



Memorial Sloan Kettering
Cancer Center

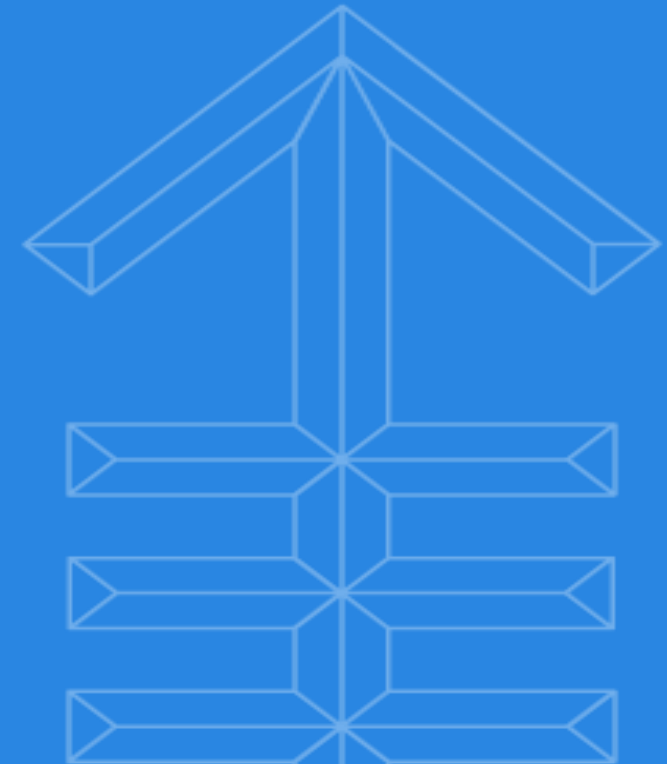
Lifestyle Modification for Improving Breast Cancer Recurrence Risk

Neil M. Iyengar, MD

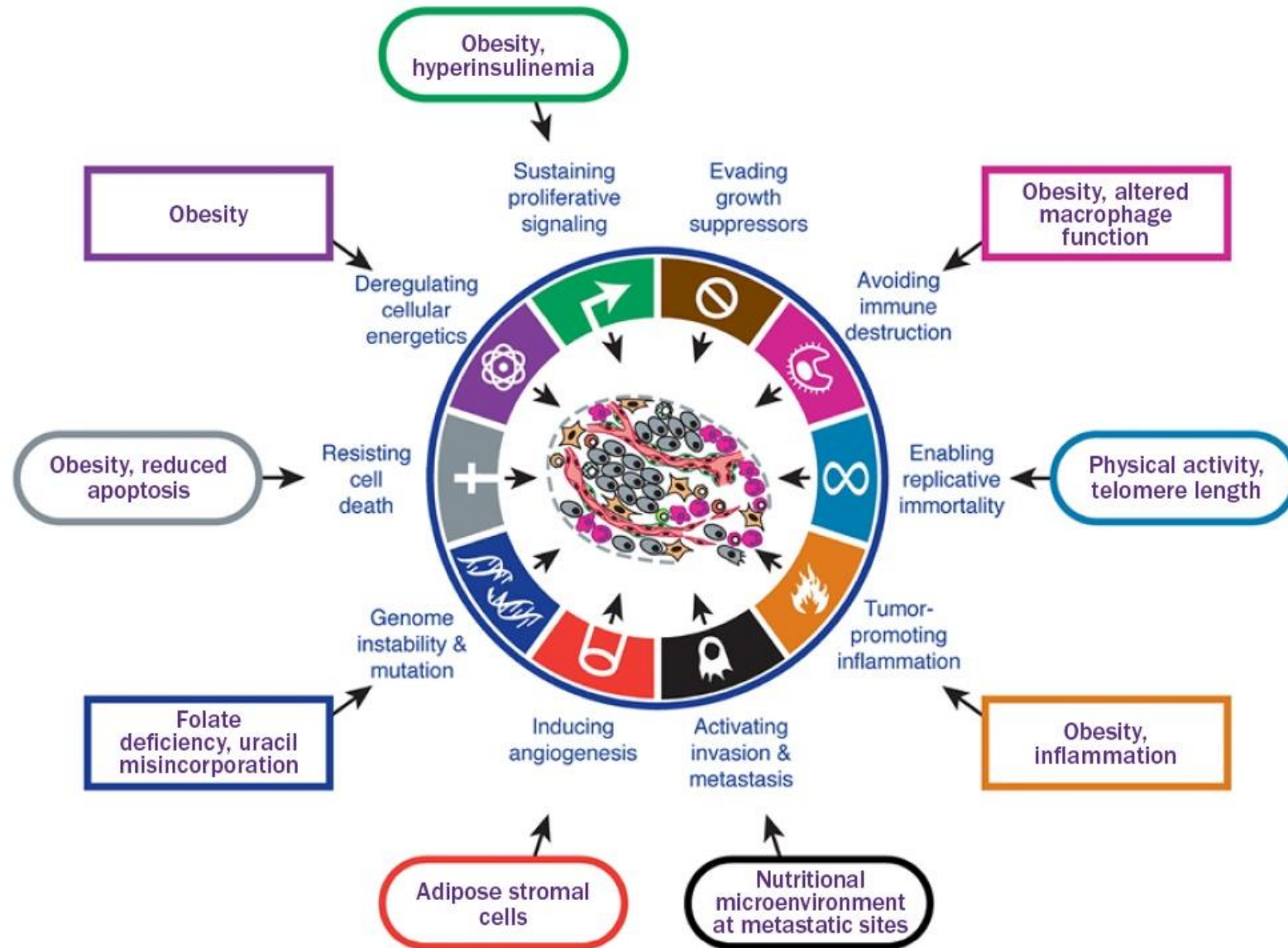
Associate Attending
Program Lead, MSK Healthy Living
Breast Medicine Service
Memorial Sloan Kettering Cancer Center
Associate Professor of Medicine
Weill Cornell Medicine

✉ iyengarn@mskcc.org

✉ @Neil_Iyengar



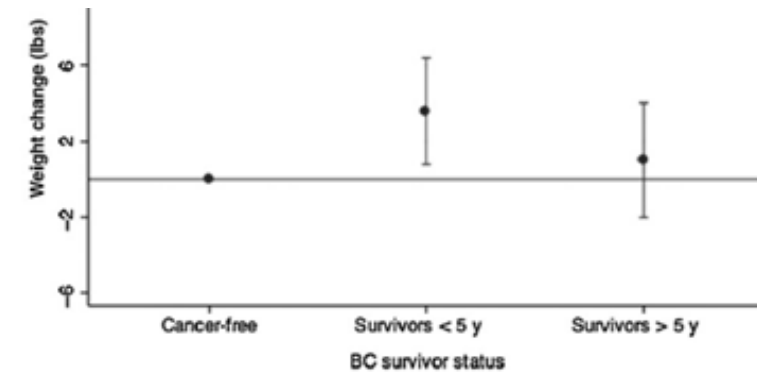
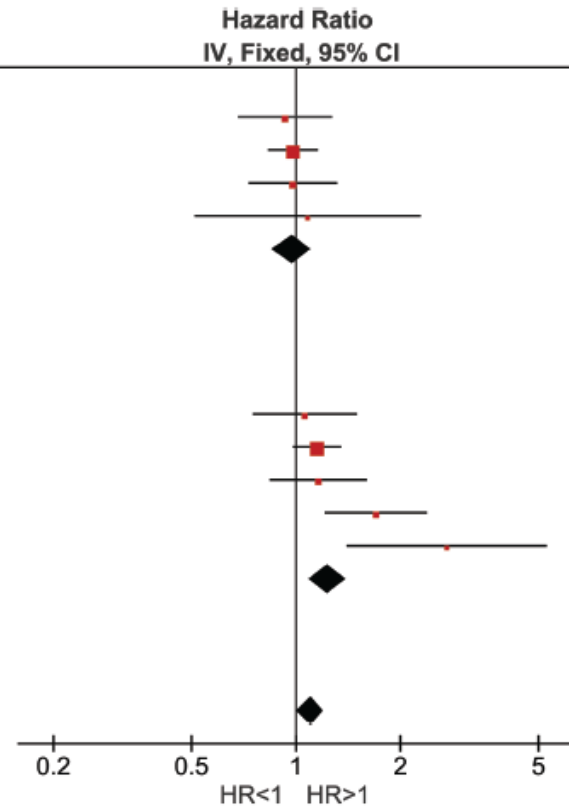
Obesity Promotes Multiple Cancer Hallmarks



