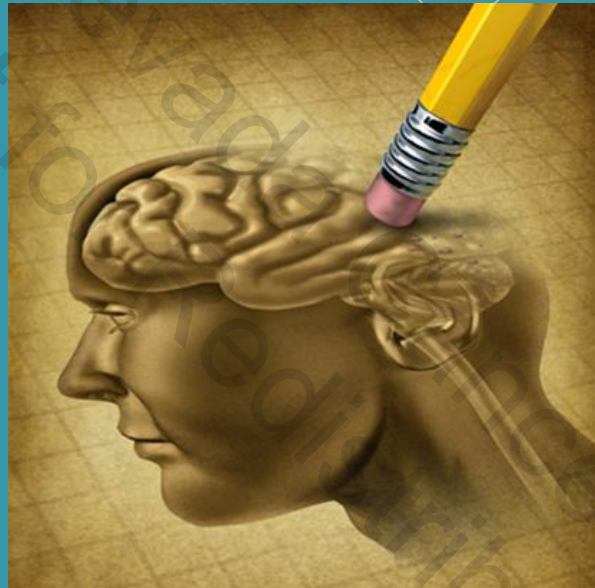


Lifestyle Interventions to Support Management of Cancer-Related Cognitive Impairment



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Patient and Family Support Program
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Disclosures

No have no relevant disclosures

2024 Nevada Cancer Summit
Not for Redistribution

Learning Objectives

1. Describe the various etiologies implicated in Cancer-Related Cognitive Impairment (CRCI)
2. Summarize potential lifestyle treatment strategies for CRCI among cancer survivors
3. Recognize opportunities for research of lifestyle strategies for CRCI

Typical concerns reported by patients

Short-term memory lapses

Difficulty concentrating or staying focused on a task

Trouble remembering details such as names, dates, or phone numbers

Difficulty multi-tasking such as carrying on a conversation and following a cooking recipe

Slower to process information

Difficulty with word retrieval



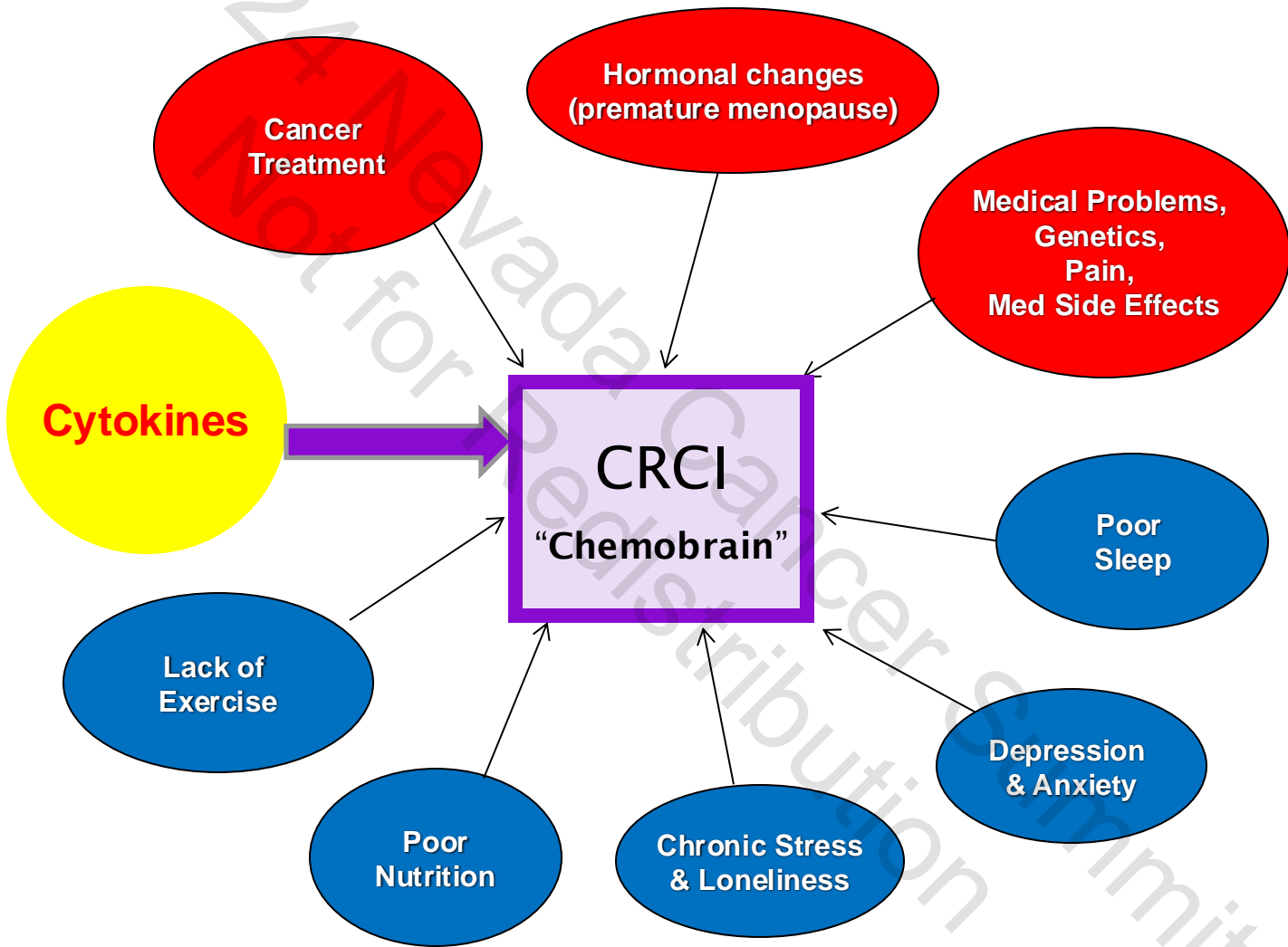
Redefining “Chemobrain”

No one size fits all

No single symptom or set of symptoms

Medical term:

