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The effects of physical activity on cancer prevention, treatment and prognosis: A review of the literature

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ABSTRACT

Introduction: The World Health Organization has reported that approximately 35% of cancer-related deaths are attributed to modifiable risk factors. Among the most important risk factors amenable to modification are obesity and lack of physical activity. The purpose of this article is to review the current evidence of the benefits of physical activity in various types of cancer.
Methods: A PubMed search for the key words “physical activity and cancer” as well as “exercise and cancer” was used to identify all indexed publications on this topic for potential utilization in this review. One MET was defined as the amount of oxygen consumed while a person is sitting quietly and is about 3.5 mL O2/kg body weight/min. MET represents the ratio of the working metabolic rate to the resting metabolic rate.
Results: Routine physical activity was found to be associated with a reduced incidence of several of the most common malignancies, including colon, breast, lung, and endometrial cancer as well as many others. Physical activity also appears to reduce all-cause mortality and cancer-related mortality among patients with breast and colon cancer, and may improve the functional status and quality of life for these patients during cancer therapy.
Conclusions: The benefits of physical activity in the prevention and progression of cancer patients are multiple. However, the strength of the available evidence is limited by the observational nature of most studies. Given the probable improvement in prevention, mortality, and quality of life with structured physical activity in different malignancies, it is important that healthcare providers discuss physical activity programs with their cancer patients. Larger randomized trials are recommended.

1. Introduction

Cancer is an important cause of mortality worldwide.[1] In addition to the various therapies available, it is important to also focus on the role of modifiable risk factors in cancer prevention and prognosis. According to the World Health Organization, approximately 35% of cancer-related deaths can be attributed to these modifiable risk factors, among which obesity and lack of physical activity (PA) play a prominent role.[2] Several mechanisms have been proposed for the beneficial effects of PA, including decreased levels of reactive oxygen species, enhancement of immune function, decreased levels of inflammation, and improved insulin sensitivity.[3–5] Moderate physical activity (PA) also induces gene expression of anti-oxidant enzymes such as superoxide dismutase, catalase, and glutathione peroxidase, which protect against oxidative DNA damage.[6,7] Furthermore, PA changes the metabolic profile of estrogens leading to reduced hormonal activity and increased anti-proliferative properties in breast cancer patients.[8]

Although, PA has been associated with improved outcomes in cancer patients, it is frequently under-emphasized by physicians. As a complement to current practices in cancer prevention through screening, PA is becoming an increasingly important strategy for modifying cancer risk, as well as, reducing pre- and post-diagnosis morbidity and mortality. The purpose of this article is to review the current literature outlining the benefits of PA in the most common

Abbreviations: CI, confidence intervals; CRC, colorectal cancer; HR, hazard ratio; MET, metabolic equivalents; NSCLC, non-squamous cell lung cancer; PA, physical activity; RR, relative risk; VO2 max, peak oxygen consumption

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forms of cancer with an emphasis on the evaluation of its effects in different stages of the disease process.

2. Methods

A PubMed search for the key words "physical activity and cancer" as well as "exercise and cancer" was used to identify all indexed publications on this topic for potential utilization in this review. One MET was defined as the amount of oxygen consumed while a person is sitting quietly and is about 3.5 mL O2/kg body weight/min. MET represents the ratio of the working metabolic rate to the resting metabolic rate.

3. Results

3.1. Colorectal cancer

3.1.1. Physical activity and primary prevention

Lack of PA is a well-known risk factor for colorectal cancer (CRC).[1] A meta-analysis of 52 studies from 1984 to 2008, which included 24 case-control studies and 28 cohort studies, demonstrated that PA reduced the risk of CRC in men (RR = 0.76; 95% CI: 0.71 – 0.82 and women (RR = 0.79; 95% CI: 0.71 – 0.88) and concluded that as much as 24% of the overall risk of CRC can be attenuated by engaging in either occupational or leisure-time PA.[9] Similar results were observed in a meta-analysis of 174 studies that included 19 studies involving colon cancer, which showed that increasing levels of PA were associated with a decreased risk of developing CRC.[10] It demonstrated that patients who engaged in PA of 600–3999 MET minutes/week, 4000–7999 MET minutes/week, or ≥8000 MET minutes/week had 10%, 17%, and 21% reductions respectively when compared with less active individuals (< 600 MET minutes/week of total PA).

