Observational and Experimental Evidence for the Role of Physical Activity in Cancer Control

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Overview

- **Physical activity and cancer risk**
  - Review of observational epidemiologic evidence
  - Biologic mechanisms
  - Randomized controlled exercise intervention trials
  - Population attributable risk for physical inactivity and cancer
  - Future research directions
Physical Activity in Cancer Control Framework


**Cancer Control Categories**

**Cancer-Related Time Periods**

**Diagnosis**

- Prevention → Detection
- → Treatment
- → Treatment Prep/Coping
- → Treatment Effectiveness /Coping
- → Recovery
- → Disease
- → Palliation
- → Survival

**Prediagnosis**

- Prescreening
- Screening

**Postdiagnosis**

- Pretreatment
- Treatment
- Survivorship
- End-of-Life

- Prevention
- Health Promotion
IARC Handbook of Cancer Prevention. Vol 6: Weight Control and Physical Activity, 2002


Chapter 23: Physical Activity, 2006

US Dept Health & Human Services 2008 Physical Activity Guidelines for Americans
Physical Activity and Cancer
Courneya and Friedenreich, editors

Topics:

- Physical Activity and Cancer Prevention
- Physical Activity and Cancer Survivorship
- Physical Activity and Cancer Special Topics

Recent Results in Cancer Research, Springer-Verlag, 2011
Methodologic Issues in Physical Activity and Cancer Research

- **Difficulty in assessing physical activity**
  - Need to assess all:
    - *Types* of activity (occupational, household, recreational, transportation)
    - *Parameters* of activity (frequency, duration, intensity)
    - *Time periods* in life (pre and post-diagnosis)
  - Validity and reliability of self-reported PA measurement
  - Need for objective measurement methods

- **Difficulty of comparisons across studies**
  - Different physical assessment methods used
  - Variable adjustments for confounders and effect modifiers
  - Not feasible to do meta-analyses since assessments are not uniform

- **Insufficient sample sizes to explore all factors that relate to physical activity**
  - Cancers of low incidence more difficult to study

- **Histologic heterogeneity within cancer sites**
  - Few studies have examined the risks associated with histologic sub-types

- **Possible selection bias if healthier, more physically active individuals participate in research studies**
# Level of Evidence on Physical Activity and Cancer Risk Reduction

<table>
<thead>
<tr>
<th>Convincing or Probable</th>
<th>Insufficient or Null</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colon</strong></td>
<td>Rectal *</td>
</tr>
<tr>
<td><strong>Breast</strong></td>
<td>Pancreatic</td>
</tr>
<tr>
<td><strong>Endometrial</strong></td>
<td>Gastric</td>
</tr>
<tr>
<td><strong>Lung</strong></td>
<td>Bladder</td>
</tr>
<tr>
<td><strong>Prostate</strong></td>
<td>Testicular</td>
</tr>
<tr>
<td><strong>Ovarian</strong></td>
<td>Kidney</td>
</tr>
<tr>
<td></td>
<td>Hematologic cancers (non-Hodgkin lymphoma, Hodgkin lymphoma, leukemia, multiple myeloma)</td>
</tr>
</tbody>
</table>

* No association

Friedenreich et al. *EJC*, 2010; 46:2593-2604
Physical Activity and Breast Cancer Risk

Lynch BM, Neilson HK, Friedenreich CM. Physical activity and breast cancer prevention.

