

Creating the Evidence Base: Challenges in Conducting Research on the Efficacy of Mind-Body Interventions

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Outline

- CAM in cancer
- Issues in mind-body research in Psycho-oncology
- Progression of a research program
- Modifications and alternatives



CAM in cancer

- High usage of CAM interventions in cancer patients – Fouladbakhsh et al, 2005
- Interviewed 968 patients with mixed dx – 30% used CAM

Therapy	n	%
Herbal and vitamin supplements	157	55
Spiritual healing or therapy	93	33
Massage	37	13
Relaxation techniques, imagery, or yoga	28	10
Chiropractic treatments	27	9
Lifestyle diets	26	9
Therapeutic audio or videotapes	18	6
Homeopathic treatments	7	3
Acupuncture or acupressure	6	2
Therapeutic spas	5	< 1
Energy balancing	2	< 1
Osteopathic treatments	4	< 1
Medication wraps	1	< 1
Hypnosis	—	—
Other complementary and alternative medicine therapies	47	16

N = 286



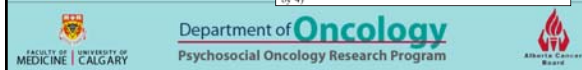
CAM in breast Cancer

- Buettner et al, 2006
- 2022 BrCa patients from Nurses' Health Study responded to survey
- 87% response rate
- 62% used CAM

Table 2 Complementary and alternative medical therapies used for any reason by respondents during the past 2 years

Therapy	N	Number using therapy	Percent of total respondents
Relaxation/imagery	1942	616	32%
Spiritual healing	1909	257	13%
Yoga	1929	228	12%
Energy healing	1929	147	8%
Acupuncture	1923	81	4%
Massage	1932	440	23%
Chiropractic	1928	225	12%
High-dose vitamins	1918	391	20%
Herbs	1895	361	19%
Homeopathy	1901	70	4%
Other CAM therapies*	1932	85	4%
Any CAM used* (Total respondents using at least 1 CAM therapy)	2022	1249	62%

*Includes infrequently used therapies, such as biofeedback (used by 24), hypnosis (used by 24), naturopathy (used by 20), osteopathy (used by 16), folk remedies (used by 16), chelation (used by 4)



Research issues in mind-body interventions

Meditation, yoga, reiki




Research Issues for CAM in cancer

- Very little empirical research on efficacy of CAM in cancer
- Lots of overblown anecdotal reports
- Seen as preying on vulnerable population
- No obvious biological mechanisms of action of many CAM therapies




Methodological Issues

- Using biomedical quantitative model to convince skeptics
- RCT as gold standard (CONSORT guidelines)
 - Problems: Blinding...triple...double...single
- Is it smart to go right to an RCT?
 - Building a research program




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Hierarchy of evidence

- Anecdotal reports/ case examples
- Program evaluation
- Qualitative research
- Pre-post study designs with validated measures
- Comparisons with other groups (non-randomized)
- Randomized trials with non-active comparison group
- Randomized trials with active comparison




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Other Quantitative Designs?

- A-B-A designs
 - Period of baseline established before introduction of treatment
 - Treatment provided for discrete time period, outcomes monitored
 - Treatment withdrawn and outcomes tracked for return to baseline
- Appropriate for treatments expected to washout



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Other Designs


- Interrupted time series
 - Basically an A-B-A design with multiple baselines of differing length between participants

Person 1: a..a..b..b..a..a..a

Person 2: a..a..a..b..b..a..a..a


Person 3: a..a..a..a..b..b..a..a

Person 4: a..a..a..a..a..b..b..a



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Other Designs

- Counterbalanced crossover design
 - Advantages: smaller sample size, recruitment...


A: Experimental Condition

5 Reiki Sessions → W → 2 Reiki Sessions → W → 5 Reiki Sessions → W → 2 Reiki Sessions

B: Rest Control Condition


5 Days of Rest → W → 5 Days of Rest → W → 5 Days of Rest → W → 5 Days of Rest → W

W = Washout Period: 7 days monitoring or 2 point increase




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Other methods?