3.1.2. Physical activity and colorectal cancer prognosis

The benefits of PA have also been demonstrated in patients diagnosed with CRC. A meta-analysis of 11 studies, which included 17295 patients with a follow-up period ranging from 3.8 to 11..8–11.9 years, demonstrated that patients who were more active prior to their initial diagnosis of CRC had lower overall and cancer-specific mortality (RR = 0.81; 95% CI: 0.72 – 0.91 and RR = 0.79; 95% CI: 0.71 – 0.89, respectively).[11] Furthermore, patients who remained physically active after the initial diagnosis also demonstrated lower CRC-specific and overall mortality (RR = 0.77; 95% CI: 0.63 – 0.94 and (RR = 0.71; 95% CI: 0.63 – 0.81, respectively). Another meta-analysis of 7 studies from 2006 to 2013, with 8056 participants, confirmed that higher levels (> 17 MET-hours/week) of PA before diagnosis was associated with a higher cancer-specific survival (HR = 0.75; 95% CI: 0.62 – 0.91) and overall survival (HR = 0.74; 95% CI: 0.62 – 0.89).[12] The benefits were also noted if PA was started after a diagnosis of CRC with an increase in cancer-specific survival (HR = 0.61; 95% CI: 0.44 – 0.86) and overall survival (HR = 0.62; 95% CI: 0.54 – 0.71). Finally, a study by Meyerhardt et al, reported the benefits of PA in a cohort of 573 females who were sedentary before the diagnosis of non-metastatic CRC.[13] They noted that women who engaged in at least 18 MET-hours per week of PA after diagnosis compared with less than 3 MET-hours per week had significant reductions in cancer-specific mortality (HR = 0.39; 95% CI: 0.18 – 0.82, p = 0.008), and overall mortality (HR = 0.39; 95% CI: 0.18 – 0.82, p = 0.003). Also, in women that were active before the diagnosis, increasing the levels of PA led to lower cancer-specific mortality (HR = 0.48; 95% CI: 0.24 – 0.97) and overall mortality (HR = 0.51; 95% CI: 0.30 – 0.85). Other benefits of PA among CRC patients include a reduction of physical fatigue among those receiving chemotherapy and an improved quality of life in stage II CRC.[14,15]

3.2. Breast cancer

3.2.1. Physical activity and primary prevention

A review of 34 case-control and 28 cohort studies prior to September 2007 evaluated the association between activity and the risk of breast cancer, as well as its effect in different population subgroups.[16] An average of 25–30% risk reduction was observed with increased PA in 47 (76%) of the 62 studies, which was noted to be a dose-response effect in 28 of 33 studies. Stronger decreases in risk were observed for recreational activity, vigorous activity, lifetime or later life activity, among postmenopausal women, women with normal body mass index, non-white racial groups, those with hormone receptor negative tumors, women without a family history of breast cancer and parous women. Additionally, a study that included 1195 breast cancer patients and 2012 control participants in the population-based Women's Contraceptive and Reproductive Experiences Study, measured several biomarkers which showed that lifetime recreational PA was inversely associated with risk for the HER2-negative subtype of breast cancer (p ≤ 0.04).[17] The risk of HER2-negative breast cancer decreased with increased MET-hours/weeks of recreational PA (at least 15.2 annual MET hour/week) in the pre or postmenopausal period examined, p = 0.04.

