

Optimizing Fitness for Transplant and Cellular Therapies

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Disclosures

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 - Views expressed are my own and not those of the FDA

10-20% of allogeneic hematopoietic stem cell transplant (HCT) patients will die of transplant complications

The better you are starting transplant,
the better you do during transplant

What does it mean to be better?
How can we make patients better?

Overview

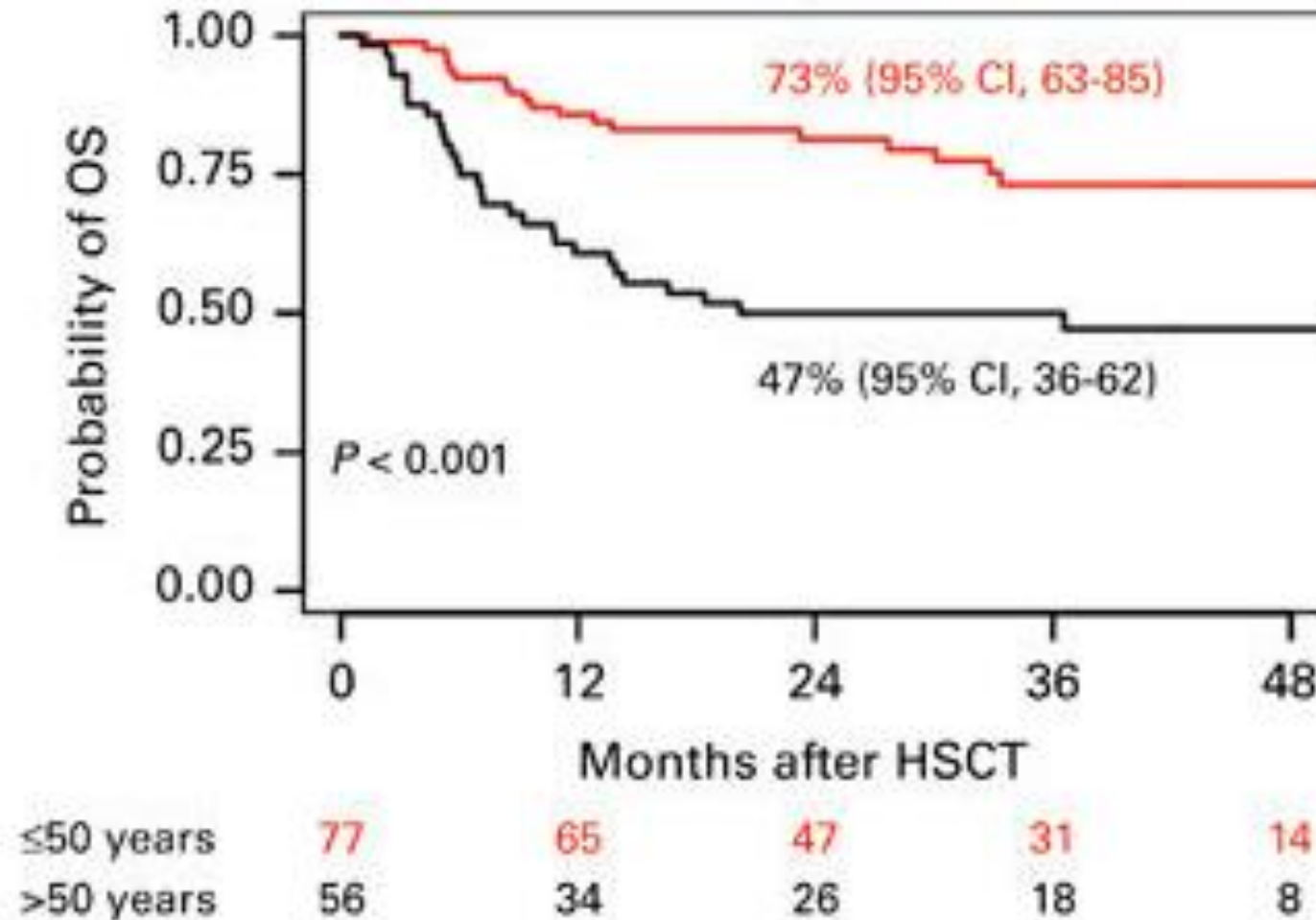
- Clinical Pre, Peri, and Post-Treatment Optimization Program (C-POP)
- Observational (O-POP)
- Interventional (I-POP)

Case 1: C-POP

- MM is a 67M seen for consideration of HCT

- Doc, what are my chances?
- Am I going to be ok?

Survival after Allogeneic HCT, >50 years



Geriatric Assessment

- Comorbidities
- Social Support
- Polypharmacy
- Physical Function
- Cognitive Function
- Mental Health
- Nutritional Status
- Food Insecurity
- Financial Toxicity
- Social Determinants of Health

Clinical Pre-HCT Optimization Program (C-POP)

- Physical Function: 6MW, SPPB, 30SSS, Fried Frailty ➤ PT/OT
- Cognitive Function: MOCA -> PROMIS Cog, TMT, DSST, HVLT ➤ Speech, psych
- Mental Health: PHQ9, PC-PTSD -> PCL5 ➤ Psych
- Nutrition: GLIM ➤ Dietitian
- Food Insecurity: USDA ➤ SW/Food Bank
- Financial Toxicity: FACIT-COST ➤ SW/grants
- Other SDOH: CMS AHC HRSN Screening Tool ➤ SW
- Other: PROMIS 29+2, EQ5D/5L, OARS IADL, Employment

New Patient Evaluation (n=318)

C-POP SDOH

- Food Insecurity: 13%
 - Malnutrition: 70% vs. 45% (p=0.034)
 - Total Parenteral Nutrition: 65% vs. 34% (p=0.013)
 - Depression: 40% vs. 10% (p=0.002)
 - Financial Toxicity: 75% vs. 25% (p<0.001)
- Financial Toxicity: 29% mild, 24% moderate-high
 - FACT-BMT at Day 180 (125.5 none vs. 122 mild vs. 92.3 mod-high) and at Day 365 (132.5 none vs. 117 mild vs. 112.6 mod-high), both p<0.05

Case 1 (cont)

- C-POP NPE 3/2018: impairments in physical function and nutrition
-> Referred to PT, dietitian, PT 3x/week at home
- C-POP SO 10/2018: resolution of impairments
-> Proceeded to HCT and doing well at last f/u 6 years later

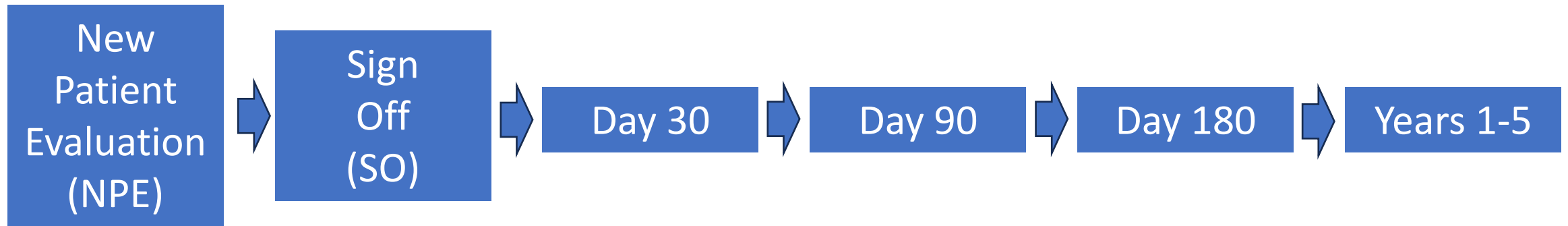
Case 2: C-POP

- CP is a 65F AML/MDS, FLT3TKD, NPM1, TET2, CR1
 - MOCA 20
 - Failed 6MW, SPPB, PONS
 - Attempted PT, OT, dietitian but didn't improve
 - After lengthy discussion with patient and daughter decided against HCT
 - Lived 3 more years before dying from disease relapse

“The better part of valor is discretion,
in the which better part I have saved my life”

- Shakespeare, Henry IV Part 1

Clinical Pre-, Peri-, and Post-Treatment Optimization Program (CPOP)



What *else* does it mean to be
“better”?

