Physical activity among childhood cancer survivors

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AICR October 30, 2014
Outline

• Childhood cancer and survival
• Chronic health conditions
• Associations between exercise/lifestyle and chronic health conditions
• Declining physical activity
• Frail health
• Physical activity guidelines
• Prevention and remediation examples
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Cancer incidence and mortality rates among U.S. children 0-19 years

In 2014, estimated 420,000 childhood cancer survivors in the U.S.

By 2020, estimated 500,000 survivors

1 in 680 is a childhood cancer survivor (ages 20 to 50 years)

Risk for adverse late effects is multifactorial, but largely determined by treatment-specific factors

www.seer.cancer.gov
Robison, Nature Reviews 2014
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## Childhood Cancer Survivor Study (CCSS) (U24 CA55727)

- Funded in 1994
- Retrospective Cohort, diagnosed 1970-1986
- 26 Contributing Centers
- 5-Year Survival
- Leukemia, Lymphoma, CNS, Bone, Wilms, NBL, Soft-tissue sarcoma
- Detailed Treatment Data, Wide Range of Outcomes
- 230+ Publications since 2001

<table>
<thead>
<tr>
<th>Count</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>20,720</td>
<td>Eligible</td>
</tr>
<tr>
<td>3017</td>
<td>Lost</td>
</tr>
<tr>
<td>17,703</td>
<td>Contacted</td>
</tr>
<tr>
<td>3189</td>
<td>Refusal</td>
</tr>
<tr>
<td>14,372</td>
<td>Participants</td>
</tr>
</tbody>
</table>

Cohort Expansion: 1987-1999  
**n=15,351**
Cumulative incidence of serious, disabling, life threatening chronic conditions

Armstrong, J Clin Oncol 2014
Chronic conditions include adverse cardiovascular outcomes

Cumulative Incidence at 45 years:
Cardiovascular Events (grade 3–5)

<table>
<thead>
<tr>
<th>Age</th>
<th>Survivor</th>
<th>Sibling</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>4.5%</td>
<td>0.8%</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Coronary Artery Disease

Survivor 4.5%
Sibling 0.8%

Congestive Heart Failure

Survivor 4.7%
Sibling 0.5%

Valve Abnormality

Survivor 1.3%
Sibling 0.1%

Arrhythmia

Survivor 0.8%
Sibling 0.0%

Armstrong, J Clin Oncol 2013
Risk of a cardiac event is magnified by the presence of known cardiovascular risk factors (CVRFC) include diabetes, dyslipidemia, hypertension, obesity

Coronary Artery Disease

- CVRFC alone: OR=6.8
- Chest RT alone: OR=6.3
- Chest RT + CVRFC: OR=28.2

Congestive Heart Failure

- CVRFC alone: OR=4.7
- Chest RT alone: OR=4.3
- Chest RT + CVRFC: OR=16.2

Armstrong, J Clin Oncol 2013
Vigorous physical activity associated with lower risk of adverse cardiovascular event

<table>
<thead>
<tr>
<th>MET hours/week</th>
<th>Any Major CV Event</th>
<th>Coronary Artery Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RR</td>
<td>95% CI</td>
</tr>
<tr>
<td>None</td>
<td>Referent</td>
<td></td>
</tr>
<tr>
<td>3 to 6</td>
<td>0.87</td>
<td>0.56 to 1.34</td>
</tr>
<tr>
<td>9 to 12</td>
<td>0.45</td>
<td>0.26 to 0.80</td>
</tr>
<tr>
<td>15 to 21</td>
<td>0.47</td>
<td>0.23 to 0.95</td>
</tr>
</tbody>
</table>

N= 1.187 Hodgkin Lymphoma Survivors from CCSS (median age 31.2 years, median follow-up 11.9 years) who did not have an adverse cardiovascular event at the baseline questionnaire

Cumulative incidence of cardiovascular event at 10 years was 12.2% for those with no MET hours/week and 5.2% for those with 9+ Met hours/week
St. Jude Lifetime Cohort (SJLIFE)

• Objective:
  – To establish a lifetime cohort of childhood cancer survivors
  – To facilitate longitudinal evaluation of health outcomes in aging adults surviving pediatric cancer

