Living with and Beyond Cancer – Brain Health

Virtual EMAS School, May 2020

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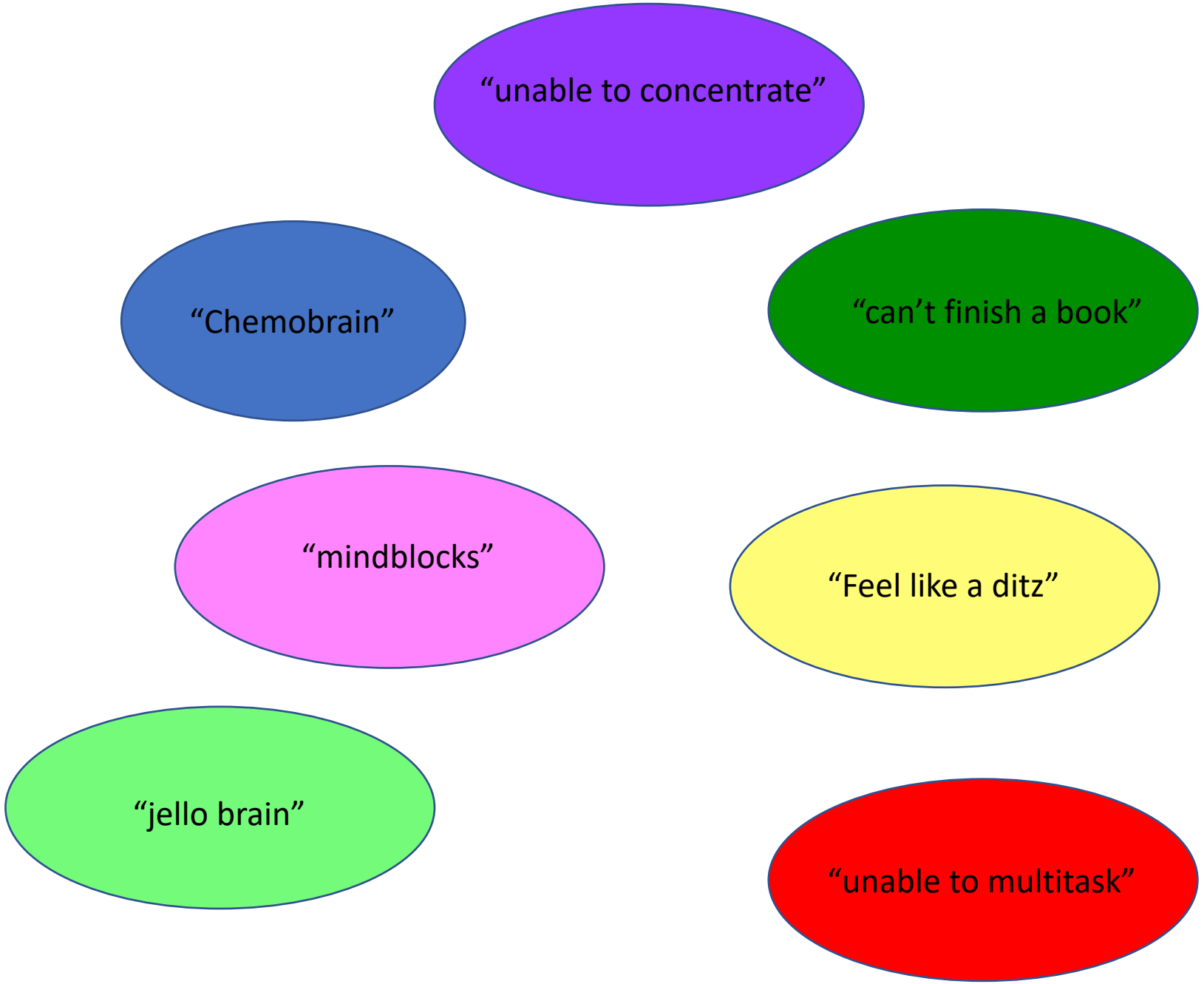
Plan

- Impact of cancer treatment on brain function
- Role of estrogen in brain function
- Interventions to improve cognition


“unable to concentrate”
“Chemobrain”
“can’t finish a book”
“mindblocks”
“Feel like a ditz”
“jello brain”
“unable to multitask”

Who needs assessment

- Persistent complaints over time
- Impact on Quality of Life
- Impact on work
- But…..
  - Major discrepancies exist in assessment of cognitive function
    - A lack of a set standard to define cognitive impairment
    - Variability in which neuropsychological tests were utilized
    - The range of statistical analyses employed across studies

Cognitive dysfunction is multifactorial

- May pre-exist diagnosis
  - 15-75% of breast cancer patients[1]
- Intimately related to
  - mood, fatigue, sleep, VSM
  - Age is a major confounder – cognitive reserve

[1]. J Clin Oncol. 2012;30(30):3675. Epub 2012 Sep 24.