Observational Pre-, Peri-, Post-Treatment Optimization Program (OPOP)

- PROMs facilitated by iPads, REDCap, MyChart, etc.
 - ACES, PRO CTCAE
- Assessments
 - CPET, Ultrasound, Body Composition
- Mobile health to monitor patients
 - Garmin, TempTraq
- Correlative studies to drive mechanistic insights and future interventions
 - Inflammation, microbiome, biological aging

How can we make patients
“better”?

I-POP: Building on CPOP: Food Insecurity

- Multi-center RCT (KUMC, Duke, Stanford, MSKCC)
- Healthcare-community partnership with food banks
- Directly deliver food in clinic

Box 3. NOURISH Contents. All bags will include shelf-stable food for 2-3 days for one individual.

A. 4,000-6,000 Kilocalories (kcal)

B. ~18-20% kcal protein (primarily lean)

C. ~50-52% kcal from carbohydrate (primarily complex)

D. ~30% kcal from fat (primarily unsaturated)

E. 10-15 servings fruits and vegetables

F. 12 – 18 oz bread, cereal, rice, or pasta (primarily whole grains)

G. 6-9 servings ultra pasteurized milk

	Workup Day -30	Sign Off Day -7	Return Home Day 90	Follow Up Day 365
Phase of Care	Pre-TCT	Peri-TCT	Post-TCT	
Location	Home	Quaternary Cancer Center (QCC)	Home	
Control Arm	Food Bank Near Home	Food Bank Near QCC	Food Bank Near Home	
NOURISH Arm	Food Bank Near Home + Food in Clinic	Food in Clinic (Twice Weekly)	Food Bank Near Home + Food in Clinic	

I-POP: Building on O-POP: CRF

Low cardiorespiratory fitness ($VO_{2peak} < 16$ ml/kg/min) is linked with:

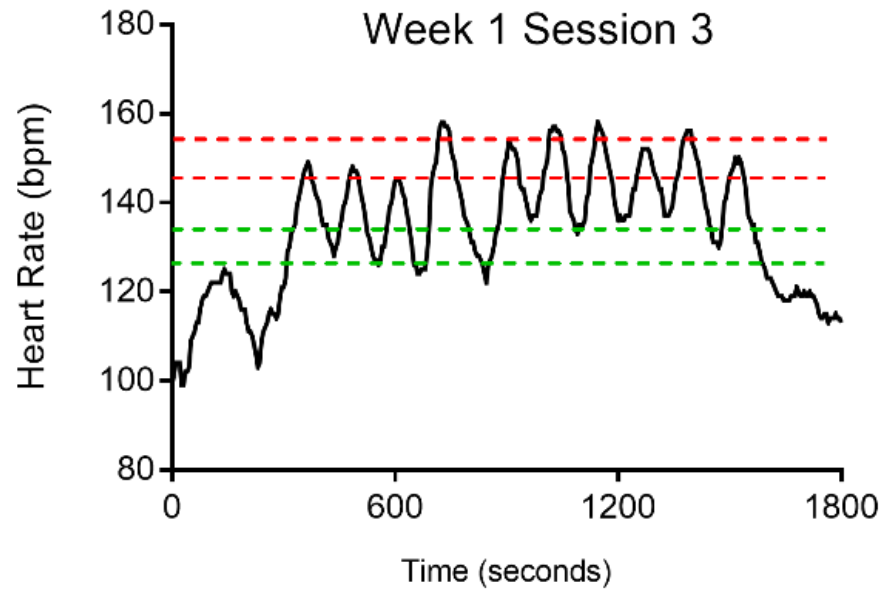
Mortality: HR 6.70 (1.29-34.75) ($p=0.02$)

Hospital Days: median 33 vs 22 ($p=0.004$)

I-POP: REMM-HIIT

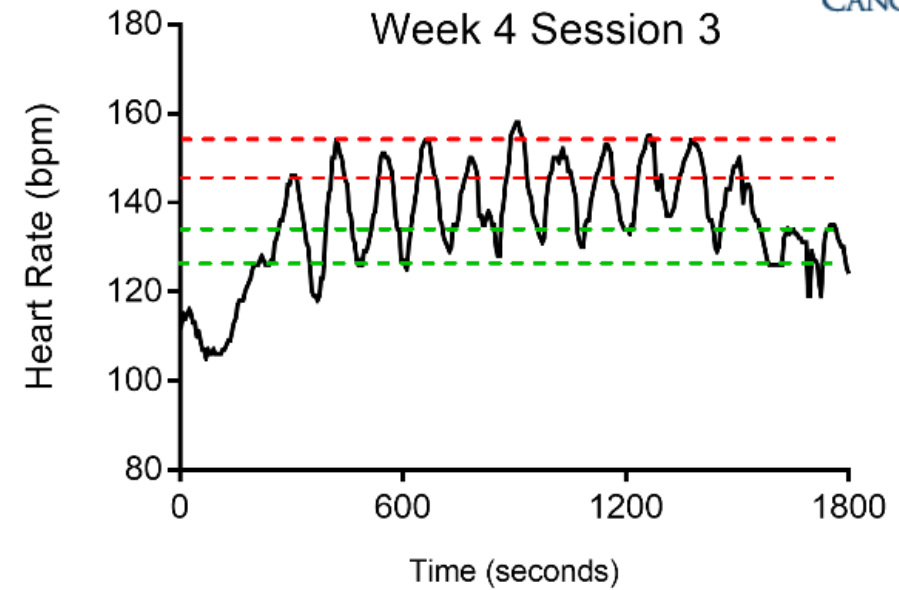
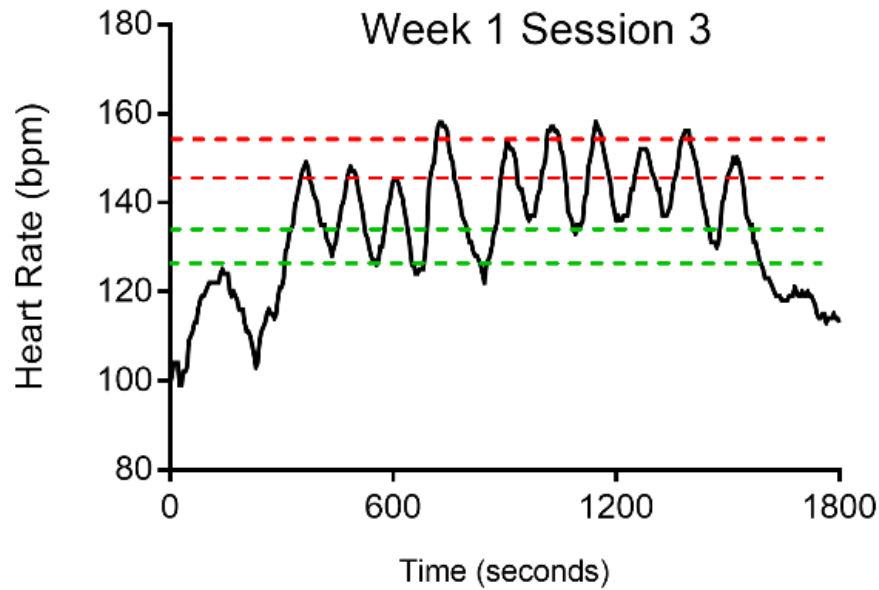
- REmotely Monitored, Mobile health supported, High Intensity Interval Training – pre-habilitation exercise program
 - Improvement in 4-8 weeks
 - Improvement with 90 minutes/week
 - Personalized to baseline fitness
- One session at Duke, the rest are at home
- All allos who will go to HCT between 1-6 months and can exercise