• Eligibility:
  – Diagnosis of cancer treated at St. Jude
  – At least 18 years of age
  – At least 10 years from diagnosis
SJLIFE assessment

**Pre-visit**
- Medical records: treatment and medical events
- Questionnaires: self-report of socio-demographics, health status, and medical events

**Clinical Assessment**
- Laboratory core battery
- Risk-based screening per COG Guidelines
- Functional assessment
- Collection of biological specimens
- Externally funded ancillary research studies
- Priority pilot studies

**Post-visit**
- Follow-up and validation of outcomes
- Use of bio-repository for biomarkers, genome wide and candidate gene studies

**SJLIFE Database**
1713 Adult Survivors
Median Age 32 years (range 18-60)
Median time from Diagnosis 25 years (range 10-47)
51% Female
87% Caucasian

Cohort Characteristics

Hudson, JAMA 2013
Chronic conditions in SJLife

<table>
<thead>
<tr>
<th>Presence of chronic health condition graded by CTCAE v4</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Totals</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least one condition</td>
<td>92.8%</td>
<td>68.8%</td>
<td>60.8%</td>
<td>17.8%</td>
</tr>
<tr>
<td>Multiple conditions</td>
<td>72.6%</td>
<td>36.4%</td>
<td>23.2%</td>
<td>1.9%</td>
</tr>
<tr>
<td>At least one grade 1 or 2 condition</td>
<td>96.7%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple grade 1 or 2 conditions</td>
<td>86.2%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least one grade 3 or 4 condition</td>
<td></td>
<td></td>
<td>67.6%</td>
<td></td>
</tr>
<tr>
<td>Multiple grade 3 or 4 conditions</td>
<td></td>
<td></td>
<td>30.3%</td>
<td></td>
</tr>
</tbody>
</table>

By age 45 years it is estimated that......

–  80% (95% CI 73.0 – 86.6%) will have a serious/disabling or life-threatening chronic health condition [CTCAE v.4 Grade 3-4]

–  95.2% (95% CI 94.8 – 98.6%) will have at least one chronic health condition

Hudson JAMA 2013
Metabolic syndrome in SJLife

<table>
<thead>
<tr>
<th></th>
<th>Male (%)</th>
<th>Female (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolic syndrome</td>
<td>32.5</td>
<td>31.0</td>
</tr>
<tr>
<td>Increased waist circumference</td>
<td>29.9</td>
<td>41.6</td>
</tr>
<tr>
<td>Increased Triglycerides</td>
<td>33.8</td>
<td>21.0</td>
</tr>
<tr>
<td>Decreased HDL</td>
<td>38.2</td>
<td>42.6</td>
</tr>
<tr>
<td>Increased blood pressure</td>
<td>53.0</td>
<td>40.6</td>
</tr>
<tr>
<td>Increased fasting glucose</td>
<td>38.2</td>
<td>24.9</td>
</tr>
</tbody>
</table>

- N=1598 (49.2% male)
- Mean age at diagnosis 7.9 ± 5.5 years
- Mean time since diagnosis 25.6 ± 7.6 years
- Cohort members with campus visit & diet data
## AICR Guidelines

<table>
<thead>
<tr>
<th>Item</th>
<th>Value</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index</td>
<td>≤ 25 kg/m²</td>
<td>1</td>
</tr>
<tr>
<td>Recreational physical activity</td>
<td>Meets CDC guidelines*</td>
<td>1</td>
</tr>
<tr>
<td>Daily fruit and vegetables</td>
<td>≥ 5 servings/day</td>
<td>1</td>
</tr>
<tr>
<td>Daily intake complex carbohydrates</td>
<td>≥ 400 g/day</td>
<td>1</td>
</tr>
<tr>
<td>Daily alcohol intake</td>
<td>&lt; 14 g/day (Females) &lt; 28 g/day (Males)</td>
<td>1</td>
</tr>
<tr>
<td>Daily red meat intake</td>
<td>&lt; 80 g/day</td>
<td>1</td>
</tr>
<tr>
<td>Daily sodium consumption</td>
<td>&lt; 2400 mg</td>
<td>1</td>
</tr>
</tbody>
</table>

