years from BMT

Why is Long Term Follow Up So Important?

Regarding BMT Survivors…

- ~500,000+ in the US by 2030
- 2 in 3 have at least one health condition = double the rate in siblings
- Early detection/prevention aims to prevent significant complications and premature mortality.

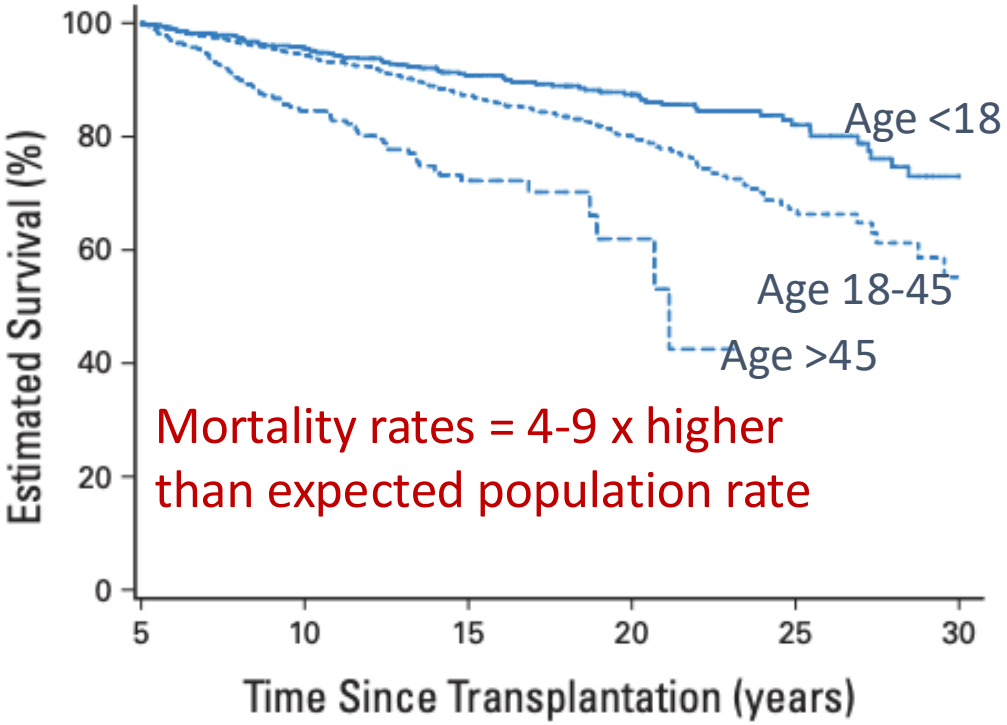
Sun et al, Blood 2010

Life expectancy in Seattle patients who survived at least 5 Years after their BMT

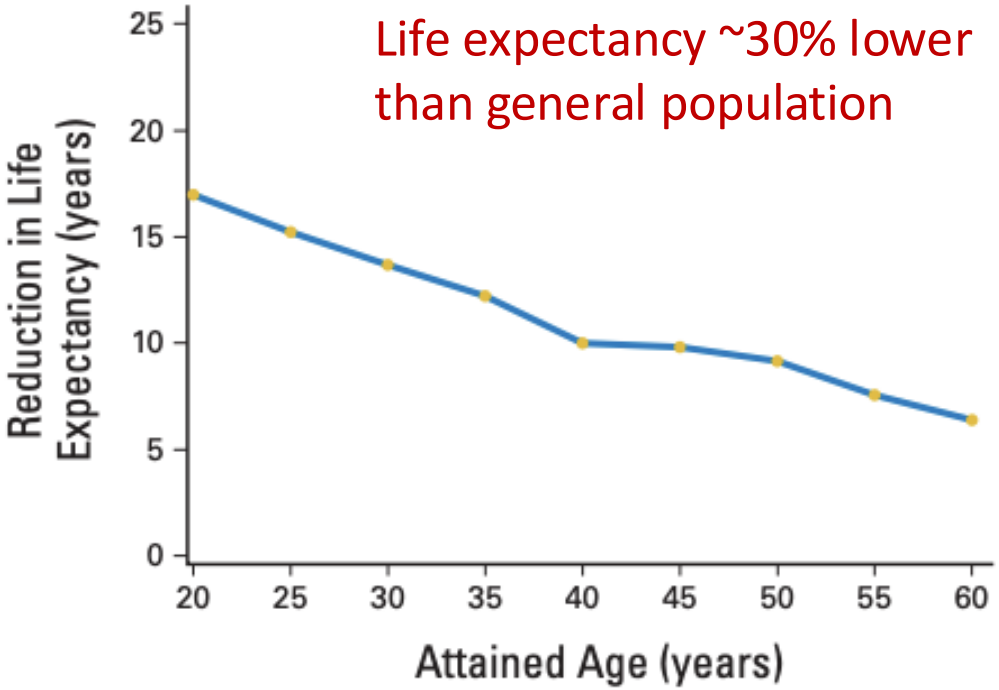
- 7,984 BMTs through 2002
  - High-dose conditioning
  - 5,410 died within 5 years, relapsed, had a 2nd BMT, or were lost to follow-up
- 2,574 ≥ 5-year survivors
  - Half were aged 46 years (range, 6-80) at analysis
  - Half were 13 years (range 5-36) post-transplant
  - 80.4% survived 20 years post-transplant

Martin et al, JCO 2010

Life expectancy in Seattle patients who survived at least 5 Years after their BMT



Mortality rates = 4-9 x higher than expected population rate



Life expectancy ~30% lower than general population

Martin et al, JCO 2010

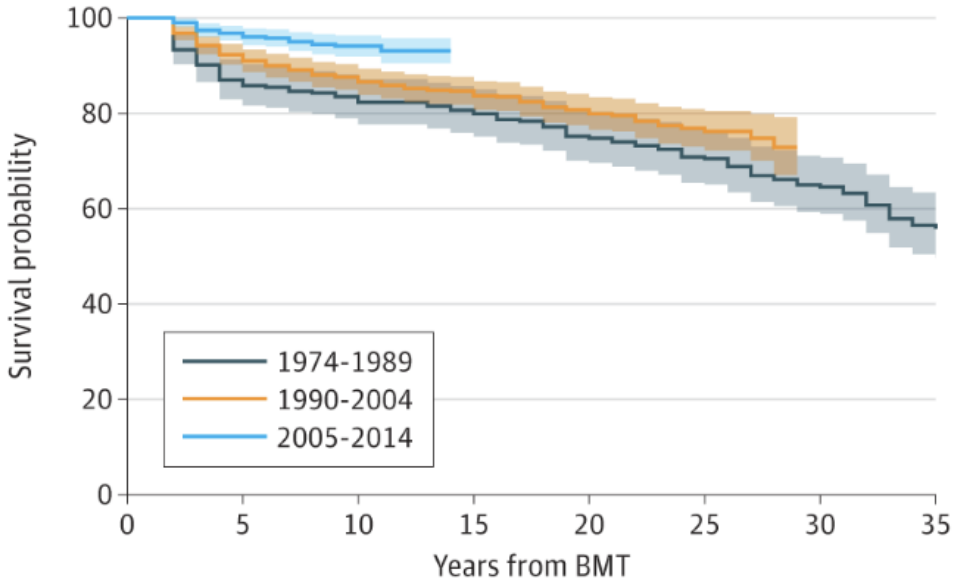
Life expectancy has improved for survivors (≥2+ y) over the past 40 years, but mainly for patients age <18 years

- 4,741 BMTs at City of Hope, University of Minnesota, and University of Alabama between 1974 and 2014
- Across the three periods:
  - More older patients received BMT
  - Conditioning got less intense
  - There was more chronic GVHD
- Half were age 12 years post-BMT (range 2-44 y) at analysis

