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Past, Present and Future: A Journey of Biobehavioral Complementary Alternative Medicine (CAM) Research for Cancer Survivors and Caregivers

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Professor and Lyall and Beatrice Thompson Nursing Professorship in Oncology
University of South Florida College of Nursing

Sigma Theta Tau Nurse Researcher Hall of Fame

Learner Objectives

At the end of this session attendees will be able to:

- Discuss research priorities in program of research.
- Identify contributions to advancement of nursing science in bio-behavioral intervention research.
- Describe sequential achievements in the development and testing of self regulated CAM interventions.
- Discuss importance of funding to move the science forward.
    - I have no Conflict of Interest to report.

Matching Passion with Research Goals

Research Priorities

- **Designing and testing bio-behavioral complementary alternative therapy interventions for cancer survivors and caregivers.**

Research Priorities

- **Testing psychological, and physiological stress, and bio-behavioral mechanisms for CAM interventions.**

Research Priorities

- **Building collaborative, diverse translational teams across cultures and disciplines, while providing leadership and mentorship for current and future research.**

Research Grant Priorities

USF CON
USF

American Cancer Society®

ONS® Oncology Nursing Society

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NIH NATIONAL CANCER INSTITUTE

1

R21
NIH/NCI
(2006 - 2009

2

R01
NIH/NCI
(2009 - 2015)

3

R01
NIH/NCI
(2015 – 2020)

First Grant

Patterns of Use of Complementary Alternative Therapies in BCS

Purpose:
Estimate the frequency use of CAM therapies among BCS.

Results related to distress:
Guided imagery was one of the most frequently used reported CAM therapy(79%).

Results: First intervention study: test a CAM intervention: Guided Imagery.

Second Grant, First Biobehavioral

Effects of Relaxation/Guided Imagery on Natural Killer Cell Cytotoxicity and Cytokine (IL-2) among BCS

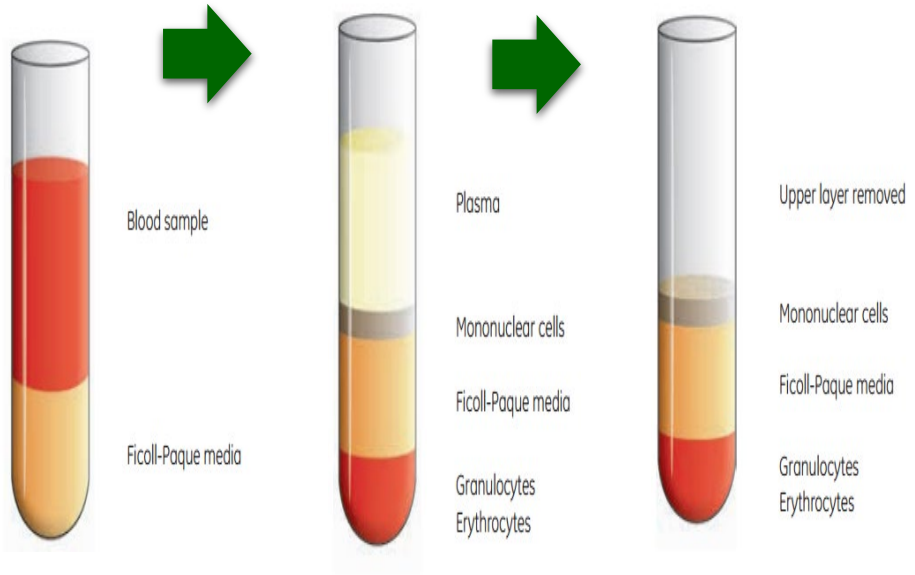
Purpose:

- Determine if relaxation/guided imagery improves immune function: (NK, IL-2) in 28 BCS (pre-surgery to 4 weeks post-surgery).

Results

- Increased NK cytotoxicity and IL-2 activation (LAK Cells) significant differences occurred in the guided imagery group compared to the UC group ($p<0.01$ to $p<0.05$).

Peripheral Blood Mononuclear Cells (PBMCs) are isolated for immune analysis



Third and Fourth Grant

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ONS Oncology Nursing Society

Although guided imagery had a positive impact, to further my research trajectory I developed an innovative and standardized stress reduction program for breast cancer survivors based on MBSR.

Third and Fourth Pilot MBSR(BC)

Purpose:

Assess feasibility of the MBSR(BC) program among BCS and effect on psychological status, physical symptoms, and QOL.

Results:

Significant decreases in:

- Fear of recurrence,
- State anxiety, Trait anxiety, Depression, and Perceived Stress.

Significant increases in:

- QOL, (emotional-well being) and general health.

