What represents success in Transplantation?

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Later measures of HCT Success

- Survival
- Free of Relapse
- Free of ongoing complications
- Recovery to autonomy without health burdens
- Return to work or school
- Quality of Life

Earlier measures of HCT Success

Survival

from pancytopenia	engraftment
from risk of infection	immune reconstitution
from GVHD	immune tolerance
from risk of Relapse	remission
from other ongoing complications	well

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Risk Factors for graft failure or delayed recovery

Patient: Donor: Treatment

Risk Factors for graft failure or delayed recovery

Patient:

Damaged microenvironment
Disturbed hematopoiesis
Alloimmunization

Acquired hematopoietic injury

Fibrosis
Aplasia
Donor Specific antibodies

HHV-6
Parvovirus
Other

Risk Factors for graft failure or delayed recovery

Donor & Graft:

HLA mismatch	Graft failure/rejection
Alloimmunization	Donor Specific antibodies (in recipient) Alloantibodies (in donor) risks for GVHD ABO mismatch risk for hemolysis or platelet delay
Graft type and cell dose	Higher risk in UCB >--BM >--PB 10-15% 5-6% 3-4%
Graft manipulation	T cell depletion RBC or plasma depletion

Graft type and cell dose graft failure	Higher risk in	UCB >	--BM >	--PB
		10-15%	5-6%	3-4%

TNC
CD34
Viability

Recent rarity of BM harvests; technique and quality declining
If coming back for Haplo grafts; training needed

Risk Factors for graft failure or delayed recovery

Treatment

Myelosuppressive drugs

MMF, anti virals,

Rarely TMP-SMX, H2 blockers

drug associated antibodies

Infections

HHV6, parvo

EBV hemophagocytosis

Risk Factors for Relapse

- Diagnosis
- Disease status Disease Risk Index (DRI)

