

Interventions to Promote Physical Activity in Cancer Survivors

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Goals

- Review of Literature
 - Focus on adult survivors
 - Focus on randomized controlled trials (RCTs)
- Challenge of Behavior Change: Exercise Adoption and Maintenance
 - Theories and Constructs
- Questions to be Explored
- Exercise in the Cancer Healthcare Continuum

Reviews

- Literature search of reviews 2013+ (keywords: reviews, meta-analyses, synthesis, cancer patients, cancer survivors, physical activity, exercise)
- **78** publications identified
- 28 excluded (e.g., editorials, epidemiology, yoga, pediatric patients)
- **52 review papers** included (heterogeneity regarding inclusion/exclusion criteria, not confined to RCTs)

Cancer Type	Number of Reviews
Mixed	14
Breast	17
Prostate	7
Lung	7
Colorectal	2
Head & neck	2
Lymphoma	1
Gynecological	1
Stem cell transplant	1

When in the Cancer Trajectory(ies)?

- Potential time-point(s) for exercise promotion

Pre-treatment (Pre-surgery: Singh et al., 2013; Neo-adjuvant therapy: Padilha et al., 2014)

During treatment

Posttreatment

Long-term survivorship

Palliative care

End of life

1. Reach

1st Generation Studies

- Majority of studies during and posttreatment
- Select group of participants (conservative eligibility criteria) limited generalizability
- Differences btw nonparticipants and participants not clear (representativeness: tumor registries vs. convenience samples)

2. Efficacy (Speck et al., 2010)

- During treatment
 - Small-to-moderate effect on fitness, upper and lower body strength, body weight, functional QOL, anxiety and self-esteem
- Posttreatment:
 - Large effect on upper and lower body strength, BrCa specific concerns
 - Small-to-moderate effects on exercise, aerobic fitness, overall QOL, fatigue, IGF-1

3. Safety/Adverse Effects

- Speck et al. (2010)
 - Of 36 studies that reported presence/absence of AEs, 29 reported no harm
- Risk of inactivity?

4. Attrition

- Speck et al. (2010)
 - 11.2 % (range: 0 – 48.3%)
 - 12.7% during treatment vs. 10.2% posttreatment

5. Settings

- Settings/Institutions: Research settings/hospitals and off-site

Feature	On-Site	Off-site (print, telephone, web, social media)
Exercise Prescription*	Yes, with training progression	Yes (FITT)
Baseline exercise testing	Yes	Seldom
Dose delivered	Moderate-to-High	Light-to-Moderate Likely to be lower than on-site
Length	12-16 weeks	12-16 weeks, longer for print-based programs
Type	Aerobic (AET) only, progressive resistance training (PRT), combined	AET only, AET+PRT
Delivery agents	Exercise physiologists, certified exercise trainers	Varies Research staff, nurses, none (print/web based)

* Principles of exercise training have not been applied: individualization, specificity, progressive overload and rest/recovery. Importance of increasing the training volume, Sasso et al., 2015

Feature	On-Site	Off-site
When?	During adjuvant therapy, post-treatment, a few at pre-operation/during neo-adjuvant therapy	Often for post-treatment and long-term survivors (> 5 years)
For whom?	Breast, prostate, CRC, lung Generally sedentary/not using PRT	Breast, prostate, CRC, lung Generally sedentary
Group-based	Yes	Likely to be exercising alone/friend/partner
Reach	Highly select, those who can travel and meet scheduling requirements	Wide

Feature	On-site	Off-site
Integrity of intervention delivery	High: Close supervision and monitoring	Variable
Adherence	Monitored	Variable (often dependent on self-reports)
Effects	Stronger effects on many outcomes (cardiorespiratory fitness, strength, fatigue, etc.)	Effects are small-to-moderate (with exceptions) Importance of objective data
Theory	Seldom reported	Yes: Many focus on behavior change and use theories

Feature	On-site	Off-site
Safety	Monitored and AEs should be reported	Level of monitoring varies
Attrition	Low (highly select participants) Some threat of contamination	Low Threat of contamination (attention control, wait-list control)
Costs	Not reported: likely to be high (resource intensive)	Few program report costs: likely to be inexpensive vs. on-site programs
Maintenance	Not frequently assessed	Possibly better than on-site

On-site supervised moderate-to-high intensity combined AET + PRT vs. low-intensity home-based program vs. usual care, BrCa patients during chemotherapy (e.g., van Waart et al., 2015).

