

Contributions of diet to metabolic problems in survivors of childhood cancer



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Chronic health conditions in adult survivors of childhood cancer

- 62.3% of cancer survivors reported at least one chronic condition.
- Survivors were 3.3 times as likely to have a chronic health condition compared to sibling controls (95% CI: 3.0-3.5)

	<u>Relative Risk (95% CI)</u>	
major joint replacement	54.0	(7.6 - 386.3)
congestive heart failure	15.1	(4.8 – 47.9)
second malignancy	14.8	(7.2 – 30.4)
coronary artery disease	10.4	(4.1 – 25.9)
cerebrovascular accident	9.3	(4.1 – 21.2)

Metabolic syndrome

Characteristics:

- Abdominal obesity
- Dyslipidemia
- Raised blood pressure
- Insulin resistance \pm glucose intolerance
- Prothrombotic state
- Proinflammatory state

Predictive of increased risk of cardiovascular disease and type 2 diabetes

Preventable with appropriate diet and physical activity

National Cholesterol Education Program ATPIII: Clinical Identification of the Metabolic Syndrome (2001)

Risk Factor	Defining Level
Abdominal Obesity	Waist Circumference [†]
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
Triglycerides	≥150 mg/dL
HDL cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/85 mmHg
Fasting glucose	≥110 mg/dL

Metabolic syndrome is identified by the presence of 3 or more risk factors listed in this table.

Prevalence of metabolic syndrome among adult survivors of childhood cancer

Author/ date	N	Age at interview	Cancer diagnoses included	Prevalence of metabolic syndrome	MetSyn criteria used
Gurney, 2006	75	Mean: 30 years	Acute lymphoblastic leukemia	17% *	ATP III
Van Waas, 2010	500	Median: 28 Range: 18-59	All childhood cancers	13% **	modified definition of MetSyn, Haugnes <i>et al</i>
Smith, 2014	1598	Range: 19-60	All childhood cancers	32% *	ATP III

* Not statistically significantly different from general population (NHANES)

** No comparison group

Prevalence of metabolic syndrome in the US adult population: 34% (NHANES 2003-2006)

Factors associated with metabolic syndrome in adult survivors of childhood cancer

- Advanced age
- Lower educational attainment
- Treatment regimens containing cranial radiotherapy (CRT)
- Failure to follow dietary recommendations
- Sedentary lifestyle

Dietary pattern scores

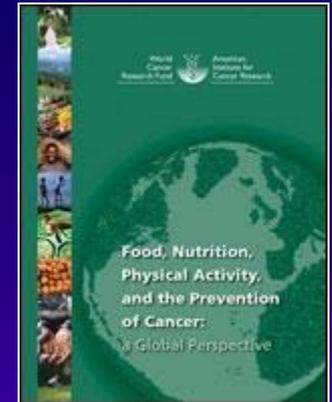
- Scores that describe adherence to recommendations on dietary factors for disease prevention
- Accounts for the complexity of diet, collinearity between dietary components
- Can be either translated into dietary recommendations, or used to test the effectiveness of existing recommendations

Examples:

- Mediterranean Diet Score
- Healthy Eating Index
- Alternate Healthy Eating Index
- DASH Score
- WCRF/AICR Adherence score

*World Cancer Research Fund /
American Institute for Cancer Research (2007)*

Food, Nutrition, Physical Activity and the Prevention of Cancer: A Global Perspective



Recommendation for Cancer Survivors:
“Follow the recommendations for cancer prevention”

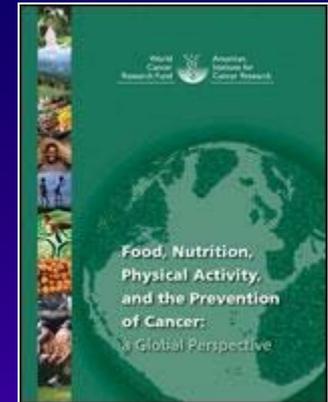
Recommendations for cancer prevention:

- Maintain body weight within the normal range.
- Be moderately physically active. Get the equivalent of 30 minutes of brisk walking every day. As fitness improves, aim for 60 minutes or more of moderate exercise (or 30 minutes vigorous exercise) each day.

(continues)

*World Cancer Research Fund /
American Institute for Cancer Research (2007)*

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Recommendations for cancer prevention (continued):

- Consume calorie-dense foods sparingly. Avoid sugary drinks. Consume 'fast foods' sparingly, if at all.
- Eat at least 5 servings of a variety of non-starchy vegetables and fruits each day.
- People who consume red meat should consume less than 18 oz per week, and very little (if any) should be processed.
- If alcohol is consumed, limit consumption to no more than two drinks a day for men, and one drink per day for women.
- Avoid salt-preserved, salted or salty foods.
- Dietary supplements are not recommended for cancer prevention.

TABLE 1. WCRF/AICR Scoring

Item Description	Value	Score
BMI, kg/m ²	≤25	1
	>25	0
Physical activity	Meets guidelines ^a	1
	Does not meet guidelines ^a	0
Daily fruit and vegetable consumption	≥5 servings/d	1
	<5 servings/d	0
Daily intake of complex carbohydrates	≥400 g/d	1
	<400 g/d	0
Daily alcohol intake	<14 g/d (females); <28 g/d (males)	1
	≥14 g/d (females); ≥28 g/d (males)	0
Daily red meat intake	<80 g/d	1
	≥80 g/d	0
Daily sodium consumption	<2400 mg	1
	≥2400 mg	0

Abbreviations: BMI, body mass index; WCRF/AICR, World Cancer Research Fund/American Institute for Cancer Research.