Bhatia et al, JAMA Oncol 2021

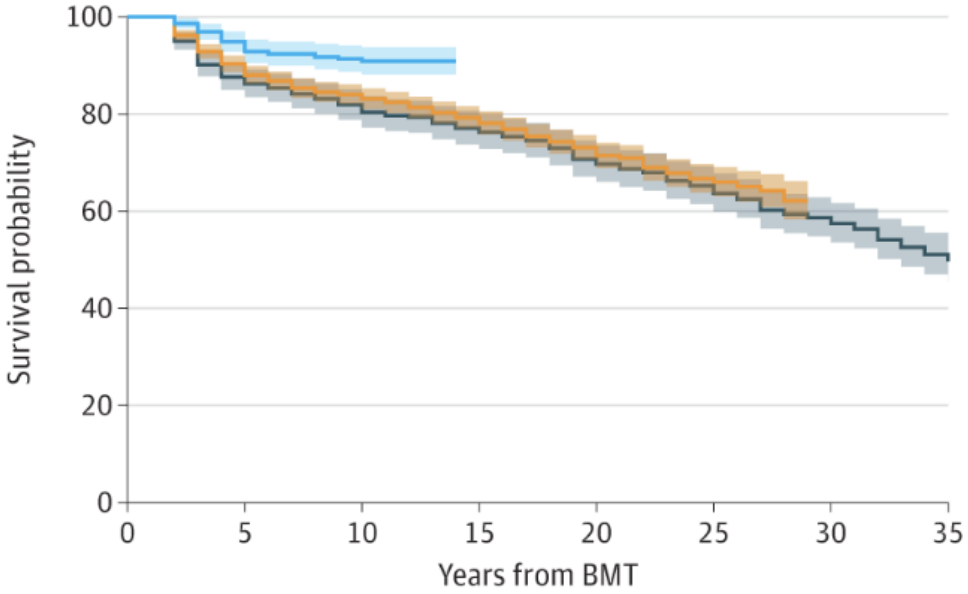
Life expectancy after transplant was better in children than in adults

Survival in patients with BMT at age <18



8.5%↓ life expectancy (= 2 years)

Survival in all BMT patients



Overall 20.8%↓ life expectancy (= 8.7 years)

- 9.7% if no CGVHD (4.4 y)
- 25% if CGVHD (9.6 y)

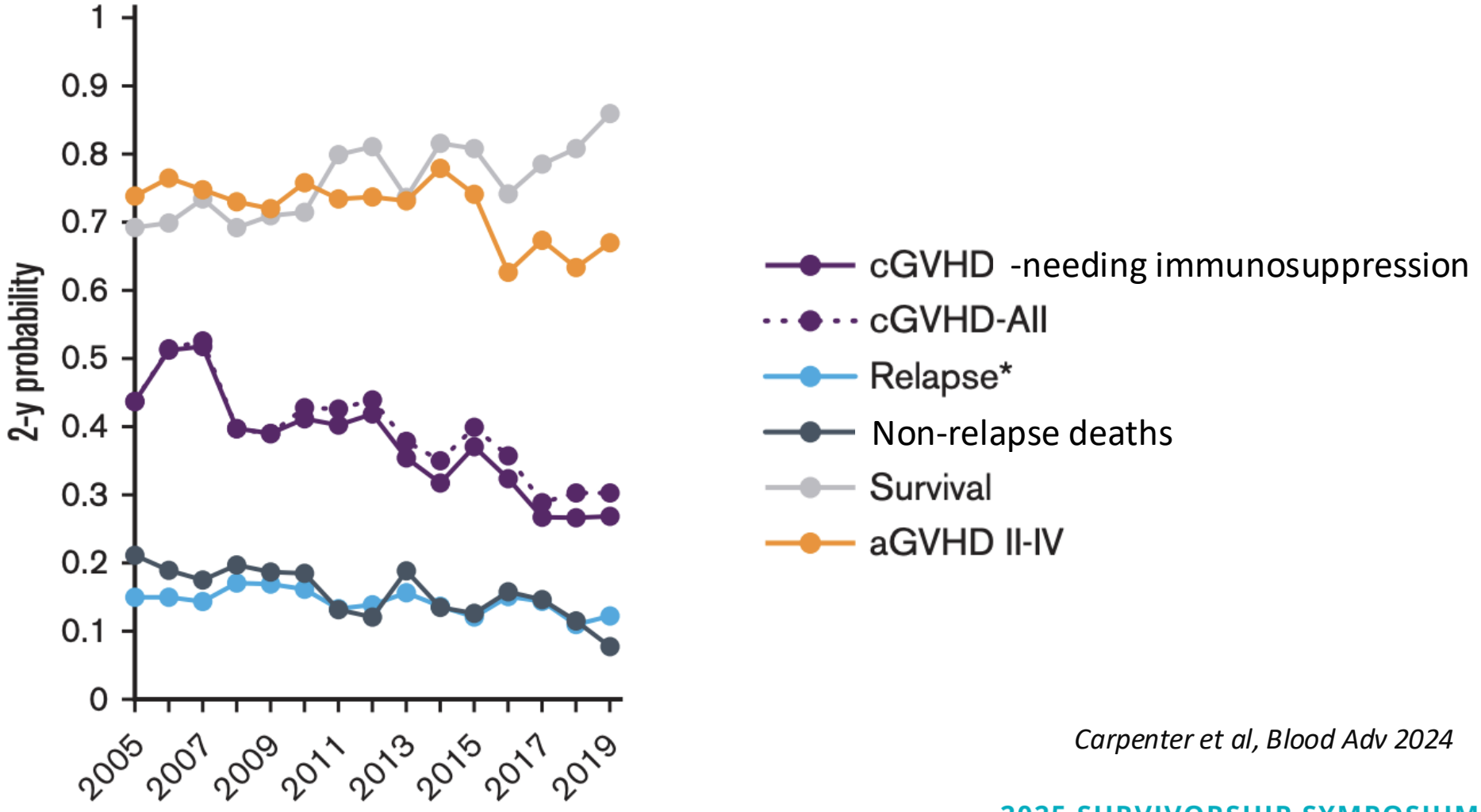
Bhatia et al, JAMA Oncol 2021

Leading Cause of Death at 30 years Post-Transplant

- Relapse = 12%
- Infection = 11%
  - 52 times higher than the general population
- Second cancer = 7%
  - 4.8 time higher than the general population
- Cardiovascular = 4.6%
  - 4.1 times higher than the general population
- Lung disease = 2.7%
  - 13.9 times higher than the general population

