Received: 6 November 2024 | Revised: 23 December 2024 | Accepted: 30 December 2024

DOI: 10.1002/cncr.35727

ORIGINAL ARTICLE

The association of physical activity with survival in colon cancer versus a matched general population: Data from Cancer and Leukemia Group B 89803 and 80702 (Alliance)

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Funding information
National Cancer Institute, Grant/Award Numbers: U10CA180821, U10CA180882

Abstract

Background: Colon cancer patients have inferior overall survival than a matched general population (MGP). It is unknown if physical activity is associated with a reduction in this survival disparity.

Methods: Data were analyzed from two National Cancer Institute–sponsored postoperative treatment trials in stage III colon cancer, Cancer and Leukemia Group B (CALGB) 89803 and 80702, with 2876 patients who self-reported physical activity. Physical activity was converted to metabolic equivalents (MET-hours/week). The MGP was derived from the National Center for Health Statistics and matched on age, sex, and year.

Results: In CALGB 89803, among patients who were alive at 3 years, those with <3.0 and ≥18.0 MET-hours/week had subsequent 3-year overall survival rates that were −17.1% (95% confidence interval [CI], −22.4 to −11.8) and −3.5% (95% CI, −7.7 to 0.3) lower than MGP, respectively. In CALGB 80702, among patients who were alive at 3 years, those with <3.0 and ≥18.0 MET-hours/week had subsequent 3-year overall survival rates that were −10.8% (95% CI, −15.4 to −6.9) and −4.4% (95% CI, −7.6 to −1.6) lower than MGP, respectively. In pooled analyses, among patients who were alive and did not have tumor recurrence by year 3 (n = 1908), those with <3.0 and ≥18.0 MET-hours/week had subsequent 3-year overall survival rates that were −3.1% (95% CI, −6.2 to −0.3) lower and 2.9% (95% CI, 1.5–4.2) higher than MGP, respectively.

Conclusions: Physical activity is associated with an attenuation of the survival disparity between patients with stage III colon cancer participating in clinical trials and MGP. Colon cancer survivors who are physically active may achieve survival that approximates the MGP.

The study was registered on Clinicaltrials.gov as NCT000038350 and NCT01150045.

KEYWORDS
cancer survivors, colonic neoplasms, exercise, matched general population, neoplasm recurrence

INTRODUCTION

Colon cancer is a leading cause of cancer-related death worldwide.[1] Observational studies report that physical activity after a colon cancer diagnosis is associated with significantly longer disease-free survival.[2,3] Among 1696 patients with stage III colon cancer, physical activity during and after chemotherapy lowered the risk of tumor recurrence in the first postoperative year, which translated into an overall survival benefit, suggesting that physical activity may prevent —as opposed to delay—tumor recurrence in some patients.[4]

A pooled analysis of clinical trials reported that the long-term survival of colon cancer patients has improved over time but remains worse than in a contemporaneously matched general population (MGP).[5] The primary determinant of achieving a survival rate comparable to the MGP was remaining free of tumor recurrence.[5] If physical activity prevents tumor recurrence,[4] it may also reduce the survival disparity between colon cancer patients and the MGP. However, the degree to which physical activity may help patients with colon cancer achieve a survival rate like that of individuals of the same age, sex, and year but without cancer is unknown.

This analysis investigated if physical activity during and after chemotherapy is associated with the survival disparity between patients with stage III colon cancer and the MGP. Enabling patients to understand how physical activity may influence their prognosis relative to a similar population without cancer may be valuable to medical and public health personnel and policymakers who seek innovative and evidence-based messages to promote physical activity to improve population health.[6]

MATERIALS AND METHODS

Study population

Patients in this analysis participated in one of two National Cancer Institute–sponsored Cancer and Leukemia Group B (CALGB, now part of Alliance for Clinical Trials in Oncology) postoperative treatment trials in stage III colon cancer. The primary objective of CALGB 89803 was to test the hypothesis of the superiority of weekly irinotecan, 5-fluorouracil, and leucovorin compared with weekly 5-fluorouracil and leucovorin (ClinicalTrials.gov NCT000038350).[7] The primary objective of CALGB 80702 was to test the hypothesis of the superiority of celecoxib compared with placebo during 5-fluorouracil, leucovorin, and oxaliplatin chemotherapy (ClinicalTrials.gov NCT01150045).[8] Both trials enrolled patients from community and academic centers across the National Clinical Trials Network.