Pre HCT MRD ALL; AML; imaging for NHL others

Conditioning MAC vs RIC vs NMA

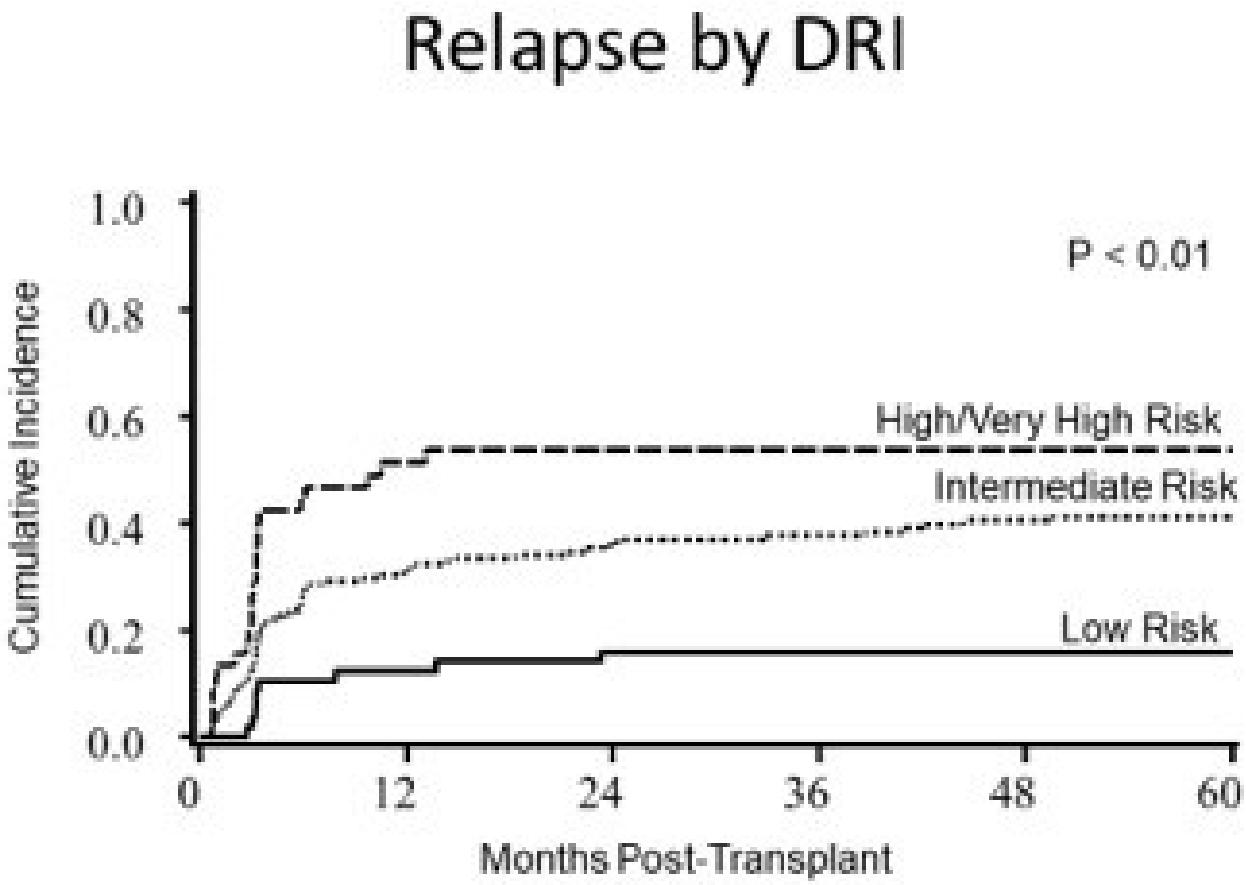
Immune competence: potency of GVL

Uncertain if differing between donor sources

Possibly more GVL with double UCB grafts

Worse with T cell depletion; ATG [no GVHD]