Summary of Evidence on Physical Activity and Breast Cancer Risk

- **Consistent evidence** *(64 out of 86 observed decreased risk)*:
  - 19 studies show no effect
  - 64 studies show decreased risk
  - 3 studies find increased risks

- **Fairly strong risk reductions** *(25% decrease for highest vs. lowest activity levels, on average)*:
  - 29% average risk reduction in case-control studies
  - 20% average risk reduction in cohort studies

- **Clear dose-response** with increasing activity and decreasing risk *(40 of 50 studies)*

- **Biologic plausibility exists** *(several possible mechanisms)*

- **Temporality exists**

Lynch et al. in Courneya and Friedenreich, *Physical Activity and Cancer*. Heidelberg: Springer-Verlag, 2011
Physical Activity and Breast Cancer Risk: Cohort Studies

Statistically significant reduction in 16 of 41 cohort studies (39%)
Statistically significant reduction in 20 of 45 case-control studies (44%)
Type, Dose and Timing of Activity: Breast Cancer

- **Type:**
  - Of four types of activity, greatest risk decreases found for recreational and household activity (average 21% decrease), followed by walking/cycling (18% decrease) and occupational activity (13% decrease).

- **Intensity:**
  - Moderate activity – average 15% risk reduction
  - Vigorous activity – average 18% risk reduction

- **Duration:**
  - 2-3 hours/week – 7%
  - 6.5+ hours/week – 28%

- **Timing:**
  - Activity during 20s – 8%
  - Activity > 50 years – 17%
  - Adult lifetime – 27%
Population Sub-groups: Breast Cancer

- Strongest associations seen in:
  - Menopausal status: Post-menopausal
  - Race / ethnicity: Non-white ethnicities
  - Body mass index: Low to medium BMI ($\leq 25$)
  - Family history: None
  - Parity: Parous

- No clear effect modification by hormone receptor status
Physical Activity and Risk of Colon Cancer
Summary of Evidence on Physical Activity and Colon Cancer Risk

- **Consistent evidence** *(72 of 85 studies observe decreased risk)*
  - 14 show no effect and no studies find increased risk

- **Fairly strong risk reductions** *(~30% decreases for highest vs. lowest activity levels)*
  - 34% average risk reduction in case-control studies
  - 23% average risk reduction in cohort studies

- **Clear dose-response** *(41 of 47 studies)*

- Biologic plausibility exists

- Temporality exists
Physical Activity and Colon Cancer Risk: Cohort Studies

Statistically significant risk reductions in 16 of 41 studies (39%)
Physical Activity and Colon Cancer Risk: Case-control Studies

Statistically significant risk reductions in 18 of 44 studies (41%)
Type, Dose and Timing of Activity: Colon Cancer

- **Type of Activity:**
  - All types may be effective for lowering risk
    - e.g., occupational activity (22% decrease in risk), recreational (23%)
  - Sedentary behaviour may increase risk

- **Intensity:**
  - Vigorous or moderate activity decrease risk

- **Timing of Activity:**
  - Inconsistent findings

- **Population Sub-groups:**
  - Relatively constant effects across BMI categories
  - Association may vary by tumour sub-site
    - i.e., proximal or distal
  - Benefit for men and women
  - Unclear effects of race/ethnicity, dietary intake, HRT use
Physical Activity and Risk of Gynecologic Cancer
Summary of Evidence on Physical Activity and Endometrial Cancer Risk

- **Consistent evidence** *(23 of 28 studies)*
  - Nearly all of studies show risk reductions

- **Fairly strong risk reductions** *(30-35% decreases for highest vs. lowest activity levels)*
  - 25% average risk reduction in cohort studies
  - 33% average risk reduction in case-control studies

- **Evidence of dose-response** *(12 of 19 studies)*

- **Biologic plausibility exists**

- Sedentary behaviour emerging as possibly important
Physical Activity and Endometrial Cancer Risk

Cohort Studies
- Prospective cohort
  - Terry et al., 1999
  - Furberg & Thune, 2003
  - Gierach et al., 2009
  - Friberg et al., 2006
  - Patel et al., 2008
  - Colbert et al., 2003
  - Friedenreich et al., 2007
- Retrospective cohort
  - Zheng et al., 1993
  - Moradi et al., 1998
- Case-cohort study
  - Schouten et al., 2004