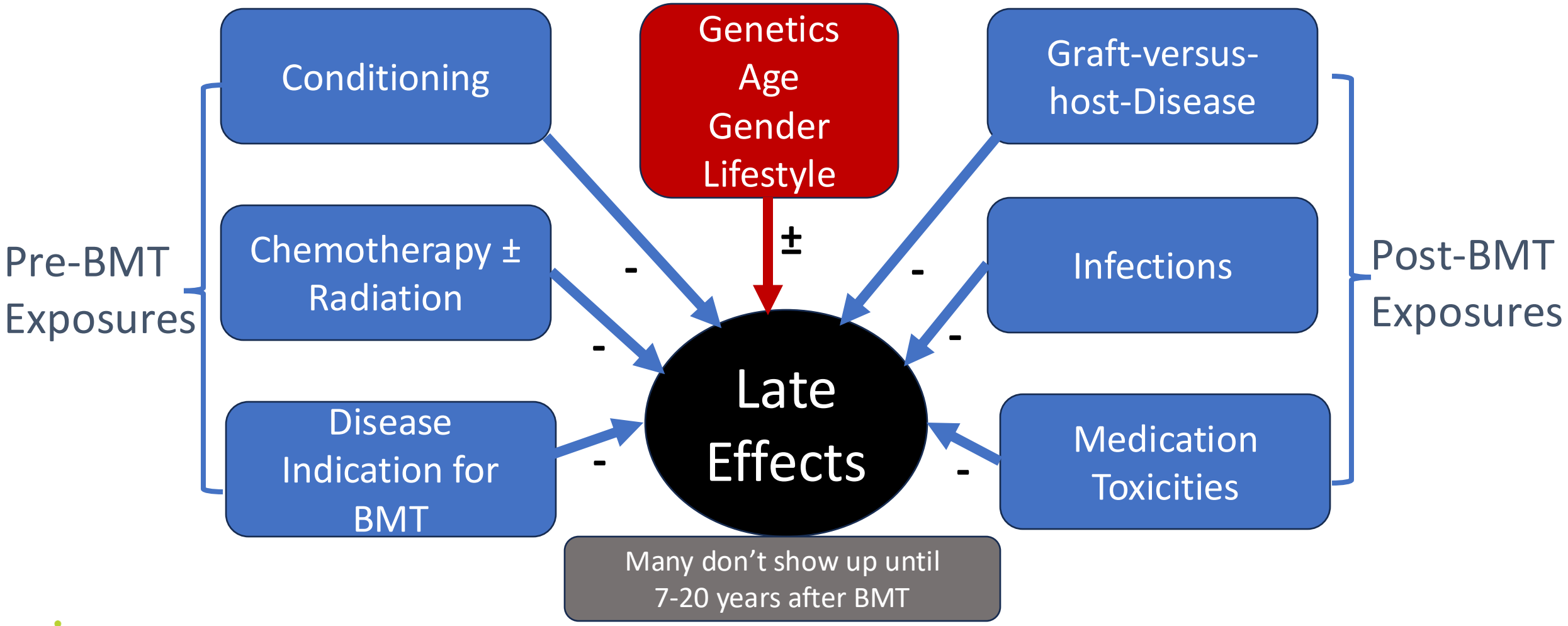
Bhatia et al, JAMA Oncol 2021

Good news is that Chronic GVHD is decreasing while survival is increasing for Seattle BMT patients



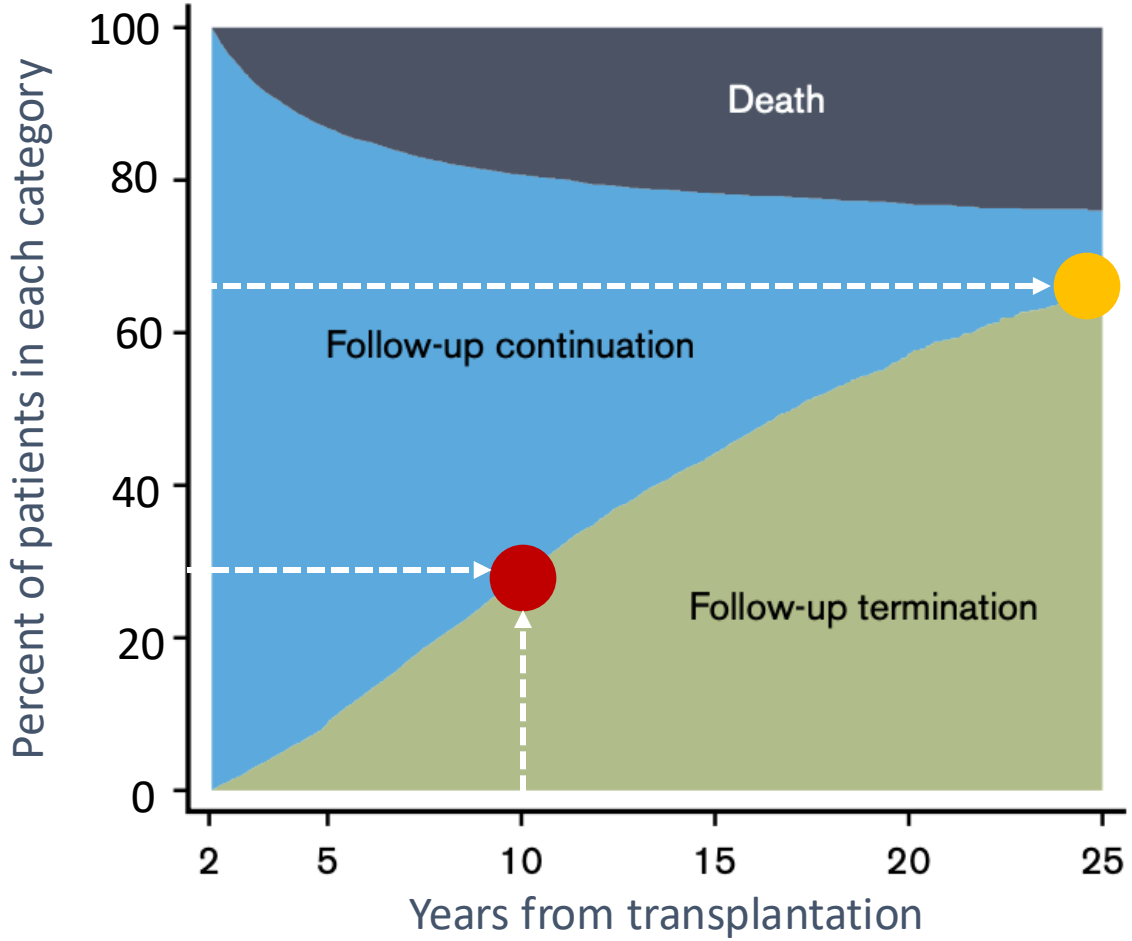
Carpenter et al, Blood Adv 2024

Beyond Survival: Why is Long-Term Follow-Up So Important?



Premature Discontinuation of Long-Term Follow-Up is a Problem

Large Japanese Study of BMT survivors: (N = 17,980)



Patients who prematurely ended long-term follow-up:

