Physical activity in older adults with metastatic gastrointestinal cancer: a pilot and feasibility study

Justin C Brown, Elizabeth Brighton, Nancy Campbell, Nadine J Mc Cleary, Thomas A Abrams, James M Cleary, Peter C Zengiver, Kimmie Ng, Douglas Robinson, Brian M Wolpin, Matthew B Yurgelun, Jeffrey A Meyerhardt

ABSTRACT

Objectives This study determined the feasibility of delivering a 12-week structured physical activity programme during chemotherapy to older adults recently diagnosed with metastatic gastrointestinal (GI) cancer.

Methods This study used a single-cohort design. Older adults (aged ≥65 years) diagnosed with metastatic oesophageal, gastric, pancreatic or colorectal cancer who planned to initiate chemotherapy were enrolled. The physical activity programme included a combination of aerobic, flexibility, strength and balance modalities delivered by a certified cancer exercise trainer during chemotherapy infusion appointments, then translated and sustained at home by participants. The co-primary endpoints included: (1) accrual of 20 participants in 12 months and (2) physical activity adherence of ≥50%.

Results Between March and October 2018, 29 participants were screened, and 20 were enrolled within 12 months (recruitment rate: 69% (90% CI: 55% to 83%); p<0.001), meeting the first co-primary endpoint. The median age of participants was 73.3 years (IQR: 69.3–77.2). At week 12, 67% (90% CI: 48% to 85%) of participants adhered to ≥50% of the prescribed physical activity (p=0.079 (statistically significant)), meeting the second co-primary endpoint. From baseline to week 12, accelerometer-measured light-intensity and moderate-intensity to vigorous-intensity physical activity increased by 307.4 min per week (95% CI: 152.6 to 462.2), and moderate-intensity to vigorous-intensity physical activity increased by 25.0 min per week (95% CI: 9.9 to 40.1).

Conclusion These results establish the feasibility of a larger scale randomised controlled trial that enrols older adults with metastatic GI cancer and delivers a structured physical activity programme during chemotherapy.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Reduced physical function predicts poor quality of life, chemotherapy toxicity and premature death in adults with metastatic cancer.
⇒ Despite the importance of preserving physical function in patients with metastatic cancer, few therapeutic options exist, and there is no standard of care.

WHAT THIS STUDY ADDS

⇒ This study established the feasibility of delivering a 12-week structured physical activity programme during chemotherapy to older adults recently diagnosed with metastatic gastrointestinal cancer.
⇒ Objectively measured light-intensity physical activity increased by 307.4 min per week (95% CI: 152.6 to 462.2), and moderate-intensity to vigorous-intensity physical activity increased by 25.0 min per week (95% CI: 9.9 to 40.1).

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE AND/OR POLICY

⇒ These results establish the feasibility of a larger scale randomised controlled trial that enrols older adults with metastatic gastrointestinal cancer and delivers a structured physical activity programme during chemotherapy.

INTRODUCTION

At the time of diagnosis of metastatic gastrointestinal (GI) cancer, 70% of patients are aged ≥65 years.1 Within the first 12–24 weeks of starting chemotherapy, 40%–60% of patients with metastatic GI cancer will experience a substantial and sustained decline in physical function.2–4 Reduced physical function predicts poor quality of life,5 chemotherapy toxicity,6,7 and premature death.8 Despite the importance of preserving physical function in patients with metastatic cancer,9 few therapeutic options exist, and there is no standard of care.10

The decline of physical function may result from the age-related and treatment-related impairments in aerobic capacity,11 ambulatory activity,12,13 and muscle strength and mass.14,15 Randomised controlled trials of older adults without cancer demonstrate that structured physical activity preserves or prevents the deterioration of physical function.16,17 Among patients with early-stage cancer, physical activity increases aerobic capacity,18 ambulatory activity,19 muscle strength and mass,20 and preserves self-reported physical
functioning. However, older adults with cancer have been under-represented in clinical trials, and the evidence establishing the feasibility of physical activity in patients with metastatic cancer receiving chemotherapy remains limited.

This pilot study aimed to determine the feasibility of delivering a 12-week structured physical activity programme to older adults recently diagnosed with metastatic GI cancer. The co-primary endpoints to establish feasibility included: (1) recruitment of 20 participants within 12 months and (2) demonstration that at least 50% of participants adhered to at least 50% of the prescribed physical activity programme.