3.2.2. Physical activity and breast cancer prognosis

Data from three female US breast cancer survivor cohorts from the After Breast Cancer Pooling Project (n = 9513) showed that low levels of PA (MET hours/week < 1.5 vs ≥1.5) was associated with a 22% increased risk of breast cancer mortality in breast cancer survivors (HR = 1.22, 95% CI: 1.05–1.42).[18] Moreover, breast cancer survivors who increased their PA, by any level from pre-diagnosis to post-diagnosis, showed a decreased total mortality risk (RR = 0.61; 95% CI: 0.46 – 0.80) compared with those who did not change their PA level after diagnosis, or remained sedentary. Furthermore, a systematic review and meta-analysis of 16 studies that compared the highest versus lowest levels of pre-diagnosis PA among breast cancer survivors showed a 23% reduction in both total (RR = 0.77; 95% CI: 0.69 – 0.88) and breast cancer-specific mortality (RR = 0.77; 95% CI: 0.66 – 0.90).[19] For post-diagnosis PA, the risks of total and breast cancer-specific mortality were reduced by 48% (RR = 0.52; 95% CI: 0.42 – 0.64) and 28% (RR = 0.72; 95% CI: 0.60 – 0.85), respectively. It was shown that for each 5, 10, or 15 MET/hour/week increase in pre-diagnosis PA, there was a 7% (95% CI: 2–12%), 13% (95% CI: 4–21%), and 19% (95% CI: 6–30%) relative risk reduction in total mortality among breast cancer survivors, respectively. Additionally, a linear response curve was observed between the levels of pre-diagnosis PA and the recurrence of estrogen/progesterone negative (ER-/PR-) breast cancer cases (HR = 0.53; 95% CI: 0.24–1.16, p = 0.033).[20] Finally, aerobic and resistance PA was shown to improve cardiorespiratory fitness measured as peak oxygen consumption (VO2 max), muscle strength, and percent body fat (p ≤ 0.001, for all) in a randomized study of early breast cancer patients.[21]

In addition to improved biologic effects, PA leads to psychological benefits in breast cancer patients. Almost 50% of women experience distress, depression, or anxiety after a diagnosis of breast cancer.[22] Saxton et al., randomized 85 women with recent treatment for breast cancer to a 6-month PA and hypocaloric healthy eating program plus usual care or usual care alone.[23] At 6-month follow-up, patients in the lifestyle intervention group exhibited a significant reduction in depressive symptoms when assessed by the Beck Depression Inventory Score (mean decrease: -3.12 points; 95% CI: -1.03 to -5.26 points, p = 0.004).

3.3. Prostate cancer

3.3.1. Physical activity and primary prevention

The data regarding the relationship between PA and development of prostate cancer appear to be equivocal. A review of 83 analyses spanning the years of 1996–2016, reported 7 studies which showed an increased incidence of prostate cancer with PA, 31 studies with no clear relationship, 24 studies with a trend towards diminished risk, and 21 studies with a significant risk reduction of up to 30%.[24] A benefit with PA was noted in the Health Professionals Follow-up Study, a prospective cohort study of 47,620 US male health professionals followed for 14 years. This study showed that men over 65 years of age who underwent the highest category of vigorous activity (≥29 vs 0 MET-hours per week) had a lower risk of developing advanced and fatal prostate cancer (RR = 0.33; 95% CI: 0.17 – 0.62) and (RR = 0.26; 95% CI: 0.11 – 0.66), respectively.[25] However, no associations were observed in men younger than 65 years of age. These findings are in contrast with a meta-analysis of 12 prospective studies, that included 1.44 million participants which found a slightly increased risk of prostate cancer with leisure time PA (HR = 1.05; 95% CI: 1.03–1.08).[26]

