Effective Approaches: Interventions for Weight Management in Cancer Survivors

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Efficacy versus Effectiveness

**Efficacy**: refers to explanatory trials to determine whether an intervention produces the expected result under ideal circumstances.

**Effectiveness**: refers to pragmatic trials that measure the degree of beneficial effect under “real world” settings.

Effectiveness = adherence in real world x efficacy

Pagoto and Leon, JAMA Intern Med, 2013;
Overview:
What makes for an effective intervention?

- The team
- The population
- Formative research
- Outcome(s)
- Intervention
  - Evidence-based components
  - Timing
  - Fidelity
  - Delivery Modalities
  - Health Behavioral Theory and Methods
  - Balancing touch and burden

- Future directions
The Team

No evidence-based, direct comparisons with variable team members

**Professional expertise:**
- Behavioral Health / Psychologist
- Biostatisticians
- Clinical Interventionists: RDN and/or Exercise physiologists
- Health coaches
- Health economists
- Oncologist / Cancer Therapy Specialists
- *Survivors*

**Community-based:**
- Community health workers / Promotoras
- Community and/or industry partners: YMCA, Curves, Weight Watchers, etc

**Robust and/or novel:**
- Software engineers
- Adaptive design specialists
The Population

Weight loss effect demonstrated largely in:

- “worried well” cancer survivor; healthier baseline health behaviors
- women

More Diversity is Necessary

- All obesity-associated cancers
- Representation of survivors with low adherence to lifestyle survivorship guidance
- and/or those with restrictions in diet and/or activity
- and/or on medications for weight, lipid, metabolic management
- Race and ethnically diverse, both males, females
- Representation of children and advanced age
- Representation of rural participants
Want greater effectiveness?
Do the formative research

Focus group; structured interviews
Stakeholders - Study population, caregivers, family members, clinical providers, etc

Data:
- General knowledge and understanding
- Recruitment potential
- Interest
- Expected adherence; barriers/ problem solving
- Preferred delivery mode(s)
- Symptoms: the case for oncology-specific interventions
  - Diet: bloating, diarrhea, constipation, flatulence, intolerances
  - Activity: fatigue, neuropathy, muscular pain (AIs), imbalance
Formative research = Intervention tailoring

Symptoms can influence behavior change and adherence: Data from the Ovarian cancer LIVES trial

MDASI Core Symptoms

RENEW trial analysis suggests symptoms do not preclude successful weight loss in older, symptomatic survivors
Kenzik K et al., J Geriatr Oncol, 2015
Outcomes: RCT Weight Loss

Effectiveness for:
- Change in weight, BMI [Thomson, 2010; Chlebowski, 2007]
- Change in QOL; select subscales SF-36 [Demark-Wahnefried, 2006; Scheier, 2005]
- Metabolic biomarkers [Goodwin, Ambrosone, Hong, 2015; 26059936]
- Less evidence: PFS, Recurrence, overall and cancer-specific mortality

Rigor and Robust Design:
- Objective measures of weight and circumferences
  - Increasing use of electronic scale
- Adjudication of outcomes (including obesity-related co-morbidities)
- Combined survival and mechanistic biomarkers
- Repeat measures (trend analysis)
- And objective lifestyle behavior change biomarkers

Thomson, Nutr Cancer, 2010; 21058203
Enhancing Effectiveness (and Impact): Focus on Outcomes

Less attention / Proposed improvements:

- Statistically powered subgroup effectiveness analysis
  - *Apriori* adherence scores/measures [Pierce, 2007; 17885013]
  - Genetic predictor of responsiveness (e.g. PNPLA3) [Shen, 2015; 25040896]
- Health-related cost effectiveness analyses [Gordon LG, 2015; ACTRN1260800399392]
- Development/assessment of cancer-associated (e.g. VEGF, e-selectin) [Linkov F, 2012; 22198242] and prognostic markers (e.g. Glasgow Prognostic Index) [Simmons, 2017; 28062344]
- Body composition [Caan and Kroenke, 2017; 28069726]
Components of Intervention

