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Physical Activity and Cancer

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Abstract

Epidemiological evidence continues to accumulate on the benefits of physical activity in relation to cancer risk, progression and mortality. Recent studies suggest that sedentary behavior may independently affect cancer risk; they also focus on factors that may explain associations with physical activity, including cancer risk factors and whether associations exist for precancerous lesions. Despite enormous efforts to examine associations between physical activity and cancer, the literature is hindered by inconsistent assessment of physical activity across studies, and incomplete consideration of variation of effects across population subgroups (for example, defined by body size, age or sex) or tumors subgroups (organ location, receptor status, or molecular subtype), and whether other factors explain study results. Clearly, public health recommendations for appropriate changes in activity levels are needed; unfortunately, at this time, we have no exact physical activity prescription to give to the public.

Keywords

Review; Physical activity; Cancer risk; Cancer survival; Recreational activity; Occupational activity; Exercise; Biological mechanisms; Methodology; Sedentary behavior; Sitting time; Breast cancer; Colon cancer

Introduction

The health benefits of participating in regular physical activity are well-documented, and include reductions in risk of cardiovascular disease, diabetes, osteoporosis, obesity, depression, fatigue, and overall mortality [1].Compelling evidence exists for inverse relationships between physical activity and risk of breast and colon cancers [2]. For these cancers, physical activity represents one of the few modifiable risk factors that can be recommended for risk reduction [2]. Evidence suggests that physical activity may also reduce the risk of endometrial and ovarian cancer, and may possibly reduce the risk of prostate and lung cancer [3, 4].

Case-control and cohort studies have been the mainstay of study designs to examine associations between physical activity and cancer. Methods for data collection physical activity vary on approach (interview, self completed questionnaire, or occupational energy expenditure), periods of life covered, and whether key elements (duration of each physical activity episode, frequency of episodes, and intensity of activity) are available. It is also

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pertinent to distinguish between broad types of physical activity: recreational (exercise activity), occupational activity (including childcare and household activity), and transportation activity (walking or biking to work). Many studies estimate metabolic equivalents (MET)-hours of energy expenditure, a composite measure that captures intensity, frequency and duration of activity, using standard values specific to each activity and multiplying these values by the number of hours spent in the specific activity per week [5].

A number of meta-analyses have been published recently; these combine effect estimates from a series of studies to provide summary estimates of cancer risk. Pooled analyses derive similar estimates of risk, but use the original data from the studies. A major challenge in combining results across studies of physical activity and cancer is that methods of quantifying physical activity vary. Most meta-analyses compare the group with the most physical activity (however defined) to that with the least activity (sometimes inactive individuals; other times those with less than some predefined amount of activity). Further, some studies examine recent activity, whereas others evaluate measures of long-term or lifetime activity; some include only recreational activity, whereas others focus on occupational activity or combine recreational and occupational activities. Therefore, one must interpret results of these studies cautiously.

Understanding the biological mechanisms underlying the associations between physical activity and cancer will provide needed insights that permit appropriate physical activity recommendations for reducing cancer risk. A number of plausible candidate mechanisms have been proposed, some specific to one particular cancer; however the single mechanism or group of mechanisms that explains the associations between physical activity and lower cancer risk have yet to be established. For colon cancer, the major hypothesis is that physical activity lowers fecal bile acid concentrations and decreases gastrointestinal transit time. For female breast cancer, physical activity alters endogenous production of sex steroid hormones by altering menstrual cycle patterns (resulting in luteal phase defects, oligomenorrhea or secondary amenorrhea) through its impact on the hypothalamic pituitary axis and, among postmenopausal women, by controlling body weight [6•]. These mechanisms, which regulate sex steroid hormones, are also potential mediators of the associations between physical activity and endometrial and ovarian cancers. Other mechanisms have been proposed that have more generalized anticancer impact and may explain associations between physical activity and several cancer sites; these include heightening immune surveillance, reducing inflammation, increasing endogenous antioxidant enzyme systems, increasing insulin sensitivity, controlling growth factor production and activation, decreasing obesity and central adiposity, optimizing DNA repair capacity, and reducing oxidative stress [6•]. It is highly plausible that several of these mechanisms act simultaneously, and that they interact synergistically to mediate the associations between physical activity and cancer.