3.3.2. Physical activity and prostate cancer prognosis

In patients diagnosed with non-metastatic prostate cancer, a case-control study that evaluated 2705 men from 1990 to 2008, demonstrated that men engaging in ≥ 3 h per week of vigorous activity (activities with a MET value of ≥6/hour such as biking, tennis, jogging, or swimming) vs less than 1 h had a 49% reduction in all-cause mortality (HR = 0.51; 95% CI: 0.36 – 0.72) and a 61% lower risk of prostate cancer-specific mortality (HR = 0.39; 95% CI: 0.18 – 0.84).[27] Another prospective study which included 1455 men with localized prostate cancer showed that men who walked briskly for ≥3 h per week had a 57% lower risk of cancer progression than men who walked at low-intensity pace for < 3 h per week (HR = 0.43; 95% CI: 0.21 – 0.91, p = 0.03).[28] A third prospective study of 830 patients with stage II-IV prostate cancer showed that post-diagnosis higher total activity (> 119 vs ≤ 42 MET-hours/week per year) was associated with lower all-cause mortality (HR = 0.58; 95% CI: 0.42–0.79, $p < 0.01$).[29] In this study, recreational PA (> 26 vs ≤4 MET-hours/week/year) was associated with lower prostate cancer-specific mortality (HR = 0.56; 95% CI: 0.35–0.90, p = 0.01). Moreover, post-diagnosis PA has been associated with better mental and physical quality of life among prostate cancer survivors.[30]

There is less evidence on the effects of PA in patients with stage IV metastatic disease. One cohort study that evaluated 55 prostate cancer patients with bone metastases showed that men who met the current aerobic PA guidelines for cancer survivors (≥150 min of moderate intensity or ≥75 min of vigorous PA per week or an equivalent combination) had better physical and mental health outcomes as well as higher physical functioning and general health scores as measure by the SF-36 questionnaire when compared with those who did not meet aerobic PA guidelines.[31]

3.4. Lung cancer

3.4.1. Benefits of physical activity on lung cancer prevention, quality of life, and prognosis

Several studies have demonstrated up to a 25% reduced risk of lung cancer with higher levels of PA.[26,32] A cohort study that involved 13,905 men free of cancer showed that over a follow-up period of 15 years, increasing levels of PA (4200–8399, 8400–12599 and > or = 12,600 kJ/week of estimated energy expenditure) were associated with a decreased risk of lung cancer (RR = 0.87; 95% CI: 0.64–1.18), (RR = 0.76; 95% CI: 0.52–1.11), and (RR = 0.61; 95% CI: 0.41 – 0.89), respectively (p = 0.0008).[32] Improvements in symptom status, quality of life, and exercise capacity with PA have been noted in patients with non-small cell lung cancer.[33,34] It is believed that these benefits are directly related to the physical improvements caused by PA, including an increase in lung volume and an improvement in oxygen uptake.[35] From a psychological standpoint, lung cancer patients have an increased prevalence of anxiety and depression. PA, including home based regimens, is associated with improved emotional well-being and a decrease in anxiety and depression levels.[35,36]

The data evaluating the effects of PA in patients with metastatic lung cancer are limited. However, a study involving 40 patients with advanced non-small cell lung cancer demonstrated that those who were compliant and able to do PA 5 days per week while in a rehabilitation facility, and 3 times per week during the outpatient setting for a total of 8 weeks, had an improvement in upper and lower extremity strength as well as increase in 6 min walk distance (28 m, $p < 0.01$).[41] In another study of 118 inoperable stage IV NSCLC patients, those who performed PA regularly and had a 6 min walk distance > 450 m had a lower all-cause mortality at a median follow-up of 27 months (HR = 0.48; 95% CI: 0.24 – 0.93) compared with those who walked less than 358.5 m.[37] Median survival was also higher for those who performed > 9 MET-hours/week of PA.

