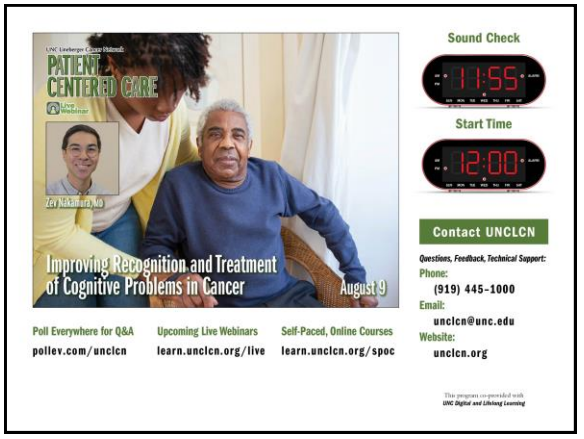
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Live Webinar
Zev Nakamura, MD
Improving Recognition and Treatment of Cognitive Problems in Cancer
August 9
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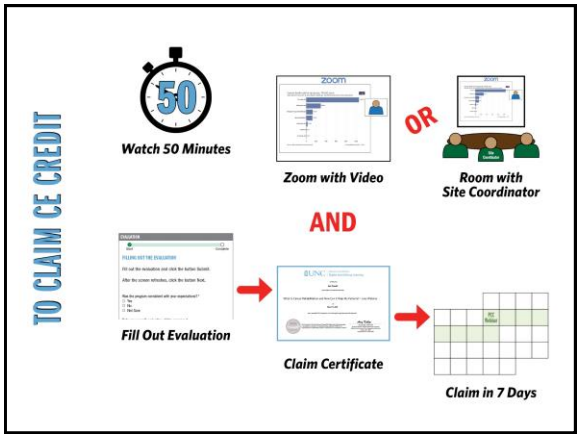
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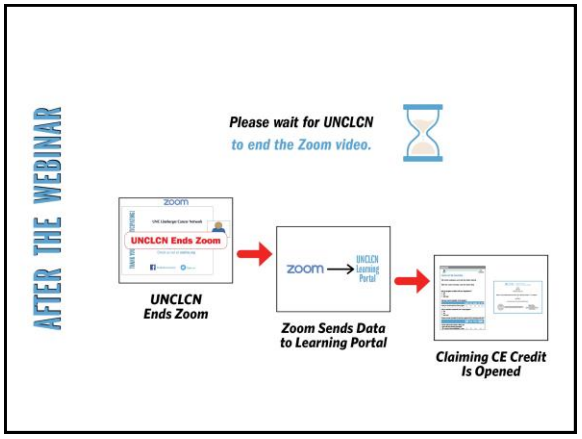
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Live Webinar
Zev Nakamura, MD
Improving Recognition and Treatment of Cognitive Problems in Cancer
August 9