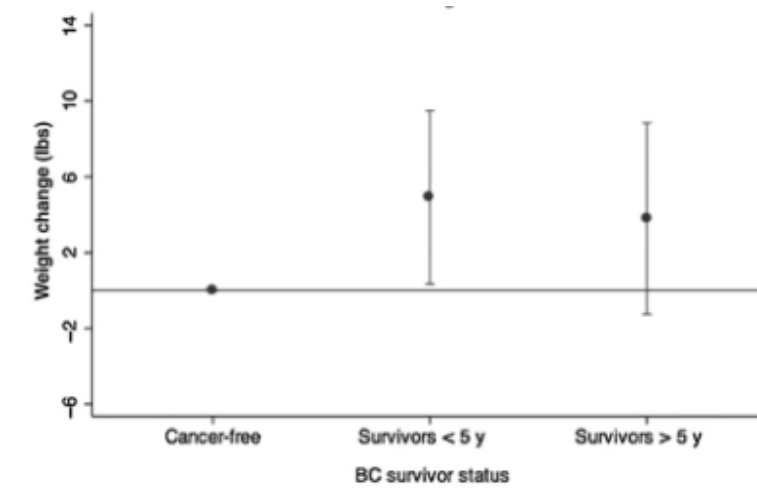
Weight Gain after Breast Cancer Diagnosis

Post-diagnosis weight gain is associated with increased mortality and happens commonly

Study or Subgroup	Hazard Ratio IV, Fixed, 95% CI
2.1.1 Moderate weight gain (5-10%)	
Caan 2012, 5-10.0% WG (SBCSS)	0.93 [0.68, 1.27]
Caan 2012, 5-10.0% WG (LACE, WHEL, NHS)	0.98 [0.83, 1.16]
Nichols 2009, 2.1-6.0kg WG	0.98 [0.73, 1.32]
Bradshaw 2012, 5-10.0% WG	1.08 [0.51, 2.29]
Subtotal (95% CI)	0.97 [0.86, 1.11]
Heterogeneity: $\text{Chi}^2 = 0.16$, $\text{df} = 3$ ($P = 0.98$); $I^2 = 0\%$	
Test for overall effect: $Z = 0.40$ ($P = 0.69$)	
2.1.2 High weight gain (>10%)	
Nichols 2009, 6.0-10.0kg WG	1.06 [0.75, 1.50]
Caan 2012, >10.0% WG (LACE, WHEL, NHS)	1.15 [0.98, 1.35]
Caan 2012, >10.0% WG (SBCSS)	1.16 [0.84, 1.60]
Nichols 2009, >10kg WG	1.70 [1.21, 2.39]
Bradshaw 2012, >10.0% WG	2.72 [1.40, 5.28]
Subtotal (95% CI)	1.23 [1.09, 1.39]
Heterogeneity: $\text{Chi}^2 = 10.48$, $\text{df} = 4$ ($P = 0.03$); $I^2 = 62\%$	
Test for overall effect: $Z = 3.38$ ($P = 0.0007$)	
Total (95% CI)	1.10 [1.01, 1.21]
Heterogeneity: $\text{Chi}^2 = 17.42$, $\text{df} = 8$ ($P = 0.03$); $I^2 = 54\%$	
Test for overall effect: $Z = 2.20$ ($P = 0.03$)	
Test for subgroup differences: $\text{Chi}^2 = 6.78$, $\text{df} = 1$ ($P = 0.009$), $I^2 = 85.3\%$	



Baseline
normal BMI



Baseline
overweight/
obese

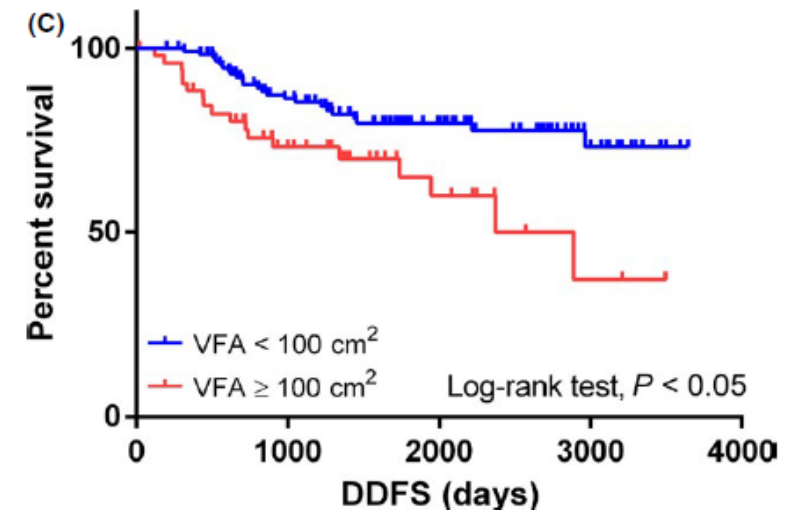
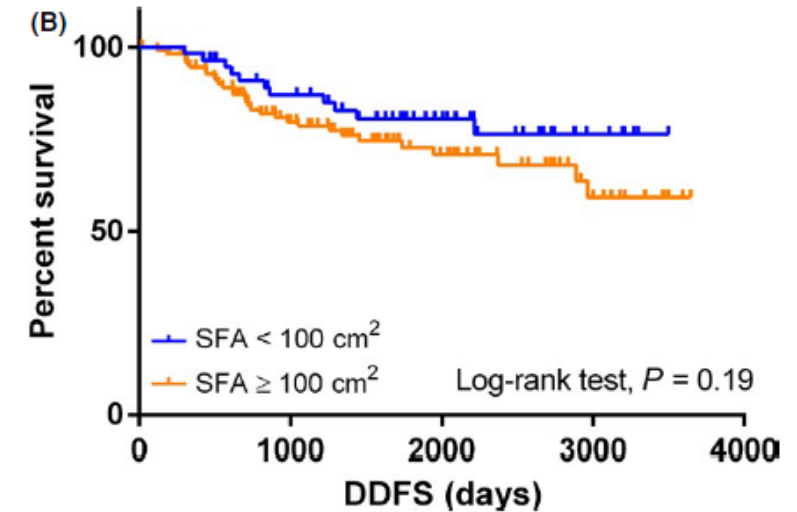
Adiposity & Outcomes in Early Breast Cancer

