ASCO Direct
Symptoms and Survivorship

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Disclosure of Conflict(s) of Interest

- Jennie R. Crews, MD MMM FACP reported **<u>no</u>** relevant financial relationships or relationships with ineligible companies of any amount during the past 24 months.
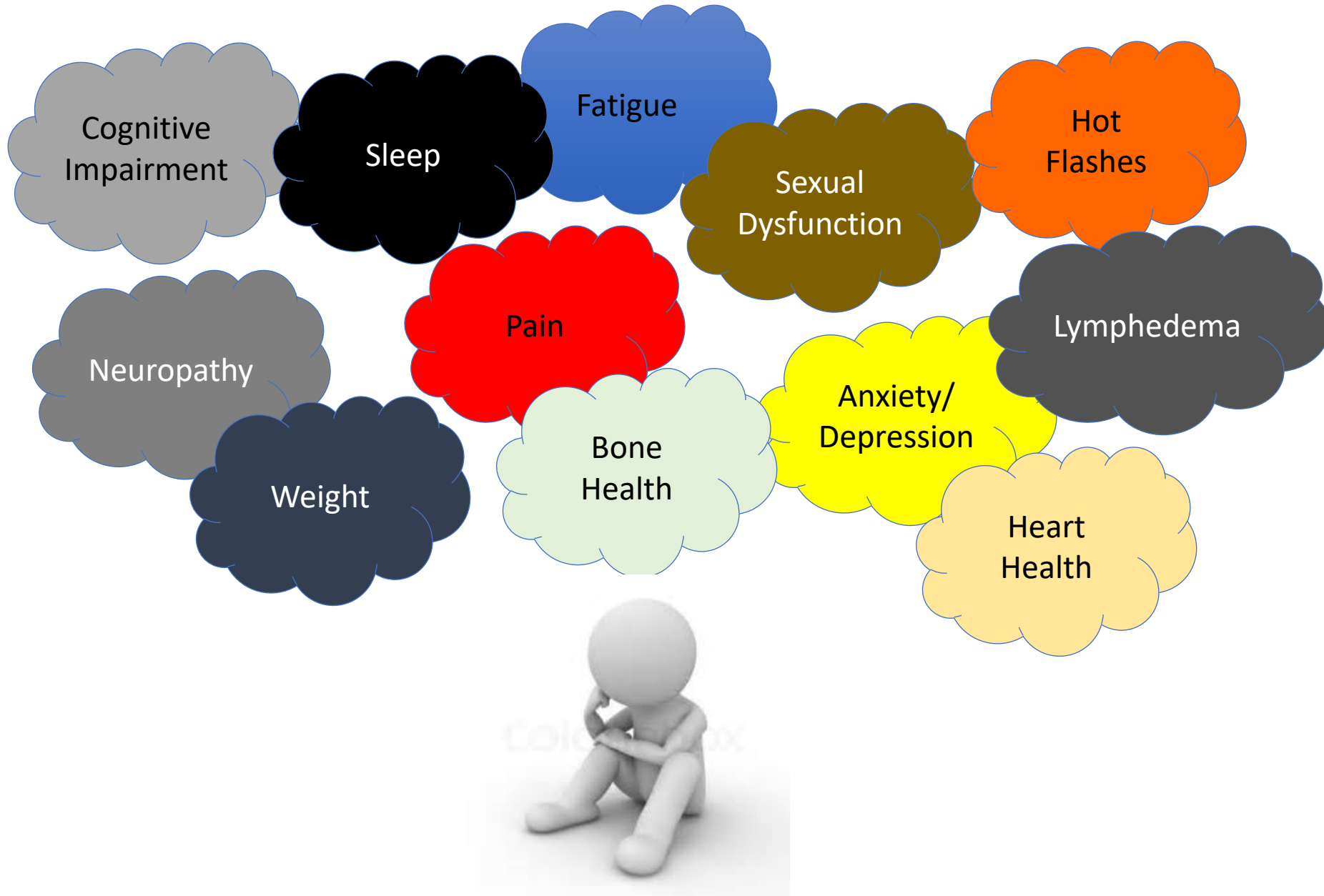
Symptoms and Survivorship: Themes from ASCO 2021

Objectives:

1. **Discuss Late and Long-Term Effects**

- Predicting Risk: Abstracts 12003, 12022, 12068,12069,
- Mitigating Effects: Abstracts 12015, 12016, 12017, 12018

2. **Review Virtual/Remote Symptom Management**
 Abstracts: 12000, 12002

**Holy Grail**: Move from Treatment to Prevention

Predicting Risk of Late and Long-Term Effects

- Not all cancer survivors experience similar side effects from similar therapies.

- There is a need to identify patients at risk of late and long-term effects to:
  - Better tailor therapy to prevent side effects
  - Customize interventions to minimize long term effects of treatment

Clinical Predictors

Genomic Predictors
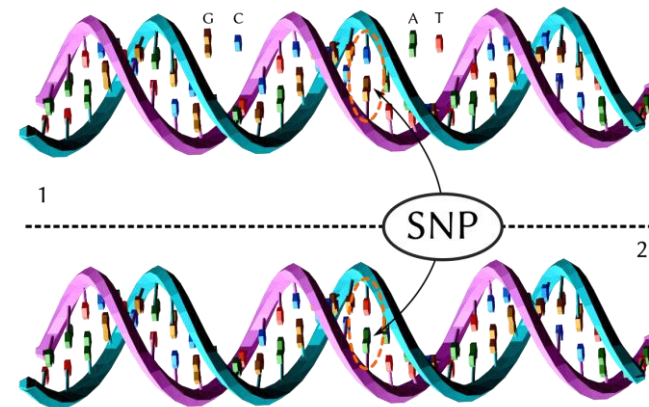
Assessing the Risk of Severe Post Treatment Cancer Related Fatigue (CRF) among Breast Cancer Survivors
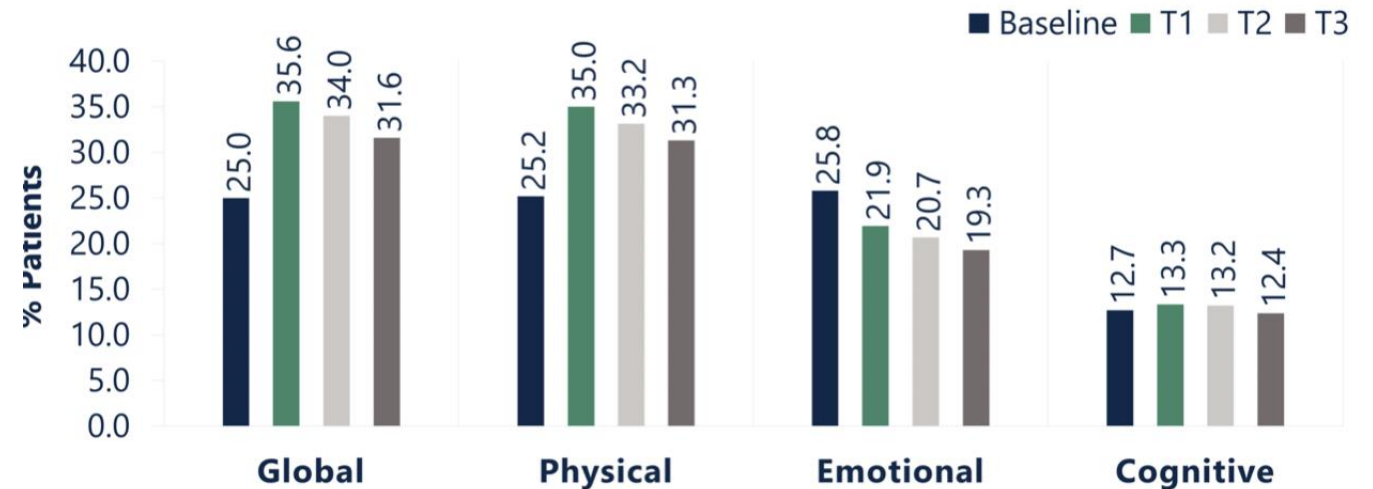## Abst #12022 (De Meglio)

