Optimizing Survivorship

The Healthy Living Program Experience

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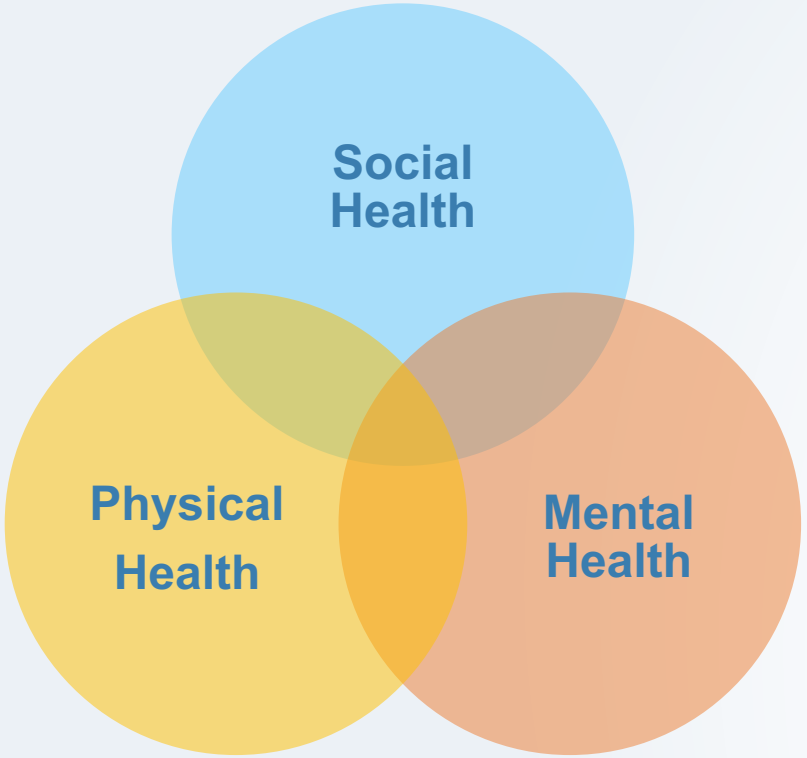
Disclosures

Consultant/Advisor/Speaker: Arvinas, AstraZeneca, BD Life Sciences, Daichii-Sankyo, Genentech/Roche, Gilead, Menarini-Stemline, Novartis, Pfizer, SynDevRx

Lifestyle Management Improves Quality of Life after Cancer Diagnosis



SOCIAL HEALTH

- Family functioning
- Marital functioning

PHYSICAL HELATH

- Physical condition
- Physical functioning
- Mobility
- Satisfaction with physical functioning
- Prior health

MENTAL HEALTH

- Mental Illness
- Anxiety
- Depression
- Psychological distress
- Psychological well-being
- Positive affect
- Cognitive functioning

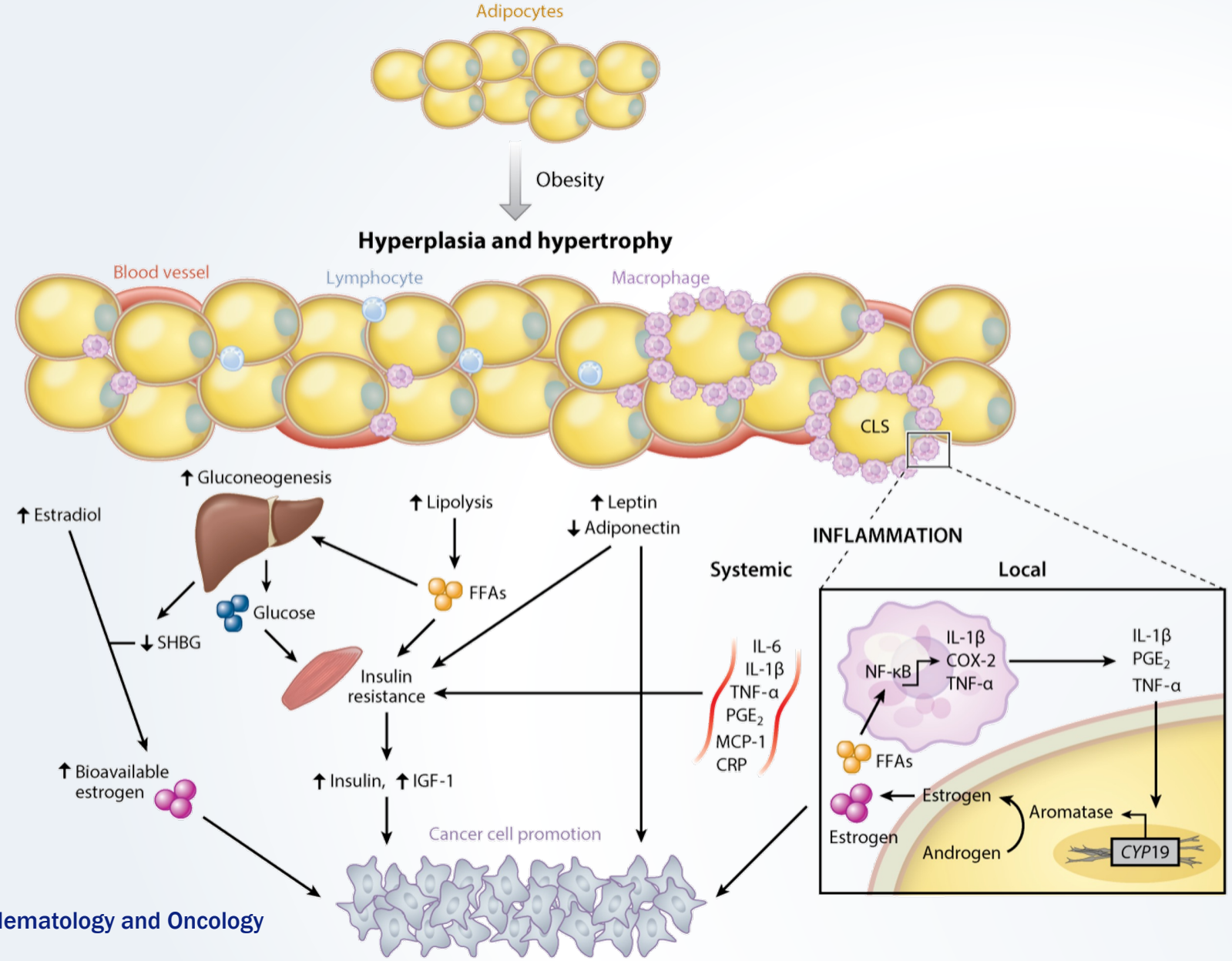
- Role limitations due to physical problems

- Energy / fatigue
- Sleep problems
- Health perceptions
- Physical symptoms
- Health distress
- Health outlook
- Pain

- Role limitations due to emotional problems
- Feelings of belonging

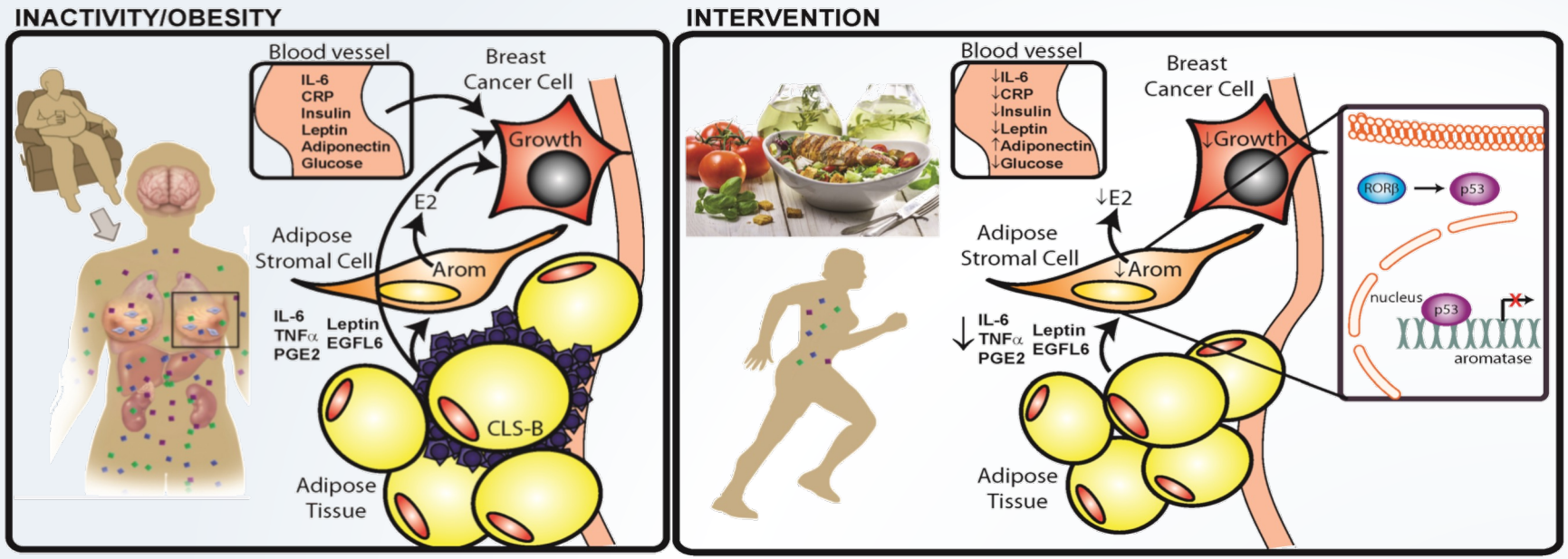
Source: van Leeuwen et al. Health Qual Life Outcomes 2018