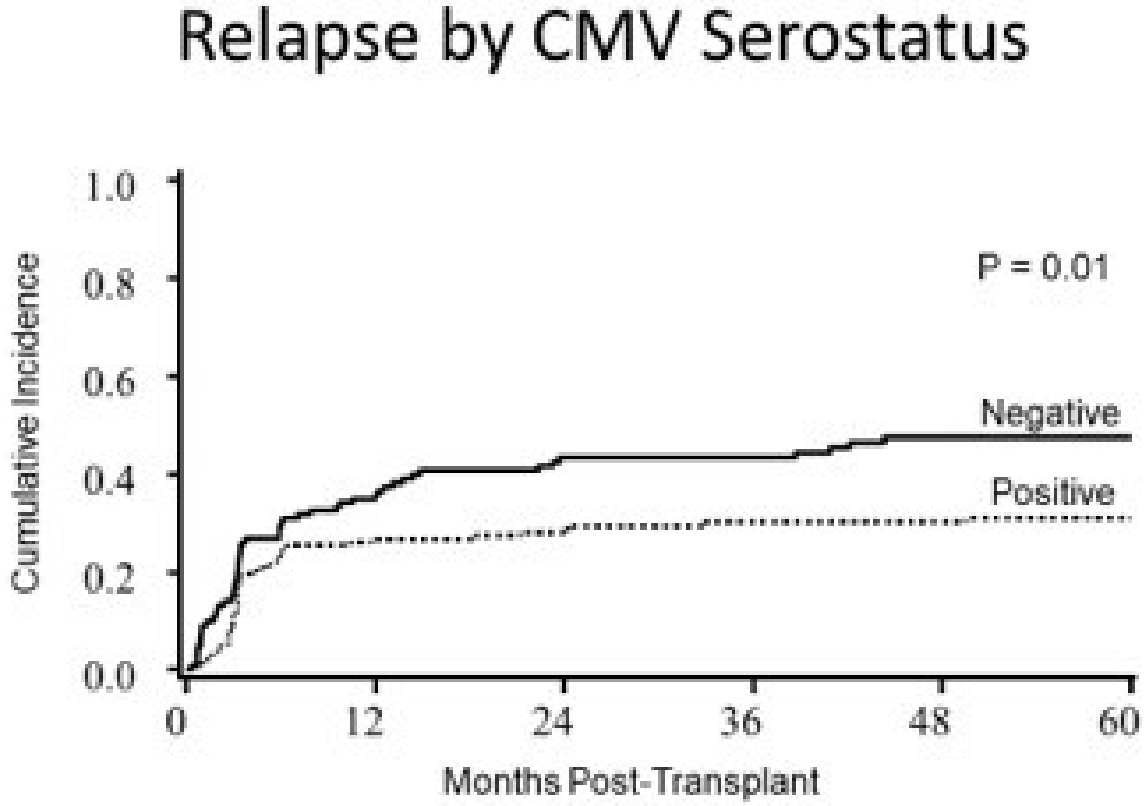
RIC HCT



Warlick, 2018

RIC HCT

Does CMV induce activated (adaptive) NK response
That limits relapse risk



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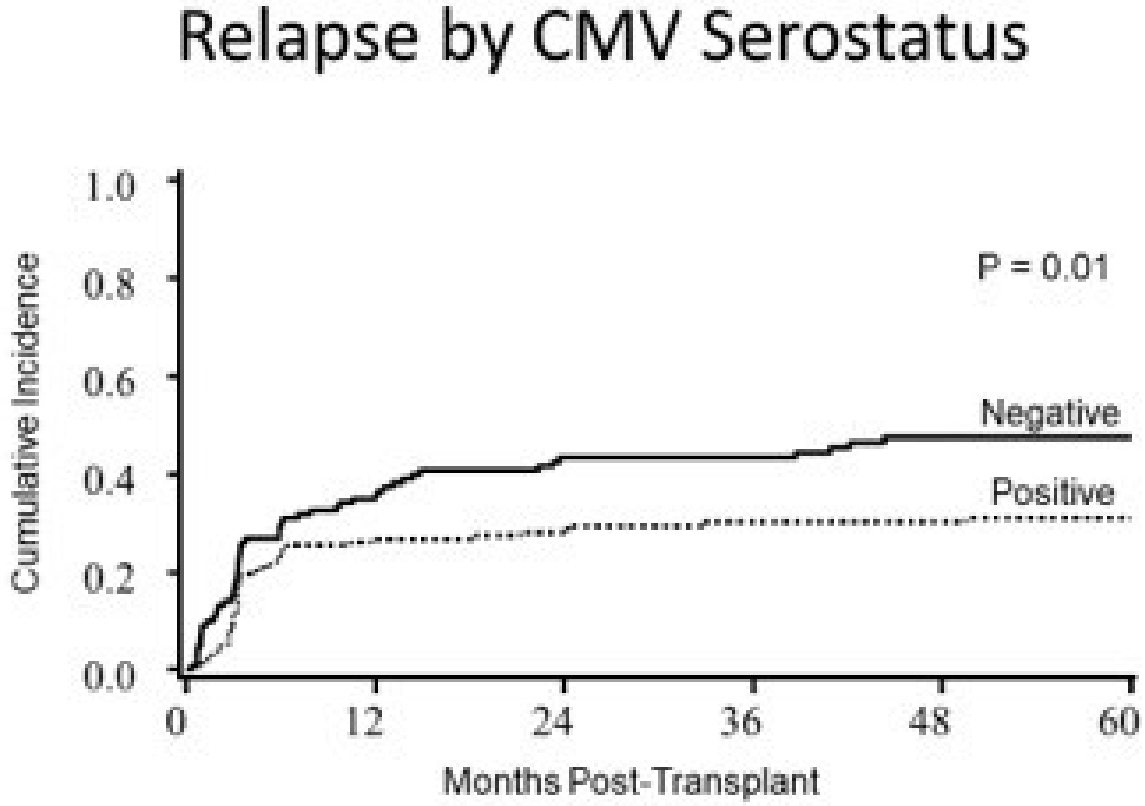