Case-control Studies
- Population-based case-control
  - Sturgeon et al., 1993
  - Salazar-Martinez et al., 2000
  - Shu et al., 1993
  - Matthews et al., 2005
  - John et al., 2010
  - Arendt et al., 2011
  - Olson et al., 1997
  - Goodman et al., 1997
  - Littman et al., 2001
  - Moradi et al., 2000
  - Friedenreich et al., 2010
- Hospital-based case-control
  - Kalandidi et al., 1996
  - Dosemeci et al., 1993
  - Levi et al., 1993
  - Hirose et al., 1996
  - Tavani et al., 2009

Statistically significant risk reduction in 14 of 28 studies (50%)
Summary of Evidence on Physical Activity and Ovarian Cancer Risk

- **Moderately consistent evidence** *(12 of 23 studies)*
  - Half studies show risk reductions
  - 3 studies show increased risk (1 is statistically significant)

- **Weak risk reductions** *(<10% average decreases for highest vs. lowest activity levels)*
  - Average 10% increased risk in cohort studies
  - Average 25% decreased risk from case-control studies

- **Some evidence of dose-response** *(9 of 11 studies)*
Physical Activity and Ovarian Cancer Studies

Cohort Studies
- Prospective cohort
  - Schnohr et al, 2005
  - Hannan et al, 2005
  - Biesma et al, 2006
  - Patel et al, 2006
  - Bertone et al, 2001
  - Weiderpass, 2006
  - Leitzmann et al, 2009
  - Lahmann et al, 2009
  - Anderson et al, 2004
  - Chionh et al, 2010

Case-control Studies
- Population-based case-control
  - Riman et al, 2004
  - Camide et al, 2009
  - Cottreau et al, 2000
  - Pan et al, 2005
  - Olsen et al, 2007
  - Moorman et al, 2011
  - Rossing et al, 2010
  - Bertone et al, 2002
  - Zheng et al, 1993

- Hospital-based case-control
  - Dosemecci et al, 1993
  - Zhang et al, 2003
  - Tavani et al, 2001
Physical Activity and Risk of Prostate Cancer
Summary of Evidence on Physical Activity and Prostate Cancer Risk

- **Less consistent evidence** *(26 of 56 studies)*
  - 25 studies find no effect
  - 26 studies find decreased risk
  - 5 studies find increased risk

- **Weak risk reductions** *(10% decreases for highest vs. lowest activity levels)*

- **Evidence of dose-response** *(12 of 18 studies)*
  - about half of the studies that examined these trends

- **Some biologic plausibility exists**
Physical Activity and Prostate Cancer: Cohort Studies

Statistically significant risk reductions in 7 of 30 studies (23%)
Physical Activity and Prostate Cancer: Case-control Studies

Statistically significant risk reductions in 8 of 26 studies (30%)
Physical Activity and Risk of Lung Cancer
Summary of Evidence on Physical Activity and Lung Cancer Risk

- **Consistent evidence** *(19 of 27 studies)*
  - 7 show no effect
  - 19 show decreased risks

- **Fairly strong risk reductions** *(25% decreases for highest vs. lowest activity levels)*

- **Evidence of dose-response** *(9 of 11 studies)*
  - about half of the studies that examined these trends

- Weaker evidence for **biologic plausibility** exists

- Effect of smoking needs to be considered
Physical Activity and Lung Cancer: Cohort Studies

Statistically significant risk reduction in 7 of 19 studies (37%)
Physical Activity and Lung Cancer: Case-Control Studies

Statistically significant risk reduction in 6 of 8 studies (75%)

Population-based
- Lam et al, 2004
- Parent et al, 2011 Overall PA
- Parent et al, 2011 Recreational
- Mao et al, 2003
- Brownson et al, 1991

Hospital-based
- Kubik et al, 2004
- Kubik et al, 2008 Ever smokers, Female
- Kubik et al, 2008 Ever smokers, Male
- Kubik et al, 2008 Never smokers, Male
- Kubik et al, 2008 Never smokers, Female
- Dosemeci et al, 1993