- Neoadjuvant chemotherapy

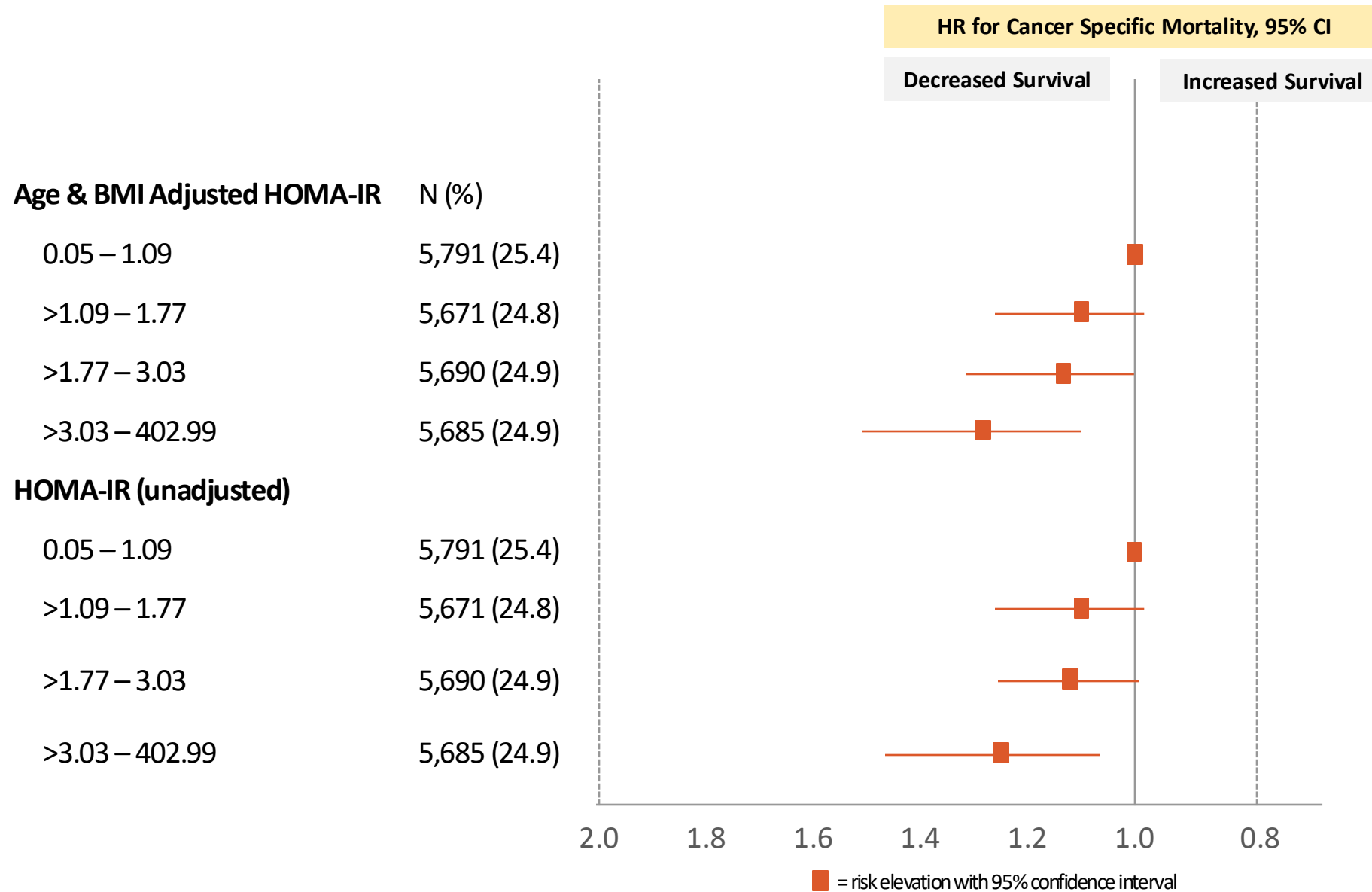
Table 5. Cox proportional hazards regression analysis of distant disease-free survival.

Variables	HR	95% CI	<i>P</i>
pCR			
No	1.00		<0.05
Yes	0.21	0.08–0.56	
Subtype			
ER (+), HER (–)	1.00		<0.05
ER (+), HER (+)	1.88	0.70–5.11	
HER2	5.62	2.49–12.68	
Triple-negative	3.83	1.62–9.03	
VFA			
<100 cm ²	1.00		<0.05
≥100 cm ²	2.42	1.28–4.57	
T			
2	1.00		0.47
3	0.92	0.35–2.42	
4	1.54	0.74–3.21	

HR: hazard ratio; CI, confidence interval; pCR, pathological complete response; ER, estrogen receptor; HER2, human epidermal growth factor 2; VFA, visceral fat area.



