Effects of exercise/physical activity on outcomes after a breast cancer diagnosis

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Outline of Presentation

- Effect of exercise/PA on clinical endpoints
- Effect of exercise/PA on cancer related side effects
- Results of a pragmatic exercise intervention during breast cancer treatment
- Macmillan’s MoveMore programme
- Current exercise guidelines
- What can you do?
- Summary
# Evidence – Clinical endpoints

**TABLE 3. Summary of risk estimates for prediagnosis and postdiagnosis physical activity in relation to cancer-specific and all-cause mortality among cancer survivors.**

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Prediagnosis Physical Activity</th>
<th>Postdiagnosis Physical Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cancer-Specific Mortality</td>
<td>All-Cause Mortality</td>
</tr>
<tr>
<td></td>
<td>N⁰</td>
<td>RR (95% CI)</td>
</tr>
<tr>
<td>Breast</td>
<td>17</td>
<td>0.82 (0.73–0.92)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>8</td>
<td>0.77 (0.68–0.87)</td>
</tr>
<tr>
<td>Prostate</td>
<td>6</td>
<td>0.99 (0.86–1.15)</td>
</tr>
<tr>
<td>Endometrium</td>
<td>2</td>
<td>1.04 (0.81–1.36)</td>
</tr>
<tr>
<td>Ovarian</td>
<td>2</td>
<td>1.01 (0.80–1.27)</td>
</tr>
<tr>
<td>Kidney</td>
<td>1</td>
<td>0.50 (0.27–0.93)</td>
</tr>
<tr>
<td>Lung</td>
<td>1</td>
<td>0.78 (0.66–0.93)</td>
</tr>
<tr>
<td>Melanoma</td>
<td>1</td>
<td>1.09 (0.69–1.70)</td>
</tr>
<tr>
<td>Non-Hodgkin Lymphoma</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Childhood cancers</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Esophageal</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Gastric</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Malignant glioma</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

*All published articles on physical activity and cancer survival were identified to January 2018 and risk estimates for the highest vs lowest quantiles of physical activity and survival outcomes were extracted. A meta-analysis was conducted to provide overall summary risk estimates by cancer site.*

START Trial – Aerobic Training vs Resistance Training vs Control

Resistance Training had significantly higher chemotherapy treatment compliance (90%) vs controls (84%)

Courneya et al. 2007, J Clin Oncol;
Does Exercise improve Treatment Tolerability & Compliance?

**Table 6. Rates of and Reasons for Chemotherapy Dose Reduction**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Total (N = 230)</th>
<th>OnTrack (n = 76)</th>
<th>Onco-Move (n = 77)</th>
<th>Usual Care (n = 77)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients requiring dose adjustments, No. (%)</td>
<td>61 (26)</td>
<td>9 (12)</td>
<td>26 (34)</td>
<td>26 (34)</td>
</tr>
<tr>
<td>Mean prescribed length of chemotherapy, days</td>
<td>118.6</td>
<td>119.2</td>
<td>119.9</td>
<td>116.7</td>
</tr>
<tr>
<td>Reasons for chemotherapy adjustment, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuropathy</td>
<td>19 (31)</td>
<td>3</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Myelosuppression</td>
<td>7 (11)</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>7 (11)</td>
<td>0</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>7 (11)</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Pain</td>
<td>6 (10)</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Infection</td>
<td>4 (7)</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>4 (7)</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Edema</td>
<td>3 (5)</td>
<td>0</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Cardiac signs or symptoms</td>
<td>2 (3)</td>
<td>0</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Obstruction/diarrhea</td>
<td>2 (2)</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Average % dose reduction*</td>
<td>9.8</td>
<td>9.7</td>
<td></td>
<td>25.2</td>
</tr>
</tbody>
</table>

*Average dose reductions per group among participants needing a dose adjustment.
Does Exercise Improves Cancer Treatment Efficacy?