Eligible patients underwent a complete surgical resection of the primary tumor within 56 days before starting protocol treatment and had pathologically confirmed stage III colon adenocarcinoma. Patients were at least 18 years old, with an Eastern Cooperative Oncology Group performance status of 0 to 2, and had normal hepatic, renal, and hematologic values. All patients provided signed informed consent, which was approved by the National Cancer Institute Cancer Treatment Evaluation Program and each participating site's institutional review board.

Physical activity assessment

At the time of trial enrollment, patients were offered the option to participate in a nested cohort study of lifestyle factors, including completing standardized assessments midway through postoperative chemotherapy and 6 months after postoperative chemotherapy (12 −14 months after primary surgical resection). Patients reported their average weekly time spent on recreational physical activities during the past 2 months using a validated questionnaire.[9] Per standardized criteria, each physical activity was assigned a metabolic equivalent (MET) value.[10,11] We calculated the MET hours per week (MET-hours/week) for each activity by multiplying the MET value by the patient's reported number of hours of physical activity each week.

Study end point

The primary end point of this analysis was overall survival, defined as the time from completing the first physical activity assessment to death from any cause.

Matched general population

For each patient in CALGB 89803 or 80702, the expected long-term survival based on the general population matched on age at cancer diagnosis, sex, and calendar year was calculated using validated life tables from the National Center for Health Statistics.[12]

Statistical analysis

Overall survival was compared between CALGB trial patients and the MGP using a one-sample log-rank test and a modified version of the Kaplan–Meier method to compare CALGB patients to the MGP derived from life table data.[13] A Kaplan–Meier survival curve with

pointwise 95% confidence intervals (CIs) for the CALGB patient cohorts was graphed with the expected survival curve based on the MGP. The observed (patients with stage III colon cancer participating in a clinical trial) minus expected (MGP) 3-year overall survival rates were calculated 1, 2, and 3 years after completing the first physical activity assessment (e.g., the probability of being alive 3 years after surviving to the 1, 2, or 3 years after completing the first physical activity assessment). A 95% CI for the absolute difference that excluded zero was considered statistically significantly different. The standardized mortality ratio (SMR) was calculated as the ratio of the observed to the expected number of deaths during follow-up with corresponding 95% CIs. A 95% CI for the SMR that excluded one was considered statistically significantly different. Analyses by category of physical activity were stratified by CALGB study cohort (89803 vs. 80702) to account for temporal changes and due to the disease-free survival and overall survival benefit of oxaliplatin chemotherapy that was used in CALGB 80702,[14] then by disease recurrence status (experienced tumor recurrence before landmark time, yes vs. no) in the sample that pooled both cohorts.[5] Data quality was ensured by review of data by the Alliance Statistics and Data Management Center and by the study chairperson following Alliance policies. Data collection and statistical analyses were conducted by the Alliance Statistics and Data Management Center using SAS (Version 9.4) and R (Version 4.1.0) on the CALGB 89803 data set locked on January 8, 2018, and the CALGB 80702 data set locked on August 10, 2020.

RESULTS

From 1999 to 2002, CALGB 89803 enrolled 1264 patients, with 1129 (89.3%) reporting their physical activity volume at both time points. From 2010 to 2016, CALGB 80702 enrolled 2524 patients, with 1643 (65.1%) reporting their physical activity volume at both time points. Differences between the patients in the analysis and the randomized sets have been reported.[2,3] In the pooled sample of 2876 patients, the median [interquartile range] age at diagnosis was 60.8 years [52.8, 68.6], and 1610 (56.0%) patients were male (Table 1). A physical activity volume <3.0, 3.0–17.9, and ≥18.0 MET-hours/week was reported by 840 (29.2%), 1264 (44.0%), and 772 (26.8%), respectively. The median [interquartile range] enrollment for CALGB 89803 was in the calendar year 2001 [2000, 2001], and for CALGB 80702 was in the calendar year 2013 [2012, 2014]. The median length of follow-up was 6.0 and 5.9 years for CALGB 89803 and 80702, respectively.

TABLE 1 Baseline characteristics overall and by study cohort.