- Qualitative methods
 - Explore the treatment from the perspective of the patient
 - can then hone in on best outcome measures
 - Case studies: Show what is possible, but won't convince the skeptics
 - Good in conjunction with quantitative methods





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The RCT: CONSORT Checklist

Interventions	4	<u>Precise details of the interventions intended for each group and how and when they were actually administered.</u>
Objectives	5	<u>Specific objectives and hypotheses.</u>
Outcomes	6	<u>Clearly defined primary and secondary outcome measures and, when applicable, any methods used to enhance the quality of measurements (e.g., multiple observations, training of assessors).</u>
Sample size	7	<u>How sample size was determined and, when applicable, explanation of any interim analyses and stopping rules.</u>
Randomization -- Sequence generation	8	<u>Method used to generate the random allocation sequence, including details of any restrictions (e.g., blocking, stratification).</u>
Randomization -- Allocation concealment	9	<u>Method used to implement the random allocation sequence (e.g., numbered containers or central telephone), clarifying whether the sequence was concealed until interventions were assigned.</u>
Randomization -- Implementation	10	<u>Who generated the allocation sequence, who enrolled participants, and who assigned participants to their groups.</u>
Blinding (masking)	11	<u>Whether or not participants, those administering the interventions, and those assessing the outcomes were blinded to group assignment. When relevant, how the success of blinding was evaluated.</u>



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Methodological Issues with RCTs

- Single-blinded possible? Ethical?
- Sham interventions
- The waitlist trial...
 - Easier to recruit but no f/u, expectancy effect
- Other control conditions?
 - Matched on contact time, social/professional support, other nonspecific factors



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Start at the beginning

Progression of a research program in Mindfulness-Based Stress Reduction



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Calgary MBSR Program

- Developed in 1996 by Michael Speca, Maureen Angen and Eileen Goodey
- Open to cancer patients and family members
- Over 1,500 patients through program
- Multiple research studies conducted
- Based on the concept of mindfulness



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Program Components

- Mindfulness – overarching theme
- Relaxation – abdominal breathing
- Gentle yoga
- Mind-body connection
- Visualization/Imagery
- Cognitive Coping Strategies
- Personal Empowerment
- Social Support



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Program Design

8-week intervention


- 1.5 hour weekly meetings with 2 instructors
- 6 hour silent “retreat” between weeks 6 and 7
- Discussion followed by mindful yoga and meditation
- Follow booklet which outlines the program
- Homework log of time spent in meditation
- Daily meditation practice encouraged and monitored - formal and informal (CDs provided)





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Group "Check-in"




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Group Yoga




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Group meditation




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TBCC Program Research

- Began with self-report outcomes
- Waitlist RCT with psychological outcomes
- Pre-post program studies
- Included biological outcomes
- Included longer follow-up
- Comparisons to other programs and groups
- Qualitative research
- RCTs with active comparison groups

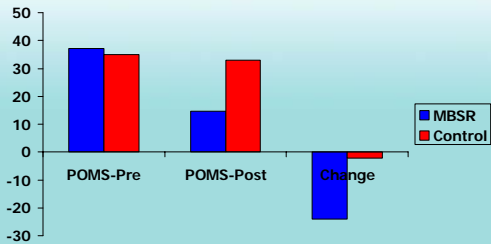

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TBCC program research



- Study 1 – Randomized controlled trial:
 - 89 patients with mixed cancer diagnoses
 - On or off treatment
 - MBSR or wait-list
- Improved symptoms of stress and less mood disturbance (Specia 2000)
- Maintenance of these improvements over 6-months (Carlson 2001)

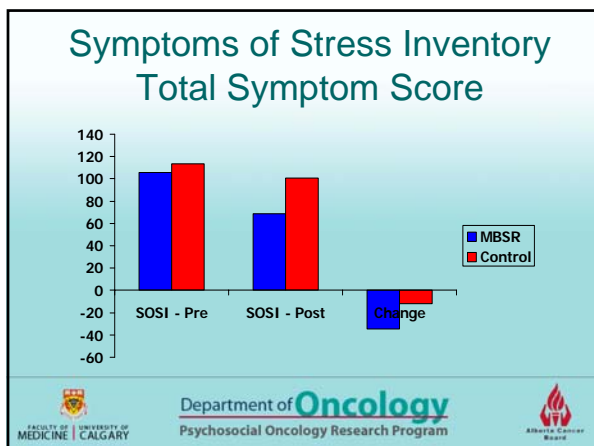

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Profile of Mood States - Total Mood Disturbance



Group	POMS-Pre	POMS-Post	Change
MBSR	~38	~15	~-23
Control	~35	~32	~-3


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Pre-post uncontrolled studies

