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

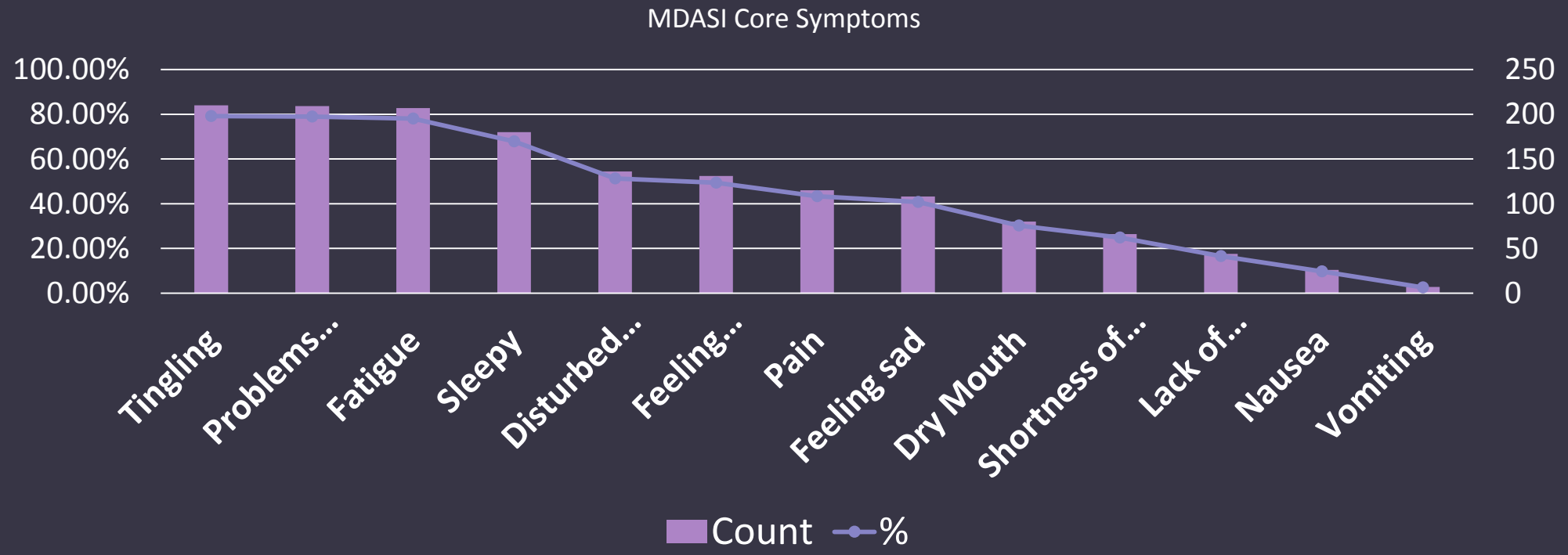
Stakeholders - Study population, caregivers, family members, clinical providers, etc

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



RENEW trial analysis suggests symptoms do not preclude successful weight loss in older, symptomatic survivors