This report provides a review of epidemiologic studies published between January 2011 and April 2012 on the associations between physical activity and cancer.

Colorectal Cancer

Colorectal Cancer Development

An inverse association between physical activity and colon cancer risk has been consistently observed among epidemiologic studies; however, the evidence for rectal cancer remains inconclusive [7, 8]. Historically, comprehensive reviews have estimated that physical activity may reduce colon cancer risk by 20–25 % when comparing individuals with the highest levels of physical activity to those with the lowest levels [9]. Risk reductions are

greater for case-control studies (24 %) than for cohort studies (17%), and risk reductions are similar for occupational activity (22 %) and recreational activity (23 %) [9]. In cohort studies, colon cancer risk reduction associated with physical activity is greater for men than for women, although case–control studies suggest similar benefits for men and women [10].

Whether physical activity preferentially protects against distal or proximal colon cancer is uncertain [11]. Boyle and colleagues studied 870 colorectal cancer cases (284 proximal, 268 distal and 318 rectal) and 996 age- matched and sex-matched healthy controls, examining the timing and intensity of recreational physical activity on subsite-specific colon cancer risk [12•]. Stronger associations were observed for distal tumors than for proximal tumors. Consistent vigorous recreational physical activity (≥ 6 MET-hours/week) during adult years was associated with 41 % lower distal colon cancer risk [95% confidence interval (CI), 0.36–0.96]. The association between vigorous recreational physical activity and distal colon cancer risk was limited to activity performed after age 51 years, with risk reductions of 49 % for 6 to 18 MET-hours per week and 55 % for 18 or more MET-hours per week. Boyle et al. did not observe any association for proximal colon cancer [odds ratio (OR)=0.93; 95 % CI, 0.59–1.45] [12•]. Although the majority of previous studies [9] have not found an association between physical activity and rectal cancer, consistent vigorous recreational physical activity averaging at least 6 MET-hours per week during adult years was associated with a reduced rectal cancer risk in one study (OR=0.62, 95 % CI, 0.39–0.98)[12•].

Sedentary behavior, defined by prolonged sitting and low energy expenditure activities (MET-value < 1.5) has been independently associated with increased risk of several cancers [13]; however, it is still unclear whether sedentary occupations modify colon cancer risk. Boyle and colleagues et al. also investigated the effect of long-term sedentary occupational work, defined by the US Department of Labor's Dictionary of Occupational Titles Demands Strength Rating, in their case-control study [14]. Participants who reported at least 10 years of sedentary work had almost two-times greater risk of distal colon cancer (OR=1.94, 95 % CI, 1.28–2.93) than those who never held a sedentary job [14]. Importantly, this association was independent of the amount of recreational physical activity reported by study participants [14].

Given that body mass index [BMI, generally measured as weight (kg)/height (m^2)] and physical activity are both risk factors for colon cancer, several analytic approaches have been employed to tease apart their joint and independent effects on colon cancer risk. The impact of occupational (longest-held and last job) and baseline recreational physical activity on the association between body size (trouser/skirt size) and colorectal cancer risk were investigated among members in the Netherlands Cohort Study (2,316 colorectal cases and 3,197 healthy cohort members) using a case-cohort analytic approach [15]. For women who were less likely to hold jobs than men, only recreational physical activity was considered. Low physical activity was associated with increased colorectal cancer risk, consistent with previous studies. In this study, the joint effects of physical activity and body size were assessed by comparing extremes. Smaller women (trouser/skirt size ≤ 44, comparable to a size 14 in the US) in the highest recreational activity category (> 90 min/day) were compared to larger women (trouser/skirt size > 44) in the lowest recreational activity category (< 30 min/day); risk for each subsite of colorectal cancer was increased [Distal: hazard ratio (HR)=1.95, 95 % CI, 1.21–3.17; Proximal: HR=1.70, 95 % CI, 1.08–2.67; Rectal: HR=2.56, 9 5% CI, 1.36–4.79]. However, the interaction between physical activity and body size was statistically significant only for proximal tumors. Among men, the combination low occupational-plus-recreational physical activity (< 8 kJ/minute) was associated with a 63 % increased risk (95 % CI, 1.03–2.56) of distal colon cancer among men whose trouser size was ≤ 52 (median of the cohort). No association was observed for proximal colon cancer or rectal cancer.

