

# Weight, Dietary Behavior, and Physical Activity in Childhood and Adolescence: Implications for Adult Cancer Risk

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## Key Words

Children · Weight · Diet · Physical activity · Cancer · Obesity · Tracking

## Summary

Lifestyle factors related to energy balance, including weight, dietary behavior and physical activity, are associated with cancer risk. The period of childhood and growth into adolescence and early adulthood may represent a 'cumulative risk' for later adult-onset cancers. We review a number of epidemiologic studies that have examined associations among childhood and adolescent body size, diet, and physical activity with adult cancer risk. These studies suggest that unhealthy behaviors that develop early in life and persist over time may increase the risk of some cancer types, such as premenopausal breast, ovarian, endometrial, colon and renal cancer, adversely affect cancer-related morbidities, and increase mortality. Continued research is needed to further determine and refine how timing and degree of such exposures in early childhood and adolescence relate to adult cancer risk. Presently, sufficient evidence suggests a continued need for stronger primary prevention in cancer and obesity research via modified lifestyle behaviors earlier in the developmental spectrum, i.e. during childhood and adolescence.

## Introduction

The rising rates of obesity both globally and in the USA are of high public health significance because of the burden that obesity has on society in terms of economic costs, loss

of productivity, disability, and overall mortality [1, 2]. The relationship between overweight (BMI = 25–29.9 kg/m<sup>2</sup>) or obesity (BMI ≥ 30 kg/m<sup>2</sup>) and childhood morbidities or adult chronic diseases has been widely studied. A growing set of studies have examined potential causal relationships between weight, diet, or physical inactivity and risk of cancer. Overall, this literature has linked obesity to increased risk of several types of cancer, including colon, endometrial, kidney, and postmenopausal breast cancer [3–6]. A recent meta-analysis also concluded that insufficient physical activity increases the risk of breast or colon cancer [7]. It has been estimated that 15–20% of cancer deaths in the USA can be attributed to overweight and obesity [8], and in the European Union 5% of cancer deaths may be related to overweight and obesity [9].

The mechanisms by which weight, diet, and physical activity influence tumor formation and progression are not completely understood. A number of putative physiological processes have been proposed. One hypothesis is that excess adipose tissue results in dysregulation of energy balance (i.e. the number of calories consumed and expended, as affected by physical activity, body size, fat and muscle, and genetics) and lipid metabolism affecting cytokine and growth factor levels (e.g. leptin, adiponectin, resistin and tumor necrosis factor alpha). These cytokines play a role in carcinogenesis [3]. Insulin and insulin-like growth factor 1 (IGF-1; once called somatomedin C) are also believed to be important. Intra-abdominal fat heightens insulin resistance, leading to increased pancreatic secretion of insulin. High concentrations of insulin reduce the synthesis of IGF-binding proteins 1 and 2, resulting in increased IGF-1 activity in the liver. This increased activity of insulin and IGF-1 reduces sex hormone binding globulin (SHBG) synthesis increasing testosterone and estradiol levels [10]. These conditions combine to influ-

ence cell proliferation and inhibition of apoptosis, especially in breast and endometrial tissues [11, 12]. Physical activity and maintenance of a normal body weight is thought to regulate these growth factor cytokines and SHBG, thus offering a potential protective effect against cancer [13–16]. Given the important role of hormones in the etiology of some cancers, these and other mechanisms continue to be investigated by basic and clinical scientists in the fields of endocrinology, metabolism, and oncology.

As is highlighted throughout this special issue of *OBSESITY FACTS*, many energy balance-related behaviors establish themselves early in childhood and may track into adulthood. The period of childhood and growth into adolescence and early adulthood could represent a ‘cumulative risk’ for later adult-onset cancers. ‘Tracking’ of behavioral risk is critical to understand in this context, in that it reflects the maintenance of a relative position in the population across time [17]. In our review, we attempt to understand the tracking of childhood weight, dietary behavior, and physical activity and its implications for cancer prevention. Thus, we review i) a large set of epidemiologic studies examining childhood and adolescent weight, diet, and physical activity as they relate to risk of adulthood cancers, and ii) discuss the implications for prevention and future directions.