CANcer Toxicity (CANTO) Cohort
- Breast cancer survivors
- Stage I-III

Collected data at 1 (T1), 2 (T2) and 4 (T3) years

CRF
- Severe = EORTC QLQ-C-30 score >40/100
- Physical, emotional, cognitive QLQ-FA12
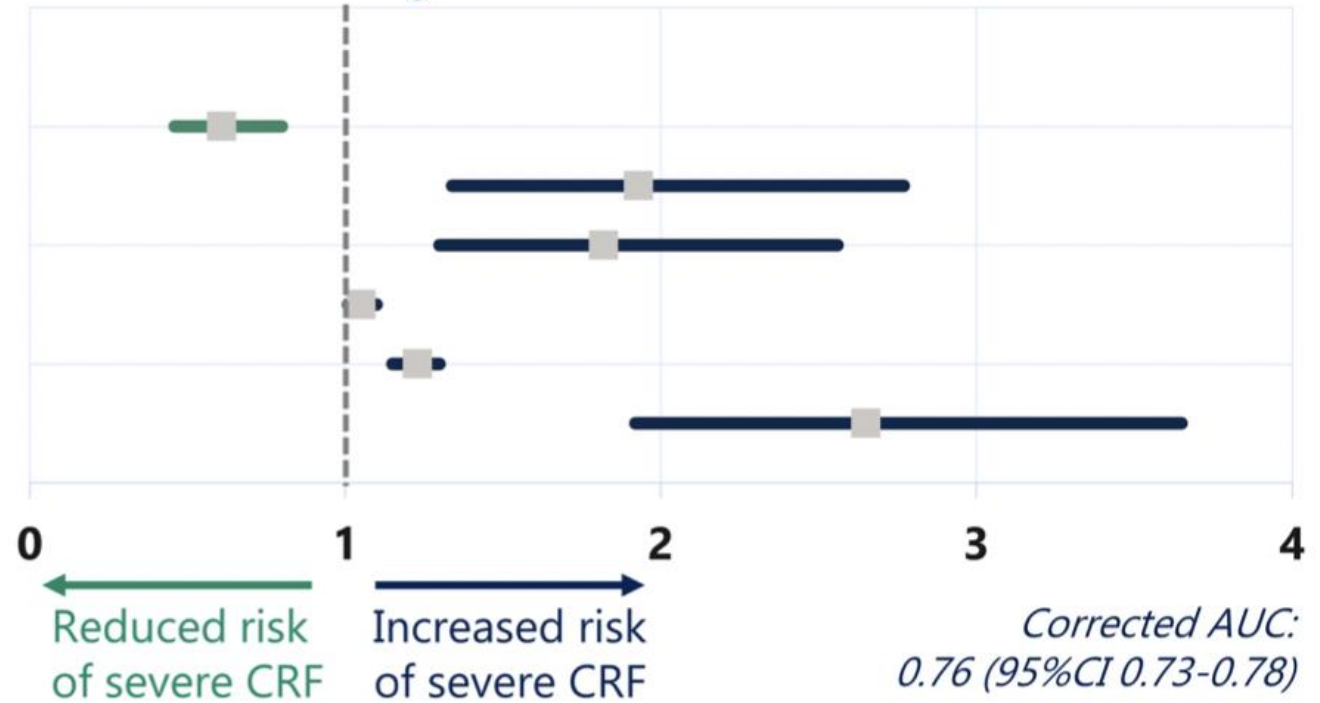
Developed Predictive model for CRF

Model of severe global CRF at T3 in the validation cohort

Menopausal status, Post- vs. Pre-
Hormonal therapy, Yes vs. No
Anxiety, Case vs. Non-case
Insomnia, additional 10 points
Pain, additional 10 points
Severe pre-tx CRF, vs. No

Odds Ratio

Reduced risk of severe CRF
Increased risk of severe CRF

Corrected AUC: 0.76 (95%CI 0.73-0.78)

Next Steps: Proactively use this predictive tool to assessment risk and assign intervention.

- Low Risk- Education, counseling and surveillance for onset of symptoms of severe CRF
- High Risk- Upfront referral for prevention and management of severe CRF

Nociplastic Pain

Altered nociception without tissue damage

Nociceptive- damage to somatic or visceral tissue

Neuropathic- damage to central or peripheral nerves

Methods:

Retrospective study → 436 patients with **newly diagnosed** breast cancer

↓

364 **female** patients with **ER and/or PR positive** disease, **without neoadjuvant** therapy, **without de novo stage 4** disease

↓

207 initiated **aromatase inhibitor therapy** (anastrozole, exemestane, letrozole)

Completed questionnaires pre-op about **overall worst pain, surgical site pain,** nociplastic pain (**fibromyalgia score**), and **anxiety**

Demographics, comorbidities, and **AI discontinuation data** were collected via chart review
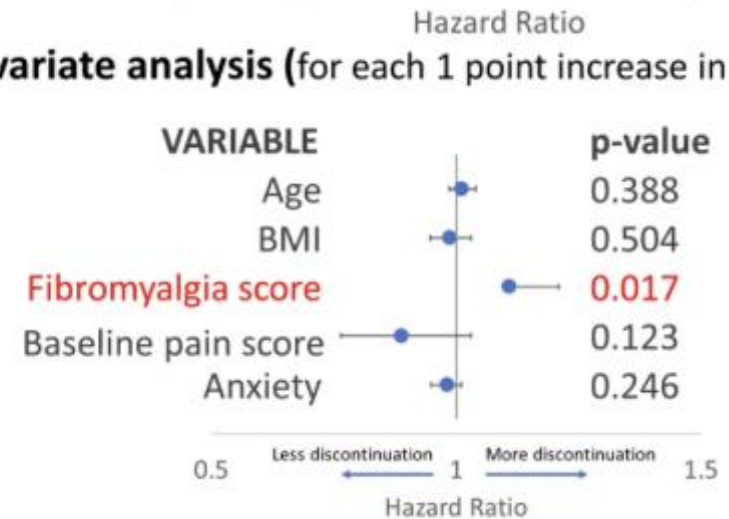
Associations Between Nociplastic Pain and Early Discontinuation of AI
Abst #12068 (Joyce)

Results/Graphs/Data:

Patient characteristics	Average
Age	61
BMI	30.3
Worst Pain	1.5/10
Surgical site pain	0.2/10
Fibromyalgia score	4.2/31
Anxiety	5.8/100

Patient Characteristics	Number (out of 207)
Menopause	
Premenopausal	181 (87%)
Postmenopausal	26 (13%)
Chemotherapy	65 (31.4%)
Initially-prescribed AI	
Anastrozole	196 (94.6%)
Letrozole	5 (2.4%)
Exemestane	6 (2.9%)

Multivariate analysis (for each 1 point increase in each variable):

VARIABLE	p-value
Age	0.388
BMI	0.504
Fibromyalgia score	0.017
Baseline pain score	0.123
Anxiety	0.246

Hazard Ratio — Less discontinuation ← 1 → More discontinuation (0.5 to 1.5)

Future Directions:
- Collect post-treatment patient-reported symptoms
- Prospectively study toxicity development and potential interventions