**MATERIALS AND METHODS**

**Study design**

This pilot and feasibility study used a single-cohort design.

**Participants**

Participants were eligible if they were aged ≥65 years, had a diagnosis of histologically confirmed oesophageal, gastric, pancreatic, or colorectal cancer that was metastatic or locally advanced (unresectable), and initiated first-line cytotoxic chemotherapy within 4 weeks of study enrolment (participants could have received prior therapy if completed >6 months before the start of first-line chemotherapy for metastatic disease). Eligible participants self-reported <150 min per week of physical activity at baseline, had an Eastern Cooperative Oncology Group (ECOG) performance status of 0–2, and at least 50% of participants adhered to at least 50% of the prescribed physical activity programme.

Participants were ineligible if they had known or suspected brain or other central nervous system metastases, uncontrolled cardiac or pulmonary disease, were pregnant or breast feeding, or had any other condition that could impede testing of the study hypothesis, making it unsafe to engage in the physical activity programme, or made the participant not available for end-of-study assessments (determined by the investigatory team).

Under approval of a Health Insurance Portability and Accountability Act (HIPAA) waiver, potentially eligible patients were identified by the study coordinator, who systematically screened all relevant oncology clinic schedules for new or follow-up appointments. The study coordinator contacted the healthcare provider to request permission to approach the patient as patients were identified. After obtaining approval, the study coordinator approached the potential participant during a clinic visit to provide information about the study and complete informed consent.

**Structured physical activity programme**

A certified cancer exercise trainer delivered the structured physical activity programme during chemotherapy infusion appointments (eg, requiring no additional appointments for participation), then translated and sustained at home by participants. The physical activity programme was 12 weeks. The programme included a combination of aerobic, flexibility, strength and balance activities, as used in the Lifestyle Interventions and Independence for Elders (LIFE) clinical trials programme.

The LIFE physical activity programme was tailored to the unique needs of patients with metastatic cancer (table 1). All participants were provided with a pedometer to objectively monitor their aerobic activity and variable ankle weights for strength activity. Physical activity goals were individualised based on each participant’s baseline physical fitness and functional status level. The programme included a weekly goal of 150 min of aerobic activity,
consistent with the Physical Activity Guidelines for Americans.26 Participants completed flexibility activities following each bout of walking. Participants completed lower extremity muscle strengthening exercises (three sets of each exercise for 10 repetitions) using variable weight ankle weights. Balance training was introduced as a complement to the aerobic and strength components. The programme included in-person instruction, home-based activity and telephone behavioural support. On the weeks that chemotherapy was not administered, the exercise trainer phoned the participant to promote exercise adherence, discuss barriers to exercise and review any changes in symptoms due to chemotherapy to develop goals for the following study week. Physical activity goals were modified in response to illness, injury or treatment-related symptoms. The programme was guided by the social cognitive model of behaviour change to improve physical activity self-efficacy, goal setting and outcome expectancy.27

Primary outcome measures
The co-primary endpoints to establish feasibility included: (1) the rate of accrual onto the study protocol and (2) adherence to the physical activity programme. Co-primary study endpoints were selected because the investigators considered the ability to recruit the target population and deliver the intervention equally important to establish feasibility for a larger scale, randomised trial designed to evaluate the efficacy of physical activity on an objectively measured physical function endpoint.

The rate of accrual co-primary endpoint was quantified as the number of days required to enrol 20 participants. The study was required to recruit 20 patients within 12 months. This endpoint was chosen to ensure that an adequate sample size could be expected to be recruited for a larger phase II multicentre trial within the scope of a research project grant programme (eg, 3-year recruitment time horizon).28 29

The adherence to the physical activity programme co-primary endpoint was quantified as the proportion of days the prescribed aerobic, flexibility, strength and balance activities were completed. Adherence was quantified from daily self-reported exercise logs that included documentation of pedometer step counts. To achieve this endpoint, the study was required to demonstrate that at least 50% of participants adhered to at least 50% of the prescribed physical activity programme. This adherence rate was chosen based on the accepted feasibility threshold for early phase clinical trial programmes.30

Secondary outcome measures
Secondary study outcomes were selected to refine and streamline the delivery and implementation of the structured physical activity programme to the target population. The secondary endpoints included: (1) rate of retention, defined as the proportion of participants who completed the study; (2) rate of assessment measure completion, defined as the proportion of participants who completed all physical function and questionnaire data collection (described below); (3) rate of adverse events, defined as the proportion of participants who experience at least one fall, hospitalisation, or musculoskeletal injury that was determined to be possibly, probably, or definitely related to the study. A post hoc descriptive endpoint was the proportion of participants who died during the 12-week study and after study completion.