		CALGB cohort	
Characteristic	**Pooled cohorts (*N* = 2876)**	**89803 (*N* = 1180)**	**80702 (*N* = 1696)**
Age, year [median (IQR)]	60.8 [52.8, 68.6]	60.0 [51.0, 69.0]	61.2 [53.4, 68.4]
Sex, No. (%)			
Male	1610 (56.0)	669 (56.7)	941 (55.5)
Female	1266 (44.0)	511 (43.3)	755 (44.5)
Year of enrollment, [median (IQR)]	2011 [2001, 2014]	2001 [2000, 2001]	2013 [2012, 2014]
1999	2 (0.1%)	2 (0.2%)	0 (0.0%)
2000	402 (14.0%)	402 (34.1%)	0 (0.0%)
2001	775 (26.9%)	775 (65.7%)	0 (0.0%)
2002	1 (<0.1%)	1 (<0.1%)	0 (0.0%)
2010	36 (1.3%)	0 (0.0%)	36 (2.1%)
2011	239 (8.3%)	0 (0.0%)	239 (14.1%)
2012	307 (10.7%)	0 (0.0%)	307 (18.1%)
2013	392 (13.6%)	0 (0.0%)	392 (23.1%)
2014	339 (11.8%)	0 (0.0%)	339 (20.0%)
2015	378 (13.1%)	0 (0.0%)	378 (22.3%)
2016	5 (0.2%)	0 (0.0%)	5 (0.3%)
Physical activity category, No. (%)			
<3.0 MET-hours/week	840 (29.2)	354 (30.0)	486 (28.7)
≥3.0–17.9 MET-hours/week	1,264 (44.0)	537 (45.5)	727 (42.9)
≥18.0 MET-hours/week	772 (26.8)	289 (24.5)	483 (28.5)

Abbreviations: CALGB, Cancer and Leukemia Group B; IQR, interquartile range; MET, metabolic equivalent.

In CALGB 89803, the absolute difference between the observed Kaplan–Meier survival rate and the expected, matched general population (MGP), 3-year overall survival conditional on surviving 1, 2, and 3 years from the first physical activity assessment was −19.2%, −15.9%, and −11.3% (Table 2; Figure 1). At each annual landmark, higher volumes of physical activity were associated with a smaller absolute difference between the observed and expected 3-year overall survival rate. For example, among patients who were alive at 3 years, those who reported <3.0 and ≥18.0 MET-hours/week of physical activity had 3-year overall survival rates that were −17.1% (95% CI, −22.4 to −11.8) and −3.5% (95% CI, −7.7 to 0.3) lower than the MGP, respectively.

In CALGB 80702, the absolute difference between the observed Kaplan–Meier survival rate and the expected (MGP) 3-year overall survival was −6.3%, −7.1%, and −6.3%, conditional on surviving 1, 2, and 3 years from the first physical activity assessment. At each annual landmark, higher volumes of physical activity were associated with a smaller absolute difference between the observed and expected 3-year overall survival rate. For example, among patients who were alive at 3 years, those who reported <3.0 and ≥18.0 MET-hours/week of physical activity had 3-year overall survival rates that were −10.8% (95% CI, −15.4 to −6.9) and −4.4% (95% CI, −7.6 to −1.6) lower than the MGP, respectively.

In analyses that pooled CALBG 89303 and 80702, the development of tumor recurrence modified the association between physical activity and the difference between the observed versus expected survival rate. The absolute difference between the observed Kaplan–Meier survival rate and the expected (MGP) 3-year overall survival was −73.2%, −59.1%, and −48.0%, conditional on being alive but developing tumor recurrence by 1, 2, and 3 years from the first physical activity assessment (Table 3; Figure 2). Among 438 patients who developed tumor recurrence by year three, those who reported <3.0 and ≥18.0 MET-hours/week of physical activity had 3-year overall survival rates that were −55.8% (95% CI, −65.2 to −47.0) and −42.5% (95% CI, −53.3 to −32.1) lower than the MGP, respectively. Among 1908 patients who were alive but had not developed tumor recurrence by year 3, those who reported <3.0 and ≥18.0 MET-hours/week had 3-year overall survival rates that were −3.1% (95% CI, −6.2 to −0.3) lower and 2.9% (95% CI, 1.5–4.5) higher than the MGP, respectively.

The conclusions from the statistical analyses that estimated the SMD (relative effect) using all available follow-up time to 6 years were not substantively different from the above-presented absolute risk differences (Tables S1 and S2). Observed absolute conditional survival for patients with stage III colon cancer participating in clinical trials by physical activity and recurrence status are presented (Tables S3 and S4).

DISCUSSION

In this analysis, we calculated conditional survival, defined as the probability of surviving three additional years, given that a patient survived 1, 2, or 3 years already, and compared that probability to what would be expected in a population of the same age, sex, and year but without cancer. We then investigated how physical activity during and after chemotherapy influences the survival disparity between patients with stage III colon cancer participating in a clinical trial and the MGP. Our analyses indicated that survival in the full population of patients with stage III colon cancer was poorer than the MGP, but higher volumes of physical activity were associated with an attenuation of the survival disparity between colon cancer patients

TABLE 2 Absolute percentage difference between the observed Kaplan–Meier and expected (population-matched) 3-year overall survival rate, overall, and stratified by physical activity category and study cohort.