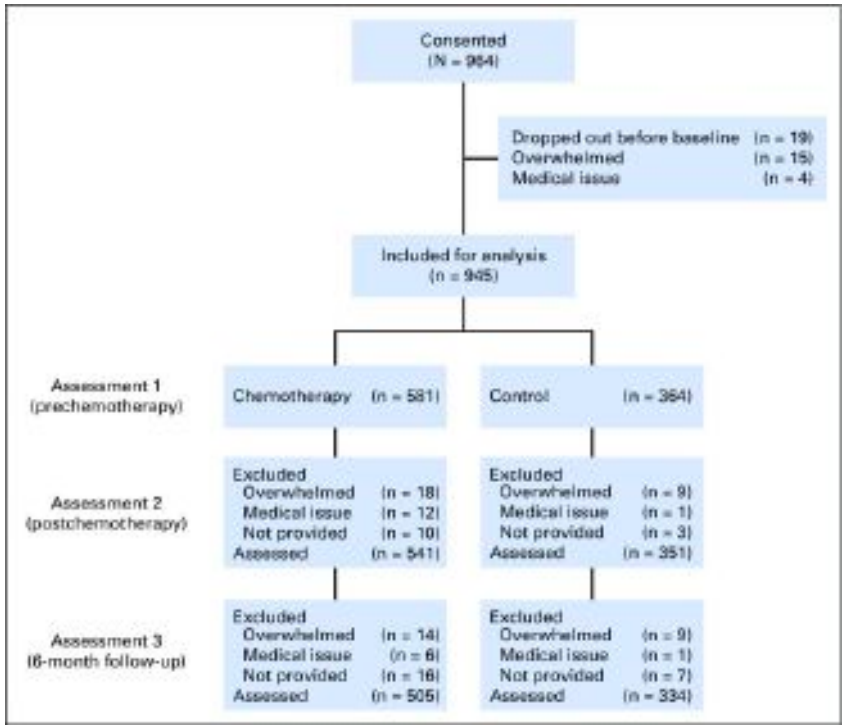
International Cognition and Cancer Task Force

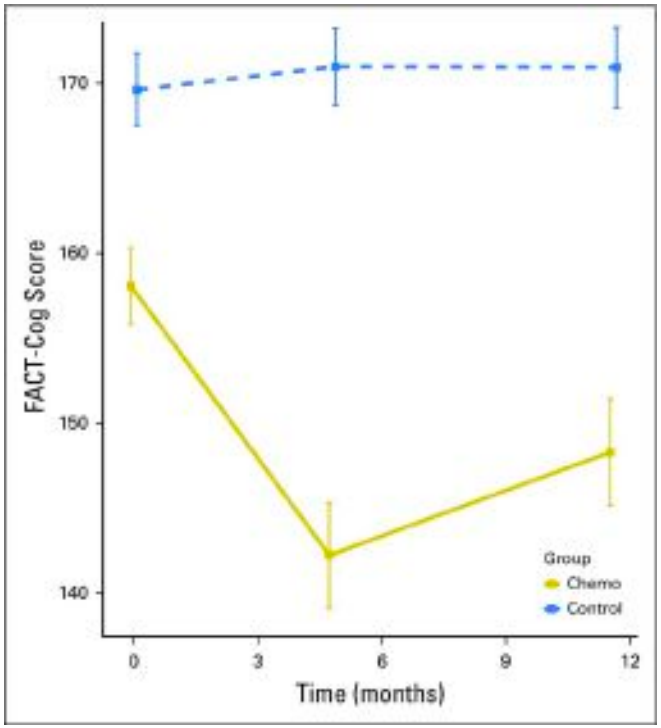
- Longitudinal studies rather than cross-sectional studies
- Studies that incorporate pretreatment cognitive assessment
- Incorporation of appropriate control groups (disease-specific and control groups)
- Encouragement for multi-institutional studies or cooperative group studies (in order to increase the sample size)

Lancet Oncol. 2011 Jul;12(7):703-8..