Formal Meditation Practice

Formal Practice

4 Meditative Practices

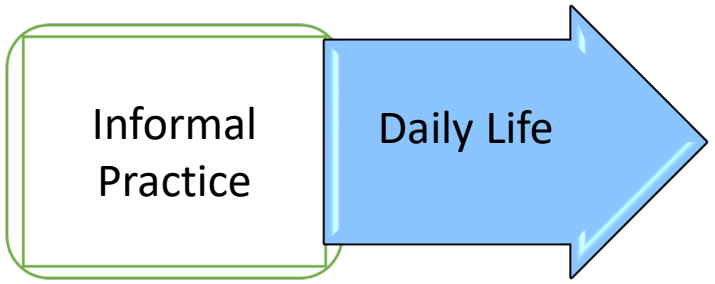
Sitting Meditation

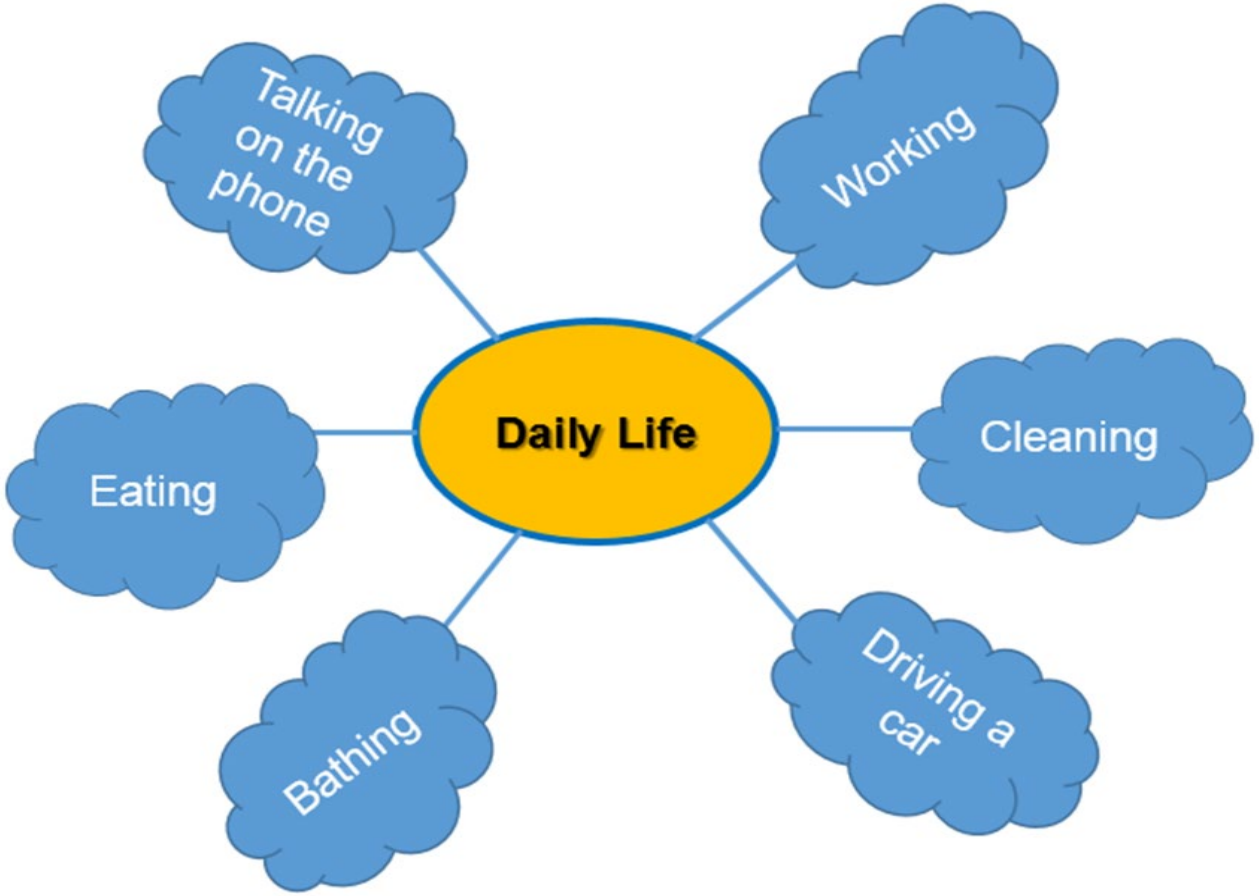
Body Scan

Yoga Posture

Walking Meditation

Informal Meditation Practice





MBSR-C Pilot Study for Advanced Stage Cancer Patients and Their Family Caregivers

Aims

- Assess the feasibility and positive psychological and physical effects of the MBSR-C program among stage 3 and 4 breast, colon, lung and prostate cancer patients and caregivers.
- Assess biological markers:
  - Cortisol, stress hormone
  - IL-6 cytokine from the MBSR-C.

Lengacher, C.A., Kip, K.E., Barta, M., Post-White, J., Jacobsen, P.B., Groer, M., Lehman, B., Moscoso, M.S., Kadel, R., Le, N., Loftus, L., Stevens, C., Malafa, M.P., Shelton, M.M. (2012). A pilot study evaluating the effect of MBSR on psychological status, physical status, salivary cortisol and interleukin-6 among advanced stage cancer patients and their caregivers. *Journal of Holistic Nursing*. doi:10.1177/0898010111435949 PMID: 22442202.

Results

Results:

Significant symptom improvements:

- Decreased patient stress and trait anxiety.
- Increased caregivers psychological QOL.
- **Dyadic** improvements in depression and QOL for both patient and caregiver.

Significant biological effects:

- Decreased **Cortisol** and **IL-6** pre-post MBSR-C classes.

Sixth Grant

1

R21
NIH/NCI
(2006 - 2009

Moving forward:

1) Larger RCT for MBSR(BC)
2) Examination of effects of MBSR(BC) on immune markers as an innovative approach for breast cancer survivors.

