

UNC Lineberger Cancer Network
PATIENT CENTERED CARE
Live Webinar
Zev Nakamura, MD
Improving Recognition and Treatment of Cognitive Problems in Cancer
August 9

Poll Everywhere for Q&A poll-ev.com/unclcn
Upcoming Live Webinars learn.unclcn.org/live
Self-Paced, Online Courses learn.unclcn.org/spoc

Sound Check
11:55

Start Time
12:00


Contact UNCLCN
Questions, Feedback, Technical Support:
Phone: (919) 445-1000
Email: unclcn@unc.edu
Website: unclcn.org

This program co-provided with
UNC Digital and Lifelong Learning

1

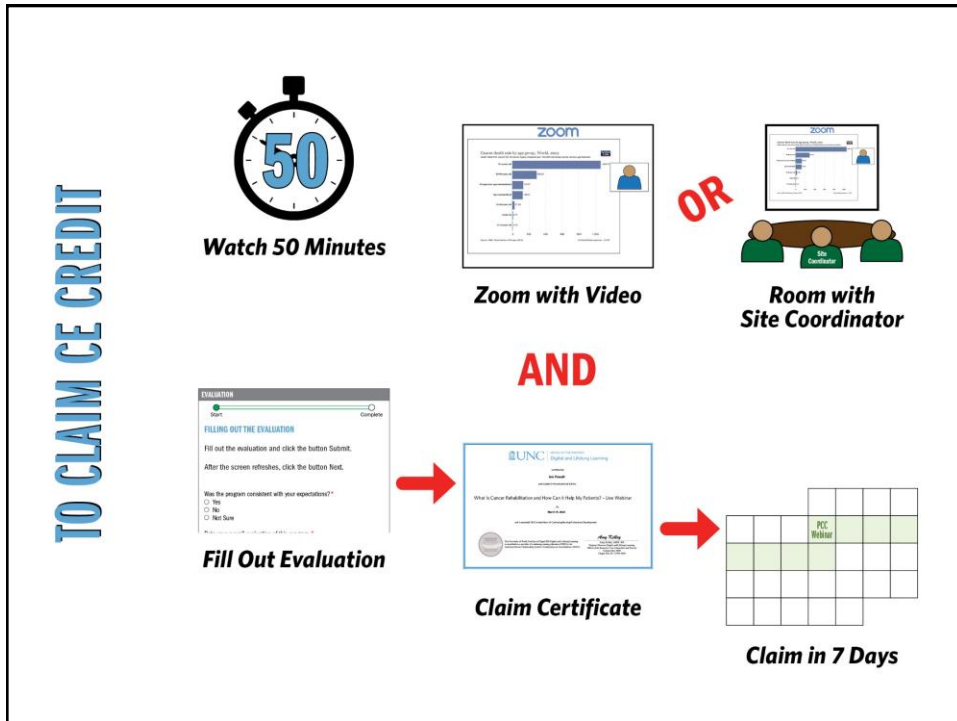
POLL EVERYWHERE

Join by Web

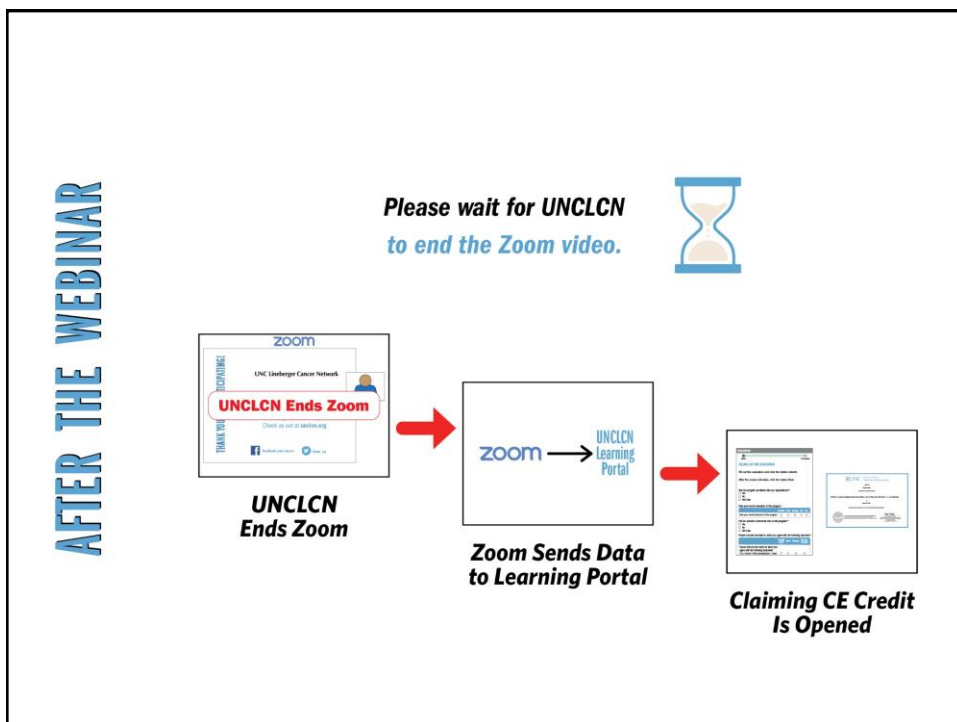


- 1 Go to PollEv.com
- 2 Enter UNCLCN
- 3 Respond to activity

2



3



4

CONTINUING EDUCATION CREDITS

FREE CE Credits with Live Webinars
Only Available at the Day and Time Indicated

<p>PATIENT CENTERED CARE</p> <p>2nd Wednesday Jan-Oct NCPD/CNE 1st Wednesday Nov-Dec ACPE ASRT CTR</p> <p>12 pm - 1 pm</p>	<p>ADVANCED PRACTICE PROVIDER</p> <p>3rd Wednesday Jan-Oct NCPD/CNE 2nd Wednesday Nov-Dec</p> <p>4 pm - 5 pm</p>
<p>RESEARCH TO PRACTICE</p> <p>4th Wednesday Jan-Oct CME 3rd Wednesday Nov-Dec NCPD/CNE ACPE ASRT CTR</p> <p>12 pm - 1 pm</p>	<p>SOUTHEASTERN AMERICAN INDIAN CANCER HEALTH EQUITY PARTNERSHIP</p> <p>1st Wednesday Feb, May, Nov CME NCPD/CNE</p> <p>12 pm - 1 pm</p>

FREE CE Credits with Self-Paced, Online Courses
Available any Day and Time

learn.unclcn.org

5

UNC Lineberger Cancer Network

PATIENT CENTERED CARE

Live Webinar

Zev Nakamura, MD

Improving Recognition and Treatment of Cognitive Problems in Cancer

August 9

6

OUR PRESENTER



Zev Nakamura, MD

Dr. Nakamura a psychiatrist and clinical researcher with advanced training in psycho-oncology and a career focus to improve cognitive outcomes in patients with cancer. His goal for this line of research is to rigorously evaluate objectively measured and patient-reported outcomes of cognition, understand how other psychosocial and biological variables impact cognition, and test interventions to prevent or treat the cognitive consequences of cancer and cancer care. Related to his interest in cognitive outcomes in cancer patients, he has led foundation and NIH-funded clinical trials to ameliorate delirium during hospitalization for stem cell transplantation and mitigate cognitive decline during chemotherapy for breast cancer. His research has also examined a wide range of neuropsychiatric symptoms (e.g., depression, anxiety, grief) in oncology and other medical illnesses.

7

OUR PRESENTER

8

OUR PRESENTER

5. Dr. Nakamura authored a review of psychiatric care for patients receiving bone marrow transplantation that was recognized as the most outstanding manuscript published in "Psychosomatics" in 2019.

9

OUR PRESENTER

5. Dr. Nakamura authored a review of psychiatric care for patients receiving bone marrow transplantation that was recognized as the most outstanding manuscript published in "Psychosomatics" in 2019.
4. He is the Associate Editor for the journal "Contemporary Clinical Trials."

10

OUR PRESENTER

5. Dr. Nakamura authored a review of psychiatric care for patients receiving bone marrow transplantation that was recognized as the most outstanding manuscript published in "Psychosomatics" in 2019.
4. He is the Associate Editor for the journal "Contemporary Clinical Trials."
3. He co-led the psychiatry arm of UNC's multidisciplinary long-haul COVID clinic.

11

OUR PRESENTER

5. Dr. Nakamura authored a review of psychiatric care for patients receiving bone marrow transplantation that was recognized as the most outstanding manuscript published in "Psychosomatics" in 2019.
4. He is the Associate Editor for the journal "Contemporary Clinical Trials."
3. He co-led the psychiatry arm of UNC's multidisciplinary long-haul COVID clinic.
2. He has been awarded the prestigious William Webb Fellowship and Early Career Research Mentee Award from the Academy of Consultation-Liaison Psychiatry.

12

OUR PRESENTER

1. He directs the UNC Comprehensive Cancer Support Program Psycho-oncology Clinic for psychiatry fellows.
2. He has been awarded the prestigious William Webb Fellowship and Early Career Research Mentee Award from the Academy of Consultation-Liaison Psychiatry.
3. He co-led the psychiatry arm of UNC's multidisciplinary long-haul COVID clinic.
4. He is the Associate Editor for the journal "Contemporary Clinical Trials."
5. Dr. Nakamura authored a review of psychiatric care for patients receiving bone marrow transplantation that was recognized as the most outstanding manuscript published in "Psychosomatics" in 2019.

13

Join by Web PollEv.com/uncfcn Join by Text Send **uncfcn** to 22333



UNC Lineberger Cancer Network

Chemobrain is the preferred medical terminology to refer to cognitive difficulties experienced by cancer patients due to cancer and its treatments.