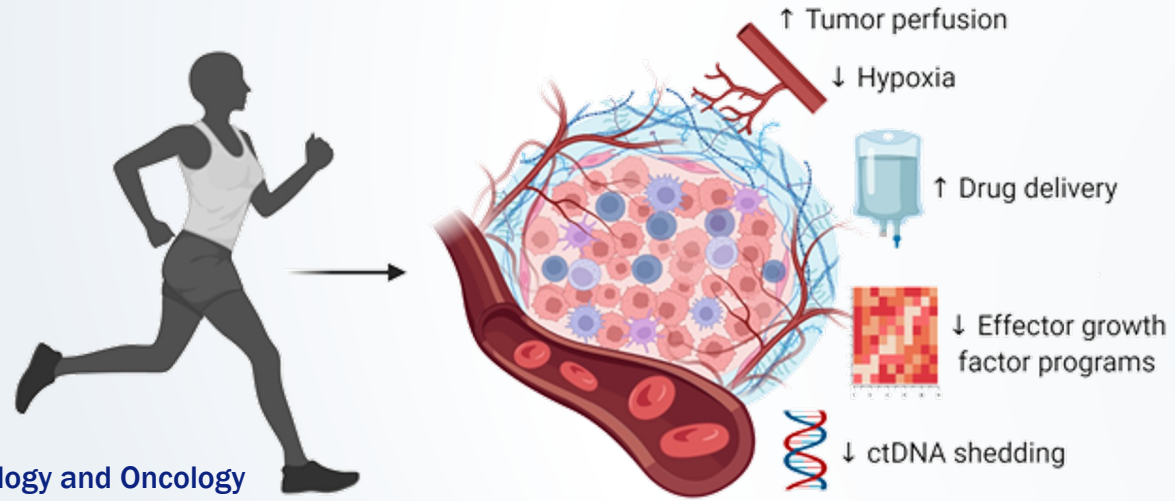
Systemic Metabolic Dysregulation Promotes Cancer Progression



Iyengar NM, et al. 2015. Annu. Rev. Med. 66:297–309

Re-establishing Energy Homeostasis as Cancer-Directed Treatment





Iyengar et al. J Clin Oncol 2016
Iyengar & Jones. JAMA Oncol 2018

Metabolic Dysfunction is Exacerbated by Chemotherapy

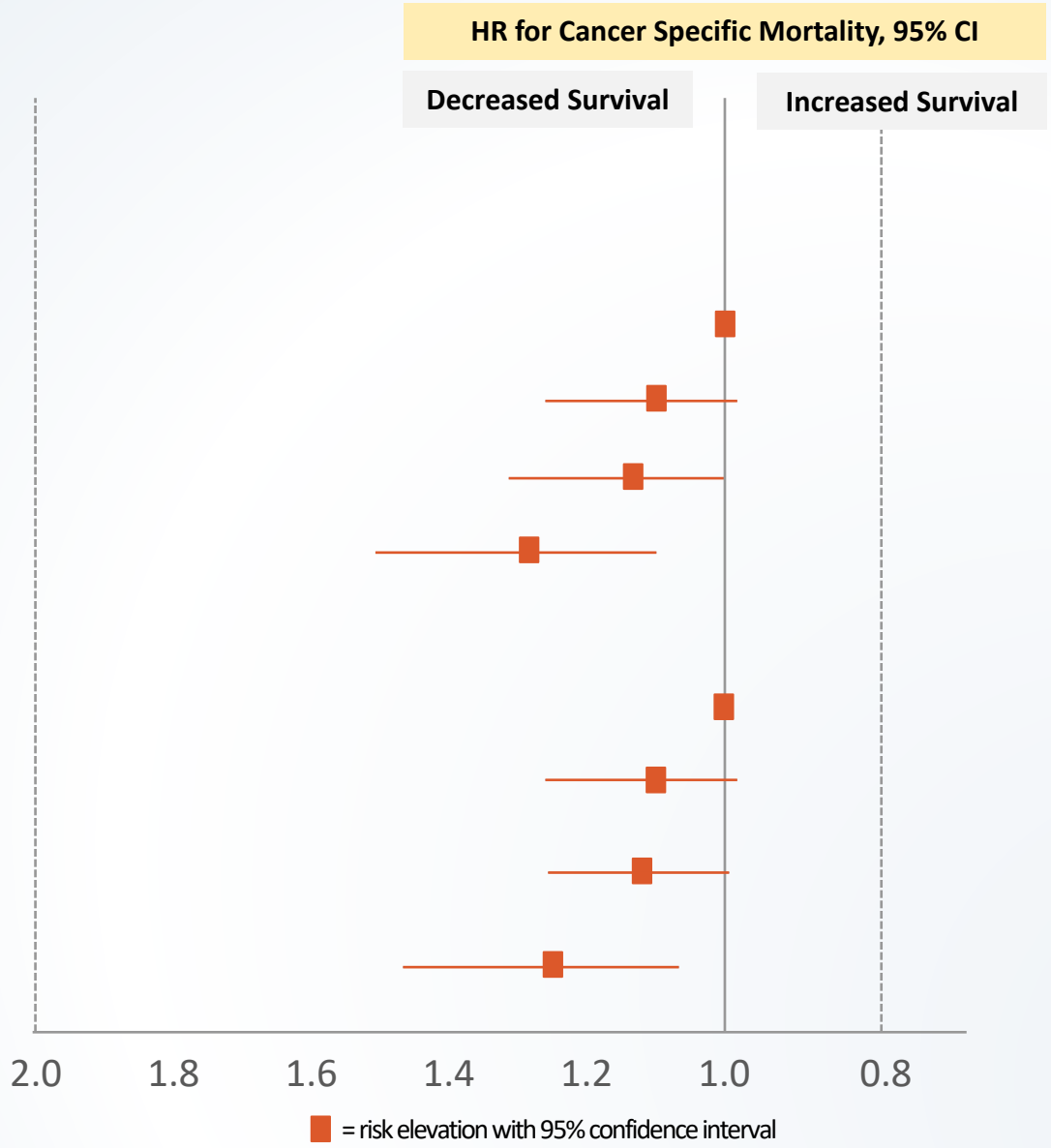
Variable	Pre-Treatment*	Post-Treatment*	% Change	*P*
Waist circumference (cm)	86.7 (12.9)	90.7 (11.2)	4.7	<0.01
BMI	25.9 (6.3)	29.0 (7.0)	11.5	<0.001
Body fat (%)	33.1 (8.2)	36.0 (5.1)	8.9	<0.001
HOMA-IR	4.52 (1.1)	9.4 (1.5)	108.3	<0.001
HbA1c (%)	5.4 (0.4)	5.9 (0.6)	8.6	<0.001
Fasting glucose (mg/dL)	97.2 (19.8)	117.0 (37.0)	20.3	<0.01
Total cholesterol (mg/dL)	185.5 (48.3)	201.9 (45.5)	8.8	<0.001
Triglycerides (mg/dL)	108.7 (47.6)	128.7 (58.9)	18.4	<0.01
CRP (mg/L)	0.37 (0.36)	0.49 (0.21)	31.9	0.04

*Mean (±S.D.)

Adapted from Dieli-Conwright et al. Cancer 2016.

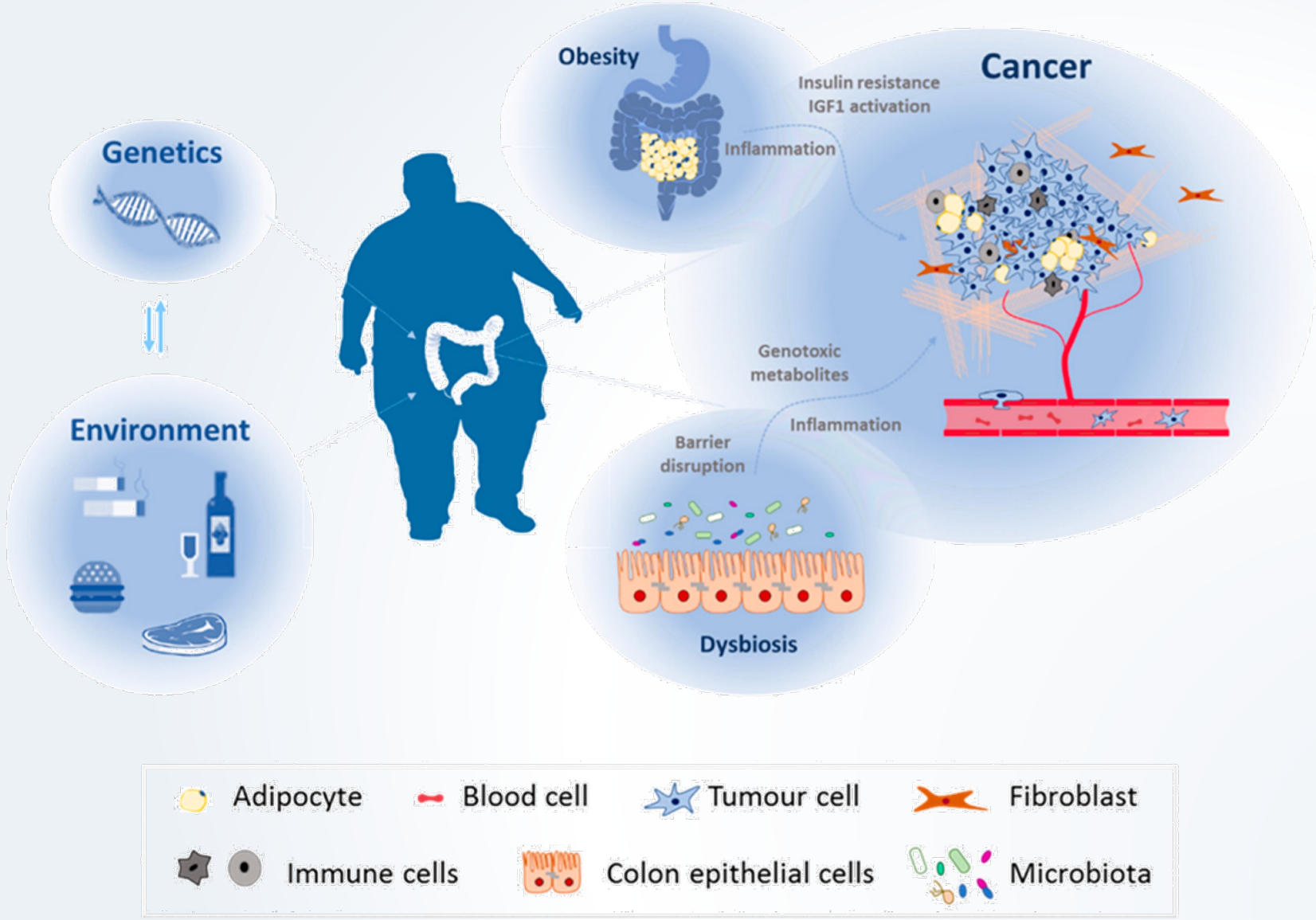
Insulin Resistance and Cancer-Specific Mortality