^aGuidelines from Centers for Disease Control and Prevention recommend 150 minutes per week of moderate physical activity.

Adherence to WCRF/AICR dietary recommendations by adult survivors of childhood cancer

Author/ date	N	Mean age at interview	Cancer diagnoses	Findings
Robien, 2008	72	29.9 years	Acute lymphoblastic leukemia	Mean adherence score: 2.9 (\pm 1.2) (out of 7)
Smith, 2014	1598	32.7 years	All childhood cancers	25.2% of males, 28.8% of females met at least 4 of the 7 recommendations

Dietary Approaches to Stop Hypertension (DASH) Diet Recommendations

Total fat:	27% of calories
Saturated fat:	6% of calories
Protein:	18% of calories
Carbohydrate:	55% of calories
Cholesterol:	150 mg
Sodium:	2,300 mg*
Potassium:	4,700 mg
Calcium:	1,250 mg
Magnesium:	500 mg
Fiber:	30 g



** 1,500 mg sodium was a lower goal tested and found to be even better for lowering blood pressure. It was particularly effective for middle-aged and older individuals, African Americans, and those who already had high blood pressure. g = grams; mg = milligrams*

Adherence to the DASH Diet by adult survivors of childhood cancer

Food group	DASH Diet Recommendation
Fruits and vegetables	<i>Daily fruit servings: ≥ 4 (women), ≥ 5 (men); Daily vegetable servings: ≥ 4 (women), ≥ 5 (men)</i>
Grains and other plant foods	<i>≥ 7 total grain servings/day (women), ≥ 10 servings/day (men); ≥ 2 whole grain servings/day (women and men)</i>
Milk or milk products	<i>≥ 2 total dairy servings/day (women), ≥ 3 servings/day (men)</i>
Meat, poultry, fish, beans	<i>≤ 2 oz/day (women), ≤ 3 oz/day (men)</i>
Fats and oils	<i>$\leq 30\%$ of total calories from fat; $\leq 10\%$ of total calories from saturated fat</i>
Sodium	<i>≤ 1500 mg sodium/day</i>
Sugar	<i>≤ 5 servings/week</i>

- 72 adult survivors of ALL
- Mean age at interview: 29.9 ± 7.3 years

Mean DASH diet score: $3.6 (\pm 1.5)$

- Mean sodium intake: 3113 mg/day
- Half the participants consumed the recommended 5 servings of fruits, vegetables - significantly better than the general population according to Behavioral Risk Factor Surveillance Survey (BRFSS)

WCRF/AICR adherence and metabolic syndrome among adult survivors of childhood cancer

Smith *et al*, 2014 (PMID: 25070001), St Jude Lifetime Cohort

- 1598 adult survivors of childhood cancers
- Participants who did not follow at least 4 of the 7 WCRF/AICR recommendations were at increased risk for metabolic syndrome

Females RR 2.4 (95% CI: 1.7-3.3)

Males RR 2.2 (95% CI: 1.6-3.0)

adjusted for age, race, CRT, education, smoking status, age at diagnosis

Mediterranean Diet and metabolic syndrome among adult survivors of childhood cancer

Tonorezos *et al*, 2012 (PMID: 23187859), ALLIFE Study

- 117 adult survivors of childhood acute lymphoblastic leukemia
- Mediterranean Diet characterized by high intake of fruits, vegetables, fish and legumes; low intake of meat and dairy products
- Mean Mediterranean Diet Score (total possible score: 8):
Females: 4.5 (\pm 1.6) Males: 3.9 (\pm 1.8)
- For each one point increase in adherence to a Mediterranean dietary pattern, odds of developing metabolic syndrome fell by 31% (OR 0.69, 95% CI: 0.50-0.94)
- Better adherence to the Mediterranean diet pattern was associated with lower visceral and subcutaneous adiposity, even after adjustment for age, gender, physical activity and total caloric intake

Additional diet related findings

- Small (n=26) study of adult survivors of childhood ALL had a mean MEDFICTS score that indicated non-compliance with the National Cholesterol Education Plan (NCEP) recommendations for total and saturated fat (PMID: 11878576)
- Among survivors of childhood ALL (n=164), less than 30% met recommended dietary intakes for vitamin D, calcium, potassium, or magnesium (PMID: 20981691)
- Children/adolescent cancer survivors tend to consume more healthful diets than adult survivors (PMID: 15812823, 7623724)

Limitations of the research to date

- Many studies have been small, single institution analyses
- Mostly cross-sectional, observational studies
- Very few studies have used comprehensive dietary assessment methods.
- Few studies have included a control group, or compared their findings to age-appropriate population data
- Lack of intervention studies to determine whether dietary intervention decreases risk of metabolic syndrome and other chronic diseases

Take-home messages

- As is true for the general US population, on average, survivors of childhood cancers are not compliant with dietary recommendations to prevent chronic diseases.
- Compliance with WCRF/AICR diet and physical activity recommendations appears to decrease the risk of metabolic syndrome, and may prevent progression to chronic disease in this high-risk segment of the population
- Intervention studies are needed to evaluate the effectiveness of diet and physical activity interventions among adult survivors of childhood cancers