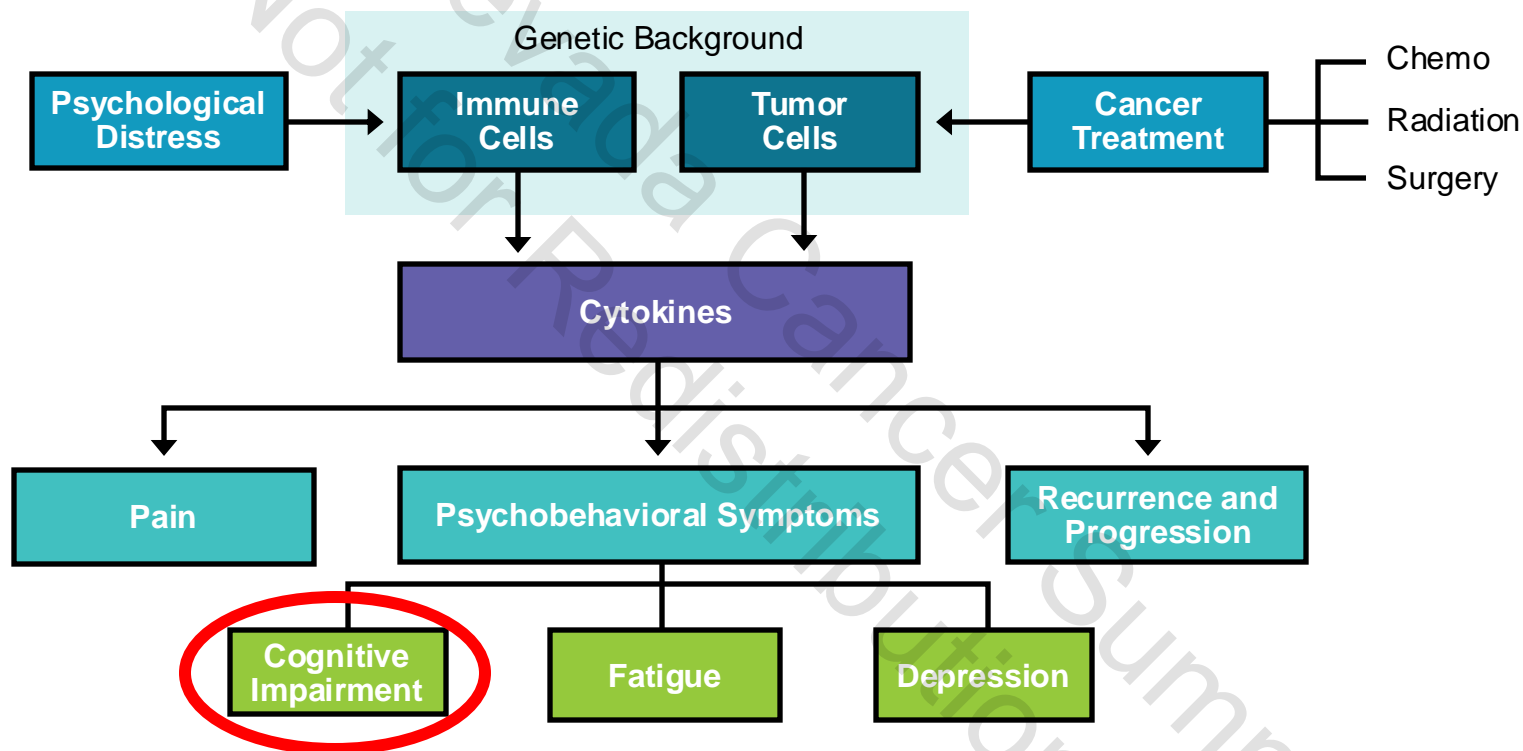
Cancer-Related Cognitive Impairment
(CRCI)



What Are Cytokines?



CRCI and Cytokines



Pharmacologic Treatments?

NO CLEAR EVIDENCE FOR EFFICACY

- Methylphenidate
- Modafinil
- Donepezil
- Memantadine
- Erythropoietin
- Gingko biloba

More rigorous clinical trials with sufficient sample sizes needed

Roadmap to Brain Health and Wellness

- **Coping Strategies**

- Mindfulness
- Mood & Negative Thoughts

- **Lifestyle**

- Exercise
- Sleep
- Nutrition
- Connectivity

- **Cognitive Strategies**

- Attention
- Memory
- Problem-Solving
- Pacing and Balance



Exercise and Cognition



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Dangers of Visceral Fat

Linked to:

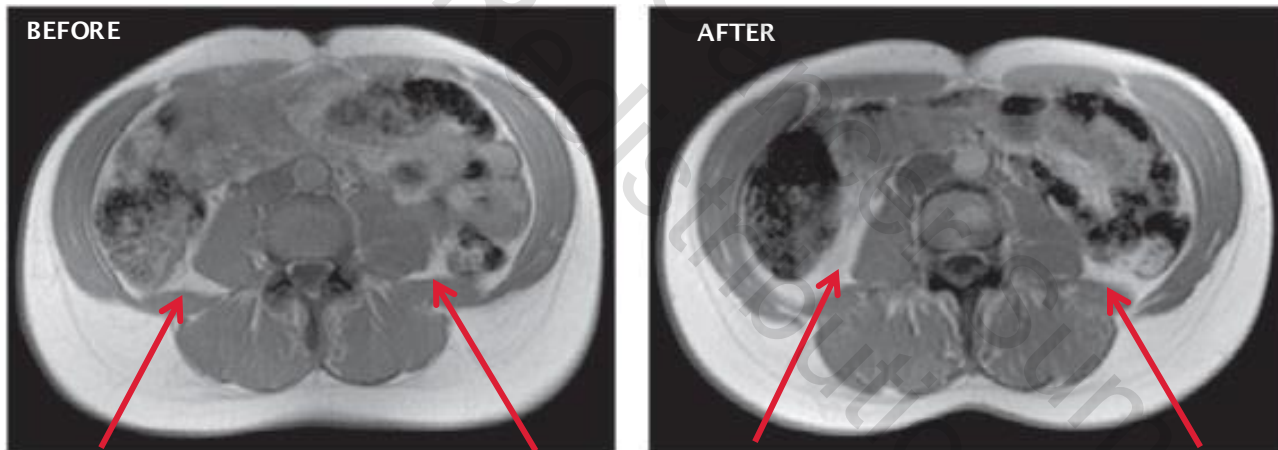
- Cardiovascular disease
- Type 2 diabetes
- **Cognitive impairment!**
- Some cancers including breast cancer, colon cancer
- Higher mortality rate



These risks may exist even if normal body mass index

Inactivity Leads to Visceral Fat: Study of Healthy Young Men

- Decreased daily stepping from 10,000 to 1,500 steps for only 2 weeks
- 7% increase in intra-abdominal fat mass
- 7% decrease in VO₂ max (fitness)
- Lean muscle mass of legs decreased



How to Reduce Visceral Fat?



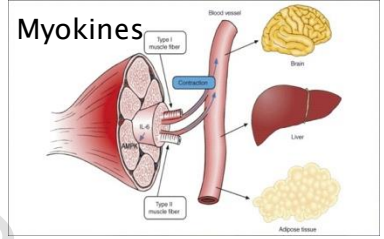
Exercise will help -- even if you don't lose weight!

