Interest in physical activity as a means for the primary prevention of cancer is increasing as the evidence for a protective effect is rapidly accumulating. Along with dietary intake and tobacco use, physical activity may be one of the main risk factors for cancer that can be modified through lifestyle/behavior change. Clear public health recommendations and health promotion campaigns have been established for diet (1) and tobacco (2) that would, if adopted, result in a clear decreased incidence of cancer worldwide. A similar focus is now being directed to the role of physical activity as a means for reducing risk for some of the major cancer sites. This report provides an updated review of the literature on physical activity and cancer for each of the main cancer sites, an overview of the hypothesized biological mechanisms that may be operative in the association between physical activity and cancer risk at these sites, a summary of the public health guidelines for physical activity for cancer prevention developed by health agencies worldwide and a brief description of how physical activity can influence all aspects of the cancer experience from prevention to palliation.

Review of evidence on physical activity and cancer prevention

Nearly 170 observational epidemiologic studies have examined the relation between physical activity and cancer prevention at specific cancer sites. Assessments of the evidence for reduced risk with increased physical activity at each site are examined here and are summarized in Table 1. The scientific evidence for the association between physical activity and cancer is categorized according to the definitions developed and used in the World Cancer Research Fund and American Institute for Cancer Research report on diet and cancer prevention (1). The categories used are “convincing,” “probable,” “possible” and “insufficient.”
Colon cancer. The most definitive epidemiologic evidence for an association between physical activity and cancer exists for colon cancer. Of the 51 studies conducted to date on colon and colorectal cancer (3–53), 43 (3.6–47) demonstrated a reduction in cancer risk among those who are most physically active male and female participants. The risk reduction averaged 40–50%, and up to 70% reductions were found in some studies when the highest and lowest activity levels were compared within each study. Increasing levels of activity were associated with a trend in decreasing risks of cancer in 25 (3.6–29) of 29 (3.5–33; 48–50) studies that examined whether a dose–response effect could be found. Despite varied and often crude physical activity assessment methods used in these studies, a very consistent risk reduction was found with the different designs and study populations. The effect was observed for both occupational and recreational activity and does not appear to be confounded by other risk factors for colon cancer, such as dietary intake or body mass index. Despite the strong association found for colon cancer, there is agreement across studies on the lack of an association between physical activity and rectal cancer.

Breast cancer. The evidence for an association between physical activity and breast cancer is neither as strong nor as consistent as that found for colon cancer but can nonetheless be classified as convincing, because >20 studies conducted worldwide have shown an association, and the risk reductions are considerable. Of 44 studies conducted thus far, 32 (35; 54–84) observed a reduction in breast cancer risk in women who were most physically active. Increased breast cancer risk was found with increased physical activity in only two studies (85,86) and the remaining studies found no association (3.87–95). Of the 32 studies that observed a decreased breast cancer risk, the reduction in risk was on average 30–40%. Evidence for a dose–response relation between increasing activity levels, however defined, and decreased breast cancer risk was found in 20 (54, 56–74) of 23 (54–76) studies that examined the trend. The inconsistent outcomes observed among studies can be attributed in part to methodological differences in assessing physical activity across these studies and in part to the fact that the relation between physical activity and breast cancer risk probably differs among subgroups of women, which has not been fully examined in previous research. In addition, the biological mechanisms for breast cancer are likely to be more complex than those for colon cancer, which may complicate the association and make it somewhat less clear to examine.

Prostate cancer. The evidence for an association between physical activity and prostate cancer is less consistent than that for either colon or breast cancer and can be classified only as probable. To date, 15 (5.26, 35.51, 52.96–105) of 30 studies have found a reduction in prostate cancer risk in men who were most physically active, with risk reductions averaging 10–30%. Two other studies found decreased risk only in subgroups of the population (106,107). No associations were found in nine (3.4; 30,108–113) studies, and increased risk was found in four (114–117) studies. Some particular methodological issues have uniquely influenced prostate cancer studies and may in part explain the inconsistencies found across these studies. For prostate cancer, high levels of activity may be needed to influence hormone levels that are potentially implicated in the etiology of this cancer (118). The majority of these studies did not have a sufficient number of study subjects who attained very high levels of activity. If a threshold effect exists, few of the studies conducted thus far would have been able to detect an association. Furthermore, most studies examined activity done later in life, closer to the time of the cancer diagnosis. However, physical activity performed early in life may be the most etiologically relevant for prostate carcinogenesis (118). A lack of understanding remains about the natural history of prostate cancer and hence the etiologic role of physical activity, including the biological mechanisms and relevant time periods in prostate carcinogenesis, are still unknown.