Remote Monitoring of High Intensity Interval Training



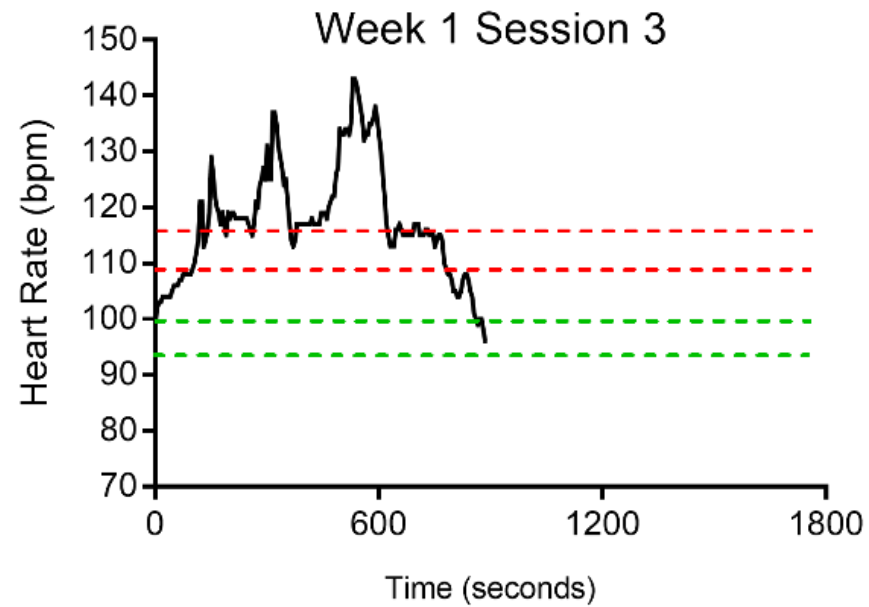
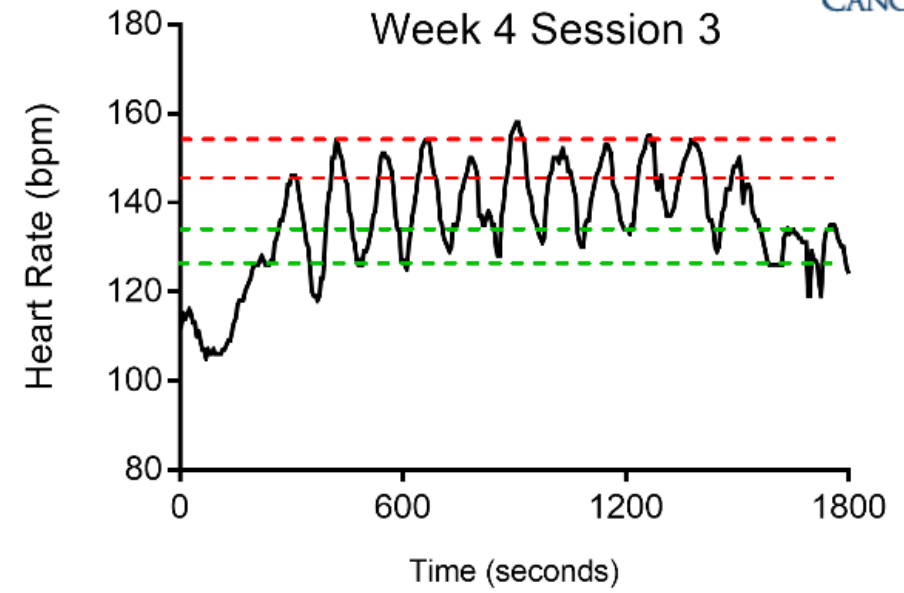
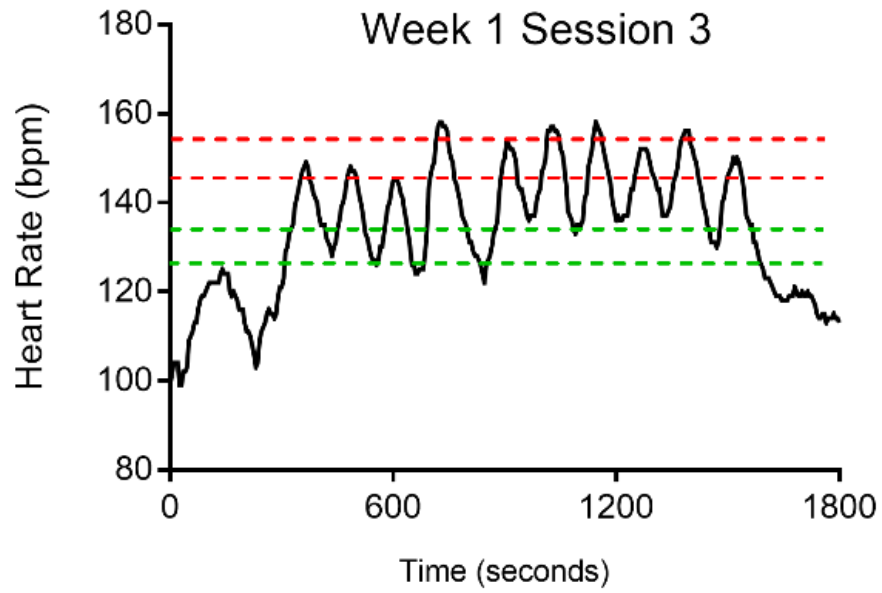
- Time: 30 min session – 5 min warmup, 20 min intervals, 5 min cool down
- Intervals: 10x, 1 minute high (80-90% HRR), 1 min low (50-60% HRR)
- Mode: home-based, patient choice
- Frequency: 3x/week
- Duration: new patient evaluation to start of transplant – variable