Exercise Is Medicine

**Exercise can reduce
inflammatory cytokines!**

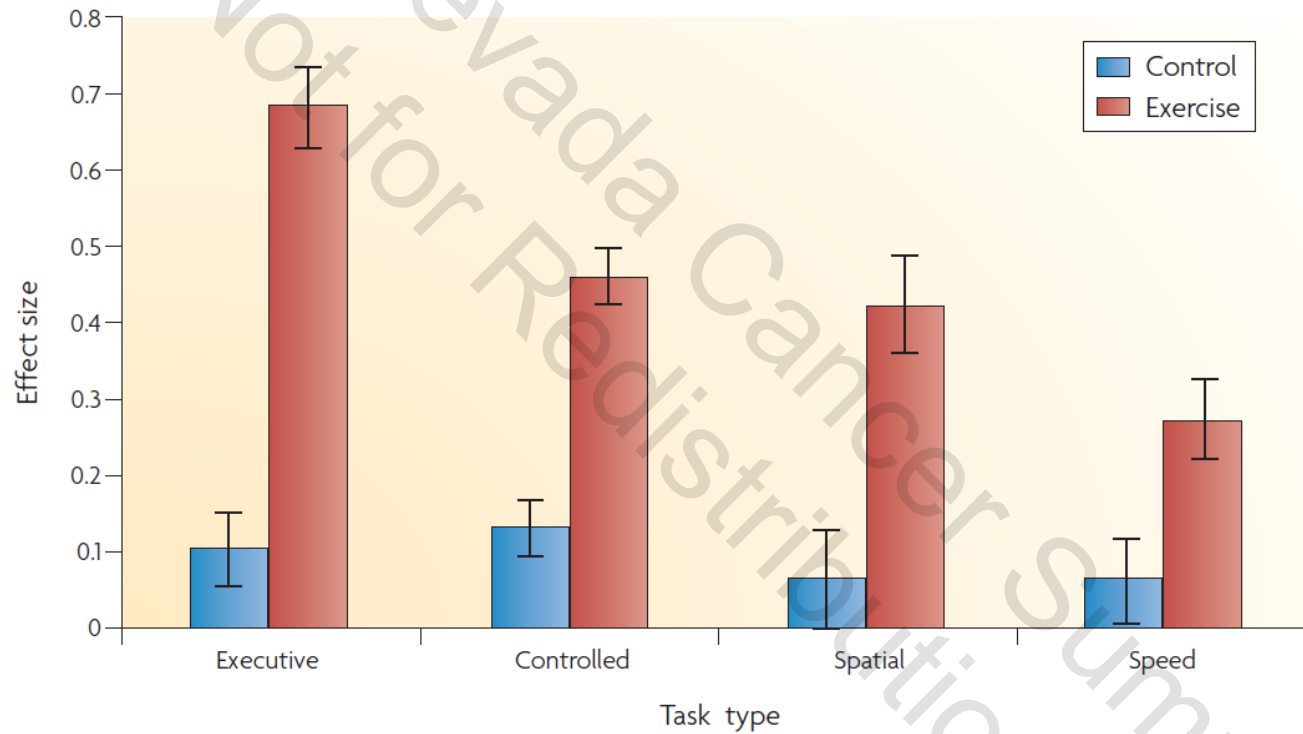


Myokines



CYTOKINES

Be Smart, Exercise Your Heart



The Bottom Line

- **Cancer survivors should be counseled regarding the benefits of exercise**
 - At least 150 minutes of moderate aerobic exercise/week
41% decrease in all cause mortality! (range from 29–52%)¹
Or 75 minutes of vigorous aerobic exercise per week
 - Strength training at least 2 days per week
- Supported by **major national guidelines**
 - American Cancer Society/ASCO Breast Cancer Survivorship Care Guidelines (JCO, 2015)
 - NCCN, Cancer Survivorship Guidelines (2021)
 - American College of Sports Medicine (2019)

Sleep and Cognition

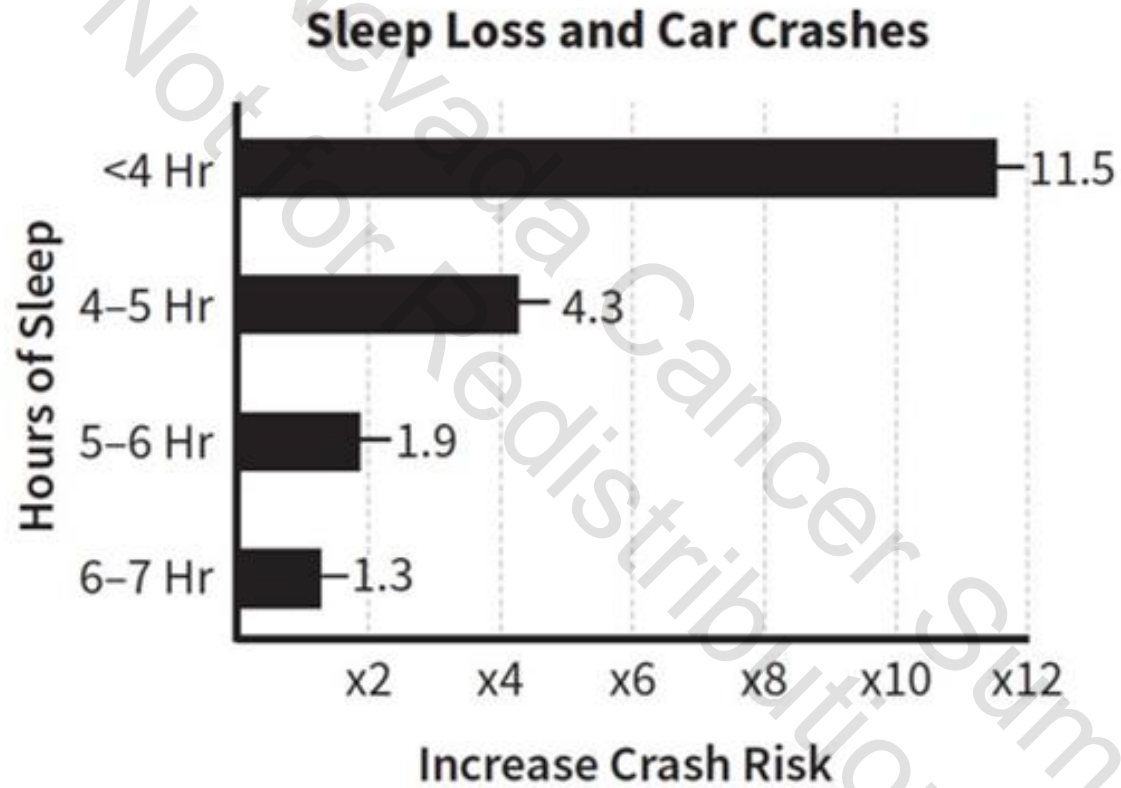


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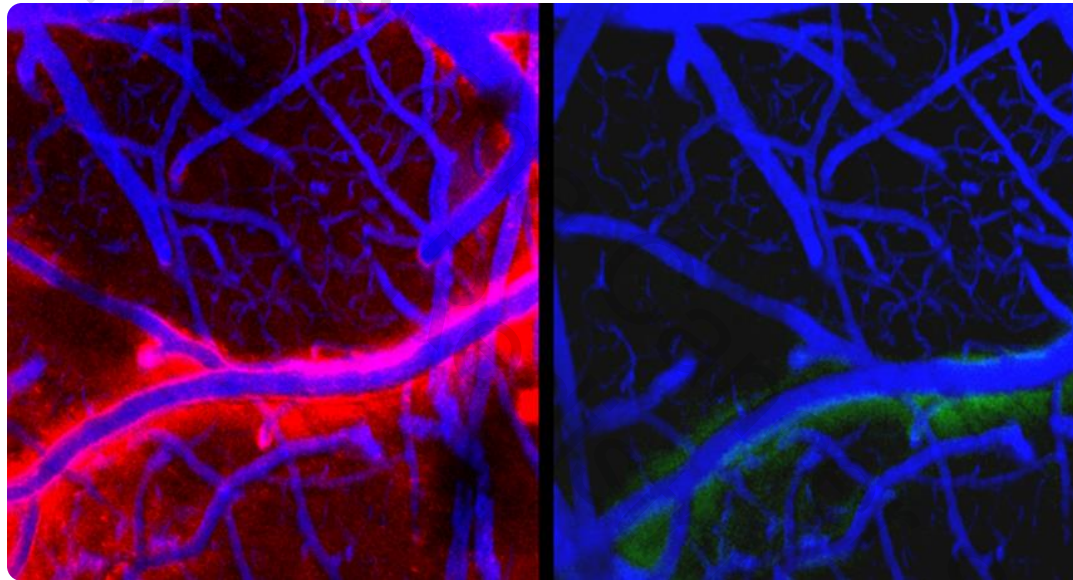
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Sleep Key to Drivers' Safety