Kenzik K et al., *J Geriatr Oncol*, 2015

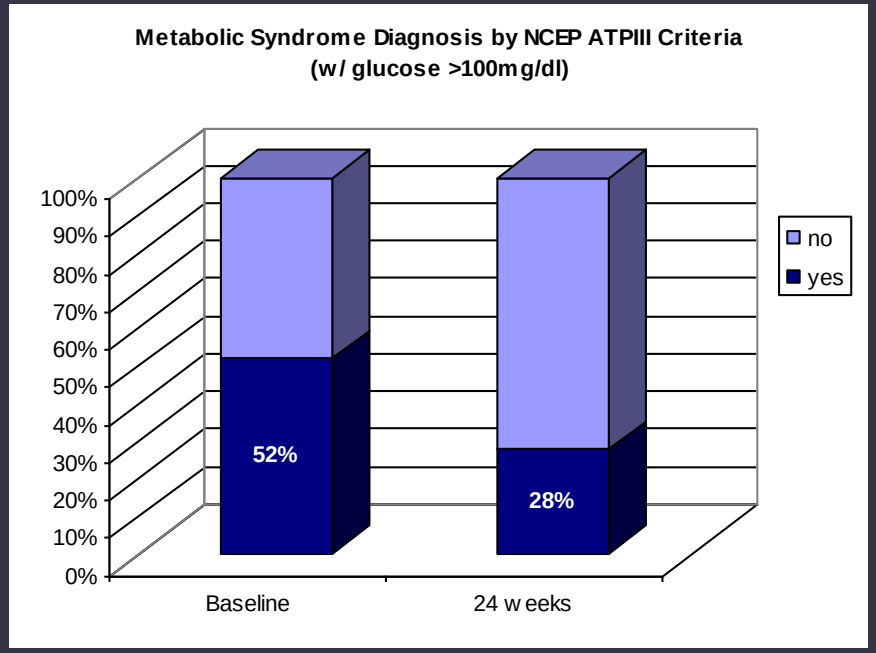
Outcomes: RCT Weight Loss

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

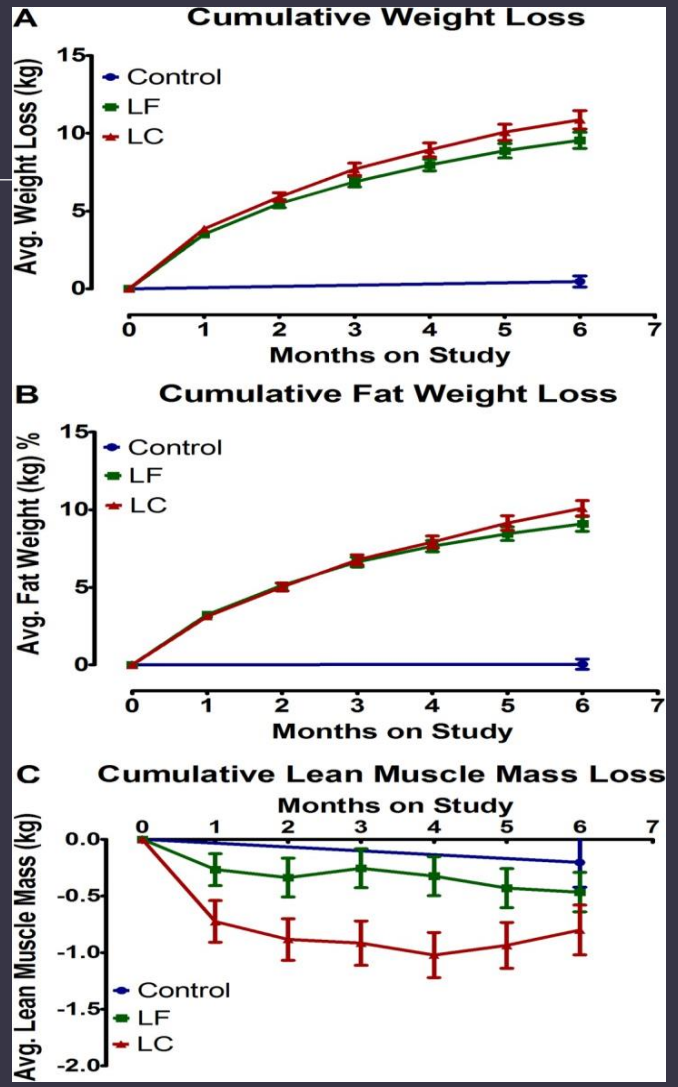
Caloric restriction more so than macronutrient distribution

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]



Managing Overweight and Obesity in Adults, NIH, 2013

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

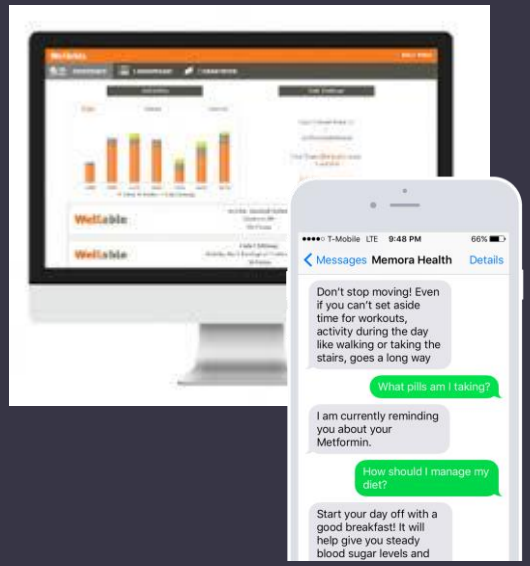
Few studies to evaluate neo-adjuvant, active treatment interventions (although common with tobacco cessation)