Endometrial cancer. There have been 13 (3.83,85,119–128) studies of endometrial cancer, of which 9 (83,119–126) have found evidence for decreased risk with increased levels of physical activity. The risk reductions have ranged quite widely in these studies from 0 to 90%, with an average reduction around 30–40%. Some evidence exists for a dose–response effect; six
(3,121–127) studies examined this trend, and of those, five (121–125) have found decreasing risks with increasing levels of activity. Given the strength of the association of endometrial cancer with breast cancer and the comparable etiologies, the possibility that physical activity might influence endometrial cancer etiology is considered fairly high. More research is needed to solidify the evidence; hence this site can be listed only as being possibly associated with physical activity.

**Lung cancer.** Physical activity as a risk factor has been examined in 11 studies of lung cancer (3,5,26,30,51,52,129–132), of which 8 (4,5,30,51,52,129–131) found a risk reduction. Because the reductions in risk have been around 30–40%, the evidence for this site can also be classified as being possibly associated with physical activity. The most important confounder for this site is smoking status, and appropriate control for this confounder was made in these studies.

**Other cancer sites.** Fewer studies have been conducted on the role of physical activity in reducing risk of cancer at other sites. Physical activity as a risk factor was examined in nine studies of testicular cancer (3,4,26,133–137), seven studies of ovarian cancer (3,83,85,138–141), six studies of renal cell (kidney) cancer (4,52,142–145), three studies of pancreatic cancer (4,146,147) and two studies each of thyroid cancer (4,148) and melanoma (4,149). These studies have provided some preliminary indications of the role of physical activity; however, the level of evidence is still too limited to make any statements regarding causal associations and must be classified as insufficient. Preliminary evidence suggests that physical activity may influence cancer risk at several of these sites, particularly the pancreas and thyroid, but results need to be corroborated before any conclusions can be made.

**Methodological considerations.**

**Assessment of physical activity.** To assess accurately the relation between physical activity and cancer risk, reliable, valid, and comprehensive measures of physical activity must be used. To date, there has been little standardization in the methods used for assessing physical activity in epidemiologic studies, and few methods have been appropriately tested for reliability and validity. The use of crude measures of physical activity has led to a large possibility of measurement error and difficulty in determining the true nature of the relation between physical activity and breast cancer risk.

For a complete analysis, all components of physical activity need to be assessed. These include type (physical activity is often thought of as recreational activity or exercise but moderate-to-high intensity occupational and household activities have also been implicated in reducing cancer risk and important differences may exist between resistance and endurance (aerobic activity), frequency (e.g., number of days per week), duration (e.g., number of hours per day), intensity [e.g., number of metabolic equivalents (150) or energy expended] and activity levels throughout the participant’s entire lifetime—information crucial for assessing the relevant times in life when physical activity influences the risk of developing cancer.

These parameters of physical activity have not been measured consistently in epidemiologic studies. Most studies have relied on recall surveys, with time frames ranging from 1 week to a lifetime. Many have focused on only one type of physical activity, such as recreational exercise, or have classified activity level by occupation. The level of detail captured on physical activity has ranged from quantitative histories that assess all types of activity—the frequency, duration and intensity of activity—over entire lifetimes (151) to a single global ques-

**Possible biological mechanisms.**

An understanding of the biological mechanisms operative in the association between physical activity and cancer risk is needed to understand more completely how changes in physical activity can influence cancer risk. Specifically, this understanding would allow more appropriate public health recommendations to be developed that would maximize the effectiveness of physical activity for cancer risk reduction because the exact type, dose and time periods in life when activity influences cancer risk at a physiological level would be understood.