(A) True	0%
(B) False	0%

14

DISCLOSURES

This activity has been planned and implemented under the sole supervision of the Course Director, William A. Wood, MD, MPH, in association with the UNC Office of Continuing Professional Development (CPD). The course director and CPD staff have no relevant financial relationships with ineligible companies as defined by the ACCME.

The University of North Carolina at Chapel Hill is accredited with distinction as a provider of nursing continuing professional development by the American Nurses Credentialing Center's Commission on Accreditation.

A potential conflict of interest occurs when an individual has an opportunity to affect educational content about health-care products or services of a commercial interest with which they have a financial relationship. The speakers and planners of this learning activity have not disclosed any relevant financial relationships with any commercial interests pertaining to this activity.

15

 **Chemobrain is the preferred medical terminology to refer to cognitive difficulties experienced by cancer patients due to cancer and its treatments.**

True 0%

False 0%

Start the presentation to see live content. For screen share software, share the entire screen. Get help at pollev.com/app

16

IMPROVING RECOGNITION AND TREATMENT OF COGNITIVE PROBLEMS IN CANCER

Zev Nakamura, MD
Assistant Professor
Department of Psychiatry
Lineberger Comprehensive Cancer Center
Patient Centered Care Series
8/9/23

17

OUTLINE

- Background
- Causes and underlying mechanisms
- Screening and diagnosis
- Treatment

18

LEARNING OBJECTIVES

1. Identify causes of cancer-related cognitive dysfunction
2. Describe the impact of cognitive problems in cancer patients on quality of life and medical outcomes
3. Recognize key aspects of workup for patients with cancer experiencing cognitive difficulties
4. Discuss available resources for patients with cancer who are experiencing cognitive problems
5. Recognize available treatments for patients with cancer experiencing cognitive dysfunction

19

HISTORICAL PERSPECTIVE

- Awareness since 1970s - “Serial Cognitive Testing in Cancer Patients Receiving Chemotherapy” (Oxman 1980)
- “Chemobrain” defined in late 1990s in cross-sectional studies in breast CA
- 2002 – Ahles et al. showed long-term effects of chemo
- 2004 – Wefel et al. first prospective longitudinal study
- Growing appreciation for cognitive difficulties resulting from cancer **and** its treatments over the last 15-20 years (i.e. CRCD, CRCI, “Tumor brain”)

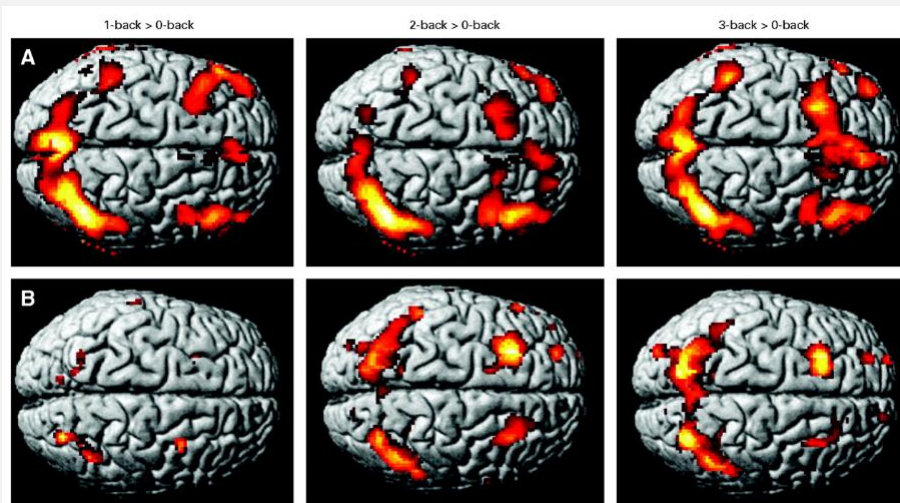
20

CANCER-RELATED COGNITIVE DYSFUNCTION (CRCDD)

- Problems in memory, concentration, executive function
- Typically subtle, but can be dramatic
- At least mild objectively measured deficits in ~50% and 75% according to self-report
- Variable course

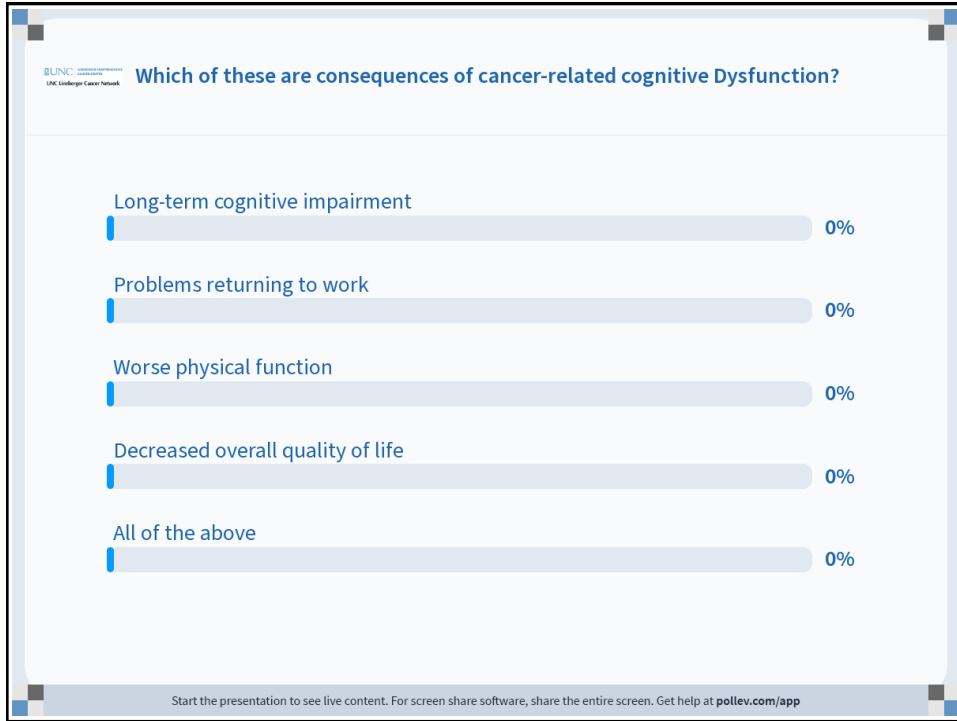
Friedman 2009, Syrjala 2011, Lin 2018, Root 2018, Gregory 2014, Buchbinder 2018