Insulin Resistance and Cancer-Specific Mortality

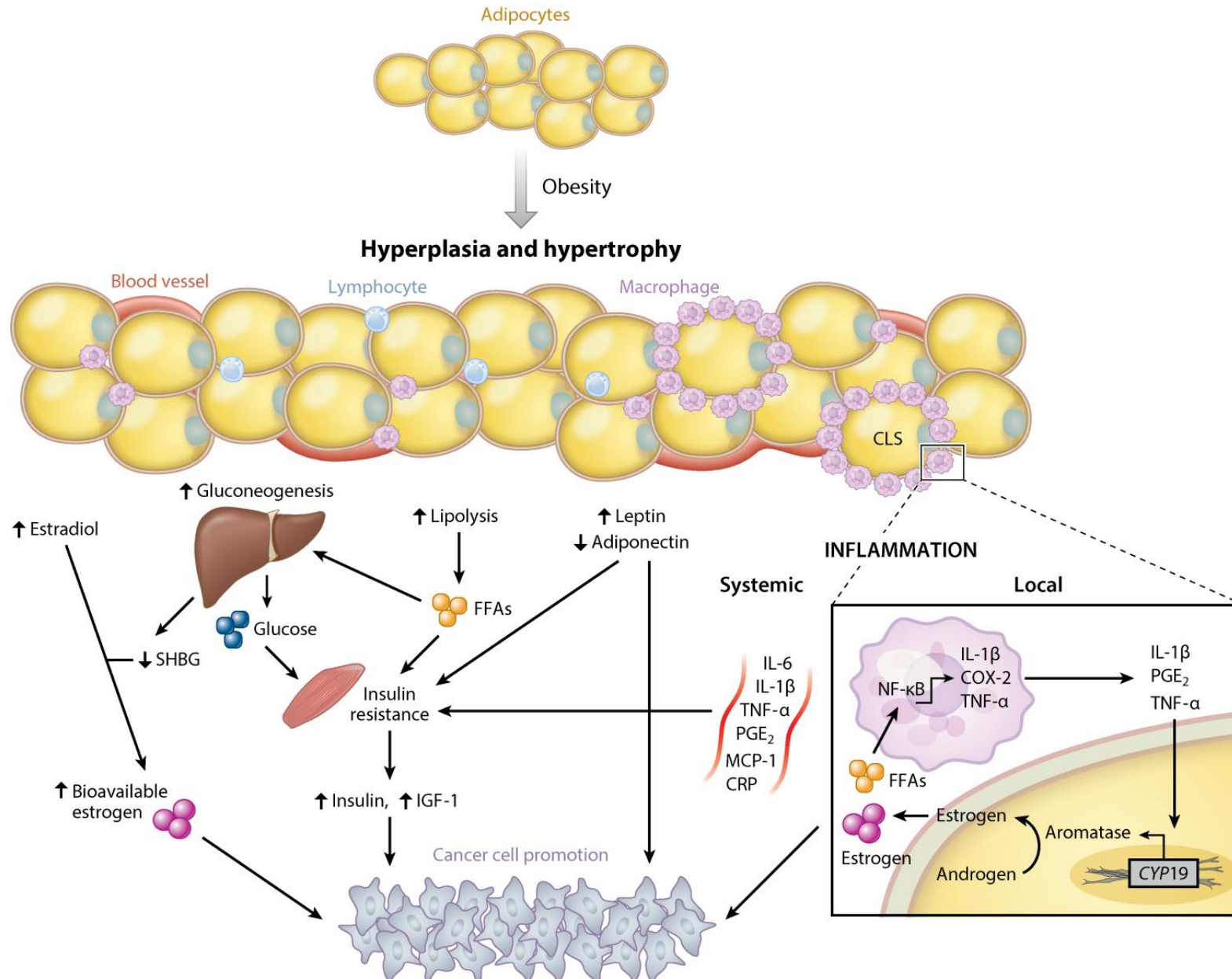


Metabolic Dysfunction is Exacerbated During Breast Cancer Treatment

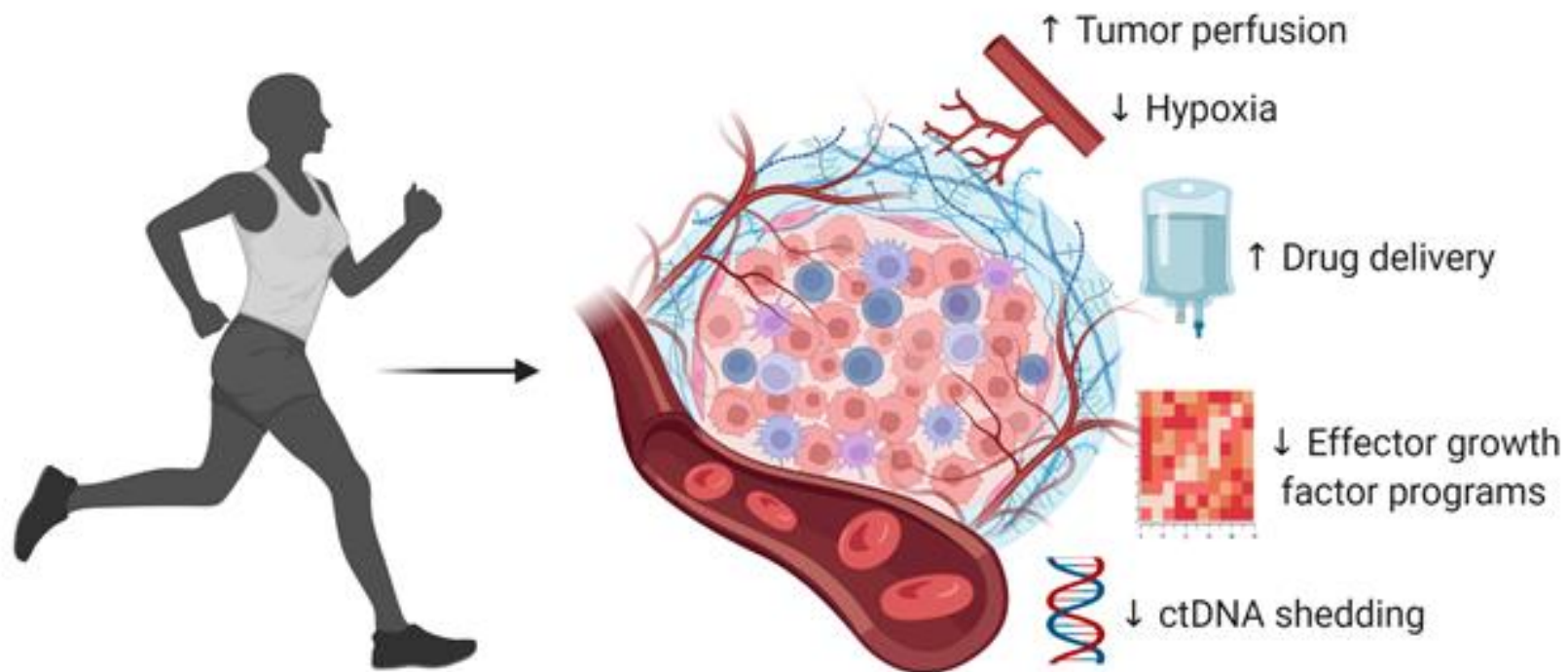
Variable	Pre-Treatment*	Post-Treatment*	% Change	<i>P</i>
Waist circumference (cm)	86.7 (12.9)	90.7 (11.2)	4.7	<0.01
BMI	25.9 (6.3)	29.0 (7.0)	11.5	<0.001
Body fat (%)	33.1 (8.2)	36.0 (5.1)	8.9	<0.001
HOMA-IR	4.52 (1.1)	9.4 (1.5)	108.3	<0.001
HbA1c (%)	5.4 (0.4)	5.9 (0.6)	8.6	<0.001
Fasting glucose (mg/dL)	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 (\pm S.D.)

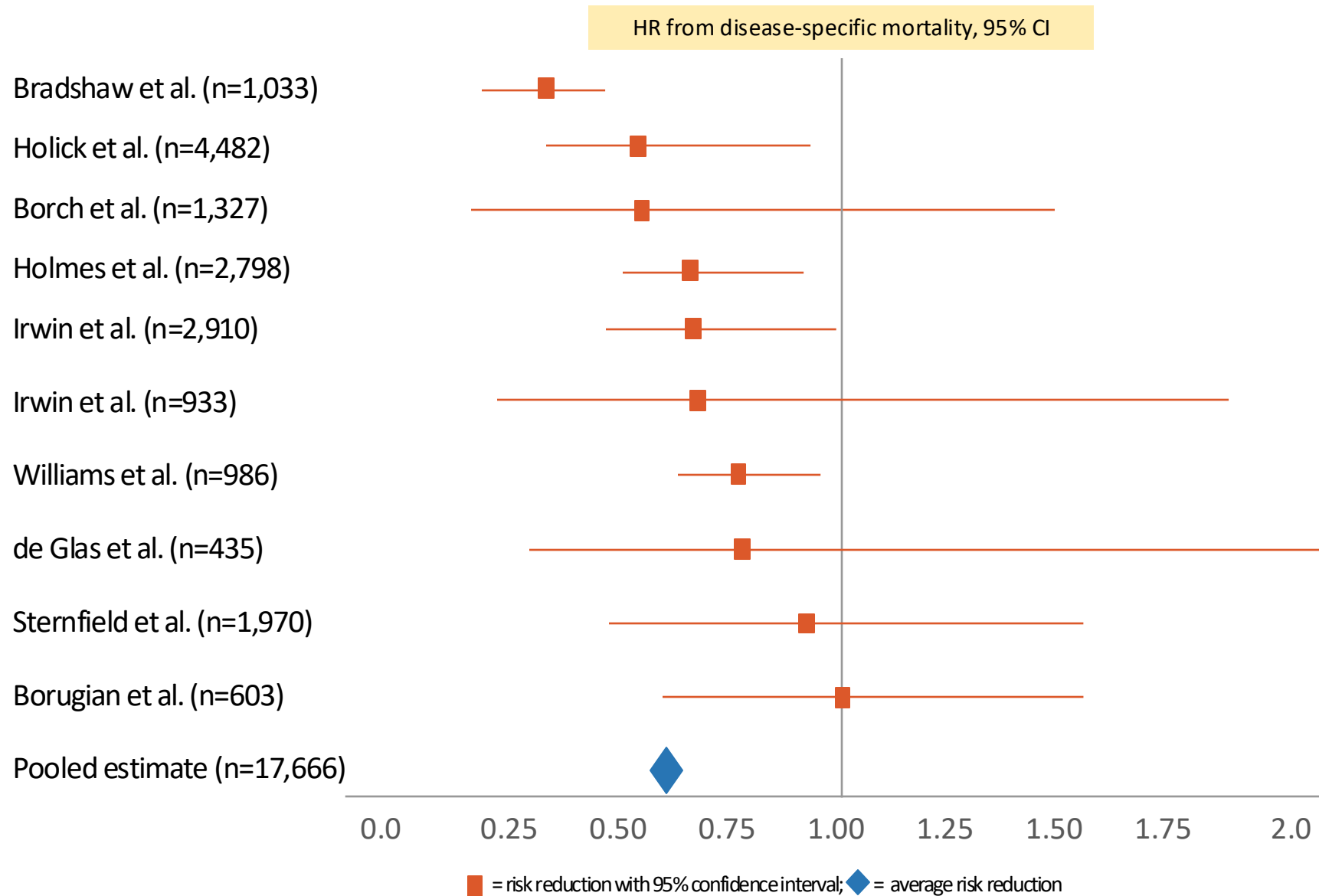
Local and Systemic Impact of Adiposity & Metabolic Dysfunction