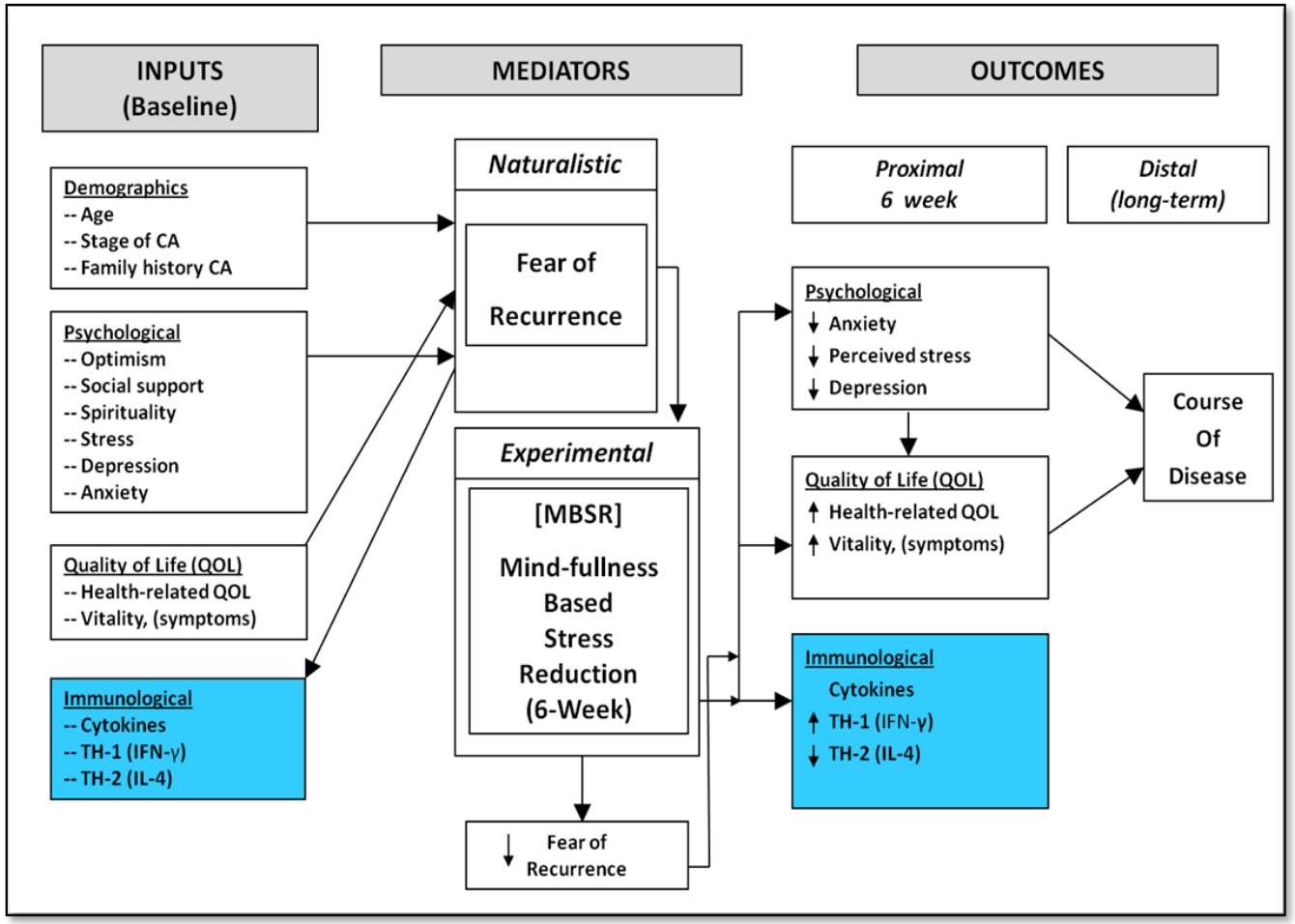
Early Stage Breast Cancer Recovery R21CA109168-02

Aim 1:

Evaluate the effect of MBSR(BC) on psychological, physical symptoms and QOL at completion of treatment.

Aim 2:

Explore mechanisms of MBSR(BC) on psychological status, QOL, and immune status.



Results

Early Stage Breast Cancer Recover R21CA109168-02

MBSR(BC) group demonstrated significant improvements compared to UC on:

- Fear of recurrence and recurrence concerns.
- State anxiety, trait anxiety and depression.
- QOL (physical functioning, role limitations and energy).
- Immune functioning significantly improved with increase ($p<0.05$) in the number of $CD4^+$ cells and activated T cells in the MBSR(BC) group ($p=0.03$).

Results

Early Stage Breast Cancer Recover R21CA109168-02

Mindfulness Based Stress Reduction (MBSR(BC)) in Breast Cancer: Evaluating Fear of Recurrence (FOR) as a Mediator of Psychological and Physical Symptoms in a Randomized Control Trial (RCT)

Cecile A. Lengacher, RN, PhD[1], Melissa M. Shelton, RN, PhD[1], Richard R. Reich, PhD[2], Michelle K. Barta, Pharm.D, MPH[1], Versie Johnson-Mallard, PhD, RN[1], Manolete S. Moscoso, PhD, PA[1], Carly Paterson, MSN[1], Sophia Ramesar, BS[1], Pinky Budhrani, BS MS[1], Irina Carranza, BS, RN[1], Jean Lucas, ARNP, MSN, MBA[1], Paul B. Jacobsen, PhD[2], Matthew J. Goodman, MD[3], and Kevin E. Kip, PhD[1]

Seventh Grant

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2

R01
NIH/NCI
(2009 - 2015)

Moving forward:

1) Larger RCT for MBSR(BC)
2) Next step: MBSR(BC) effects on multiple individual and clusters of symptoms, stress hormones, cytokines and immune markers.

Seventh Grant

MBSR(BC) Symptom Cluster Trial: R01 CA13108-01A2

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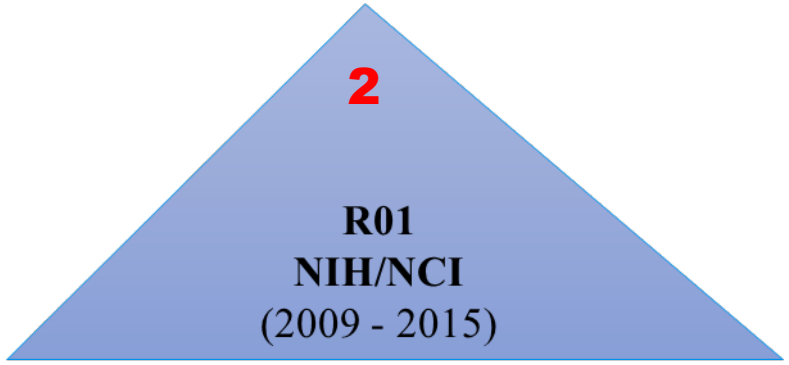