Challenge of Behavior Change

Theories and Constructs

- Majority of on-site programs have been atheoretical
- Social cognitive theory (self-efficacy, outcome expectations, social support been explored) (Loprinzi & Lee, 2014)
- Theory of Planned Behavior: individual, normative, control beliefs and behavioral intention
- Transtheoretical Model: Motivational readiness, decisional balance and processes of change

Pinto, B. M. & Ciccolo, J. (2010). Physical activity motivation and cancer survivorship. *Recent Results in Cancer Research*, 186, 367-387.

Theories: Social Cognitive Theory

Review of 12 RCTs: 10 exercise, 1 diet, 7 exercise +diet (Stacey et al., 2015)

- Small-to-moderate effects on PA after about 12 weeks
- Self-efficacy (SE) frequently targeted via pedometer/PA logs
- Social support targeted in outcome expectancy
- ↑SE associated with ↑PA in 3 trials
 - Moderator analyses: those with higher SE increased PA ↑ faster than those with lower SE
 - Mediation analyses showed partial mediation by SE

Key Components

- Goal setting, monitoring via pedometer/wearables, clear recommendations
- Getting social support, behavioral and cognitive skills are evidence-based but role for cancer survivors less clear

Behavior Change Studies

- Meta-analyses of 14 RCTs among bca survivors (2005-2013) (Bluethmann et al., 2015)
 - <5 years post-diagnosis
 - Mean 153 participants/study (white, well-educated women living in metropolitan areas)
 - 17 weeks in duration
 - Moderate-intensity exercise
- Majority were wholly-to-partially home-based

Perhaps More is not Better?

- Standardized mean difference=0.47
- Larger effects produced by highly structured programs BUT interventions via phone or email also effective (e.g., brisk walking)
- Components: self-monitoring (e.g., pedometers), individual counseling, or coaching, workshops/peer support groups

Intensive Hybrid Approach

- Challenge trial, n=273 CRC, Canadian Cancer Trials Group
- Structured exercise vs. health education
- Based on Diabetes Prevention Program and Theory of Planned Behavior
- 6 months for adoption, 6 months for consolidation (face-to-face or by phone)
- ↑ recreational PA and ↑ fitness at one-year (Courneya et al., 2016)
- Components
 - Supervised exercise
 - free or access to a fitness facility
 - frequent and on-going contact with qualified staff
 - individual tailoring
 - written materials
 - use of 17 behavior change techniques

Maintenance

- Maintenance of outcomes important:
 - Mgt of CVD, diabetes, etc., potentially for cancer survival (Holmes et al. 2005, Irwin et al., 2011, Meyerhardt et al., 2006; 2009)
 - Psy. benefits of exercise may not be sustained if the behavior is not maintained for at least 6 months (Pinto, Dunsiger & Waldemore, 2013)

Maintenance of Exercise and Outcomes

- Spark et al., 2013 review of 63 exercise and dietary interventions for bca survivors
 - 10 (16 %) assessed post-intervention (at least 3 months after last contact) outcomes; four of these 10 trials achieved successful maintenance (fitness, strength, PA, energy expenditure)
- Intervention studies have begun to address examining long-term maintenance of exercise (e.g., Morey et al., 2009; Mutrie et al., 2012)
- Additional challenges related to long-term or late effects of treatment

Long-term Outcomes

- Effects on recurrence, cancer-specific mortality/survival
- Effects on all-cause mortality
- Effects of exercise on non-cancer mortality esp. CVD-related: unknown

*And the Yet to Be: Where Are We
Going? Consider.....*



Moving to 2nd Generation of Studies

- Caveat: Still first generation for some cancers and patient subgroups
- One size doesn't fit all
- What works for whom, under which circumstances and for which outcomes?