Remote Monitoring of High Intensity Interval Training

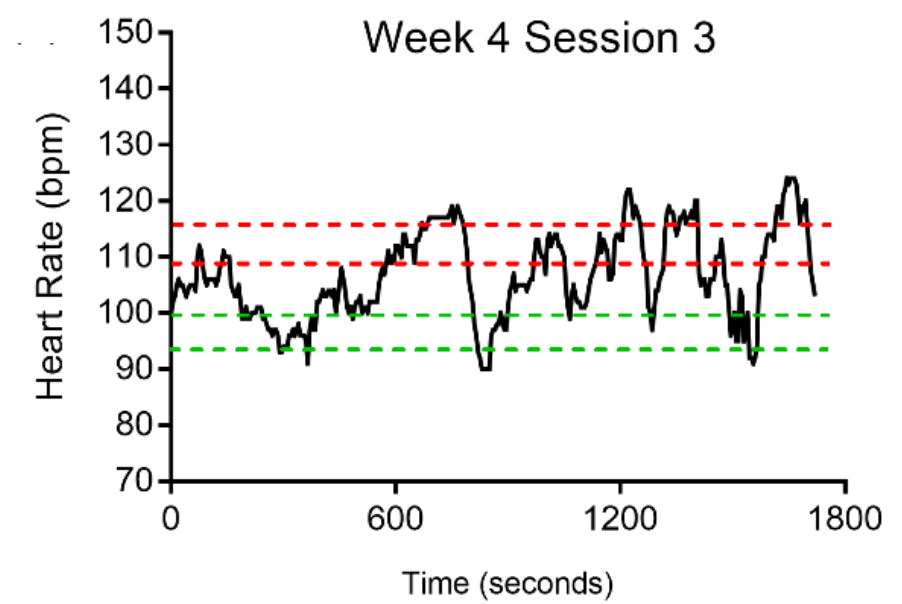
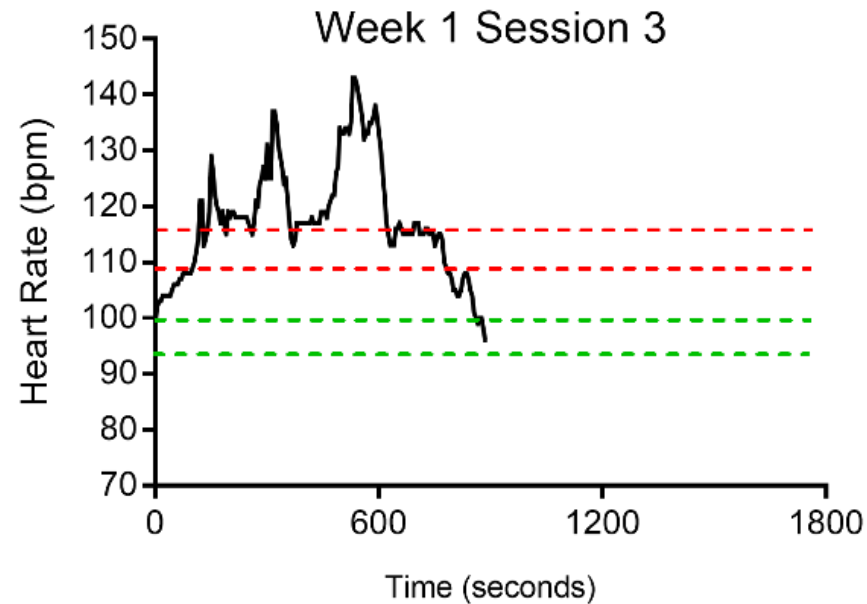
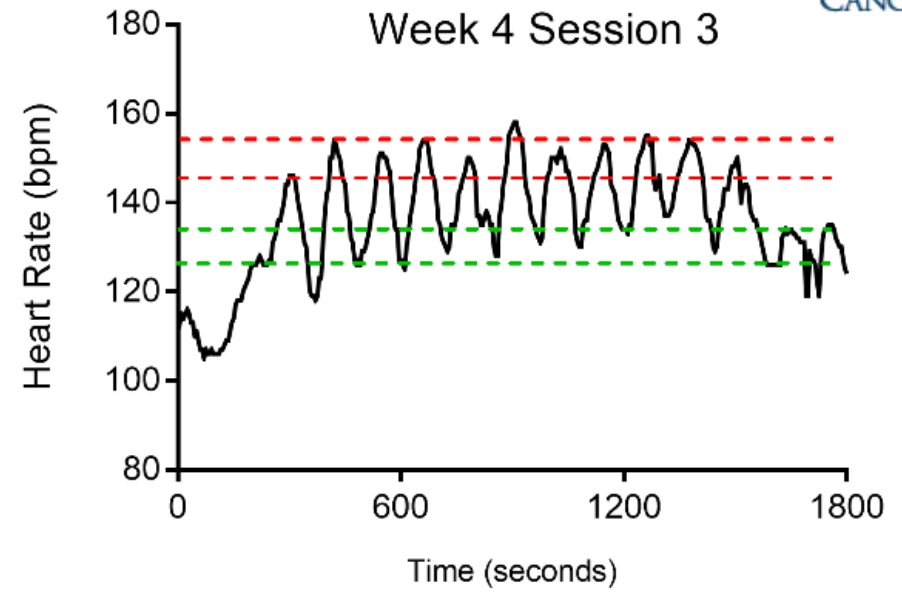
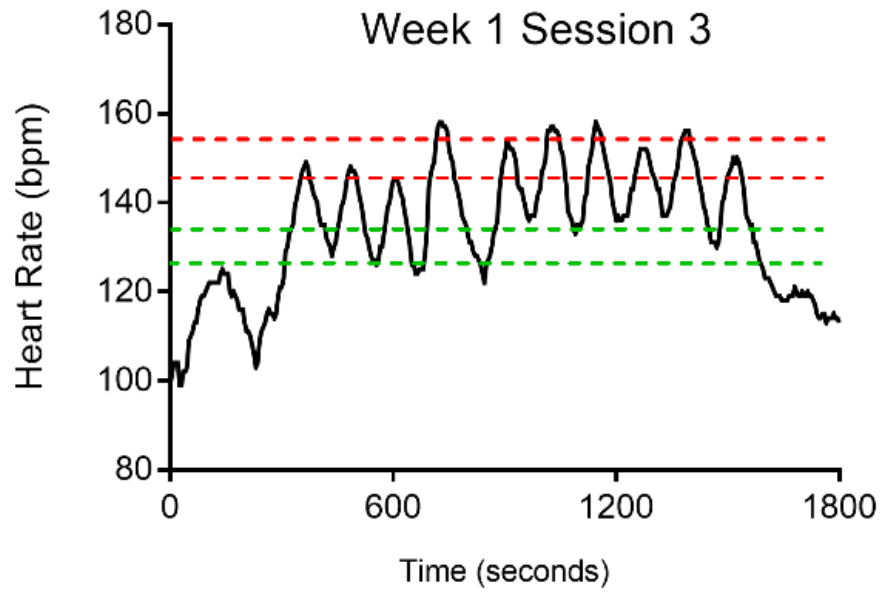