Impact of cancer treatment on cognition

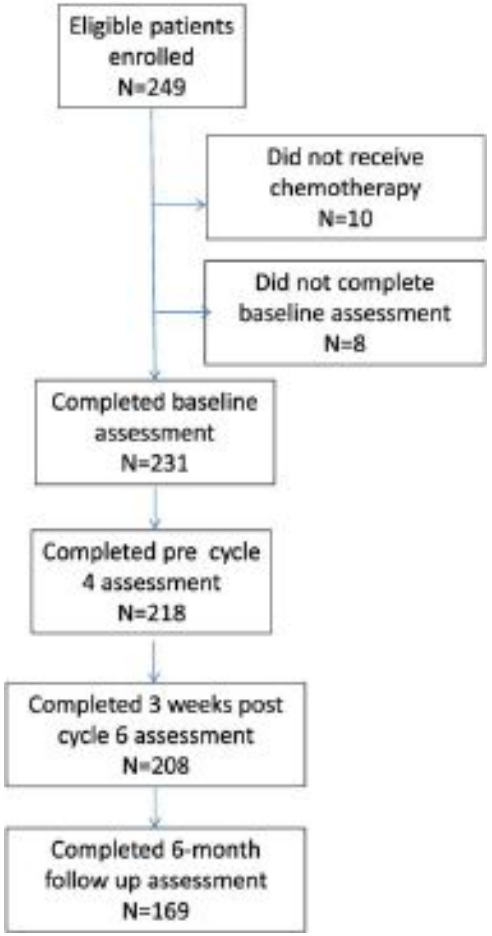
- Breast cancer
  - Chemo > 6 months reduced of verbal and visuospatial ability[1]





[1]Jim et al J Clin Oncol. 2012;30(29):3578. [2] Janelsins J Clin Oncol 35:506-514.

Ovarian Cancer



Number and percent of patients with impaired cognitive function, by domain.

Time point	Processing		Attention		Motor	
	Evaluable N	Impaired N (%)	Evaluable N	Impaired N (%)	Evaluable N	Impaired N (%)
Pre-cycle 4	191	9 (4.7%)	183	36 (19.7%)	216	16 (7.4%)
3 wks post cycle 6	187	5 (2.7%)	171	23 (13.5%)	206	22 (10.7%)
26 wks post cycle 6	159	2 (1.3%)	152	18 (11.8%)	168	12 (7.1%)

Cognitive index scores (CIS).

Time point	No. Evaluable	CIS = 0 N (%)	CIS = 1 N (%)	CIS ≥ 2 N (%)
Pre cycle 4	218	163 (74.8%)	49 (22.5%)	6 (2.7%)
3 weeks post cycle 6	208	164 (78.9%)	39 (18.8%)	5 (1.9%)
26 weeks post cycle 6	169	139 (82.3%)	28 (16.0%)	2 (1.2%)

Hess et al. Gynecol Oncol. 2015;139(3):541.

Role of Estrogen in Cognition


Clinical Review & Education

JAMA Insights | WOMEN'S HEALTH

The Menopause Transition and Cognition

Gail A. Greendale, MD; Arun S. Karlamangla, PhD, MD; Pauline M. Maki, PhD

- Biochemical basis
- Currently no evidence to support MHT to treat cognitive dysfunction
- Addressing other symptoms (VMS, sleep, mood) may improve symptoms

