

Supplementary Material

The Time-Course of Cancer Recurrence with Physical Activity in Stage III Colon Cancer

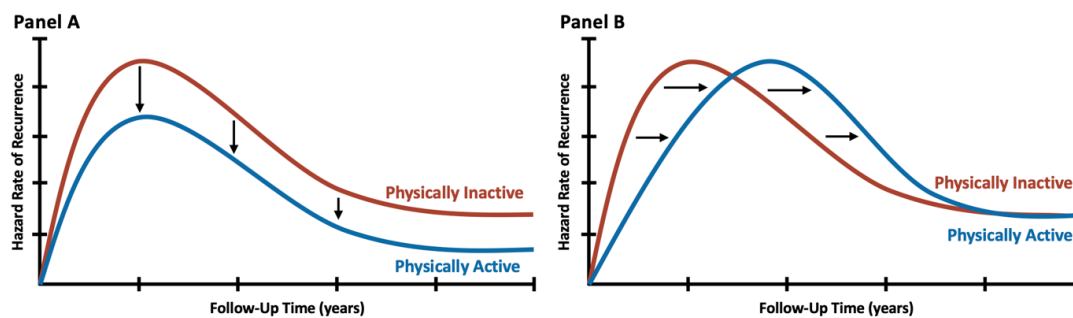
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Supplementary Figure 1. Graphical sketch of confounder-adjusted hazard rates by physical activity category. In Panel A, the hazard rate of cancer recurrence in the physically active group (blue line) is never higher than in the physically inactive group (red line), and the lines remain separated during follow-up. Panel A is consistent with the hypothesis that physical activity prevents cancer recurrence. In Panel B, the hazard rate of recurrence is initially higher in the physically inactive group, but with advancing time, the hazard rate of the physically active group becomes higher, and the lines eventually converge during follow-up. Panel B is consistent with the hypothesis that physical activity delays cancer recurrence.



Supplementary Table 1. Association of physical activity with time to cancer recurrence

| Physical Activity Volume (MET-h/wk) | 1-y Recurrence Rate (95% CI)^{a,b} | 2-y Recurrence Rate (95% CI)^{a,b} | 3-y Recurrence Rate (95% CI)^{a,b} | 5-y Recurrence Rate (95% CI)^{a,b} | Hazard Ratio (95% CI)^a |
|---|---|---|---|---|--|
| <9.0 | 6.7 (4.8, 9.5) | 13.1 (9.5, 18.3) | 19.3 (14.0, 26.8) | 31.5 (22.8, 44.2) | 1.00—Reference |
| ≥9.0 | 4.4 (3.1, 6.0) | 8.5 (6.1, 11.5) | 12.5 (9.1, 16.9) | 20.4 (14.8, 27.6) | 0.65 (0.49, 0.82) |
| Absolute Risk Difference^c | 2.3 (0.1, 4.5) | 4.6 (1.7, 7.5) | 6.8 (3.3, 10.2) | 11.1 (7.0, 15.2) | — |
| P^d | 0.040 | 0.002 | <0.001 | <0.001 | <0.001 |
| NNT^e | 44 (22, 1000) | 22 (13, 59) | 15 (10, 30) | 9 (7, 14) | — |

Abbreviations: MET-h/wk, metabolic equivalent total physical activity energy expenditure; y, year; NNT, number needed to treat

^aAdjusted for age, sex, race, extent of invasion through the bowel wall, nodal stage, tumor location, ECOG performance status, low dose aspirin use, smoking history, body mass index (time-varying), western dietary pattern (time-varying), prudent dietary pattern (time-varying), chemotherapy randomization, and pharmacotherapy randomization. Continuous covariates were modeled linearly, and categorical covariates were modeled using the categories presented in Table 1.

^bCovariates for predicting recurrence rates were set to the mean of the study population for continuous variables and most common categories for categorical variables.

^c95% confidence intervals were calculated via the bootstrap method with 1,0000 replicates.

^dP values are two-sided.

^eThe number needed to treat (NNT) was calculated as 1/Absolute Risk Difference. The NNT quantifies the number of patients who would need to be become physically active to prevent one cancer recurrence.

Supplementary Table 2. Model performance between the flexible parametric model with Weibull distribution and Cox proportional hazards model

| Endpoint | Akaike Information Criterion (AIC) | | Bayesian Information Criterion (BIC) | |
|---------------------------|---|------------|---|------------|
| | Weibull | Cox | Weibull | Cox |
| Disease-Free Survival | 3177 | 6384 | 3303 | 6462 |
| Time to Cancer Recurrence | 2843 | 5551 | 2968 | 5626 |
| Overall Survival | 2308 | 3932 | 2434 | 4001 |