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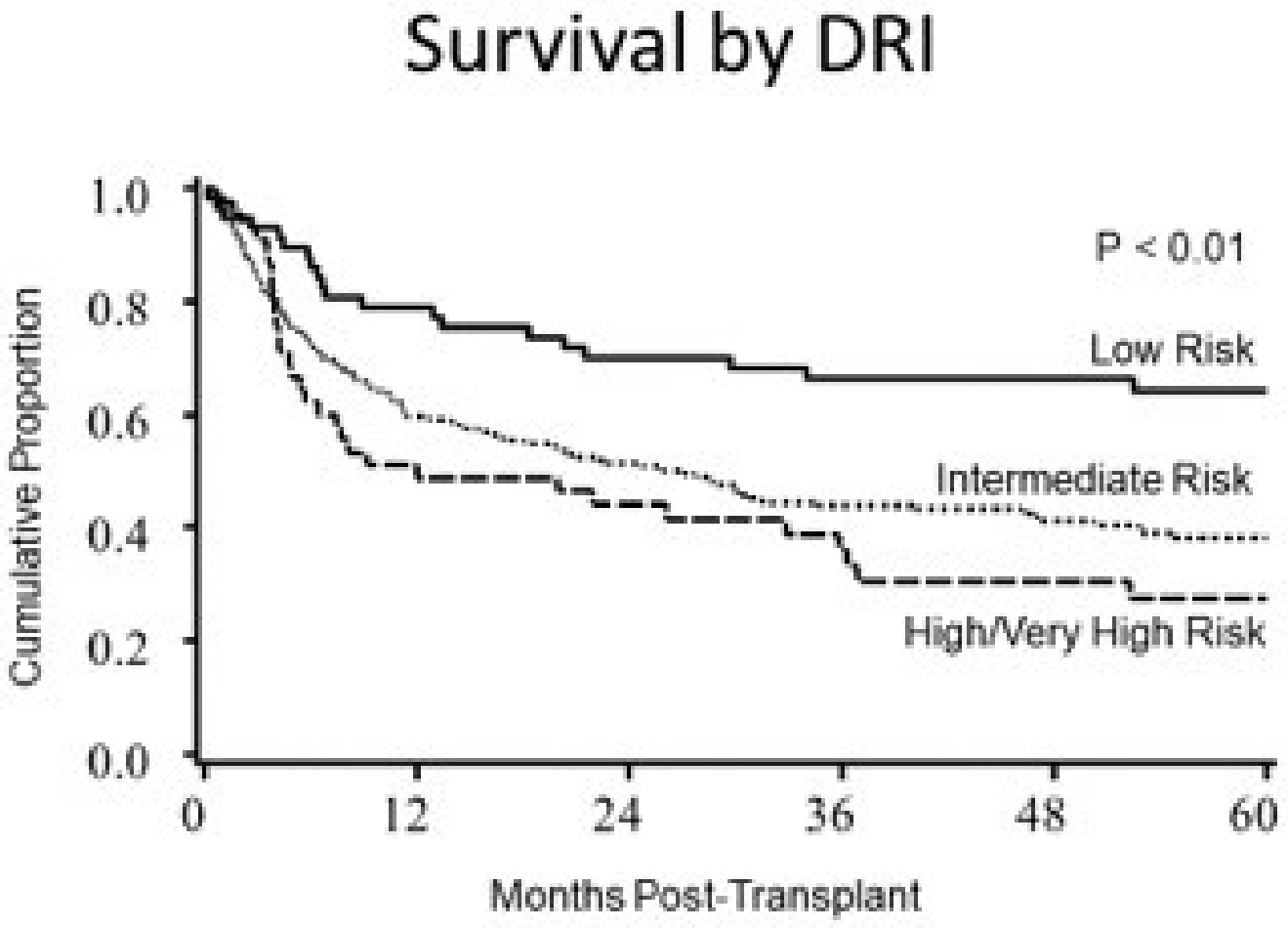


Warlick, 2018

Prevention of Relapse

- Post-HCT maintenance
  - TKI for CML, Ph+ ALL
  - Azacytidine for AML
  - Len or other for myeloma

- Immune stimulation
  - Early tapering of GVHD prophylaxis
  - Donor lymphocyte infusion pre-emptive if T depleted graft

  - T cell modulation
    - Low dose IL2 for Treg enhancement; Teffector permissive
    - ? Checkpoint inhibitors
    - Vaccines
  - NK cell augmentation
    - IL-15/IL-15Ra

Treatment of Relapse [best if later relapse]

Withdrawal of immunosuppression
with or without GVHD flare

DLI in some diseases myeloid > lymphoid
if no prior serious GVHD
Dose uncertain in HLA mismatch or Haplo
? Ineffective if mismatched HLA lost

Checkpoint inhibitors GVHD risks

Chemotherapy to achieve CR
Generally recover to donor hematopoiesis
Supplement with DLI or other