3.4.2. Effects of pre-operative physical activity on outcomes of lung cancer surgery

Pre-operative PA programs have shown mixed results in terms of improving functional capacity or reducing post-operative complications.[35] Several reports have shown benefits associated with pre-operative PA including better exercise capacity, increased quality of life, and a lower hospital length of stay with fewer post-operative complications.[37–39] A 2013 Cochrane review demonstrated greater exercise capacity, measured by the 6 min walk distance in physically active patients that underwent lung resection of NSCLC versus sedentary patients (mean difference + 50.4 m; 95% CI: 15.4–85.2 m).[40] However, a randomized controlled trial involving 151 patients with operable NSCLC showed that patients who underwent supervised high-intensity interval training for median 25 days before surgery did not have a lower rate of death or in-hospital postoperative complications (RR = 0.70; 95% CI: 0.48–1.02, p = 0.08) when compared with the usual care group.[41]

3.5. Endometrial cancer

3.5.1. Physical activity and primary prevention

A meta-analysis of 9 prospective studies with 3463 patients demonstrated that recreational activity was associated with 27% (pooled RR = 0.73, 95% CI: 0.58 – 0.93) reduction in endometrial cancer, while occupational activity was associated with a 21% (RR = 0.79, 95% CI: 0.71 – 0.88) reduction.[42] Data from a systematic review based on 20 observational studies (7 cohort and 13 case-control studies) published between 1993 and 2006 suggested that PA is associated with a 20%–40% decreased risk of endometrial cancer.[43] A meta-analysis evaluating the dose response of PA in epidemiological studies demonstrated that an increase in leisure-time PA by 3 MET-hours/week was associated with a 2% lower risk of endometrial cancer (RR = 0.98; 95% CI: 0.95–1.00, p = 0.02).[44] The data, albeit limited, shows that PA may decrease the endometrial cancer risk

3.6. Other malignancies

Although overall scarce, the evidence suggesting a potential role for leisure time PA in the reduction of less common malignancies, has been previously reported.[26] For instance, reductions in the incidence of gastroesophageal, liver, renal, and hematologic cancers have been observed. A meta-analysis of 24 studies with over 15,000 patients showed that at higher levels of PA there were reductions of 21% (RR = 0.79, 95% CI: 0.66 – 0.94), 17% (RR = 0.83, 95% CI: 0.69 – 0.99), and 28% (RR = 0.72, 95% CI: 0.62 – 0.84) in the incidence of esophageal, gastric cardia, and gastric non-cardia adenocarcinomas, respectively.[45] However, more data is needed before firm conclusion can be made concerning the effect of PA on the primary prevention and prognosis of these malignancies.

Table 1
Effects of Physical Activity on Malignancy.

Malignancy	Effects of Physical Activity
Colorectal	• Reduces incidence of colorectal cancer among men and women.[9,10] • Decreases mortality of colorectal cancer when performed before or after a diagnosis.[11–13] • Reduces fatigue aong patients receiving chemotherapy and improves quality of life.[14,15]
Breast	• Decreases risk of breast cancer.[16,17] • Any level of physical activity before or after the diagnosis significantly decreases the relative risk of total and breast cancer-specific mortality.[18,19] • There appears to be a linear dose response curve between volume of physical activity and cancer recurrence.[20]
Prostate	• Mixed findings regarding the relationship between physical activity and incidence of prostate cancer.[24] • Few studies have observed a higher incidence of prostate cancer among patients with higher levels of physical activity.[26] • Post-diagnosis physical activity was associated2 with lower prostate cancer-specific mortality as well as better mental and physical quality of life.[27,29,30]
Lung	• Higher levels of physical activity appear to reduce risk.[32] • Preoperative physical activity may confer benefits to patients undergoing lung cancer surgery.[37–40]
Endometrial	• May decrease endometrial cancer risk.[42–44] • The benefits of physical activity on survival after endometrial cancer are unknown.

4. Discussion

The exact biologic connection between cancer risk and physical activity has not been established. However, some of the postulated mechanisms include changes in endogenous sexual and metabolic hormone levels and growth factors.[46] Adiposity and obesity also appear to play a role in the mechanistic process. Weight loss through diet and PA leads not only to a significant decrease in the availability of certain sex hormones, but also to a decrease in pro-inflammatory markers and insulin levels, all of which are known to promote and maintain a pro-carcinogenic state.[47] Given that various factors have been reported to reduce the risk of malignancy through PA, it is likely that the mechanistic link between PA and cancer risk is multifactorial.