The underlying mechanisms operative in the association between physical activity and cancer have not been established; however, several plausible biological mechanisms have been proposed (Table 2). These hypothesized mechanisms...
include changes in endogenous sexual and metabolic hormone levels (155,156) and growth factors (157), decreased obesity and central adiposity (152) and possibly changes in immune function (158).

Physical activity appears to lower levels of biologically available sex hormones, which could lead to decreased risk of hormone-related cancers, including cancers of the breast, endometrium, ovaries, prostate and testes. Increased lifetime exposure to endogenous estrogens through natural reproductive events (e.g., early menarche, late age at menopause, late exposure to endogenous estrogens through natural reproductive events) or through individual variation in estrogen levels is known to increase the risk of breast cancer in both premenopausal and postmenopausal women. Prostate cancer has been linked with increased levels of biologically available testosterone in men. Physical activity may affect risk of these hormone-related cancers not only by decreasing the endogenous production of estrogens and androgens but also by increasing amounts of circulating sex-hormone binding globulin, which binds to these sex hormones and reduces their ability to influence target tissues.

Other metabolic hormones and growth factors may also be reduced with increasing physical activity. Regular physical exercise significantly lowers insulin levels, which may be associated with decreased cancer risk (159). Exercise may also affect cancer risk through its effects on insulin-like growth factors (IGFs) (157), because high levels of circulating IGF-I have been associated with increased risk of colorectal, breast, prostate and lung cancers (160–163). There is mixed evidence from studies on the influence of exercise on IGF-I levels (164,165), although this effect may vary by population and type of activity. The evidence is more consistent that physical activity, decreased energy intake and decreased body weight have all been shown to increase levels of IGF binding protein-3, which binds to IGF in the blood and decreases its ability to affect potential cancer sites (157).

**Weight control**

Of the possible biological mechanisms mediating an association between physical activity and cancer prevention, weight control may be particularly important. Weight control and physical activity are very strongly associated through the concept of energy balance—whether an individual consumes and expends the same amount of energy. A positive energy balance results in increased weight and increased fat mass, or adiposity; a negative balance results in weight loss; and a balance results in the maintenance of a stable body weight. Energy intake comes solely through food consumption but

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1 Adapted from Friedenreich (154) with permission.

**TABLE 2**

<table>
<thead>
<tr>
<th>Cancer site</th>
<th>Possible mechanisms involved</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>Decreased gastrointestinal transit time</td>
<td>Physical activity increases gut motility and reduces mucosal exposure time to carcinogens.</td>
</tr>
<tr>
<td></td>
<td>Decreased ratio of prostaglandins</td>
<td>Strenuous exercise may increase prostaglandin (PG) F, which inhibits colonic cell proliferation and increases gut motility while not increasing PGE2, which affects colonic cell proliferation, opposite to the effect of PGF.</td>
</tr>
<tr>
<td></td>
<td>Lowered bile acid secretion or enhanced acid metabolism</td>
<td>Bile acid concentrations may be decreased in physically active (confounding by diet?) persons.</td>
</tr>
<tr>
<td>Breast</td>
<td>Decreased lifetime exposure to estrogen</td>
<td>Physical activity delays menarche, reduces the number of ovulatory cycles, and reduces ovarian estrogen production. It also reduces body fat and could reduce fat-produced estrogens. It increases the production of sex hormone-binding globulin, resulting in less biologically available estrogen.</td>
</tr>
<tr>
<td>Prostate</td>
<td>Reduced exposure to testosterone</td>
<td>Physical activity increases production of sex hormone-binding globulin, resulting in lower levels of free testosterone.</td>
</tr>
<tr>
<td>All cancers, especially breast, endometrial and ovarian</td>
<td>Decreased percent body fat</td>
<td>Obese women have increased infertility, which may increase breast cancer risk. Fat storage of carcinogens can occur in visceral fat, which can be released in overweight individuals.</td>
</tr>
<tr>
<td>All cancers</td>
<td>Genetic predisposition of habitually active people</td>
<td>Constitutional factors influence athletic selection or interest in physical activity and susceptibility to cancer.</td>
</tr>
<tr>
<td></td>
<td>Exercise-induced increase in antitumor immune defenses</td>
<td>Exercise may increase number and activity of macrophages, lymphokine-activated killer cells and their regulating cytokines; it may increase mitogen-induced lymphocyte proliferation.</td>
</tr>
<tr>
<td></td>
<td>Improved antioxidant defense systems</td>
<td>Strenuous exercise increases the production of free radicals, whereas chronic exercise improves free radical defenses by up-regulating both the activities of free scavenger enzymes and antioxidant levels.</td>
</tr>
<tr>
<td></td>
<td>Decreased circulating insulin and glucose</td>
<td>The extent of exercise-induced changes in antioxidant defenses is unknown.</td>
</tr>
<tr>
<td></td>
<td>Decreased insulin and insulin-like growth factors (IGFs)</td>
<td>Increased exercise may decrease levels of insulin and bioavailable IGF-I, both of which enhance division of normal cells and inhibit cell death.</td>
</tr>
</tbody>
</table>