Genomic instability is known to drive several carcinogenic pathways [16]. Epigenetic silencing of gene expression, primarily mediated by aberrant DNA methylation, has been implicated for colon cancer; however, its role in modifying the association between colon cancer and physical activity is not well understood [16]. Within a subset of the Netherlands Cohort Study population (603 colorectal cancer cases and 4,631 controls), Hughes and colleagues investigated the combined effects on colon cancer risk of CpG island methylator phenotype (CIMP) and physical activity [17]. Combined occupational-plus-recreational physical activity at baseline was associated with decreased colorectal cancer risk, regardless of molecular subtype (CIMP+/non-CIMP) (*P*-heterogeneity=0.33)[17]. Among CIMP+ tumors, a 50 % lower colorectal cancer risk (95 % CI, 0.30–0.82) was observed for men and women in the intermediate activity category compared to those in the low physical activity; however, high activity was not associated with risk (HR=0.82, 95 % CI, 0.49–1.38) [17]. For non-CIMP tumors, high and intermediate levels of physical activity were not associated with colorectal cancer risk (High: HR=0.69, 95 % CI, 0.47–1.01; Intermediate: HR=0.81, 95 % CI, 0.61–1.07) [17]. The study lacked the statistical power to stratify by tumor subsite (proximal and distal colon cancer and rectal cancer).

An emphasis has been made on trying to identify risk factors for colon adenomas, which are considered a precursor lesion for colon cancer that is detected and removed during colonoscopy or sigmoidoscopy. Wolin et al. conducted a meta-analysis of twenty studies that investigated the association between recreational physical activity and colon adenomas published through April 2010 [18•]. An inverse relationship with a 19 % reduction in adenoma risk among men (95 % CI, 0.67–0.98) and a 13 % risk reduction among women (95 % CI, 0.74–1.02) [18•] was observed. Among men and women combined, the association was strongest, for large/advanced polyps (OR=0.30; 95 % CI, 0.56–0.88) [18•].

Colorectal Cancer Survival

Physical activity before as well as after colorectal cancer diagnosis is associated with improved survival [19•, 20•]. One study examined whether CTNNB1 (beta-catenin), which is known to play a critical role in colorectal carcinogenesis and metabolic diseases, modifies the association between physical activity and colorectal cancer survival among participants in two prospective cohort studies (the Nurses Health Study and the Health Professionals Follow-up Study) conducted in the US [21]. Colorectal cancer-specific mortality was inversely associated with increasing levels of post-diagnosis physical activity among patients whose tumors were CTNNB1-negative (HR=0.33, 95 % CI, 0.13–0.81 comparing ≥ 18 vs. < 18 MET-hours/week), but not among patients with CTNNB1-positive colorectal cancers [21].

Breast Cancer

Breast Cancer Development

The evidence for an association between physical activity and breast cancer has been classified as convincing [2]. Results from case–control studies and cohort studies have shown that invasive breast cancer risk is reduced by 20–40 % among physically active women [2]. One of the earliest studies, a case–control study of women 40 years or younger, showed a dramatic reduction in risk (approximately 50%) among women who averaged about 4 hours of activity per week during their reproductive years [22]. Similarly, among postmenopausal women, those with higher amounts of recreational physical activity during their lifetimes have been shown to have lower breast cancer risk [23, 24].