Prevalence and Predictors of Peripheral Neuropathy after Chemotherapy
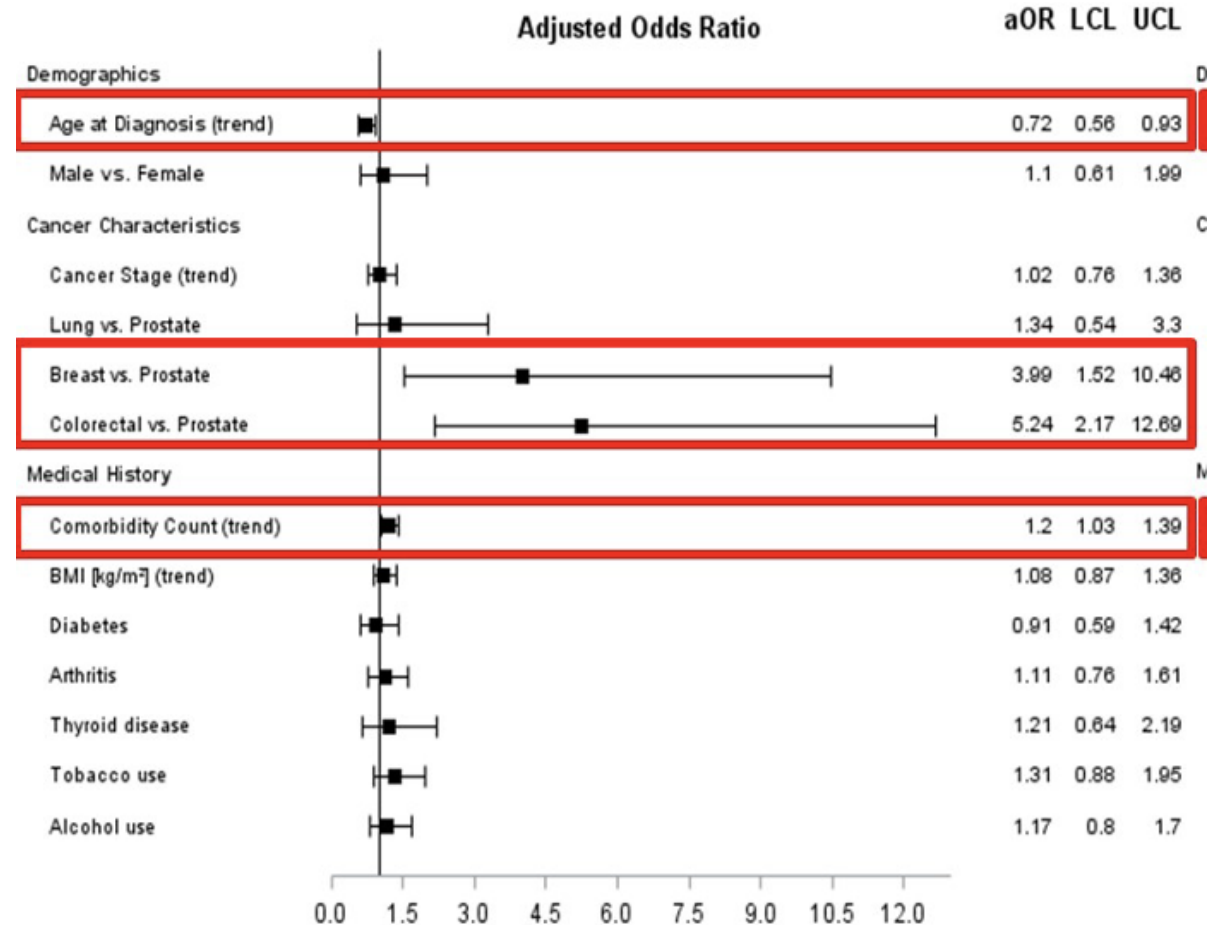Abst #12069 (Sreeram)

Detroit Research on Cancer Survivorship Cohort (ROC)
- AA Survivors
- Breast, Lung, Prostate, Colon Cancer
- Any Stage

Main Results:
- **CIPN**: 422/633 (67%) in a median of survey response time 21 months after diagnosis
- **CIPN Severity**:
  - Mild (32.2%)
  - Moderate (30.8%) and
  - Moderate to Severe (36.9%)
- **Persistent CIPN**: 324/633 (51% of cohort)
- **Persistence Probability**: 324/422 (77% of afflicted)

	Adjusted Odds Ratio	aOR	LCL	UCL
Demographics				
Age at Diagnosis (trend)		0.72	0.56	0.93
Male vs. Female		1.1	0.61	1.99
Cancer Characteristics				
Cancer Stage (trend)		1.02	0.76	1.36
Lung vs. Prostate		1.34	0.54	3.3
Breast vs. Prostate		3.99	1.52	10.46
Colorectal vs. Prostate		5.24	2.17	12.69
Medical History				
Comorbidity Count (trend)		1.2	1.03	1.39
BMI [kg/m²] (trend)		1.08	0.87	1.36
Diabetes		0.91	0.59	1.42
Arthritis		1.11	0.76	1.61
Thyroid disease		1.21	0.64	2.19
Tobacco use		1.31	0.88	1.95
Alcohol use		1.17	0.8	1.7

**Graph 1: Multivariable Analysis of Predictors of CIPN**

A Prospective Validation Study of Genetic Predictors of Aromatase Inhibitor Musculoskeletal Symptoms (AIMSS): Results from E1Z11
Abst #12003 (Stearns)

- AIMSS common side effect with AI and reason for discontinuation

- Primary Objective: to validate previously identified associations between 10 specific SNPs and discontinuation of treatment with AI due to AIMSS among women with breast cancer

10 SNPs identified in MA27 and exemestane & letrozole pharmacogenetic (ELPh) studies
- *ESR1* (rs2234693, rs2347868, rs9340835)
- *CYP19A1* (rs1062033, rs4646)
- *TCL1A* (rs11849538, rs2369049, rs7158782, rs7159713)
- *HTR2A* (rs2296972)

Stearns et al: Study Schema
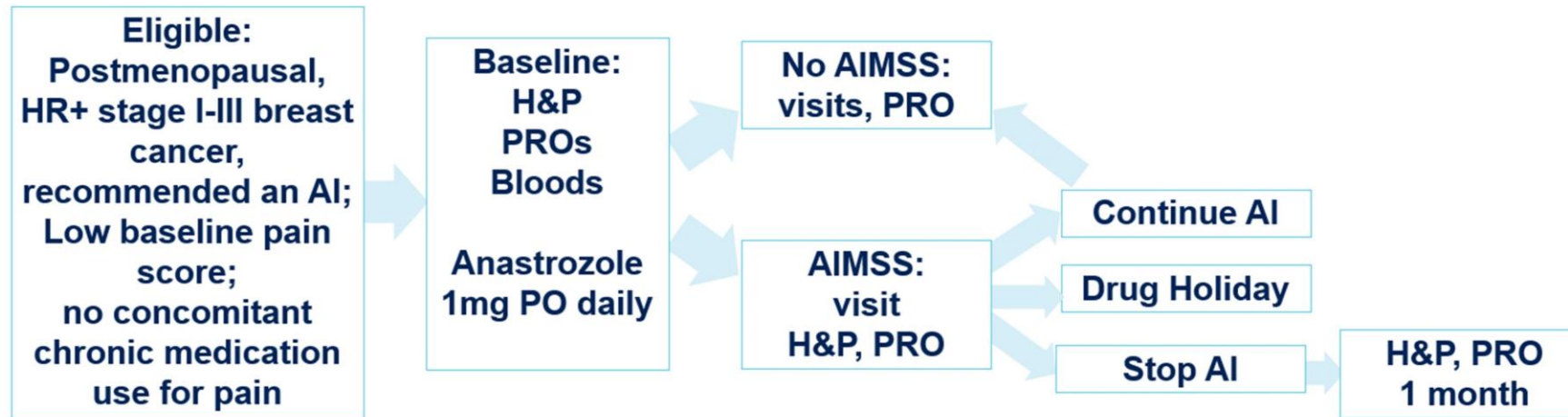
- Notable for diverse study population
- SNP analysis
  - High genotyping success in all racial and ethnic cohorts (>95%)

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Patient Accrual and Follow up

Characteristic	Cohort			Total
	African-American	Asian	Caucasian	
Enrolled	201	205	640	1046
Institution Type, N (%)				
NCORP	68 (34)	49 (24)	348 (54)	465 (44)
Minority/Underserved NCORP	28 (14)	90 (44)	7 (1)	125 (12)
Academic site/Other	105 (52)	66 (32)	285 (45)	456 (44)
First and last accrual dates	July 2013- July 2015	November 2013- October 2018	June 2013- April 2014	June 2013- October 2018
Median follow up, years (95% CI)	4.91 (4.89-4.95)	3.39 (3.06-3.94)	4.95 (4.93-4.96)	4.9 (4.88-4.93)