Other measures
Light-intensity and moderate-intensity to vigorous-intensity physical activity (minutes per week) were quantified using a triaxial waist accelerometer (Actigraph GT3X+) with established intensity thresholds.31 Four days of valid wear with ≥600 min each day were required for analysis. Handgrip strength was quantified using a hydraulic dynamometer (Jamar).32 Aerobic capacity was quantified by the long-distance (400 m) corridor walk.33 Lower extremity function was quantified by the Short Physical Performance Battery (SPPB), a standardised measure that includes walking, balance and strength.34 35 The Medical Outcome Survey Short Form (SF)-36, and Functional Assessment of Cancer Therapy (FACT-G, V.4), were used to quantify the patient-reported health-related quality of life.36 37 Follow-up measures were collected during a chemotherapy infusion visit after the 12-week physical activity intervention. Baseline characteristics, including the type of GI cancer, sites of metastases and ECOG performance status, were obtained from healthcare provider records. Questionnaires developed by the National Center for Health Statistics were used to ascertain demographic characteristics. A validated self-reported questionnaire ascertained adverse events related to physical activity (eg, musculoskeletal injury).38 Overall survival was monitored using the medical record and death registry.

Statistical analysis
A target accrual of 20 participants was selected on what investigators hypothesised to be a reasonable sample size to accrue at a single site over a 1-year time horizon. Twenty participants would provide sufficient data to calculate the rate of accrual onto the study protocol and stable estimates regarding the extent to which participants could adhere to the prescribed physical activity programme. Under the null hypothesis of a 5% recruitment rate, a 25% recruitment rate would provide 79% statistical power for a one-sided test hypothesis test with an alpha error of 10% (eg, a p value less than 0.10 would be declared statistically significant). Under the null hypothesis for a 25% physical activity adherence rate, a 50% adherence rate provides 83% statistical power for a one-sided hypothesis test with an alpha error of 10%. The null hypotheses for both outcomes were set at the point at which investigators would be unwilling to pursue a larger scale trial (eg, 1 in 20 patients who were approached choose to enrol in the study and one-quarter of all prescribed physical activity could be completed). The ability to simultaneously reject
both hypotheses would provide sufficient confidence to move this study into a larger setting designed to evaluate efficacy. Rates and CIs were calculated using the binomial method. Changes in accelerometer-measured physical activity were used as an objective measure to supplement self-reported physical activity logs. All other analyses are descriptive and hypothesis-generating.

Patient and public involvement
No patients or members of the public were involved in the design, conduct, reporting or dissemination plans of our research.

RESULTS
Between March and October 2018, 29 patients were assessed for eligibility and 20 participants were recruited, with primary data collection completed in January 2019. Of the nine patients who were not enrolled, six were ineligible because they were already sufficiently physically active and three reported a general theme of being overwhelmed with their recent diagnosis and unwilling to assume additional demands on their time.

The first co-primary study endpoint to recruit 20 participants within 12 months was met; 29 participants were screened, and 20 were enrolled over 240 days (recruitment rate: 69% (90% CI: 55% to 83%); p<0.001). The median (IQR) time from diagnosis of metastatic cancer to study enrolment was 26 days (14–43), and the physical activity programme was initiated with a median of 10 days (7–14) after study enrolment.

The median age of enrolled participants was 73.3 years (69.3–77.2); six (30%) participants were aged ≥75.0 years (table 2). Participants were most often diagnosed with pancreatic cancer (n=13 (65%)), had liver metastases (n=14 (70%)) and had baseline ECOG performance status of 1 (n=14 (70%)). After enrolment and before providing baseline study measures, two participants withdrew due to declining health (n=1) and transition to hospice care (n=1; figure 1).

Among the 18 participants who provided baseline study measures, the median handgrip strength was 32.5 kg (26.0–36.0), 400-metre walk time was 5.5 min (4.9–6.5), SPPB score was 11 (10–12) and 4-metre gait speed was 1.0 m/s (0.9–1.3), indicating good objectively measured physical function. At baseline, the median SF-36 physical health subscale score was 50.0 (30.6–67.5), mental health subscale score was 47.5 (36.6–57.5) and FACT-G score was 64.0 (33.7–82.5), indicating a good self-reported quality of life.