	Lived 1 year		Lived 2 years		Lived 3 years	
CALGB 89803	**No.**	**Difference (95% CI)**	**No.**	**Difference (95% CI)**	**No.**	**Difference (95% CI)**
Overall	1129	−19.2% (−22.1 to −16.8)	1003	−15.9% (−18.5 to −13.5)	903	−11.3% (−14.0 to −8.7)
Physical activity category						
<3.0 MET-hours/week	334	−26.1% (−31.7 to −21.6)	285	−22.1% (−27.1 to −17.1)	246	−17.1% (−22.4 to −11.8)
≥3.0–17.9 MET-hours/week	515	−16.3% (−20.3 to −13.1)	473	−16.2% (−19.7 to −12.6)	432	−12.0% (−16.1 to −8.2)
≥18.0 MET-hours/week	280	−16.7% (−21.6 to −11.9)	245	−9.0% (−13.4 to −4.9)	225	−3.5% (−7.7 to 0.3)
CALGB 80702						
Overall	1643	−6.3% (−7.8 to −4.8)	1548	−7.1% (−8.9 to −5.5)	1443	−6.3% (−8.2 to −4.5)
Physical activity category						
<3.0 MET-hours/week	465	−12.1% (−15.6 to −8.7)	420	−12.6% (−16.6 to −9.0)	376	−10.8% (−15.4 to −6.9)
≥3.0–17.9 MET-hours/week	706	−5.2% (−7.4 to −3.0)	672	−5.1% (−7.6 to −2.7)	634	−5.0% (−7.7 to −2.4)
≥18.0 MET-hours/week	472	−2.4% (−4.9 to −0.4)	456	−5.0% (−7.9 to −2.4)	433	−4.4% (−7.6 to −1.6)

Note: Estimates are computed 3 years following conditional survival to years 1, 2, and 3 from the first physical activity assessment.
Abbreviations: CALGB, Cancer and Leukemia Group B; CI, confidence interval; MET, metabolic equivalent.