Treatment of Relapse

2nd Transplant

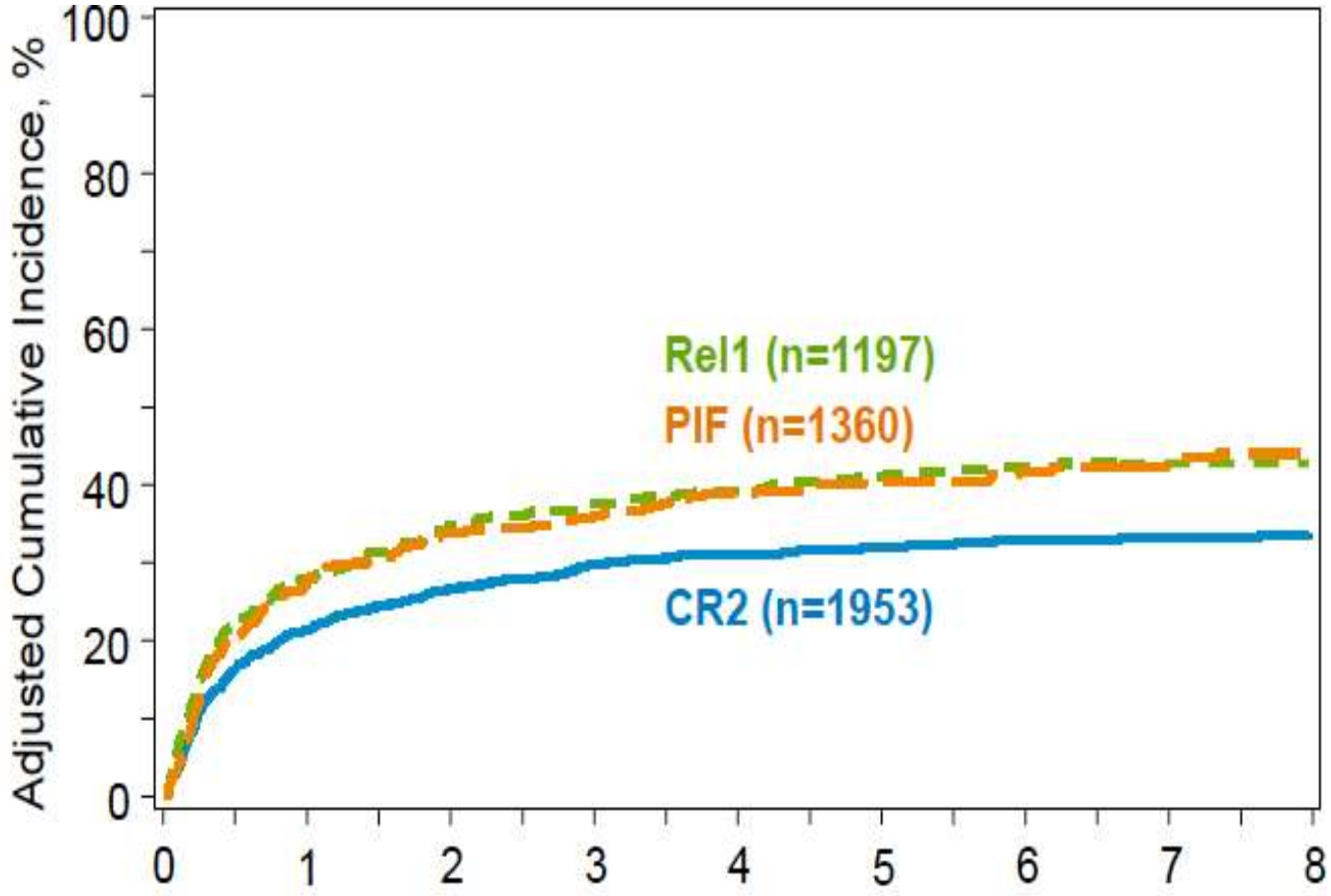
Only for late relapse longer remission implies GVL responsi
(recovered performance status and complications)