Sleep for Brain Cleanup

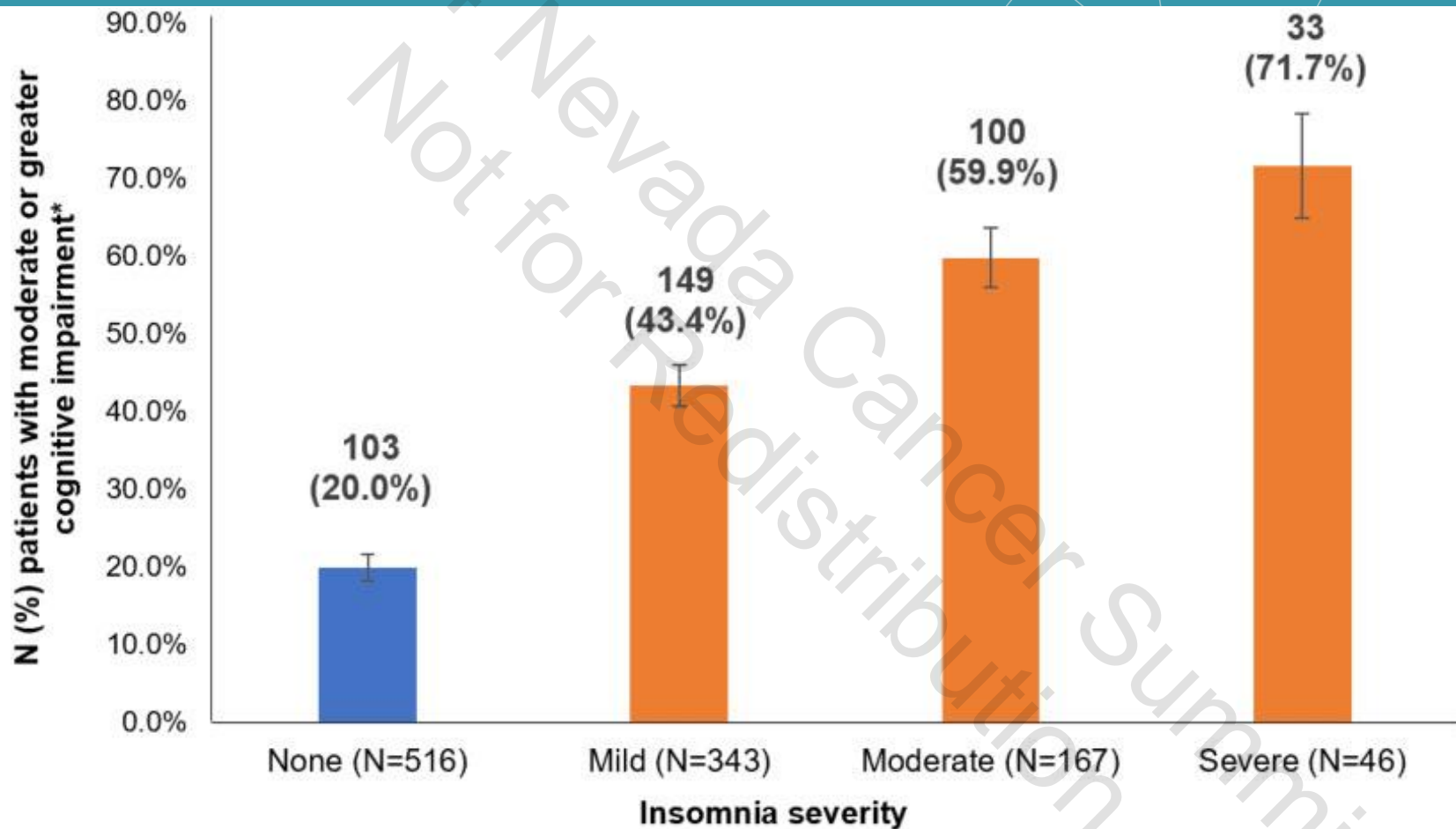
Asleep



Awake

- During sleep, channels between brain cells open
 - Cerebrospinal fluid washes out neurotoxins
- **No evidence** that **sleeping pills** are as effective as natural sleep for the “glymphatic system”

Prevalence of moderate or greater perceived cognitive impairment among breast cancer survivors by severity of comorbid insomnia



What Can I Do to Try to Facilitate the BEST Sleep Naturally?



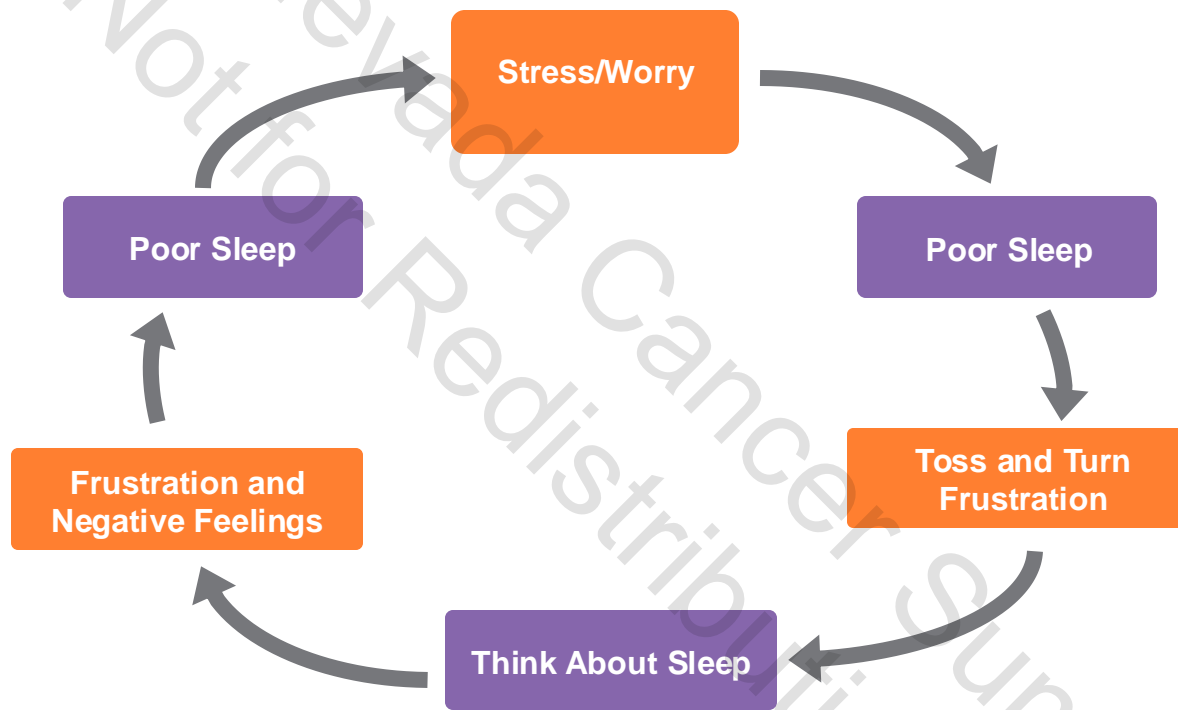
Natural Circadian Rhythm



Associations between day and night light exposure and psychiatric outcomes

- **For individuals with the brightest night-time light quartile:**
 - 30% higher risk of depression and self-harm
 - 20% higher risk of generalized anxiety disorder
 - 20% higher risk of psychosis
 - Higher risk of bipolar disorder, PTSD
- **Individuals with the brightest daytime light quartile:**
 - 20% lower risk of depression and self-harm
 - 30% lower risk for PTSD
 - Lower risk of PTSD