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Study 2: Immune and endocrine effects

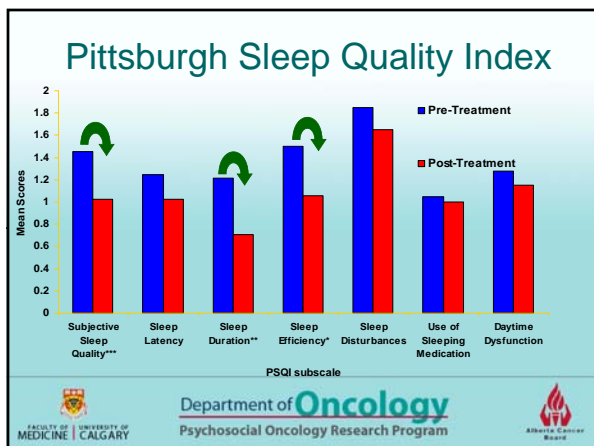
- Pre-post study with more complicated outcomes and more controlled group of subjects
- 60 early stage breast or prostate cancer patients
- At least 3-months post-treatment
 - Enhanced Quality of Life (Carlson 2003)
 - Enhanced immune function (Carlson 2003)
 - Normalized cortisol secretion patterns (Carlson 2004)
 - Maintenance at 1-year follow up (Carlson 2007)

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Study 3: Sleep outcomes

- Mixed sample of 63 Cancer patients
- Variety of dx, on and off treatments
- Improvements in a variety of sleep measures (Carlson & Garland, 2005)
- Improvements in stress, mood and fatigue levels

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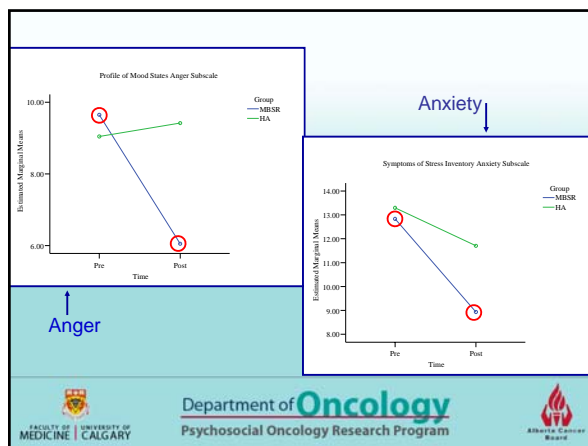


Studies with non-randomized comparison groups

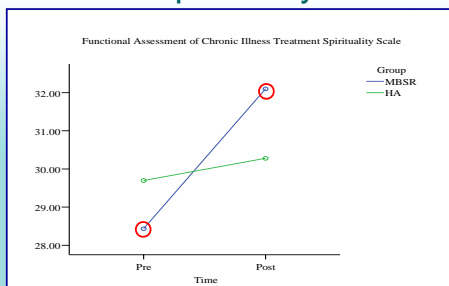
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Study 4: MBSR compared to Healing Arts

- 60 MBSR patients; 44 HA patients
- Both groups measured pre-post program and compared
- Greater improvements in MBSR in mood, stress and spirituality (Garland et al, 2007)



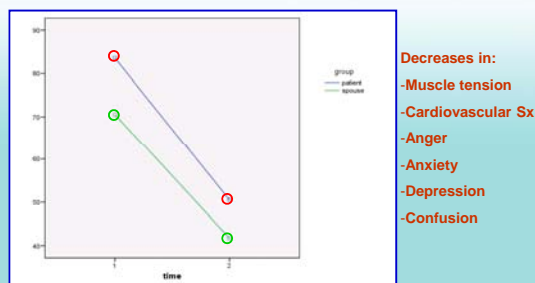
Spirituality



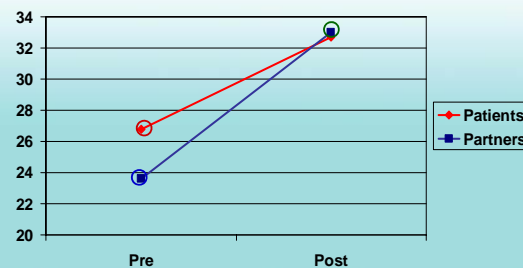
Study 5: MBSR for partners

- Compared responses of patients and their partners to MBSR
- 41 pairs on stress and mood symptoms
- 17 pairs on positive outcomes
 - Post-traumatic growth
 - Spirituality