*150 minutes of at least moderate physical activity
Association between meeting AICR guidelines & metabolic syndrome

- RR among females 2.4 (95% CI 1.7-3.3) & among males 2.2 (95% CI 1.6-3.0) for those who met 4+ compared to those who did not meet at least 4 of the AICR guidelines

- Adjusted for race, age, educational attainment and CRT exposure

Smith, Cancer 2014
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Physical activity declines over time in childhood cancer survivors

- 7,287 survivors and 2,107 siblings in CCSS completed questionnaires ~ 5 years apart
- Median age at follow-up 36 (21-58) years survivors
- Median age at follow-up 38 (21-62 siblings)
- 47.5% of survivors and 41.5% of sibling did not participate in at least 150 minutes/week of moderate physical activity
- 19.0% of survivors and 17.6% of siblings reported declining activity over the 5 years

Wilson, CEBP 2014
Declining physical activity is associated with chronic conditions

Cardiac condition  Neurologic condition  Musculoskeletal condition

Wilson, *CEBP* 2014
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Frailty and function in childhood cancer survivors

Exposures
- Anthracycline/platinum
- Chest radiation
- Limb sparing

Lifestyle choices
- Sedentary behavior
- Poor diet

Barriers or access to tailored interventions

Adapted from Buchner Clin Geriatr Med. 1992; 8
Can this phenomenon be explained by a frailty phenotype?

- Pre-frailty and Frailty are defined by a cluster of five measurements of physical state/abilities
  - Lean muscle mass - DEXA and height
  - Exhaustion - Vitality subscale of the SF-36
  - Energy expenditure – Kilocalories/week (NHANES)
  - Walking speed – 15 feet, adjusted for height/sex
  - Muscle weakness – Hand grip strength, dynamometer

Pre-frail = 2 items      Frail = 3+ items
Frailty in the SJLIFE cohort

- N=1922 (50.3% male)
- Mean age 33.6±8.1 years
- Mean time since diagnosis 25.5±7.7 years
- Mean age at diagnosis 8.2±5.6 years
- 43% leukemia
- 33% with CRT


Control participants age range 18-50 years (mean 29.0±7.5 years)
Function in childhood cancer survivors is impaired even when as physically active as siblings.

183 survivors
Mean age of 13.5±2.5 years
Mean time since diagnosis 9.3±3.0 years
147 siblings
Outline

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• Frail health
• **Physical activity guidelines**
• Prevention and remediation examples
### Consensus based recommendations for exercise among children during treatment for or following a cancer diagnosis

<table>
<thead>
<tr>
<th>Source</th>
<th>Age</th>
<th>Aerobic</th>
<th>Resistance Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>American College of Sports Medicine</td>
<td>None specified</td>
<td>15-40 minutes of moderate to vigorous intensity</td>
<td>1-2 sets of 8-10 exercises at 8 repetition maximum 1-2 times per week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Light to moderate levels – individualized with progressive dose – include weight bearing – during maintenance chemotherapy &amp; after treatment some days of the week</td>
<td></td>
</tr>
</tbody>
</table>
## Consensus based recommendations for exercise among children during treatment for or following a cancer diagnosis

<table>
<thead>
<tr>
<th>Source</th>
<th>Age</th>
<th>Aerobic</th>
<th>Resistance Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>American Cancer Society</td>
<td>Children and adolescents</td>
<td>60 minutes of moderate to vigorous physical activity 5 days per week</td>
<td>None specified</td>
</tr>
<tr>
<td>Braith (2005)</td>
<td>None specified</td>
<td>30-40 minutes at 65-85% of heart rate reserve 3 days per week if no cardiomyopathy</td>
<td>1 set 8-12 reps all major muscle groups 2 times per week</td>
</tr>
<tr>
<td></td>
<td></td>
<td>HR 10 beats below any symptoms detected during exercise testing.  Start with 2-6 minutes activity alternating with 1-2 minutes rest if cardiomyopathy</td>
<td>1 set 8-12 reps at 40-60% one rep max 8-10 machines 2-3 times per week</td>
</tr>
</tbody>
</table>
The status of fitness guidelines for childhood cancer survivors