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

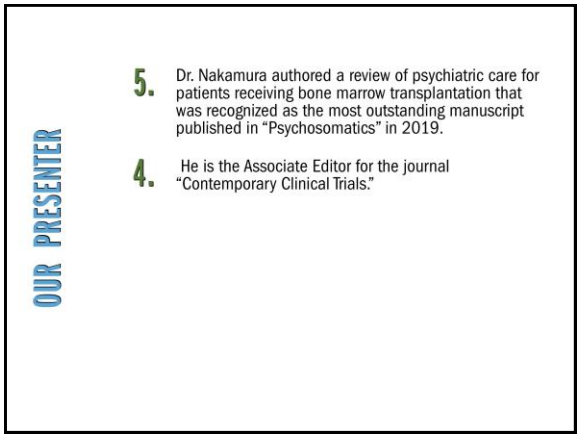
OUR PRESENTER

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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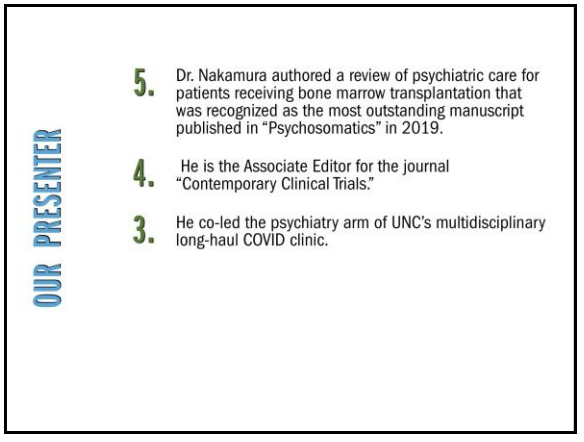
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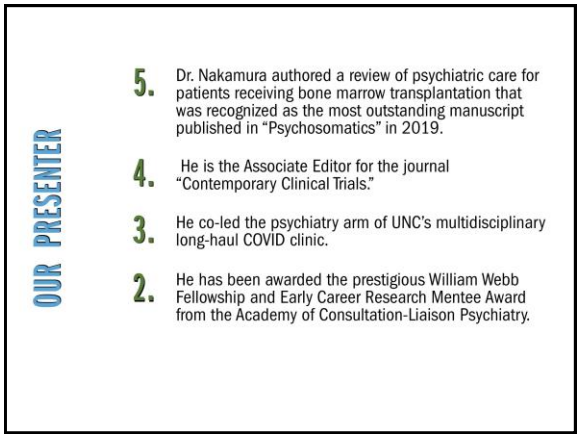
11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12

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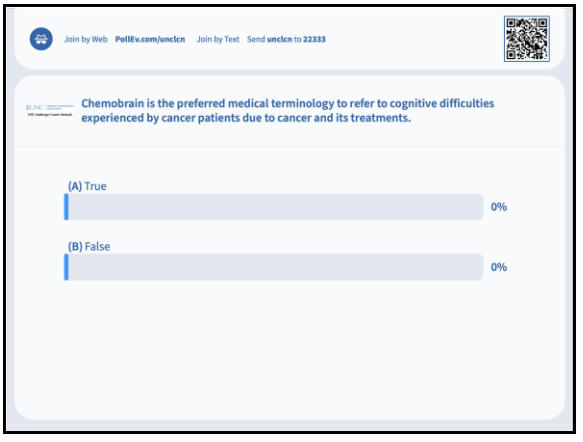
1. He directs the UNC Comprehensive Cancer Support Program Psycho-oncology Clinic for psychiatry fellows.

13



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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.

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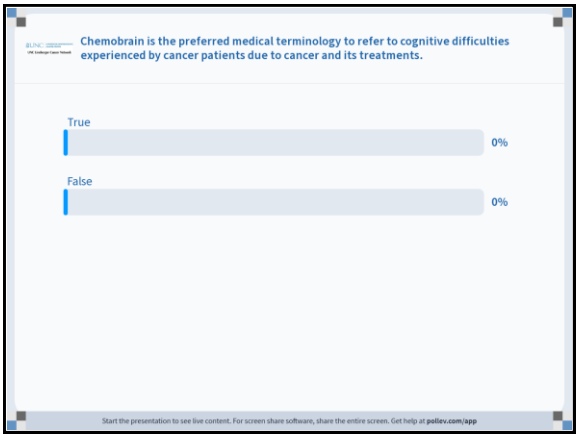
Chemobrain is the preferred medical terminology to refer to cognitive difficulties experienced by cancer patients due to cancer and its treatments.
True
0%
False
0%
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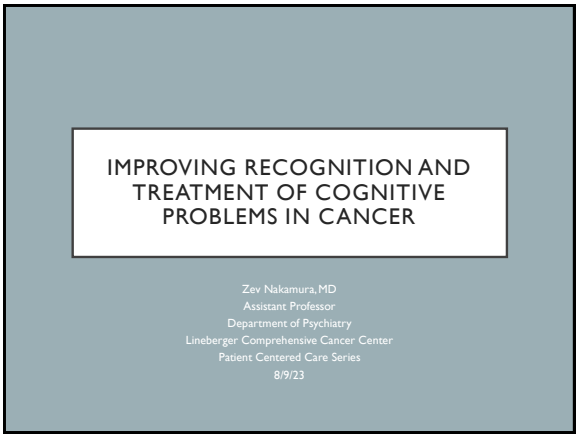
IMPROVING RECOGNITION AND TREATMENT OF COGNITIVE PROBLEMS IN CANCER
Zev Nakamura, MD
Assistant Professor
Department of Psychiatry
Lineberger Comprehensive Cancer Center
Patient Centered Care Series
8/9/23