One participant did not begin the physical activity programme due to declining health (this participant was analysed as having 0% physical activity adherence in the analysis). Two participants transitioned to hospice care after starting the physical activity programme. One participant transitioned care to another health system (these participants were analysed as having 0% physical activity adherence after transitioning out of the study). The second co-primary study endpoint to demonstrate that at least 50% of participants adhered to at least 50% of the prescribed physical activity programme was met; at week 12, 67% (90% CI: 48% to 85%) of participants adhered to at least 50% of the prescribed physical activity

| Characteristic | Median (IQR) or N (%) |
|----------------|-----------------------|

Table 2: Characteristics of study participants (N=20)

| Characteristic | Median (IQR) or N (%) |
|----------------|-----------------------|
| Age            | Continuous, years     |
|                | 73.3 (69.3–77.2)      |
|                | Categorical, %        |
|                | 65.0–74.9             |
|                | 14 (70)               |
|                | ≥75.0                 |
|                | 6 (30)                |
| Sex, %         | Male                  |
|                | 13 (65)               |
|                | Female                |
|                | 7 (35)                |
| Race, %        | White                 |
|                | 17 (85)               |
|                | Black                 |
|                | 2 (10)                |
|                | Other                 |
|                | 1 (5)                 |
| Ethnicity, %   | Non-Hispanic          |
|                | 19 (95)               |
|                | Hispanic              |
|                | 1 (5)                 |
| Type of cancer, % | Pancreatic           |
|                | 13 (65)               |
|                | Oesophageal           |
|                | 3 (15)                |
|                | Gastric               |
|                | 2 (10)                |
|                | Colorectal            |
|                | 2 (10)                |
| Site(s) of metastases, % | Liver         |
|                | 16 (80)               |
|                | Lung                  |
|                | 5 (25)                |
|                | Peritoneum            |
|                | 4 (20)                |
|                | Other                 |
|                | 2 (10)                |
| ECOG performance status, % | 0            |
|                | 3 (15)                |
|                | 1                     |
|                | 14 (70)               |
|                | 2                     |
|                | 2 (10)                |
|                | Not available         |
|                | 1 (5)                 |
| Handgrip strength, kg          |
|                | 32.5 (26.0–36.0)      |
| 400 m walk time, min           |
|                | 5.5 (4.9–6.5)         |
| SPPB total score, 0–12         |
|                | 11 (10–12)            |
| 4 m gait speed, m/s            |
|                | 1.0 (0.9–1.3)         |
| SF-36 quality of life, 0–100   |
|                | 5.0 (30.6–67.5)       |
| Physical health subscale       |
|                | 50.0 (30.6–67.5)      |
| Mental health subscale         |
|                | 47.5 (36.6–57.5)      |
| FACT-G, 0–100                 |
|                | 64.0 (33.7–82.5)      |

ECOG, Eastern Cooperative Oncology Group; FACT-G, Functional Assessment of Cancer Therapy; SF-36, Medical Outcome Survey Short Form; SPPB, Short Physical Performance Battery.
programme (p=0.079 (statistically significant); figure 2).

From baseline to week 12, light-intensity physical activity increased by 307.4 min per week (95% CI: 152.6 to 462.2; p<0.001) and moderate-intensity to vigorous-intensity physical activity increased by 25.0 min per week (95% CI: 9.9 to 40.1; p=0.001; table 3).

The retention rate at week 12 was 78% (90% CI: 62% to 94%). Among participants retained at week 12, the rate of assessment measure completion was 100%. From baseline to week 12, we observed a non-significant decline in handgrip strength (−2.6 kg (95% CI: −5.7 to 0.4)), but 400-metre walk time (−0.01 min (95% CI: −0.1 to 0.1)), SPPB score (−0.1 points (95% CI: −3.3 to 3.1)) and gait speed (−0.02 m/s (95% CI: −0.13 to 0.09)) remained stable. The SF-36 physical health subscale score modestly but non-significantly declined (−3.4 points (95% CI: −9.6 to 2.7)), whereas the mental health subscale score modestly but non-significantly increased (7.8 (95% CI: −1.7 to 17.3)); the FACT-G score declined on average, but variation was wide (−4.4 (95% CI: −20.5 to 11.6)).