Epidemiologists require that a risk factor demonstrate consistency across populations before considering it as “accepted.” In the past year, studies have been published on the association between physical activity and breast cancer risk among Japanese [25], Chinese [26],

Mexican [27], Tunisian [28], and US African American women [29]. A prospective study in Japan observed a 27 % decrease risk of breast cancer (95 % CI, 0.54–1.00) comparing women whose recreational physical activity was ≥ 3days/week to women who reported ≤ 3 days/month of physical activity [30]. One interesting result in this study is that the association was strongest among women with a BMI ≥ 25 kg/m^2 [30]. Similar results were observed in a cohort study of Chinese women in Shanghai, with a marked 27 % reduction in breast cancer risk (95% CI, 0.57–0.92) among postmenopausal women who expended at least 8 MET-hours/week/year compared to women who exercised < 8 MET-hours/week/year [26]. This association, too, was restricted to 'heavier' women, in this study, those with a BMI ≥ 23.73 kg/m^2. Both premenopausal and postmenopausal women in this Shanghai study showed increasing breast cancer risk with increasing lifetime occupational sitting time and decreasing occupation energy expenditure [26].

Several other case-control studies published in the past 18 months have some shortcoming (limited history of breast cancer, small sample size, hospital-based study design). A population-based case-control study of 1,000 incident breast cancer cases and 1,074 healthy controls in Mexico only considered physical activity in the previous 12 months, with minimal although statistically significant decreases in breast cancer risk among both premenopausal and postmenopausal women [27]. A small hospital-based case-control study in Tunisia assessed lifetime total physical activity (recreational, occupational and housework activity), showing marked reductions in postmenopausal, but not premenopausal breast cancer risk associated with lifetime physical activity [28]. Another case-control study with limited information on physical activity (past year) and small sample size, conducted among African American women in the Washington DC metropolitan area, observed 64 % reduced risk (95 % CI, 0.17–0.75) among women who engaged in ≥ 2 hours/week of vigorous physical activity (e.g., running, aerobics) in the past year compared to women who did not participate in any vigorous activity [29]. The study lacked sufficient statistical power to assess risk among premenopausal women, a common limitation of studies. Thus, the association was limited to postmenopausal women.

Risk specific to breast cancer subtypes defined by estrogen receptor (ER), progesterone receptor (PR) and HER-2/neu status of the tumor is of great interest. The Women's Health Initiative (WHI) observed decreases in breast cancer risk associated with recreational physical activity among postmenopausal women with ER-positive breast cancer [31•]. The highest tertile of moderate/low-intensity physical activity was associated with a 15 % decrease in ER-positive breast cancer risk (HR=0.85; 95 % CI, 0.74–0.98) [31•]. Similar results were observed for triple-negative breast cancer and for strenuous recreational physical activity; however, the findings were not statistically significant [31•]. A major limitation to this and previous studies stratifying by hormone receptor status is the inability to comprehensively classify triple negative breast cancer, due to missing HER2 status (unknown in 40 % of cases in WHI study). Another limitation of the WHI study was its failure to break down the ER-positive subtype by PR and HER-2 status.

The Women's Contraceptive and Reproductive Experiences (CARE) Study investigated whether the use of menopausal hormone therapy modified the inverse association between recreational physical activity and breast cancer risk in postmenopausal women reported in a prior publication [32]. Similar risk reductions were observed among women who never used hormones, those who used hormones for less than 5 years and women who were currently taking estrogen only. Associations were not observed among other hormone use subgroups; however, despite the large size of this study, tests of homogeneity were not able to statistically demonstrate that hormone therapy modified the association between physical activity and breast cancer risk.