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4 Abbreviation used: IGF, insulin-like growth factor.
### TABLE 3

**Public health recommendations on physical activity and cancer risk reduction**

- Physical activity recommendations should be included in primary prevention interventions for cancer prevention.
- All messages for physical activity should be in the context of reducing the risk of cancer rather than of preventing cancer.
- To reduce cancer risk, physical activity should comprise at least 30 to 45 minutes of moderate-to-vigorous activity on most days of the week.
- Examples of moderate and vigorous physical activities should be provided as part of messaging; these should include activities appropriate to various age, sex and culture groups.
- Messaging should recognize the variation in maximal cardiorespiratory capacity within the population. For example, because maximal capacity declines, on average, with increasing age, the upper end of the recommended activity level (i.e., 45 minutes of vigorous exercise) is in general more appropriate for youth, and the lower end (i.e., 30 minutes of moderate exercise) is more appropriate for those who have been sedentary should initially be less than for those who are already active.
- Physical activity messages can be linked to other risk reduction messages, such as maintaining a healthy body weight.
- Physical activity should be encouraged at all ages.
- Advocacy is required for policies and environmental supports for physical activity.
- A surveillance and measurement system should be implemented for tracking population levels of physical activity.

1 Reprinted from Marrett et al. (171) with permission.

Energy is expended in one of three ways: through the basal/resting metabolic rate, physical activity and the thermic effect of digesting food (166). The basal metabolic rate represents the energy expended to maintain normal body functions, including respiration, circulation, endocrine secretion, kidney filtration, etc. Physical activity refers to voluntary physical activities, such as walking, jogging or climbing stairs, in which energy is mainly expended through muscle action. The digestion, absorption and metabolism of food also represent significant energy expenditures. The amount of energy that is required depends in part on the composition of the food; dietary fats, for example, are more readily converted to body fat and require less energy to do so than do carbohydrates. Although the amount of energy expended through physical activity can be adjusted voluntarily, the energy expended through metabolism and through digestion of food is governed by a number of endogenous and exogenous factors, including metabolism, genetics and endocrine responses (167). Energy balance has become an important concept in exploring the etiology of a number of chronic diseases, including cancer, because of its close association with weight gain and overweight, conditions known to increase the risk of many chronic diseases. Epidemiologic studies have shown positive associations between various measures of overweight and adiposity and a variety of cancers. There is moderate-to-strong evidence for greater body weight being associated with increased risk of colon, kidney, esophagus, endometrium, thyroid and postmenopausal breast cancer (168). However, greater weight appears to protect against premenopausal breast cancer and lung cancer, although the latter association may be confounded by cigarette use. Abdominal fat (as opposed to fat accumulated on other parts of the body, such as the hips or buttocks) is particularly metabolically active (169) and may confer greater disease risk than fat deposited elsewhere (170).

One mechanism whereby physical activity may prevent cancer development is through a reduction in abdominal fat mass. Although both decrease in dietary intake and increase in physical activity are effective in decreasing body weight, physical activity appears in some studies to preferentially reduce intra-abdominal fat (170) and is more strongly associated with weight maintenance after a weight loss intervention. Another possible link among excess body weight, physical inactivity and cancer risk is through hormone metabolism. Both obesity and physical inactivity cause problems with insulin metabolism, which in turn leads to disease-inducing alterations in blood glucose, IGF-I, IGF-binding proteins, sex hormones and sex hormone–binding globulin.