Negative Sleep Associations & Patterns



Cognitive Behavioral Therapy for Insomnia

- **Try this first**, according to most recent guidelines
- Stimulus control, relaxation techniques, sleep hygiene
- Cognitive restructuring
 - Challenges you to reframe negative ways of thinking that can be self-fulfilling prophecies.
 - If you're lying awake thinking about what a basket case you'll be tomorrow because you're not asleep, well, that thought alone will keep you awake.
 - Asks you to look at the situation differently and replace the negative thought with a positive one.
 - "I'll fall asleep eventually," or "I can handle this if it only happens a few nights a week."
- Try an online program or train with a CBT-I therapist.

Peoples A. *J Clin Sleep Med*. 2019.

Tips for Healthy Sleep

- Stick to a schedule
- Avoid caffeine in the afternoon (can take 8 hours to wear off fully)
- Avoid alcoholic drinks before bed (reduces REM sleep)
- Don't take naps after 3 p.m.
- Take a hot bath before bed (reduces body temperature)
- Keep your bedroom cool (ideally about 65 degrees)
- Don't lie in bed awake for more than 20 minutes



Social Connectivity and Cognition



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What increases the risk of death as much as smoking cigarettes & more than inactivity or obesity?



Social Isolation Impact

Social Isolation = Smoking 15 Cigarettes a Day



Loneliness is a risk factor for:

- **In the general population:**
 - Poorer overall cognitive performance
 - Faster cognitive decline
 - Poorer executive functioning
 - More negativity and depressive cognition
- **Linked as a risk factor for cognitive complaints among breast cancer survivors**



Loneliness and Social Isolation



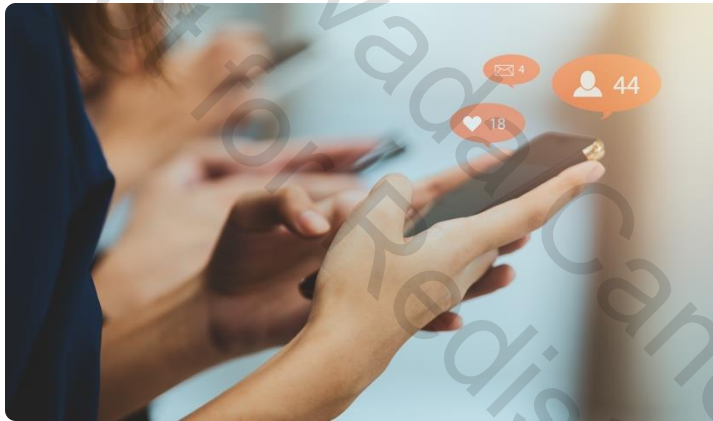
Loneliness —
“The unpleasant experience that occurs when a person’s network of social relations is deficient in some important way, either quantitatively or qualitatively.”¹



Social Isolation —
“The absence of relationships with other people.”²

Loneliness Is a *Subjective* Experience

- Some people are socially isolated but not lonely



- Some people are lonely even with a lot of social contacts

You Can Overcome Loneliness

- **Stay connected**
- Cognitive behavioral therapy
 - Shift people's attention and interpretation of social situations in a more positive direction
- Know where your own thermostat is set and try to stay in your comfort zone
 - "The degree of social connection that can improve our health and happiness... is both as simple and as difficult as *being open and available to others.*"
— Cacioppo. 2011.

Emerging from the Haze Program



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NCCN Survivorship Guidelines 2023: Cognitive Function

CANCER-ASSOCIATED COGNITIVE DYSFUNCTION INTERVENTIONS

Patient/Family Education and Counseling

- Validation of experience of cognitive dysfunction associated with cancer diagnosis and treatment
- Reassurance that cancer-associated cognitive dysfunction is often not a progressive neurologic disorder like progressive dementias^b
- Support self-management and coping strategies

General Strategies for Management of Cancer-Associated Cognitive Dysfunction

- Teach enhanced organizational strategies (ie, using memory aids like notebooks and planners, keeping items in the same place, using reminder notes, smart phone technology)
- Encourage patients to do the most cognitively demanding tasks at the time of day when energy levels are highest
- Provide information about relaxation or stress management skills for daily use
- Recommend routine physical activity ([HL-1](#))
- Recommend limiting use of alcohol and other agents that alter cognition and sleep
- Consider meditation, yoga, mindfulness-based stress reduction, and cognitive training (ie, brain games)
- For older adults also see the cognitive function section of the [NCCN Guidelines for Older Adult Oncology \(OAO-F\)](#)
- Optimize management of:
 - Depression or emotional distress (See appropriate survivorship guidelines or NCCN Guidelines for Distress Management)
 - Sleep disturbance ([SSD-1](#))
 - Fatigue ([SFAT-1](#))
 - Contributing symptoms such as pain ([SPAIN-1](#))
 - Medical comorbidities

EMERGING FROM THE HAZE™:

A 10-Week Workshop in Strategies to Combat “Chemobrain”