Consensus
◦ Diet, physical activity, behavior modification
◦ Other:
   * meal replacement  *sleep hygiene  *stress management  *microbiome

Caloric restriction more so than macronutrient distribution

Low CHO vs Low Fat weight loss intervention trials in breast cancer
◦ 24 weeks: -5.9 Low CHO vs -6.3 Low fat (p= <0.001)
  Thomson, 2010 [21058203]
◦ 24 weeks: NS across groups; 9 kg
  Thompson, 2015 [26010254]
Health Behavior Theory and Methods

Commonly applied theories
- Social Cognitive Theory
- Theory of Planned Behavior
- Health Belief Model

Applications/Strategies
- Self-monitoring (weight, diet, physical activity, sedentary time)
- Build self-efficacy
  
  *Well-established evidence for non-survivor and survivor populations*

Need to identify predictors of weight loss and long-term weight maintenance in cancer survivors
Systematic Review: MI with Cancer Survivors

15 studies utilizing MI in cancer survivors for a range of behaviors

- Efficacious across a variety of cancer types
- MI patient-centered approach useful for:
  - Working through ambivalence,
  - Building self-efficacy,
  - Tailoring re: emotional and physical repercussions of cancer diagnosis and treatment

Telephone-based interventions most commonly apply MI

Spencer, JC and Wheeler SB Patient Education and Counseling 2016
Timing of Intervention: Cancer Continuum

“Teachable moment”: Risk-benefit

- US Health and Retirement Study analysis: new chronic disease diagnosis increased preventive medical procedures, but not physical activity
- PASS study demonstrate only 7.5% of men in active surveillance lost > 5% body weight during observational period
- Oncology nurses report high patient receptiveness to health behavior change during treatment
- Greater time since diagnosis predicted less healthy behaviors; interventions in closure proximity to diagnosis are warranted

Few studies to evaluate neo-adjuvant, active treatment interventions (although common with tobacco cessation)

Xiang X, 2016,26634998 ; Liss MA, 2016; 27431498; Karvinen, 2015, 2648830; Bluethmann, 2015, 26060053
Delivery

- Mail/print education and counseling
- Multimodal counseling
- Telephonic counseling
- Onsite 1:1 and Group counseling