21



Ferguson 2007

22



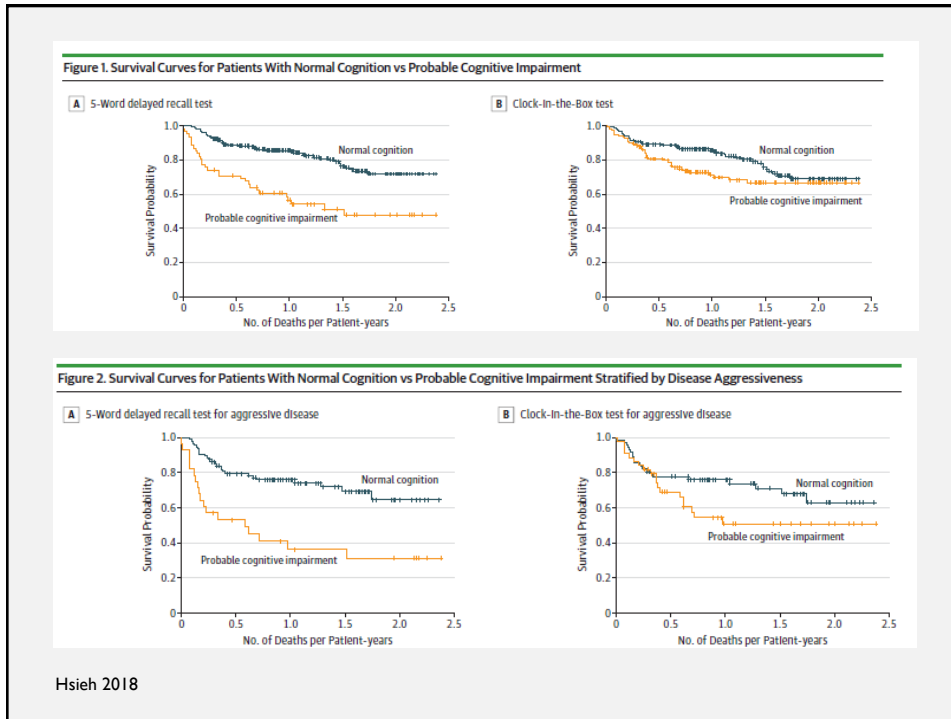
23

SIGNIFICANCE OF CRCD

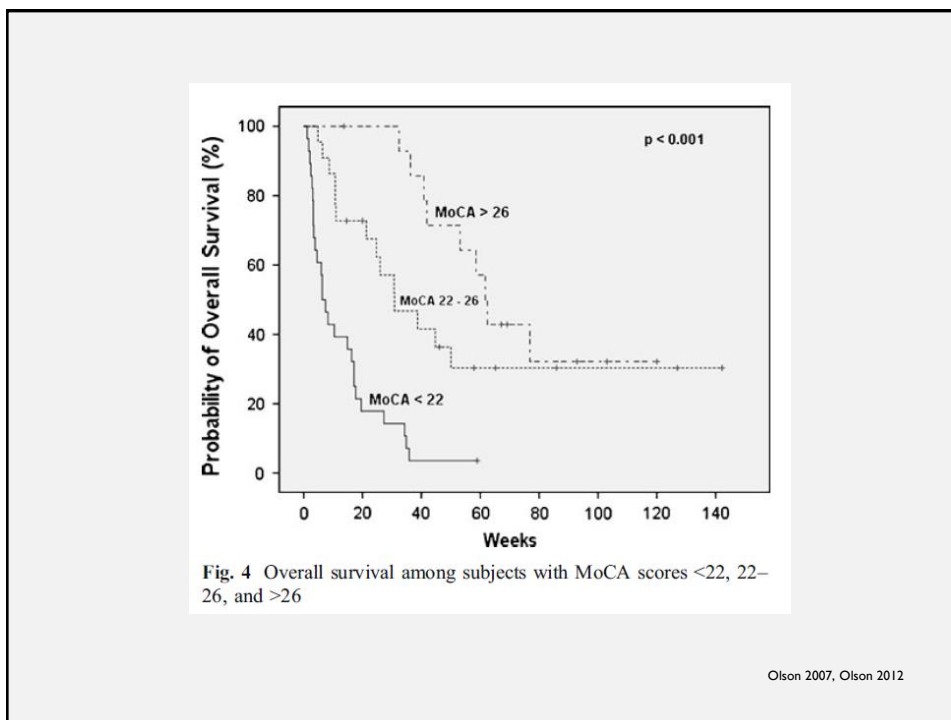
- Greater influence on chemotherapy prescribing than age or functional status
- Worsens medication compliance
- Decreased occupational productivity
- Associations
 - adverse mental health
 - worse emotional and social well-being
 - impaired physical function
 - frailty
 - increased mortality
- One of the most feared problems among cancer survivors

Janelsins 2014, Yang 2018, Von Ah 2021, Von Ah 2015, Klaver 2020, Nakamura 2020, Hshieh 2018, Mohile 2018

24




25



26

CRCD AND CHEMOTHERAPY TOXICITY



Journal of Geriatric Oncology
Volume 11, Issue 2, March 2020, Pages 284-289


Association between a cognitive screening test and severe chemotherapy toxicity in older adults with cancer

Reena V. Jayani^a, Allison M. Magnuson^b, Can-Lan Sun^a, Huiyan Ma^a, William P. Tew^a, Supriya G. Mohile^a, Ajeet Gajra^a, Heidi D. Klepin^a, Cary D. Gross^b, Hyman B. Muss^a, Andrew F. Chapman^a, Vani Katheria^a, Arti Hurria^a, William Dale^a & ^a ^b

- 703 pts ≥ 65 yo
- Potential cognitive impairment in 36% (BOMC 5-10)
- Grade 3+ chemotherapy toxicity in 55%
- Potential cognitive impairment increased risk of severe toxicity

	Univariate Analysis			Adjusted Analysis ^a				
	Severe Chemotherapy Toxicity		OR (95% CI)	p-value	Severe Chemotherapy Toxicity		OR (95% CI)	p-value
	No	Yes			No	Yes		
Overall								
Cognition								
Normal	222	231	1.54 (1.13-2.11)	0.007	211	222	1.35 (0.96-1.90)	0.08
Potential Impairment	96	154			92	144		
High School Education or Less								
Normal Cognition	75	78	1.94 (1.10-3.08)	0.02	72	77	1.87 (1.06-3.29)	0.03
Potential Impairment	36	69			33	64		
Greater than High School Education								
Normal Cognition	146	153	1.35 (0.91-2.02)	0.14	138	145	1.13 (0.73-1.74)	0.58
Potential Impairment	60	85			59	80		

27

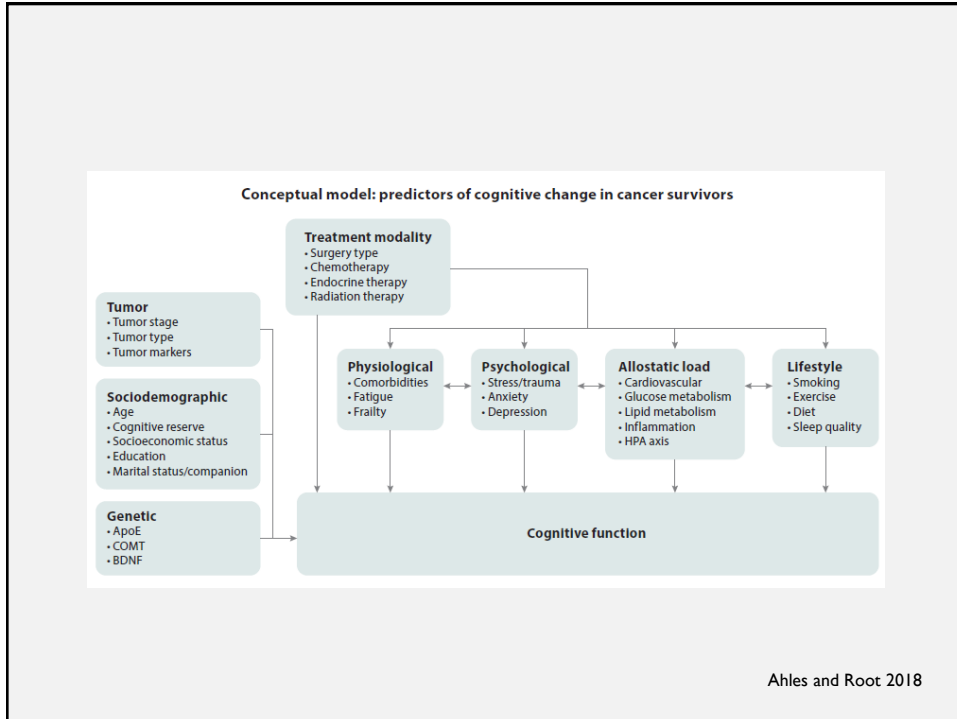


Which of These Contribute to the Development of CRCD?

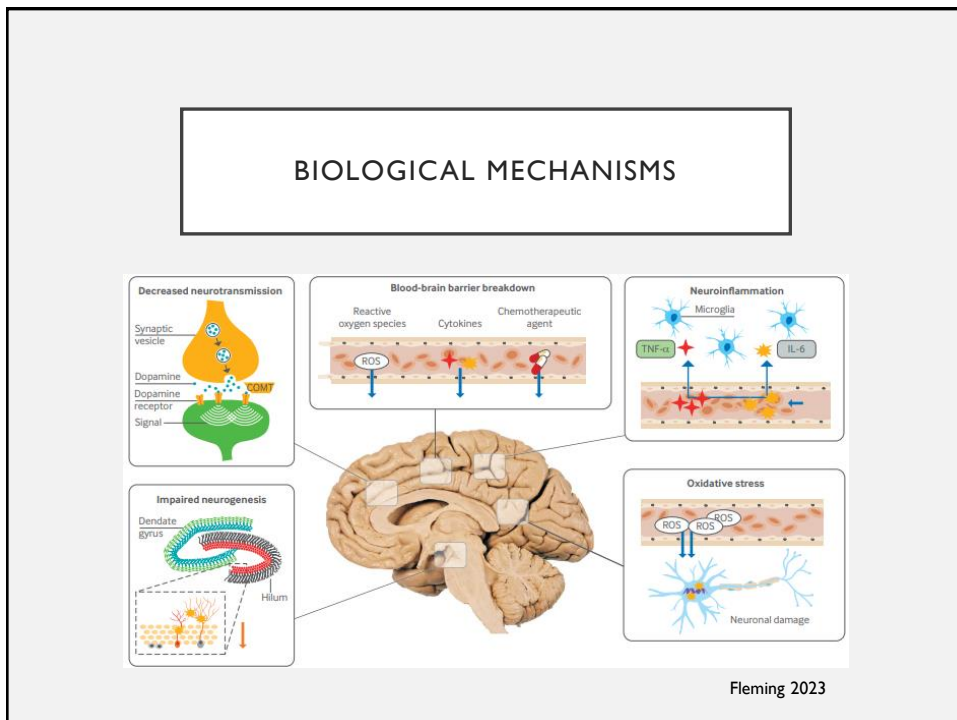
- 0%
- 0%
- 0%
- 0%
- 0%

Start the presentation to see live content. For screen share software, share the entire screen. Get help at pollev.com/app

28



29



30

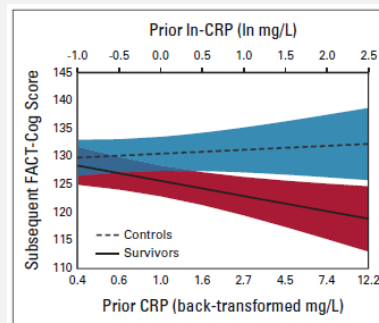
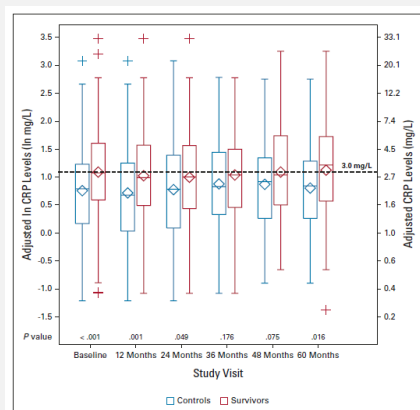
INFLAMMATION

- Associated with ↑ risk for cancer and neurocognitive disorders
- ↑ cytokine levels in CA pts at baseline relative to controls
- ↑ during chemo and during hospitalization for HSCT
- ↓ (but stay elevated) with time
- Correlate with objective and self-reported CRCD