- 28% by 10 yrs
- 67% by 25 yrs

Miyamura et al, Blood Advances 2019

Why Long-Term Follow-Up was Discontinued

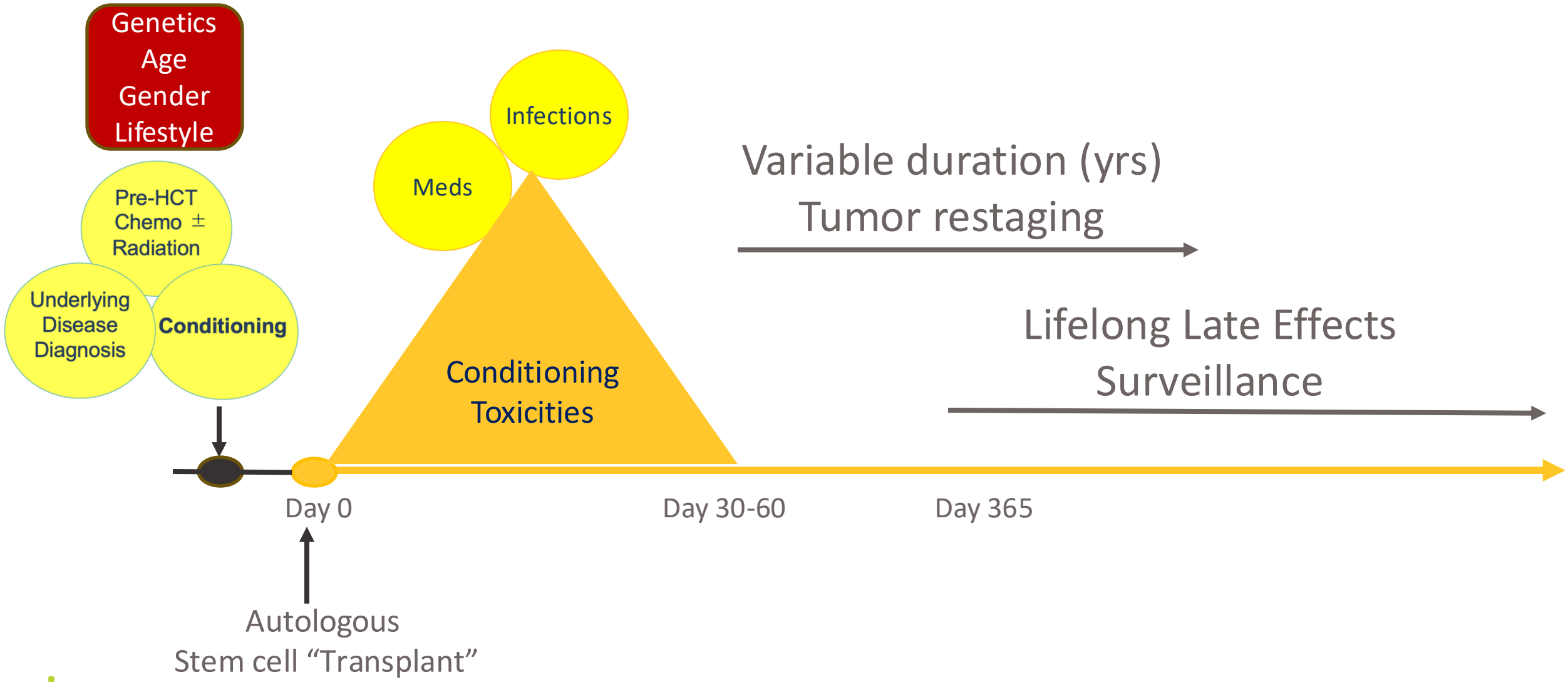
Large Japanese Study of BMT survivors: (N = 17,980)

- Most often, doctor-instigated based on “patient’s good physical condition”
- Most likely at-risk are adolescents and young adults but also:
  - BMT for non-malignant disease or standard-risk malignancy
  - Those without chronic GVHD

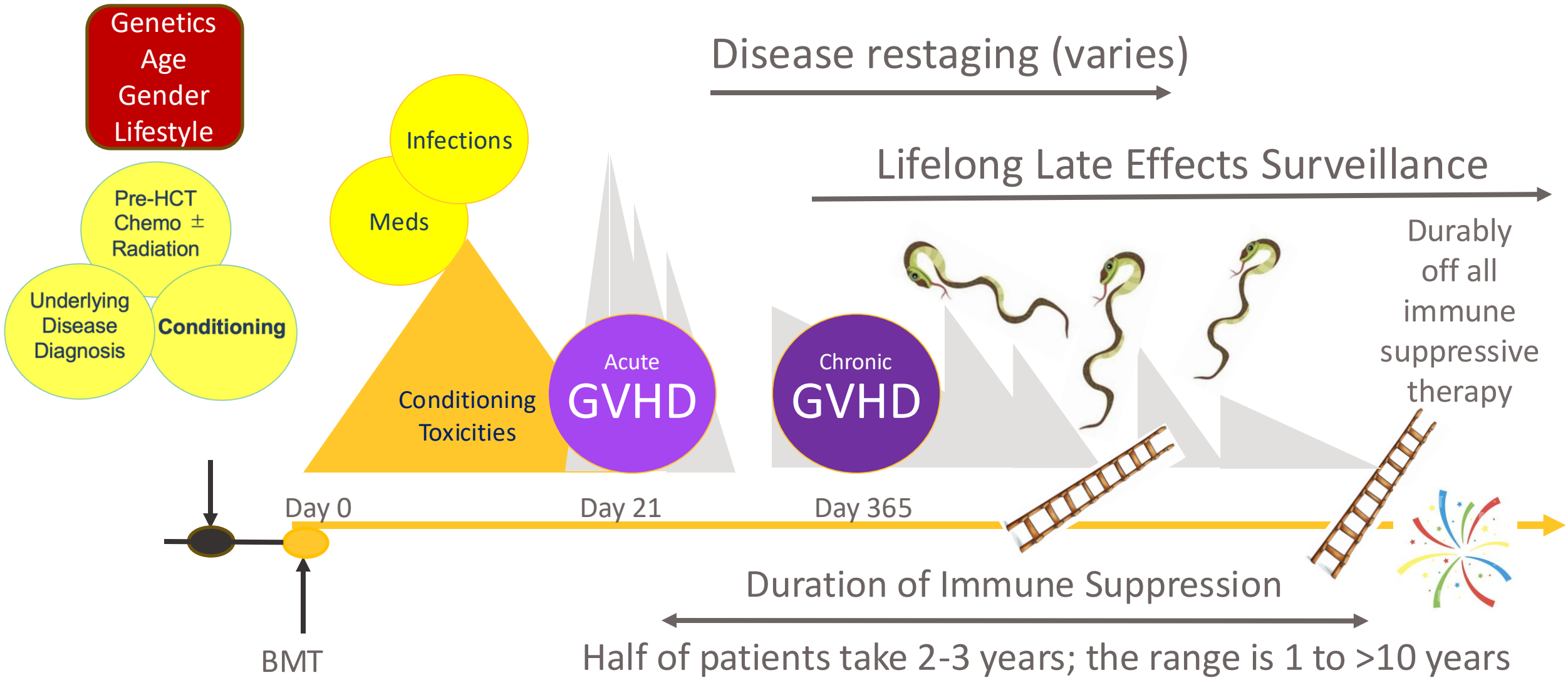
Miyamura et al, Blood Advances 2019

Long-Term Follow-Up Differs after a Transplant With Your Own Cells (Autologous) versus a Transplant with Donor Cells (Allogeneic)!

Autologous Stem Cell Transplant: LTFU Timeline



Allogeneic Stem Cell Transplant: LTFU Timeline



Why is Chronic GVHD Such a Burden?

- Moderate/Severe chronic GVHD is associated with worse quality of life, higher symptom burden, pain medication use, and depression.
- 1-in-4, to 1-in-3 people with active chronic GVHD are unable to work compared to one-in-eight with resolved chronic GVHD
- Caregivers have more depression and sleep disorders than the general population
- Patients with chronic GVHD have 4-5 times the rate of moderately severe to life-threatening health conditions than their siblings.