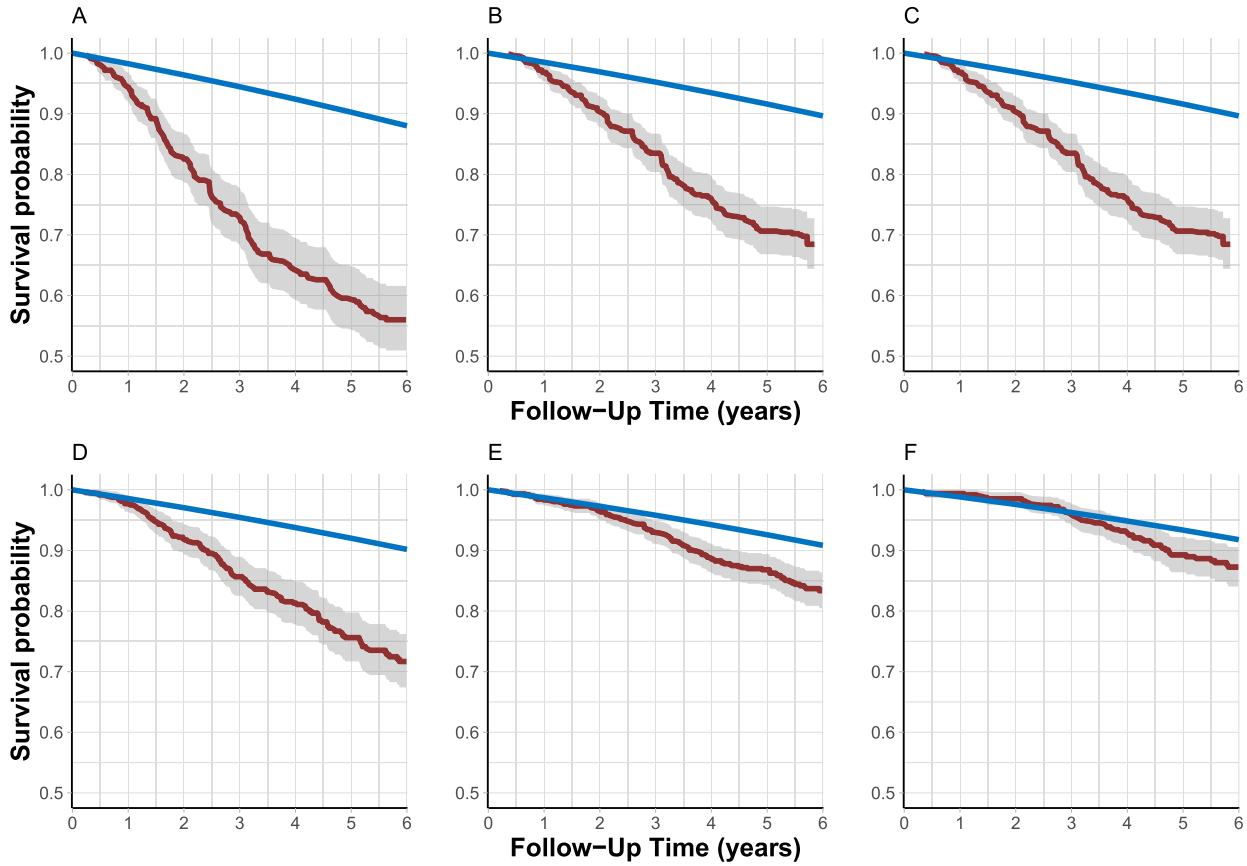

FIGURE 1 Kaplan–Meier survival curves with 95% pointwise confidence intervals, superimposed on matched population survival curves in CALGB 89803 (A–C) and CALGB 80702 (D–F), by physical activity category of <3.0 MET-hours/week (A and D), ≥3.0–17.9 MET-hours/week (B and E), and ≥18.0 MET-hours/week (C and F). CALGB indicates Cancer and Leukemia Group B; MET, metabolic equivalent.

TABLE 3 Absolute percentage difference between the observed Kaplan–Meier and expected (population-matched) 3-year overall survival rate stratified by physical activity category and tumor recurrence status.

	Alive but with tumor recurrence at year 1		Alive but with tumor recurrence at year 2		Alive but with tumor recurrence at year 3	
Patients with tumor recurrence	**No.**	**Difference (95% CI)**	**No.**	**Difference (95% CI)**	**No.**	**Difference (95% CI)**
Overall	241	−73.2% (−78.4 to −67.6)	417	−59.1% (−63.9 to −54.6)	438	−48.0% (−52.9 to −42.9)
Physical activity category						
<3.0 MET-hours/week	92	−79.1% (−85.6 to −72.6)	132	−70.3% (−77.8 to −62.2)	125	−55.8% (−65.2 to −47.0)
≥3.0–17.9 MET-hours/week	90	−72.7% (−82.0 to −63.6)	185	−53.4% (−60.8 to −46.0)	207	−45.6% (−52.3 to −38.4)
≥18.0 MET-hours/week	59	−66.6% (−78.0 to −54.5)	100	−56.2% (−66.4 to −45.5)	106	−42.5% (−53.3 to −32.1)
Patients without tumor recurrence	**Alive and without tumor recurrence at year 1**		**Alive and without tumor recurrence at year 2**		**Alive and without tumor recurrence at year 3**	
Overall	2531	−5.7% (−6.9 to −4.5)	2134	−1.0% (−2.0 to −0.04)	1908	0.75% (−0.3 to 1.9)
Physical activity category						
<3.0 MET-hours/week	707	−9.9% (−12.7 to −7.4)	573	−3.6% (−6.1 to −1.1)	497	−3.1% (−6.2 to −0.3)
≥3.0–17.9 MET-hours/week	1131	−4.9% (−6.7 to −3.3)	960	−1.2% (−2.8 to 0.4)	859	1.6% (−0.02 to 3.1)
≥18.0 MET-hours/week	693	−2.7% (−4.8 to 0.8)	601	1.9% (0.3–3.2)	552	2.9% (1.5–4.2)

Note: Estimates are computed 3 years following conditional survival to years 1, 2, and 3 from the first physical activity assessment.

Abbreviations: CI, confidence interval; MET, metabolic equivalent.