Nested case-control study (within a cohort)
- Rundle et al, 2010 Recreational
### Summary of Evidence on Physical Activity and Cancer Risk by Site

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Number of Studies</th>
<th>Studies found reduced risk</th>
<th>Consistency of evidence</th>
<th>Magnitude of risk reduction</th>
<th>Dose-response effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>85</td>
<td>72</td>
<td>Yes</td>
<td>30%</td>
<td>Yes</td>
</tr>
<tr>
<td>Breast</td>
<td>86</td>
<td>64</td>
<td>Yes</td>
<td>25%</td>
<td>Yes</td>
</tr>
<tr>
<td>Endometrial</td>
<td>28</td>
<td>23</td>
<td>Yes</td>
<td>30-35%</td>
<td>Yes</td>
</tr>
<tr>
<td>Lung</td>
<td>27</td>
<td>19</td>
<td>Some</td>
<td>25%</td>
<td>Some</td>
</tr>
<tr>
<td>Prostate</td>
<td>56</td>
<td>26</td>
<td>No</td>
<td>10%</td>
<td>Limited</td>
</tr>
<tr>
<td>Ovarian</td>
<td>23</td>
<td>12</td>
<td>No</td>
<td>&lt;10%</td>
<td>Limited</td>
</tr>
<tr>
<td>All Others</td>
<td></td>
<td></td>
<td></td>
<td>Insufficient or Null</td>
<td></td>
</tr>
</tbody>
</table>
Biologic Mechanisms
How physical activity could interact with carcinogenesis