Lifestyle Interventions May Reduce Risk of Cancer Recurrence



Exercise & Breast Cancer-Specific Mortality



Selected Diet and Exercise Trials in Early Breast Cancer

Study	Intervention	BMI	Primary Endpoint	Outcomes
COMPLETED				
WINS	Diet	All	RFS	↓ 24% recurrence in low fat vs. control
WHEL	Diet	All	Event-free interval, OS	No effect on recurrence
RENEW	Diet + PA	25-40	PF scale	Durable improvement in PF, weight, and behavioral patterns
DAMES	Diet + PA	25-39.9	BMI	↑ weight loss in individual-tailored arm (-3.77 kg) and team-tailored arm (-2.09 kg) vs control (-0.87 kg)
LISA	Diet + PA	24-50	DFS*	12 months: -5.5 kg in telephone v -0.7 kg in mail arms 24 months: -3.6 kg in telephone v -0.4 kg in mail arms
ENERGY	Diet + supervised exercise	25-45	Weight loss	12 months: -6% in supervised v -1.5% in control arms 24 months: -3.7% in supervised v -1.3% in control arms
LEAN	Diet + PA	≥ 25	Weight loss	6 months: -5.6 kg in-person v -4.8 kg telephone v -1.7 kg control arms 12 months: (6 months post-intervention): -5.6 kg in-person v -6.3 kg telephone v -3.8 kg control

*Not reached. Abbreviations: PA, physical activity; RFS, relapse-free survival; PF, physical functioning; OS, overall survival; DFS, disease free survival

Breast Cancer Weight Loss (BWEL) Trial

 3136 Participants

Key Eligibility*

- Stage II-III Breast Cancer
- HR+/HER-2- or TNBC
- Diagnosed w/in past 14 months
- Completed with surgery and any chemotherapy and/or radiation
- BMI \geq 27 kg/m²

*Patients planning on taking medications for the purpose of weight loss and/or undergoing a surgical weight loss procedure within 2 years were not eligible



Standardized Program:

- Telephone-based weight loss program
- Based on Social Cognitive Theory
- Adapted from Diabetes Prevention Program, Look AHEAD, LISA



Centralized Delivery:

- 42 calls over 2 years
- Each patient paired with a weight loss coach, based at Dana-Farber
- Weekly months 1-3
- Biweekly months 3-12
- Monthly months 13-24



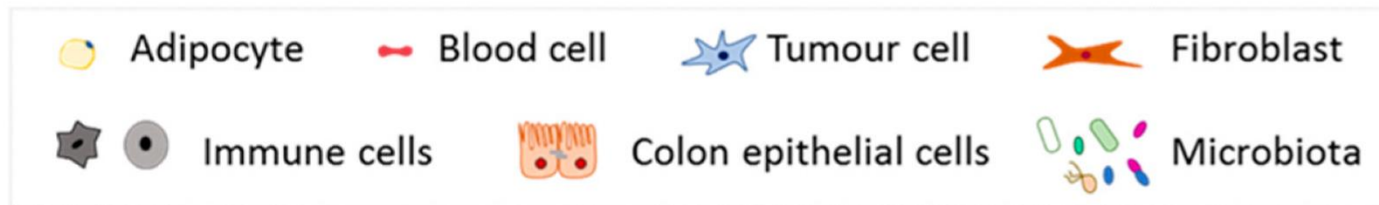
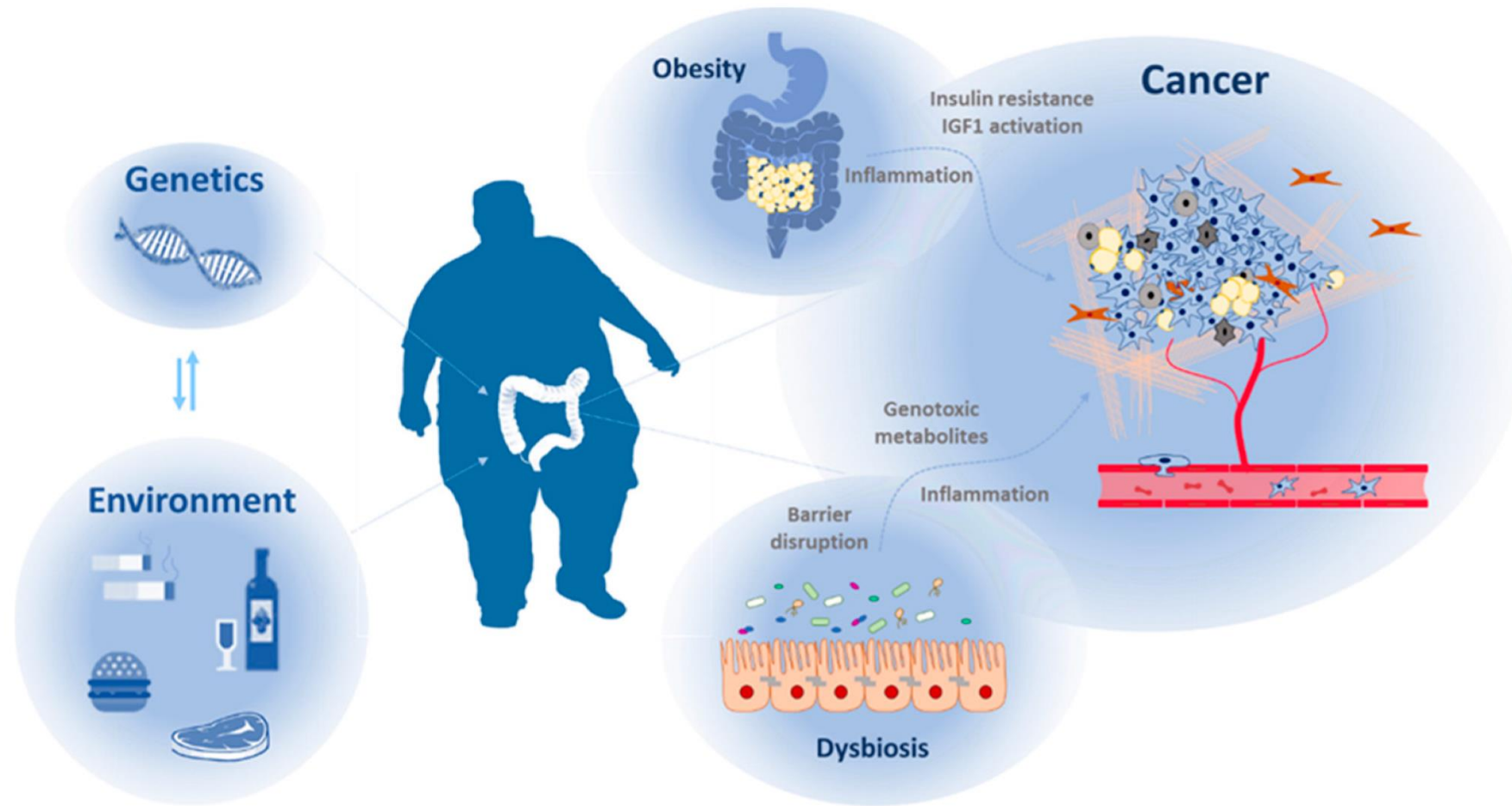
Intervention Goals:

- 10% weight loss
- 500-1000 kcal/day deficit
- Increased physical activity
150-225 minutes moderate-intensity activity/week