WEEK 1 - Introduction & Program Overview

Neuroplasticity. Understanding Cancer-Related Cognitive Impairment

WEEK 2 - Mindfulness, Stress Management and Relaxation Techniques

WEEK 3 - Lifestyle and Cognition: Exercise

WEEK 4 - Mood and Negative/Automatic Thoughts

WEEK 5 - Lifestyle and Cognition: Sleep

WEEK 6 - Cognitive Strategies: Attention

WEEK 7 - Lifestyle and Cognition: Nutrition

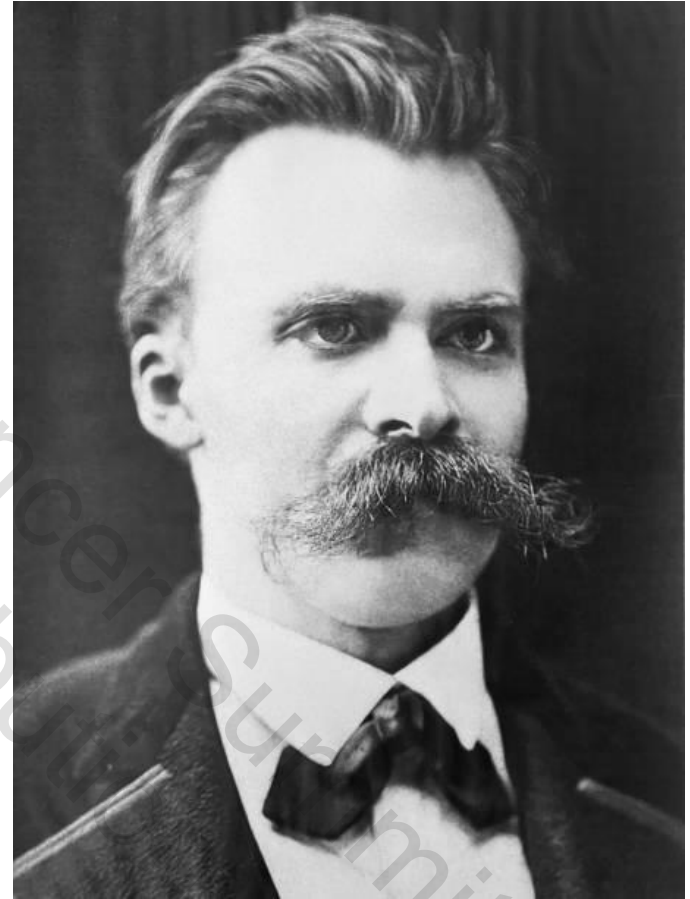
WEEK 8 - Cognitive Strategies: Memory

WEEK 9 - Cognitive Strategies: Problem Solving. Pacing and Balancing.

WEEK 10 - Lifestyle and Cognition: Social Support. Summary and Review

**He who has a why to
live for can bear
almost any how.**

— Friedrich Nietzsche



Emerging from the Haze™: Prospective, Multicenter Controlled Study

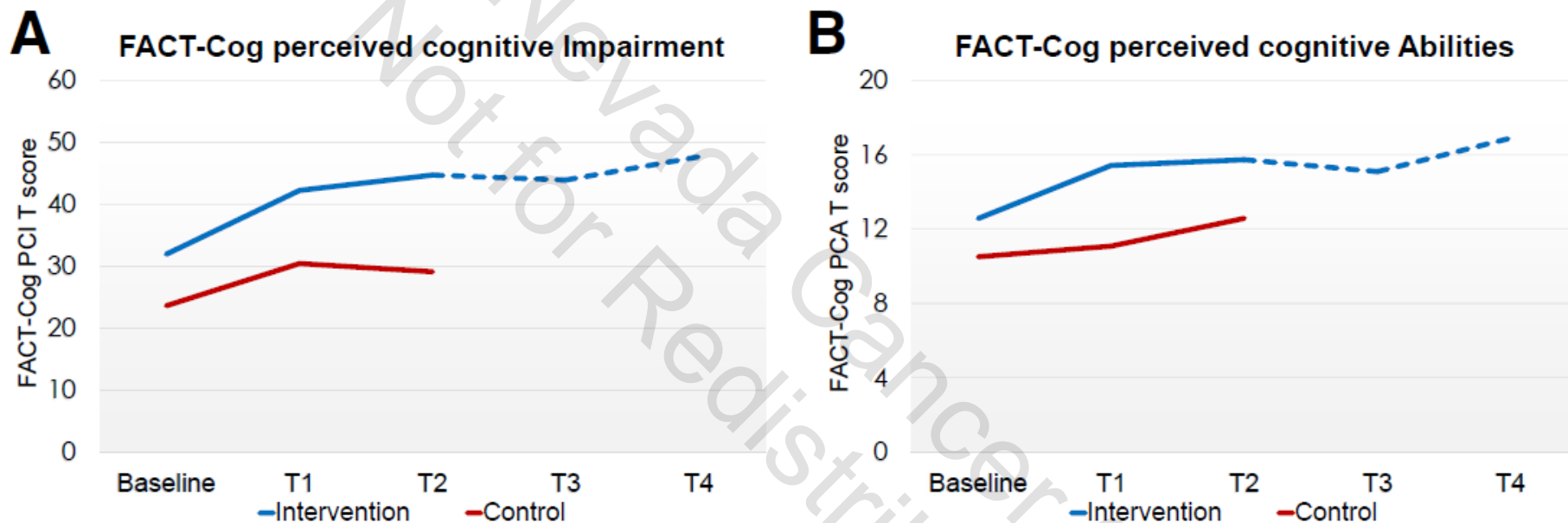


Fig 2 Lower scores on the FACT Cog PCI (A) and PCA (B) indicate more severe cognitive symptoms. The dotted line indicates continued long-term follow-up for the intervention group (with no direct comparison for the wait list control because they were offered the intervention after T2).

ASCO Quality Care Symposium 2021: Abstract 347169 *Emerging from the Haze*: Feasibility pilot of a virtual multi-dimensional psycho-educational cognitive rehabilitation intervention for cancer survivors with decreased perceived cognitive function after cancer therapy

Arash Asher, MD¹, Celina Shirazipour, PhD¹, Jeffrey Wertheimer, PhD, ABPP-CN¹, Jamie Myers, PhD, RN, AOCNS²

¹ Cedars-Sinai Medical Center, Los Angeles, CA

² Univ of Kansas School of Nursing, Kansas City, KS

Background:

- Standardized, effective cognitive rehabilitation interventions that can be widely disseminated are urgently needed for cancer-related cognitive impairment.
- The purpose of this single-arm pilot study was to test the feasibility of a virtual delivery of a cognitive rehabilitation intervention for participants in virtual groups.
- Study aims included:
 - (1) Recruit 30 participants and achieve a 70% retention rate
 - (2) Demonstrate feasibility/acceptability of measures assessing determinants of behavior change (missing data <25%; reliability $\geq .70$)
 - (3) Explore interventional impact on perceived cognitive function (PCF), determinants of behavior change, and loneliness.

Methods:

- Adult cancer survivors reporting impaired cognitive function following primary treatment were enrolled from two cancer centers and affiliates.
- Two cohorts (N=37) attended six weekly sessions and completed pre-/post- patient reported outcome questionnaires designed to measure PCF, loneliness, and determinants of behavior change for exercise, sleep, and mindfulness.

- Virtual delivery of cognitive rehabilitation interventions may be feasible and acceptable to cancer survivors
- Loneliness may be an important predictor of both issues with cognitive function and intention to change behavior.