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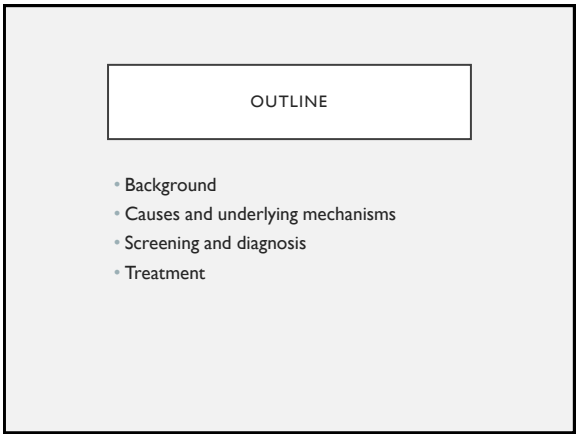
OUTLINE
Background
Causes and underlying mechanisms
Screening and diagnosis
Treatment

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

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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")

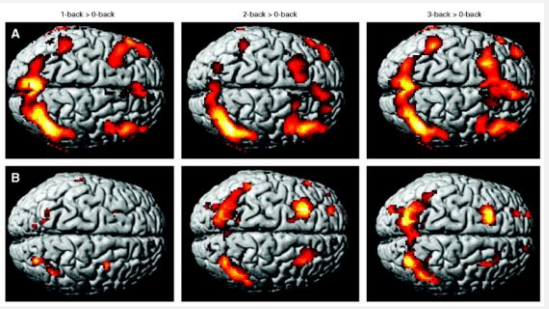
20

CANCER-RELATED COGNITIVE DYSFUNCTION (CRCD)

- 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

Which of these are consequences of cancer-related cognitive Dysfunction?

Long-term cognitive impairment 0%

Problems returning to work 0%

Worse physical function 0%

Decreased overall quality of life 0%

All of the above 0%

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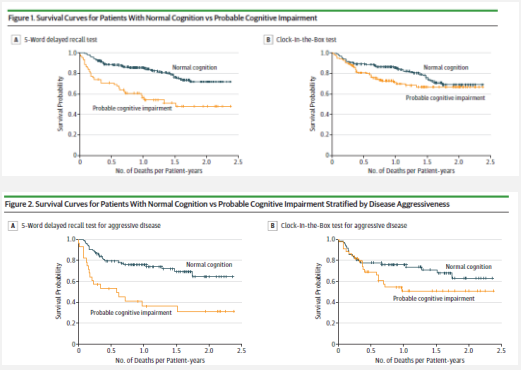
SIGNIFICANCE OF CRCD