As with colorectal cancer, an emphasis has been made on trying to detect risk factors earlier in the disease process. A report from the Nurses' Health Study II cohort showed that lifetime recreational physical activity was associated with risk of benign breast disease and columnar cell lesions, which may be precursors to breast cancer [33•]. Women who engaged in 39–53.9 MET-hours/week (equivalent to 13 hours/week of walking or 3.25 hours/week of running) had substantially reduced risk of proliferative benign breast disease [Relative Risk (RR)=0.63; 95 % CI, 0.33–1.19] [33•]. Although risk reduction was greater for women with low BMI at age 18 years, no statistical differences in RR could be demonstrated when comparing women with BMI < 21 $kg/^2$ to those with higher BMI in late adolescence. These results suggest that the benefit of physical activity may be initiated early in the carcinogenic process and emphasize the importance of starting physical activity at young ages and maintaining physical activity throughout life.

Breast Cancer Survival

Breast cancer survivorship literature has shown evidence that pre-diagnosis and post-diagnosis physical activity reduce all-cause and breast cancer-specific mortality among breast cancer survivors [19•]. A recently published meta-analysis reported that pre-diagnosis physical activity was associated with lower all-cause mortality (OR=0.82, 95 % CI, 0.67–0.99), and that post-diagnosis activity was associated with reduced all-cause mortality (OR=0.59, 95 % CI, 0.53–0.65), breast cancer-specific mortality (OR=0.66, 95 % CI, 0.57–0.77) and disease recurrence (OR=0.76, 95 % CI, 0.66–0.87) [34•]. These associations were modified by BMI and hormone receptor status. Pre-diagnosis physical activity was associated with lower breast cancer-specific mortality among women with a BMI < 25 kg/m^2 (not overweight or obese), whereas post-diagnosis physical activity was associated with reductions only among women with a BMI ≥ 25 kg/m^2. Further, reductions in both breast cancer-specific and all-cause mortality were observed among women diagnosed with ER-positive, but not ER-negative, tumors. Chen et al. assessed associations between post-diagnosis recreational physical activity and survivorship among 4,826 women diagnosed with stages I-III breast cancer identified 6 months after diagnosis through the population-based Shanghai Cancer Registry, and observed similar results [35]. Compared to women who did not participate in any recreational activity, reductions in breast cancer-specific mortality were observed for women who participated in regular physical activity (≥ 8.3 MET-hours/week) within 18 months after diagnosis (HR=0.72, 95 % CI, 0.57–0.93) and within 36 months after diagnosis (HR=0.59, 95 % CI, 0.45–0.76) [35]. Likewise, reductions in all-cause mortality were observed for women who participated in regular physical activity within 18 months after diagnosis (HR=0.65, 95 % CI, 0.51–0.83) and within 36 months after diagnosis (HR=0.65, 95 % CI, 0.51–0.84) [35]. Contrary to what was observed in the meta-analysis, Chen et al. observed reduced mortality only among women with ER-negative breast tumors ($HR_{all\text{-}cause}$ = 0.40, 95 % CI, 0.29–0.59; $HR_{breast\ cancer\text{-}specfic}$ = 0.36, 95 % CI, 0.24–0.56) [35].

Other Cancer Sites

Cancer Development

Endometrial Cancer—The evidence showing that regular physical activity lowers endometrial cancer risk is accumulating, but is less convincing than that for breast or colon cancer [2]. A meta-analysis of prospective cohort studies considering the literature published through 2009 indicates that recreational physical activity lowers endometrial cancer risk by 27 % (95 % CI, 0.58–0.93) and occupational activity lowers risk by (95 % CI, 0.71–0.88) [36•]. The authors further investigated sitting time in relation to endometrial cancer risk using data from the NIH-AARP Diet and Health Study, and observed that greater sitting time was independently associated with increased endometrial cancer risk [36•]. Two case-