Both physical activity and weight reduction are important risk factors for cancer, and although they are strongly linked, each appears to confer an independent benefit to reduce cancer risk. The International Agency for Research on Cancer has estimated that between one fourth and one third of cancer cases may be attributable to the combined effects of elevated body weight and inadequate physical activity (168).

### Summary of biological mechanisms

Other biological mechanisms for the association between physical activity and cancer risk have been proposed, and it is likely that multiple, interrelated actions are involved. However, the level of scientific evidence for any of these possible mechanisms is still minimal, and much further research is needed to determine which mechanisms are operative for each type of cancer.

### Public health recommendations for cancer prevention

On the basis of the existing evidence, public health organizations have issued physical activity guidelines for individuals, with the intention of reducing cancer rates in the general population. These organizations (including the American Cancer Society, U.S. Department of Health and Human Services, International Union against Cancer, World Cancer Research Fund and American Institute for Cancer Research, Harvard Center for Cancer Prevention, Canadian Cancer Society and Health Canada) have generally recommended a minimum of 30 min/d of moderate-to-vigorous intensity activity on 5 d/wk or more. Moderate-to-vigorous intensity activity is any physical activity that raises the heart rate or causes the individual to sweat. Examples include brisk walking, recreational sports and heavy housework or yard work.

The Workshop on Physical Activity and Cancer Prevention convened in March 2000 by Cancer Care Ontario (171) developed recommendations for practitioners and health professionals on appropriate ways and contexts in which to convey these physical activity guidelines to the general public. These recommendations are summarized in Table 3.

### Physical activity in other aspects of cancer

Although most attention has been focused on the efficacy of physical activity in cancer prevention, it must be emphasized that physical exercise may also be useful in improving other aspects of the cancer experience. Figure 1 provides a conceptual model for organizing research into the antecedents and consequences of physical exercise for cancer control. Framework PEACE (Physical Exercise Across the Cancer Experience) (172) (Fig. 1) highlights the need to examine physical exercise across each of six discrete time periods that...
demarcate the cancer experience and for each of eight general cancer control outcomes that may be amenable to physical exercise interventions. As shown at the bottom of the figure, research is already under way for several time periods and outcomes.

Conclusion

The evidence for a beneficial effect of physical activity on cancer incidence is accumulating rapidly and can be classified as “convincing” for colon and breast and “probable” for prostate. To increase our understanding of the possible etiologic role of physical activity in cancer etiology, it will be necessary to conduct more well-designed studies that include detailed, quantitative lifetime histories of physical activity and examine the effects across varied populations and subgroups of populations. More consideration of the underlying biological mechanisms that are operative is also necessary both to refine the scientific understanding of the causal pathways between activity and cancer incidence and to provide public health recommendations regarding physical activity and weight control as means for the primary prevention of cancer. Based on the current level of knowledge, general recommendations can be made for the public that are aligned with those developed for other major chronic diseases. When each cancer site has accumulated more specific dose information, more detailed recommendations for physical activity and cancer prevention can be formulated. Until then, sufficient evidence already exists to recommend that the general population try to achieve at least moderate intensity activity of a minimum of 30 min/d on 5 d/wk or more. For some cancer sites, the level of activity required may be vigorous and the duration of the activity may be at least 45–60 min. At this time, these public health guidelines on physical activity for cancer prevention are preliminary. However, given the clear health benefits for physical activity for many other chronic diseases, adoption of these guidelines for cancer prevention can be considered sound public health practice without harmful consequences. In fact, given the high level of obesity and inactivity in the population and the clear economic and health burdens on society because of these two major modifiable lifestyle risk factors, urgency exists to ensure that the general population becomes more active.

LITERATURE CITED

10. Brownson, R. C., Zahm, S. H., Chang, J. C. & Blair,


[The rest of the text contains references to various studies on colorectal cancer, physical activity, and its relation to cancer risk, including studies on the risk of colorectal cancer among women, the role of dietary factors, and the impact of physical activity on cancer risk in different populations and settings.]
PHYSICAL ACTIVITY AND CANCER PREVENTION