Patel 2015, Wang 2016, Kesler 2013, Lyon 2016, Hoogland 2019

31

ELEVATED C-REACTIVE PROTEIN PREDICTIVE OF SELF-REPORTED COGNITIVE PROBLEMS

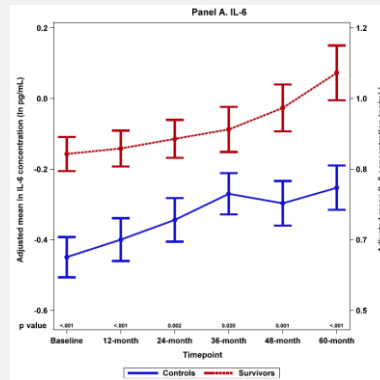


Carroll, Nakamura, Small et al. 2022

32

INTERLEUKIN-6 PARTIALLY ACCOUNTS FOR WORSE COGNITION IN CANCER SURVIVORS COMPARED TO CONTROLS

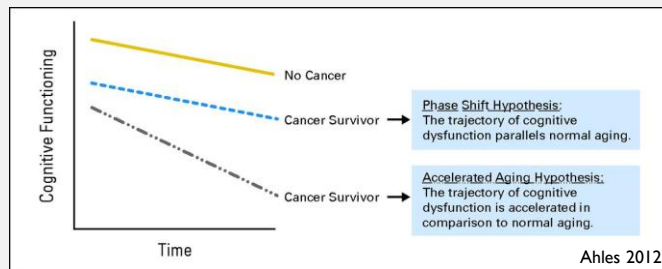
- Survivors had significantly higher IL-6 levels than controls over time
- Survivors had lower attention/executive function scores than controls ($p < .05$).
- Levels of IL-6, IL-10, and TNF- α related to cognitive performance
- IL-6 mediated the relationship between survivor/control group and cognition ($p = .01$).



Mandelblatt 2023

33

CRCD IN THE CONTEXT OF ACCELERATED AGING



- Inflammation, oxidative stress, DNA damage, shortening of telomeres, cellular senescence
- Increased expression of p16^{INK4a} in breast cancer after chemotherapy (10 yrs chronological aging) and after autologous HSCT for multiple myeloma (34 yr of chronologic aging)

Sanoff 2014, Rosko 2015, Salas-Ramirez 2015

34

IMAGING FINDINGS

- Altered functional brain activation
- ↓gray matter volume
- ↓white matter connectivity
- Decreased volume and connectivity correlate with worse function

Sousa 2020, Kesler 2020, Deprez 2018

35

CANCER/TUMOR

- Non-CNS Cancers
 - Immune system dysfunction → disrupt brain structure and function
 - Feeling physically ill, fatigued, depressed, etc.
- Primary brain tumors and brain metastases
 - ↑ Intracranial pressure
 - Edema
 - Displacement of brain tissue
 - ↓ blood supply

36

CHEMOTHERAPY

- Most chemo cannot cross the BBB
 - CA increases BBB permeability
 - Even small amounts can cause significant damage
- Increases levels of pro-inflammatory cytokines
- Cytokines increase BBB permeability
- Elevated cytokines can lead to damage through oxidative stress and DNA damage
- Diminution of neurogenesis
- Disruption of myelin and oligodendrocyte precursors

Lange 2019

37

SURGERY

- Mastectomy implicated in cognitive effects
- May be 2/2 increased inflammation, pain, psychological effects
- Impact of anesthesia (especially in elderly)
- In pts w/ brain tumors, can improve or worsen cognitive function

Reid-Arndt 2012, Cimprich 2010, Su 2020

38

RADIATION

- **Cranial, Head & Neck**
 - Radiation necrosis
 - Disrupts creation of new neurons in the hippocampus
- **Local**
 - Some evidence for adverse cognitive effects
- **Mechanisms**
 - Chronic oxidative stress and inflammation
 - Neuronal damage
 - Changes to BBB, ischemia, oligodendrocyte function

Wilke 2018, Dong 2015, Carvalho 2018

39

HORMONAL THERAPY

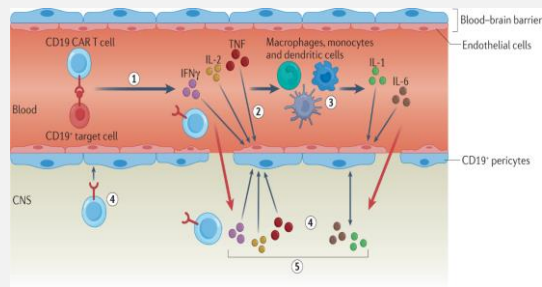
- Estrogen and testosterone support brain function
- Tamoxifen and aromatase inhibitors
 - Smaller hippocampal size
 - Combination with chemo may lead to greater cognitive difficulties
 - Other studies show no association
- ADT with adverse cognitive consequences

Ganz 2014, Van Dyk 2019, Bender 2015

40

CAR T CELL THERAPY

- 30-62% develop acute encephalopathy (ICANS), which resolves with steroids, tocilizumab
- At least one small study demonstrated patient-reported cognitive concerns in memory (35%), word-finding (30%), attention (23%), executive function (13%) 1-5 years after CAR T (Ruark 2020)



Lee 2019, Gust 2017, Santomaso 2018

41

IMMUNE CHECKPOINT INHIBITORS

- Encephalitis occurs in <1% from 4 days to 28 weeks after exposure
- May lead to neuroinflammation, which in combination with other treatments, could increase risk for CRCD
- Other candidate mechanisms include: cross-reaction w/ auto-antigens in the CNS (e.g., paraneoplastic syndrome), autoimmune, T-cell mediated direct injury
- Indirect effects via endocrinopathies (e.g. hypo/hyperthyroidism)
- Up to 37% of metastatic melanoma survivors treated with ICIs had cognitive impairment when tested 6 months after treatment
- Systematic studies are lacking

Touts 2017, Schagen 2022, Rogiers Support Care Cancer 2020, Rogiers J Immunol Res 2020

42

MEASUREMENT

No standard for screening, diagnosis, monitoring (measures or schedule)

CCF recommends

- Hopkins Verbal Learning Test
- Trail Making Test
- Controlled Oral Word Association Test

Self-report measures

- EORTC-QLQ-30
- FACT-Cog
- PROMIS Cognitive Function

Objective screening instruments

- Montreal Cognitive Assessment (MOCA)
- Mini Mental Status Exam
- Mini-Cog
- Blessed Orientation Memory Concentration Test

Computerized/digital tasks

- NIH Toolbox
- CANTAB

43

PROMIS COGNITIVE FUNCTION SHORT FORM

Please respond to each question or statement by marking one box per row.

In the past 7 days...

	Never	Rarely (Once)	Sometimes (Two or three times)	Often (About once a day)	Very often (Several times a day)
My thinking has been slow.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
It has seemed like my brain was not working as well as usual.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
I have had to work harder than usual to keep track of what I was doing.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
I have had trouble shifting back and forth between different activities that require thinking.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
I have had trouble concentrating.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
I have had to work really hard to pay attention or I would make a mistake.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
I have had trouble forming thoughts.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1
I have had trouble adding or subtracting numbers in my head.....	<input type="checkbox"/> 5	<input type="checkbox"/> 4	<input type="checkbox"/> 3	<input type="checkbox"/> 2	<input type="checkbox"/> 1

44

MOCA

MONTREAL COGNITIVE ASSESSMENT (MOCA)
Version 7.1 Original Version

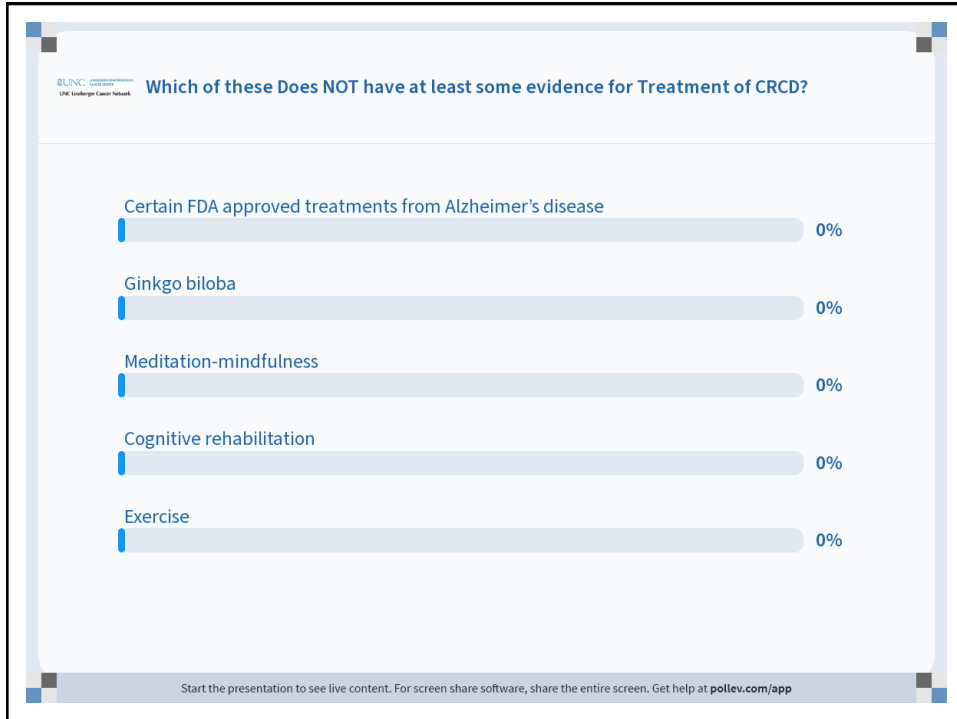
NAME: _____
Education: _____
Sex: _____
Date of birth: _____
DATE: _____

VISUOSPATIAL / EXECUTIVE	Copy cube	Draw CLOCK (Ten past eleven) (3 points)	POINTS
		<input type="checkbox"/> Contour <input type="checkbox"/> Numbers <input type="checkbox"/> Hands	___/5
NAMING			___/3