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Results:

- Participant retention rate was 85%.
- Measures of determinants of behavior change were reliable ($r \geq .70$) across all three behaviors.
- Post-intervention scores for PCF, determinants of behavior change, and loneliness ratings significantly improved

Significant Results for Wilcoxon Signed Rank Test

Measure	Baseline		Post-Intervention		Sig	
	N	Mean, SD	Measure	N		Mean, SD
PROMIS Cognitive Function	37	35.86, 7.72	PROMIS Cognitive Function	33	40.42, 6.58	.000
PROMIS Cognitive Function Abilities	37	38.44, 6.40	PROMIS Cognitive Function Abilities	33	43.90, 6.52	.000
UCLA Loneliness	37	42.22, 9.80	UCLA Loneliness	34	29.94, 14.66	.001

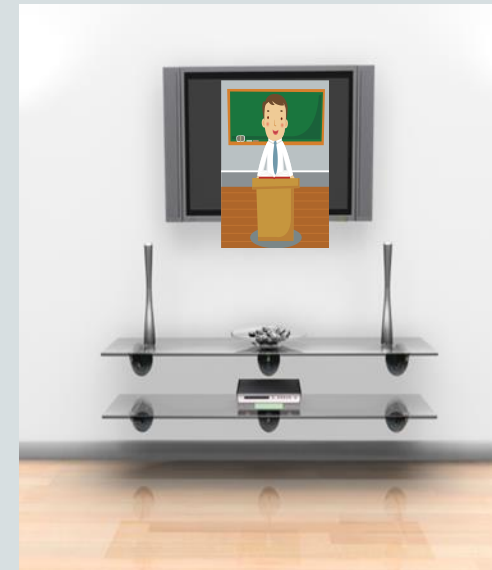
How do we *effectively* disseminate novel interventions for common cognitive concerns related to cancer and its treatment?

Standardized Video Productions



EMERGING FROM THE HAZE™

- **Recent Pilot**
 - Enrolling 90 adults with stage I-III solid tumors, HD or NHL
 - Report cognitive issues after receiving chemotherapy
 - Between 6 months and 5 years of chemotherapy completion
- Block randomization into 3 Groups:
 - Group 1: real-time virtual delivery in groups
 - Group 2: pre-recorded virtual delivery in groups
 - Group 3: wait-list control
- **Participants will:**
 - Attend 10 weekly zoom sessions
 - Complete study questionnaires at 3 timepoints (one week prior, at week 10, and week 14)
 - Receive a small stipend for completion of all 3 study questionnaires (\$50)



Next Step: Evaluate use of pre-recorded version

Co-I's: Arash Asher, MD Celina Shirazipour, PhD; Jeffrey Wertheimer, PhD (Cedars-Sinai)

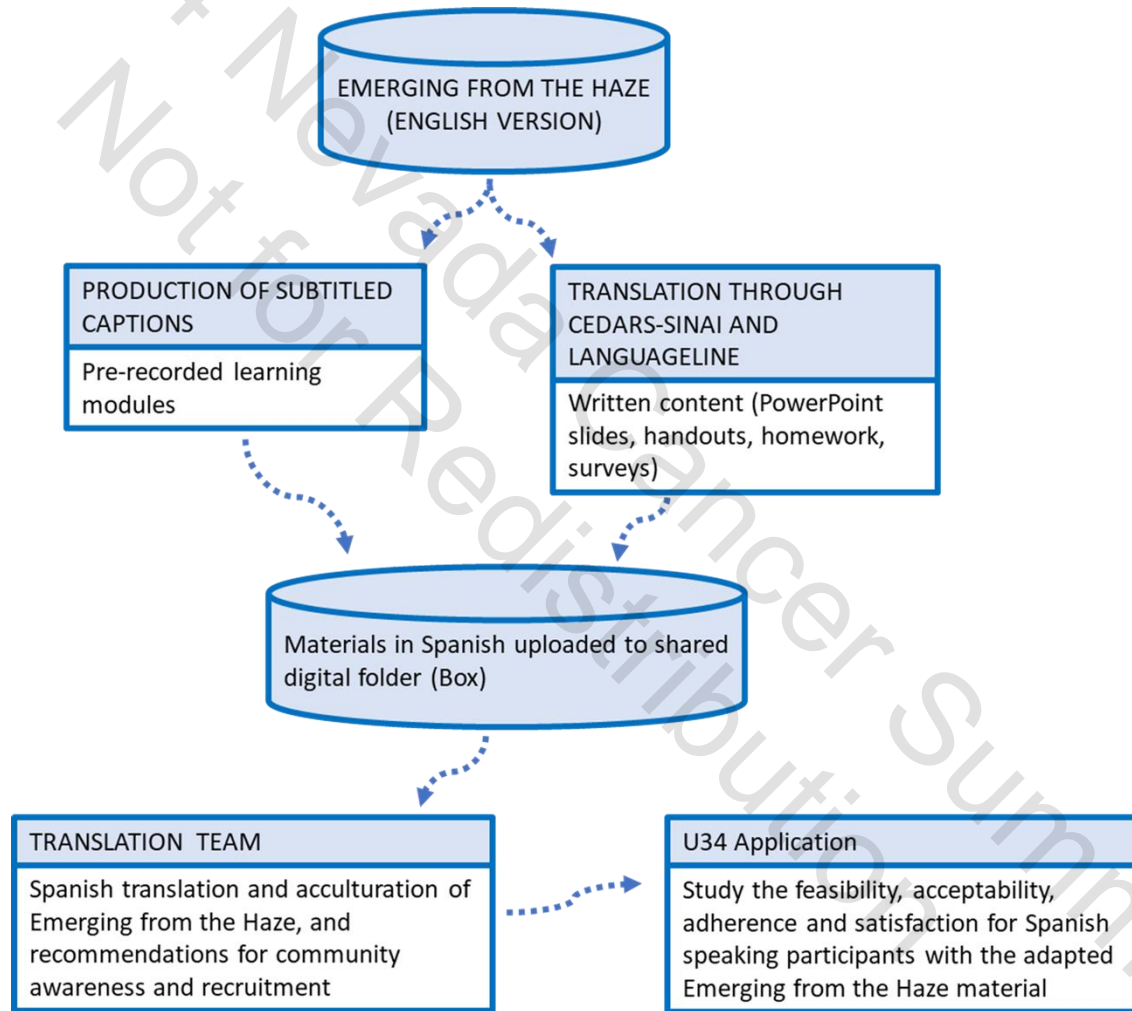
PI: Jamie Myers PhD, RN, AOCNS (University of Kansas).

Funded by the Oncology Nursing Foundation RE03 Award.

Emerging from the Haze: Randomized, wait-list controlled pilot comparing two virtual delivery formats of a cognitive rehabilitation intervention for cancer survivors reporting impaired cognitive function following chemotherapy

- Target enrollment was exceeded (n=93/90). Overall retention was 88% with 84% for the live group, 87% for the pre-recorded group and 90% for WLC.
- Significant perceived cognitive functioning reported for the “live” group versus WLC (PCA- $p=0.010$, $d=.707$) at week 10. PCF improvement reported for the “pre-recorded” group versus WLC was clinically meaningful with a moderate effect size (PCI- $p=0.10$, $d=0.443$) at week 10.
- No significant between-group difference for perceived cognitive functioning
- Study results need future multi-site research powered to detect moderate effect sizes to demonstrate efficacy for “pre-recorded” group delivery.

Community Outreach and Engagement, Diversity Equity and Inclusion: Emerging from the Haze: A multidialectal approach to improve access for Spanish speaking cancer survivors



Pilot Study of *Individual* Viewing of Haze

Primary Aim: Demonstrate the feasibility of a virtually delivered individual viewing format for Emerging from the Haze.

Aim 2: Explore the impact of the virtually delivered individual viewing format on change in perceived cognitive function (PCF).

Aim 3: Explore the impact of the virtually delivered individual viewing format on changes in health behaviors (physical activity, sleep) and health related quality of life (HRQOL).