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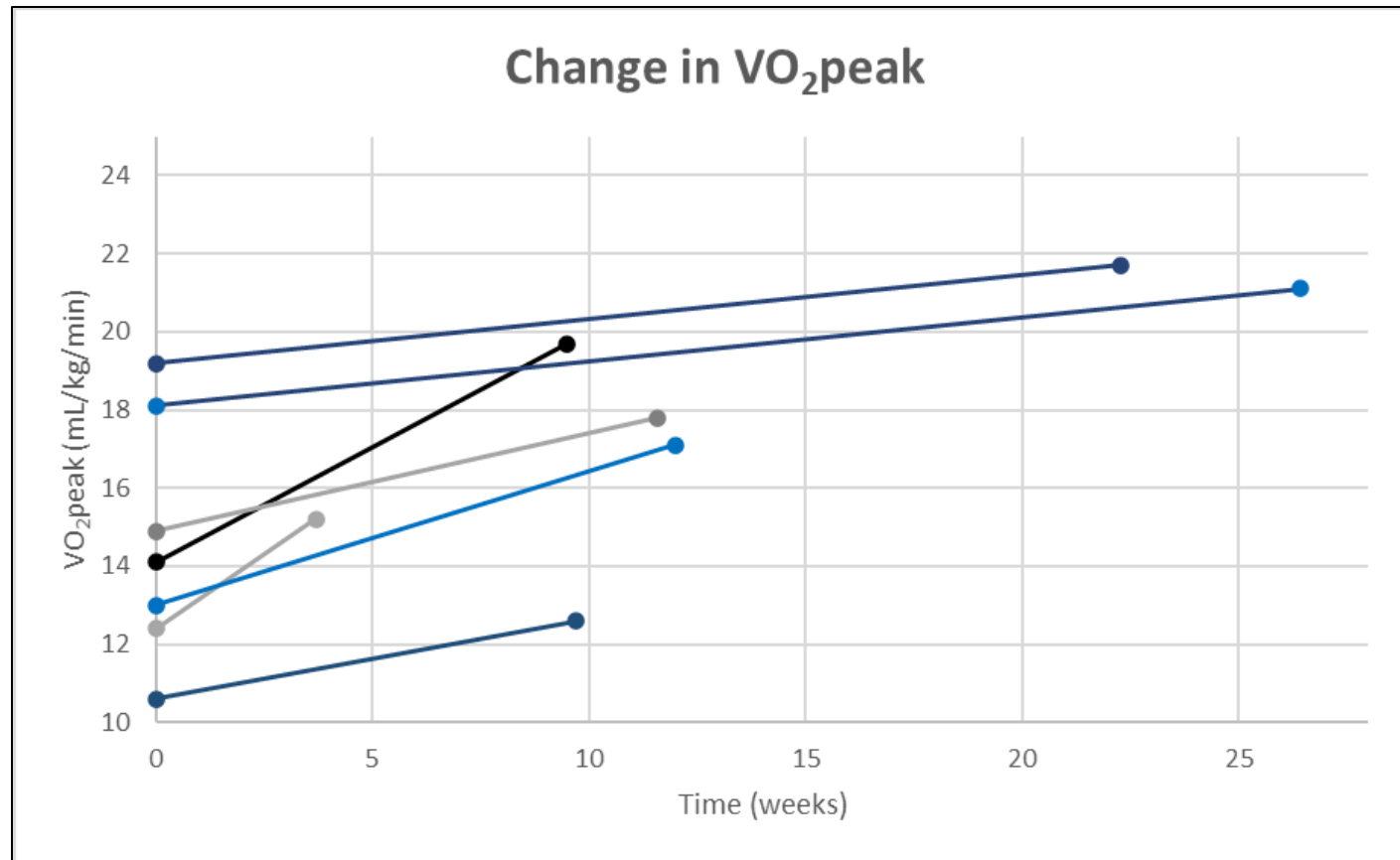
Remote Monitoring of High Intensity Interval Training



Remote Monitoring of High Intensity Interval Training



Results – Outcomes



- VO₂peak increased by 3.2 mL/kg/min (23.1%) (p=0.002)
- 30sSS increased by 2.7 reps (p=0.086)
- 6MW increased by 41.0m (p=0.229)

How *else* can we make patients “better”?

Resilience is defined as a dynamic property which enables cells, organs, organisms or **individuals** to resist or recover from the effects of a physiological or pathological stressor

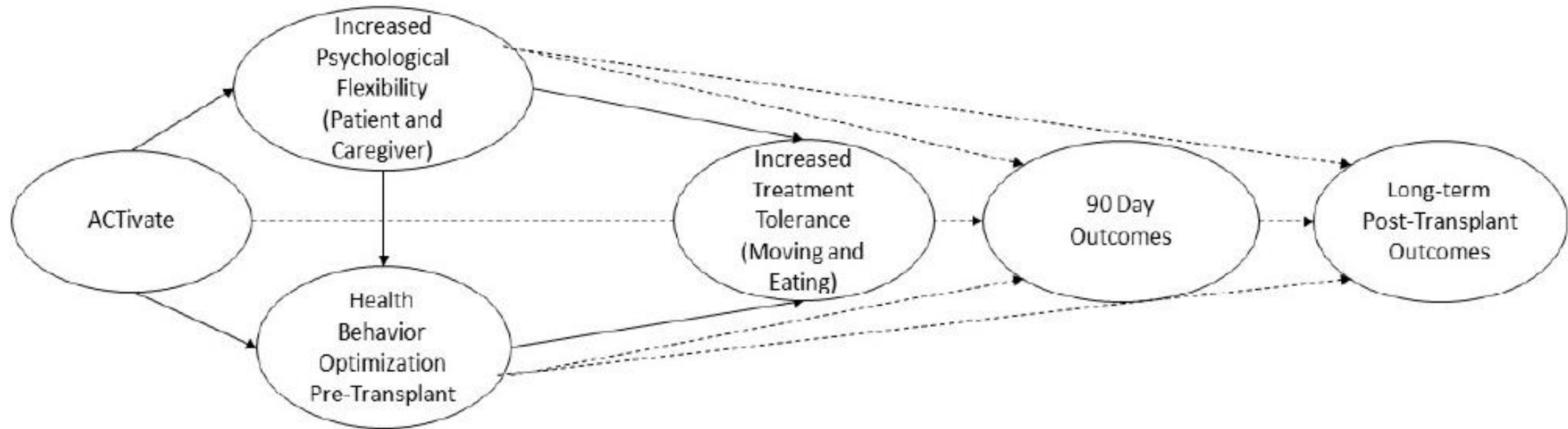
Case 3: Psychological Resilience

- RW was a 67yoF with high-risk MDS s/p Bu/Flu MUD + pasireotide
 - Developed GI GVHD, after steroids didn't work, decided to enter hospice

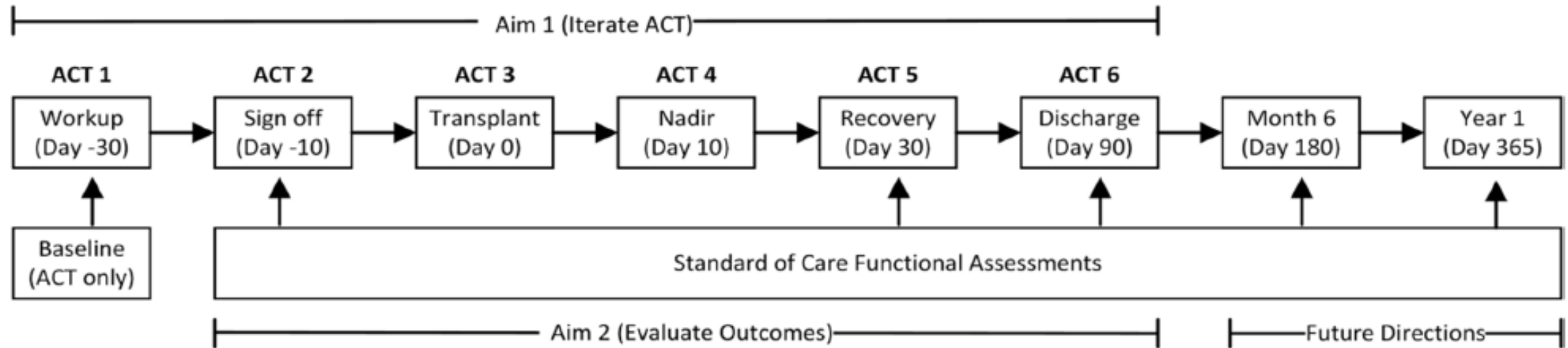
“I shouldn't have pushed her into it, she wasn't ready.”

Acceptance and Commitment Therapy (ACT)

- Goal: improve psychological and physical resilience -> improve physical activity and HCT outcomes.