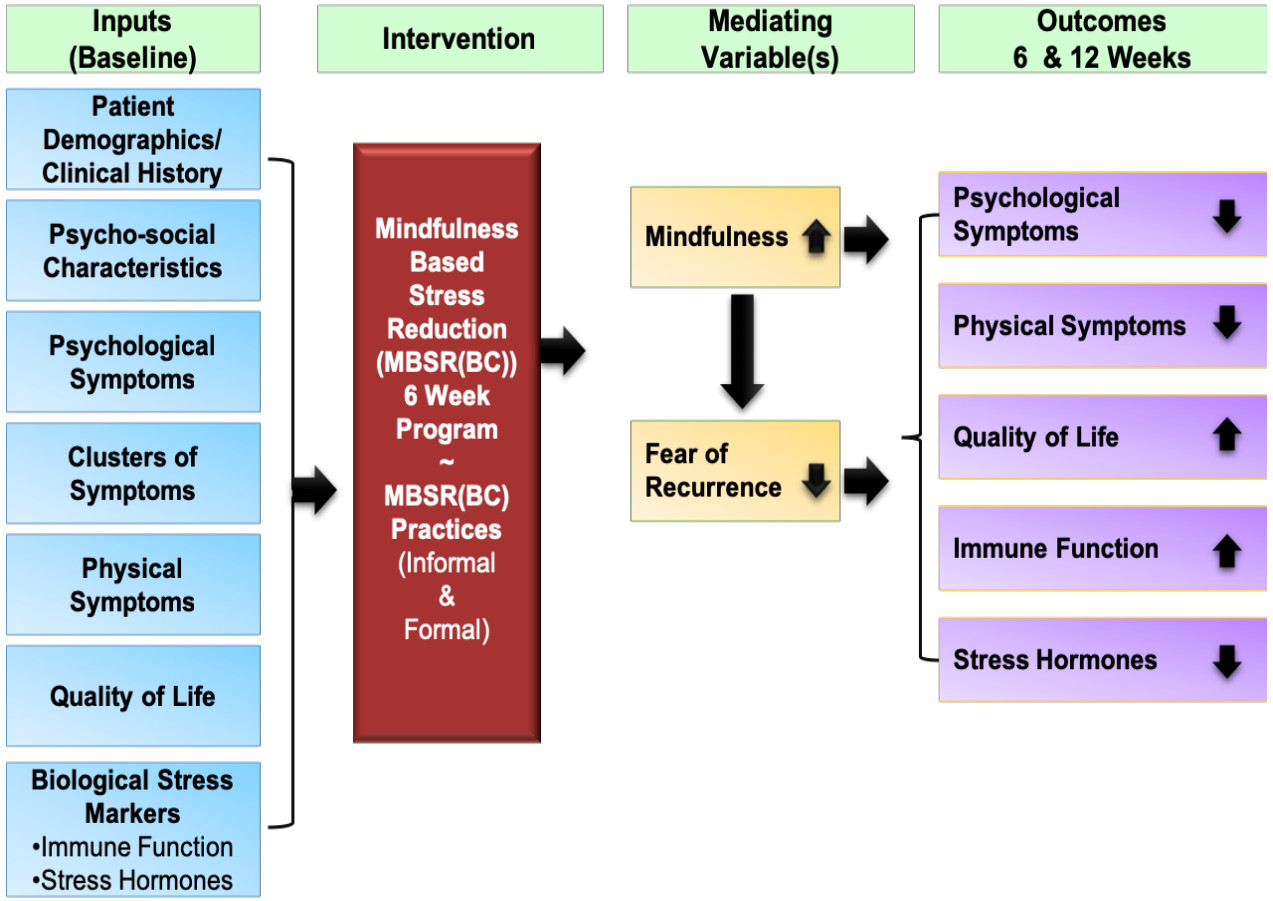
- URL of Registry: ClinicalTrials.gov, www.ClinicalTrials.gov Registration Number: NCT01177124
- Lengacher, C.A., Reich, R., Paterson, C.L., Ramesar, S., Park, Y. J., Alinat, C., Johnson-Mallard, V., Moscoso, M., Budhrani-Shani, P., Miladinovic, B., Jacobsen, P.B., Cox, C.E., Goodman, M., and Kip, K. E (2016). Examination of Broad Symptom Improvement Resulting From Mindfulness-Based Stress Reduction in Breast Cancer Survivors: A Randomized Controlled Trial. *Journal of Clinical Oncology*. doi: 10.1200/JCO.2015.65.7874

Aims and Logic Model

Aim 1
- Evaluate the efficacy of MBSR(BC) for improving psychological and physical symptoms, QOL, and measures of immune function and a stress hormone (cortisol).

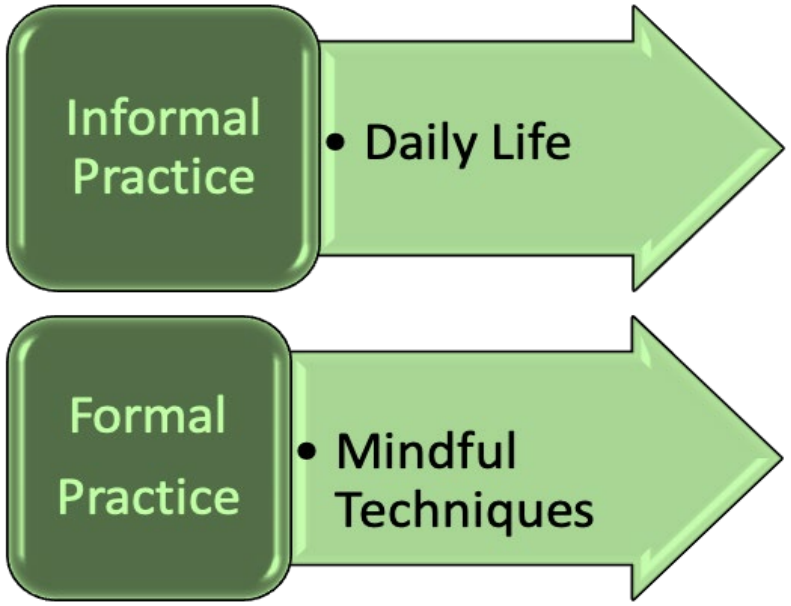
Aim 2
- Test whether positive effects achieved from the MBSR(BC) program are mediated through increased mindfulness and decreased fear of recurrence.