NCORP: NCI Community Oncology Research Program

Presented By: Vered Stearns, MD FASCO, vstearn1@jhmi.edu
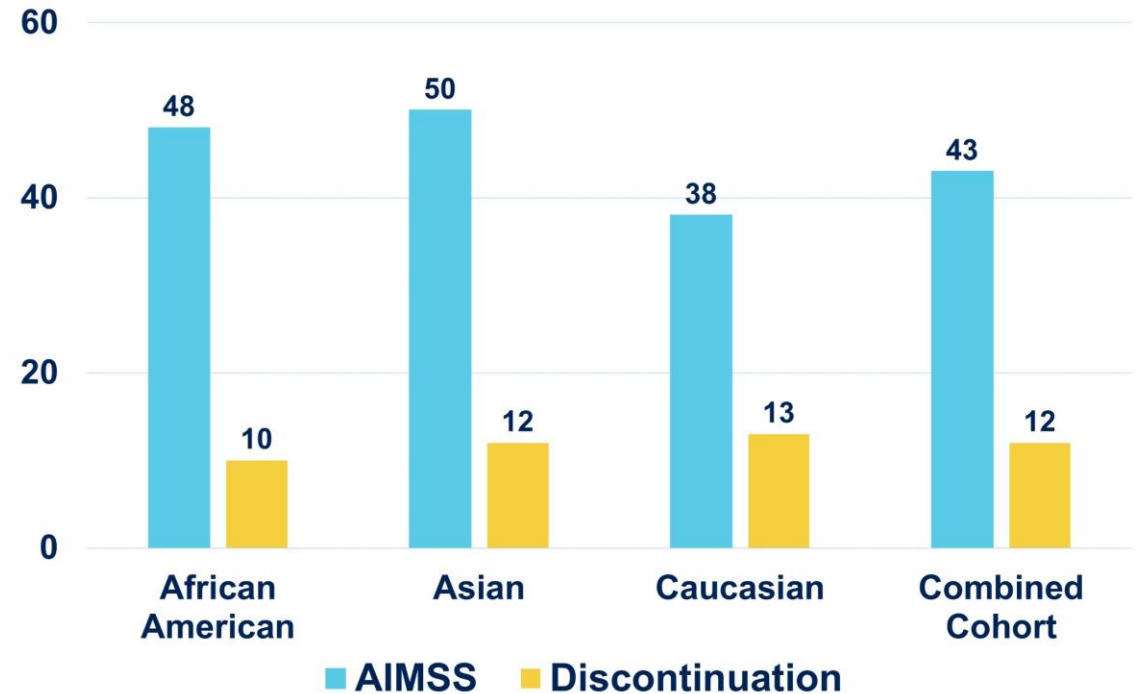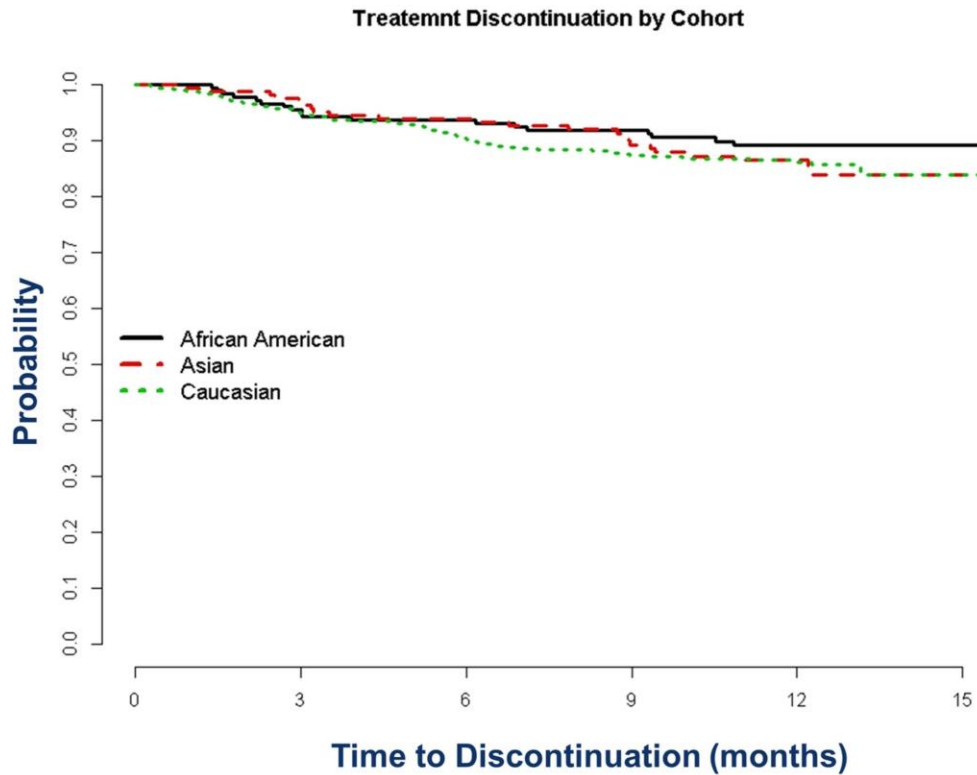
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AIMSS and discontinuation

-More AA and Asians developed AIMSS compared to Caucasians (AA compared to Caucasians p=0.017; Asian compared to Caucasians p=0.004)
-Similar AI discontinuation rate in all 3 cohorts

Stearns et al: Results

-More AA and Asians developed AIMSS compared to Caucasians (AA compared to Caucasians p=0.017; Asian compared to Caucasians p=0.004)
-Similar AI discontinuation rate in all 3 cohorts
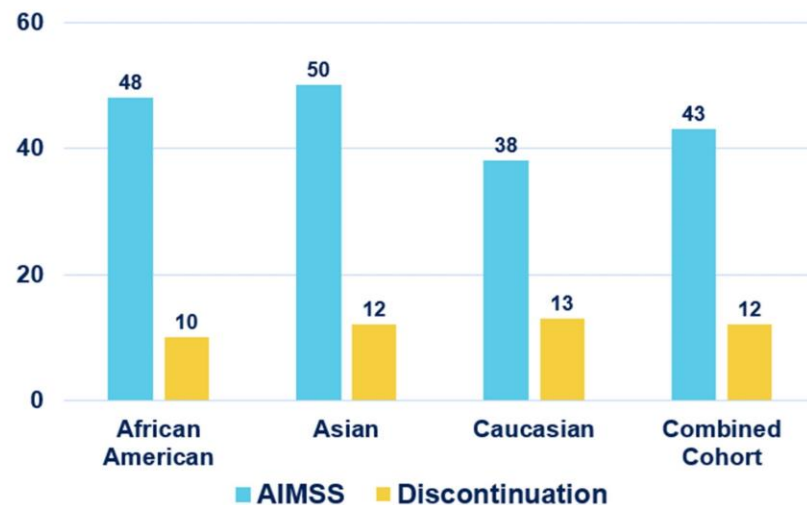
Vered Stearns, MD FASCO, vstearn1@jhmi.edu

SNP Analysis:

- Unable to prospectively validate 10 candidate SNPs as predictors of AIMSS or AI discontinuation
- Trend for an association between *rs2296972/HTR2A* and development of AIMSS

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# Conclusions: Predictors of Late and Long-term Effects

- Clinical markers show some correlation but need further validation and defined tools
- Genomic markers are not ready for clinical use, but more potential candidates are being identified
  - Abst. 12004 and 12005 identified SNPs that may predict for platinum-induced neurotoxicity and anthracycline-induced cardiotoxicity
- Likely will need a combination of clinical and genomic markers
- Important to include racial and ethnic minorities in trials looking at clinical and genomic markers of risk
- For now, best strategy is mitigation of long-term effects with evidence-based interventions

Long-term Results from Randomized Blinded Sham- and Waitlist-Controlled Trial of Acupuncture for Joint Symptoms Related to AI in Early-Stage Breast Cancer S1200 [1]
Abstract #1208 (Hershman)

- Post menopausal women
- AI >30 days
- 3/10 BPI-WP score
- TA and SA for 12 weeks v. Waitlist
  - 2 sessions/wk x 6 wks
  - 1 session/wk x 6 wks
- At W24, all subjects offered 10 TA