**Chemotherapy:** 25% lower risk for disease progression for AT+RT (16%) vs Con (22%) -- START Trial 8-year follow up data

**Radiotherapy:** Lower risk of local progression for RT (0%) vs CON (17%) in pts with spinal metastasis during radiotherapy

**Chemoradiotherapy:** Higher TNM-downstaging after neoadjuvant chemoradiotherapy in pts with rectal cancer

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Potential mechanisms for exercise’s protective effects with breast cancer survivors

(Mostly preclinical studies)

- Reduced adiposity
- Metabolic regulation: Insulin/IGF-1/IGF-BP3
- Regulation of anti-inflammatory system - CRP, interleukins, adipokines
- Better immune surveillance and function: NK cells, T cells
- Regulation of circulating sex steroid hormones: oestrogen
- Less oxidative stress to DNA damage and resulting gene mutations
- Better tumour vasculature: less hypoxic environment
- Direct effects on tumour milieu & tumour cell gene expression
Exercise During Chemo-infusion

Campbell et al. Case Report in Oncology (2019)
The problem....

Consequences of cancer treatment:

Physical
- Fatigue
- Weight changes
- Reduced fitness - C/V & MSE
- Endocrine problems
- Osteoporosis
- Cardiotoxicity
- Lymphoedema
- Limited range of movement
- Pain and arthralgia
- Peripheral neuropathy
- Sexual dysfunction

Psychological
- Lack of confidence
- Loneliness
- Social isolation
- Changes in body image
- Anxiety
- Depression
- Cognitive dysfunction
- Loss of control
- Self esteem
- Helplessness
How strong is the evidence that staying active after a cancer diagnosis is beneficial?

Rigorous approach to locate, appraise & grade evidence as high, moderate, low, or very low quality.
What is best way to provide this information for health care professionals?

• Only systematic reviews of RCTs
• Grade the strength of the evidence (WCRF model)
• Separate findings into stage of cancer trajectory
• Separate findings into each cancer type
• Look at each outcome individually
  – Physical function (cardiorespiratory fitness, muscular function and strength)
  – Fatigue
  – Well being (quality of life, depression, anxiety, sleep)
  – Specific side effects (neuropathic pain, lymphoedema, osteoporosis)
1. Physical Activity Pre-Surgery

**Physical function:** (Preliminary)

Lung cancer: improved CRF and lung function (5 RCTs) aerobic exercise

Abdominal cancers: improved CRF (7 RCTs) walking or cycling programmes

**Post operative complications:** (Preliminary)

Lung cancer: fewer post operative complications and shorter hospital stays (5 RCTs) aerobic exercise

Prostate cancer: reduced rates of urinary incontinence post prostatectomy (6 RCTs) pelvic floor exercises

Breast cancer: Three studies of exercise during neoadjuvant chemotherapy: exercise training was safe and feasible; adherence rates were acceptable (66–96%). In-hospital exercise training improved physical fitness however impact on HRQoL and other clinical important outcomes uncertain.

[Exercise intervention in people with cancer undergoing neoadjuvant cancer treatment and surgery: A systematic review Loughney et al (2016)]
2. Physical Activity During Treatment

**Physical function:**

*All cancers:* prevent decline in CRF and MF (14 RCTs). Increase in MS (16 RCTs) (Preliminary)

*Breast cancer:* improvements in CRF (15 RCTs) and MF (9 RCTs) (Promising)

*Prostate cancer:* increase/maintain MF and CRF (5 RCTs – ADT and 4 RCTs during radiotherapy) (Preliminary)

*Haematological cancer:* improved CRF and MF (10 RCTs while hospitalised for SCT) (Preliminary)
2. Physical Activity During Treatment

Fatigue:

All cancers: small reduction in fatigue (25 RCTs during chemotherapy and radiotherapy) Promising

Breast cancer: small reduction in fatigue (19 RCTs during chemo and radiotherapy) Promising

Prostate cancer: Fatigue associated with ADT was controlled or reduced (5 RCTs) Reduced fatigue during radiotherapy (4 RCTs) Preliminary

Haematological cancer: reduced fatigue while hospitalised for SCT (3RCTs) Preliminary

Head and Neck cancer: Control of fatigue (2 RCTs during radiotherapy or chemoradiation) Preliminary
2. Physical Activity During Treatment

**Wellbeing:**

*All cancers:* improvement in depression (6 RCTs) no change in anxiety (2 RCTs) improved sleep quality (9 RCTs) **Preliminary**