Aim 3
- Evaluate whether positive effects achieved are modified by patient characteristics.



MBSR(BC)

MBSR(BC) is a standardized stress-reducing intervention that combines sitting and walking meditation, body scan, and yoga adapted for BC survivors.



Results: Significant Symptom Improvement

MBSR(BC) vs. UC individual symptom improvement:

- **Psychological symptoms** (anxiety, fear of recurrence overall and fear of recurrence problems.
- **Physical symptoms** (fatigue severity, fatigue interference.
- **QOL** (general health).

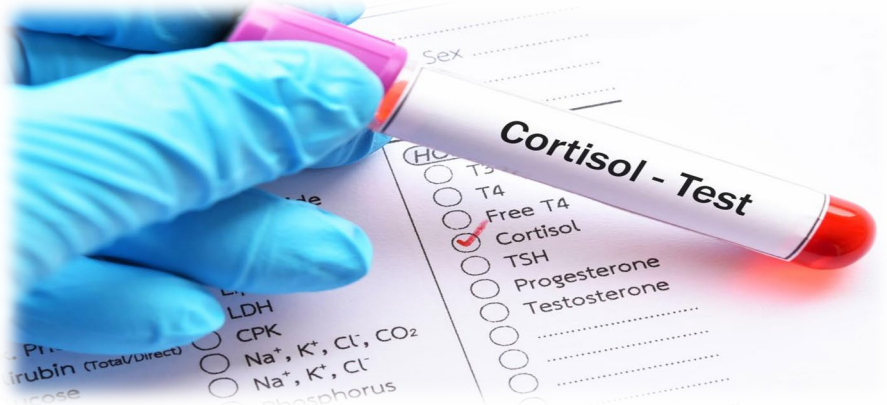
Symptom **cluster** improvement for MBSR(BC) baseline-6 weeks:

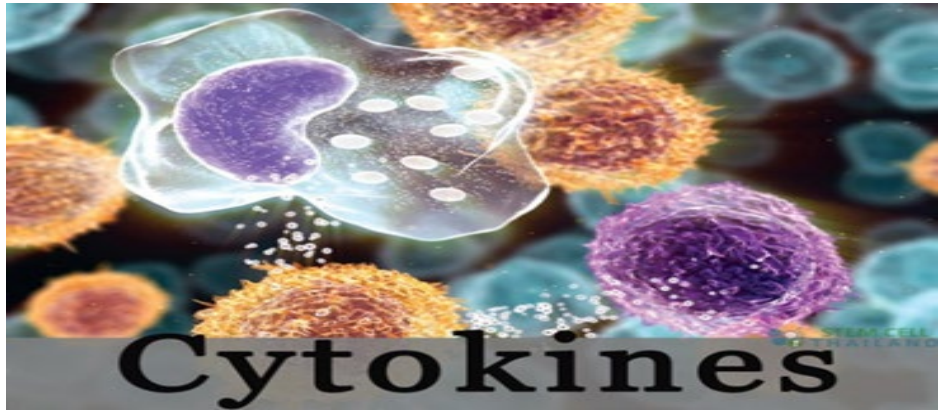
- **Psychological** cluster (anxiety, depression, perceived stress and QOL, emotional well-being).
- **Physiological** cluster, and fatigue (fatigue, sleep, and drowsiness).

Results: Stress Hormone, IL-6 and TNF-α

MBSR(BC) group:

- Cortisol levels decreased between pre- and post- MBSR(BC) assessments at week 1 and week 6 ($p<0.01$), pre- and post- intervention session.
- **IL-6 levels were reduced within** the MBSR(BC) group, at baseline and week 6 ($p<0.05$).
- **TNF**-α levels were reduced during the MBSR(BC) 6 week intervention.





Lengacher, C. A., Reich, R.R., Paterson, C.L., Shelton, M., Shivers, S., Ramesar, S., Pleasant, M.L., Budhrani-Shani, P., Groer, M., Post-White, J., Johnson-Mallard, V., Kane, B., Cousin, L., Moscoso, M. Romershausen, T.A., & Park, J.Y. (2018). A large randomized trial: Effects of mindfulness-based stress reduction (MBSR) for breast cancer survivors (BC) on salivary cortisol and IL-6. *Biological Research for Nursing*, 1-11. doi: 10.1177/1099800418789777 PMID: 30079756

Associated Symptoms and Biomarkers

Significant relationships were found between:

- IL-6 and pain (r=.21, p<0.02),
- IL-6 and QOL
  - Physical Functioning,
  - Energy, General Health, Pain, Physical Health, Role Limits-Physical
    r's ranged -.18 and -.25, p<0.05.

- Cortisol was significantly related to QOL (physical health r=-.11, p<0.05).

NCI Economic Administrative Supplement

Aims

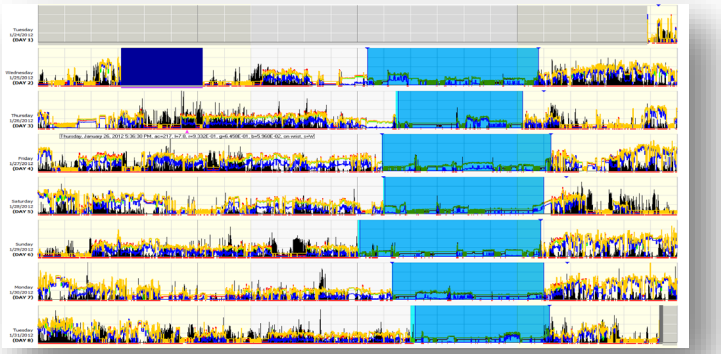
- **Estimate** costs of the MBSR(BC) for healthcare providers and out-of-pocket costs for an individual patient.
- **Estimate** the cost-effectiveness of MBSR(BC) compared to UC with respect to psychological QOL.