Lee et al, Haematologica 2018
Jamani et al, BBMT 2018
Sun et al, Blood 2010

Some Causes of Late Effects

Complications by organ (representative example)	Chronic GVHD or its therapies	Conditioning	Infection
Ocular: (dry eyes)	+++	++	+/-
Oral: (dry mouth)	+++	++	+/-
GI tract: (late dysphagia)	++	-	+/-
Liver: (elevated ALT/AST and/or alkaline phos)	+++	-	++
Lung: (airflow obstruction)	++	+	++
Bone: (decreased bone mineral density or AVN)	+++	+	-
Endocrine: (secondary adrenal insufficiency)	+++	-	+/-
Metabolic: (insulin resistance, hypertension)	+++	+/-	+/-
Musculofascial: (myopathy/myositis)	+++	-	+/-
Vulvovaginal: (erythema, erosions)	+++	-	+
Rare: (myasthenia gravis)	+	-	-

Excerpt from: ***Carpenter et al****, Best Pract & Res Clin Haematol:* ***2008****;21:309-331*

20-point Head-to-Toe Long-Term Follow-Up List

ORGAN-based	
1.Ocular	FA
2. Ear	FA
3. Oral	FA
4. Lung	
5. Heart	FA
6. GI / hepatic	
7. Musculo-skeletal	FA
8. Renal / GU	FA
9. Skin	FA

SYSTEMS-based	
10. Graft/chimerism	
11. Immunity	
12. Endocrine/ metabolic	FA
13. Neurocognitive	FA
14. Psychological	FA

PROBLEM-based	
15.Chronic GVHD	
16.Infection	
17. Infertility	FA
18. Iron Overload	FA
19. Quality of life	FA
20. Subsequent Neoplasms	FA

DISEASE-based overlay
Always consider 1-20 via the lens of underlying disease indication for transplant

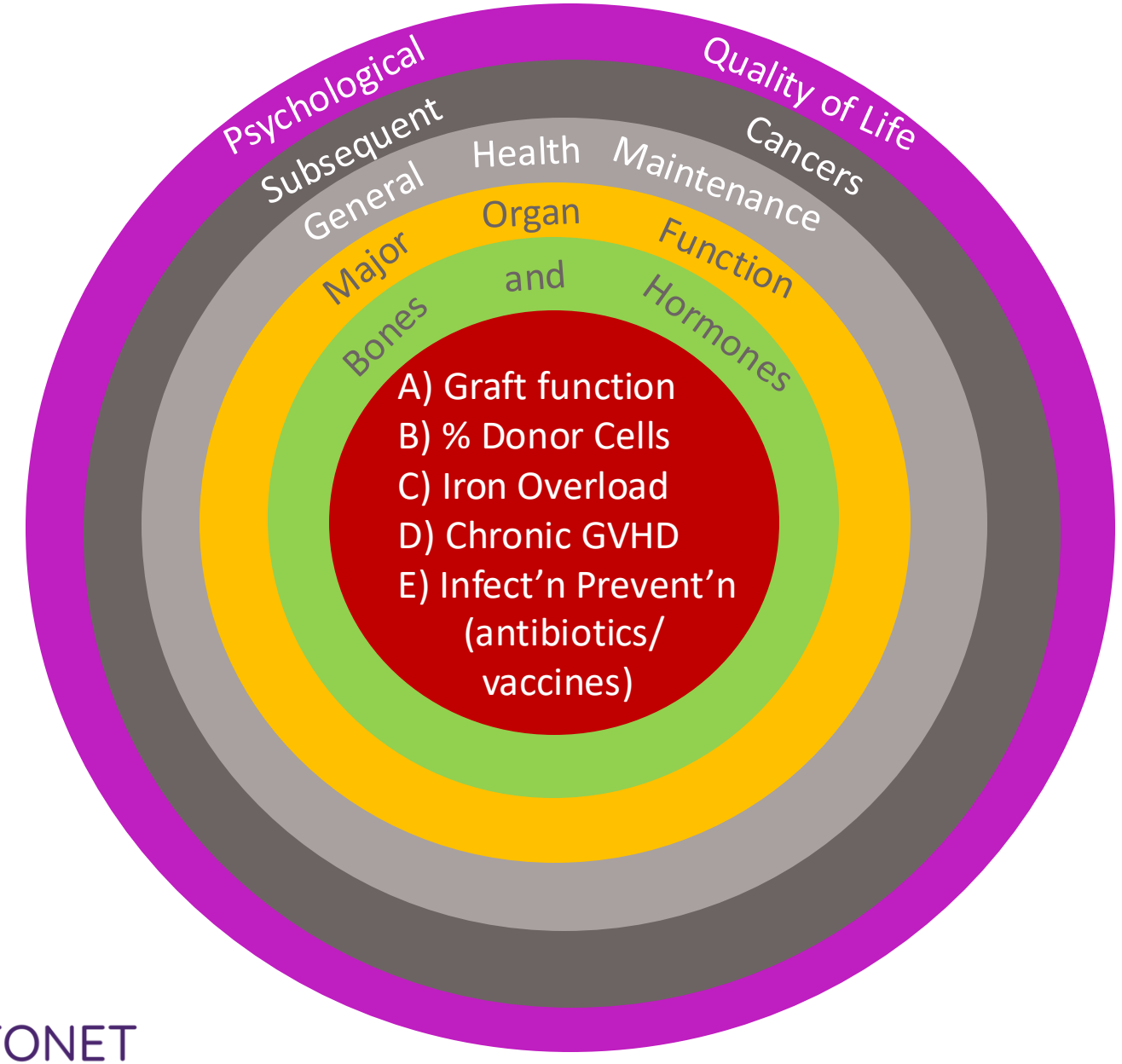
example

Fanconi Anemia

LTFU Providers need to organize this List

- LTFU care plans have core elements for every survivor.
- After Allo-transplant, providers should diligently conduct chronic GVHD screening exams every 1-2 months during and up to 1 year after tapering immune suppressive therapy
- LTFU care plans are also individualized and prioritized accordingly
- My approach is to consider the following spheres of evaluation…

Dr. C's "Core to Outer Spheres for Comprehensive LTFU"



- Core elements
- Bone health, thyroid
  Children: growth/puberty
  Adults: fertility/menopause
- Lungs, heart, kidneys, eyes, liver, GI tract, brain
- BMI, Blood pressure, urinalysis, nutrition, fasting metabolic labs
- Skin, oral, breast, colon, others if genetic risk or predisposition syndrome
- At a minimum, screen annually

How is Long-Term Follow-Up Best Conducted?

BMT Long-Term Follow-Up Survey
American Society for Transplant and Cellular Therapy (ASTCT)

- ~5,000 accredited US hospitals: ~177 (3.5%) contain a BMT center
- Survey response rate 38.5%:
  - 45% had an LTFU clinic
    - ≥85% agreed Nurse Practitioners/Physician Assistants were essential
    - allo-BMT survivors should be seen lifelong
    - clinics help provide preventive guidelines
  - 55% had no LTFU clinic
    - only 28% felt they had too few patients to establish one.
    - 100% agreed allo-BMT survivors have needs separate from GVHD, and transitions of care (peds to adult, or away from transplant center) can lead to complications.
    - 84% prefer to provide survivorship care as individual practitioners