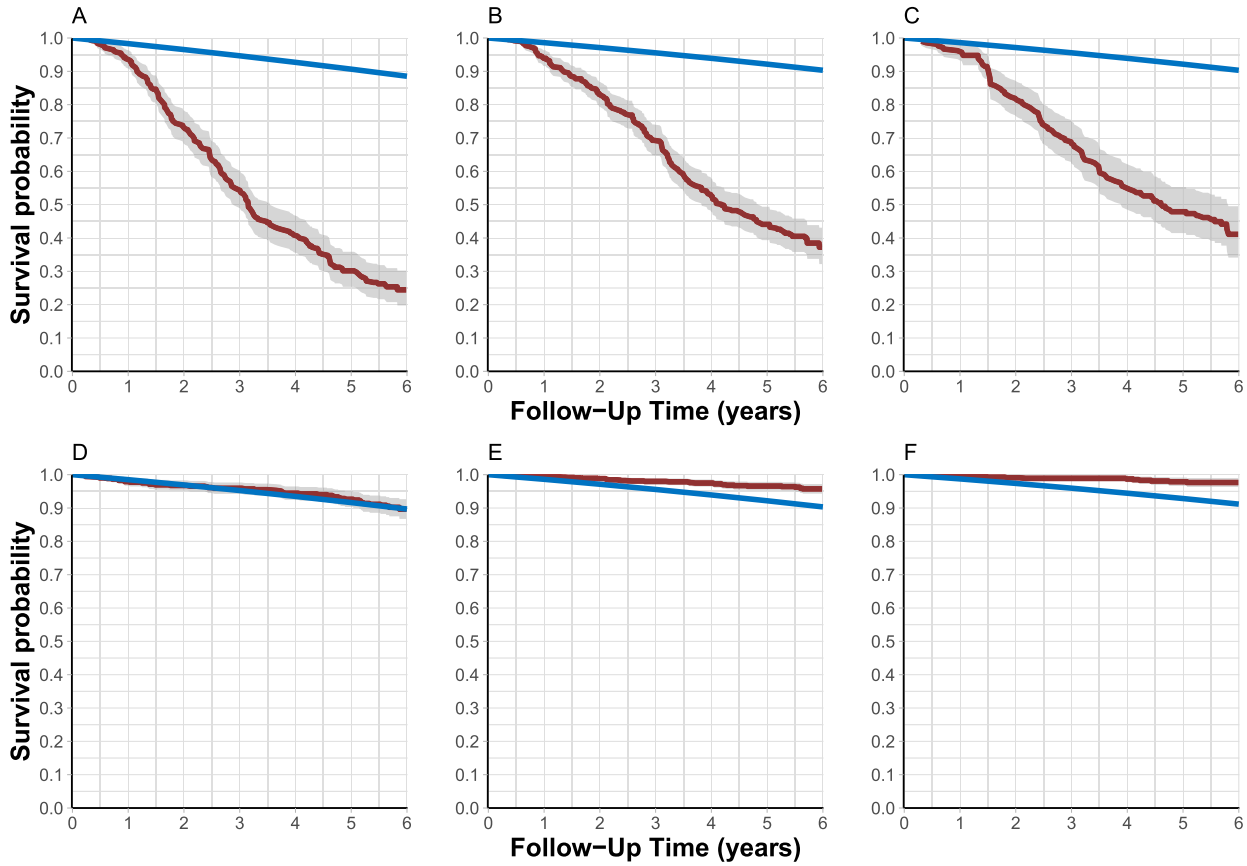

FIGURE 2 Kaplan–Meier survival curves with 95% pointwise confidence intervals, superimposed on matched population survival curves in patients with tumor recurrence (A–C) and without tumor recurrence (D–F), by physical activity category of <3.0 MET-hours/week (A and D), ≥3.0–17.9 MET-hours/week (B and E), and ≥18.0 MET-hours/week (C and F). MET indicates metabolic equivalent.

and the MGP. In both clinical trial cohorts, the difference between the observed and the expected (MGP) 3-year overall survival rates decreased with higher volumes of physical activity. Contrasting patient overall survival to that of the general population, such as the comparisons reported here, may help inform future strategies to optimize cancer survivorship.

Among patients enrolled in CALGB 89803, 3-year overall survival began to approximate the MGP with higher volumes of physical activity and on conditional survival to additional landmarks. In contrast, among patients enrolled in CALGB 80702, 3-year overall survival began to approximate the MGP with higher volumes of physical activity but was less impacted upon conditional survival to additional landmarks. A key distinction between CALGB 80702 and CALGB 89803 was using a chemotherapy regimen containing oxaliplatin. A regimen containing fluoropyrimidine and oxaliplatin has been proven to improve disease-free survival and overall survival in patients with stage III colon cancer versus fluoropyrimidine alone.[14] However, the median enrollment between CALGB 89803 and CALGB 80702 also differed by a decade; thus, we cannot exclude the possibility that other temporal-related factors—such as advances in early detection, surgical staging, postoperative medical management, and the early identification of tumor recurrence—may have also influenced this observation.[15]