Increasing Efficacy and Effect Size

## Delivery Modalities: Diet ± Physical Activity for Weight Loss

<table>
<thead>
<tr>
<th>Delivery Mode</th>
<th>Advantages</th>
<th>Disadvantages</th>
<th>Cancer type</th>
<th>Weight/ BMI</th>
<th>Examples from Survivorship interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinically-based/Supervised (1:1 w or w/out grps)</td>
<td>Treatment fidelity Safety Integration w/ care delivery</td>
<td>Cost Participant burden Access barriers</td>
<td>Mixed</td>
<td>Range 2-9 kg at 6 months; 5 kg at 12 months</td>
<td>CHOICE, Sedlackeck, 2011; Campbell, 2012; Get Fit for the Fight, Swisher, 2015; SUCCEED, McCarroll, 2014; Travier, 2014; Harris, 2012</td>
</tr>
<tr>
<td>Community-based/diverse populations</td>
<td>Reach Dissemination</td>
<td>Fidelity</td>
<td>Breast</td>
<td>-2.6 kg vs -1.5 kg @ 12 w Active trial</td>
<td>Cocinar Para Su Salud, Greenlee, 2016; Moving Forward, Stolley, 2015</td>
</tr>
<tr>
<td>Commercial programs</td>
<td>Availability Normalization Fidelity (?)</td>
<td>Cost Access in rural areas</td>
<td>Breast</td>
<td>-2.6 kg WW; -9.4 kg WW + 1:1; +0.85 kg control -3.3(±3.5)% vs -1.8(±2.9)%</td>
<td>Weight Watchers, Djuric, 2002 Curves, Greenlee, 2016</td>
</tr>
<tr>
<td>Home-based</td>
<td>Privacy Cost savings</td>
<td>Safety (?)</td>
<td>Breast, prostate, colorectal Breast</td>
<td>-2.06 kg vs -0.92 kg BMI @ 12 mo: -1.4 mom/ -1.38 daughter</td>
<td>RENEW, Morey, 2009; DAMES, Demark-Wahnefried, 2014</td>
</tr>
<tr>
<td>Telephone / Group Phone</td>
<td>Cost savings Reach (geographic) Social support</td>
<td>Less personal Safety(?)</td>
<td>Breast</td>
<td>-5.4% tele vs -2.0% usual -4.8 kg tele vs -1.7 kg usual -5.3 vs 0.7% (6m) / -3.6 vs 0.4% (12 m)</td>
<td>LEAN, Harrigan, 2016; Befort, 2014; LISA, Goodwin, 2014</td>
</tr>
<tr>
<td>Technology-based</td>
<td>Reach/ Dissemination Technology IQ, access IT support req Safety(?)</td>
<td>Childhood Endometrial</td>
<td>Over 14 yr less weight gain -6.4 kg @ 6 mo</td>
<td>Fit4Life, Huang, 2014 McCarroll ML, 2015</td>
<td></td>
</tr>
<tr>
<td>Print materials</td>
<td>Reach/ Dissemination Cost savings</td>
<td>Safety(?)</td>
<td>Breast, prostate</td>
<td>-0.3 vs +0.1 BMI No change</td>
<td>FRESH START, Demark-Wahnefried, 2007; Park CL, 2016</td>
</tr>
<tr>
<td>Mixed-delivery modalities</td>
<td>As above</td>
<td>As above</td>
<td>Breast Endometrial</td>
<td>6% vs 1.5% control (12 mo) -3.5 kg vs +1.4 kg -0.8 kg vs +0.2 kg</td>
<td>ENERGY, Rock, 2015; Von Gruenigan, 2008; Stepping STONE, Sheppard, 2016</td>
</tr>
</tbody>
</table>
Balancing Intervention Intensity and Duration: Effect, Adherence, Retention

**Indirect/Unintentional touch**
- healthcare team;
- family members/caregivers;
- social media

**Cancer Weight Management Studies:**
- Most trials high, early touch
- Short to moderate duration (12w-12m)
Adherence and Retention: Weight loss studies

Overall adherence is similar to non-survivor weight loss

Overall retention is greater than for general obese, adult population; lower for pragmatic, community-based trials

Approaches to enhance adherence and retention

◦ Multimodal communications
◦ Adherence “challenges” with prizes
◦ Tracking / self-monitoring
◦ Report back of behavior change (from validated instruments)
◦ Study identity items and study progress updates
◦ Compensation vs reward

Fidelity of intervention


Manuscripts commonly do not robustly describe fidelity-related information

Review of “convenience” sample of 10 studies of weight loss in cancer survivors

- Program content, # contacts, duration: 9/10
- Provider training: 8/10
- Post-training skills assessment: 2/10
- Ensure content delivery: 5/10
- Treatment manual: 3/10
- Participant comprehension assessment: 1/10
- Adherence assessment: 7/10

*Risk of bias for majority of studies is high:* Reeves et al, *Obesity Reviews*, 2014
Where are we?

We can promote weight change in survivors.....

Effective and efficacious approaches have been developed and delivered.....

Gaps and opportunities remain.....

Probably time to get more pragmatic in terms of establishing effectiveness, including more focus on primary prevention

Dissemination/implementation science [Eakin EG, 2015, HCTRN 12615000882527]
Future Directions

Adaptive Designs
- Cost-effectiveness
- Identify and remove less effective interventions earlier; Move survivors into high-reward interventions sooner
- Opportunity to integrate multiple behaviors that may cluster
- Test medication + lifestyle [Patterson RE et al., Weight loss + metformin, Contemp Clin Trials, 2016]

Applications of behavioral approaches/theories from tobacco and substance abuse literature
- Self-expansion [Xu X, ....Wing, RR, Ann Behav Med, 2-17]

Precision Medicine
- Genetics: Risk perception and responsiveness
- Molecular basis of variability in weight change: NIH workshop, Bray MS et al., Obesity, 2016 [26692578]