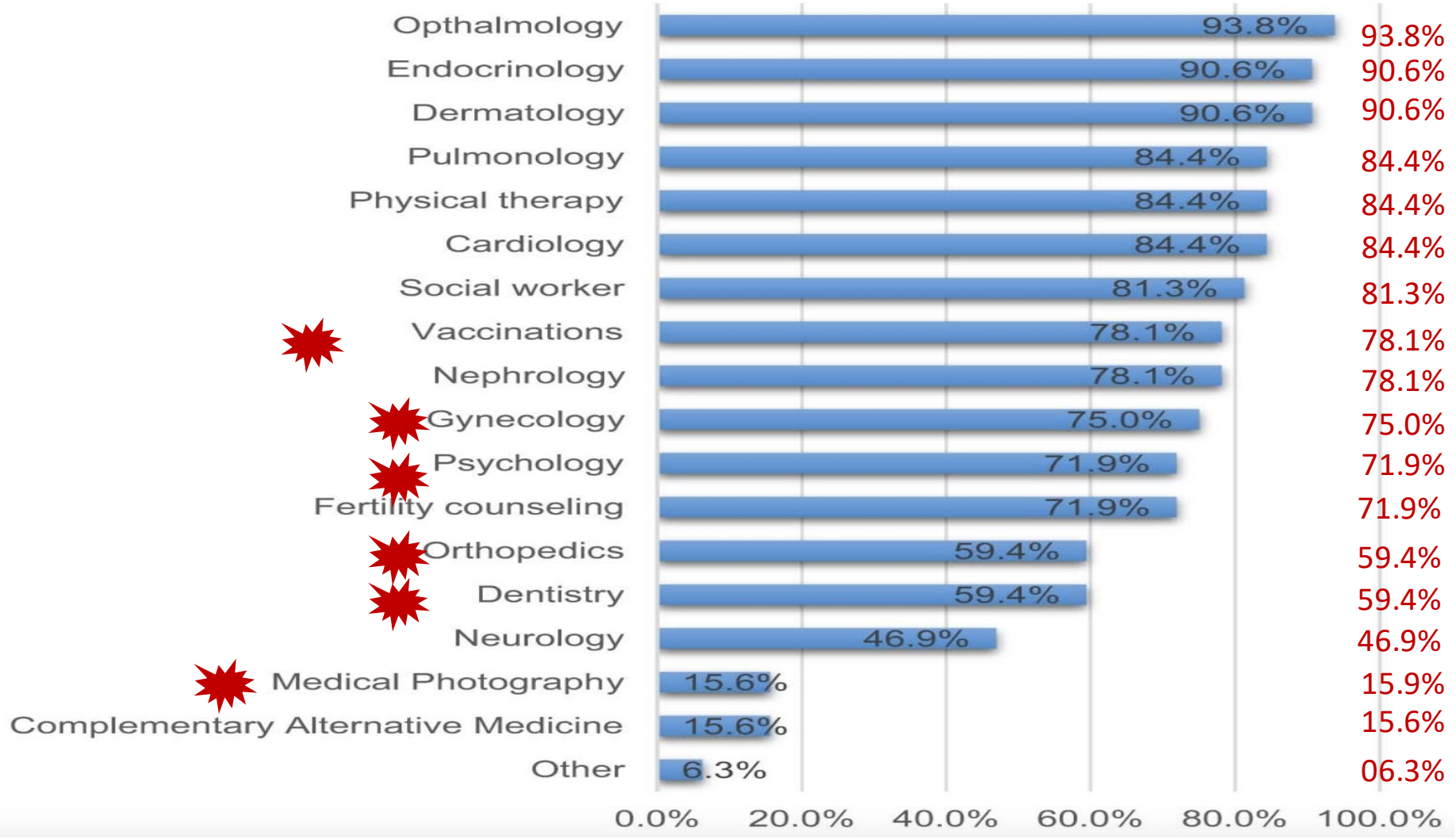
Hashmi et al, BBMT 2018

Obstacles to LTFU Clinics

- Lack of Expertise
- Logistics (space, infrastructure, commitment)
- Fiscal
- Preference for individual practitioner continuity care model

Hashmi et al, BBMT 2018

Availability of Sub-Specialists at BMT Centers with Long-Term Follow-Up Clinics



Model of LTFU Care Often Depends on HCT Center Size

Large Centers ⟷ NCI-Designated Comprehensive Cancer Centers **Smaller Centers**

<u>>500 HCT/yr</u>

A. Dedicated LTFU Dept.

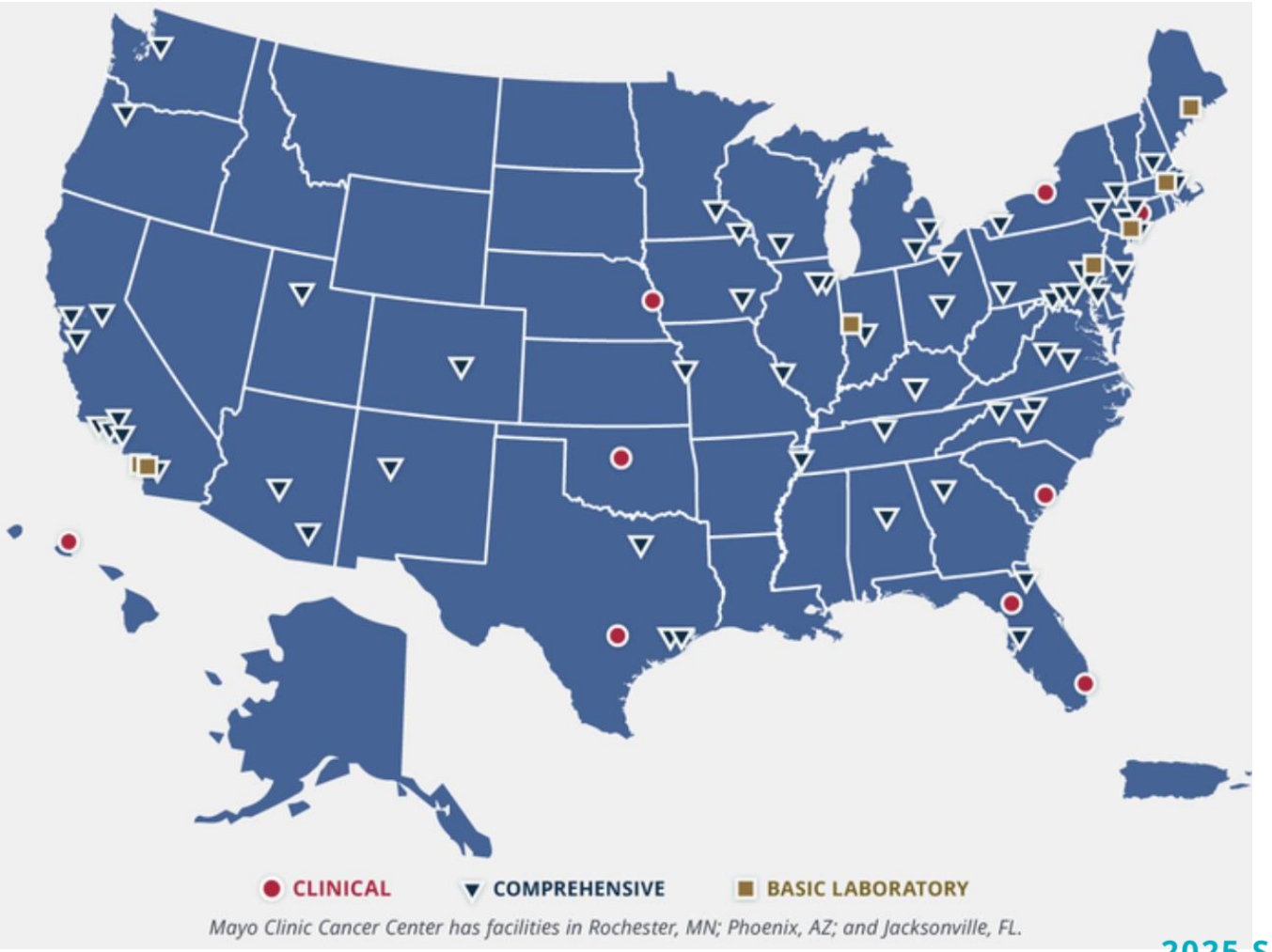
Expert LTFU

Providers rotate

B. LTFU Continuity Clinics

No rotation

C. =A+B



<u>100-200 HCT/yr</u>

Continuity Clinics

<u>≤50 HCT/yr</u>

Individual provider follows a small patient panel

Models of LTFU Care: Center with <30 BMT per year

"Jack-of-all-Trades"

Single Provider

Pros	Cons
Better Continuity	Harder to develop depth of chronic GVHD "playbook scenarios at smaller center"
Easier to establish Rapport	Minimal to no chronic GVHD subspecialty expertise
Efficiency via legacy of Continuity	"Jack-of-all-Trades" maybe too stretched to do justice for chronic GVHD/LTFU patients
Patients and Providers often prefer this model	Limited experience with full range of Late Effects