Results: Costs per year declined.

- **Providers**: BCS who survived 10 or 20 years would have a discounted provider cost per QALY gained of $650 or $457.
- **Patients:** An individual who survived 10 or 20 years would have a discounted cost per QALY gained of $577 or $407.

Lengacher, C. A., Kip, K. E., Reich, R. R., Craig, B. M., Mogos, M., Ramesar, S., Paterson, C., Farias, J., & Pracht, E. (2015). A cost-effective mindfulness stress reduction Program: A randomized control trial for breast cancer survivors. Nursing Economics, 33(4), 210-232.

NCI Sleep Administrative Supplement



Aim

- **Evaluate** the efficacy of the MBSR(BC) program for improving both self-report and objective sleep quality.

Significant Results

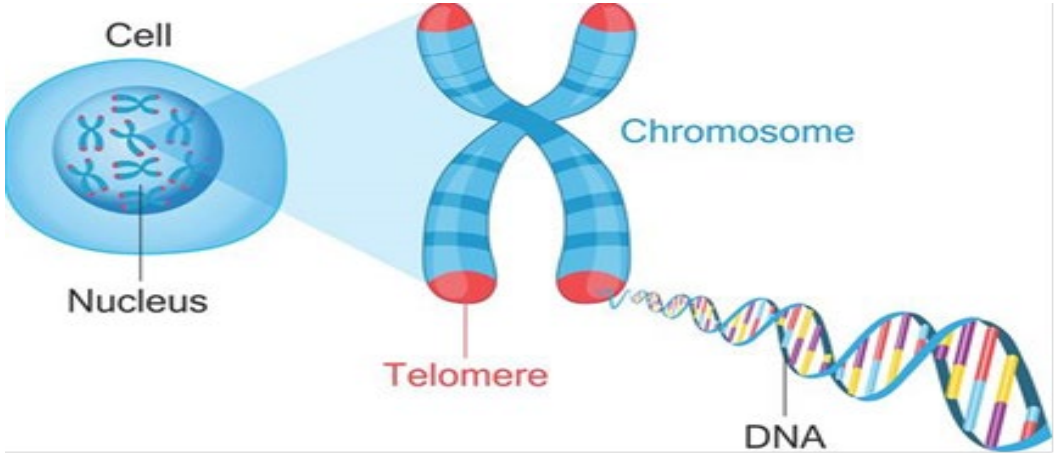
- MBSR(BC) improved objective sleep parameters at 12 weeks on sleep efficiency compared to UC group, percent of sleep time and less number waking bouts.

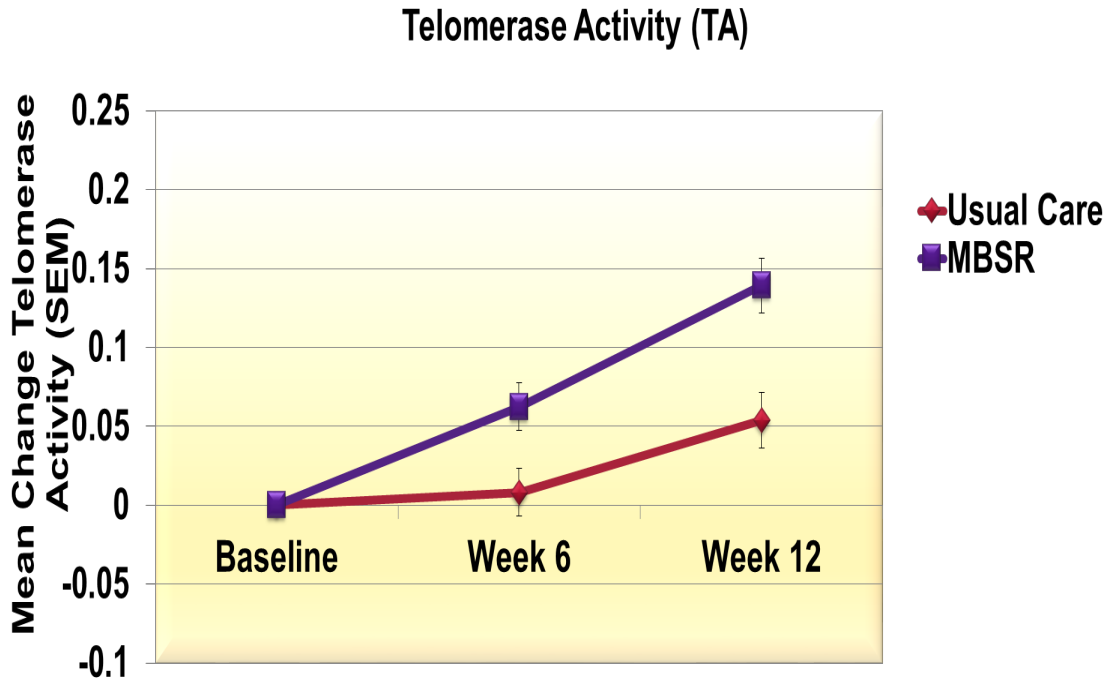
USF Established Researcher Award Telomeres

Aim:

Evaluate the effects of MBSR(BC) compared to UC on Telomere Length and Telomerase activity.