Age & BMI Adjusted HOMA-IR	N (%)
0.05 – 1.09	5,791 (25.4)
>1.09 – 1.77	5,671 (24.8)
>1.77 – 3.03	5,690 (24.9)
>3.03 – 402.99	5,685 (24.9)
HOMA-IR (unadjusted)	
0.05 – 1.09	5,791 (25.4)
>1.09 – 1.77	5,671 (24.8)
>1.77 – 3.03	5,690 (24.9)
>3.03 – 402.99	5,685 (24.9)



Adapted from Pan et al. JNCI 2020.

Precision Lifestyle Interventions: Host + Tumor Targeting



Aguirre-Portoles et al. Nutrients 2017.

Phase 2 RCT: Precision Nutrition + Structured Exercise

Eligibility

- Stage I-III ER+ breast cancer
- Completed curative surgery, radiation, and cytotoxic treatment
- Current treatment with adjuvant aromatase inhibitor
- BMI ≥ 27
- Sedentary (< 90 min exercise / wk)

Randomize

6 months

Structured Exercise + Plant-based diet (N=28)

Attention Control Telephone counseling + Treadmill (N=28)

Post-study Visit

- **Breast biopsy**
- **DEXA**
- **Fasting blood**
- **CPET**
- **Stool**

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- **DEXA**
- **Fasting blood**
- **CPET**
- **Stool**

Study Endpoints

Primary: Breast aromatase level
Secondary: Breast tissue gene expression changes, Blood markers, body composition, weight loss, adherence, microbiome, QOL / PROs

Biostatistical Design

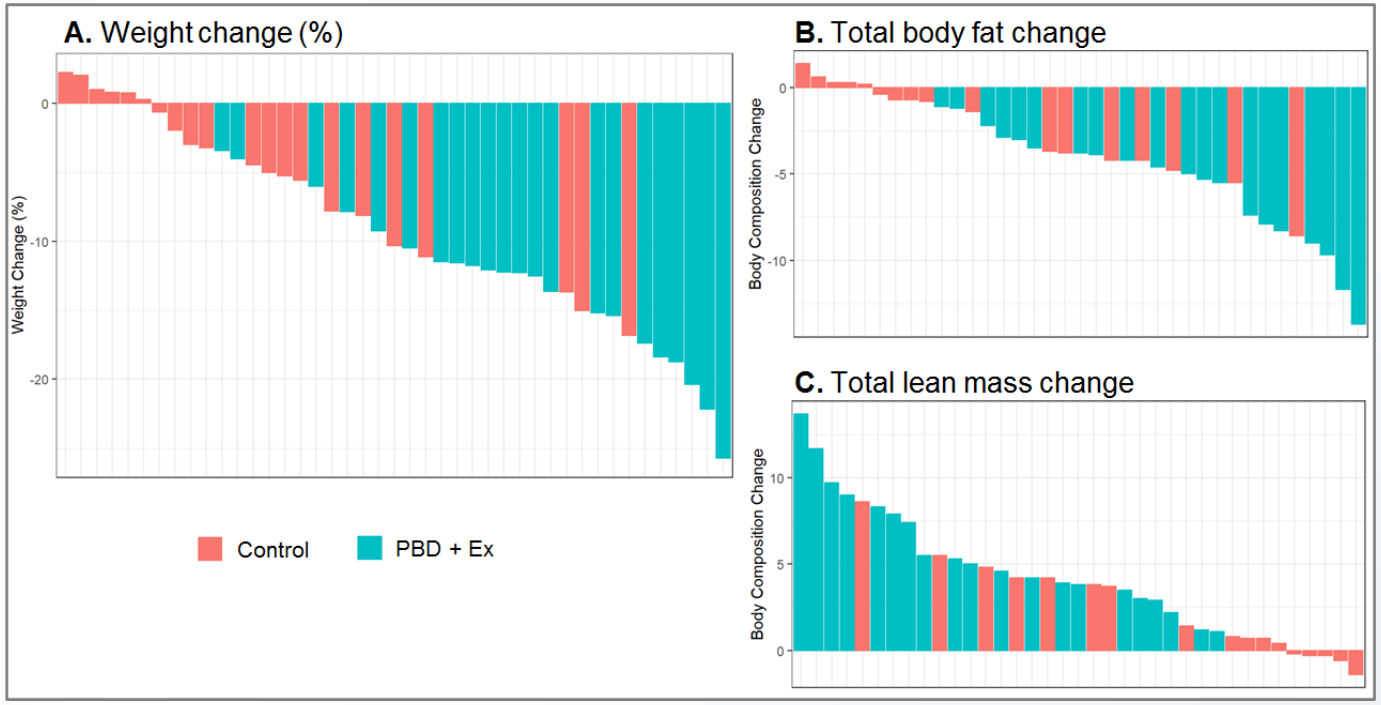
- 1 unit decrease in BMI = 0.06 mean reduction in aromatase (SD 0.81, log scale)
- Goal BMI reduction is 3 kg/m^2

NCT04298086

Phase 2 RCT: Precision Nutrition + Structured Exercise

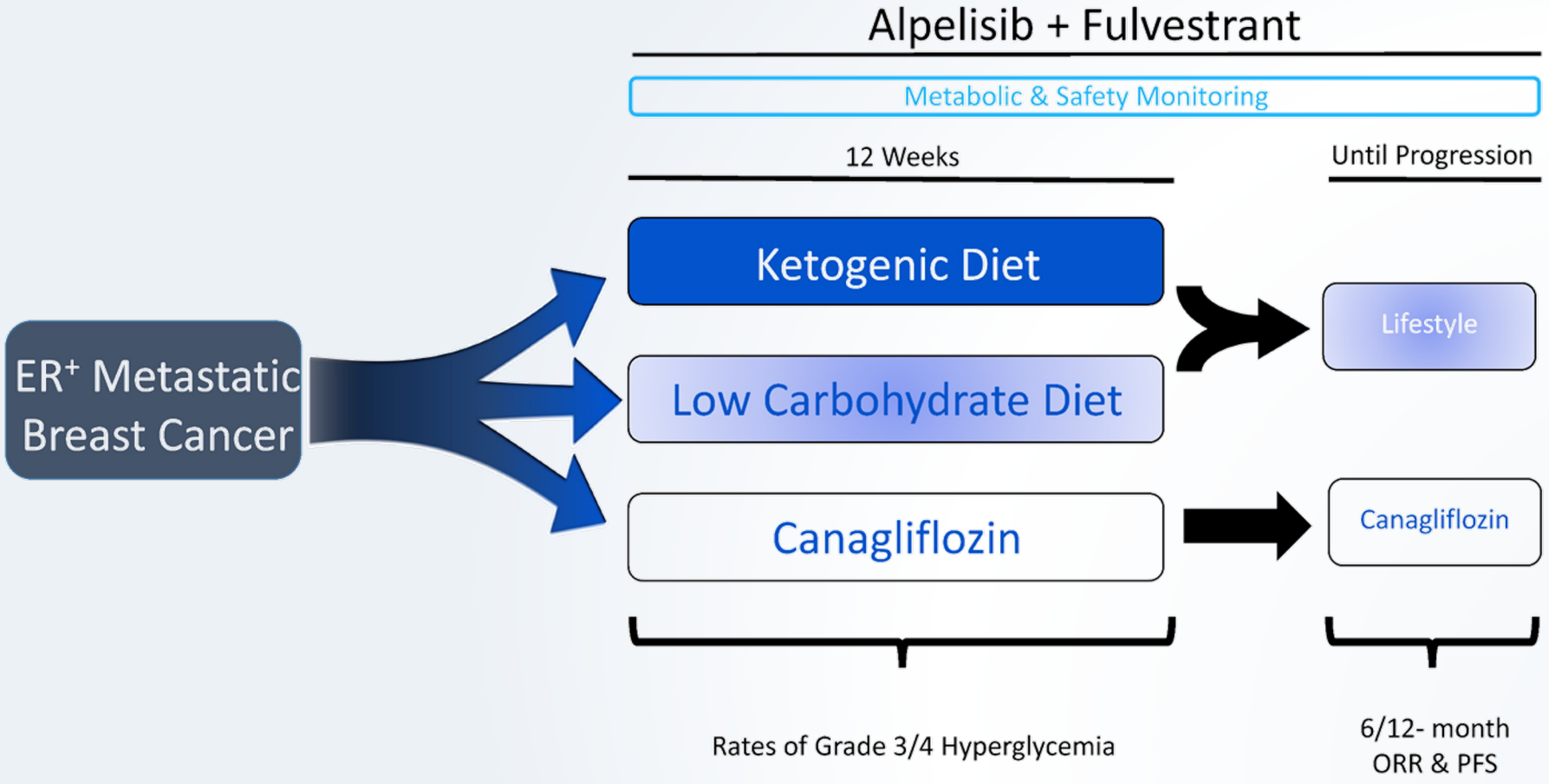
Characteristic	Control (N = 21)	PBD + Ex (N = 22)
Age at consent, mean (SD)	58 (7)	56 (7)
Race, number (%)		
White	16 (76%)	15 (68%)
Black	4 (19%)	3 (14%)
Other	0 (0%)	3 (14%)
Unknown	1 (5%)	1 (5%)
Ethnicity, number (%)		
Non-Hispanic	15 (71%)	18 (82%)
Hispanic	4 (19%)	4 (18%)
Unknown	2 (10%)	0 (0%)
BMI, mean (SD)	34.2 (4)	34.3 (5)
Smoking, number (%)		
Never	13 (62%)	14 (64%)
Prior/quit	8 (38%)	8 (36%)
Alcohol intake, number (%)		
Never	2 (9%)	4 (18%)
Prior/quit	1 (5%)	2 (9%)
Yes	18 (86%)	16 (73%)
Stage, number (%)		
I	11 (52%)	12 (55%)
II	7 (33%)	8 (36%)
III	3 (14%)	2 (9%)
Receptor status, number (%)		
ER+/PR–/HER2–	1 (5%)	1 (4%)
ER+/PR+/HER2–	19 (90%)	18 (82%)
ER+/PR+/HER2+	1 (5%)	3 (14%)
Chemotherapy, number (%)	6 (29%)	8 (36%)
Radiation, number (%)	18 (86%)	17 (77%)
Ovarian suppression, number (%)	5 (24%)	14 (64%)