Table. The Menopausal Transition and Cognition—An Approach to Patient Education

Examples of Patient Questions	Examples of Clinician Responses
I'm having memory problems (eg, forgetfulness, difficulty retrieving names, losing train of thought). Is this part of menopause?	This is a common symptom. About half of women experience forgetfulness and other cognitive problems as a part of their menopausal transition.[a]
Are other menopausal transition symptoms (eg, hot flashes, poor sleep, and feelings of anxiety or depression) responsible for the memory difficulties?	Although menopausal transition symptoms are associated with cognitive difficulties, changes in cognition across menopause stages occur independently of those symptoms. Cognitive difficulties can occur in women without any other menopausal transition symptoms.
If I treat my other menopausal transition symptom(s), will my memory problems improve?	There is general evidence (in circumstances other than the menopausal transition) that treating depression, anxiety, and sleep disturbance improves memory. No studies directly address whether treating these symptoms during the menopausal transition improves cognition. Treating your other menopausal transition symptom(s) may or may not have a cognitive benefit.[b]
Are the (menopausal transition-related) cognitive symptoms a sign that I am developing dementia?	Dementia is very rare at midlife unless a person has a family history of early-onset Alzheimer disease. In one study, mild cognitive test effects seen in the menopausal transition resolved in postmenopause. Another study showed that difficulty remembering words persisted in postmenopause, but verbal memory test scores remained well within the normal range.
Should I have my memory tested?	In most cases, testing is not necessary. However, if your cognitive symptoms are significantly interfering with your daily life, a referral for a neuropsychological evaluation could be helpful in determining the nature and severity of the problem.[c]
Are there any nonpharmacological things I can do to manage my cognitive symptoms during the menopause?	Mild attention deficits contribute to misplacing keys, forgetting a parking spot, or not registering the name of a new acquaintance. This can be mitigated by focusing attention (eg, consciously landmarking the car location) and using mnemonic devices (eg, repeating new names aloud). Physical activity and control of cardiometabolic risk factors are possible strategies to prevent cognitive decline, but whether they improve menopausal transition-related cognitive symptoms is unknown.[4]

[a] Assess for other conditions that can affect cognitive function such as anxiety and depressive or sleep disorders. These symptoms are common during the menopausal transition and can have independent effects on cognition. If present, discern whether they are clinically meaningful and warrant treatment or a consultation with a clinician with the requisite expertise.

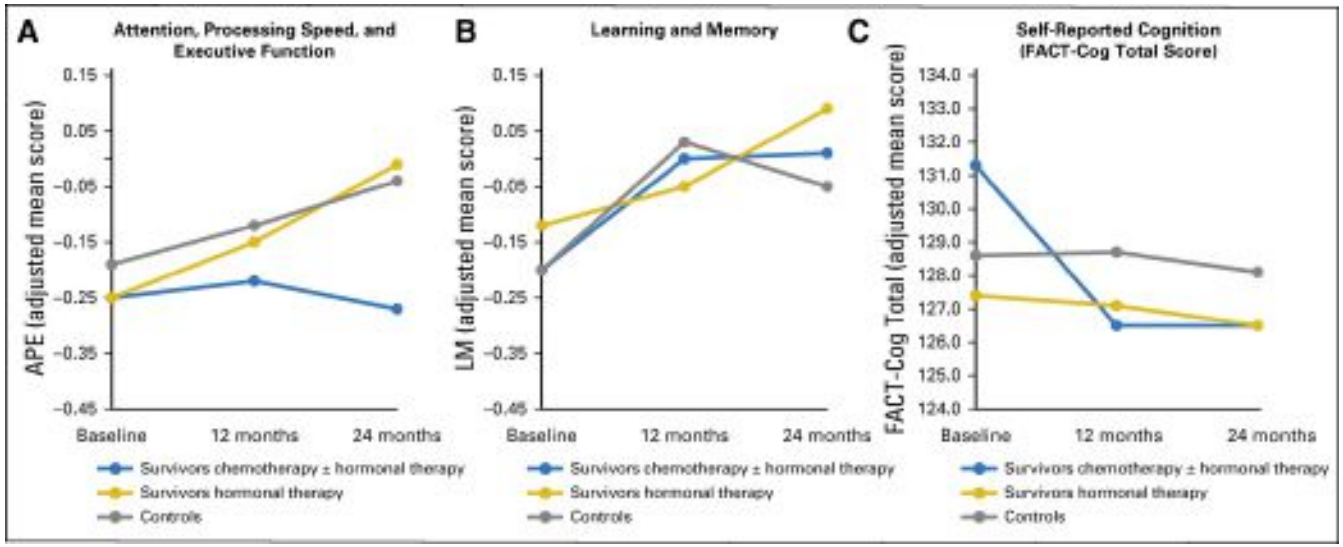
[b] Assess the severity and impact of other symptoms and the patient's desire for intervention (with possible side benefit on cognition). There is preliminary evidence that treating hot flashes benefits cognitive function, but more research is needed.

[c] Women report that cognitive symptoms can interfere with work and relationships.[10] However, clinically significant functional impairment, such as a decrement in job performance or problems managing daily activities, would be unusual in association with menopausal transition-related cognitive symptoms and would merit consultation.