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

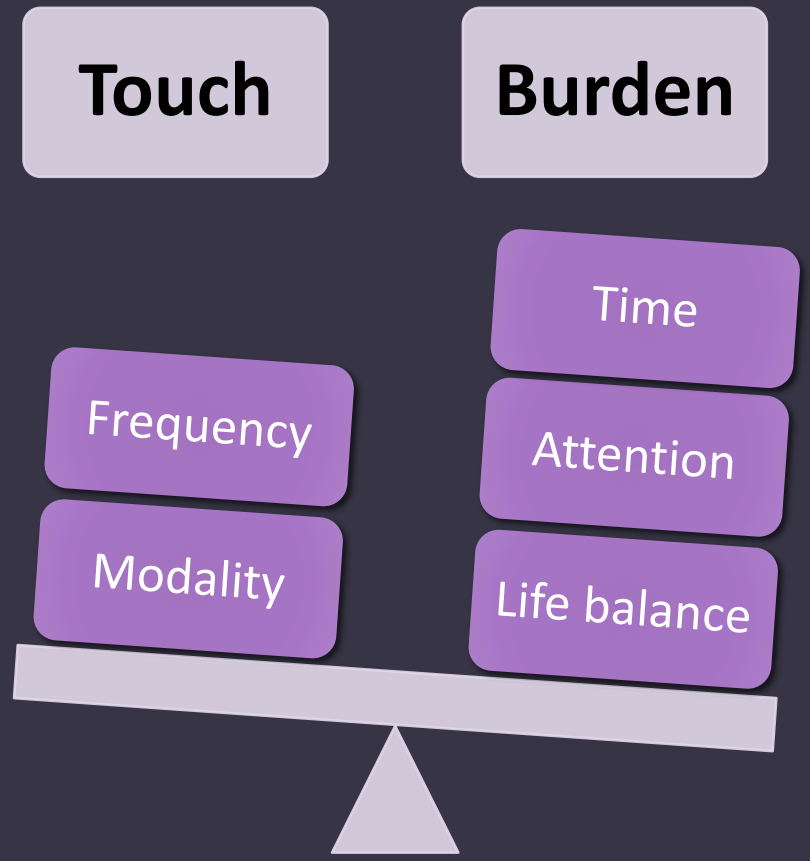
Increasing Efficacy and Effect Size

West & Mitchie, University College of London, Guide to Development and Evaluation of Digital Behavior Change Interventions in Healthcare, 2016

Delivery Modalities: Diet ± Physical Activity for Weight loss

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

Balancing Intervention Intensity and Duration: Effect, Adherence, Retention



Cancer Weight Management Studies:

- Most trials high, early touch
- Short to moderate duration (12w-12m)

Indirect/ Unintentional touch

- healthcare team;
- family members/ caregivers;
- social media

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

<u>Approaches to enhance adherence and retention</u>

- 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

Delhanty, Obes Sci Pract, 2016; Warner CT, BMC Pub Health, 2013; Goldberg and Kiernan, Health Educ Res, 2004

Fidelity of intervention

NIH Behavior Change Consortium, *Health Psychology*, 2004

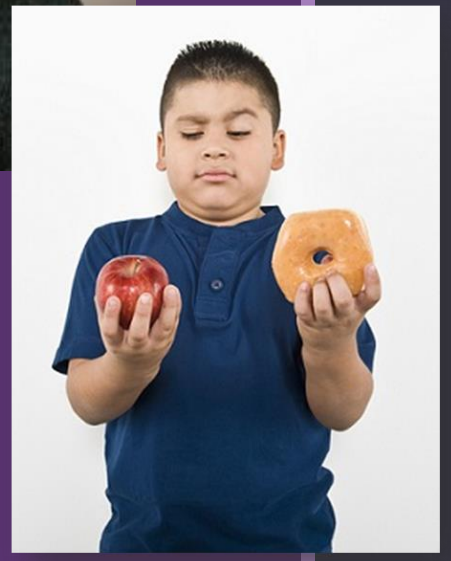
Manuscripts commonly do not robustly describe fidelity-related information

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]***