Due to the increasing number of individuals diagnosed with cancer, it is important to understand the role of PA in cancer prevention and therapy (Table 1). The benefits of PA in cancer patients are multifaceted, as they have been observed within the primary prevention of certain malignancies, and in diverse clinical outcomes at the time of diagnosis and throughout their treatment phase. However, the strength of the available evidence is hampered by the observational nature of the majority of the studies, and the overall lack of standardization in the methods used for assessing PA level. The current literature is further weakened by the fact that most studies did not evaluate the effect of PA in different epidemiologic subgroups, as the majority of them were carried out in Western countries and included a predominantly white population. Hence, the results may not be applicable to other ethnic groups. However, the majority of studies selected adjusted for other important confounding factors, such as age, smoking, race, education level, energy intake, BMI, occupational exposure, alcohol, and social class. Given the overwhelming body of literature demonstrating the benefits of PA on cancer prevention, mortality, and quality of life, the American Cancer Society recommends that adults obtain at least 150 min of moderate intensity or 75 min of vigorous intensity activity on a weekly basis to lower cancer risk, in combination with a diet based on vegetables, fruits, and whole grains with minimal red meat, processed foods, and refined grains.[48] Because each cancer patient or survivor have different levels of tolerance to PA, establishing a personalized approach to each patient is important in increasing the level of adherence and desire in the patient to incorporate greater PA into their daily life.[48,49]

Several areas need further analysis in order to define more precisely the PA recommendations in cancer patients, including what type of PA, the level of intensity and the frequency needed to obtain optimal benefit. Moreover, the literature in patients with metastatic disease is tenuous, making it dangerous to draw any concrete conclusions in such individuals. For all the aforementioned reasons and considering the growing population suffering from cancer, it is imperative that larger, randomized studies with pre-specified measures are accordingly designed and developed promptly.

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Conflict of interest

None.

References

1. Jemal A, Bray F, Center MM, et al. Global cancer statistics. *CA Cancer J Clin.* 2011;61:69–90.
2. Danaei G, Vander Hoorn S, Lopez AD, et al. Causes of cancer in the world: Comparative risk assessment of nine behavioral and environmental risk factors. *Lancet.* 2005;366:1784–1793.
3. Marzatico F, Pansarasa O, Bertorelli L, et al. Blood free radical antioxidant enzymes and lipid peroxides following long-distance and lactacidemic performances in highly trained aerobic and sprint athletes. *J Sports Med Phys Fitness.* 1997;37:235–239.
4. Bradley RL, Jeon JY, Liu FF, et al. Voluntary exercise improves insulin sensitivity and adipose tissue inflammation in diet-induced obese mice. *Am J Physiol Endocrinol Metab.* 2008;295:586–594.
5. Pedersen L, Idorn M, Olofsson GH, et al. Voluntary running suppresses tumor growth through epinephrine and IL-6 dependent NK cell mobilization and redistribution. *Cell Metab.* 2016;23:554–562.
6. Selamoglu S, Turgay F, Kayatekin BM, et al. Aerobic and anaerobic training effects on the antioxidant enzymes of the blood. *Act Physiol Hung.* 2000;87:267–273.
7. Fisher-Wellman K, Bloomer RJ. Acute exercise and oxidative stress: a 30 year history. *Dyn Med.* 2009;8:1–11.
8. Zhu BT, Conney AH. Functional role of estrogen metabolism in target cells: Review and perspectives. *Carcinogenesis.* 1998;19:1–27.
9. Wolin KY, Yan Y, Colditz GA, Lee IM. Physical activity and colon cancer prevention: a meta-analysis. *Br J Cancer.* 2009;100:611–616.
10. Kyu HH, Bachman VF, Alexander LT, et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and stroke events: Review and dose-response meta-analysis for the global burden of disease study 2013. *BMJ.* 2016:354–357.
11. Wu W, Guo F, Ye J, et al. Pre- and post-diagnosis physical activity is associated with a survival benefit of colorectal cancer patients: a systematic review and meta-analysis. *Oncotarget.* 2016;7:52095–52103.
12. Gaetan Des G, Bernard U, Thierry B, et al. Impact of physical activity on cancer-specific and overall survival with colorectal cancer. *Gastroenterol Res Pract.* 2013;2013:1–6.
13. Meyerhardt JA, Giovannucci EL, Holmes MD, et al. Physical activity and survival after colorectal cancer diagnosis. *J Clin Oncol.* 2006;24:3527–3534.
14. Van Vulpen JK, Velthuis MJ, Steins Bisschop CN, et al. Effects of an exercise program in colon cancer patients undergoing chemotherapy. *Med Sci Sports Exerc.* 2016;48:767–775.
15. Lewis C, Xun P, He K. Physical activity in relation to quality of life in newly diagnosed colon cancer patients: A 24 month follow up. *Qual Life Res.* 2014;23:2235–2246.
16. Friedenreich CM, Cust AE. Physical activity and breast cancer risk: Impact of timing, type and dose of activity and population subgroup effects. *Br J Sports Med.* 2008;42:636–647.
17. Ma H, Xu X, Ursin G, et al. Reduced risk of breast cancer associated with recreational physical activity varies by HER2 status. *Cancer Med.* 2015;4:1122–1135.
18. Nelson SH, Marinac CR, Patterson RE, et al. Impact of very low physical activity, BMI, and comorbidities on mortality among breast cancer survivors. *Breast Cancer Res Treat.* 2016;155:551–557.
19. Schmid D, Leitzmann MF. Association between physical activity and mortality among breast cancer and colorectal cancer survivors: a systematic review and meta-analysis. *Ann Oncol.* 2014;25:1293–1311.