JAMA. 2020;323(15):1495-1496. doi:10.1001/jama.2020.1757

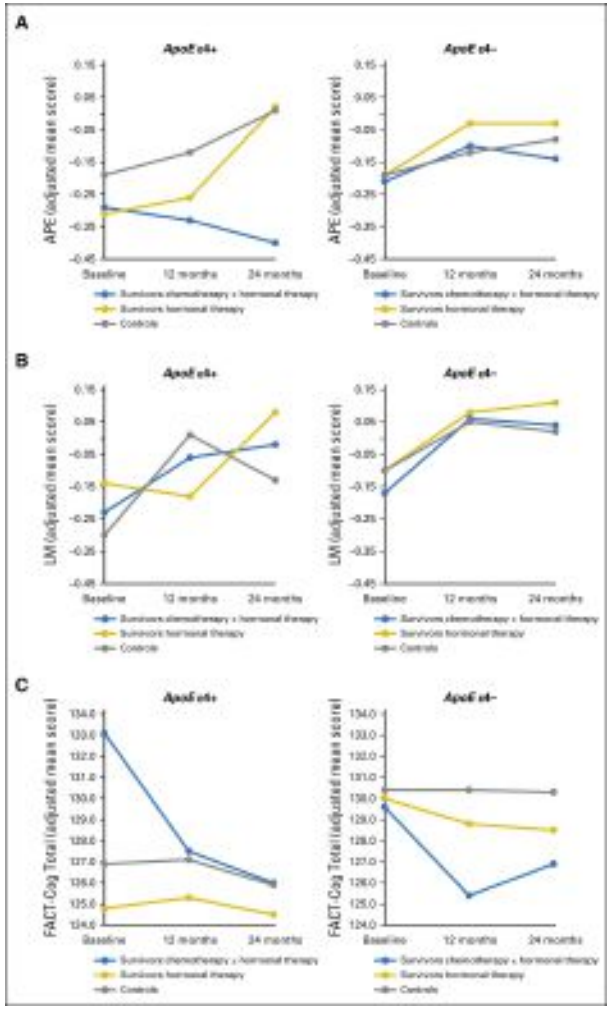
What about anti-endocrine therapy?