- 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



Hsieh 2018

25

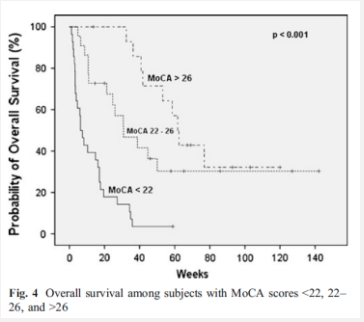


Fig. 4 Overall survival among subjects with MoCA scores <22, 22–26, and >26

Olson 2007, Olson 2012

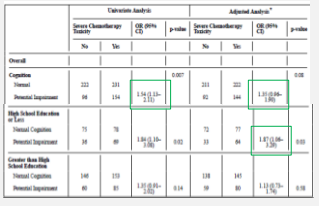
26

CRCD AND CHEMOTHERAPY TOXICITY

Journal of Geriatric Oncology

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

- 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



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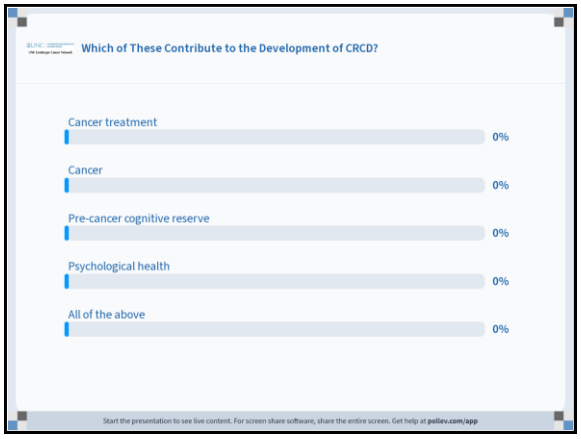
Which of These Contribute to the Development of CRCD?
Cancer treatment
0%
Cancer
0%
Pre-cancer cognitive reserve
0%
Psychological health
0%
All of the above
0%
Start the presentation to see live content. For screen share software, share the entire screen. Get help at pollev.com/app

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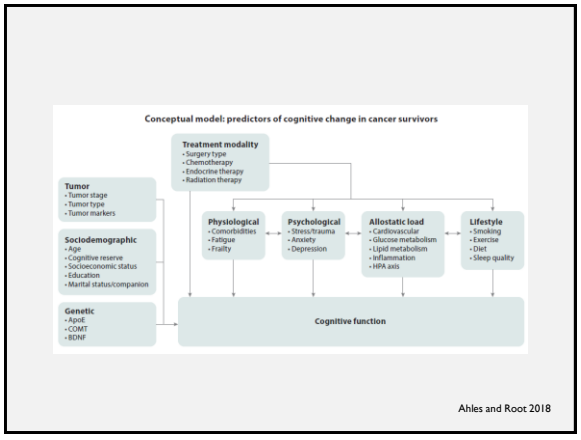
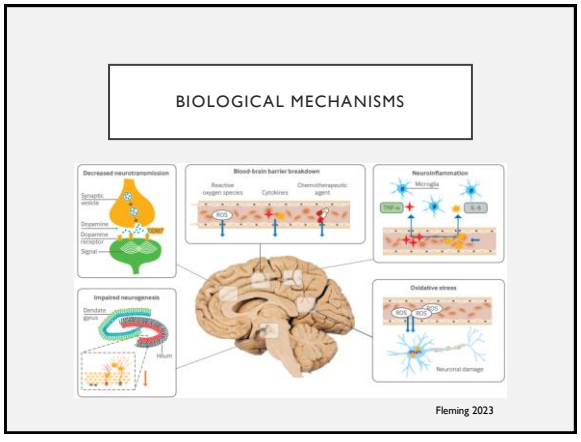

Conceptual model: predictors of cognitive change in cancer survivors
Treatment modality
• Surgery type
• Chemotherapy
• Endocrine therapy
• Radiation therapy
Tumor
• Tumor stage
• Tumor type
• Tumor markers
Sociodemographic
• Age
• Cognitive reserve
• Socioeconomic status
• Education
• Marital status/companion
Genetic
• ApoE
• COMT
• BDNF
Physiological
• Comorbidities
• Fatigue
• Frailty
Psychological
• Stress/trauma
• Anxiety
• Depression
Allostatic load
• Cardiovascular
• Glucose metabolism
• Lipid metabolism
• Inflammation
• HPA axis
Lifestyle
• Smoking
• Exercise
• Diet
• Sleep quality
Cognitive function
Ahles and Root 2018

29


BIOLOGICAL MECHANISMS
Decreased neurotransmission
Blood-brain barrier breakdown
Neuroinflammation
Impaired neurogenesis
Oxidative stress
Fleming 2023

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

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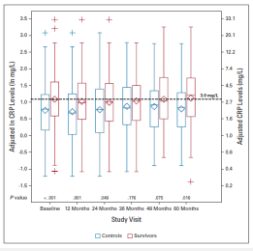
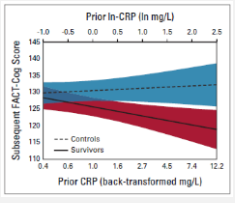
ELEVATED C-REACTIVE PROTEIN PREDICTIVE OF SELF-REPORTED COGNITIVE PROBLEMS