There were no adverse events that were determined to be considered by the medical investigator as definitely, probably or possibly related to the study. No participants died during the 12-week intervention. The median overall survival was 16.2 months (8.4–22.4); 70% of participants were alive at 12 months (figure 3).

**DISCUSSION**

The co-primary endpoints of this pilot and feasibility study of physical activity for older adults with metastatic GI cancer were met. Twenty participants were recruited within 12 months and at least 50% of participants adhered to at least 50% of the prescribed physical activity programme. In addition, the accelerometer-measured light-intensity and moderate-intensity to vigorous-intensity physical activity increased by 307 and 25 min per week, respectively. No unexpected or serious safety signals were identified, and no participants died during the 12-week intervention. This pilot and feasibility study provides critical foundational data to inform a randomised trial designed to evaluate the efficacy of physical activity on an objectively measured physical function endpoint.

The population of older adults with metastatic GI cancer face dual challenges: (1) the decline in physiological reserve due to both metastatic cancer and ageing; and (2) the toxicities from treatment. The unfavourable synergy from ageing with cancer and chemotherapy—a double hit to key physiological systems—manifests as accelerated declines in function. We hypothesise that the deterioration of physical function in patients with cancer is from age-related and cancer treatment-accelerated declines in aerobic capacity, ambulatory activity, and muscle strength and mass. Supporting this hypothesis is the observation that patients with cancer have a lower aerobic capacity, ambulatory activity, muscle strength and muscle mass, compared with matched control participants who do not have a history of cancer.

Examining the feasibility of a structured physical activity programme in older adults with metastatic GI cancer was motivated by the observation that participation in physical activity is one of the strongest predictors of physical function among older adults without cancer. Physical functions, such as walking or locomotion, have been a primary emphasis of natural selection throughout human evolution. This has resulted in redundant sets of physiological systems—including the cardiovascular, pulmonary, neurological and musculoskeletal—that work in conjunction to enable physical function. When
one physiological system becomes compromised, other systems compensate. Consequently, declines in physical function become clinically evident only when this extensive network of physiological reserves becomes depleted, and other compensatory systems have failed. This decline in physical function erodes quality of life, which constrains opportunities to receive additional life-sustaining therapies and consequently increases the risk of death. We have proposed physical function as a biomarker that synchronously describes the performance and coordination of various physiological systems that may be impaired because of ageing and cancer treatment.

The increase of 307 min per week light-intensity physical activity and 25 min per week of moderate-intensity to vigorous-intensity physical activity may be clinically valuable. Higher volumes of light-intensity physical activity are associated with a reduced risk of developing mobility disability among older adults. Moderate-intensity to vigorous-intensity physical activity is associated with dose-dependent changes in the SPPB and gait speed, and relatively small increases (~48 min per week) in moderate-intensity to vigorous-intensity physical activity are associated with meaningful reductions in the risk of major mobility disability. In a meta-analysis of 11 studies, higher volumes of light-intensity physical activity were associated with a lower risk of death, independently of the volume of moderate-intensity and vigorous-intensity physical activity. It is important to recognise that accelerometer-defined light-intensity physical activity may be consistent with the energy expenditure of moderate or vigorous-intensity physical activity in older adults.

Recently introduced treatment options for patients with metastatic GI cancers have significantly extended overall survival. Among patients with metastatic colorectal cancer, overall survival has improved threefold in the past 20 years. Among patients with metastatic pancreatic cancer, a chemotherapy regimen consisting of oxaliplatin, irinotecan, fluorouracil and leucovorin compared with gemcitabine as first-line therapy improves overall survival by 40%. Among patients with metastatic gastric cancer, a combination of nivolumab and chemotherapy compared with chemotherapy alone as first-line therapy improves overall survival by 30%. This has created an opportunity to develop interventions that prevent the loss of physical function to maximise quality of life while patients receive life-prolonging therapy.

There are limitations to this study. The principal limitation is the small sample size of recruited participants from a single cancer centre. It is possible that the participants who chose to enrol in this study were not like patients who did not enrol. The intervention length was limited to 12 weeks, which precludes our ability to comment on the ability of participants to adhere to this programme over a longer time horizon. Our study was not designed with the intent of conducting extensive null hypothesis significance testing on study outcome measures.