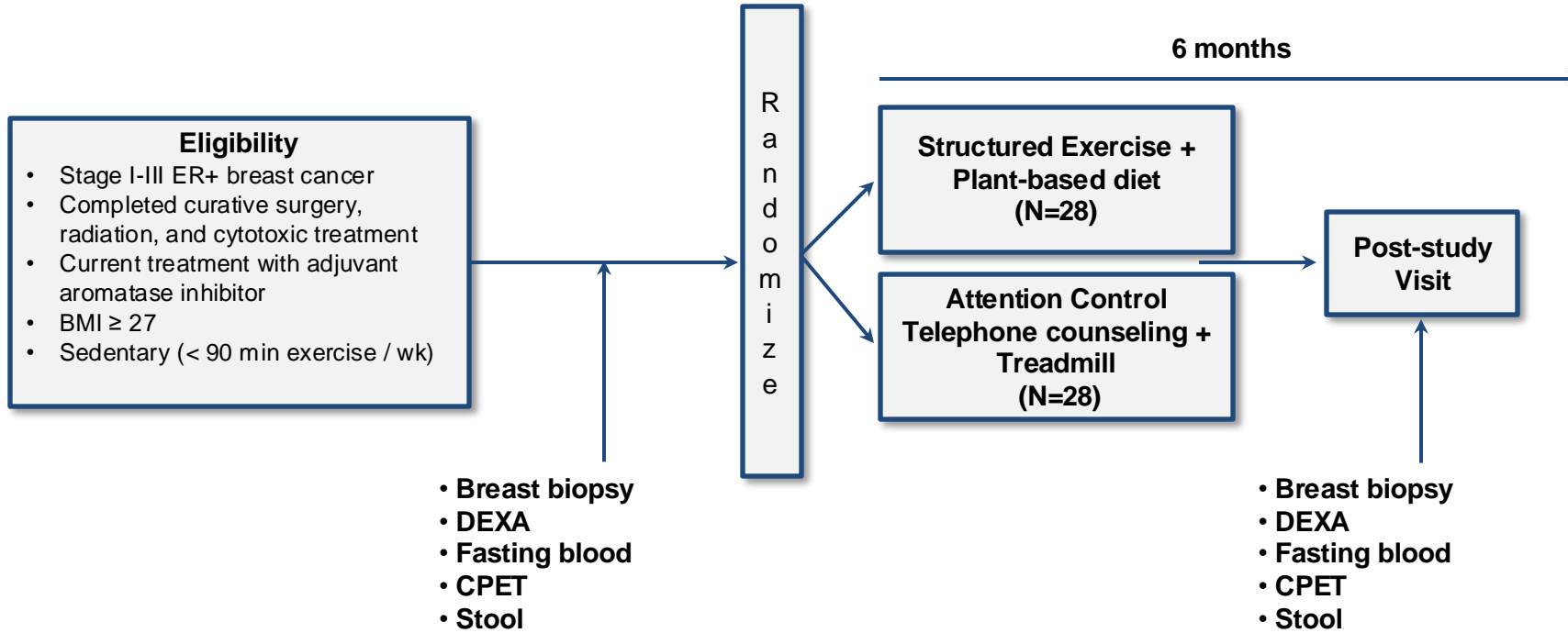


	CONTROL (n=1173)	WLI (n=1222)	P VALUE
Absolute Weight Change at 6-months	+ 0.2 kg	- 4.4 kg	<0.0001
% Weight Change at 6-months	+ 0.3%	- 4.8%	<0.0001
Absolute Weight Change at 12-months	+ 0.7kg	- 4.4kg	<0.0001
% Weight Change at 12-months	+ 0.9%	- 4.8%	<0.0001

Looking to the Future: 'Precision' Lifestyle Interventions



Phase 2 RCT: Precision Nutrition + Structured Exercise



Study Endpoints

Primary: Breast aromatase level

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

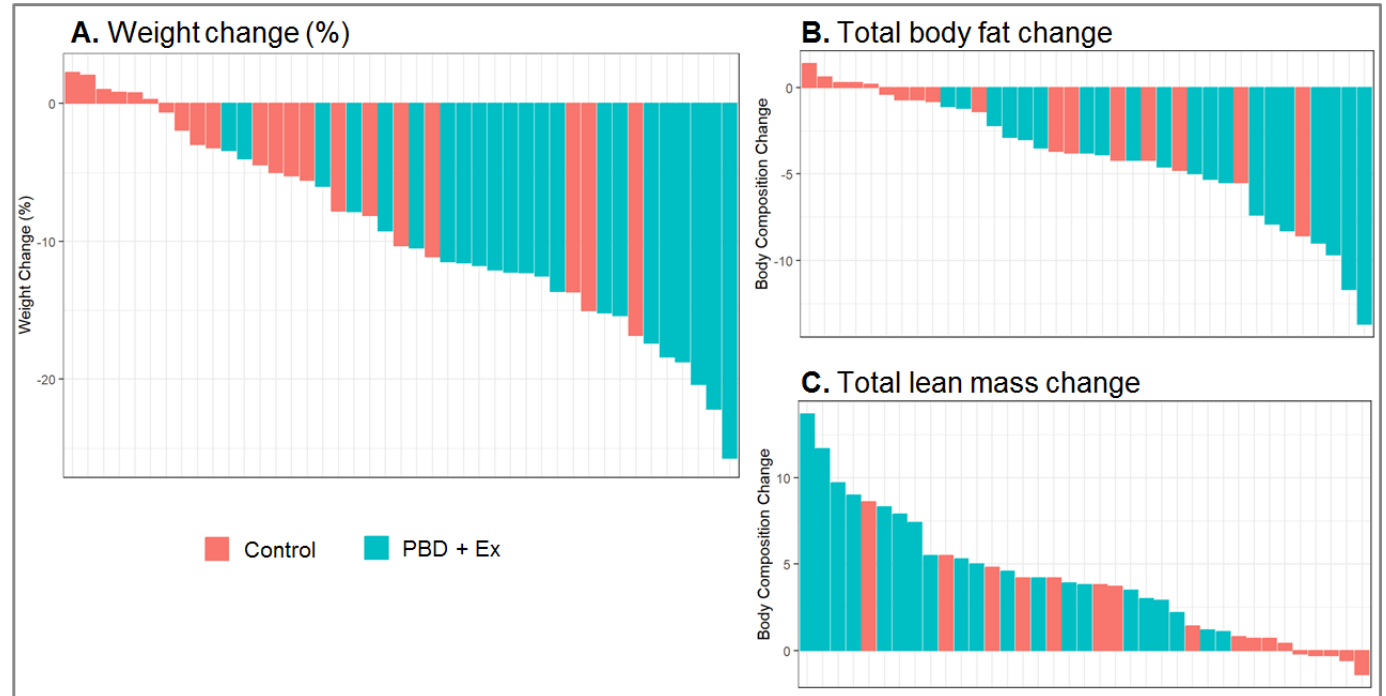
Biostatistical Design

- 1 unit decrease in BMI = 0.06 mean reduction in aromatase (SD 0.81, log scale)
- Goal BMI reduction is 3 kg/m²