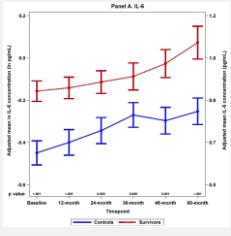


Carroll, Nakamura, Small et al. 2022

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

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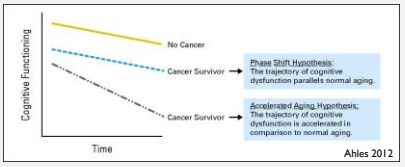
CRCD IN THE CONTEXT OF ACCELERATED AGING



Ahles 2012

- 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

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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

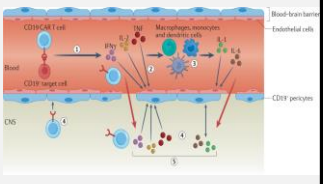
- Estrogen and testosterone support brain function
- Tamoxifen and aromatase inhibitors
  - Smaller hippocampal size
  - Combination with chemo may lead to greater cognitive difficulties
  - Other studies show no association
- ADT with adverse cognitive consequences

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, Santomasso 2018

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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

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MEASUREMENT

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

ICCTF 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

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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	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
It has seemed like my brain was not working as well as usual	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
I have had to work harder than usual to keep track of what I was doing	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
I have had trouble shifting back and forth between different activities that require thinking	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
I have had trouble concentrating	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
I have had to work really hard to pay attention or I would make a mistake	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
I have had trouble forming thoughts	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1
I have had trouble adding or subtracting numbers in my head	☐ 5	☐ 4	☐ 3	☐ 2	☐ 1

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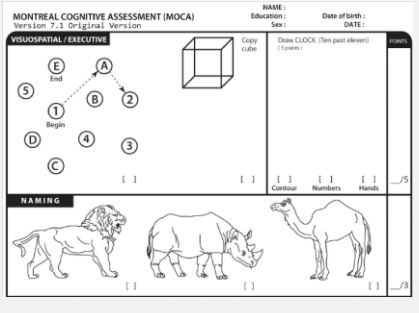
MOCA



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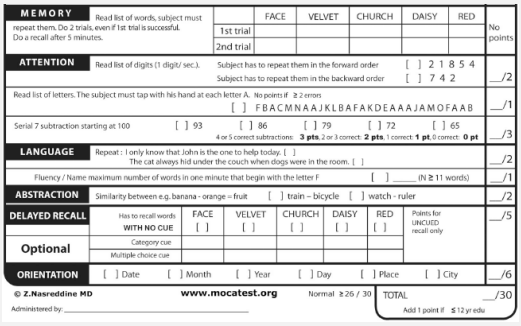
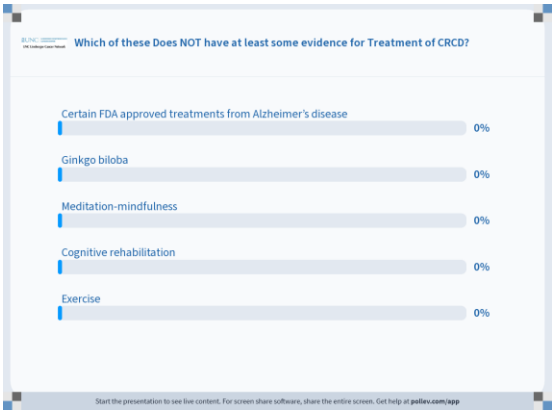


MEMORY	Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.		FACE	VELVET	CHURCH	DAISY	RED	No points
		1st trial						
		2nd trial						
ATTENTION	Read list of digits (1 digit/ sec.).	Subject has to repeat them in the forward order [ ] 2 1 8 5 4						
		Subject has to repeat them in the backward order [ ] 7 4 2						/2
Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors [ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B								/1
Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65 4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**								/3
LANGUAGE	Repeat : I only know that John is the one to help today. [ ] The cat always hid under the couch when dogs were in the room. [ ]							/2
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 /5
Optional	Category cue							
	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

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CRCD 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

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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

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COGNITIVE TRAINING

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

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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

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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