**Update at 52 weeks shows
TA reduces AI joint pain
Effect durable at 52 weeks**

Adjusted Mean Differences by Arm
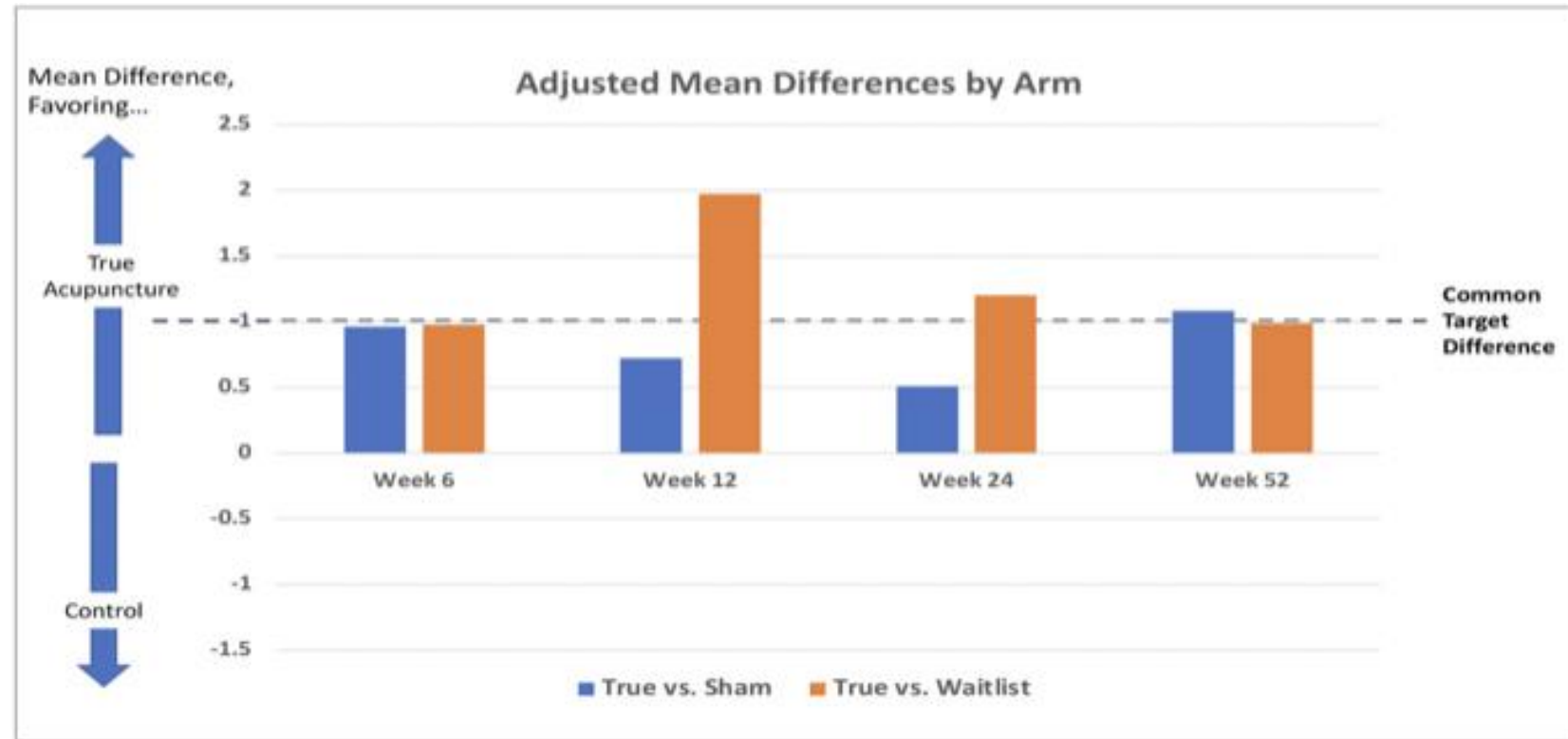
[1] Hershman JAMA 2018

Effects of Yoga, Cognitive Behavioral Therapy and a Behavioral Placebo on Sleep: A Nationwide Multicenter Phase III RCT in Cancer Survivors
Abst #12017 (Lin)

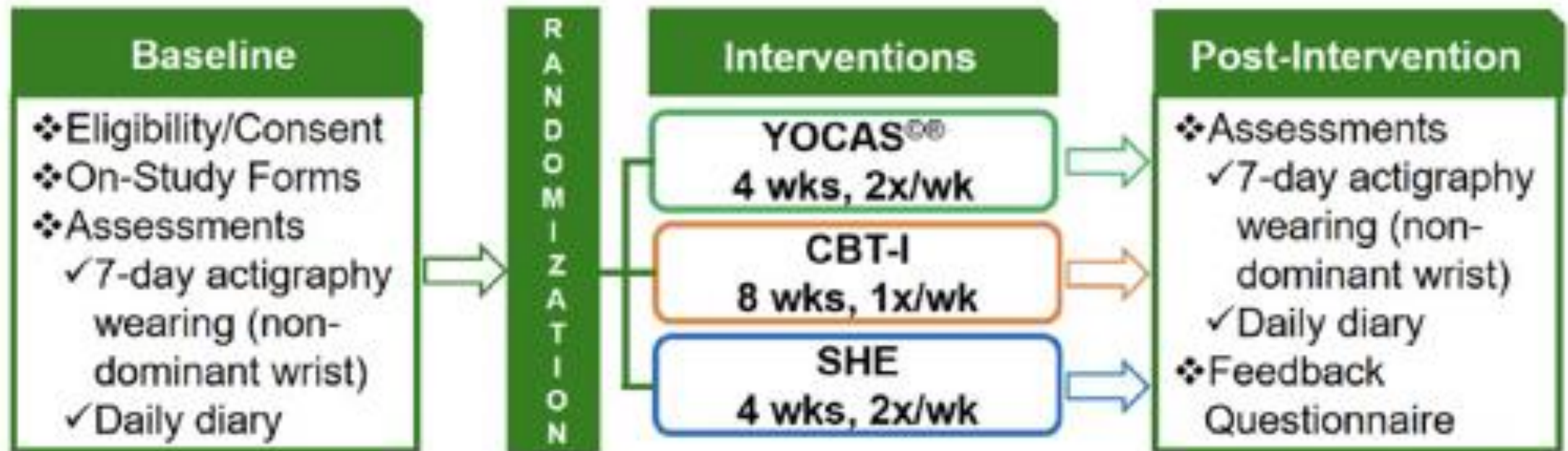YOCAS: Yoga for Cancer Survivors (Hatha and Restorative)

CBT-I : Cognitive Behavioral Therapy for Insomnia

SHE: ASCO Survivorship Health Education (control)

All sessions led by certified health professionals in a small group setting

Actigraph (T3x or GT9x) worn on the non-dominant wrist 24h/d

N = 740

Baseline
❖ Eligibility/Consent
❖ On-Study Forms
❖ Assessments
  ✓ 7-day actigraphy wearing (non-dominant wrist)
  ✓ Daily diary

RANDOMIZATION

Interventions
YOCAS©®
4 wks, 2x/wk

CBT-I
8 wks, 1x/wk

SHE
4 wks, 2x/wk

Post-Intervention
❖ Assessments
  ✓ 7-day actigraphy wearing (non-dominant wrist)
  ✓ Daily diary
❖ Feedback Questionnaire