Only if in CR

No advantage of changing donors

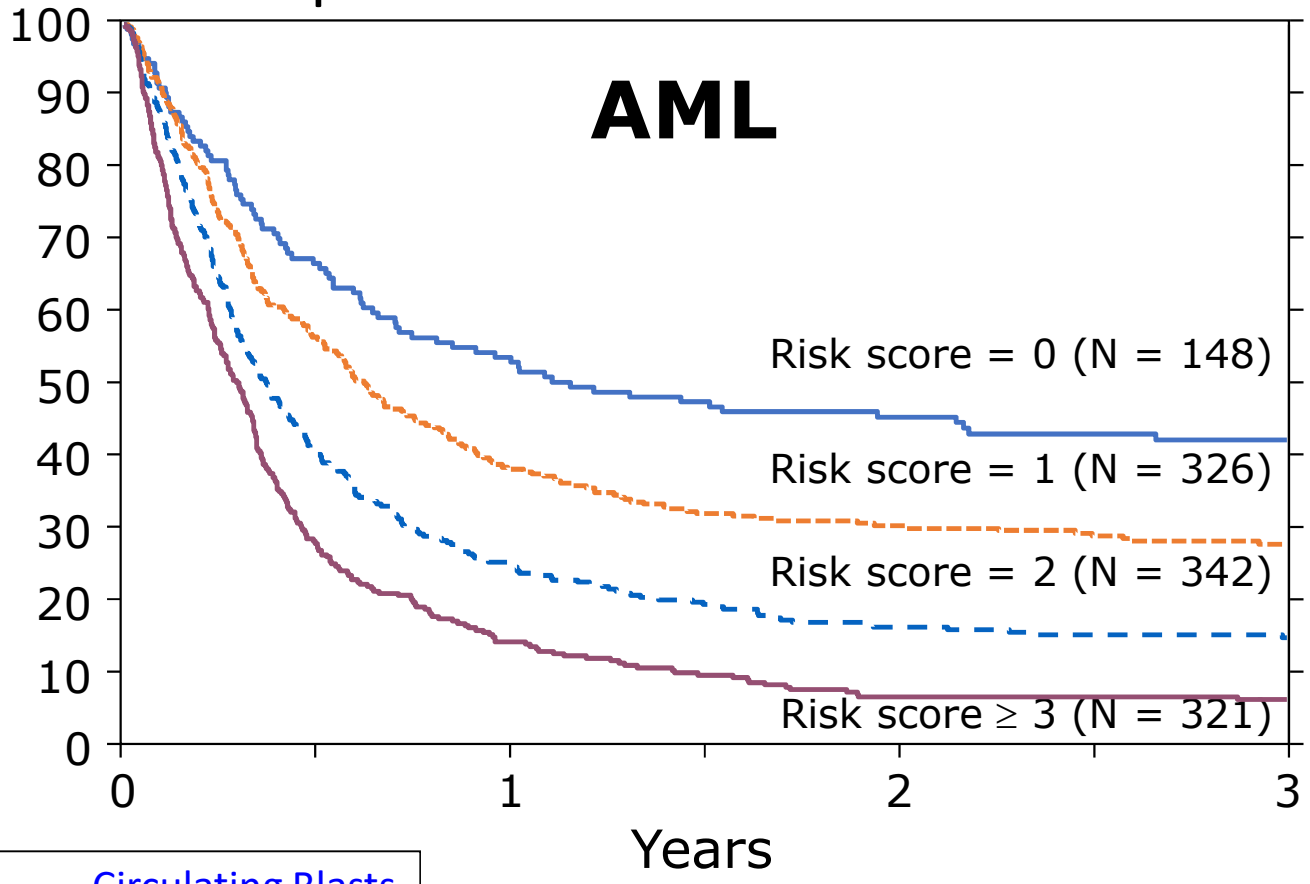
20-40% survival [selected series]

Relapse risk after allotransplantation: CR2 better than PIF or 1st Relapse



Weisdorf, Cancer, 2017

HCT in relapse: Survival



CR1 <6 months
Poor risk cytogenetics
MM URD or other related
KPS <=80

Circulating Blasts

Duval
JCO, 2010

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Recovery post HCT

Resolved chronic GVHD

Residual organ dysfunction [renal, hepatic]

2nd malignancy

Bone and endocrine health

Growth (children & adolescents)

Metabolic syndrome

BP, lipids, cardiovascular risks (smoking)

Neurologic & emotional

Survivorship Screening and Guidance