45

MEMORY	Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED		No points
		1st trial							
		2nd trial							
ATTENTION	Read list of digits (1 digit/ sec.). Subject has to repeat them in the forward order [] 2 1 8 5 4								___/2
	Subject has to repeat them in the backward order [] 7 4 2								
	Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors [] FBACMNAAJKLBFAFKDEAAAJAMOFAB								___/1
	Serial 7 subtraction starting at 100 [] 93 [] 86 [] 79 [] 72 [] 65								___/3
	4 or 5 correct subtractions: 3 pts. 2 or 3 correct: 2 pts. 1 correct: 1 pt. 0 correct: 0 pt								
LANGUAGE	Repeat : I only know that John is the one to help today. []								___/2
	The cat always hid under the couch when dogs were in the room. []								
	Fluency / Name maximum number of words in one minute that begin with the letter F [] _____ (N ≥ 11 words)								___/1
ABSTRACTION	Similarity between e.g. banana - orange = fruit [] train - bicycle [] watch - ruler								___/2
DELAYED RECALL	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	[]	[]	Points for UNCUED recall only
	Category cue	[]	[]	[]	[]	[]	[]	[]	
Optional	Multiple choice cue								
ORIENTATION	[] Date	[] Month	[] Year	[] Day	[] Place	[] City			___/6
© Z.Nasreddine MD		www.mocatest.org		Normal ≥ 26 / 30		TOTAL		___/30	
Administered by: _____								Add 1 point if ≤ 12 yr edu	

46



47

ADDRESS REVERSIBLE CONTRIBUTORS

- Sleep disorders (insomnia, sleep apnea)
- Depression, anxiety, distress
- Pain and pain medications
- Other physical illnesses
- Fatigue
- Vitamin/Mineral deficiencies
- Anemia

48

CRCO INTERVENTIONS

Behavioral: Cognitive rehabilitation, Cognitive training, Combination

Physical activity: Aerobic, strength exercise programs; Yoga

Mind-Body: Meditation, Mindfulness, Acupuncture

Pharmacotherapies: Donepezil, Memantine, Modafinil, Methylphenidate, Epo-stimulating agents, Vitamin E, Ginkgo biloba, SSRIs

49

COGNITIVE REHABILITATION ("STRATEGY TRAINING")

- Increase awareness and problem solving around difficulties
- Weekly, face-to-face sessions with Speech or Occupational Therapist
- Aids: planner, alerts, sticky notes

50

COGNITIVE TRAINING

- AKA “Brain Training”, “Brain Games”
- Repetitive, increasingly challenging tasks (often via computer)
- 4-5 days/week, 30 min/session
- HappyNeuron, Luminosity, BrainHQ

51

PHYSICAL ACTIVITY

- ↓ risk of Alzheimer’s and slows age-related cognitive decline
- Research in CRCD is growing
- Moderate intensity aerobic exercise ~150 min/week
- Get Real & Heel
- LIVESTRONG at the YMCA
- Yoga

Campbell 2020

52

MIND-BODY

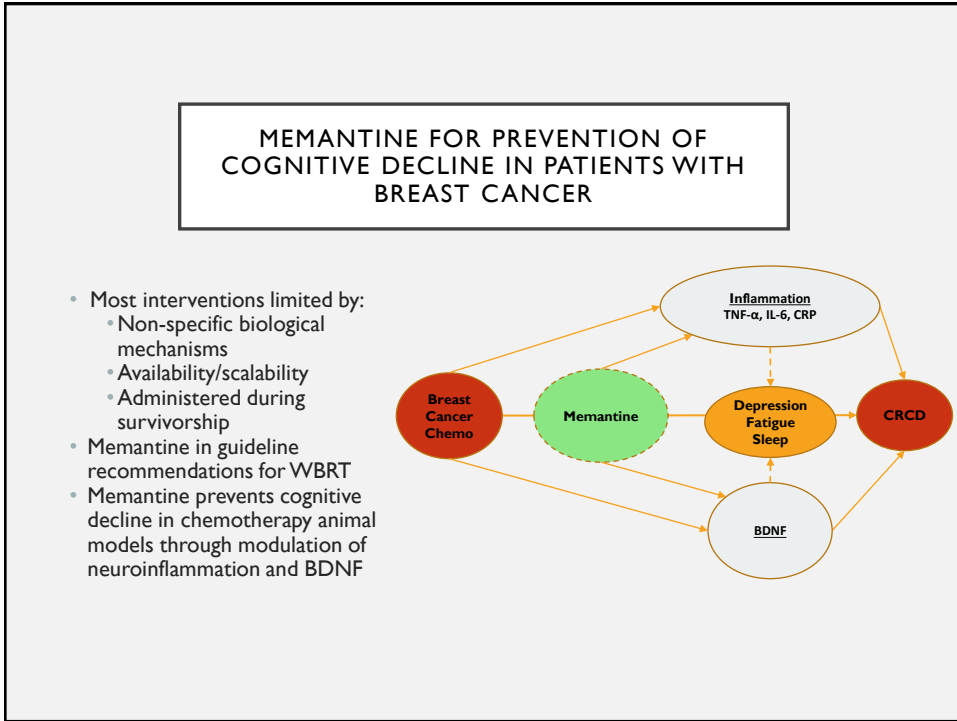
- Guided imagery
- Mindfulness
 - UCLA MAPS classes
 - UNC and Duke Integrative Medicine
 - Apps: The Mindfulness App, Sitting Still, Headspace, Insight Timer, Mindfulness Bell
- Acupuncture
 - UNC Family Medicine Acupuncture Clinic
 - NC Society of Acupuncture and Asian Medicine

53

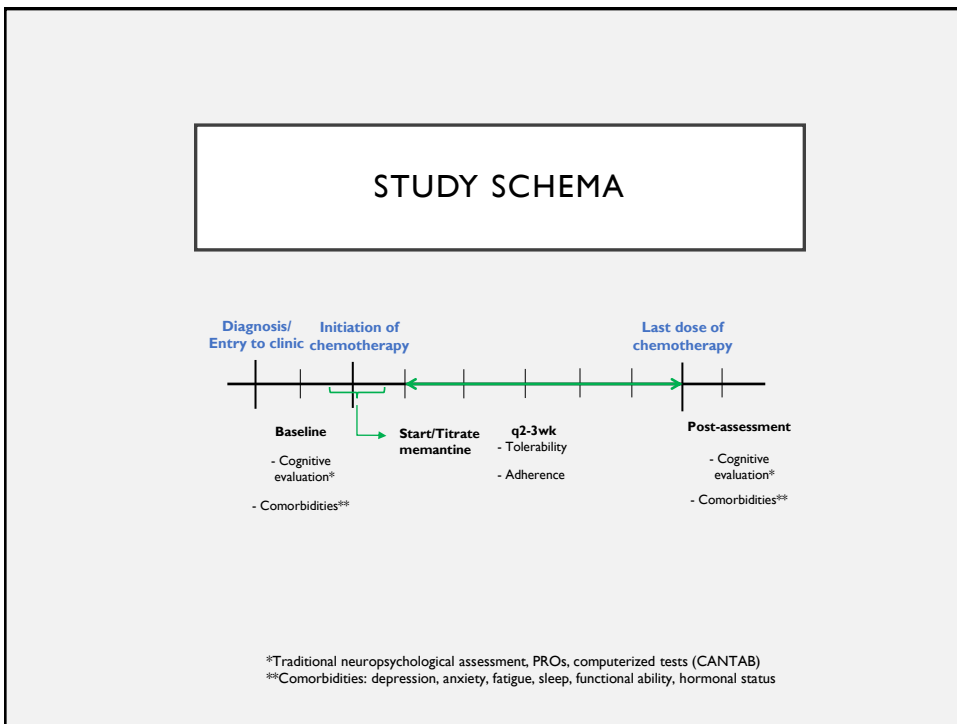
MEDICATIONS

- Stimulants (Ritalin and modafinil)
- Alzheimer's medications (donepezil and memantine)
- SSRI antidepressants
- Weigh risk/benefit

54



55



56

FEASIBILITY, TOLERABILITY, AND ACCEPTABILITY

Participant Characteristics (N=56)

	% (N)
Age, mean (SD)	56.2 (12.8)
Female	98 (55)
Race	
White	77 (43)
Black or African-American	18 (10)
More than one race	3 (5)
Education, mean (SD)	15.8 (2.2)
Stage	
I	57 (32)
II	27 (15)
III	16 (9)
HER2+	29 (16)
HR+	68 (38)
Adjuvant	64 (36)
Anthracycline-based regimens	43 (24)

Feasibility and Safety

- **Recruitment Rate:** 44%
- **Retention Rate:** 80%
- **Adherence:** 76% received \geq 90% scheduled doses
- **AEs:** 2 at least probably related to memantine; both grade I

Acceptability

	Agree or Strongly Agree (%)	Uncertain (%)	Disagree or Strongly Disagree (%)
Having to take memantine worried me	7	7	86
I sometimes worried about long-term effects of memantine	16	12	72
Memantine disrupted my life	5	5	91

Nakamura 2023

57

COGNITIVE CHANGES

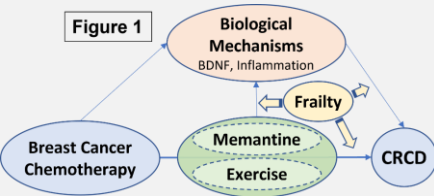
Measure	Improved (%)	No Change (%)	Declined (%)
Attention/Executive Function	22	64	13
Digit Span Forwards	16	69	15
Digit Span Backwards	35	35	29
Controlled Oral Word Association Test	40	40	20
Animal Naming	22	36	42
Delayed Matching to Sample	36	29	36
Rapid Visual Processing	32	55	13
One Touch Stockings of Cambridge	29	52	19
Learning/Memory	47	40	13
HVLT-R Total Recall	49	36	16
HVLT-R Delayed Recall	51	36	13
Global	24	67	9