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MEDICATIONS

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

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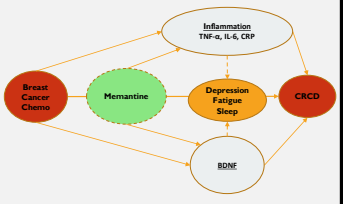
MEMANTINE FOR PREVENTION OF COGNITIVE DECLINE IN PATIENTS WITH BREAST CANCER

- Most interventions limited by:
  - Non-specific biological mechanisms
  - Availability/scalability
  - Administered during survivorship
- Memantine in guideline recommendations for WBRT
- Memantine prevents cognitive decline in chemotherapy animal models through modulation of neuroinflammation and BDNF



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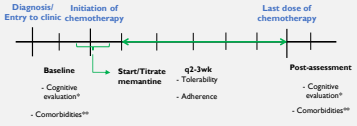
STUDY SCHEMA



*Traditional neuropsychological assessment, PROs, computerized tests (CANTAB)
**Comorbidities: depression, anxiety, fatigue, sleep, functional ability, hormonal status

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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 ≥ 90% scheduled doses
- **AEs:** 2 at least probably related to memantine; both grade 1

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

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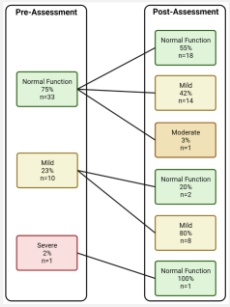
COGNITIVE CHANGES



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**

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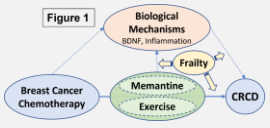
RATIONALE FOR MULTICOMPONENT TREATMENTS

- 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

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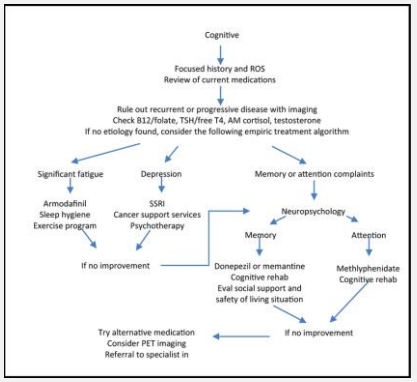

Cramer 2019

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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

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UNC COMPREHENSIVE CANCER SUPPORT PROGRAM (CCSP)

https://unclineberger.org/ccsp/

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CRCD AND FRAILTY

- 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)

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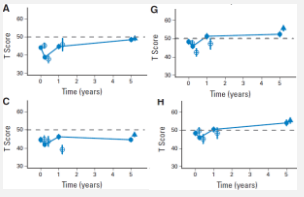
TRAJECTORY AFTER TRANSPLANT

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



Syrjala 2011

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EFFECT OF AGE

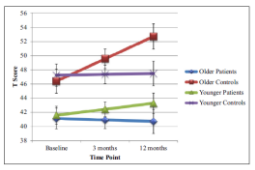

Figure 2. Covariate-adjusted (IQ and sex) estimated means with standard error bars for verbal memory in older (≥65 years) and younger (<65 years) patients and controls.

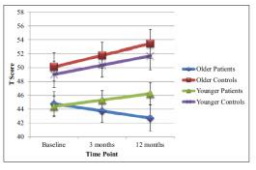

Figure 3. Covariate-adjusted (IQ and sex) estimated means with standard error bars for verbal fluency in older (≥65 years) and younger (<65 years) patients and controls.

Hoogland 2017

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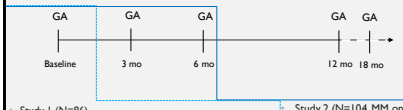
LEVERAGING A CANCER REGISTRY TO BETTER UNDERSTAND COGNITIVE DIFFICULTIES IN THE OUTPATIENT SETTING



Eligibility

- **Plasma Cell Disorders**
- **Current or Prior Therapy**
- **English-Speaking**
- **18+ yo**

- Study 1 (N=86)
  - Describe cognition using MoCA, BOMC, EORTC, and PROMIS
  - Examine correlations between cognitive measures
  - Explore GA variables associated with objective vs. self-reported CRCD
- Study 2 (N=104, MM only)
  - Describe longitudinal changes in self-reported cognition (EORTC) over the first three study timepoints (6 mo after enrollment)
  - Explore predictors of worsening cognition