What Works (on-site, off-site, hybrid)?

- Closer attention to exercise “dose” so that the linkages to outcomes become clear

Importance of training volume (Kiwata et al., 2016)

- What is the minimal exercise dose (FITT) and for which outcome (PA behavior, body weight, QOL, specific symptoms such as pain, survival)?

ARTICLE

Effects of Exercise Dose and Type During Breast Cancer Chemotherapy: Multicenter Randomized Trial

Kerry S. Courneya, Donald C. McKenzie, John R. Mackey, Karen Gelmon, Christine M. Friedenreich, Yutaka Yasui, Robert D. Reid, Diane Cook, Diana Jespersen, Carolyn Proulx, Lianne B. Dolan, Cynthia C. Forbes, Evyanne Wooding, Linda Trinh, Roanne J. Segal

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- Background** Exercise improves physical functioning and symptom management during breast cancer chemotherapy, but the effects of different doses and types of exercise are unknown.
- Methods** A multicenter trial in Canada randomized 301 breast cancer patients to thrice-weekly supervised exercise during chemotherapy consisting of either a standard dose of 25 to 30 minutes of aerobic exercise (STAN; $n = 96$), a higher dose of 50 to 60 minutes of aerobic exercise (HIGH; $n = 101$), or a combined dose of 50 to 60 minutes of aerobic and resistance exercise (COMB; $n = 104$). The primary endpoint was physical functioning assessed by the Medical Outcomes Survey-Short Form (SF)-36. Secondary endpoints were other physical functioning scales, symptoms, fitness, and chemotherapy completion. All statistical tests were linear mixed model analyses, and the P values were two-sided.
- Results** Follow-up assessment of patient-reported outcomes was 99.0%. Adjusted linear mixed-model analyses showed that neither HIGH (+0.8; 95% confidence interval [CI] = -0.8 to 2.4 ; $P = .30$) nor COMB (+0.5; 95% CI = -1.1 to 2.1 ; $P = .52$) were superior to STAN for the primary outcome. In secondary analyses not adjusted for multiple comparisons, HIGH was superior to STAN for the SF-36 physical component summary ($P = .04$), SF-36 bodily pain ($P = .02$), and endocrine symptoms ($P = .02$). COMB was superior to STAN for endocrine symptoms ($P = .009$) and superior to STAN ($P < .001$) and HIGH ($P < .001$) for muscular strength. HIGH was superior to COMB for the SF-36 bodily pain ($P = .04$) and aerobic fitness ($P = .03$). No differences emerged for body composition or chemotherapy completion.
- Conclusions** A higher volume of aerobic or combined exercise is achievable and safe during breast cancer chemotherapy and may manage declines in physical functioning and worsening symptoms better than standard volumes.
- J Natl Cancer Inst;2013;105:1821-1832

What Works?

- Need to offer programs that can improve outcomes and adherence
- Offer programs that will be effective for older patients (re-design PA programs for older adults)
- Use of pragmatic designs (e.g., 1 in-person+ 3 phone calls, Lahart et al., 2016)

When to Intervene?

- When is the optimal time to intervene for patients and family members?
 - Soon after diagnosis? (e.g., improve post-surgery recovery, aerobic capacity, etc.)
 - During treatment and posttreatment? (e.g., for symptom relief from treatment toxicities, adjuvant treatment completion, dose alterations)
 - Long-term survivorship? (e.g., for chronic and late effects, recurrence, cancer mortality, non cancer mortality)
 - Exercise in palliative care and end-of life? (e.g., for symptom relief, improve mood)
- Is it a teachable moment/month/year(s)? Do the moments wax and wane?

For Whom?

- Among BrCa and PrCa
 - Low SES, minorities, rural, older
 - Larger samples
 - Wider generalizability of samples
- CRC, lung, brain, endometrial
- Select patients who are in need: fatigued, poorer QOL
- What works for which subgroup of patients?
Moderators: demographic, clinical and psy. variables

Mechanisms for Exercise-related Outcomes (Why?)