## Methods

This review is focused on peer-reviewed, published studies examining childhood and/or adolescent (up to age 18) exposures (specifically, body size, diet, physical activity) as they relate to adult cancer risk. We conducted multiple searches using the U.S. National Library of Medicine’s online PubMed/MEDLINE interface, including root search terms and permutations such as ‘child’, ‘adolescent’, ‘youth’, ‘obesity’, ‘adult’, ‘neoplasm’, ‘risk factor’, ‘observational study’, ‘cohort study’, and ‘prospective study’. Reference lists in identified studies and review papers were also culled for other relevant citations which were not identified via our original search. We excluded studies that focused primarily on maternal weight gain during pregnancy, pre-, peri-, and postnatal infant weight and the role of breastfeeding, achieved adult height only, or exposures that were assessed for ages older than 18 years. Although these are both important and relevant (as they have been associated with cancer risk), they were beyond the scope of this particular review. Table 1 presents a list of resulting studies, cataloged by risk (i.e. positive association with cancer) or protective (i.e. negative association with cancer) factor, and cancer type examined, including indicators of body size, diet, physical activity, adult cancer risk. These results are described and summarized in the narrative that follows.

## Weight and Cancer

A total of 45 studies, conducted over the past 30 years, examining potential associations between childhood and adolescent weight on cancer risk were identified. A majority were case-control studies, with fewer nested case-control and retrospective cohort studies. A challenge in conducting this type of research is capturing the key exposure of interest, namely childhood and adolescent weight and height. A common method has been to ask individuals to self-report on their weight or body size relative to their peer group at certain ages [18–25]. Some studies used figure drawings depicting progressively larger body shapes as proxy measures of body size at certain age periods [26–30]. In some cases, studies assessed only weight at the late adolescent period, relying mainly on participants’ retrospective recall of their weight during a period of adolescence, and current height was either self-reported or measured to calculate BMI [31–50]. Measured height and weight from childhood or adolescence were available in a small subset of studies [51–61]. These differences in methodology are important to note as they affect the quality of the evidence associated with each of the cancer types discussed below.

### *Breast Cancer*

The association between childhood and adolescent body weight and breast cancer has received considerable attention: greater BMI at age 18, or higher perceived body fat relative to others during childhood, is associated with an approximately 20–50% decreased risk of breast cancer. This inverse association was reported among 22 studies; however, a small set indicted null findings when investigating the relationship between child indicators of weight and breast cancer [21, 35, 45, 47, 48, 52, 57, 60]. Only one study found a positive (increased risk) relationship between the highest perceived weight category and breast cancer; that same study also reported an inverse relationship among those in the lowest weight category and risk of cancer relative to the average [19]. Many others found significant inverse associations mainly among women developing premenopausal breast cancer [26, 27, 29, 30, 41, 47, 50, 53, 60, 62, 63]. Studies examining different time periods in childhood found significant inverse associations for taller body size during the prepubertal stages [26, 60]. Among women with predominately postmenopausal breast cancer (or when data are stratified by menopausal status), no consistent association between adolescent weight or childhood body size and postmenopausal breast cancer risk emerges [28, 37, 47, 60]. Some studies do note that observed weight gain from late adolescence to adulthood increases risk of postmenopausal breast cancer [18, 28, 37, 39, 47]. Although there remains a possibility of misclassification of exposure due to reliance on adult retrospective recall of childhood size, four of the five studies that had measured height and weight data in childhood or adolescence observed an inverse relationship between BMI and breast cancer risk [53, 58, 60, 64].

**Table 1.** Summary of studies addressing tracking of childhood energy balance-related risks for select cancers in adulthood<sup>a</sup>

Childhood risk/protective factor	Cancer type						
	menopause unspecified breast cancer	premenopausal breast cancer	postmenopausal breast cancer	ovarian cancer	endometrial cancer	colon cancer	others
<i>Weight</i>							
+	19			36 (preM), 38 (preM), 42, 55	25, 33, 34, 46	52, 61, 65	31 (RCC men only), 33, 52, 54, 59
-	18, 19, 22-24, 39, 58, 64	26-30, 41, 47, 50, 53, 60, 62, 63	27				
0	21, 52, 57	45, 48	37, 47, 60	32, 36 (postM), 38 (postM and BMI), 40, 44, 56	43, 49		20 (RCC)
<i>Weight change</i>							
+	27, 60, 64		18, 28, 35, 37, 39, 47	56 (nulliparous)	25, 34, 43		31 (RCC men only)
-	19	18, 47					
0		30		42	49		
<i>Physical activity</i>							
+							93, 95
-	68-77, 119	63			94	96	95, 97-99
0	81, 82, 84, 85, 86, 91, 92, 95	29, 69, 79, 80, 83, 87, 88	78, 89, 90	79			79, 95, 97, 100
<i>Diet</i>							
+	105-107	104					110, 113
-	102, 103, 105-107	101	101				112
0	22, 110	108, 109, 120	120				100, 110

preM = Premenopausal women; postM = Postmenopausal women; RCC = renal cell carcinoma.