*Breast cancer:* no clear effects on depression (5 RCTs) anxiety (2 RCTs) or QoL (12 RCTs) **Preliminary**

*Prostate cancer:* no clear effects on QoL (5 RCTs) during ADT **Preliminary**

*Haematological cancer:* no clear changes in psychological well being or distress while undergoing SCT (4 RCTs) **Preliminary**

*Head and Neck cancer:* Improvement of QoL during radiotherapy or chemoradiation (2 RCTs) **Preliminary**
2. Physical Activity During Treatment

Treatment side-effects

**Breast cancer:**
1. Neuropathic pain – 2 RCTS - unclear
2. Shoulder mobility – 1 RCT – improvements
3. Lymphoedema – 2 RCTs – reduced risk
4. Sarcopenia – 1 RCT – reversal with resistance training
3. Physical Activity After Treatment

Physical function:

All cancers: *improved* outcomes CRF (7 RCTs) & MF (3 RCTs) **Promising**

Breast cancer: *improved* CRF and MF (10 RCTs) **Promising**

Lung cancer: *Increase* in CRF (3 RCTs after lung resection) **Promising**

Colorectal cancer: *improved* CRF (3 RCTs) **Promising**

Fatigue:

All cancers: *reduction* in fatigue (15 RCTs) **Promising**

Breast cancer: *reduction* in fatigue (9 RCTs) **Promising**

Colorectal cancer: *no change* in fatigue (3 RCTs) **Preliminary**

Body Composition:

All cancers: *reduction* in body weight (16 RCTs) **Preliminary**

Breast cancer: *reduction* in body fat % (10 RCTs) **Promising**
3. Physical Activity After Treatment

Wellbeing:

All cancers: improved QoL (11 RCTs) less anxiety (4 RCTs) depression (9 RCTs) Preliminary
Breast cancer: reduction in depression (3 RCTs) increase in QoL (6 RCTs) Promising
Lung cancer: no change in QoL (3 RCTs) Preliminary
Colorectal: no change in QoL (3 RCTs) Preliminary

Treatment side effects:

Breast cancer: reduction in joint pain (1 RCT on aromatase inhibitors) 12 months Preliminary
Prostate cancer: Increase improvements with less urinary incontinence (4 RCTs) pelvic floor training Preliminary
4. Physical Activity Advanced / Palliative Care

Breast cancer: no change in CRF 16 wk home based programme (1 RCT) Preliminary

Fatigue:

All cancers: controlled fatigue (6 RCTs) or reduced (3 RCTs) Preliminary
GI cancers: reduction in fatigue in CRF 16 wk home based programme (1 RCT) Preliminary
Prostate cancer: clinical improvements fatigue after 12-week supervised exercise & maintained over 6 months (1 RCT) Preliminary

Wellbeing:

All cancers: improvements in sleep quality (2RCTs) unclear effects on QOL (9 RCTs: 3 RCTs with improvements and 6 RCTs no change) Preliminary

Body Composition:

All cancers: improvements in bone density with spinal bone mets (1 RCT) 3-6 months after resistance training Preliminary
From pilot study to community-based physical activity behaviour change programmes (2000 – 2018)
The Glasgow Studies (2000-2012)

- 2000: Pilot study with 23 women with breast cancer - selected?
- 2003: CRUK Glasgow Study - randomised control trial
- Women with breast cancer on chemotherapy or radiotherapy
- Dedicated recruiters
- Group exercise classes
- Twice a week for 12 weeks
- 7 Glasgow city council venues and classes (morning afternoon & eve / weekends also)
- Behaviour change component
Cost effectiveness of exercise during treatment

- Cost for exercise programme was ~£300 per woman
- Safe - no adverse events
- Participants spent significantly less nights in hospital and less visits to GP
- An economic saving to NHS of £1507 per person
- Intervention achieved conventional standards of cost-effectiveness (QALYs)

A little less conversation, a little more action!

I certainly preferred the exercise class (to a support group). I get bored listening to myself far less anybody else! Just want to get away from it .. I mean there is something else in life as well (as cancer).