Nakamura 2023

58

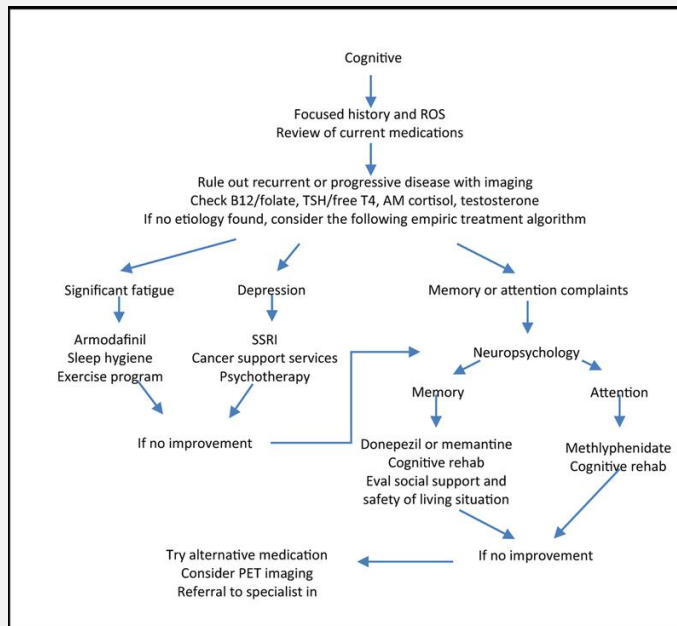
RATIONALE FOR MULTICOMPONENT TREATMENTS

- Limited efficacy for monotherapeutic approaches
- Inter-individual variability in mechanisms driving CRCD
- Opportunities to augment highly targeted medications with biobehavioral interventions that have more diffuse targets
- Exercise stimulates BDNF, lowers inflammation, but also a promising treatment for frailty
- Exercise safe during cancer treatment and beneficial for fatigue, physical function, mood



Campbell 2020, Ligibel 2022, Racey 2021, Cesari 2015

59



Cramer 2019

60

SUMMARY

- CRCD is common and consequential
- Multiple mechanisms, converging on inflammation and accelerated aging
- Measurement
 - Self-report and objective measures
 - Self-report should include FACT-Cog or, at minimum, the PROMIS Cognitive Function Short Form 8a
 - Neuropsych batteries should reflect ICCTF recommendations
- Workup/Treatment
 - B12, folate, vitamin D, TSH/FT4
 - Address depression/anxiety, sleep problems (e.g., sleep study)
 - Consider referral for neuropsychological testing
 - Referral for cognitive rehab (e.g., SLP, OT)
 - Trials of memantine/donepezil vs. stimulants

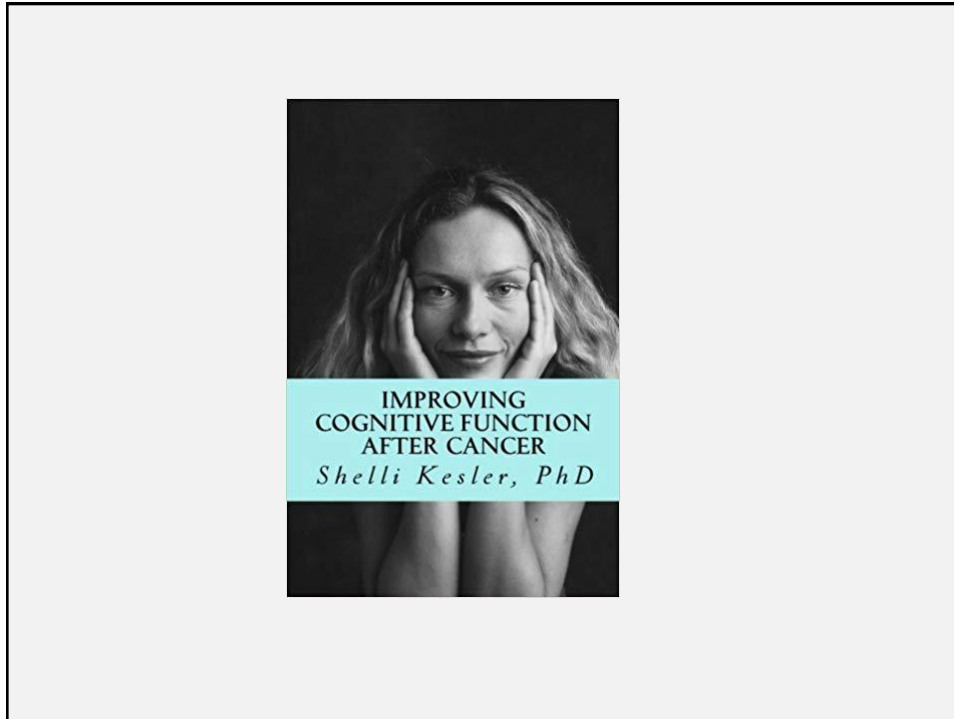
61

UNC COMPREHENSIVE CANCER SUPPORT PROGRAM (CCSP)



<https://unclineberger.org/ccsp/>

62



63

REFERENCES

- Ahles, T. A., & Root, J. C. (2018). Cognitive Effects of Cancer and Cancer Treatments. *Annual Review of Clinical Psychology, 14*, 425–451. <https://doi.org/10.1146/annurev-clinpsy-050817-084903>
- Ahles, T. A., Root, J. C., & Ryan, E. L. (2012). Cancer- and cancer treatment-associated cognitive change: An update on the state of the science. *Journal of Clinical Oncology, 30*, 3675–3686. <https://doi.org/10.1200/JCO.2012.43.0116>
- Allemann-Su, Y.-Y., Vetter, M., Koechlin, H., Conley, Y., Paul, S. M., Cooper, B. A., Kober, K. M., Levine, J. D., Miaskowski, C., & Katapodi, M. C. (2023). Distinct cognitive function profiles are associated with a higher presurgery symptom burden in patients with breast cancer. *Cancer Nursing, 46*(4), E208–E217.
- Campbell, K. L., Zadavec, K., Bland, K. A., Chesley, E., Wolf, F., & Janelsins, M. C. (2020). The Effect of Exercise on Cancer-Related Cognitive Impairment and Applications for Physical Therapy: Systematic Review of Randomized Controlled Trials. *Physical Therapy, 100*(3), 523–542.
- Cimprich, B., Reuter-Lorenz, P., Nelson, J., Clark, P. M., Therrien, B., Normolle, D., Berman, M. G., Hayes, D. F., Noll, D. C., & Peltier, S. (2010). Prechemotherapy alterations in brain function in women with breast cancer. *Journal of Clinical and Experimental Neuropsychology, 32*(3), 324–331.
- Cramer, C. K., Cummings, T. L., Andrews, R. N., Strowd, R., Rapp, S. R., Shaw, E. G., Chan, M. D., & Lesser, G. J. (2019). Treatment of radiation-induced cognitive decline in adult brain tumor patients. *Current Treatment Options in Oncology, 20*, 1–16.
- Deprez, S., Kesler, S. R., Saykin, A. J., Silverman, D. H. S., De Ruiter, M. B., & McDonald, B. C. (2018). International cognition and cancer task force recommendations for neuroimaging methods in the study of cognitive impairment in non-CNS cancer patients. *Journal of the National Cancer Institute, 110*, 223–231. <https://doi.org/10.1093/jnci/djx285>
- Dong, X., Luo, M., Huang, G., Zhang, J., Tong, F., Cheng, Y., Cai, Q., Dong, J., Wu, G., & Cheng, J. (2015). Relationship between irradiation-induced neuro-inflammatory environments and impaired cognitive function in the developing brain of mice. *International Journal of Radiation Biology, 91*(3), 224–239.

64

REFERENCES

- Ferguson, R. J., Ahles, T. A., Saykin, A. J., McDonald, B. C., Furstenberg, C. T., Cole, B. F., & Mott, L. A. (2007). Cognitive-behavioral management of chemotherapy-related cognitive change. *Psycho-Oncology*, *16*(8), 772–777. <https://doi.org/10.1002/pon.1133>
- Hoogland, A. I., Nelson, A. M., Gonzalez, B. D., Small, B. J., Breen, E. C., Sutton, S. K., Syrjala, K. L., Bower, J. E., Pidala, J., & Booth-Jones, M. (2019). Worsening cognitive performance is associated with increases in systemic inflammation following hematopoietic cell transplantation. *Brain, Behavior, and Immunity*, *80*, 308–314.
- Hsieh, T. T., Jung, W. F., Grande, L. J., Chen, J., Stone, R. M., Soiffer, R. J., Driver, J. A., & Abel, G. A. (2018). Prevalence of cognitive impairment and association with survival among older patients with hematologic cancers. *JAMA Oncology*, *4*(5), 686–693.
- Janelins, M. C., Kesler, S. R., Ahles, T. A., & Morrow, G. R. (2014). Prevalence, mechanisms, and management of cancer-related cognitive impairment. *International Review of Psychiatry*, *26*(1), 102–113. <https://doi.org/10.3109/09540261.2013.864260>
- Karschnia, P., Parsons, M. W., & Dietrich, J. (2019). Pharmacologic management of cognitive impairment induced by cancer therapy. *The Lancet Oncology*, *20*, e92–102. [https://doi.org/10.1016/S1470-2045\(18\)30938-0](https://doi.org/10.1016/S1470-2045(18)30938-0)
- Kesler, S., Janelins, M., Koovakkattu, D., Palesh, O., Mustian, K., Morrow, G., & Dhabhar, F. S. (2013). Reduced hippocampal volume and verbal memory performance associated with interleukin-6 and tumor necrosis factor-alpha levels in chemotherapy-treated breast cancer survivors. *Brain, Behavior, and Immunity*, *30*(Supplement), S109–S116. <https://doi.org/10.1016/j.bbi.2012.05.017>
- Kesler, S. R., Petersen, M. L., Rao, V., Harrison, R. A., & Palesh, O. (2020). Functional connectome biotypes of chemotherapy-related cognitive impairment. *Journal of Cancer Survivorship*, *14*(4), 483–493. <https://doi.org/10.1007/s11764-020-00863-1>