In a pooled analysis of more than 32,000 patients with colon cancer enrolled in clinical trials, the primary determinant of achieving a survival rate comparable to the MGP was remaining free of tumor recurrence.[5] Most tumor recurrences after stage III colon cancer occur within 2 or 3 years of diagnosis.[16] Tumor recurrence is often metastatic to the liver or lung,[17] and curative-intent surgery is typically not feasible.[18] Consequently, in the decade after colon cancer diagnosis, 80% of all deaths are preceded by tumor recurrence.[19] In our analysis, the development of tumor recurrence modified how physical activity attenuated the survival disparity between colon cancer patients and the MGP.

Among patients alive and without tumor recurrence at years 1 and 2, higher volumes of physical activity were associated with an attenuation of the overall survival disparity between patients with stage III colon cancer and the MGP. However, among patients who were alive and without tumor recurrence at year 3, the survival rate approximated the MGP, regardless of the volume of physical activity. This observation is consistent with the hypothesis that the primary means by which physical activity attenuates the survival disparity between colon cancer patients and the MGP may be through the prevention of tumor recurrence. An observational analysis examining the effects of physical activity on tumor recurrence using continuous time statistical modeling showed a significantly lower risk of tumor

recurrence in physically active patients in the first postoperative year, translating into an overall survival benefit for the first 3 postoperative years.[4]

Among patients who developed tumor recurrence, higher volumes of physical activity and conditional survival to additional landmarks were associated with an attenuation of the survival disparity between colon cancer patients and the MGP; however, the magnitude of the survival disparity remained large due to the lethal nature of most tumor recurrences in colon cancer. For example, among patients alive but with tumor recurrence by 3 years, the survival disparity with the MGP was −50.5% (95% CI, −58.8 to −42.1) with <3.0 MET-hours/week and −33.2% (95% CI, −42.5 to −24.4) with ≥18.0 MET-hours/week of physical activity. This finding complements prior reports that physical activity during and after chemotherapy is associated with a 33% relative extension in overall survival time after tumor recurrence in patients initially diagnosed with stage III colon cancer.[20] This extension in overall survival time may be partly attributed to physical activity delaying tumor progression,[21] a validated surrogate end point of overall survival in advanced colon cancer.[22] Nonetheless, most deaths in this patient subset are due to colon cancer, contributing to the high global burden of colon cancer death rates.

The biological mechanisms by which physical activity reduces tumor recurrence, improves overall survival, and enables colon cancer patients to achieve long-term survival that approximates the MGP remain incompletely characterized.[23] This is due to the pleiotropic effects of physical activity, which affect all cells and tissues to produce health benefits.[24,25]

In randomized trials of patients with stage I-III colon cancer, physical activity favorably shifts the host tumor microenvironment by reducing systemic inflammation,[26] improving insulin sensitivity,[27] and reducing intraabdominal visceral adipose tissue.[28] Moderate-intensity aerobic physical activity, such as brisk walking, lowers circulating tumor cells in surgically resected stage I-III colon cancer patients.[29] The clinical benefits of physical activity in patients with colon cancer may occur through two synergistic processes: indirect (systemic) effects in the host tumor microenvironment and direct (physical) effects on cancer cells.[23]

Cancer control initiatives, such as the American Cancer Society 2035 Challenge,[30] have proposed focusing on modifiable risk factors, such as insufficient physical activity, to reduce cancer mortality. Identifying evidence-based framing to promote physical activity is critical because two-thirds of colon cancer survivors self-report insufficient physical activity.[31] In an American Society of Clinical Oncology survey, 78.6% of practicing oncologists regularly assessed physical activity, and 72.3% advised patients to increase or maintain physical activity.[32] The results of this analysis may be particularly relevant for patients who want to understand how physical activity may improve their long-term health and how their health with physical activity may compare to their friends and family members without cancer.[33]

Maximizing how patients feel, function, and survive is critical to cancer survivorship and control. Many patients with colon cancer have comparable quality of life and physical functioning compared with population-based normative values.[34] Among the subgroups with impairments in quality of life and physical functioning,[35] participation in physical activity is associated with improved physical activity in observational cohorts and randomized trials.[36,37] This analysis contributes information about how physical activity can promote an overall survival experience after colon cancer that begins to approximate the overall survival experience of individuals of the same age, sex, and year but without cancer. The myriad health benefits achieved by physical activity make promoting physical activity a cornerstone to optimizing colon cancer survivorship.[38]