Physical Activity

Metabolism/Detoxification

Chemical Carcinogens

Reactive Oxygen Species

Endogenous Oxidative Stress

DNA Damage

Initiation

Promotion and Progression

Clinical Disease

Positive Association

Negative Association

Adapted from Rundle A. CEBP 2005;14:227-36
<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Possible effect of Physical Activity</th>
<th>Cancer Sites</th>
</tr>
</thead>
</table>
| **Body fat**                    | * Reduces fat → lowers adipokines, inflammatory markers, estrogens, testosterone  
* Improves insulin sensitivity, ↑ SHBG levels                                                                                                                                                                           | Colon                        |
|                                 |                                                                                                                                                                                                                                     | Postmenopausal breast        |
|                                 |                                                                                                                                                                                                                                     | Endometrium                 |
|                                 |                                                                                                                                                                                                                                     | Ovaries                      |
| **Insulin resistance**          | * Improves insulin sensitivity, ↓ plasma insulin, C-peptide, glucose levels since body fat reduced and skeletal muscle increased  
* Increased glucose transport into muscle and decreased fatty acid synthesis                                                                                                                                                 | Colon                        |
|                                 |                                                                                                                                                                                                                                     | Breast                       |
|                                 |                                                                                                                                                                                                                                     | Endometrium                 |
|                                 |                                                                                                                                                                                                                                     | Ovaries                      |
|                                 |                                                                                                                                                                                                                                     | Prostate                     |
| **Improved pulmonary function** | * Lowers concentration of carcinogens in lungs  
* Shortens exposure time b/w lung tissue and carcinogens                                                                                                                                                                         | Lung                         |
| **Sex hormones**                | * Postmenopause: Body fat loss ↓ aromatase & 17β-dehydrogenase levels in adipose tissue → can lower estrone, estradiol and testosterone synthesis  
* Hepatic synthesis of SHBG increases with lower insulin levels, ↓ estradiol and testosterone                                                                                                                                 | Breast                       |
<p>|                                 |                                                                                                                                                                                                                                     | Endometrium                 |
|                                 |                                                                                                                                                                                                                                     | Ovaries                      |</p>
<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Possible effect of Physical Activity</th>
<th>Cancer Sites</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D</td>
<td>• Associated with higher 25-hydroxyvitamin D blood levels</td>
<td>Colon, Breast</td>
</tr>
<tr>
<td>Insulin-like growth factors</td>
<td>• Might ↓IGF-1 and ↑IGFBP-3</td>
<td>Colon, Premenopausal breast, Endometrium, Ovaries, Prostate, Lung</td>
</tr>
<tr>
<td>Sex hormones</td>
<td>• <strong>Pre-menopause</strong>: Ovarian production of estrogens may decrease → delay menarche, menstrual dysfunction, anovulation</td>
<td>Breast, Endometrium, Ovaries, Prostate</td>
</tr>
<tr>
<td>Adipokines</td>
<td>• Decreases body fat (main source of leptin)</td>
<td>Colon, Breast, Endometrium, Prostate, Lung</td>
</tr>
<tr>
<td></td>
<td>• ↑Adiponectin levels by ↓IL-6 and TNF-α but possibly only with weight loss</td>
<td></td>
</tr>
<tr>
<td>Chronic low-grade inflammation</td>
<td>• May ↓ inflammatory markers (CRP, IL-6, TNF-α) partly through fat loss</td>
<td>Most cancers</td>
</tr>
<tr>
<td>Mechanism</td>
<td>Possible effect of Physical Activity</td>
<td>Cancer Sites</td>
</tr>
<tr>
<td>-----------------------------------</td>
<td>--------------------------------------------------------------------------------------------------------</td>
<td>---------------</td>
</tr>
<tr>
<td>Immune function</td>
<td>• May improve innate and acquired immune responses to recognize and eliminate cancer cells&lt;br&gt;• Effects of long-term, moderate intensity PA on humans at risk not well understood</td>
<td>Most cancers</td>
</tr>
<tr>
<td>Oxidative stress, anti-oxidant defense and DNA repair</td>
<td>• May reduce oxidative stress, increase anti-oxidant enzymes (e.g. superoxide dismutase), and/or enhance DNA repair</td>
<td>Most cancers</td>
</tr>
<tr>
<td>Prostaglandins</td>
<td>• May inhibit synthesis of prostaglandins synthesis</td>
<td>Colon</td>
</tr>
<tr>
<td>Gastrointestinal transit time</td>
<td>• ↑ gut motility and may ↓ transit time → less interaction between mucosa and carcinogens but changes may not be large enough to alter risk</td>
<td>Colon</td>
</tr>
</tbody>
</table>
Randomized Controlled Exercise Intervention Trials for Breast Cancer Prevention

- Three year-long RCTs conducted to date on aerobic exercise and breast cancer biomarkers among postmenopausal, inactive, 50-75 yr old healthy women:
  - McTiernan et al. (*Physical Activity for Total Health Trial*) (N=173)
  - Monninkhof et al. (*Sex Hormones and Physical Exercise Trial*) (N=189)
  - Friedenreich et al. (*Alberta Physical Activity and Breast Cancer Prevention Trial*) (N=320)
Hypothesized Biologic Mechanisms Between Physical Activity and Breast Cancer

Friedenreich CM, Neilson HK, Lynch BM. *Eur J Cancer*. 2010; 46:2593-2604
<table>
<thead>
<tr>
<th>Endpoint</th>
<th>PATH Trial</th>
<th>SHAPE Trial</th>
<th>ALPHA Trial</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex hormones</strong></td>
<td>↓estrone and estradiol restricted to women who lost &gt;2% body fat</td>
<td>No effect on estrogens or androgens</td>
<td>↓estradiol and ↑SHBG</td>
</tr>
<tr>
<td><strong>Obesity</strong></td>
<td>↓ all adiposity measures</td>
<td>↓ body fat but no effect on weight, BMI or hip circumference</td>
<td>↓ all adiposity measures</td>
</tr>
<tr>
<td><strong>Insulin resistance</strong></td>
<td>↓insulin, leptin, HOMA score</td>
<td>Not reported</td>
<td>↓ insulin, HOMA-IR, leptin, adiponectin/leptin ratio</td>
</tr>
<tr>
<td><strong>Inflammation</strong></td>
<td>↓C-reactive protein</td>
<td>Not reported</td>
<td>↓ C-reactive protein</td>
</tr>
<tr>
<td><strong>Publications</strong></td>
<td>Irwin 2003; McTiernan 2004; Frank 2005; Campbell 2009</td>
<td>Monninkhof 2009; Velthuis, 2009</td>
<td>Friedenreich 2010a; Friedenreich 2010b, Friedenreich 2011</td>
</tr>
</tbody>
</table>