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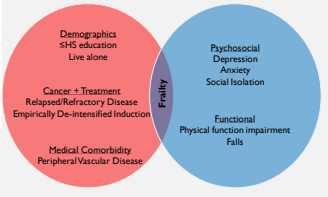
STUDY 1: CROSS-SECTIONAL



- **MoCA and BOMC:** ρ =-0.51, p<0.001
- **EORTC and PROMIS:** ρ =0.69, p<0.001
- **BOMC and EORTC/PROMIS:** ρ =-0.21, p=0.06
- **MoCA and EORTC:** ρ =0.19, p=0.08
- **MoCA and PROMIS:** ρ =0.05, p=0.66

Nakamura 2022

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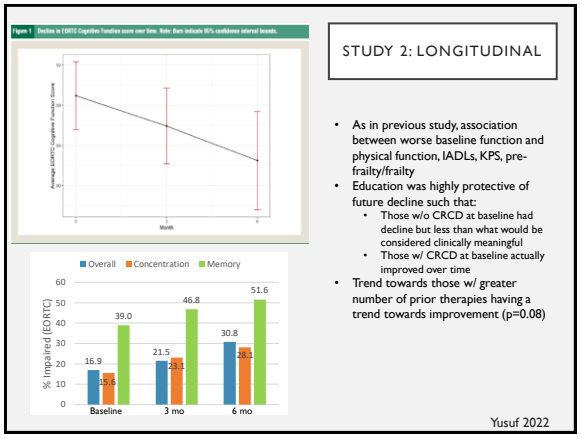

STUDY 2: LONGITUDINAL

- As in previous study, association between worse baseline function and physical function, IADLs, KPS, pre-frailty/frailty
- Education was highly protective of future decline such that:
  - Those w/o CRCD at baseline had decline but less than what would be considered clinically meaningful
  - Those w/ CRCD at baseline actually improved over time
- Trend towards those w/ greater number of prior therapies having a trend towards improvement (p=0.08)

Yusuf 2022

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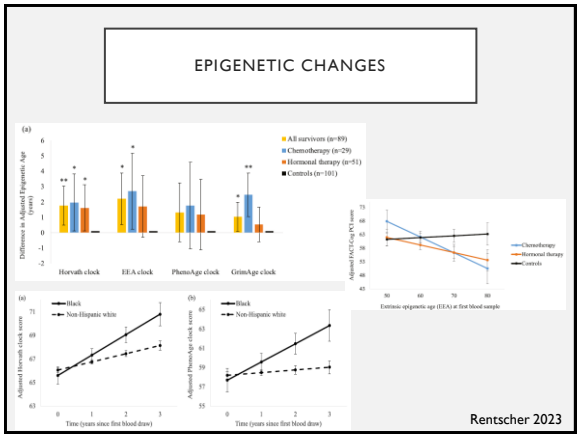

Rentscher 2023

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THANK YOU!

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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

RESEARCH TO PRACTICE
Self-Paced, Online Course

No CME credit available for August 23 webinar

August 23
12:00 PM

H&N Cancer Management in NC: Updates for 2023
Siddharth Sheth, DO, MPH **Colette J. Shen,** MD, PhD
Wendell Yarbrough, MD, MMHC, FACS

PATIENT CENTERED CARE
Self-Paced, Online Course

September 13
12:00 PM

Improving the Lives of AYA with Cancer
Lauren Lux, MSW **Catharine Swift,** MSW, LCSW
Melissa Matson, MSN, RN, AGPCNP-BC

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

Complete details on Self-Paced Online Courses:
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SELF-PACED, ONLINE COURSES

ADVANCED PRACTICE PROVIDER
Self-Paced, Online Course

Parenting with Cancer
Justin Yopp, PhD

RESEARCH TO PRACTICE
Self-Paced, Online Course

The Ketogenic Diet for Brain Tumor Patients: A Phase 1 Trial and Beyond...
Jethro Hu, MD

PATIENT CENTERED CARE
Self-Paced, Online Course

Cancer Pathology: How Diagnosis Drives Treatment
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