<sup>a</sup>The numbers in the table correspond to citations appearing in the reference list. '+' = Positive (risk) relationship between factor and cancer; '-' = Negative/inverse (protective) relationship between factor and cancer; '0' = null (uncertain or equivocal) relationship between factor and cancer. The determination of a positive, negative, or null association was based on p-values and confidence intervals reported in the actual studies.

### *Ovarian and Endometrial Cancer*

The relationship between child and adolescent weight and ovarian cancer has received less attention despite a plausible biological connection, as adiposity has been associated with some of the risk factors for ovarian cancer (e.g. ovulatory function, infertility, endometriosis, and inflammation) [56]. In eight recent studies, seven asked respondents to recall their weight at age 18 [32, 36, 38, 40, 42, 44, 56], and one measured height and weight available from age 14–17 years [55]. The results of these studies were mixed: four indicated a positive association between late adolescent BMI and risk of ovarian cancer [36, 38, 42, 55], and three reported a null or lack of association [32, 40, 56]. At least two of the studies showed risk may be more salient for premenopausal than for postmenopausal women [36, 38]. The single nested case-control study observes a significant relative risk of adult ovarian cancer of 1.56 in those whose adolescent BMI was in the 85th percentile (overweight range) compared to those women whose adolescent BMI was in the 25th–74th percentile (low normal range) [55].

Only nine studies of the relationship between body mass and endometrial cancer risk included measures of childhood or adolescent body mass. Most asked participants to recall their adolescent weight (ages 16–18) [25, 33, 34, 43, 46, 49] or rate it relative to others [25]: four indicated a positive association [25, 33, 34, 46], and one remained significant after adjusting for adult or current body mass [33]. Regarding weight gain, a single study found it to be a risk factor but only during the 4th decade of life [25]. Weight gain from 18 years of age was also a risk, mainly among women who were already overweight during adolescence [34].

### *Colon and Renal Cancer*

Higher BMI has been associated with colon cancer in several epidemiologic studies; less is known about whether or not larger body mass (or greater BMI) in childhood and adolescence or change since adolescence confers greater risk. Studies indicate a positive association between larger body mass in youth and later adult colon cancer risk [52, 61, 65]. A recent study found a two-fold increase in risk of death from colon cancer related to BMI > 85th percentile measured during adolescence [52]. In two studies of renal cancer, one found a weakly positive association with cancer risk among men related to retrospective report of BMI at age 18 [31]; another found no association between perceived body size at age 12 and renal cancer risk [20]. Adolescent weight may also moderate effects. Leaner adolescents with stable weight in adulthood have low risk, and markedly increased risk results with weight gain in adulthood [31]; heavy adolescents have elevated risk regardless of gain.

## **Physical Activity and Cancer**

Several studies have examined the relationships between physical activity and breast [66] or endometrial cancers [67].

Both found evidence of reduced risk of breast and endometrial cancers with increased physical activity for adults though these trends are not necessarily reproduced for physical activity during childhood and adolescence [66, 67].

### *Breast Cancer*

Significant risk reduction is observed among those who report being physically active as adolescents [68–77]. Participation in college athletics was associated with reduced risk of developing breast cancer [77] as well as breast and reproductive system cancers [76]. Modest risk reductions are also found among women reporting being physically active in their child and teen years [78, 79] or teen years only [80–82]. Eleven studies did not find an association between adolescent physical activity and breast cancer risk [29, 83–85] in the general population and in African-American women only [86]; no association with leisure or recreational activity [87–90], in relation to peers [91], or in a study where <25% of the study population had been engaged in vigorous physical activity were reported [92].

### *Other Cancers*

Studies examining the relationship between youth physical activity and other cancers were also reviewed and are evaluated together. Strenuous physical activity (e.g. activities that make individuals sweat or breathe hard) between the ages of 12–18 was associated with a significant reduction in risk for Hodgkin's lymphoma in women [93] as well as endometrial [94], rectal [95], colorectal [96], and renal cell cancer [97–99]. A single study showed a slightly reduced, but not significant trend for prostate cancer [100] – another found a significantly increased risk [95].

## **Diet and Cancer**

Many studies focus on the relationship between the intake of different types of foods and nutrients and the development of cancer. These studies often examine contemporary dietary practices of adults. Diet and nutritional intake during childhood and adolescence has also been reported, and these works are summarized below.