* Only statistically significant results shown.
**Study design:** Two-armed, two-centered RCT

**Intervention:** Year-long, 5 days/week, 45 mins/session (3 supervised, 2 unsupervised), aerobic exercise only, no change in diet

**Eligibility criteria:** Postmenopausal, 50-74 yrs, no previous cancer, healthy, BMI=22-40, no HRT use, non-smoker, non-excessive alcohol, inactive

**Control:** No change in exercise or diet

**Sample size:** 320

**Outcomes:** Sex hormones, adiposity, insulin resistance, inflammation, mammographic density
ALPHA Trial Flow Chart

Recruitment

- Attend information session and remain eligible and interested (n=542)
  - Did not meet inclusion criteria (n=1840)
    - Refused (n=798)
    - Other reasons (n=274)
  - Assessed for eligibility (n=3454)

Randomization

- Randomized (n=320)
  - Exercise Group (n=160)
  - Control Group (n=160)

Data Collection

- 12 month blood samples (n=154)
- 12 month blood samples (n=156)
ALPHA Trial: Average Number of Minutes Exercised by Week on Trial

Target of 225 mins/week

3 month ramp-up

9-month maintenance
Change in Physical Activity Levels from Baseline to 12 Months (MET-hrs/wk)

- Total PA: Exercisers vs. Controls, p = 0.001
- Recreational: Exercisers vs. Controls, p < .001
- Occupational: Exercisers vs. Controls
- Household: Exercisers vs. Controls
Change in Fitness from Baseline to 12 Months

Exercisers vs. Controls

p < .001
Impact of Exercise Intervention on Endogenous Estrogens: Estradiol

Mean Change in log(Estradiol) During 12 Months Follow-up by Groups

P=0.001

Friedenreich et al., JCO, 2010; 28:1458-66
Impact of Exercise Intervention on Sex Hormone Binding Globulin

Mean Change in log(SHBG) During 12 Months Follow-up by Groups

Exercisers: Mean 95%CI

Controls: Mean 95%CI

P=0.002

Friedenreich et al., JCO, 2010; 28:1458-66
## Impact of Exercise Intervention on Adiposity Outcomes

<table>
<thead>
<tr>
<th>Change from Baseline</th>
<th>Exercisers</th>
<th>Controls</th>
<th>Difference</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>-2.3</td>
<td>-0.5</td>
<td>-1.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>-0.9</td>
<td>-0.2</td>
<td>-0.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>-2.2</td>
<td>0.1</td>
<td>-2.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Abdominal fat area (cm²)</td>
<td>-48.5</td>
<td>-9.6</td>
<td>-38.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intra-abdominal fat area (cm²)</td>
<td>-16.5</td>
<td>-1.6</td>
<td>-14.9</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Friedenreich et al., *Int J Obes* 2010; 35:427-35
### Impact of Exercise Intervention on Adiposity Outcomes

<table>
<thead>
<tr>
<th>Change from Baseline</th>
<th>Exercisers</th>
<th>Controls</th>
<th>Difference</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subcutaneous fat area (cm²)</td>
<td>-32.0</td>
<td>-7.9</td>
<td>-24.1</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Percent body fat</td>
<td>-2.0</td>
<td>-0.2</td>
<td>-1.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>-2.4</td>
<td>-0.4</td>
<td>-2.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Lean muscle mass (kg)</td>
<td>-0.0</td>
<td>-0.1</td>
<td>0.1</td>
<td>0.564</td>
</tr>
</tbody>
</table>

Friedenreich et al., *Int J Obes* 2010; 35:427-35
Percent Change of Total Body Fat and Intra-abdominal Fat by Average Weekly Duration of Exercise

* Significant difference compared with control group ($P<0.05$).
† Significant difference compared with low-active group ($P<0.05$).