Models of LTFU Care: Center with ≥100-200 BMT/yr

Leverages Non-BMT Cancer Survivorship Clinic

- Subspecialties are available

Pros	Cons
Continuity can vary from moderate to high	Easier to develop reasonable chronic GVHD "playbook scenarios" depending on continuity model
Subspecialties more available	Chronic GVHD subspecialty expertise still variable
This model can work well for autologous transplants because no GVHD	Busy clinics may have insufficient time for comprehensive chronic GVHD exams
Higher access to cutting edge chronic GVHD therapies on research studies vs small center	Variable experience with full range of Late Effects
Patients / Providers often prefer a continuity model	

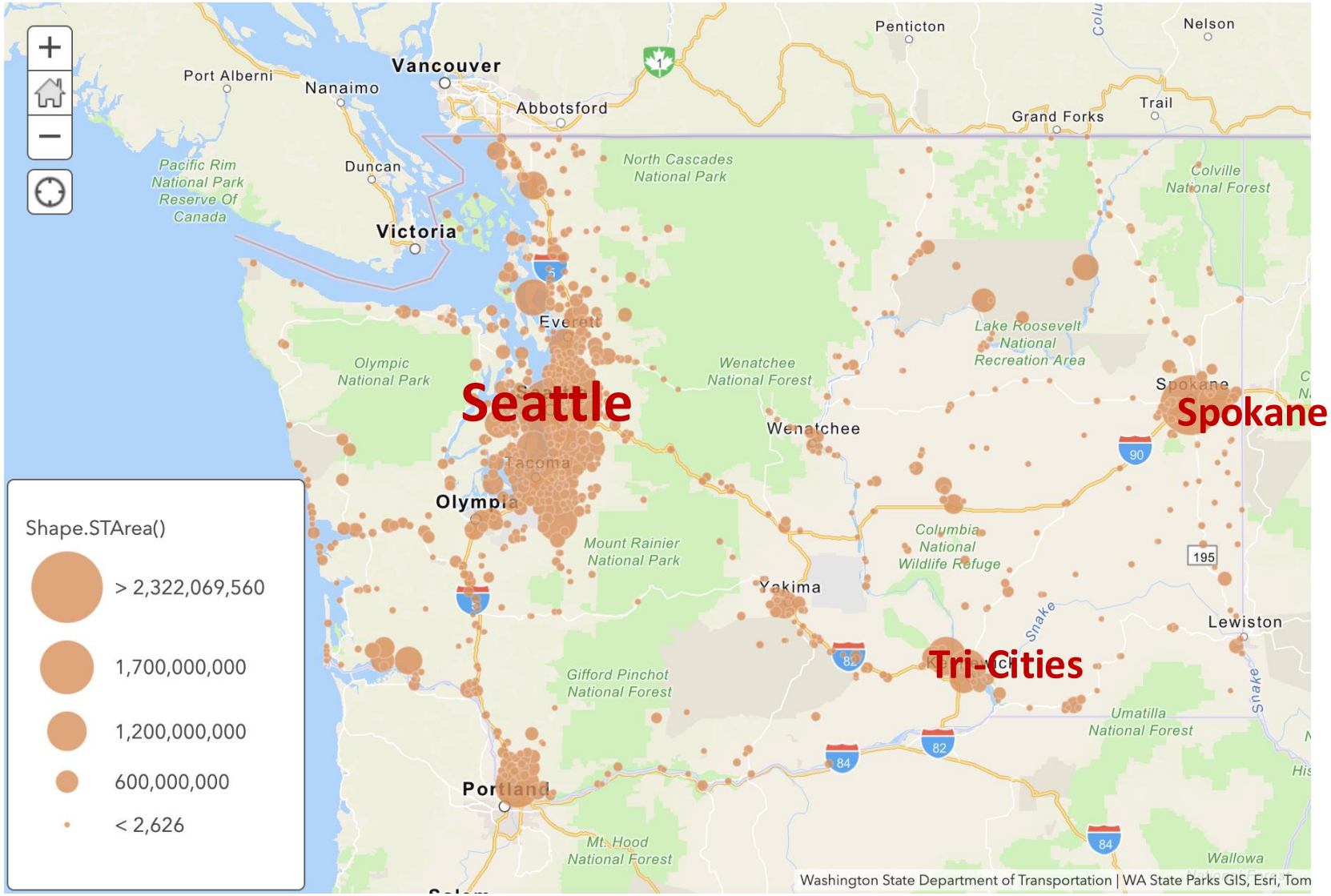
Models of Long-Term Follow-Up Care: Centers with ≥500 BMT/year

More often have dedicated BMT LTFU

- Relevant subspecialties

Pros	Cons
Continuity suffers in rotational models	Harder to maintain rapport in rotational model for patients with cGVHD
Deep knowledge of cGVHD	Limited capacity if large survivor panels
Full Spectrum of Subspecialties	Finite capacity limits in-person consultations to more complex patients or annually
Highest access to cutting edge cGVHD research therapeutics	Hospital administrators need convincing why longer clinic visits are necessary
Telemedicine can assist management in remote hometowns	Mostly unbillable

What about patients far away from NCI-designated Comprehensive Cancer Centers?



Drivetimes to Seattle from

- Spokane: 4-5 hours
- Tri-Cities: 3.5-4 hours (If not snowing!)
- Even harder to get to from remote, smaller towns!

How to address this?

- Telehealth
- Outreach clinics

Long-Term Follow-Up Models of Care

A. No LTFU Clinic (Traditional)

Jack-of-All-Trades

- Soley responsible for patient panel
- Small TC option

B. Shared Cancer Survivorship Clinic (CSC)

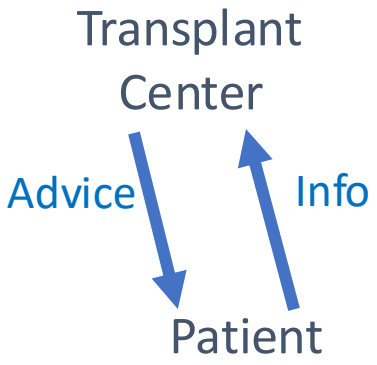
- Transplant center continuity provider leverages CSC infrastructure
- Tend to lack CGVHD expertise relative to C

C. Dedicated BMT LTFU Clinic

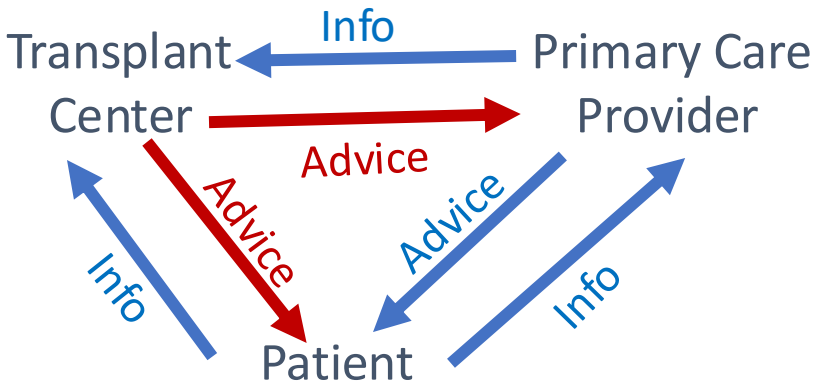
- Rotating BMT LTFU Experts
- Breadth of subspecialties
- Limited Capacity (e.g. 6000 prevalent survivors at Fred Hutch)