### *Breast Cancer*

Studies examining the relationship between child and adolescent diet and cancer have primarily focused on risk of breast cancer. Consumption of specific foods at various ages in women's lives have differentially reported associations with risk, making it difficult to draw clear and well-informed conclusions. A study that assessed diet both at cancer diagnosis and in adolescence found that among premenopausal women, high-fat foods (such as beef, pork, and gravy) increased risk, and consumption of fish decreased risk. In postmenopausal women only, pork consumption increased risk, and carrots decreased risk; none of these adult risk trends appeared in

adolescence [22]. Today, pork (like chicken) is often bred and processed to be leaner than in the past – making some trimmed pork cuts now a lean meat.

Several researchers have examined the relationship between the consumption of specific food types or nutrients during childhood and their impact on the risk of breast cancer. Phytoestrogens (or dietary estrogens), which are found in foods such as soy, flaxseeds, grains, nuts, fruits and vegetables, reduced the risk of breast cancer when consumed during adolescence [101–103]. Eating red meat [104], butter [105], French fries [106], and a diet with a higher glycemic index (i.e. measured carbohydrate effects on blood glucose levels) [107] during childhood increased the risk of breast cancer. Conversely, decreased risk was associated with consumption of eggs, vegetable fat, fiber, and vitamin E (a known antioxidant) [105, 107]. Moderately reduced risk may have been related to the consumption of fruits and vegetables [108] and milk [109], though benefits remain unproven in that context [110].

#### *Other Cancers*

In two studies using the same cohort [111], increased childhood fruit intake decreased risk of adult cancer [112], and increased childhood energy intake increased risk of adult cancer mortality [113]. Studies of childhood diet and prostate cancer risk have found either no association [100] or a slightly decreased but not significant risk with dairy consumption [110]. High dairy intake in childhood is associated with increased risk of colorectal cancer, but not associated with risk of stomach cancer [110].

### **Limitations**

There are several limitations with this research, including the review's methodology and its studies reviewed. Though literature searches were thorough, some might have been incomplete. Capturing exposures of interest were also challenging, specifically childhood and adolescent body size and diet. Examining the association between childhood body size, diet or and physical activity and risk of adult cancer is limited in that recall over extended periods of time might be inaccurate. There is also the possibility of selection bias among controls who agreed to participate in research studies concerning physical activity; healthier and more physically active individuals may have been more likely to participate. Finally, measurement of physical activity and age ranges in which childhood physical activity was assessed differ across studies, making comparisons complex and challenging to interpret.

The major limitation to assessing the relationship between diet during early life and adult cancers is recall accuracy of foods consumed decades ago, although some focused on more specific and limited time periods. Limiting recall to a narrower time window, or focused only on the intake of a particular food, further affects this. Accuracy could be improved in future studies through assessment of childhood diet at the be-

ginning of a prospective cohort study. Studies included in this review also relied on older cohorts, and it is not clear if associations hold up over time as populations become heavier, more sedentary, had different nutritional histories with increased consumption of processed foods (and differently processed foods) containing food additives.

### **Prevention and Future Directions**

Cancer is the summation of different risks and exposures over the course of many years, including genetic susceptibility, environmental exposures, and modifiable risk factors. From birth to young adulthood, the human body is rapidly growing and developing, and exposures during this time period can be related to the development of cancer later in life [114]. As noted throughout this review, the implications of childhood overweight and obesity on future cancer risks accrued into adulthood are numerous and significant. As this evidence continues to mount from basic and clinical research investigations, the focus of our attention must ultimately turn toward prevention and intervention. From the standpoint of primary and secondary prevention of obesity, a recent review concludes that exercise and physical activity promotion are critical to achieving these ends [115]. We underscore the importance of these activities related to adult-onset cancers.

The World Health Organization has taken a strong stance on the prevention of obesity, noting its global health threat [116]. In the USA, the Institute of Medicine's Committee on Prevention of Obesity in Children and Youth developed a comprehensive strategy for America, detailing how key institutions in children's lives (families, schools, industry, communities, and government) can change the outcome of childhood obesity [117]. As the USA leads the world in its obesity epidemic, so too may it lead by example with respect to prevention. It is clear that the problem of childhood obesity must be viewed at the macro level, targeting the broad population of children. Until these goals are reached, a number of intermediate steps are also required. Chief among these are modifications to youth dietary and physical activity practices. As the evidence base for efficacious interventions in these areas continues to grow [118], so too will opportunities for interdisciplinary prevention interventions that address a more complete range of children's biopsychosocial risks and protections targeting obesity and cancer.

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