Results:

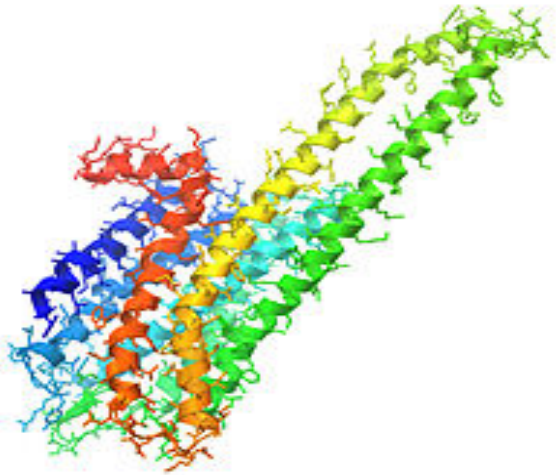


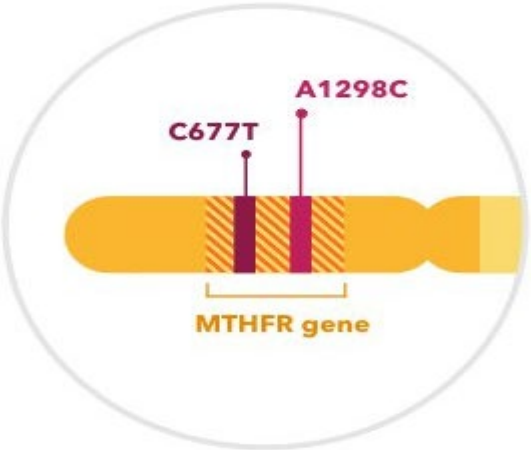


Lengacher C.A., Reich, R., Kip, K.E., Barta, M., Ramesar, S., Paterson, C.L., Moscoso, M.S., Carranza, I., Budhrani, P.H., Kim, S.J., Park, H.Y., Jacobsen, P.B., Schell, M.J., Jim, H.S.L., Post-White, J., Farias, J.R., & Park, J.Y. (2014). Influence of mindfulness-based stress reduction (MBSR) on telomerase activity in women with breast cancer (BC). *Biological Research for Nursing*, 16(4), 438-47. doi: 10.1177/1099800413519495 PMID: 24486564 PMCID: PMC4559344

Results: USF Established Researcher Award

- Genetic variants in HTR2A, APOE, and MTHFR were significantly associated with post-chemotherapy cognitive impairment among BCS.
- A larger study is warranted for confirmation. Once established, these associations may be applied in determining the impact of genetic profile on CI after CT or the efficacy of CI improvement interventions for the individual patient.
- The current R01 grant has genetic variants as moderators of effects of MBSR(BC) on cognitive functioning.





R01 CA199160-01

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R01
NIH/NCI
(2015 – 2020)

Moving forward current grant:

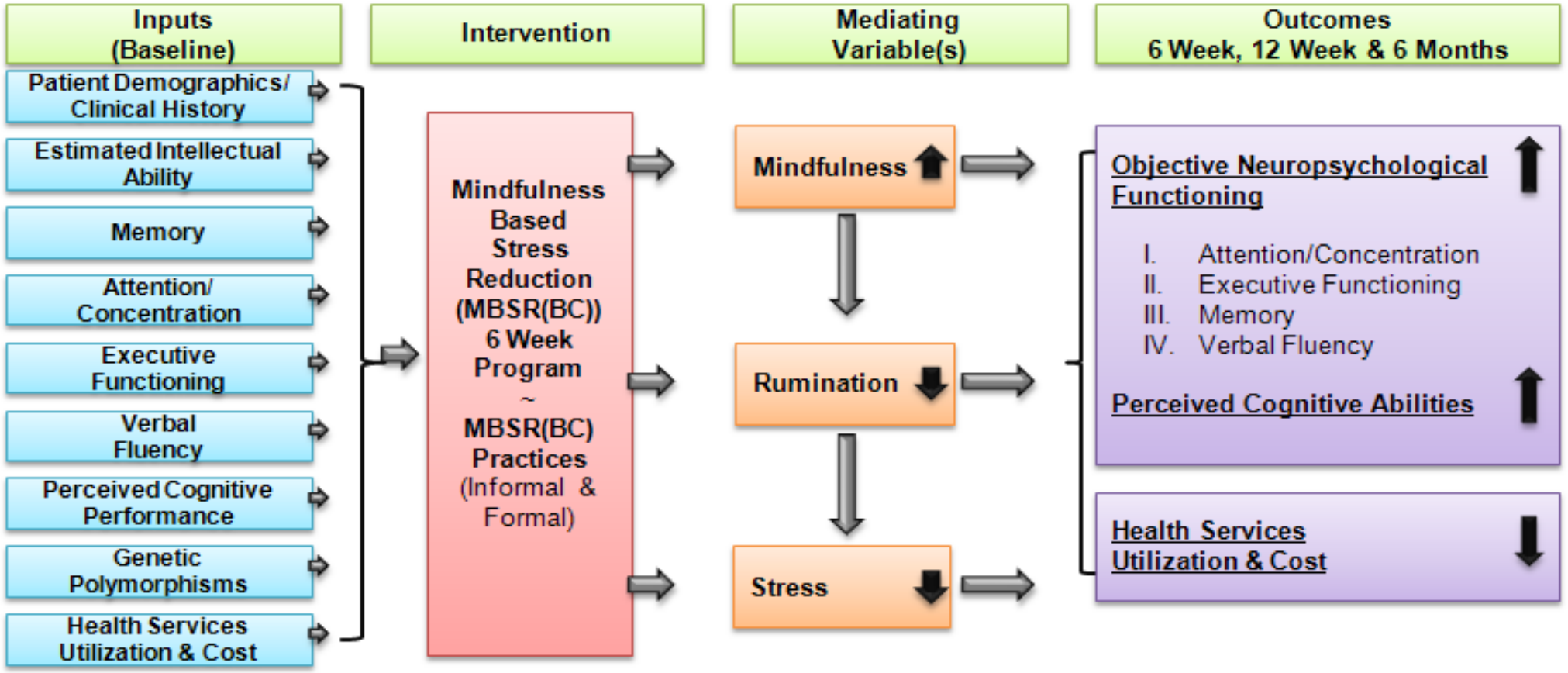
1) "Efficacy of MBSR Treatment of Cognitive Impairment Among Breast Cancer Survivors" R01 CA199160-01