There are several important limitations to this analysis. This was an observational data analysis; therefore, uncertainty persists if the identified associations are causal or if the ability to engage in physical activity is simply an indicator of better health, thus reversing the causality of the associations reported. The patients included in our analysis were enrolled in randomized treatment trials. Patients who enroll in randomized trials may differ from the underlying source population.[39] Clinical trial participants may have fewer chronic health conditions, thus making comparisons appear more favorable than in the general population of patients with colon cancer. Physical activity was self-reported in this study. Although the questionnaire is validated,[9] it was limited to several recreational physical activities and not a comprehensive assessment of all domains of physical activity. Race and ethnicity were unavailable for some patients in these two clinical trials. Thus, we could not use race and ethnicity to refine our matching to the MGP. We matched colon cancer patients on age, sex, and year, which, before the SARS-CoV-2 pandemic, were the primary predictors of longevity.[40] Despite these limitations, this analysis offers a novel population-level perspective on the benefits of physical activity in patients with colon cancer.

This analysis has several important strengths. Physical activity is often not measured in large real-world data sets. Pooling the data from two CALGB clinical trial cohorts enabled us to study patients over nearly 2 decades of treatment. The larger sample size also enabled us to examine the effects of physical activity stratified by recurrence status.

Among patients with stage III colon cancer enrolled in trials of postoperative treatments, participation in physical activity was associated with an attenuation of the survival disparity between colon cancer patients and the MGP. Achieving a survival rate comparable to the MGP is conditional on remaining tumor recurrence-free. Select colon cancer survivors who are physically active may achieve long-term survival that approximates the MGP.

AUTHOR CONTRIBUTIONS

Justin C. Brown: Conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, resources, supervision, validation, writing–original draft, and writing–review and editing. **Chao Ma**: Conceptualization, data curation, formal analysis, investigation, methodology, project administration, resources, validation, visualization, and writing–review and editing. **Qian Shi**: Data curation, formal analysis, investigation, methodology, project

administration, resources, supervision, validation, visualization, and writing–review and editing. **Leonard B. Saltz**: Data curation, investigation, methodology, project administration, resources, and writing–review and editing. **Anthony F. Shields**: Data curation, investigation, methodology, project administration, resources, and writing–review and editing. **Jeffrey A. Meyerhardt**: Conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, supervision, validation, and writing–original draft, writing–review and editing. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

ACKNOWLEDGMENTS

Research reported in this publication was supported by the National Cancer Institute of the National Institutes of Health under award numbers U10CA180821 and U10CA180882 (to the Alliance for Clinical Trials in Oncology) (https://acknowledgments.alliancefound.org). Justin C. Brown is supported by R00CA218603, R01CA270274, U01CA271279, and OT2CA278684. Jeffrey A. Meyerhardt is supported by the Douglas Gray Woodruff Chair fund, the Guo Shu Shi Fund, the Project P fund, Anonymous Family Fund for Innovations in Colorectal Cancer, and the George Stone Family Foundation. The National Cancer Institute Cancer Treatment Evaluation Program and each participating site's institutional review board approved the study protocol. All patients provided signed informed consent.

CONFLICT OF INTEREST STATEMENT

Justin C. Brown reports grants from the National Institutes of Health, the American Institute for Cancer Research, and Cancer Research UK paid to his institution. Qian Shi reports institutional grant support from Celgene–Bristol-Myers Squibb and Roche/Genentech; consulting fees from Yiviva Inc and Boehringer Ingelheim Pharmaceuticals; and stock ownership in Johnson & Johnson, Merck, and Amgen. Anthony F. Shields reports grants from the National Cancer Institute. Jeffrey A. Meyerhardt reports personal fees for serving on the advisory boards of Merck Pharmaceutical. The other authors declare no conflicts of interest. The National Cancer Institute was involved in the study's design and reviewing and approving the manuscript. However, it was not involved in the conduct of the study, collection, management, analysis, interpretation of the data, or decision to submit the manuscript for publication. The content is solely the authors' responsibility and does not necessarily represent the official views of the National Institutes of Health.

DATA AVAILABILITY STATEMENT

Data cannot be shared to preserve the anonymity of patient-protected health information.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Brown JC, Ma C, Shi Q, Saltz LB, Shields AF, Meyerhardt JA. The association of physical activity with survival in colon cancer versus a matched general population: data from Cancer and Leukemia Group B 89803 and 80702 (Alliance). *Cancer*. 2025;e35727. doi:10.1002/cncr.35727