	Control (N=21)	PBD + Ex (N=22)	P
	Change (95% CI)	Change (95% CI)	
Weight (kg)	-4 (-6.6, -2.2)	-12 (-15, -9.4)	<0.001
Total body fat (kg)	-2 (-3.5, -0.71)	-6 (-7.3, -4.1)	<0.001
Trunk fat (kg)	-3 (-4.4, -0.73)	-7 (-8.9, -4.9)	<0.001
Total body lean mass (kg)	2 (0.71, 3.5)	6 (4.1, 7.3)	<0.001
Total body fat to lean mass ratio	-0.01 (-0.02, 0.00)	-0.02 (-0.03, 0.00)	0.4



Iyengar et al. ASCO 2024.

Targeting Insulin Feedback to Enhance Alpelisib (TIFA) Trial

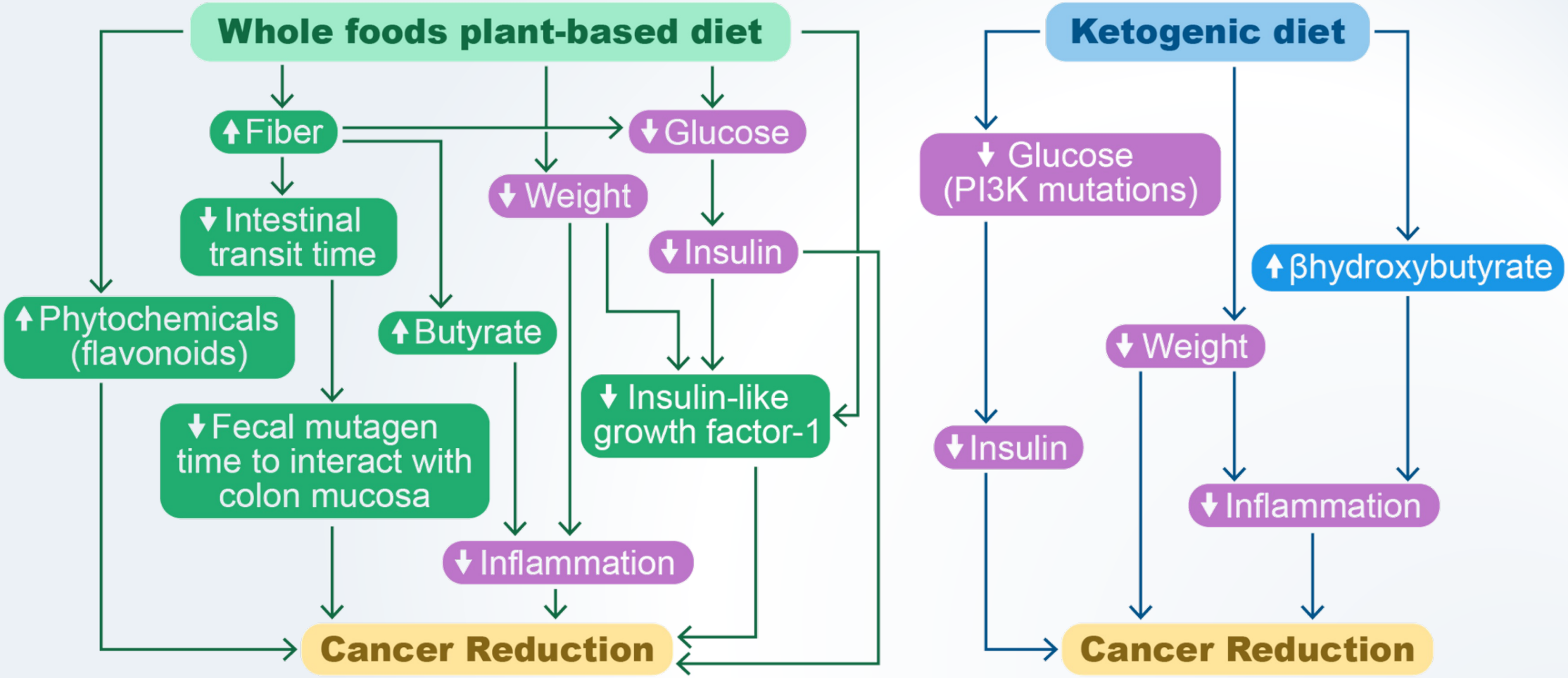


Memorial Sloan Kettering Cancer Center

Weill Cornell Medicine

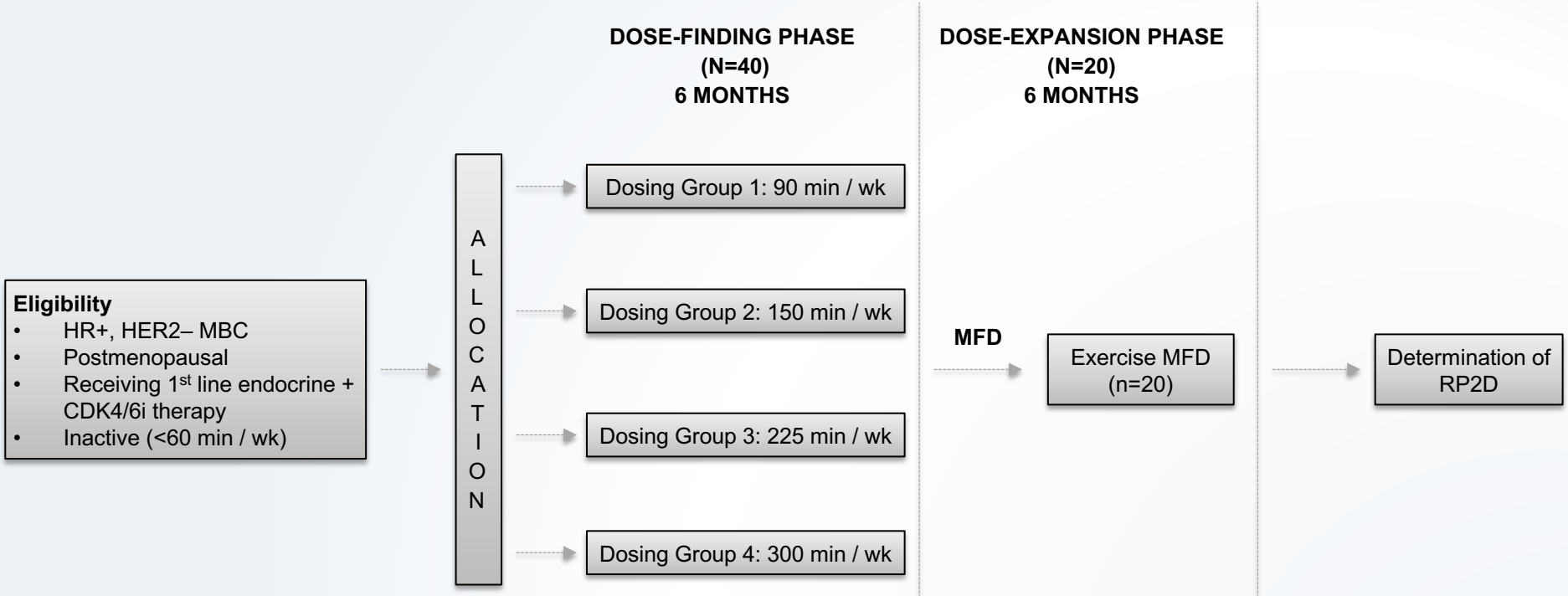
The Ohio State University

Plant-based vs. Ketogenic Diets



Shah & Iyengar. JAMA Oncology 2022.