Name and URL of Registry: ClinicalTrials.gov, www.ClinicalTrials.gov Registration Number: NCT

Innovation

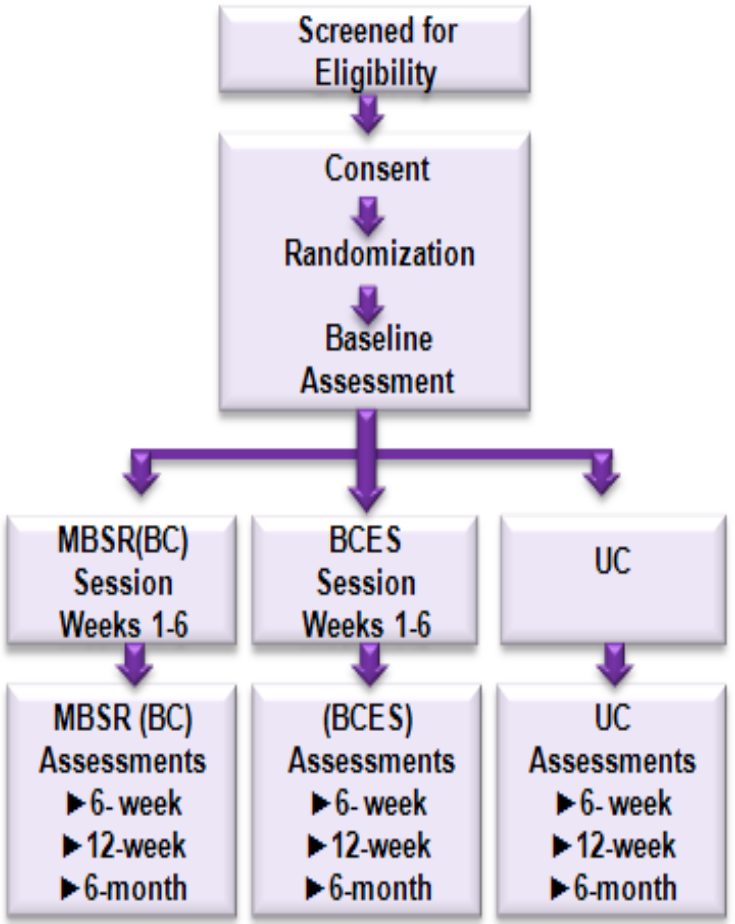
- **First R01 to:**
  - Evaluate the efficacy of MBSR(BC) among BCS for neuropsychological cognitive improvements.
  - Design and test the MBSR(BC) program in English and Spanish, and adapted for improving cognition.
  - Evaluate genetic variants as moderators of MBSR(BC) on improvements in cognitive impairment.
  - Determine the impact of MBSR(BC) on health services utilization and costs.

Biobehavioral Logic Model



Innovation

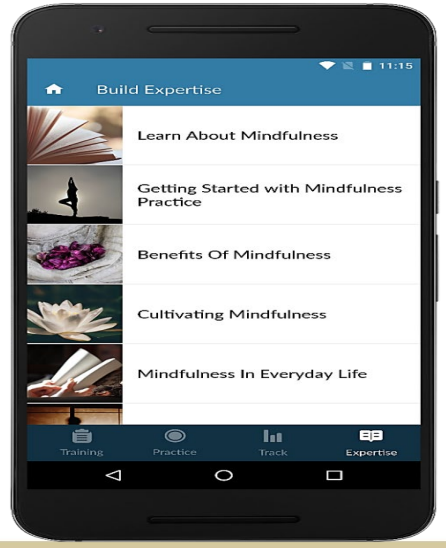
MBSR(BC)



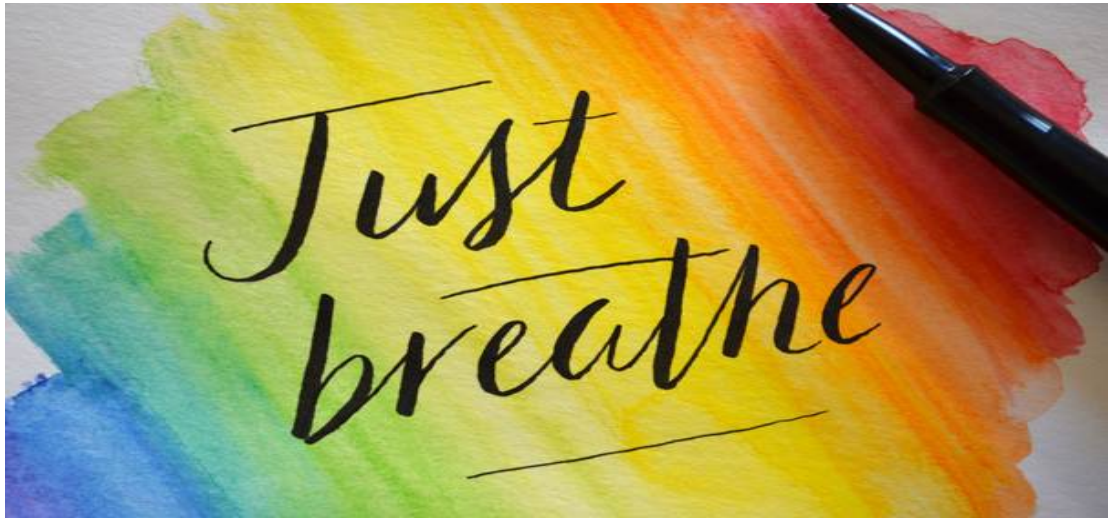
BCES

Future Directions

Next steps towards progress



Future Directions



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Takes a Team

A PREEMINENT RESEARCH UNIVERSITY

Support of Family

Support of Mentors

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Thank you!

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