control studies found similar results [37, 38]. In one study, endometrial cancer risk was reduced 39 % (95 % CI, 0.43–0.87) among women with the highest level of lifetime, combined, occupational and recreational activity (≥ 91.9 MET-hours/week) when compared to women with the least activity; moderate intensity lifetime activity alone also resulted in a substantial risk reduction [37]. Activity performed at younger and older adult ages produced similar risk reductions. Further, the inverse associations were strongest in obese and overweight women. Arem et al. also observed that moderate-intensity to vigorous-intensity sports/recreational physical activity was associated with a 34 % reduction in endometrial cancer risk (95% CI, 0.50–0.87) comparing active to inactive women (≥ 7.5 MET-hours/week versus 0 MET-hours/week); however, in contrast with the John et al. study [37], the associations were stronger among women with BMI < 25 [38]. Further, risk was greater among women sitting more than 8 hours/day than among women sitting less than 4 hours/day (OR=1.52, 95 % CI, 1.07–2.16).

Prostate Cancer—The evidence for an association between physical activity and prostate cancer has been classified as probable [2]. In a 2002 review of the literature, Friedenreich and Orenstein suggested that prostate cancer risk is reduced 10–30 % when comparing the most active men to the least active men [4]. An update to this review, based on 22 additional studies, indicates that the majority of recent research studies observed protective effects [39]. Leitzmann and Rohrmann added that the associations with reduced risk may be most apparent for fatal prostate cancer [40] A current systematic review and meta-analysis, including 19 cohort and 24 case-control studies, agrees [41•]. A pooled 19 % reduction in risk (95% CI, 0.73–0.91) was observed for occupational physical activity, and a 5 % reduction (95 % CI, 0.89–1.00) was observed for recreational physical activity, comparing the most physically active men to the least active. An issue that somewhat reduces our confidence in these estimates is that considerable heterogeneity between studies was observed. Further analysis of this compilation of studies suggested that only physical activity performed between the ages of 20 and 65 years was associated with prostate cancer risk [41•].

Lung Cancer—Physical activity may reduce lung cancer risk 30–40 % [4], but the literature is not convincing, as one cannot ignore potential residual confounding or effect modification due to smoking. Recent studies have attempted to address this issue by estimating risk within subgroups defined by smoking status. A recent review suggests an inverse relationship between heavy lifetime physical activity and lung cancer in former and current smokers that is consistent across all histologies, but is not observed not among those who have never smoked [6•]. A small case-control study of current and former smokers enrolled in the Cologne Smoking Study came to a similar conclusion, observing a lower risk of lung cancer among participants who were physically active compared to those who were not (OR = 0.53, 95 % CI, 0.29–0.97) [42]. Due to sex differences in lung cancer pathology, risk factors and prognosis, current research has also begun to investigate the association for men and women separately [43]. The recent literature consists of small case-control studies [44] that suffer from an inability to examine risk in subgroups by histology, smoking status or sex (reduced statistical power), and a survival bias in that rapidly fatal cases or those who are too ill to be interviewed are excluded from the study population.

Ovarian Cancer—Existing literature on risk of ovarian cancer in relation to physical activity is inconclusive [2]. A previous meta-analysis of 12 studies observed a 21 % reduction in ovarian cancer risk (95 % CI, 0.70–0.85) for case-control studies and a 19 % reduction in risk (95 % CI, 0.57–1.17) in cohort studies, when comparing the women who performed the most recreational physical activity to those performing the least amount [45]. Three additional studies showed no association [46–48], and the most recent study observed

a nonsignificant 10–20 % reduction in ovarian cancer risk for those who engaged in one or more hours/week of recreational aerobic activity [49].

Renal Cell Carcinoma—Physical activity has been studied in relation to renal cell carcinoma, in part because of the known deleterious effects of high body mass index and hypertension on the risk of renal cell cancer; however, no association has been established. A review of genitourinary cancers observed significant protective effects in 8 of 15 studies of physical activity in relation to renal cell carcinoma, with an average 8 % reduction in risk comparing individuals with the highest level of physical activity to those with the lowest level of activity [50•]. Reductions in risk were greater for recreational than for other forms of activity and for activity performed later in life.