Total symptoms of stress



Spirituality



Qualitative Research




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Study 6: Grounded Theory Study

- Interviewed long-term MBSR participants
- 7 females and 2 males
- 43-77 years in age (average age 60.8 years).
- Active in the drop-in group for between 1 and 6 years (average time 2.8 years).
- Individual interviews followed by focus group
- Data analyzed using Q6 Nudist and grounded theory approach




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Personal Transformation


- Lessening of cancer as part of identity
I'm not feeling my cancer is growing, it's becoming less and less. It's secondary. I'm looking at the positive aspects of becoming healthier, maybe even healthier than I was before.
- Change in perspective
Cancer can make a person very bitter or it can make them very wise. I'm not crazy about having had cancer but it has certainly done a lot in my life.
- Developing feelings of gratitude
How did I make a switch from being negative to positive in dealing with cancer? It was gratitude.
- Change in the relationship to oneself – knowing oneself better
It's changed my outlook on life, my relationship to other people and, most importantly, my relationship to myself. A person has to go inside and find out who they are, what their motivating factors are and what is good for them.



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Spirituality




Whenever I find that I'm really bogged down I go and I meditate. I've become a lot more spiritual.


I would say, to use a cliché, it is about spirituality. What is the definition of spirituality. It's about your connection. You're connected to something outside of yourself.

this is exercise of the spirit... You come for not only learning how to connect more with yourself, but you're also connecting with other people who understand the pain.

It's wise, there's this universality about it. You don't have to come from a certain faith tradition to take some of these things away.




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Current Studies - RCTs


- MASTER
- MINDSET
- MINDMAP



- Studies of MBSR for women diagnosed with breast cancer




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MASTER: Mindfulness-based stress reduction and Acute Stress Test Experimental Reactivity in women with cancer

Linda Carlson
Laura Van Wielingen
Tavis Campbell

Funded by the Canadian Breast Cancer Research Alliance Survivorship Grants



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Study Design

- Nonrandomized waitlist trial of women diagnosed with cancer participating in MBSR
- Tested pre-post MBSR or wait-period with laboratory stress protocol
- Blood pressure monitored weekly throughout MBSR



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Results: Psychological

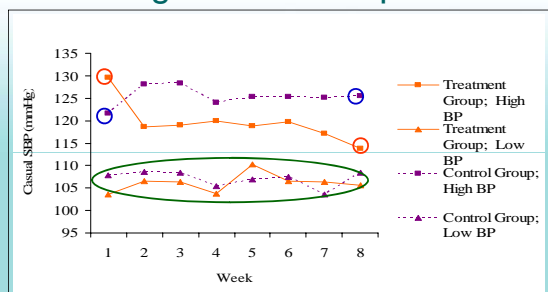
- Improvements in the treatment group:
 - 26% ↓ symptoms of stress
 - 49% ↓ symptoms of depression
 - 68% ↓ mood disturbance
 - ↓ rumination
 - ↑ mindful attention-awareness



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Resting home blood pressure



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MINDSET: MINDfulness-based stress reduction versus Supportive Expressive Therapy in breast cancer survivors

Linda E. Carlson
Michael Specca
Richard Doll
Joanne Stephen

Funded by the Canadian Breast Cancer
Research Alliance Survivorship Grants



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Study Design

- 3-armed randomized controlled trial in distressed breast cancer survivors
 - MBSR
 - Supportive-Expressive Therapy (SET)
 - One-day Stress Management Seminar
- Pre-Post, 6, 12 month assessment
- Psychological, biological, moderators



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MINDMAP

A pilot study of MINDfulness Meditation
(M) and AcuPuncture (A) for the
treatment of pain in women with bone
metastases receiving palliative radiation
therapy

Linda E. Carlson, PhD
Michael Specca, PsyD
Jackson Wu, MD



Funded by the Canadian Breast Cancer Research Alliance
Developmental and Exploratory Grants




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MINDMAP Study Design


- Pilot feasibility study of a 3-arm randomized control trial (RCT)
- Patients randomized to one of three treatment groups:




Radiation Therapy (RT) only




Radiation Therapy (RT) plus MM



Radiation Therapy (RT) plus Acupuncture
- Assessed with pain diaries, cortisol, questionnaires and followed for 4 months




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