- Mediators of effects on various outcomes: personal, psychological, social, physiological, endocrine, immunological)
- For exercise-cancer prognosis: insulin glucose axis, immune functioning, endocrine?
- For exercise-psychosocial outcomes: fitness, behavior change, social support, others?

Helping Patients to Become Physically Active: Lessons Learned



- Tailor to the needs of cancer patients
 - Disease type (breast vs. CRC, lung etc., stage, treatment type, time since diagnosis age, weight, genetics)
- Focus on outcomes of relevance to patients (e.g., symptoms of fatigue, pain, survival) (evidence will facilitate reimbursement)
- Patients want individualized programs with achievable and meaningful goals, focused on symptom mgt. and functional independence (Granger et al., 2016)

Patient Needs

- Recognize that patients have strengths (resilience, social support); emphasize the specific anticipated benefits for them
- Patient preferences for various types of exercise programs (e.g., Courneya et al., 2016)
- Choice and flexibility (when, where and how they will exercise)
- Cultural tailoring (Latina survivors, Mama et al., 2015; Hawaiian dance, football clubs in Denmark, Nordic walking, Fischer et al., 2015)

Barriers: Individual-level

- Barriers (real and perceived, strength and frequency of barriers)
 - Disease of the aging: co-morbid diseases, physical capacity
 - Treatments (side-effects, long-term and late effects) and phase (during, post-treatment)
 - Anxieties and fears
 - Attitudes and beliefs about exercise
- General barriers (time pressures, weather, etc.) similar to non-cancer populations



Wish List



- RCTs of high quality
 - Detailed descriptions of the intervention: s
delivery agent training, type of exercise (FITT)
(AET, PRT, combination, HIIT), progression,
supervision details, blinding of assessor,
concealment of treatment allocation, intention-to-
treat analyses
- Challenge re. delivery channel: Efficacy and feasibility

Wish list

- Use of theories of behavior change-comparison of theories
- Use of telehealth, mHealth, social media (majority of cancer survivors are older adults)
 - (e.g., FB for YACs, Valle et al., 2013)
- Cost effectiveness understudied (important for reimbursement/3rd party payment)
- Document safety (and AEs)
- Plan for maintenance of behavior change

Exercise Promotion in the Healthcare Continuum

Multiple Missed Opportunities

After diagnosis, during treatment, post-treatment, follow-ups

- Exercise is not part of cancer treatment plan or follow-up (may improve with survivorship care plans)
- Reluctance of oncologists to prescribe exercise (lack of knowledge, time, etc.)
 - Jones et al., 2004 Importance of MD advice
 - Pinto et al., 2013 (use of the 5 A's: Ask, Assess, Advise, Assist, Arrange referral/follow-up)
 - Need guidance on programs to refer patients
 - ASCO's tool-kit
- Lack of prioritization of exercise in healthcare setting and reimbursement

Exercise in the Cancer Care Continuum:

After diagnosis, during treatment, post-treatment, follow-ups

- Need for triage (by whom? HCP-oncologist, NP, PCP) (NCCN guidelines)
 - Need for PT
 - On-site medical supervised: like cardiac rehab. for those who have medical needs/comorbidities
 - Supervised community-based programs that have shown to be effective and safe
 - Those who can exercise safely without close supervision (distance-based: print, telephone, web/e-health)

Healthcare Transitions

- When patients transition back to PCP/FP
 - Opportunities to promote healthy lifestyles
 - Recognize risk of late effects (e.g., lymphedema)
 - Referral resources for triage

Go beyond the Individual-level for Implementation

- Larger context and potential partners
 - Cancer survivors
 - Role for cancer rehab. programs
 - Family and care-givers
 - Healthcare system
 - Community programs (e.g., commercial programs Curves©, LiveStrong at the Y)
 - Organizations (e.g., non-profit organizations for cancer survivors)





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**"I'm trying to be more active.
Which one burns more calories,
Twittering, Blogging or Googling?"**