Multicenter Phase 1a Trial of Exercise in ER+ Metastatic Breast Cancer: TBCRC 054

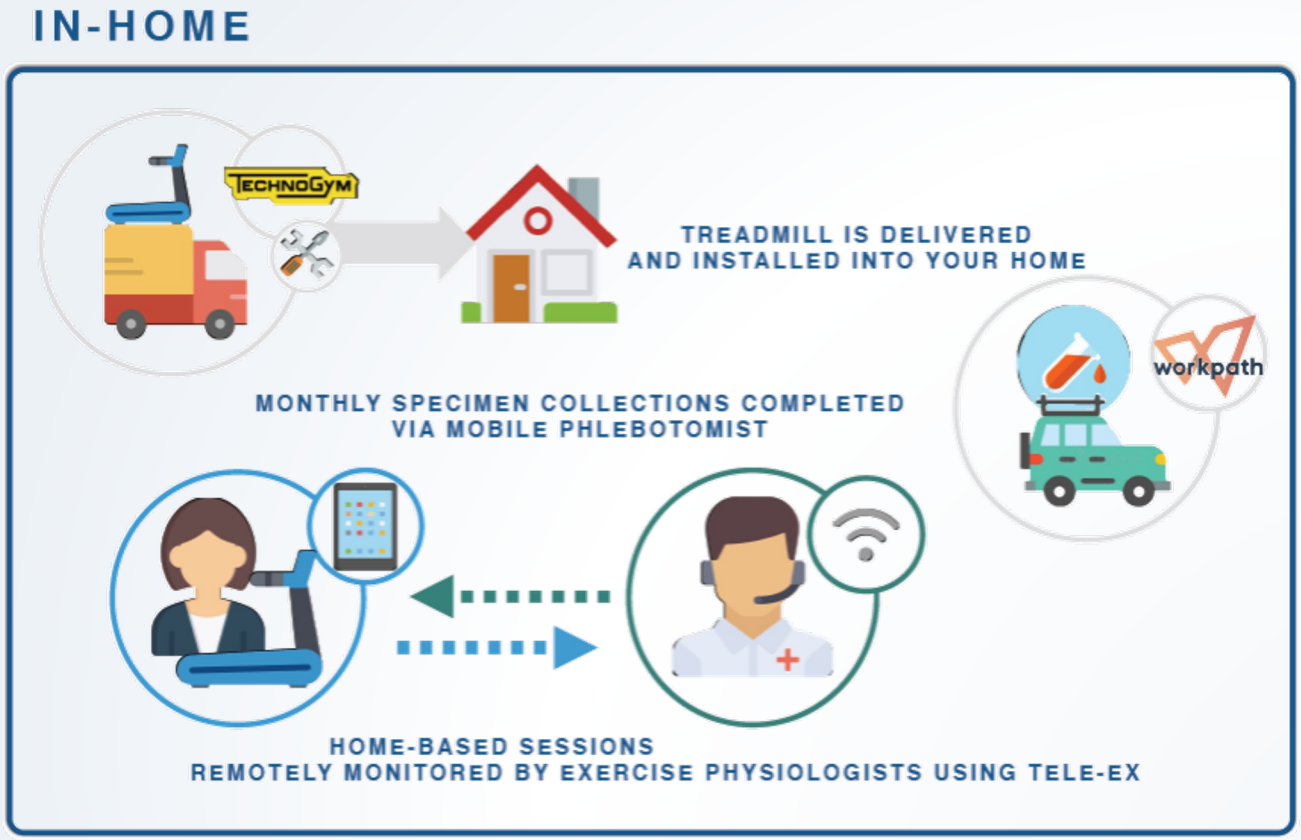


Statistical Design: **Time-to-event continual reassessment method (TITE-CRM)**

Dose escalation and assignment to dosing group will be determined by continual assessment of exercise RDI

R01CA235711

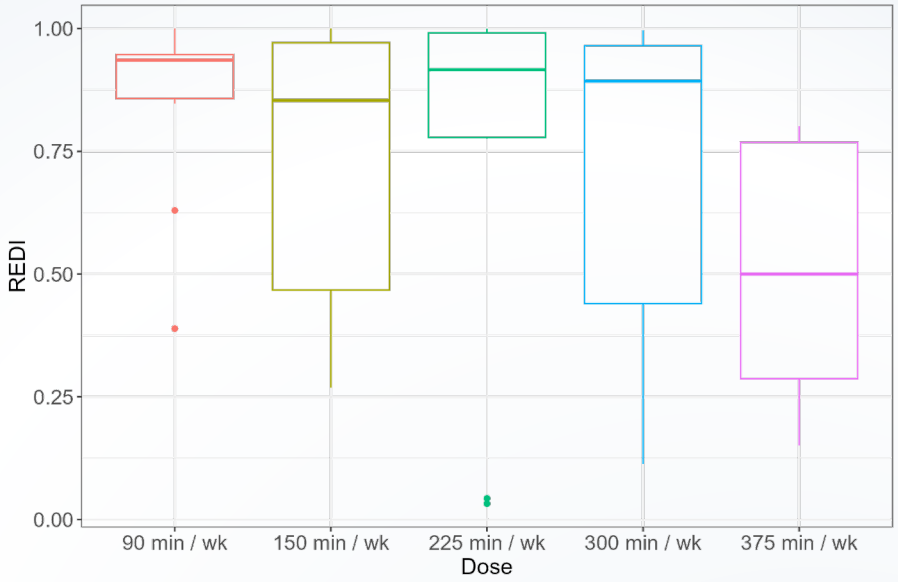
Multicenter Phase 1a Trial of Exercise in ER+ Metastatic Breast Cancer: TBCRC 054

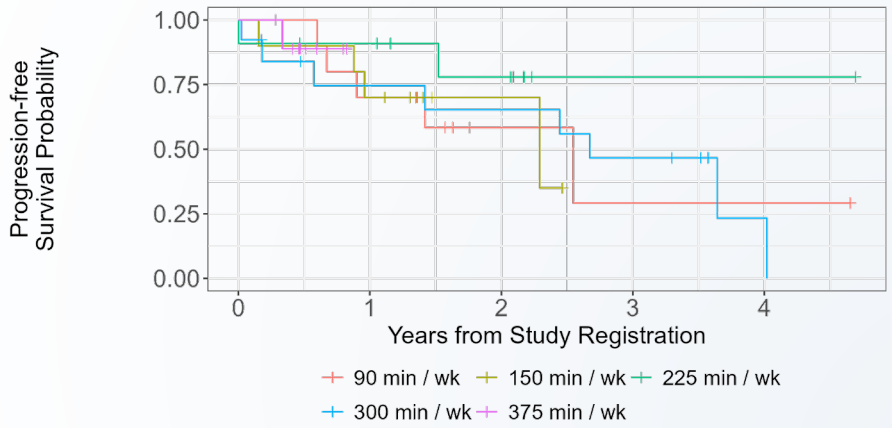


R01CA235711

Multicenter Phase 1a Trial of Exercise in ER+ Metastatic Breast Cancer: TBCRC 054

Characteristics (N=54)		Median (IQR) or N (%)
Age		53 (46 – 63)
BMI (kg/m²)		27 (23 – 33)
Race/Ethnicity	Asian	3 (6%)
	Black or African American	5 (10%)
	White	35 (73%)
	Other	5 (10%)
	Unknown	6
Smoking & Alcohol Use	Current smoker	1 (2%)
	Current alcohol use	37 (69%)
Hormone Receptor Status	ER+	54 (100%)
	PR+	40 (74%)
Cancer Burden	De novo metastasis	12 (22%)
	Visceral metastasis	23 (43%)
	1 metastatic site	37 (69%)
	2 metastatic sites	10 (19%)
	≥ 3 metastatic sites	7 (12%)
Endocrine Therapy	Aromatase inhibitor	43 (80%)
	Fulvestrant	11 (20%)
Ovarian Suppression		1 (2%)
CDK4/6 Inhibitor	Palbociclib	33 (62%)
	Ribociclib	12 (23%)
	Abemaciclib	8 (15%)
	Unknown	1



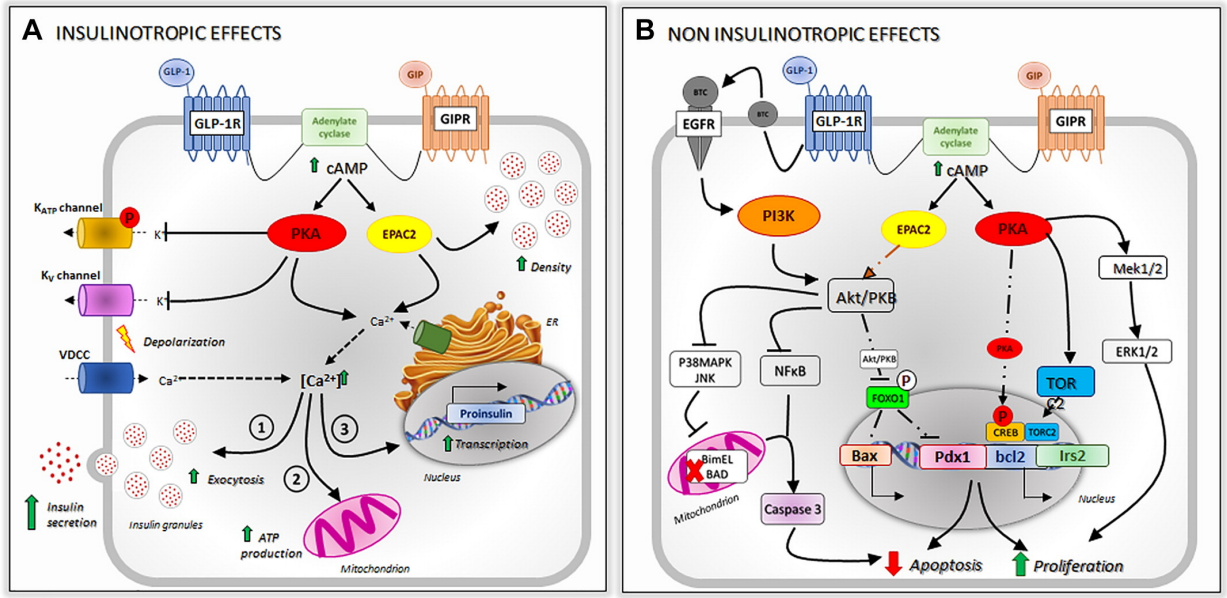


At Risk

90 min / wk	10	7	2	1	1
150 min / wk	10	7	2	0	0
225 min / wk	11	9	6	1	1
300 min / wk	13	8	7	5	1
375 min / wk	10	0	0	0	0

Iyengar et al. ASCO 2025.