• No clearly established, published, risk-based, limitation-specific guidelines exist for exercise among children with cancer or who have survived cancer

• Cochrane reviews support benefits for persons with coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, diabetes, osteoporosis, peripheral neuropathy, and chronic fatigue syndrome, all potentially late effects of childhood cancer and/or its treatment .... and supervised exercise for children with leukemia
Examples - approaches

• Among adult survivors
  – Safety
  – Efficacy

• Among children on therapy
  – Prevention

• Among children/adolescents off therapy
  – Lifestyle modification (habits)
Resistance and aerobic exercise for subclinical anthracycline cardiomyopathy

- 12 week exercise intervention in survivors of childhood cancer with anthracycline induced cardiomyopathy
- Aerobic exercise (20-45 min sessions, 3-5 times/wk.)
- Resistance training (8-10 exercises, 12-15 reps each exercise, 2-3 times/wk.)
- Compliance monitored with logs and weekly phone calls from exercise specialist

Smith, *Pediatr Blood Cancer*. 2013; epub
## Mean values for outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Pre</th>
<th>Post</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (Kg)</td>
<td>65.7</td>
<td>64.5</td>
</tr>
<tr>
<td>Body Fat (%)</td>
<td>28.1</td>
<td>27.0</td>
</tr>
<tr>
<td>Maximal Oxygen Consumption (ml/kg/min)</td>
<td>21.6</td>
<td>26.0</td>
</tr>
<tr>
<td>Leg Extension at 60 degree per second (Nm)</td>
<td>172.3</td>
<td>198.7</td>
</tr>
<tr>
<td>Ejection Fraction (%)</td>
<td>43.8</td>
<td>49.4</td>
</tr>
</tbody>
</table>

N=5, 3 males, median age 38 (range 33-41) years  
Diagnoses 4 osteosarcoma, 1 Ewing’s sarcoma
To evaluate the effects of 24-week supervised resistance training with protein supplementation compared to resistance training alone or usual care on muscle mass and strength, physical performance and biomarkers of metabolic health among young adult survivors of childhood cancer.
Aerobic and strength training during maintenance therapy for childhood ALL

<table>
<thead>
<tr>
<th>% change</th>
<th>Body Mass Index</th>
<th>Knee extension strength</th>
<th>Grip strength</th>
<th>Sit and reach test</th>
<th>Ankle Dorsiflexion</th>
<th>Six minute walk distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>-3.0</td>
<td>11.1</td>
<td>16.9</td>
<td>42.2</td>
<td>81.4</td>
<td>16.0</td>
<td></td>
</tr>
</tbody>
</table>

12 children with ALL, age 5-10 years, receiving maintenance therapy, in first remission.

Six month home-based intervention, with written and video instruction, was supervised with weekly calls from an exercise coach. Results: Seventeen patients enrolled (participation 63%).
To evaluate the impact of aerobic training intervention on fitness, neurocognitive function, physical performance, fatigue and quality of life in children with medulloblastoma.
Future - web-based intervention to promote physical activity among children and adolescents with ALL

Baseline assessment

Website access, accelerometer & educational materials

Accelerometer & educational materials

End of intervention assessment

End of intervention assessment

Six months post intervention assessment

Six months post intervention assessment

One year post intervention assessment

One year post intervention assessment

Randomization

Reminder to connect at 2 and at 6 weeks

First 3 months after completion of therapy

To evaluate the effects of a six month rewards-based physical activity intervention delivered via an interactive website in children following treatment for ALL
What's Zamzee?

Zamzee records your physical activity, and transforms it into zamz that power you through levels filled with prizes and surprises. You can also use your zamz to buy stuff. With Zamzee, the more you move, the more you get.

Wear the Zamzee meter near your waist or in your pocket all day, every day. Plug your Zamzee into any computer with the Zamzee Upload Center installed, and your data is transformed into zamz!

Zamzee is a project of HopeLab. To learn more about HopeLab and its work, visit www.hopelab.org.

Need to download the Zamzee Upload Center for this computer?

DOWNLOAD!

Sign In

Member Name: bear5
Password: 

Remember me
Forgot your password?

SIGN IN

Need to Sign Up?

SIGN UP NOW

Need Help or Having Trouble?
Thank You!