Loneliness as a Risk Factor for Cancer-Related Cognitive Impairment

	FACT CogPCI	FACT CogPCA	PROMIS Cog Ability	Promis Cog Concerns	N=53
UCLA Loneliness Scale	- .63	- .57	- 0.49	0.50	Spearman Correlation
	<.0001	<.0001	0.0002	0.0002	p-value

What else can be offered outside of a formal cancer-focused cognitive rehabilitation program?



NCCN Survivorship Guidelines 2023: Cognitive Function

CANCER-ASSOCIATED COGNITIVE DYSFUNCTION-SPECIFIC INTERVENTIONS

FIRST-LINE INTERVENTIONS

- Neuropsychological evaluation/testing and recommendations^c
- Cognitive rehabilitation
 - ▶ Occupational therapy^d
 - ▶ Speech therapy
 - ▶ Neuropsychologist
- Psychotherapy
- Recommend routine physical activity [\(HL-1\)](#)

SECOND-LINE INTERVENTIONS

- Consider referral to a clinician with expertise in memory or cognitive concerns for further evaluation and care for survivors who continue to have memory problems after rehabilitation
- Consider trial use of medications (methylphenidate, modafinil, or donepezil)^e



Coordination of Care

Occupational Therapy

- Encourage patients to do the most cognitively demanding tasks at the time of day when energy is highest
- Support coping and self-management strategies

Using the Rehab Team

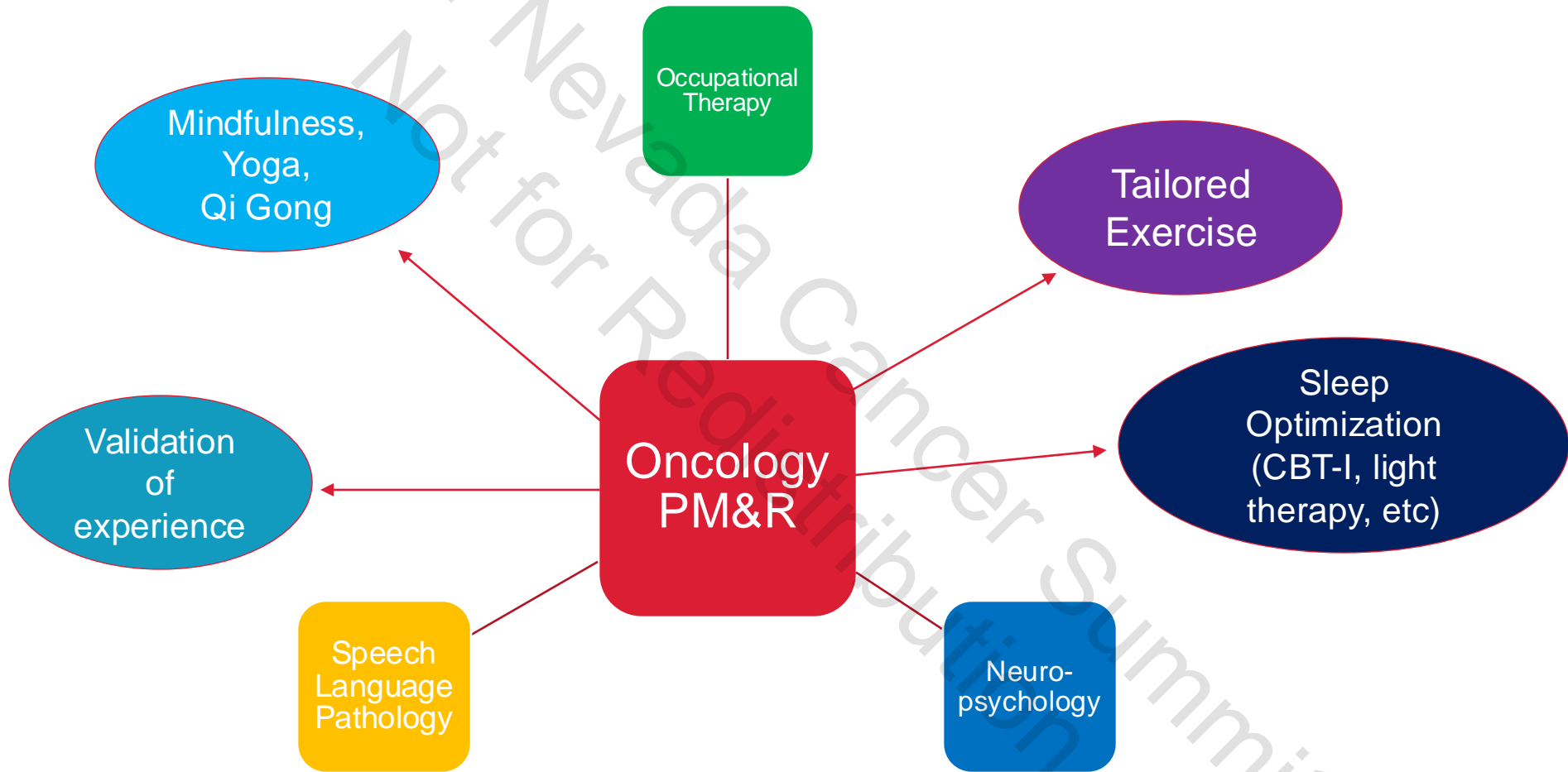
Speech Language Pathology

- Teach enhanced organizational strategies

Neuro-
psychology

- Stress Management
- Testing (select cases)
- Cognitive Rehab (if available)

Coordination of Care



Photobiomodulation Pilot Study for CRCI



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THOR LED Helmet



The THOR LED helmet has been reviewed by the FDA through the 510(k) process and received the 510(k) number K033923.

Study Arms

Randomized, double blinded, pilot study of Photobiomodulation for Cancer-Related Cognitive Impairment

- Single site study: Cedars-Sinai Medical Center (CSC at SOCC)
- 30 cancer survivors with cancer-related cognitive impairment

Arm A

- Intervention Group – use of a PBM helmet 3x per week for 6 weeks. Helmet will be in 'therapeutic setting', $35\text{mW}/\text{cm}^2=42\text{J}/\text{cm}^2$

Arm B

- Control Group – Use of a PBM helmet 3x per week for 6 weeks. Helmet will be in 'placebo setting', $0\text{mW}/\text{cm}^2=0\text{J}/\text{cm}^2$

Pilot Study of Photobiomodulation for Cancer Related Cognitive Impairment

A research study:

Cedars-Sinai Cancer is seeking participants for a research study that will examine how a 6-week intervention wearing a helmet which emits nonionizing light sources can impact cancer-related cognitive impairment.

To be eligible for this study, you must be:

- Aged 18 or over
- Previous diagnosis of stage I-III non-central nervous system solid tumor malignancy, Hodgkin, or Non-Hodgkin lymphoma
- Completed cancer treatment more than 6 months ago but less than 5 years ago
- Self-reported cognitive complaints
- English or Spanish speaking



If you choose to participant you will be asked to:

- Attend 3 in-person sessions per week for 6 weeks at the Cedars-Sinai Rehab Gym at 250 N. Robertson, Beverly Hills, 90211
- Sessions will include wearing a helmet which emits nonionizing light for up to 40 mins and completing study questionnaires

Thank you



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