

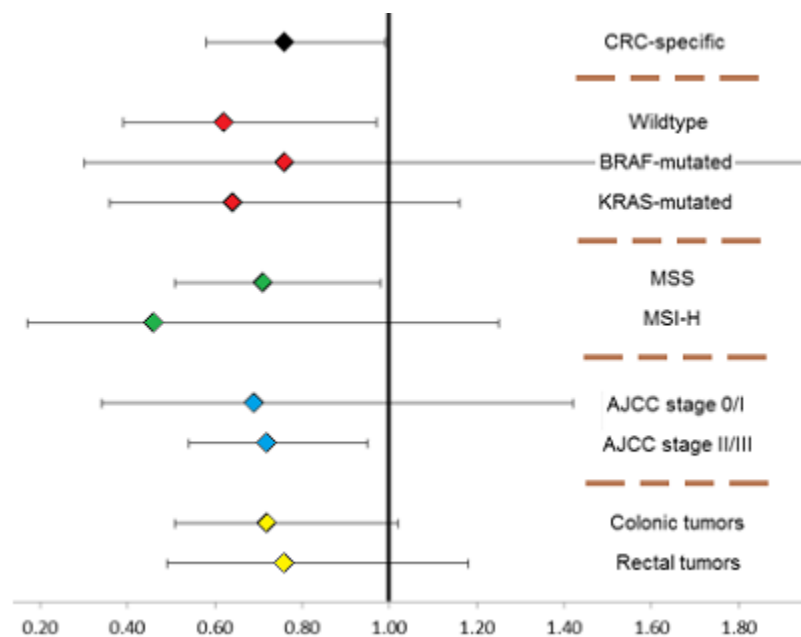
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SCIENCE SPOTLIGHT

Physical Activity before Colorectal Cancer Diagnosis Improves Survival

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Hazard ratio estimates and 95% confidence intervals for the association between pre-diagnostic physical activity level (at least 8.75 MET-hours/week versus less) and colorectal cancer specific survival. This relationship did not significantly vary when stratified by BRAF/KRAS mutation status (red), microsatellite instability status (green), cancer stage (blue), and tumor location (yellow).

Image provided by Dr. Sheetal Hardikar

Physical activity throughout life is beneficial for lowering the risk of developing or dying from several forms of cancer. Consequently, guidelines for cancer survivors generally recommend at least 150 minutes of moderate intensity or 75 minutes of vigorous exercise per week. While there is consistent evidence that post-diagnostic physical activity improves both overall and colorectal cancer-specific survival, the evidence for pre-diagnostic physical activity is less clear. To further explore this relationship, Drs. Sheetal Hardikar and Amanda Phipps in the Public Health Sciences Division evaluated the association between physical activity and colorectal cancer survival while accounting for potential epidemiologic and molecular sources of heterogeneity. As recently reported in *Cancer Epidemiology, Biomarkers & Prevention*, the authors observed that individuals who were physically active before colorectal cancer diagnosis had significantly better survival than those who had been inactive or minimally active.

Colorectal cancer is a heterogeneous disease, and recent work has identified molecular characteristics within the tumor that can differentiate different subtypes of disease. These colorectal cancer subtypes have been shown to have differential associations with survival: the presence of somatic mutations in the *BRAF* or *KRAS* oncogenes has been associated with poorer survival, while

the presence of microsatellite instability (MSI) has been associated with better survival. Additionally, evidence has suggested that the association of other lifestyle factors, such as smoking, with colorectal cancer risk and survival may also vary according to these tumor markers. Therefore the inconsistent associations previously seen for pre-diagnostic physical activity could have been due to those studies not accounting for these molecular characteristics.

To evaluate this relationship, the authors analyzed pre-diagnostic physical activity and outcomes data in more than 1,300 colorectal cancer patients from the Seattle Colon Cancer Family Registry. Participants were asked about their recreational physical activity during defined age periods, which were converted into standard metabolic equivalent of task hours per week (MET-h/wk). At least 8.75 MET-h/wk of physical activity was the threshold for meeting the recommended level of exercise. Tumor markers were assayed from banked tissue samples. After a median follow-up time of 6.1 years, pre-diagnostic physical activity levels were evaluated for an association with both overall and colorectal cancer specific survival using Cox regression.

The authors found that being physically active was associated with statistically significant improvements in both overall and colorectal cancer-specific survival. Importantly, patients who reported at least 8.75 MET-/wk of pre-diagnostic physical activity had better survival regardless of their tumor-markers, cancer stage, or tumor site (see figure). "Our results support these recommendations for colorectal cancer patients and suggest that physical activity in the years preceding cancer diagnosis may offer a survival benefit," said lead author Dr. Hardikar. "This survival benefit did not appear to differ for patients with different molecular subtypes of disease."

These results solidify the importance of maintaining sufficient levels of physical activity to not only reduce the risk of colorectal cancer, but also to improve prognosis should the disease develop. Importantly this study shows that this holds true regardless of the molecular characteristics of the tumor, leading to broad generalizability of this finding. "Further studies are needed to better understand the underlying mechanisms through which pre-diagnostic physical activity may impart survival benefit," said Dr. Hardikar. "This may aid us to better inform physical activity recommendations to the public." In the meantime, people have yet another reason to be physically active.

Other PHS investigators contributing to this project were Drs. Polly Newcomb, Karen Makar, and John Potter.

Citation:

[Hardikar S, Newcomb PA, Campbell PT, Win AK, Lindor NM, Buchanan DD, Makar KW, Jenkins MA, Potter JD, Phipps AJ](#). 2015. Prediagnostic physical activity and colorectal cancer survival: overall and stratified by tumor characteristics. *Cancer Epidemiol Biomarkers Prev.* 24(7):1130-7. doi: 10.1158/1055-9965.EPI-15-0039.