Pancreatic Cancer—A meta-analysis of 28 studies of pancreas cancer showed total lifetime physical activity and occupational activity were associated with reduced risk [51]. Non-significant reductions in risk were observed for recreational physical activity and transportation (walking and cycling as a form of commuting). Significant heterogeneity was present across the studies, making it difficult to find a definitive answer. An analysis of a prospective study conducted in the Netherlands indicated that risk of pancreatic cancer was reduced 20 % (95 % CI, 0.64–0.99) among those who ever versus never participated in a sports activity [52]. Pancreatic cancer was not associated with physical activity among individuals whose past participation in sports activity was < 2 hours/week (versus those with no activity (HR=1.18, 95 % CI, 0.78–1.79), whereas risk of pancreatic cancer was reduced among those whose participation in sports activity ranged from 2 to < 4 hours/week (HR=0.67, 95 % CI, 0.47–0.96) or was ≥ 4 hours/week (HR=0.76, 95 % CI, 0.57–1.00; *P-trend*=0.05) [52]. No associations were noted for other recreational activities or occupational activity.

Non-Hodgkin's Lymphoma (NHL)—Recently, three studies have investigated the association between NHL and physical activity. The Women's Health Initiative (WHI) combined clinical trial and observational cohort study observed statistically non-significant positive associations between total recreational physical activity (MET-hours/week), as well as hours of moderate or strenuous recreational physical activity per week, and risk of NHL; however, no specific subtype associations were observed [53]. The European Prospective Investigation into Cancer and Nutrition (EPIC) found no evidence that total physical activity influenced the risk of NHL or B-cell NHL, overall or by subtype, for either men or for women [54]. Similarly, the American Cancer Society Cancer Prevention Study-II Cohort observed no association [55]. However, women who reported sitting at least six hours/day (versus those reporting sitting for fewer than 3 hours/day) had increased risk of multiple myeloma (HR = 2.40, 95 % CI, 1.45–3.97).

Other Cancer Sites Survival

Evidence that physical activity reduces cancer patients' mortality is beginning to accumulate for prostate and lung cancers. Results of one study indicate that post-diagnosis physical activity is associated with a 46–49 % reduction in all-cause mortality among prostate cancer survivors and a 61 % reduction in prostate cancer-specific mortality [56]. Further, among prostate cancer patients, Richman et al. found those who engaged in at least 3 hours of brisk walking per week had the lowest risk of disease progression [57]. The latest lung cancer literature has focused on increasing cardiorespiratory fitness [58]. Sui et al. observed an inverse association between cardiorespiratory fitness and lung cancer-specific mortality among current and former smoking men, and a 12-fold increase in risk of death among current smokers with low cardiorespiratory fitness level [58]. Moorman et al. observed modest reductions in ovarian cancer mortality among non-obese women who reported

engaging in at least 2 hours of recreational physical activity per week one year prior to cancer diagnosis [49].

Conclusion

The evidence of a beneficial effect of physical activity on cancer risk is accumulating rapidly and can be classified as “convincing” for colon and breast cancer and “probable” or “possible” for several other cancer sites. To increase our understanding of these associations, it will be necessary to conduct studies that are optimally designed, collect detailed lifetime histories of physical activity, and examine the effects across different population subgroups. By considering the potential, underlying biological mechanisms that are operative, it should be possible to refine study designs, questionnaires, and biomarker measures to enhance our understanding of the causal pathways that define the relationships between physical activity and cancer incidence, and to make our public health recommendations regarding physical activity more specific. Although it is clear that recommendations for appropriate changes in physical activity levels are important public health messages, we still have no exact physical activity prescriptions to give the public generally for all cancers and specifically for individual cancers. Further, we still need to be able to address the following questions: What are the ages when physical activity provides its greatest benefit? What types of activity will provide the greatest protection against cancer or enhance survival? What activity patterns (intensity, frequency, duration of activity) are optimal? Can enhancements of the built environment facilitate participation in physical activity?

Acknowledgments

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