Communication Approach

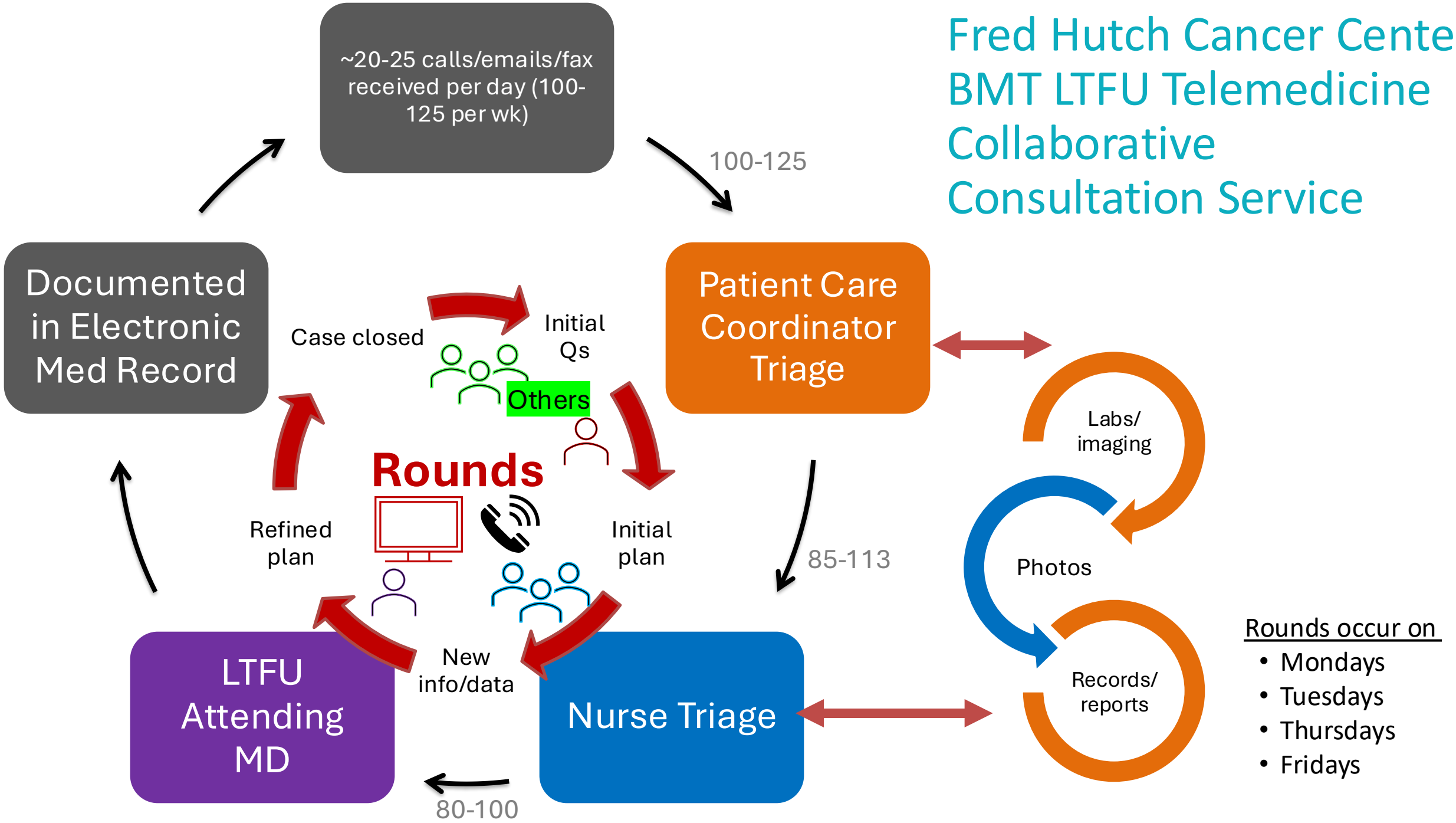
Traditional



Collaborative



Fred Hutch Cancer Center BMT LTFU Telemedicine Collaborative Consultation Service



Rounds occur on

- Mondays
- Tuesdays
- Thursdays
- Fridays

Does Telemedicine Help Patients Who Live Far from Their BMT Center?

…we think probably yes but need to study it more!

- Seattle study found no impact of distance or urban/rural residence on clinical outcomes
- CIBMTR registry study reported good survival after chronic GVHD for low-risk (group 1) patients but step-downs in survival for higher-risk groups 2 to 6, fully explained by step-ups in non-relapse deaths
- In contrast, a Seattle Study showed better survival for higher-risk groups explained by no increment in non-relapse deaths, possibly attributed to the dedicated LTFU program and robust telemedicine

Khera et al, BBMT 2016
Inamoto et al, Blood 2014

What about Survivorship Care Plans?

- A randomized trial tested whether survivorship care plans *mailed* to transplant survivors and created by the Center for International Blood & Marrow Transplant Research (CIBMTR) improved confidence in survivorship info at 6 months compared to baseline (based on phone surveys with ~87% completion rate)

Majhail et al, Haematologica 2019

Did Survivorship Care Plans Help?

- Survivorship Care Plans did not improve confidence in
  - survivorship info
  - knowledge of BMT exposures
  - health care utilization
- Survivorship Care Plans did reduce treatment distress and the mental aspects of quality of life
- While Survivorship Care Plans are generally considered valuable, more work needs to be done!

Majhail et al, Haematologica 2019

ASTCT Long-Term Follow-Up Survey: Conclusions

- One-size-fits-all clinic specifications are not feasible:
  - Center size, resources vary widely
  - The relative merits of shared long-term follow-up clinics (integrating single continuity providers) vs. centralized clinics (rotational provider model) are unclear
  - Need to accommodate survivors at distant locations from the transplant center.
- We need to figure this out!

Characteristics of the Ideal BMT Long-Term Follow-Up Healthcare Provider

- Committed to the needs of this population and critically understands that:
  - Early detection of chronic GVHD is vital to survivors' quality of life and even life expectancy
  - Late effects have latency, and survivors need annual follow-up even if they "look fine"
  - Focus on "core elements" is critical, with "Dr. C's outer spheres" tackled at least annually
- Conducts robust monthly symptom evaluation, exams, and medication reconciliation
- Authentically commits to collaborative communication with the Transplant Center –
  - Timely and thorough bidirectional responses are key!

Barriers to Finding the Ideal BMT Long-Term Follow-Up Healthcare Provider

- Not all patients live close to a transplant center, let alone a high-volume one experienced in chronic GVHD management.
- Bandwidth of some providers is so stretched that there can be insufficient time to address even the “core elements” – especially thorough exams to check for GVHD
- Non-reimbursement for time spent communicating with Transplant Center
- Not all transplant centers have a well-developed telemedicine service

Long-Term Follow-Up Takeaways

- LTFU starts 60-100 days post-BMT and is more complex after allo-HCT (cGVHD)
- LTFU Care Models vary by transplant center size, feasibility, MD preference, patient hometown location, and resources; a one-size-fits-all approach is unlikely
- Comprehensive BMT LTFU care starts with core elements, then moves to other aspects, always considering patient exposures, genetics, lifestyle, mood, and quality of life.
- Survivorship Care Plans reduce distress but determining their larger role needs more work – referring MDs prefer concise to-do list over multiple-page reports

Long-Term Follow-Up Takeaways, cont'd

- Survivorship Care Plans reduce distress but determining their larger role needs more work
  - referring MDs prefer a concise to-do list over multiple-page reports
- Telemedicine ± and perhaps Outreach Clinics are likely key elements to delivering LTFU to a growing number of BMT survivors spread far and wide

Questions?

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Let Us Know How We Can Help You

Visit our website: bmtinfonet.org

Email us: help@bmtinfonet.org

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