There are strengths to this study. This study successfully recruited older adults, who are often under-represented in clinical trials. Moreover, study participants had a variety of GI malignancies, such as pancreatic cancer, which are less commonly studied in the context of lifestyle modification trials. This study used an evidence-based physical activity programme that has been proven efficacious in preventing a functional decline in healthy older adults. The physical activity programme was tailored to the unique needs of patients with metastatic cancer. The physical activity programme required minimal equipment and was predominately home based in a manner that could be broadly disseminated in a nationwide trial. Moreover, during the COVID-19 pandemic, virtual physical functioning assessments were validated for cancer survivors, and the implementation of these methods may improve the accessibility of clinical trials to older adults.

**CONCLUSION**

Prolonging the overall survival of patients with metastatic GI cancer is an important clinical objective.
However, of even greater importance is that extensions in overall survival include a preserved capacity to live independently and function well. Upon commencing life-sustaining chemotherapy, many older adults with metastatic GI cancer experience precipitous declines in physical function. Despite the importance of preserving physical function in this vulnerable population, few therapeutic options exist. Preventing physical function decline is an important goal in providing evidence-based, patient-oriented, geriatric palliative cancer care. The results from this study establish the feasibility of a larger scale randomised controlled trial that recruits older adults with metastatic GI cancer and delivers a structured physical activity programme during chemotherapy.

Acknowledgements We thank Melissa Harris, Phillip Nauta and Harrison Travis for assistance with accelerometer data curation and analysis.

Contributors JCB and JAM contributed to conceptualisation and project planning. JCB, EB and JAM had full access to the data in the study and take responsibility for the integrity and accuracy of the data analysis. All authors performed interpretation of data. All authors contributed significantly to the writing of this paper. All authors have read and approved the final version of the manuscript to be submitted. JCB is responsible for the overall content as the guarantor of this report.

Funding This work was supported by the National Cancer Institute of the National Institutes of Health under Award Number R00-CA218603; the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health under Award Number P30-DK072476; and the National Institute of General Medicine Sciences of the National Institutes of Health under Award Number U54-GM104940.

Competing interests JCB reported receiving grants from the National Institutes of Health and the American Institute for Cancer Research. JCB reported research funding to his institution from Merus, Roche and Bristol Myers Squibb; he reported research funding from Merck, AstraZeneca, Esperas Pharma, Bayer and Tesaro; he reported honorarium for being on the advisory board of Syros Pharmaceuticals and Blueprint Medicines. MY reported receiving grants from Janssen Pharmaceuticals and personal fees from UpToDate for peer review services. JM reported receiving personal fees from Taiho for grant review for the National Comprehensive Cancer Network, fees for serving on the advisory boards of COTA Healthcare and Ignyta Single, and institutional support from Boston Biomedical for a clinical trial outside the submitted work.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The study was conducted following Good Clinical Practice and the ethical principles in the Declaration of Helsinki. The study protocol and informed consent document were reviewed and approved by the Institutional Review Board of Dana-Farber/Harvard Cancer Center (protocol #17.350) before engaging in study-related activities. All participants provided written informed consent and received approval from their qualified healthcare provider to enrol in the study.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/.