Friedenreich et al., *Int J Obes* 2010; 35:427-35
Impact of Exercise Intervention on Insulin

Mean Change in log(Insulin) During 12 Months Follow-up by Groups

Exercisers: Mean 95%CI
Controls: Mean 95%CI

Friedenreich et al., Cancer Prev Res 2011;4 (epub)
Impact of Exercise Intervention on Leptin

Mean Change in log(Leptin) During 12 Months Follow-up by Groups

Exercisers: Mean 95%CI
Controls: Mean 95%CI

Friedenreich et al., Endocrine Related Cancer 2011
Percent Change in Insulin Biomarkers by Adherence Levels

Friedenreich et al., *Endocrine Related Cancer* 2011
Impact of Exercise Intervention on C-reactive Protein

Mean Change in CRP During 12 Months Follow-up by Groups

Breast Cancer and Exercise Trial in Alberta: Study Design

Recruit 330 postmenopausal women 50-74 years

Randomize

High volume exercise group (5 days/wk x 60 mins/session)

Moderate volume exercise group (5 days/wk x 30 mins/session)

Compare high vs moderate exercise groups on endogenous sex hormones, obesity and inflammatory markers, insulin, glucose
## Estimated Preventable Cancers Associated with Physical Inactivity, USA, 2011

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>No. of cancers in USA, 2011*</th>
<th>PAR for physical inactivity</th>
<th>Estimated preventable cancers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>141,210</td>
<td>30.4%</td>
<td>42,933</td>
</tr>
<tr>
<td>Breast</td>
<td>230,480</td>
<td>21.2%</td>
<td>48,948</td>
</tr>
<tr>
<td>Endometrial</td>
<td>46,470</td>
<td>25.8%</td>
<td>11,973</td>
</tr>
<tr>
<td>Prostate</td>
<td>240,890</td>
<td>12.7%</td>
<td>30,620</td>
</tr>
<tr>
<td>Lung</td>
<td>221,130</td>
<td>16.8%</td>
<td>37,200</td>
</tr>
<tr>
<td>Ovarian</td>
<td>21,990</td>
<td>8.2%</td>
<td>1,797</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>902,170</strong></td>
<td></td>
<td><strong>173,470</strong></td>
</tr>
</tbody>
</table>

*SEER Data for 2011  PAR=Pe(RR-1)/Pe(RR-1)+1 where Pe=0.754 from CDC PA data
Future Research Directions

- Investigate sedentary behaviour and light intensity activity as risk factors for cancers
- Improve PA measurements including objective assessments
- More precision on type, dose, timing of activity in relation to cancer risk
- Examine effect modification by other factors
- Conduct prospective observational studies of new biomarkers
- Need more mechanistic RCTs that evaluate different doses and types of PA
- Conduct RCTs of combined physical activity and diet for cancer prevention
- **Ultimate objective:** provide more quantitative data to enhance public health recommendations regarding PA type, dose, timing for cancer risk reduction
Conclusion

- Strong, consistent evidence worldwide that PA reduces colon, breast, endometrial cancer risks and possibly also prostate, lung and ovarian cancers by 10-30% with a dose-response effect and some sub-group effects.
- Several plausible biologic mechanisms exist.
- RCTs are finding support for these mechanisms.
- 8-30+% of cancers may be attributable to physical inactivity.
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