- **Thinking and Living With Cancer (TLC)**



Journal of Clinical Oncology 2018 363211-3222. DOI: 10.1200/JCO.18.00140

Stratification based on genetic risk



Journal of Clinical Oncology 2018 363211-3222. DOI: 10.1200/JCO.18.00140

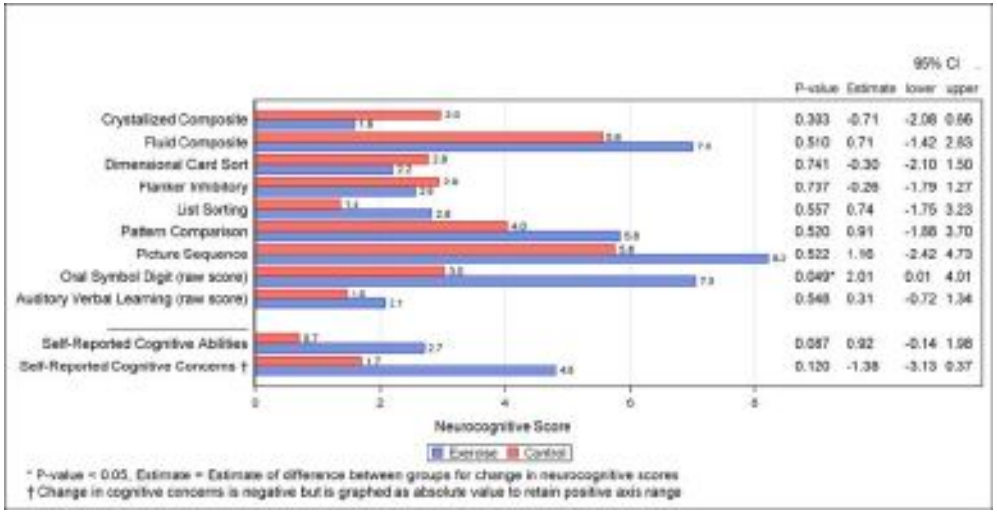
Surgical Menopause

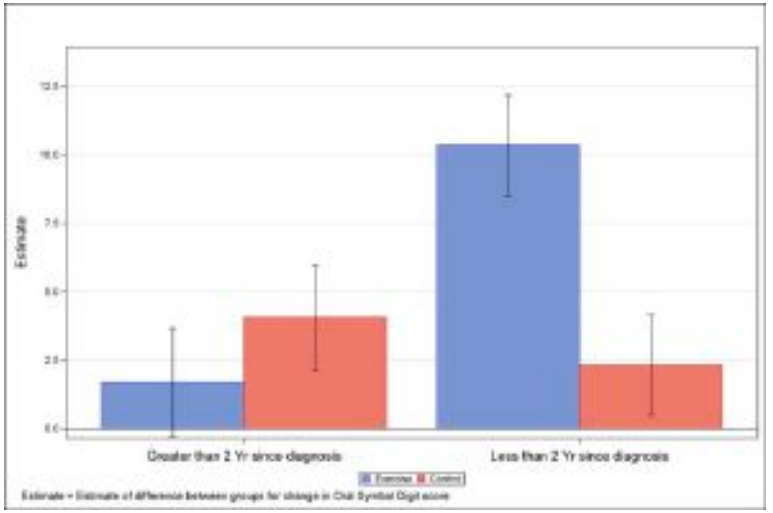
- Mayo Clinic Cohort of Oophorectomy and Aging
- BSO increased risk of cognitive impairment or dementia compared to those without oophorectomy (HR 1.46, 95% CI 1.13–1.90).
- Risk was higher for women undergoing BSO before age 49 that were not treated with estrogen until age 50 (HR 1.89, 95% CI 1.27–2.83, p = 0.002).
- In women who took estrogen until age 50, risk of cognitive impairment or dementia was not significantly different (HR 0.79, 95% CI 0.25–2.54, p = 0.69)

Neurology 69 (2007) 1074–1083, doi.org/10.1212/01.wnl.0000276984.19542.e6

Interventions to improve cognition

- MHT – to address other symptoms – may help
- Pyschoeducation and cognitive rehabilitation
  - Educate patients – pre-treatment
- Exercise

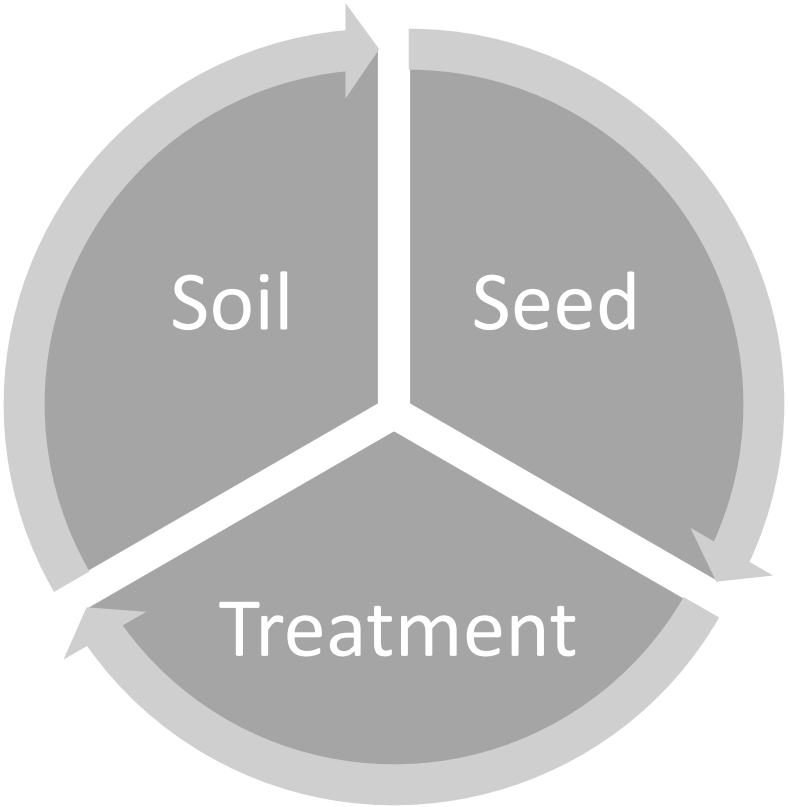




Hartman et al. Cancer. 2018;124(1):192.

Summary and conclusion

Host Factors
Genetics
Cognitive reserve
Age
Co-morbidities



Disease Factors
Cancer type
Cancer stage
Para-neoplastic disorders
Time since dx

Radiotherapy
Chemotherapy
Endocrine tx
Immunotherapy