RE: Physical Activity and Risks of Proximal and Distal Colon Cancers: A Systematic Review and Meta-Analysis

We read with great interest the systematic review and meta-analysis by Boyle et al. (1) on physical activity and risks of proximal colon cancers (PCCs) and distal colon cancers (DCCs), under the hypothesis that PCCs and DCCs may be two distinct cancer types with different genetic and environmental risk factors. The results suggested that physical activity is associated with a reduced risk of both PCCs and DCCs. This is a very important investigation because colorectal cancer is the third most common cancer in both men and women (2). However, as a limitation of their study, the authors stated that future research should focus on whether the intensity of physical activity influences the association between physical activity and the risk of colorectal cancer, which was also stressed in the recent article by Barton (3). Recently, we published a systematic review and meta-analysis (4) on physical activity and risk of breast cancer and found that intensity of physical activity influences its association with the risk of breast cancer. Thus, in this letter, we explore whether the intensity of physical activity influences its association with the risk of PCCs and DCCs.

A two-stage, random-effects, dose-response meta-analysis taking into account the between-study heterogeneity was performed, as has been well described by Orsini et al. (5). Briefly, three knots at the 25th, 50th, and 75th percentiles of the levels of physical activity were first estimated in a restricted cubic spline model using generalized least square regression taking into account the correlation within each set of published relative risk. Then a multivariable random-effects meta-analysis was conducted to combine the study-specific estimates using the restricted maximum likelihood method. Metabolic equivalent (MET) is the most commonly used measurement of physical activity intensity (6). Thus studies were included if they provided the following information (7): relative risk with 95% confidence interval (CI) for three or more quantitative categories (MET-hours) of physical activity (we presented all results with relative risk for simplicity), as well as the number of cases and participants (or person-years) for each category of physical activity. The median or mean level of physical activity for each category was assigned to the corresponding relative risk for every study.

For PCC, data from seven studies [references (9,19,20,27,32,33,39) in the study by Boyle et al. (1)], which included 1534 PCC case subjects, were used. A linear relationship was found, and the risk of PCC was 0.97 (95% CI = 0.90 to 1.04), 0.94 (95% CI = 0.83 to 1.07), 0.90 (95% CI = 0.77 to 1.03), 0.85 (95% CI = 0.73 to 0.98), 0.79 (95% CI = 0.67 to 0.93), and 0.74 (95% CI = 0.59 to 0.92) for 10, 20, 30, 40, 50, and 60 MET-hours/week, respectively (Figure 1).

For DCC, data from the above-mentioned seven studies, which included 1583 DCC case subjects, were used. Some evidence of a nonlinear relationship was found, and the risk of DCC was 0.90 (95% CI = 0.83 to 0.96), 0.80 (95% CI = 0.69 to 0.92), 0.77 (95% CI = 0.67 to 0.91), 0.81 (95% CI = 0.71 to 0.93), 0.84 (95% CI = 0.71 to 0.99), and 0.86 (95% CI = 0.70 to 1.06) for 10, 20, 30, 40, 50, and 60 MET-hours/week, respectively.

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Figure 1. The dose–response analysis between physical activity and proximal colon cancer with restricted cubic splines in a multivariable, random-effects, dose–response model. The solid line and the long dash line represent the estimated relative risk and its 95% confidence interval. The short dash line represents the linear relationship.
and colleagues’ analysis of increasing amounts of metabolic-equivalent (MET) hours per week is assessing the impact of volume (or dose) of total physical activity (ie, frequency x duration x intensity), rather than intensity, on the risks of proximal and distal colon cancers. As noted in Barton (2), the same level of MET hours per week can be achieved by performing vigorous-intensity physical activity for a short time, moderate-intensity physical activity for a relatively longer period, or a combination of vigorous- and moderate-intensity physical activity.

It is possible that the intensity at which physical activity is performed (ie, light, moderate, or vigorous) may influence the impact that it has on different health outcomes (3,4), so this is an important research topic. Our recent narrative review concerning physical activity and colon cancer risk concluded that there was some evidence indicating that vigorous-intensity activity may confer a greater risk reduction than moderate-intensity activity in men but not women (5). However, it is possible that measures of vigorous-intensity activity may simply be better able to classify study participants as having performed a high or low level of physical activity, because measurement of vigorous-intensity activity may be less prone to exposure misclassification than measurement of moderate-intensity activity (6).

Important issues to consider when combining intensity-specific results from different studies include the inconsistent use of the terms light, moderate, and vigorous, with some studies using these terms to describe increasing volumes or “doses” of physical activity rather than intensity, and the range of terms that have been used to describe activity intensities (7). For example, although five studies have investigated different physical activity intensity levels in relation to the risks of proximal and distal colon cancers [references (9,19,33,35,39) in Boyle et al. (1)], the different levels and combinations of intensity categories used in these studies make it very difficult to draw any overall conclusions. Given the importance of this topic, we support previous calls for greater consistency in the terminology used to describe intensity (7) and recommend that different activity intensity categories be treated as having potentially independent influences on disease risk (3).

References


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Response

We thank Zhang et al. for their comment and dose–response meta-analysis in response to our review (1). Their analysis provides some interesting data to suggest that the dose–response relationship between physical activity and the risk of colon cancer may differ slightly by subsite and a full systematic review and dose–response meta-analysis of this topic would be a valuable addition to the literature. However, we would suggest that Zhang

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