Results

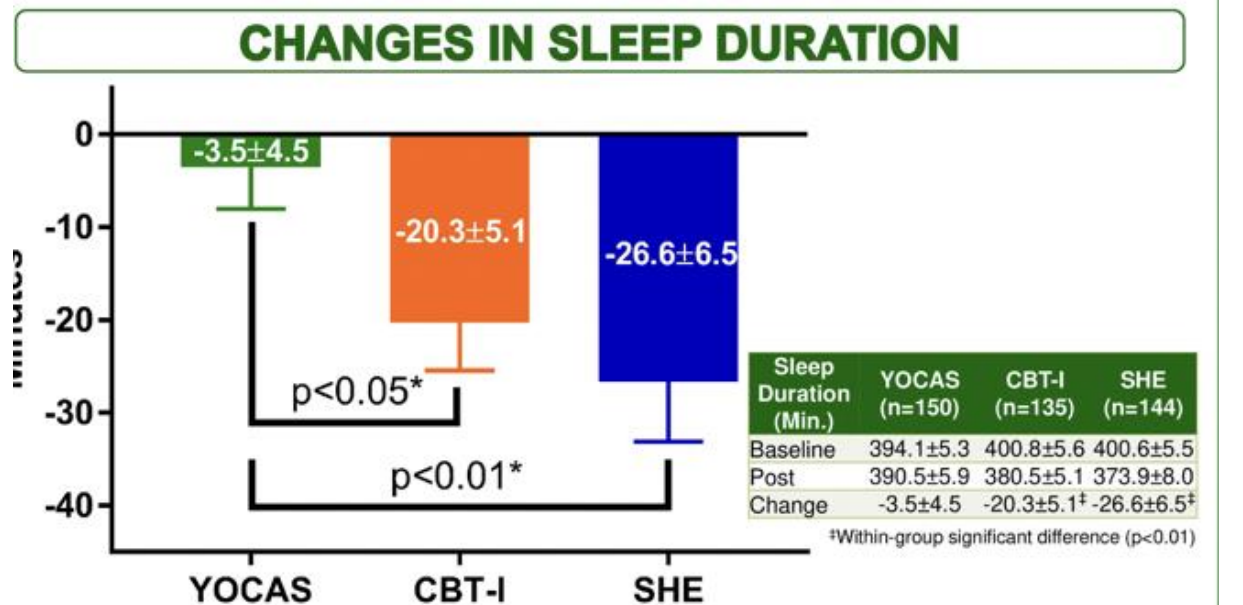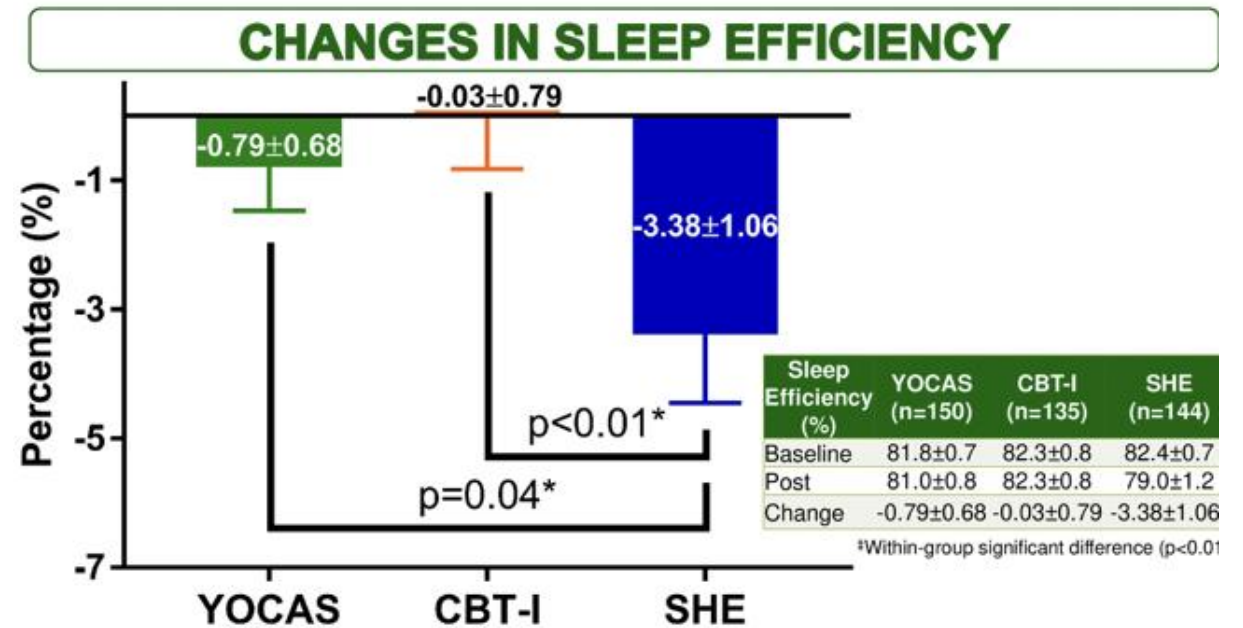Sleep Efficiency:
YOCAS and CBT-I subjects maintained
SHE reduced

Sleep Duration:
YOCAS maintained
CBT-I and SHE reduced

WASO (wake after sleep onset)
No difference
Trend toward lower with CBT-I

CHANGES IN SLEEP EFFICIENCY

-0.03±0.79

-0.79±0.68

-3.38±1.06

p<0.01*

p=0.04*

Sleep Efficiency (%)	YOCAS (n=150)	CBT-I (n=135)	SHE (n=144)
Baseline	81.8±0.7	82.3±0.8	82.4±0.7
Post	81.0±0.8	82.3±0.8	79.0±1.2
Change	-0.79±0.68	-0.03±0.79	-3.38±1.06

‡Within-group significant difference (p<0.01

CHANGES IN SLEEP DURATION

-3.5±4.5

-20.3±5.1

-26.6±6.5

p<0.05*

p<0.01*

Sleep Duration (Min.)	YOCAS (n=150)	CBT-I (n=135)	SHE (n=144)
Baseline	394.1±5.3	400.8±5.6	400.6±5.5
Post	390.5±5.9	380.5±5.1	373.9±8.0
Change	-3.5±4.5	-20.3±5.1‡	-26.6±6.5‡

‡Within-group significant difference (p<0.01)

Phase II Study of Exercise and Low Dose Ibuprofen for Cognitive Problems During Chemo
Abst #2016 (Janelsins)

Cancer Related Cognitive Impairment

　　75% of patients undergoing treatment [1]

　　Can persist long term in 35% [1]

　　　Includes memory loss, difficulty concentrating, impaired executive functioning

Possible mechanisms
- Impaired blood flow
- Direct neuron damage
- Metabolic Syndrome (Abst #12013 ASCO 2021 Alexander, et al)
- Inflammation

[1] Janelsins, et al. Int Rev Psych 2014

Phase II Study of Exercise and Low Dose Ibuprofen for Cognitive Problems During Chemo
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- Inflammation

Exercise +/- Ibuprofen

[1] Janelsins, et al. Int Rev Psych 2014

Janelsins et al: Study Schema

Baseline–Prior to Initiation of Next Chemotherapy Cycle

Informed Consent
Assessments
- Daily Diary & Steps
- Cognitive Tasks
  - CANTAB
  - Paper-Based
- Blood Collection
  - Inflammation Markers
- Fitness Assessments

- Symptom Measures

RANDOMIZE

Placebo

Exercise + Placebo

Ibuprofen

Exercise + Ibuprofen

Intervention– Beginning Day 1 of On-Study Chemotherapy Cycle for 42 days

- Exercise Diary (if randomized)

- Weekly phone calls

Post-Intervention Assessment– Between Day 42 and prior to last on-study chemotherapy

Assessments
- Daily Diary & Steps
- Cognitive Tasks
  - CANTAB
  - Paper-Based
- Blood Collection
  - Inflammation Markers
- Fitness Assessments

- Symptom Measures

Michelle Janelsins, PhD, MPH

Notable Eligibility Criterion:

- At chemotherapy cycle 1 or after, report cognitive difficulties of 3 or higher (on a scale of 0 = "Not Present" to 10 = "As Bad As You Can Imagine")

- Be scheduled to receive at least 2 additional cycles of oral or IV chemotherapy over the 42-day study period

- **Study Medication:** Ibuprofen 200 mg po bid vs placebo
- **Exercise:** Walking & Resistance Training with therapeutic bands

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EXCAP©® Intervention

- **Exercise Modes**
  - **Aerobic**
    - Walking with a pedometer
  - **Non-Aerobic/Resistance**
    - Therapeutic bands
- **Frequency**
  - **Walking (pedometer):** daily
    - Number of steps
  - **Resistance bands (10 exercises):** daily
    - Number of sets and repetitions
- **Duration**
  - **6 weeks**

- **Intensity**
  - **Low to Moderate**
  - **RPE of 2-4** on a 0-10 scale
  - **40-70% Heart Rate Reserve**
  - **Progressive Tailoring**
- **Standardization**
  - **EXCAP©® Instructional Kit** with pedometer, therapeutic bands and a manual
  - ACSM-certified exercise physiologists delivery of **EXCAP©®**

Presented By: Michelle Janelsins, PhD, MPH

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Both Interventions Improved Attention Performance (TMT-A)