20. Schmidt M, Chang-Claude J, Vrieling A, et al. Association of pre-diagnosis physical activity with recurrence and mortality among women with breast cancer. *Int J Cancer.* 2013;133:1431–1440.
21. Casla S, López-Tarruella S, Jerez Y, et al. Supervised physical exercise improves VO2max, quality of life, and health in early stage breast cancer patients: a randomized controlled trial. *Breast Cancer Res Treat.* 2015;153:371–382.
22. Burgess C, Cornelius V, Love S, et al. Depression and anxiety in women with early breast cancer: Five year observational cohort study. *BMJ.* 2005;330:702–705.
23. Saxton JM, Scott EJ, Daley AJ, et al. Effects of an exercise and hypocaloric healthy eating intervention on indices of psychological health status, hypothalamic-pituitary-adrenal axis regulation and immune function after early-stage breast cancer: a randomized control trial. *Breast Cancer Res.* 2014;16:R39.
24. Shephard RJ. Physical activity and prostate cancer: an updated review. *Sports Med.* 2016:1–19.
25. Giovannucci EL, Liu Y, Leitzmann MF, et al. A prospective study of physical activity and incident and fatal prostate cancer. *Arch Intern Med.* 2005;165:1005–1010.
26. Moore SC, Lee IM, Weiderpass E, et al. Association of leisure-time physical activity with risk of 26 types of cancer in 1.44 million adults. *JAMA Intern Med.* 2016;176:816–825.
27. Kenfield SA, Stampfer MJ, Giovannucci E, et al. Physical activity and survival after prostate cancer diagnosis in the health professionals follow-up study. *J Clin Oncol.* 2011;29:726–732.
28. Richman EL, Kenfield SA, Stampfer MJ, et al. Physical activity after diagnosis and risk of prostate cancer progression: data from the cancer of the prostate strategic urologic research endeavor. *Cancer Res.* 2011;71:3889–3895.
29. Friedenreich CM, Wang Q, Neilson HK, et al. Physical activity and survival after prostate cancer. *Eur Urol.* 2016;70:576–585.
30. Ferris MS, Kopciuk KA, Courneya KS, et al. Associations of post-diagnosis physical activity and change from pre-diagnosis physical activity with quality of life in prostate cancer survivors. *Cancer Epidemiol Biomarkers Prev.* 2016;26:1–9.
31. Zopf EM, Newton RU, Taaffe DR, et al. Associations between aerobic exercise levels and physical and mental health outcomes in m prostate cancer: a cross-sectional investigation. *Eur J Cancer Care.* 2016;70:586–587.
32. Lee IM, Sesso HD, Paffenbarger Jr RS. Physical activity and risk of lung cancer. *Int J Epidemiol.* 1999;28:620–625.
33. Rochester CL, Fairburn C, Crouch RH. Pulmonary rehabilitation for respiratory disorders other than chronic obstructive pulmonary disease. *Clin Chest Med.* 2014;35:369–389.
34. White J, Dixon S. Nurse led patient education programme for patients undergoing a lung resection for primary lung cancer. *J Thorac Dis.* 2015;7:131–137.