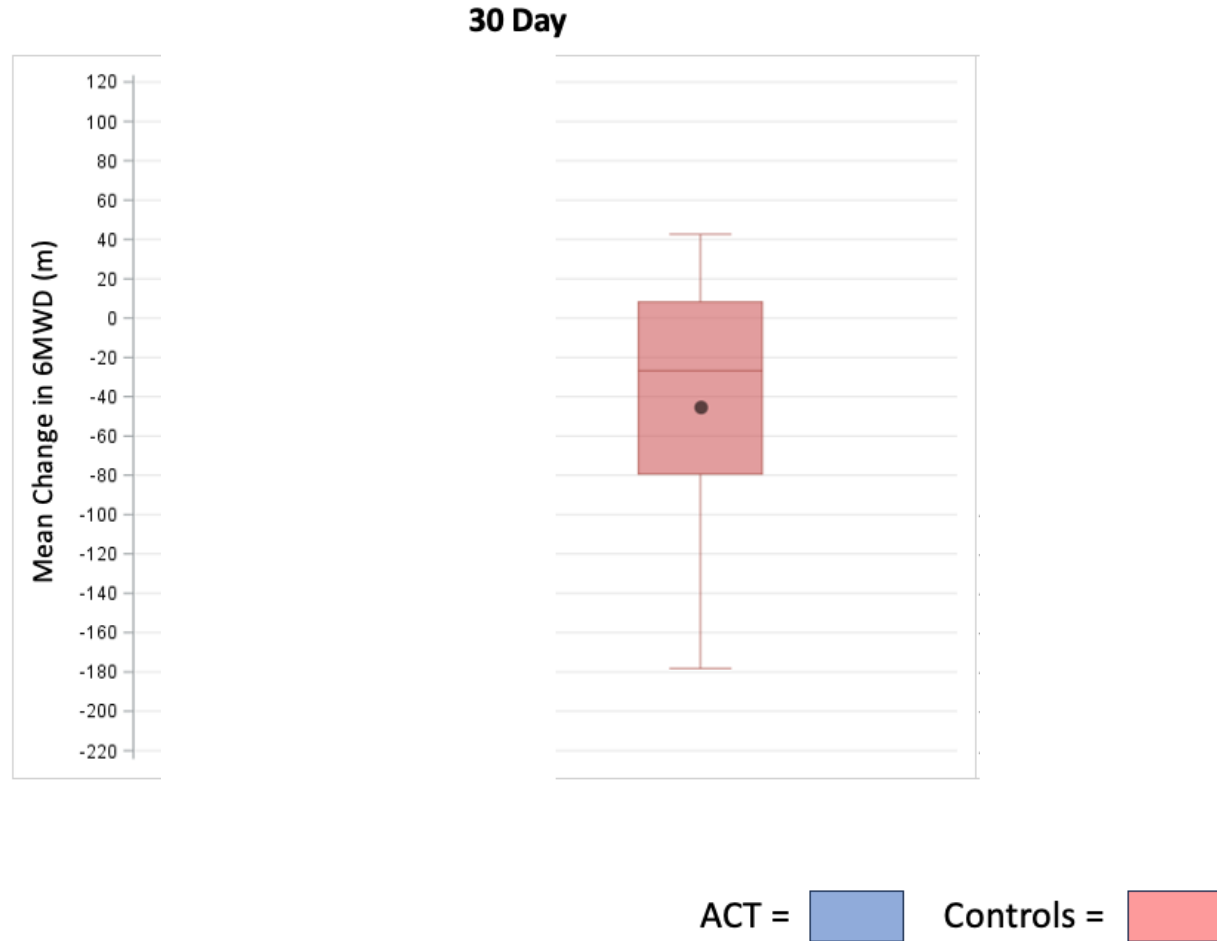


I-POP: ACTivate



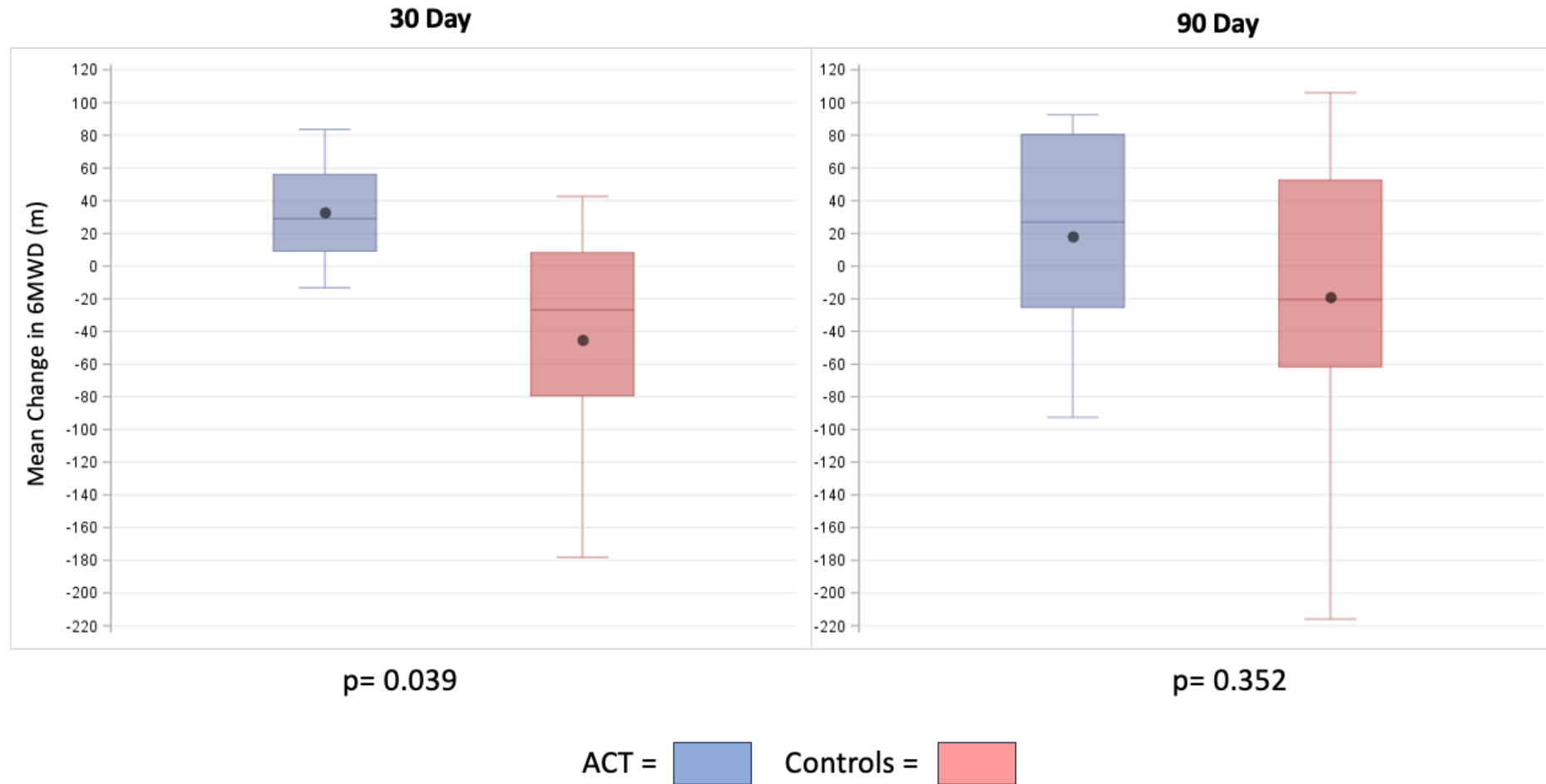
ACTivate Results

6 Minute Walk Distance, Average
Change From Baseline



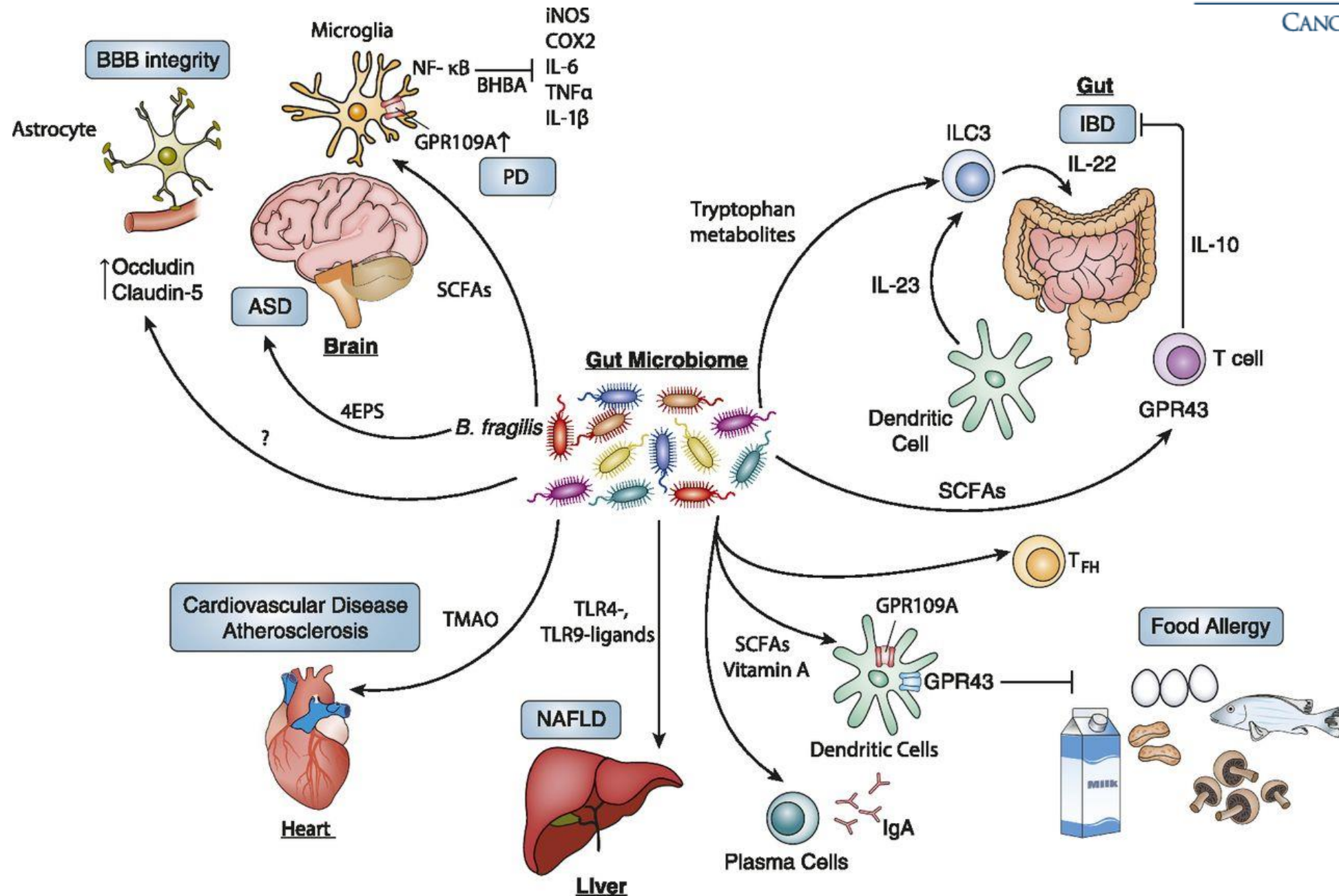
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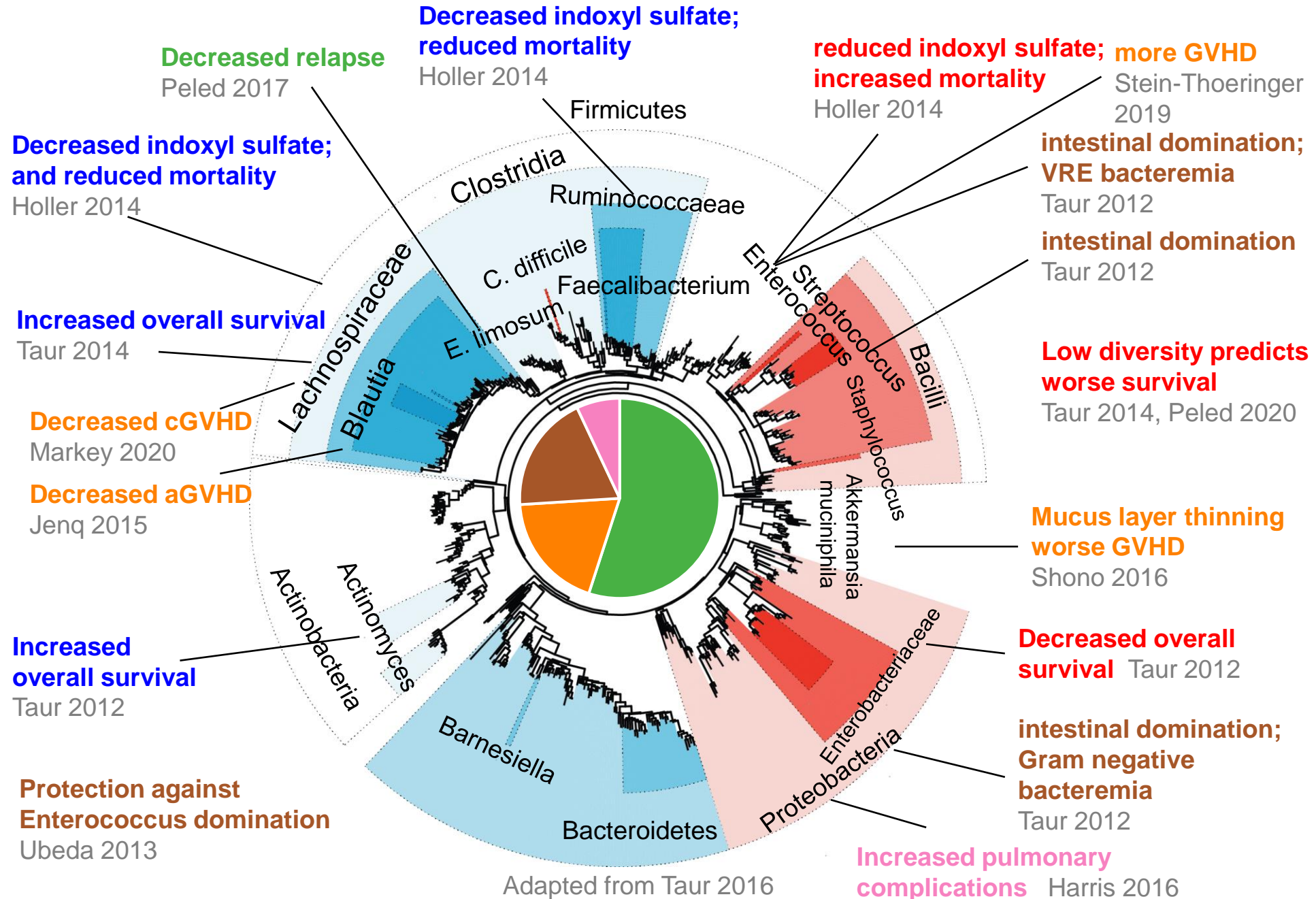
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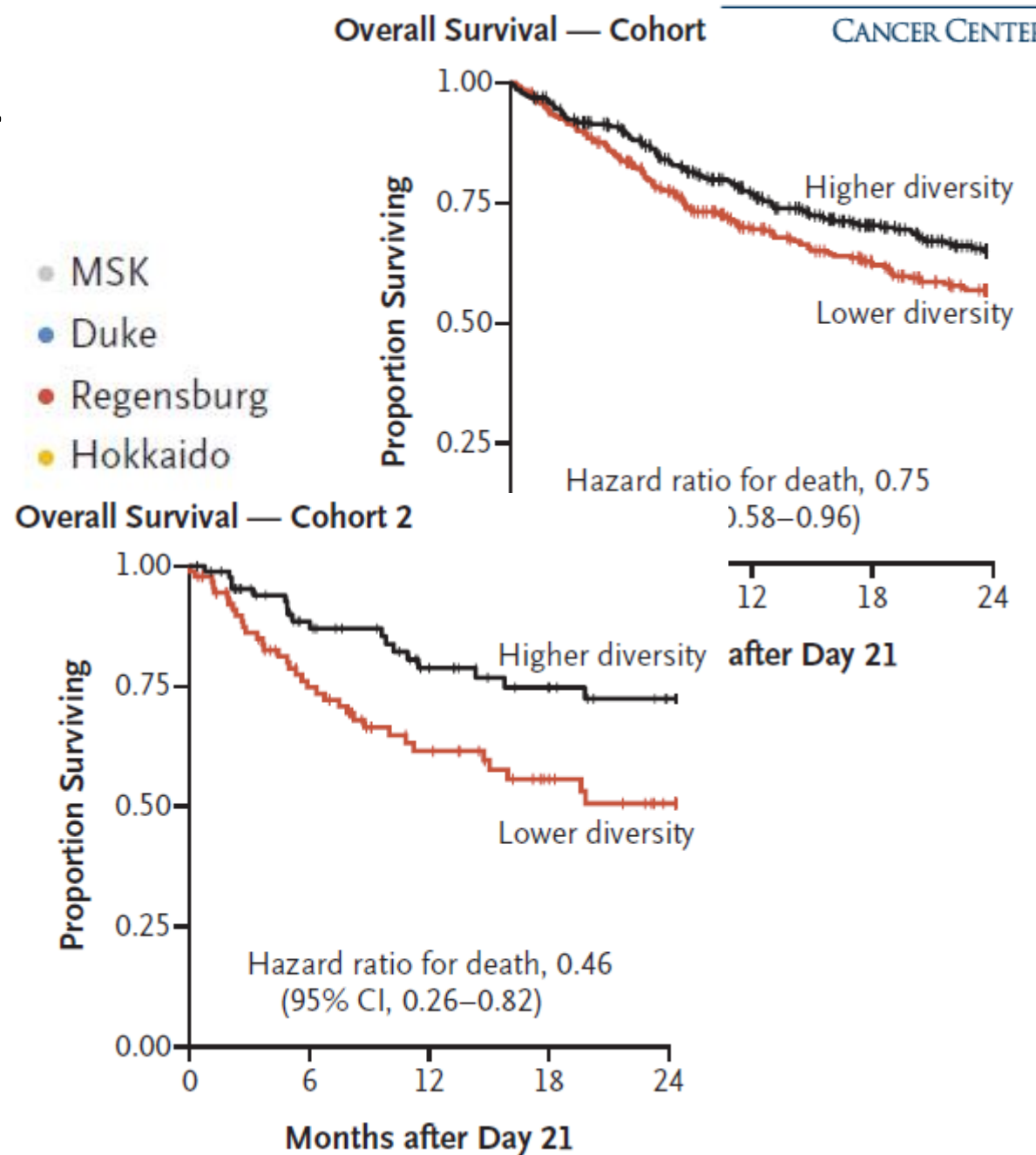