65

REFERENCES

- Lange, M., Joly, F., Vardy, J., Ahles, T., Dubois, M., Tron, L., Winocur, G., De Ruyter, M. B., & Castel, H. (2019). Cancer-related cognitive impairment: an update on state of the art, detection, and management strategies in cancer survivors. *Annals of Oncology : Official Journal of the European Society for Medical Oncology*, *30*(12), 1925–1940. <https://doi.org/10.1093/annonc/mdz410>
- Lyon, D. E., Cohen, R., Chen, H., Kelly, D. L., McCain, N. L., Starkweather, A., Ahn, H., Sturgill, J., & Jackson-Cook, C. K. (2016). Relationship of systemic cytokine concentrations to cognitive function over two years in women with early stage breast cancer. *Journal of Neuroimmunology*, *301*, 74–82. <https://doi.org/10.1016/j.jneuroim.2016.11.002>
- Mohile, S. G., Magnuson, A., Pandya, C., Velarde, C., Duberstein, P., Hurria, A., Loh, K. P., Wells, M., Plumb, S., Gilmore, N., Flannery, M., Wittink, M., Epstein, R., Heckler, C. E., Janelins, M., Mustian, K., Hopkins, J. O., Liu, J., Peri, S., & Dale, W. (2018). Community oncologists' decision-making for treatment of older patients with cancer. *JNCCN Journal of the National Comprehensive Cancer Network*, *16*(3), 301–309. <https://doi.org/10.6004/jnccn.2017.7047>
- Reid-Arndt, S. A., & Cox, C. R. (2012). Stress, coping and cognitive deficits in women after surgery for breast cancer. *Journal of Clinical Psychology in Medical Settings*, *19*, 127–137.
- Sanoff, H. K., Deal, A. M., Krishnamurthy, J., Torrice, C., Dillon, P., Sorrentino, J., Ibrahim, J. G., Jolly, T. A., Williams, G., Carey, L. A., Drobish, A., Gordon, B.-B., Alston, S., Hurria, A., Kleinhans, K., Rudolph, K. L., Sharpless, N. E., & Muss, H. B. (2014). Effect of cytotoxic chemotherapy on markers of molecular age in patients with breast cancer. *Journal of the National Cancer Institute*, *106*(4), dju057. <https://doi.org/10.1093/jnci/dju057>
- Schagen, S. B., Tsvetkov, A. S., Compter, A., & Wefel, J. S. (2022). Cognitive adverse effects of chemotherapy and immunotherapy: are interventions within reach? *Nature Reviews. Neurology*, *18*(3), 173–185. <https://doi.org/10.1038/s41582-021-00617-2>

66

REFERENCES

Sousa, H., Almeida, S., Bessa, J., & Pereira, M. G. (2020). The Developmental Trajectory of Cancer-Related Cognitive Impairment in Breast Cancer Patients: A Systematic Review of Longitudinal Neuroimaging Studies. *Neuropsychology Review*, *30*(3), 287–309. <https://doi.org/10.1007/s11065-020-09441-9>

Von Ah, D., & Crouch, A. (2021). Relationship of perceived everyday cognitive function and work engagement in breast cancer survivors. *Supportive Care in Cancer*, *29*, 4303–4309. <https://doi.org/10.1007/s00520-020-05950-8>

Wilke, C., Grosshans, D., Duman, J., Brown, P., & Li, J. (2018). Radiation-induced cognitive toxicity: pathophysiology and interventions to reduce toxicity in adults. *Neuro-Oncology*, *20*(5), 597–607.

Zimmer, P., Baumann, F. T., Oberste, M., Wright, P., Garthe, A., Schenk, A., Elter, T., Galvao, D. A., Bloch, W., Hübner, S. T., & Wolf, F. (2016). Effects of exercise interventions and physical activity behavior on cancer related cognitive impairments: A systematic review. *BioMed Research International*, *2016*, 1820954. <https://doi.org/10.1155/2016/1820954>

67

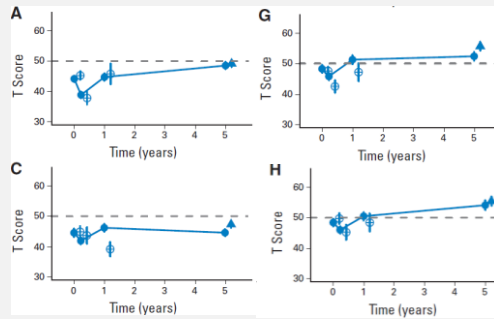
CRCD AND FRAILITY

- Frailty is the phenotypic representation of dysregulation across multiple physiological systems
- Higher prevalence in cancer populations and accelerated by cancer treatments
- In breast cancer, longitudinal objective and self-reported decline in cognitive function from pre- to 6 months post-chemotherapy was associated w/ increase in frailty over the same period (Magunuson 2019)
- In breast cancer survivors 5-15 years post-treatment, frailty and *pre-frailty* predicted cognitive decline over 2 yr observation in cancer survivors but not controls (Ahles 2022)
- In outpatients with plasma cell disorders (n=86), we have shown that frailty is uniquely associated with *both* objective (RR 1.49, p=0.04) and self-reported (RR 3.60, p=0.02) CRCD (Nakamura 2022)

68

TRAJECTORY AFTER TRANSPLANT

- Cognitive dysfunction at baseline is prevalent
- Worsens immediately after transplant
- Recovers over time, but persists in a subset



Syrjala 2011

69

EFFECT OF AGE

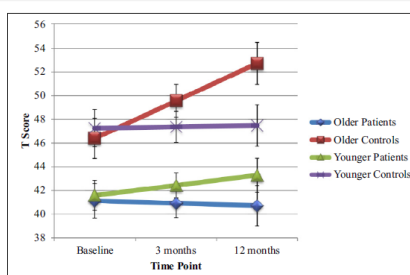


Figure 2. Covariate-adjusted (IQ and sex) estimated means with standard error bars for verbal memory in older (≥ 65 years) and younger (< 65 years) patients and controls.

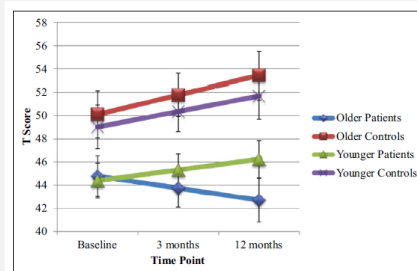
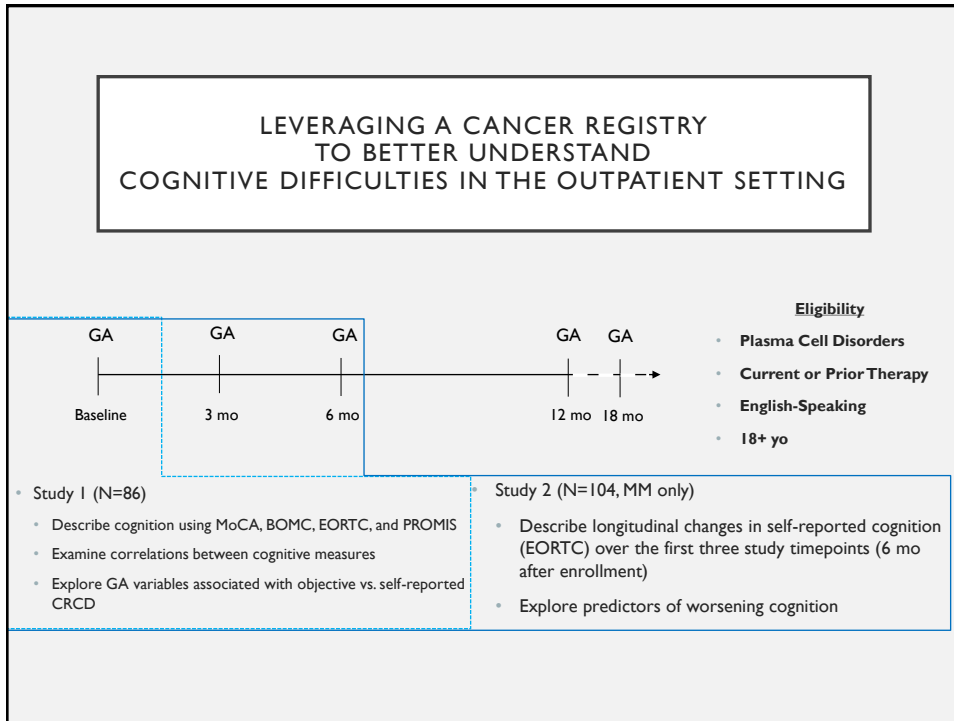