35. Bade BC, Thomas DD, Scott JB, et al. Increasing physical activity and exercise in lung cancer: reviewing safety, benefits, and application. *J Thorac Oncol.* 2015;6:861–871.
36. Chen HM, Tsai CM, Wu YC, et al. Randomized controlled trial on the effectiveness of home based walking exercise on anxiety, depression and cancer-related symptoms in patients with lung cancer. *Br J Cancer.* 2015;112:438–445.
37. Jones LW, Hornsby WE, Goetzinger A, et al. Prognostic significance of functional capacity and exercise behavior in patients with metastatic non-small cell lung cancer. *Lung Cancer.* 2012;76:248–252.
38. Singh F, Newton RU, Galvão DA, et al. A systematic review of pre-surgical exercise intervention studies with cancer patients. *Surg Oncol.* 2013;22:92–104.
39. Crandall K, Maguire R, Campbell A, et al. Exercise intervention for patients surgically treated for non-small cell lung cancer (NSCLC): a systematic review. *Surg Oncol.* 2014;23:17–30.
40. Cavalheri V, Tahirah F, Nonoyama M, et al. Exercise training undertaken by people within 12 months of lung resection for non-small cell lung cancer. *Cochrane Database Syst Rev.* 2013;7:1–37.
41. Licker M, Karenovics W, Diaper J, et al. Short-term preoperative high-intensity interval training in patients awaiting lung cancer surgery: a randomized controlled trial. *J Thorac Oncol.* 2017;12:323–333.
42. Moore SC, Gierach GL, Schatzkin A, et al. Physical activity, sedentary behavior, and the prevention of endometrial cancer. *Br J Cancer.* 2010;108:933–938.
43. Voskuil DW, Monninkhof EM, Elias SC, et al. Task force physical activity and cancer. Physical activity and endometrial cancer risk, a systematic review of current evidence. *Cancer Epidemiol Biomarkers Prev.* 2007;16:639–648.
44. Keum N, Ju W, Lee DH, et al. Leisure time physical activity and endometrial cancer risk: dose-response meta-analysis of epidemiological studies. *Int J Cancer.* 2014;135:682–694.
45. Behrens G, Jochem C, Keimling M, et al. The association between physical activity and gastroesophageal cancer: Systematic review and meta-analysis. *Eur J Epidemiol.* 2014;29:151–170.
46. Friedenreich CM, Orenstein MR. Physical activity and cancer prevention: etiologic evidence and biological mechanisms. *J Nutr.* 2002;132(November 11 Suppl):3456S–3464S.
47. DeSantis CE, Lin CC, Mariotto AB, et al. Cancer treatment and survivorship statistics. *CA Cancer J Clin.* 2014;65:252–271.
48. Kushi LH, Doyle C, McCullough M, et al. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin.* 2012;62:30–67.
49. Campbell KL, Foster-Schubert KE, Alfano CM, et al. Reduced-calorie dietary weight loss, exercise, and sex hormones in postmenopausal women: randomized controlled trial. *J Clin Oncol.* 2012;30:2314–2316.