Change Score in Seconds

* p <0.05

Score worsened

Placebo   EXCAP + Placebo   Ibuprofen   EXCAP + Ibuprofen

Score improved

* p <0.032
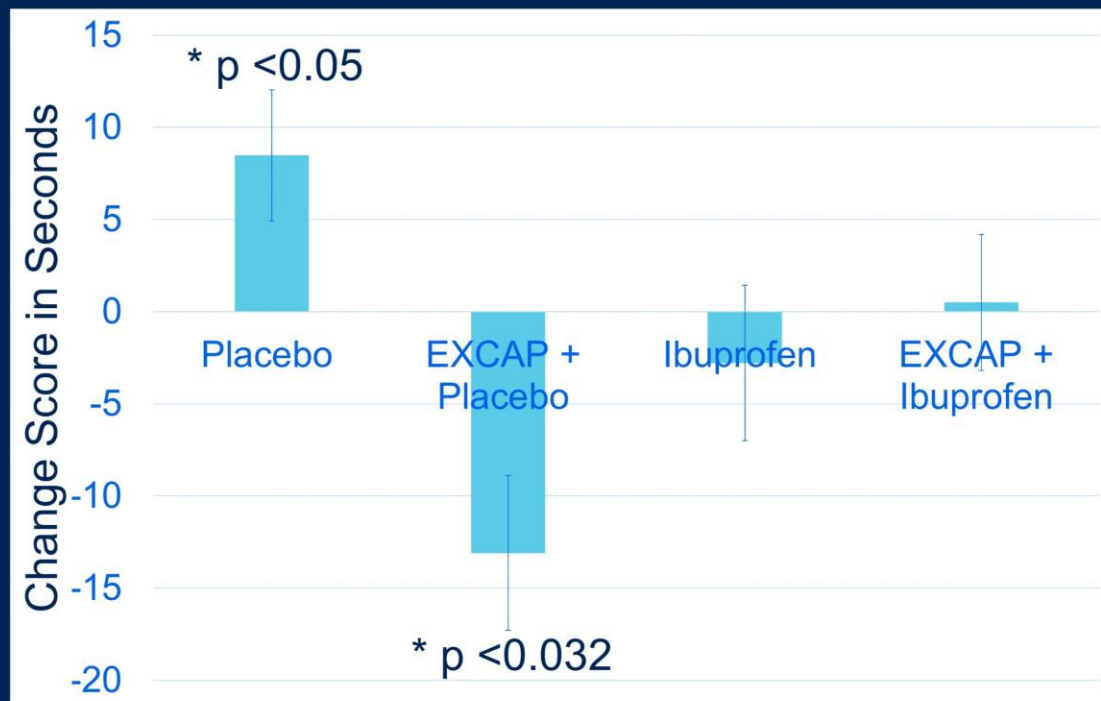
ANCOVA adjusted for baseline score

Between Group: EXCAP vs. Placebo; -21.57 seconds, p<0.001
Ibuprofen vs. Placebo; -11.3 seconds, p=0.048
EXCAP + Ibuprofen vs. Placebo; -7.98 seconds, p=0.122

Main effect: All EXCAP; -9.14 seconds, p=0.02
All Ibuprofen; 1.16 seconds, p=0.77

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Exercise Improved Cognitive Symptoms
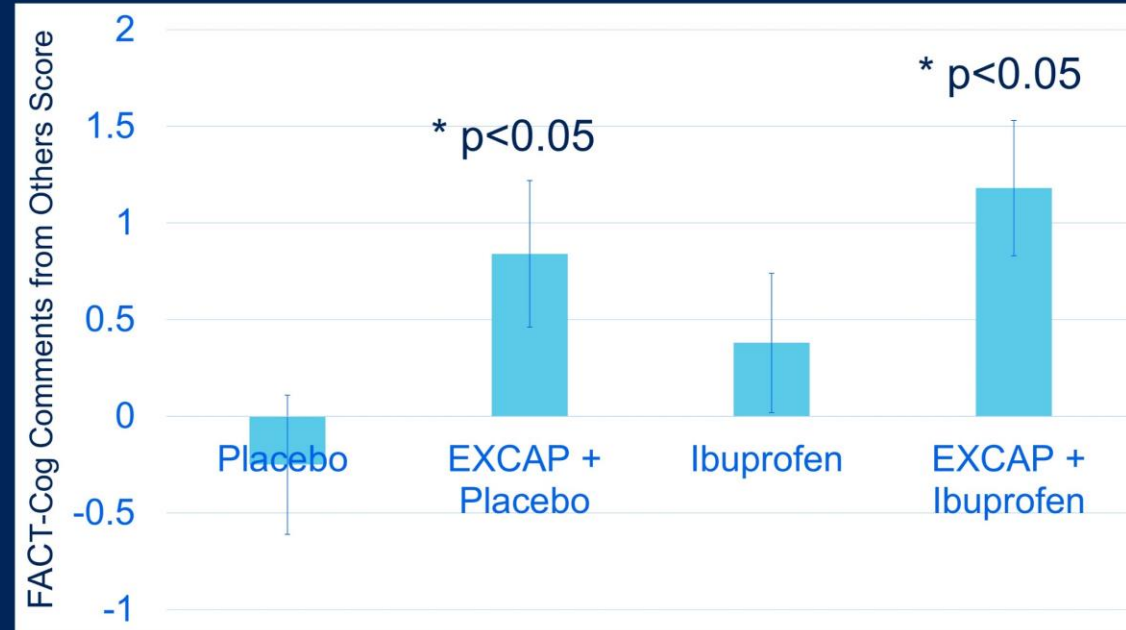
Between Group: EXCAP vs. Placebo; 1.08 points, p=0.033
Ibuprofen vs. Placebo; 0.63 points, p=0.200
EXCAP + Ibuprofen vs. Placebo; 1.43 points, p=0.004

Main effect: All EXCAP; 0.94 points, p=0.009
All Ibuprofen; 0.48 points, p=0.180

Presented By: Michelle Janelsins, PhD, MPH

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Both Interventions Dampened Inflammation

Presented By: Michelle Janelsins, PhD, MPH

Conclusions: Mitigating Late and Long-Term Effects

AI Induced Joint Symptoms

- True Acupuncture benefit is still seen with longer term follow up
- Other interventions- exercise, yoga

Sleep

- YOCAS beneficial for sleep efficiency and duration
- CBT-I beneficial for efficiency
- Other interventions: correct underlying conditions

Cancer Related Cognitive Impairment

- Need to understand effects of inflammation on cognitive function
- Phase III RCTs of exercise needed
  - Abst #12015 Benefit of exercise seen on self-reported but not tested cognitive function but some benefit in highly fatigued patients
- Other interventions: cognitive rehabilitation, organization training, correct underlying conditions

Virtual/Remote Symptom Management

- Remote Symptom monitoring can improve patient outcomes and reduce ED/hospitalizations
  - Ethan Basch JCO 2016
  - Denis ASCO 2019
- COVID 19 accelerated need for remote monitoring
- Technology opened doors for at home care delivery of support services and can include supervised at home supportive care

Randomized Trial of Remote Symptom Monitoring During COVID19: Impact on Symptoms, QOL and Unplanned Healthcare Utilization
Abst #12000 (Mooney)

Purpose:

- To determine if remote symptom monitoring and management of cancer patients during COVID would
  - Reduce symptom burden
  - Decrease unplanned healthcare use
  - Improve QOL

Used Symptom Care At Home (SCH)

- Daily PRO evaluating presence and severity of common symptoms
- Algorithm to triage to self-care coaching vs. NP intervention using decision support tool
- Previously tested and published (Mooney Cancer Med Mar;6(3):537-546)

Feasibility of a Virtual Hybrid Resistance and Balance Training Program for Older Patients with Cancer and Its Preliminary Effects on Lower Body Strength and Balance
Abst #12002 (Sattar)

Risk of falls

- Is associated with older age and having cancer

- Can be decreased with resistance and balance training

Design

- Remote, 8 week exercise program (3x per week) supervised by CEP

- 25 patients aged 65 or older with breast, colorectal, prostate, lung ca on active treatment or completed within 6 months

- No brain or unstable bone mets

- Isometric leg strengthening

- Otago program (https://www.physio-pedia.com/Otago_Exercise_Programme)

Outcome measures

Lower body strength	• 5-times chair stand
Balance	• Balance test
Falls	• Self-report

RQ 1: Feasibility

- **Recruitment rate: 60% (27/45)**
- **Attendance rate:**
  - Virtual component: 97.6%
  - Independent component 84.7%
- **Program completion rate: 96%**
- **Attrition rate: 4%**
- **Outcome capture: 100%**
- **Program acceptability:**
  - Perceived program as rewarding and enjoyable (100%)
  - Felt this program prepared them to exercise on their own (92%)
  - Confident to continue exercising on their own (81%)
  - Would recommend program to other patients (100%)