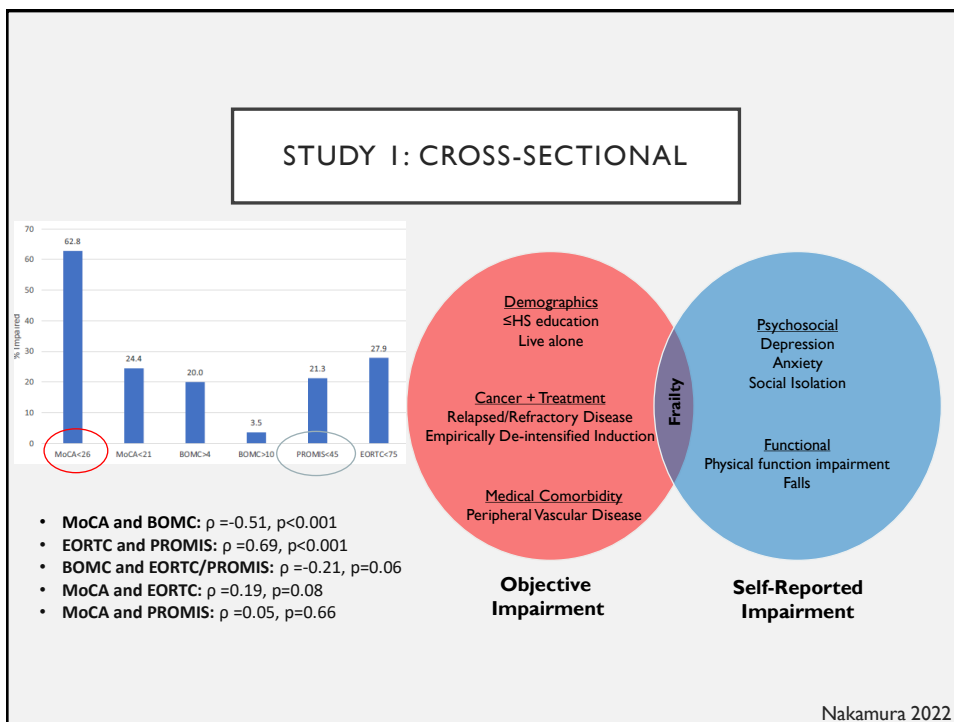
Figure 3. Covariate-adjusted (IQ and sex) estimated means with standard error bars for verbal fluency in older (≥ 65 years) and younger (< 65 years) patients and controls.

Hoogland 2017

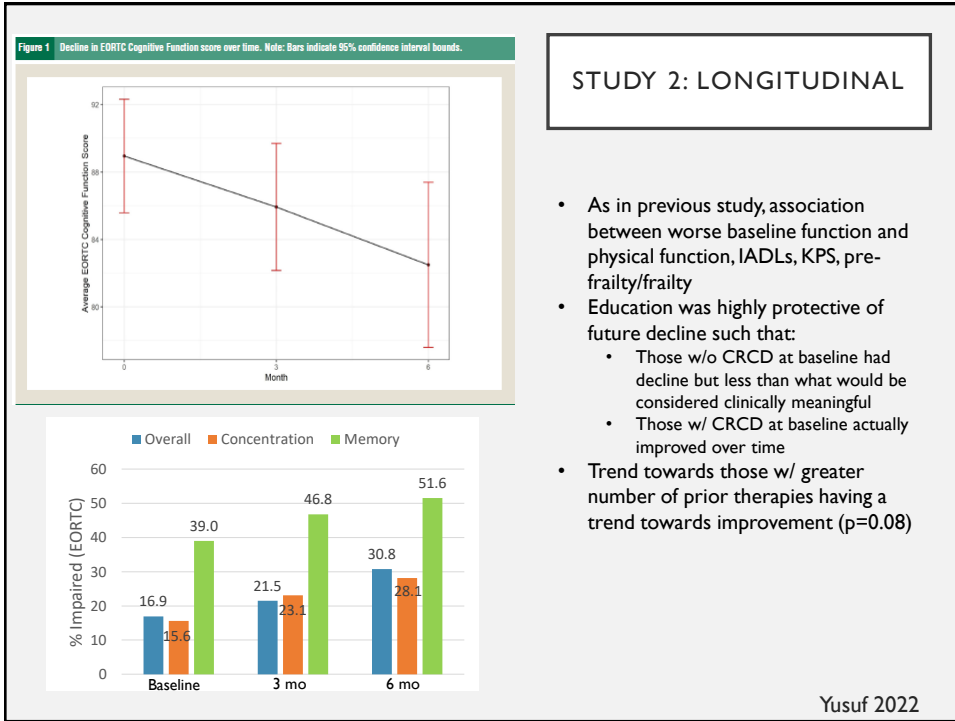
70



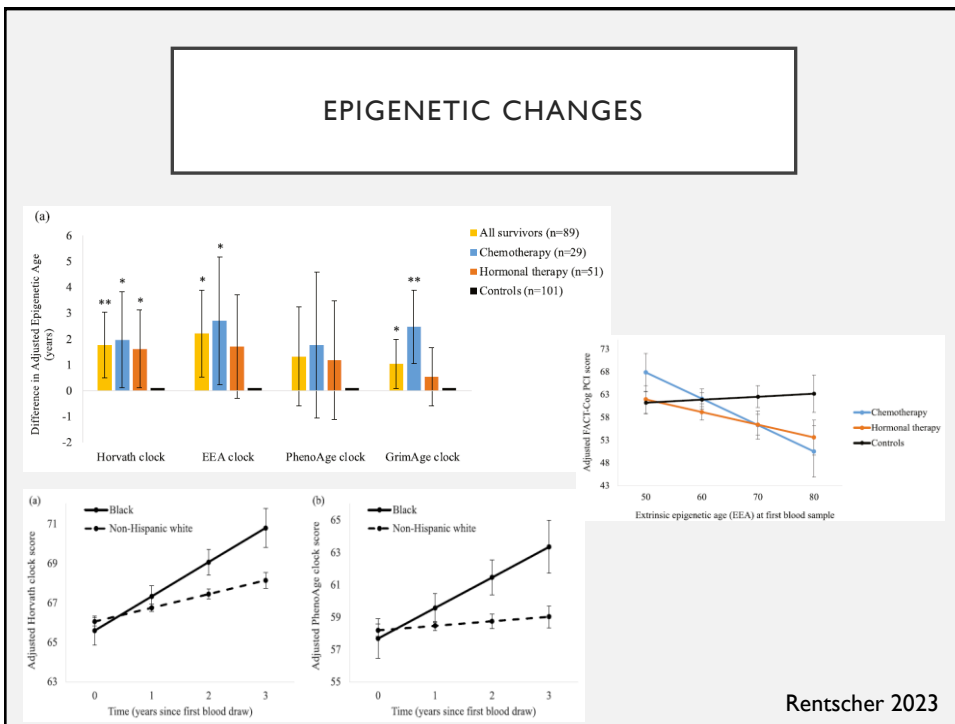
71



72



73



74

UNC Lineberger Cancer Network Questions/Comments?

Nobody has responded yet.
Hang tight! Responses are coming in.

Start the presentation to see live content. For screen share software, share the entire screen. Get help at pollev.com/app

75

THANK YOU!

University Cancer Research Fund

UNC | LINEBERGER COMPREHENSIVE CANCER CENTER

UNC Lineberger Cancer Network


The Telehealth Team

Tim Poe, Director

Veneranda Obure , Technology Support Specialist	Nadja Brown , Interim Administrative Support Specialist
Jon Powell , PhD, Continuing Education Specialist	Patrick Muscarella , Technology Support Technician
Oliver Marth , Technology Support Technician	Lindsey Reich , Public Communication Specialist
Andrew Dodgson , DPT, Continuing Education Specialist	Barbara Walsh , DNP, MPH, MSN, RN, Nurse Planner

76

SELF-PACED, ONLINE COURSES



ADVANCED PRACTICE PROVIDER
Self-Paced, Online Course

August 16
4:00 PM

Developing Comprehensive Exercise Programming for People Affected by Cancer

Carly Bailey, MA

August 23
12:00 PM




RESEARCH TO PRACTICE
Self-Paced, Online Course

No CME credit available for August 23 webinar

H&N Cancer Management in NC: Updates for 2023

Siddharth Sheth, DO, MPH Colette J. Shen, MD, PhD
Wendell Yarbrough, MD, MMHC, FACS

September 13
12:00 PM



PATIENT CENTERED CARE
Self-Paced, Online Course

Improving the Lives of AYA with Cancer

Lauren Lux, MSW Catharine Swift, MSW, LCSW
Melissa Matson, MSN, RN, AGPCNP-BC


September 13
12:00 PM

Today's webinar will be available in about one month as a **FREE**, Self-Paced, Online Course

Complete details on Self-Paced Online Courses: learn.unclcn.org/spoc

77

SELF-PACED, ONLINE COURSES




ADVANCED PRACTICE PROVIDER
Self-Paced, Online Course

Parenting with Cancer

Justin Yopp, PhD

September 13
12:00 PM




RESEARCH TO PRACTICE
Self-Paced, Online Course

The Ketogenic Diet for Brain Tumor Patients: A Phase 1 Trial and Beyond...

Jethro Hu, MD

September 13
12:00 PM



PATIENT CENTERED CARE
Self-Paced, Online Course

Cancer Pathology: How Diagnosis Drives Treatment

Yuri Fedoriw, MD

September 13
12:00 PM

Complete details on our Self-Paced, Online Courses: learn.unclcn.org/spoc

78

THANK YOU FOR PARTICIPATING!

UNC Lineberger Cancer Network

Email: unclcn@unc.edu
Call: (919) 445-1000

Send us an email to sign up for our monthly e-newsletter.

Check us out at unclcn.org

 facebook.com/unccn  unclinebergercancernetwork

 @unc_cn  linkedin.com/in/unccn

79