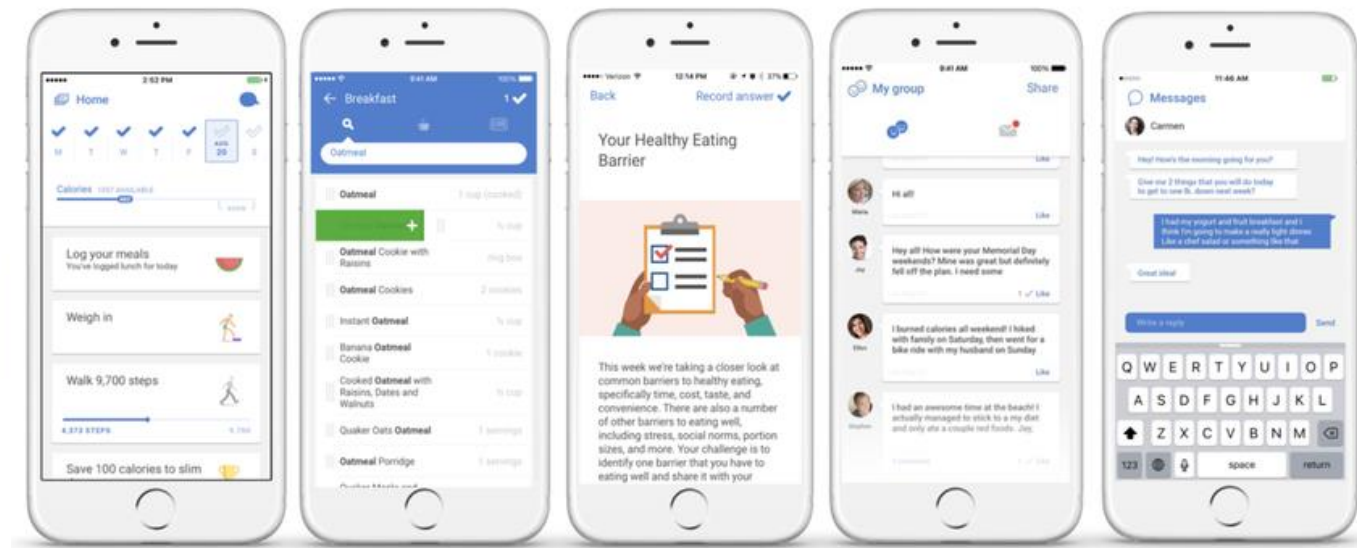
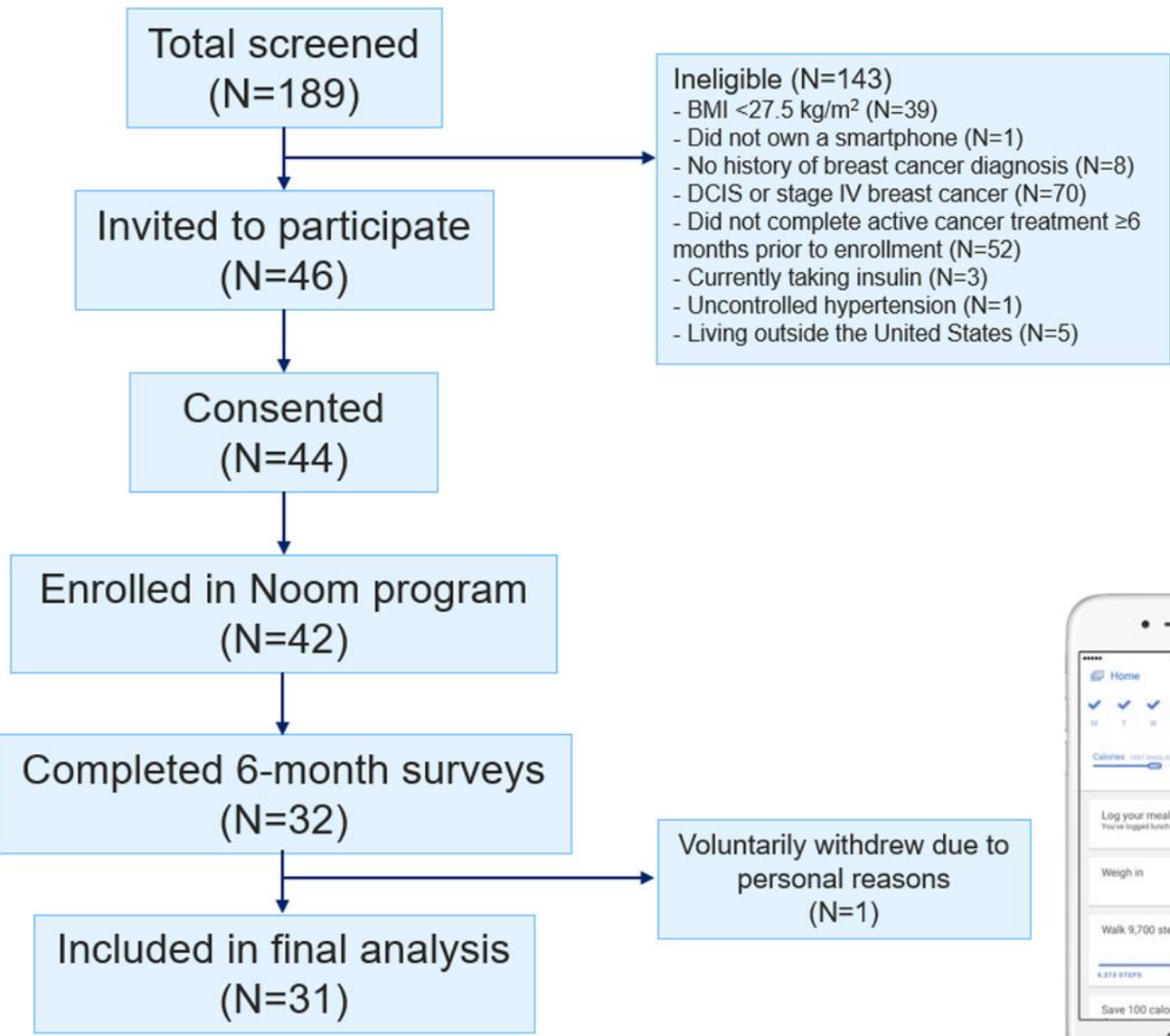
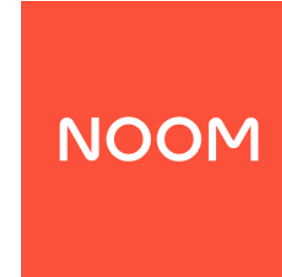
Phase 2 RCT: Precision Nutrition + Structured Exercise

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%)