Incretin Mimetics (GLP1-RA) – Mechanisms & Effects



Folli et al. Am J Physiol Endocrinol Metab 2023
Gutgesell et al. Diabetes Ther 2024

Glucagon GLP-1 GIP

Liver	Intestine	Brain	Muscle	Pancreas	Adipose	Cardiovascular	Plasma
↑↓ Gluconeogenesis	↓ Gastric emptying	↓↓↓ Food intake	↑ Insulin sensitivity	↑↑↑ Insulin secretion	↓ Lipogenesis	↓ Cardiovascular events	↓ Triglycerides
↓ Steatosis	↓ Gastrointestinal motility	↓ Reward behaviour	↓↑ Glucose uptake	↓ Glucagon secretion	↑ Lipolysis	↓ Blood pressure	↓ LDL-cholesterol
↑ Bile acid production		↓ Palatability		↑↑ β-Cell survival	↓ Fat mass		↓ Fasting insulin
↑ Lipid oxidation		↑↓ Nausea			↓ Inflammation		↓ Fasting glucose
↓ Lipid synthesis					↑ Thermogenesis		

PRESENTED BY: Neil M. Iyengar, MD; Memorial Sloan Kettering Cancer Center

Mobile Behavior Change Application in Breast Cancer

Total screened (N=189)

Ineligible (N=143)
- BMI <27.5 kg/m² (N=39)
- Did not own a smartphone (N=1)
- No history of breast cancer diagnosis (N=8)
- DCIS or stage IV breast cancer (N=70)
- Did not complete active cancer treatment ≥6 months prior to enrollment (N=52)
- Currently taking insulin (N=3)
- Uncontrolled hypertension (N=1)
- Living outside the United States (N=5)

Invited to participate (N=46)

Consented (N=44)

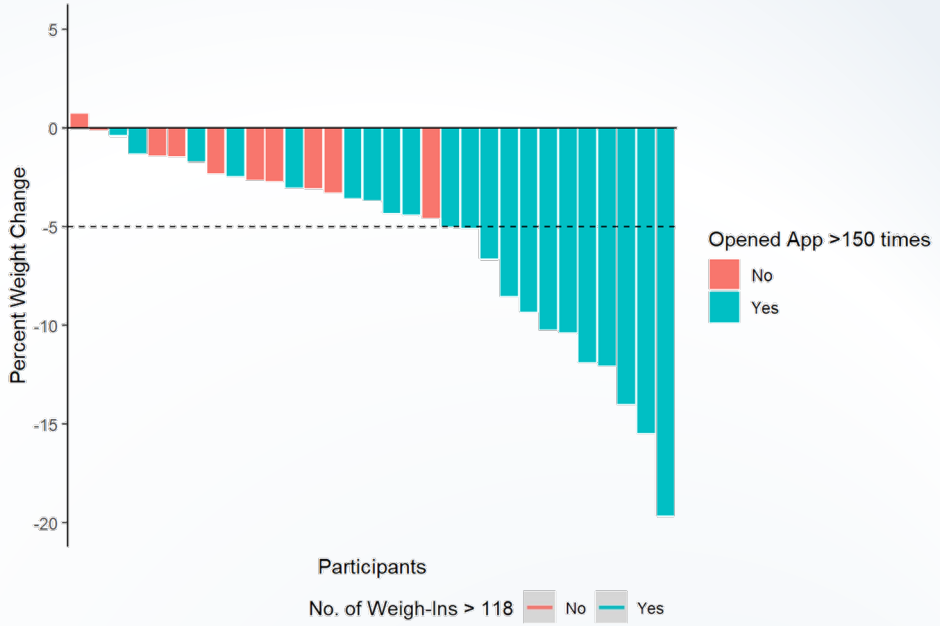
Enrolled in Noom program (N=42)

NOOM

Completed 6-month surveys (N=32)

Voluntarily withdrew due to personal reasons (N=1)

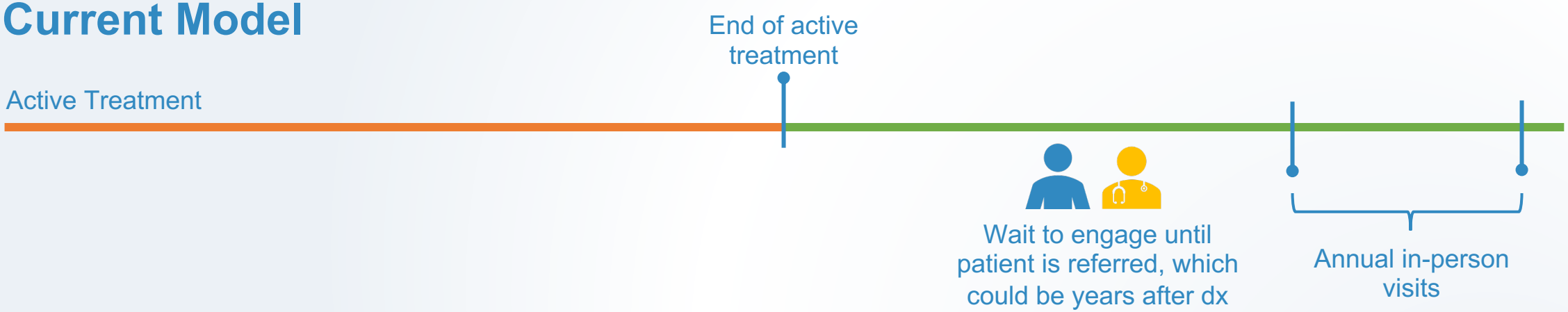
Included in final analysis (N=31)



Shen et al. NPJ Breast Ca 2024.

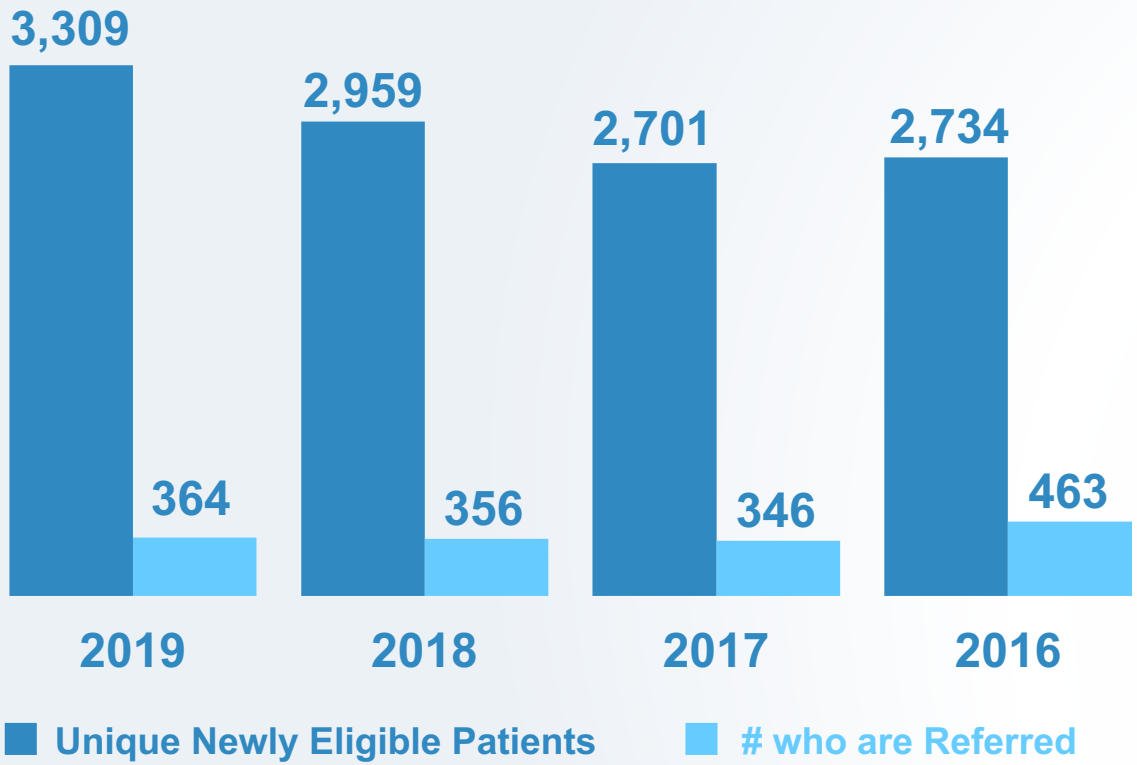
Lifestyle management is a central feature of survivorship care, yet referral to Survivorship occurs years after diagnosis