I wouldn’t have been interested in just sitting round a table talking about cancer, that’s really the last thing you want to do. I mean we did talk about it quite a lot because we were right in the middle of treatment, but it was kind of alongside of what you were doing (exercise), it wasn’t the main focus of why you got together.
Long term effects: 18 month & 5 year follow up
5 year follow up

- Of the 203 women in the original study, 114 attended the 18 months follow up and 87 at 5 years.

- Women in the original exercise group still reported significantly more leisure time physical activity and a more positive mood than women in the original control group.

- Those engaging in sufficient physical activity recorded a larger decrease in depression levels at all follow-up points.

THE UNDERRATED 'WONDER DRUG'
Macmillan’s Move More Programme
“Everyone living with and beyond cancer is aware of the benefits of physical activity and enabled to choose to become and to stay active at a level that’s right for them”
MOVE MORE
NORTHERN IRELAND

LIVING WITH CANCER?
WE’LL HELP YOU GET ACTIVE

CONSULTATION WITH MOVE MORE COORDINATOR
DIVERSE MENU OF PHYSICAL ACTIVITY OPPORTUNITIES TAILORED TO YOUR NEEDS
MINIMUM OF 12 MONTHS FOLLOW UP SUPPORT

WALKING, SPORTS, GYM, SWIMMING ACTIVE AT HOME
GROUP-BASED OR INDIVIDUAL
CANCER SPECIFIC OR NON-CANCER SPECIFIC
INCENTIVES: FREE SESSIONS, DISCOUNTED RATES, MOVE MORE EVENTS
Behaviour Change Support Provided

Physical Activity Levels

- Referral Follow Ups
- Brief Intervention Completed
- Follow Up 1 Completed
- Follow Up 2 Completed
- Additional Follow Ups Completed

- None
- Very Little
- Moderate
- A Lot
Current exercise guidelines
1. Evidence and Mechanisms Primary and Secondary Cancer Prevention [Patel et al, MSSE (2019)]

2. New International Exercise Guidelines (based on specific side effects) [Campbell et al, MSSE (2019)]

3. Guidelines on implementation of exercise programmes in clinical and community settings [Schmitz et al, CA Cancer (2019)]
"Exercise is safe both during and after most types of cancer treatment."
Activity Recommendations

Exercise can be safely performed during and after cancer treatment, if individual limitations are considered.

All cancer survivors, including those with existing disease or who are undergoing difficult treatments, should be encouraged, as a minimum, to avoid being sedentary.

Unless advised otherwise, follow the physical activity guidelines provided for the general UK population.
What can you do?
Cancer diagnosis can signal an enhanced motivation to change lifestyle behaviours - become more receptive to health behaviour change interventions
GOALS OF EXERCISE PROGRAMME

- Improve functional status prior to treatment or prevent/attenuate functional decline during treatment
- Address treatment-specific impairments during and following treatment
- Optimize general health in the recovery period following cancer treatment
EXERCISE AFTER A CANCER DIAGNOSIS
Changing a paradigm...

Physical Activity as a Standard Cancer Treatment
Edward L. Giovannucci

Correspondence to: Department of Nutrition, Harvard School of Public Health, 665 Huntington Ave, Boston, MA 02115 (e-mail: egiovann@hsph.harvard.edu).

Giovannucci 2012, J Natl Cancer Inst (Editorial)

Therapeutic Properties of Aerobic Training After a Cancer Diagnosis: More Than a One-Trick Pony?
Lee W. Jones, Mark W. Dewhirst

Correspondence to: Lee W. Jones, PhD, Memorial Sloan-Kettering Cancer Center, Department of Cardiology, New York, NY, 10065 (e-mail: joneslw@mskcc.org).

Jones & Dewhirst 2014, J Natl Cancer Inst (Editorial)
Advanced Inoperable Lung Cancer Patients in Denmark
Take Home Messages

• Convincing evidence is strong that exercise interventions have short & long term physical & psychological benefits
• Emerging evidence that exercise reduces risk of cancer recurrence and improves treatment efficacy
• Strong rationale for provision of exercise/ ways to staying active as a part of cancer care package
• Community MoveMore programmes available with trained CanRehab instructors UK wide
• Need simple effective referral pathway and links between NHS and community services
• After a breast cancer diagnosis: Movement Matters!
Acknowledgements

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