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RQ 2: Efficacy

- ## Lower body strength
  - Baseline: median 9.2s (IQR = 3.13)
  - Follow-up: median 7.7s (IQR = 4.6)
  - *p* = .001
  - N=6 (23%) surpassed MCID (2.3s)
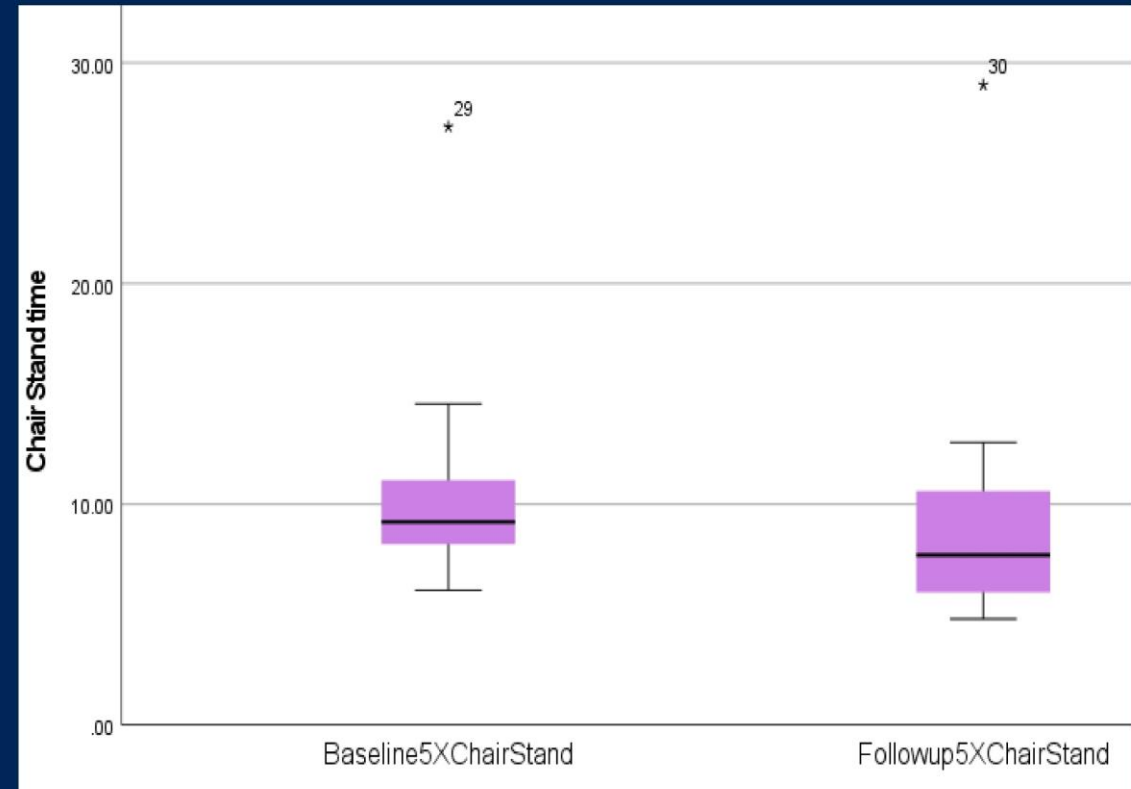
Randomized Trial of Remote Symptom Monitoring During COVID19: Impact on Symptoms, QOL and Unplanned Healthcare Utilization
Abst #12000 (Mooney)

Design:
- Randomized, controlled trial of
  - Symptom Care at Home
  - Usual Care (control)
- Patients 18 or older on chemo and/or radiation
- 4/21/20-12/31/20
- Baseline and monthly questionnaires

Outcomes:
- Health care utilization: unplanned, ED, hospitalization, urgent care
- Patient reported symptom burden, HRQOL, mental health, loneliness, isolation using EHR, MDASI, PROMIS, Pendo, HADS, UCLA loneliness and isolation score

Results: Health Care Utilization
Decreased unplanned visits in SCH group

Unique participants with 1 or > unplanned health care visits (n= 128 SCH; 124 UC)			
Group	**N (%)**		
SCH	15 (11.7%)	$\chi2 = 5.25$	
UC	28 (22.6%)	$p = .022$	
Type and frequency of unplanned health care visits			
Group	**Type of Health Care Use**	**Freq**	**%**
SCH	Acute Care Clinic	6	25.0
	Emergency Department	3	12.5
	Hospitalized	15	62.5
	Total	24	100%
UC	Acute Care Clinic	5	12.5
	Emergency Department	10	25.0
	Hospitalized	25	62.5
	Total	40	100%

Results: Symptom burden over time

ANCOVA models of MDASI Symptom Severity
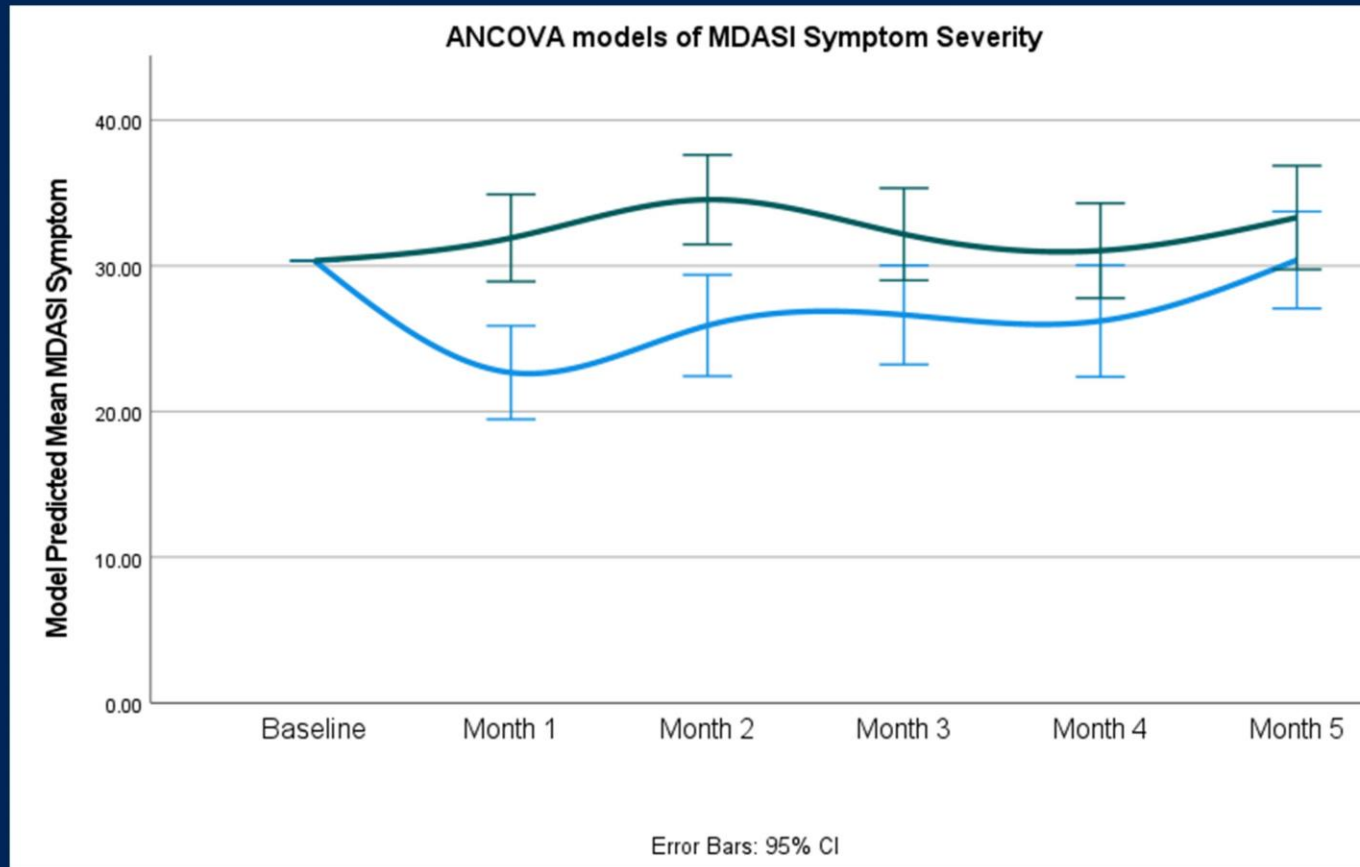
Legend: Usual Care, SCH Intervention

Error Bars: 95% CI

Presented By: Kathi Mooney

Results: HRQOL over time

Presented By: Kathi Mooney

Conclusions: Virtual/Remote Symptom Management

- Remote monitoring/management improves patient outcomes and reduces health care utilization

- Can deliver remote supportive care via exercise with good participatiioin and demonstrable benefits

- Potential Barriers to remote/virtual management
  - Patient access
  - Practice cost
  - Varying reimbursement
  - Implementation may be difficult in smaller practices

Thank you
jcrews@seattlecca.org