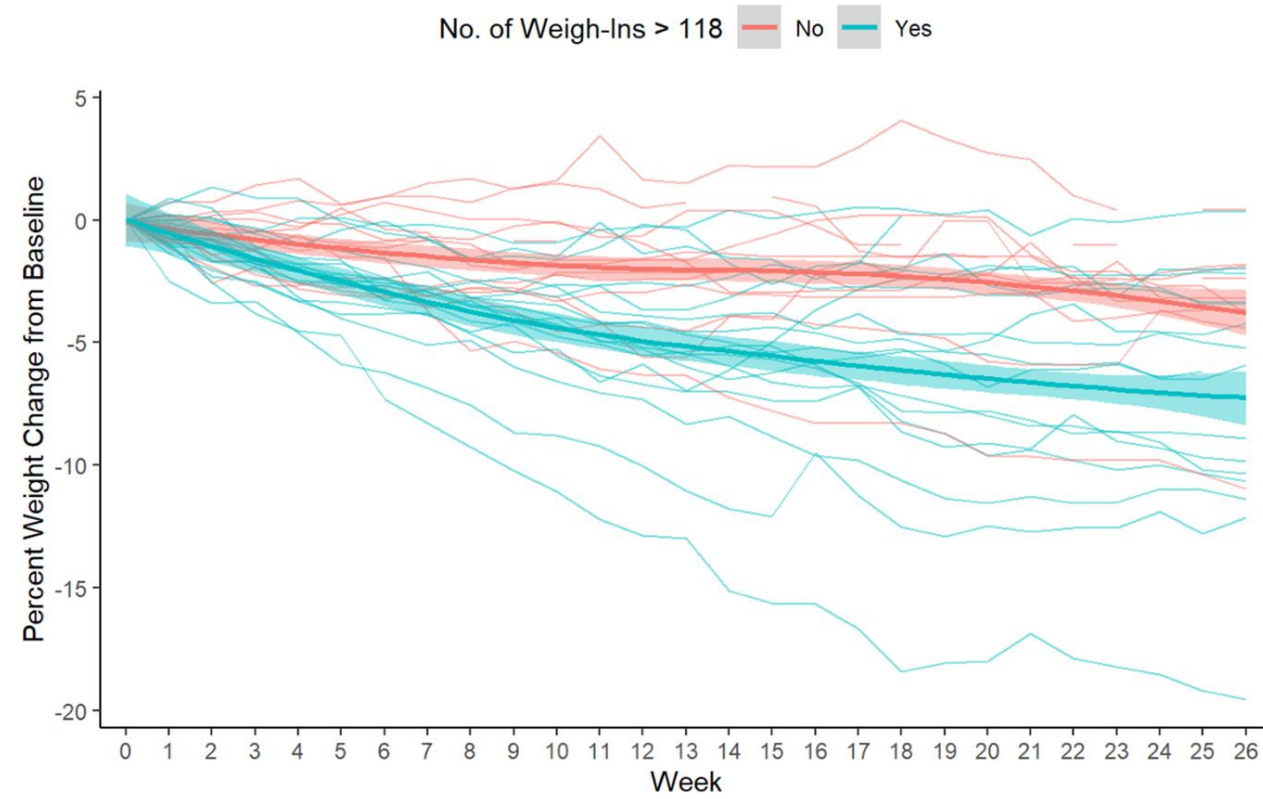
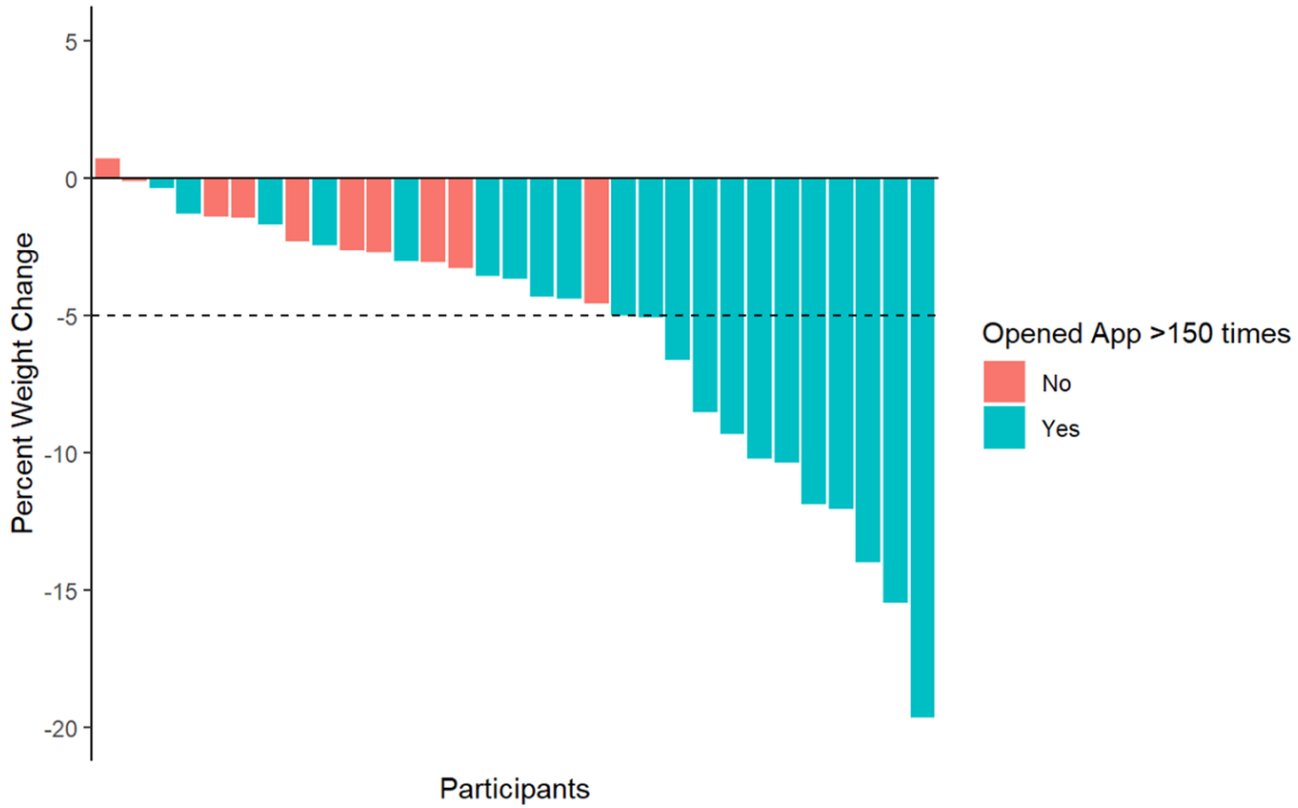
	Control (N=21)	PBD + Ex (N=22)	P
	Change (95% CI)	Change (95% CI)	
Weight (kg)	-4 (-6.6, -2.2)	-12 (-15, -9.4)	<0.001
Total body fat (kg)	-2 (-3.5, -0.71)	-6 (-7.3, -4.1)	<0.001
Trunk fat (kg)	-3 (-4.4, -0.73)	-7 (-8.9, -4.9)	<0.001
Total body lean mass (kg)	2 (0.71, 3.5)	6 (4.1, 7.3)	<0.001
Total body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



Mobile Behavior Change Application in Breast Cancer



Mobile Behavior Change Application in Breast Cancer



Summary of Lifestyle Impact

Exposure	Effect	Strength	Outcome
Physical activity	Decreases risk	Strong	Primary and recurrence risk
Alcohol	Increases risk	Strong	Primary and recurrence risk
Non-starchy vegetables	Decreases risk	Limited	Primary and recurrence risk
Foods containing carotenoids	Decreases risk	Limited	Primary and recurrence risk
Dairy products	Decreases risk	Limited	Primary risk
High calcium diet	Decreases risk	Limited	Primary risk

Summary of Dietary Evidence

Exposure	Direction of effect	Outcomes
Wholegrains	Decreases risk	<ul style="list-style-type: none">• Colorectal cancer
Foods containing dietary fibre	Decreases risk	<ul style="list-style-type: none">• Colorectal cancer• Weight gain, overweight and obesity
'Fast foods' 'Western type' diet	Increases risk	<ul style="list-style-type: none">• Weight gain, overweight and obesity
Glycaemic load	Increases risk	<ul style="list-style-type: none">• Endometrial cancer
Red meat	Increases risk	<ul style="list-style-type: none">• Colorectal cancer
Processed meat	Increases risk	<ul style="list-style-type: none">• Colorectal cancer

Summary of Dietary Evidence

Exposure	Direction of effect	Outcomes
Sugar sweetened drinks	Increases risk	<ul style="list-style-type: none">• Weight gain, overweight and obesity
Alcoholic drinks	Increases risk	<ul style="list-style-type: none">• Mouth, pharynx and larynx• Oesophagus (adenocarcinoma)• Liver• Colorectum• Breast• Stomach

Summary of Dietary Evidence



RECOMMENDATION

Eat a diet rich in wholegrains, vegetables, fruit and beans

Make wholegrains, vegetables, fruit, and pulses (legumes) such as beans and lentils a major part of your usual daily diet

- GOAL** Consume a diet that provides at least 30 grams per day of fibre¹ from food sources
- GOAL** Include in most meals foods containing wholegrains, non-starchy vegetables, fruit and pulses (legumes) such as beans and lentils
- GOAL** Eat a diet high in all types of plant foods including at least five portions or servings (at least 400 grams or 15 ounces in total) of a variety of non-starchy vegetables and fruit every day
- GOAL** If you eat starchy roots and tubers as staple foods, eat non-starchy vegetables, fruit and pulses (legumes) regularly too if possible

¹ Measured by the AOAC method.

Summary of Dietary Evidence



RECOMMENDATION

Limit consumption of red and processed meat

Eat no more than moderate amounts of red meat¹, such as beef, pork and lamb. Eat little, if any, processed meat²

GOAL If you eat red meat, limit consumption to no more than about three portions per week. Three portions is equivalent to about 350 to 500 grams (about 12 to 18 ounces) cooked weight of red meat.³ Consume very little, if any, processed meat

¹ The term 'red meat' refers to all types of mammalian muscle meat, such as beef, veal, pork, lamb, mutton, horse and goat.

² The term 'processed meat' refers to meat that has been transformed through salting, curing, fermentation, smoking or other processes to enhance flavour or improve preservation.

³ 500 grams of cooked red meat is roughly equivalent to 700–750 grams of raw meat, but the exact conversion depends on the cut of meat, the proportions of lean meat and fat, and the method and degree of cooking.

2018 WCRF/AICR Guidelines to Reduce Cancer Risk



Additional Resources

- Lifestyle Intervention Clinical Trials
- The Healthy Living Program at MSK
 - <https://www.mskcc.org/cancer-care/types/breast/msk-healthy-living>
- MSK Blog Updates
 - <https://www.mskcc.org/news/breast-cancer-and-weight-gain-how-to-control-it-during-and-after-treatment>
- American Institute for Cancer Research Continuing Update Project
 - <https://www.aicr.org/>
- Digital Therapeutics
 - Smartphone Apps
- Comprehensive Weight Control Centers: role for weight loss drugs?
 - <https://www.mskcc.org/news/cancer-benefits-and-risks-from-ozempic-wegovy-and-other-weight-loss-drugs>

 iyengarn@mskcc.org

 @Neil_Iyengar