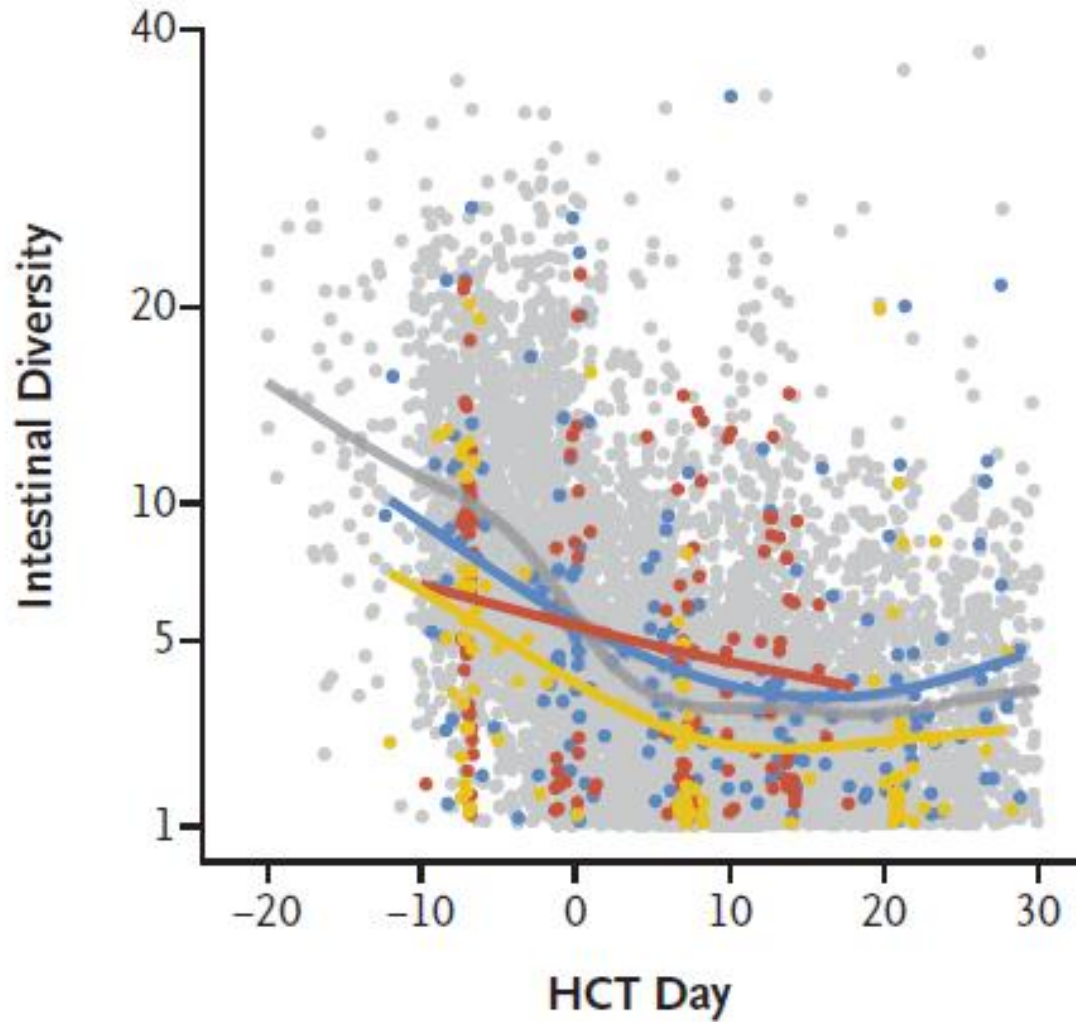


Gut bacteria associated with allo-HCT outcomes

Slide courtesy of Tsoni Peled, MSKCC



Not just single-center



I-POP: GOS

- Phase 1 Trial of GOS in HCT patients completed
- Randomized Phase 2 trial ongoing
- Hypotheses:
 - Decrease GVHD
 - Microbiome signature to predict response



Bringing It Home



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Bringing It Home

- It's about our patients
- PROs/QOL/Function
- Biomarkers/Microbiome
- Mobile Health (Telehealth, Devices)
- Resilience, Accelerated Aging



Improve Pre-, Peri, and Post-HCT Care to
Improve Patient Outcomes

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