ORCID iD Justin C Brown http://orcid.org/0000-0001-7540-4913

REFERENCES

1. Parry C, Kent EE, Mariotto AB, et al. Cancer survivors: a booming population. Cancer Epidemiol Biomarkers Prev 2011;20:1996–2005.
2. Bonnetain F, Dahan L, Maillard E, et al. Time until definitive quality of life score deterioration as a means of longitudinal analysis for treatment trials in patients with metastatic pancreatic adenocarcinoma. Eur J Cancer 2010;46:2753–62.
3. Hamidou Z, Chibaudel B, Hebbard M, et al. Time to definitive health-related quality of life score deterioration in patients with resectable metastatic colorectal cancer treated with FOLFIRI versus sequential dose–dense FOLFOX7 followed by FOLIRI: the MIROX randomized phase III trial. PLoS One 2016;11:e0157067.
4. Quach C, Sanoff HK, Williams GR, et al. Impact of colorectal cancer diagnosis and treatment on health-related quality of life among older Americans: a population-based, case-control study. Cancer 2015;121:943–50.
5. Kluetz PG, Slagle A, Papadopoulos EJ, et al. Focusing on core patient-reported outcomes in cancer clinical trials: symptomatic adverse events, physical function, and disease-related symptoms. Clin Cancer Res 2016;22:1555–63.
6. Hurria A, Togawa K, Mohile SG, et al. Predicting chemotherapy toxicity in older adults with cancer: a prospective multicenter study. JCO 2011;29:3367–76.
7. Quinten C, Coens C, Mauer M, et al. Baseline quality of life as a prognostic indicator of survival: a meta-analysis of individual patient data from EORTC clinical trials. Lancet Oncol 2009;10:865–71.
8. van Abbema DL, van den Akker M, Janssen-Heijnen ML, et al. Patient- and tumor-related predictors of chemotherapy intolerance in older patients with cancer: a systematic review. J Geriatr Oncol 2019;10:31–41.
9. Burg MA, Adorno G, Lopez EDS, et al. Current unmet needs of cancer survivors: analysis of opened-ended responses to the American cancer society study of cancer survivors II. Cancer 2015;121:623–30.
10. Jones LW, Eves ND, Haykowski M, et al. Exercise intolerance in cancer and the role of exercise therapy to reverse dysfunction. Lancet Oncol 2009;10:598–605.
11. Innominato PF, Focan C, Gorlia T, et al. Circadian rhythm in rest and activity: a biological correlate of quality of life and a predictor of survival in patients with metastatic colorectal cancer. Cancer Res 2009;69:4700–7.
12. Mornmont MC, Waterhouse J, Bleuzen P, et al. Marked 24-h rest/activity rhythms are associated with better quality of life, better response, and longer survival in patients with metastatic colorectal cancer and good performance status. Clin Cancer Res 2000;6:3038–45.
13. Christensen JF, Jones LW, Andersen JL, et al. Muscle dysfunction in cancer patients. Ann Oncol 2014;25:947–58.
14. Martin L, Birdsell L, MacDonald N, et al. Cancer cachexia in the age of obesity: skeletal muscle depletion is a powerful prognostic factor, independent of body mass index. JCO 2013;31:1539–47.
15. LIFE Study Investigators, Pahor M, Blair SN, et al. Effects of a physical activity intervention on measures of physical performance: results of the lifestyle interventions and independence for elders pilot (LIFE-P) study. J Gerontol A Biol Sci Med Sci 2006;61:1157–65.
16. Pahor M, Guralnik JM, Ambrosius WT, et al. Effect of structured physical activity on prevention of major mobility disability in older adults: the life study randomized clinical trial. JAMA 2014;311:2387–96.
17. Jones LW, Liang Y, Pituskin EN, et al. Effect of exercise training on peak oxygen consumption in patients with cancer: a meta-analysis. Oncologist 2011;16:112–20.
18. Spence RR, Heesich KC, Brown WJ. Exercise and cancer rehabilitation: a systematic review. Cancer Treat Rev 2010;36:185–94.
19. Steine GB, Helbstoad JL, Balstad TR, et al. Effect of physical exercise on muscle mass and strength in cancer patients during treatment—A systematic review. Crit Rev Oncol Hematol 2013;88:573–93.
20. Mishra SI, Scherer RW, Geijle PM, et al. Exercise interventions on health-related quality of life for cancer survivors. Cochrane Database Syst Rev 2012;CD007566.
21. Mishra SI, Scherer RW, Snyder C, et al. Exercise interventions on health-related quality of life for people with cancer during active treatment. Cochrane Database Syst Rev 2012:390–2.
22. Wilk M, Kepska J, Kepska J, et al. Exercise interventions in metastatic cancer disease: a literature review and a brief discussion.
on current and future perspectives. BMJ Support Palliat Care 2020;10:404–10.
24 Mikkelsen MK, Juhl CB, Lund CM, et al. The effect of exercise-based interventions on health-related quality of life and physical function in older patients with cancer receiving medical antineoplastic treatments: a systematic review. Eur Rev Aging Phys Act 2020;17:18.