Current Model

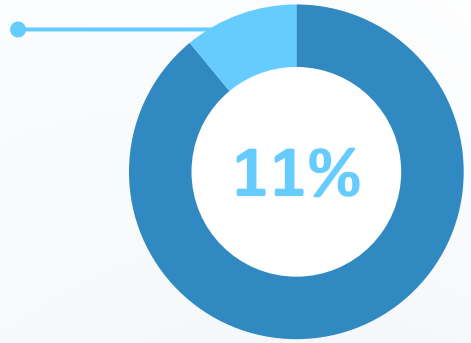


Low engagement with a growing population of eligible survivors

Within Breast Medicine Service at MSK



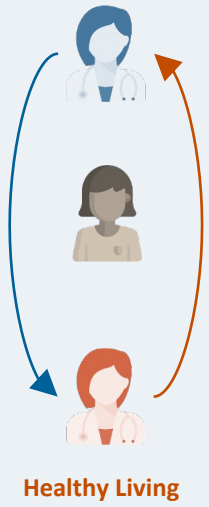
Eligible BMS patients referred to Survivorship Program in 2019

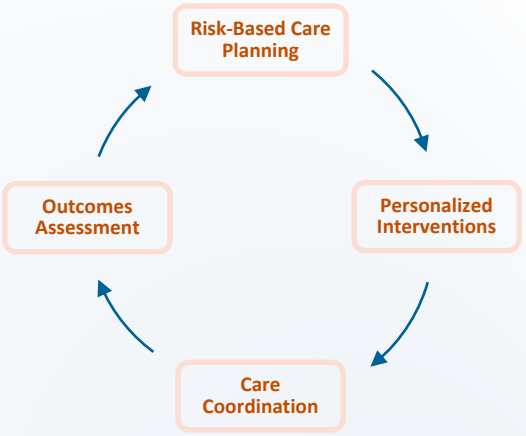


The Healthy Living Model: Core Components

A risk-based approach to assessment and management of a patient's lifestyle, behaviors, psychosocial context, and needs, delivered at the start of cancer care through a hybrid model.

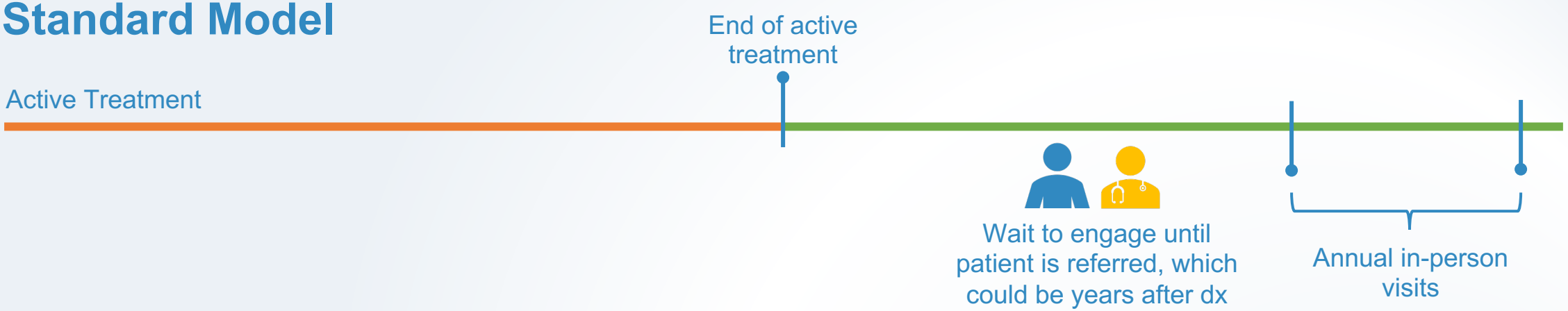
1. Engage Early
2. Deliver Risk-Stratified Care
   - Assess Risk
   - Personalize Interventions
3. Centralize Coordination
4. Monitor & Evaluate



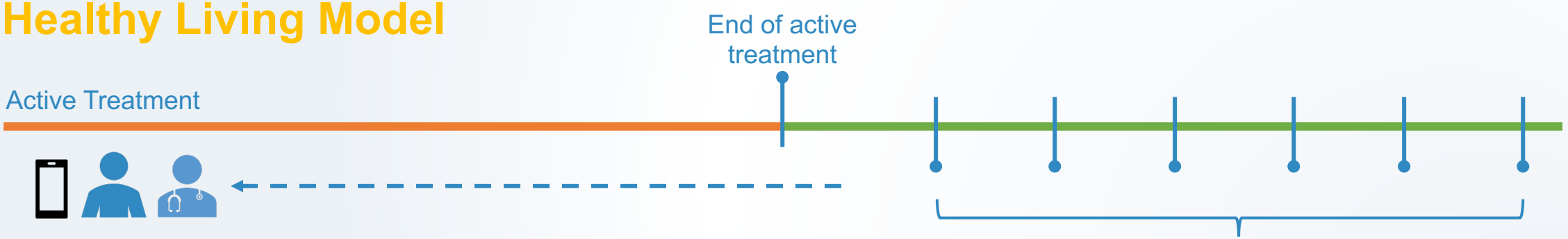


Support During Treatment, Bridge to Survivorship

Standard Model



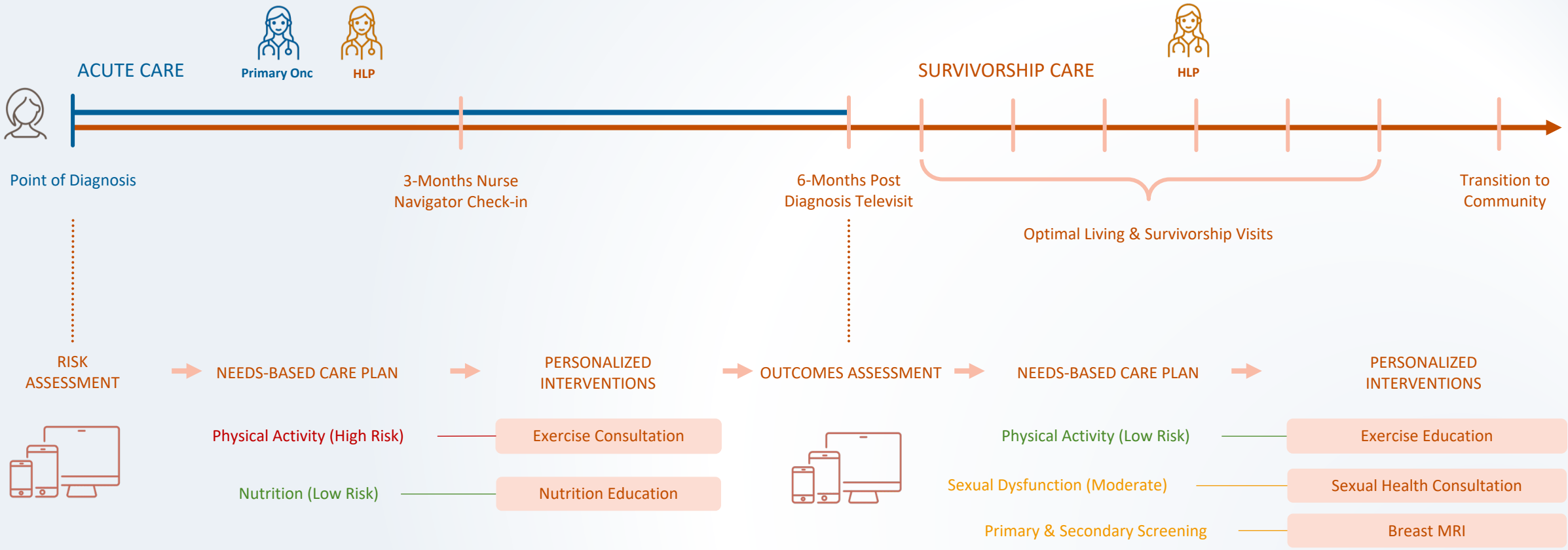
Healthy Living Model



- Engage patient early in their cancer journey
- Use of digital tools to collect relevant insights to create personalized wellness plans and identify research interest

Healthy Living Program Patient Journey

Healthy Living leverages a whole person approach as a bridge to post-treatment care.



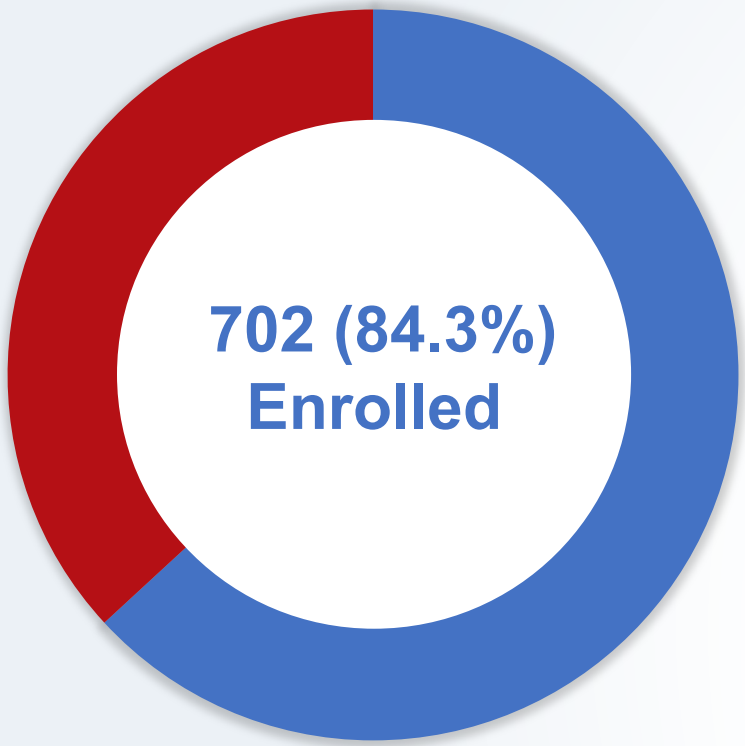
Proof of Concept: Pilot Study

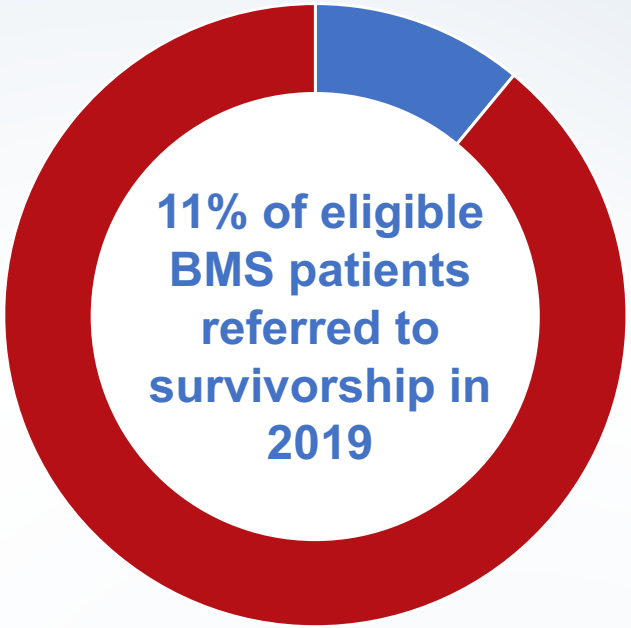
Baseline characteristic	N=399
Age, median	58
Baseline BMI, median (kg/m^2)	26.1
Stage	
Ductal carcinoma in situ	45 (11.2%)
Stage I	296 (74.2%)
Stage II	51 (12.8%)
Stage III	7 (1.8%)
Receptor status	
Hormone receptor-positive	317 (89.5%)
HER2-positive	24 (6.8%)
Triple-negative	26 (7.3%)
Chemotherapy	135 (33.9%)

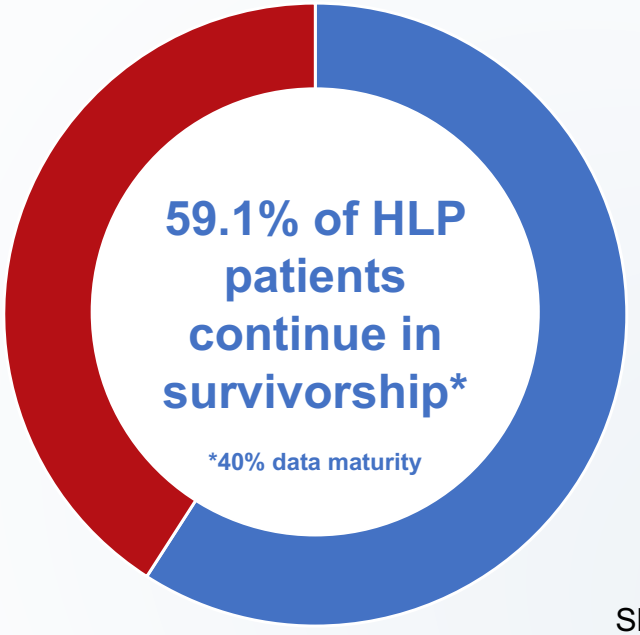
Shen et al, under review

Pilot Study: Feasibility

833 surveys assigned

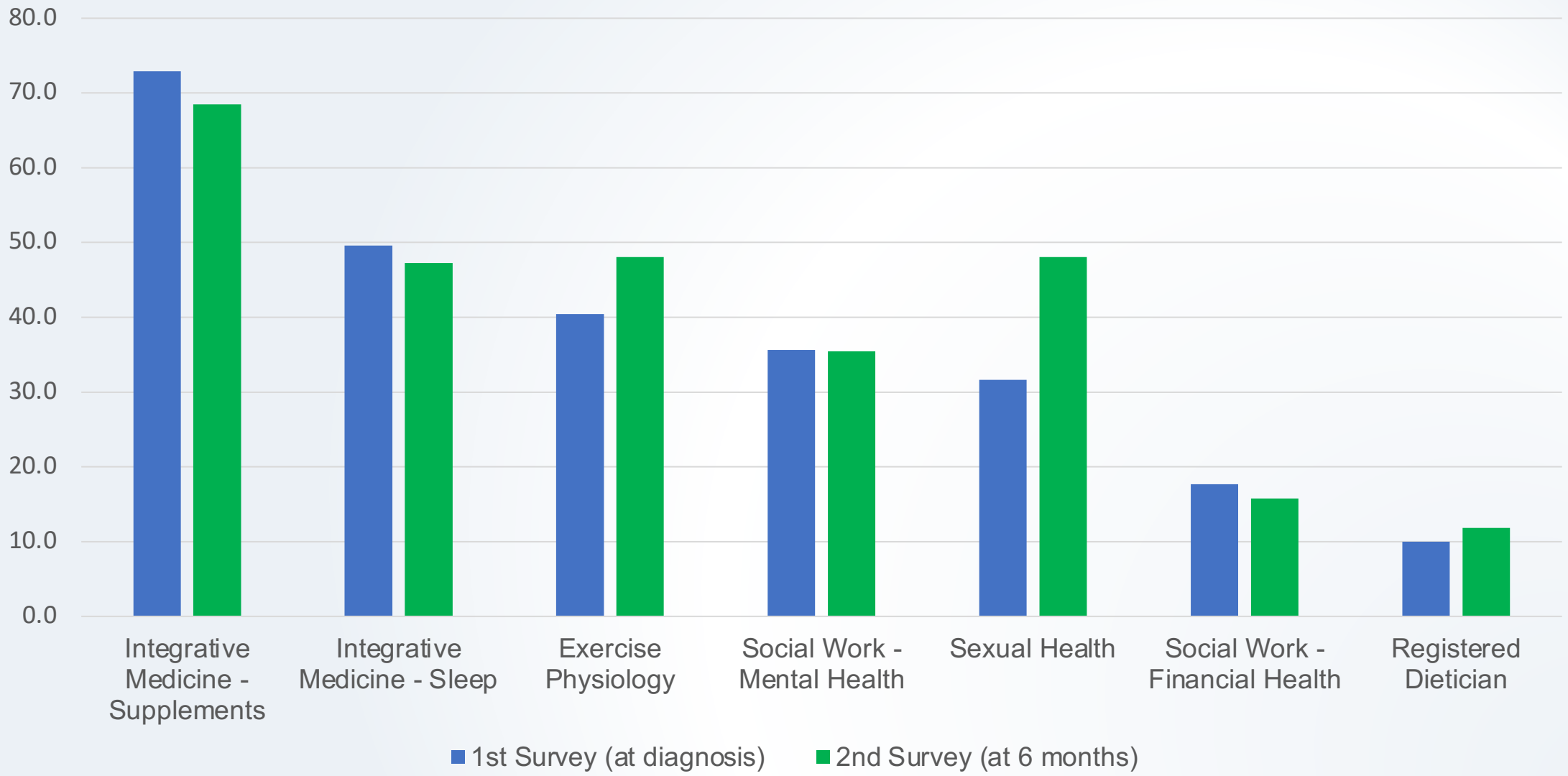






Shen et al, under review

Pilot Study: Lifestyle risk profiles at diagnosis and 6 months post



HEALTHY LIVING

Collaborative approach to program development & implementation

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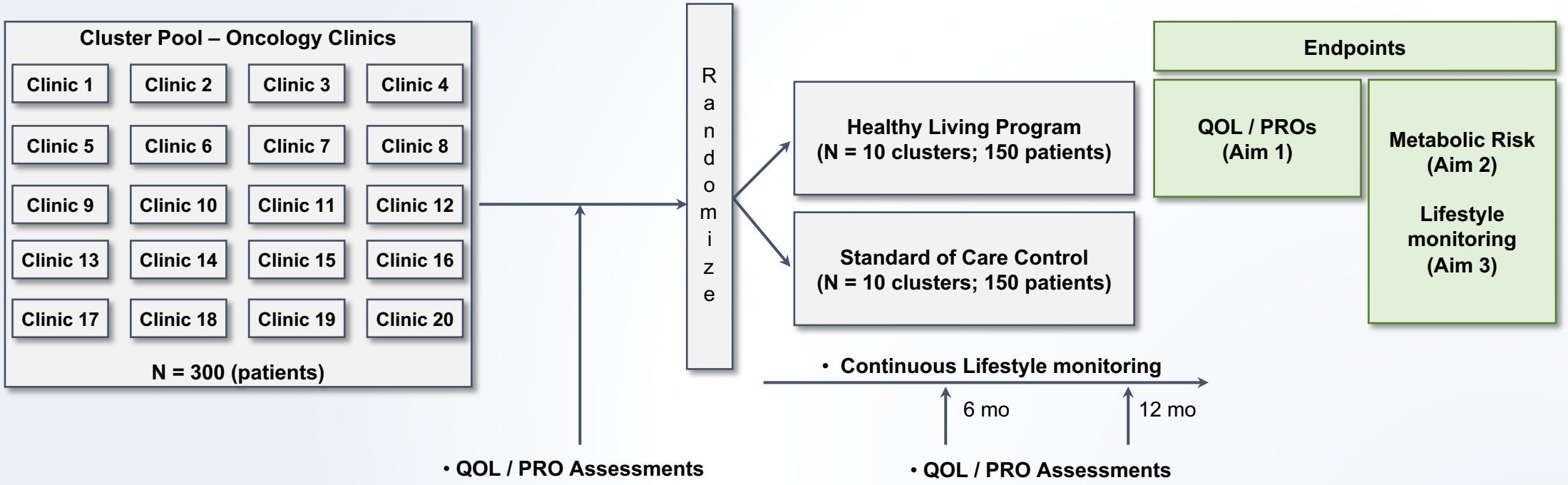
Future Directions: R01 submission



Future Directions: Platform to promote rigor in lifestyle / survivorship research