25 Paffenbarger R, Wing A, Hyde R. Paffenbarger physical activity questionnaire. Am J Epidemiol 1978;108:161–75.
26 Piercy KL, Troiano RP, Bouchard C. The physical activity guidelines for Americans. JAMA 2018;320:2000–8.
27 Glanz K, Rimer BK, Viswanath K. Health behavior and health education: theory, research, and practice. John Wiley & Sons, 2008.
28 Moore CG, Carter RE, Niswander PJ, et al. Recommendations for planning pilot studies in clinical and translational research. Clin Transl Sci 2011;4:332–7.
29 Julious SA. Sample size of 12 per group rule of thumb for a pilot study. Pharm Stat 2005;4:287–91.
30 Gupta A, Stewart T, Bhandari N, et al. Feasibility of wearable physical activity monitors in patients with cancer. JCO Clin Cancer Inform 2018;2:1–10.
31 Troiano RP, Berrigan D, Dodd KW, et al. Physical activity in the United States measured by accelerometer. Med Sci Sports Exerc 2008;40:181–8.
32 Rogers BH, Brown JC, Gater DR, et al. Association between maximal bench press strength and isometric handgrip strength among breast cancer survivors. Arch Phys Med Rehabil 2017;98:264–9.
33 Nienhuis AB, Simonsick EM, Naydeck BL, et al. Association of long-distance corridor walk performance with mortality, cardiovascular disease, mobility limitation, and disability. JAMA 2006;295:2018–26.
34 Gurin JM, Ferrucci L, Simonsick EM, et al. Lower-Extremity function in persons over the age of 70 years as a predictor of subsequent disease. N Eng J Med Overseas Ed 1995;332:556–62.
35 Gurin JM, Simonsick EM, Ferrucci L, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol 1994;49:M85–94.
36 Ware JE, Kosinski M, Bayliis MS, et al. Comparison of methods for the scoring and statistical analysis of SF-36 health profile and summary measures: summary of results from the medical outcomes study. Med Care 1995;33:AS264–79.
37 Cella DF, Tuleyky DS, Gray G, et al. The functional assessment of cancer therapy scale: development and validation of the general measure. J Clin Oncol 1993;11:570–9.
38 Brown JC, Troxel AB, Schmitz KH. Safety of weightlifting among women with or at risk for breast cancer-related lymphedema: musculoskeletal injuries and health care use in a weightlifting rehabilitation trial. Oncologist 2012;17:1120–8.
39 Blyth CR, Still HA. Binomial confidence intervals. Br J Cancer 2005;11:449–60.
40 Sehl M, Sawhney R, Naeim A. Physiologic aspects of aging: impact on cancer management and decision making, part I. Cancer J 2005;11:449–60.
41 Sehl M, Sawhney R, Naeim A. Physiologic aspects of aging: impact on cancer management and decision making, part II. Cancer J 2005;11:461–73.
42 Petrick JL, Foraker RE, Kucharska-Newton AM, et al. Trajectory of overall health from self-report and factors contributing to health declines among cancer survivors. Cancer Causes Control 2014;25:1179–86.
43 Petrick JL, Reeve BB, Kucharska-Newton AM, et al. Functional status declines among cancer survivors: trajectory and contributing factors. J Geriatr Oncol 2014;5:359–67.
44 Jones LW, Courneya KS, Mackey JR, et al. Cardiopulmonary function and age-related decline across the breast cancer survivorship continuum. JCO 2012;30:2530–7.
45 McDonald L, Oguz M, Carroll R, et al. Comparison of accelerometer-derived physical activity levels between individuals with and without cancer: a UK Biobank study. Future Oncol 2019;15:3763–74.
46 Winters-Stone KM, Medysky ME, Savin MA. Patient-Reported and objectively measured physical function in older breast cancer survivors and cancer-free controls. J Geriatr Oncol 2019;10:311–6.
47 Bernabeu-Wittell M, Gonzalez-Molina Alvaro, Fernández-Ojeda R, et al. Impact of sarcopenia and frailty in a multicenter cohort of Polypathological patients. JCM 2019;8:535.
48 Buchner DM, Beresford SA, Larson EB, et al. Effects of physical activity on health status in older adults. II. intervention studies. Ann Rev Public Health 1992;13:469–88.
49 Wagner EH, LaCroix AZ, Buchner DM, et al. Effects of physical activity on health status in older adults. I: observational studies. Ann Rev Public Health 1992;13:451–68.
50 Dickinson MH, Farley CT, Full RJ, et al. How animals move: an integrative view. Science 2000;288:100–6.
51 Ferrucci L, Bandinelli S, Buxenutti E, et al. Subsystems contributing to the decline in ability to walk: bridging the gap between epidemiology and geriatric practice in the InCHIANTI study. J Am Geriatr Soc 2000;48:1618–25.
52 Chou LS, Draganchic LF. Stepping over an obstacle increases the motions and moments of the joints of the trailing limb in young adults. J Biomech 1997;30:331–7.
53 Brown JC, Harhay MO, Harhay MN. Physical function as a prognostic biomarker among cancer survivors. Br J Cancer 2015;112:194–8.
54 Fanning J, Rejeski WJ, Chen S-H, et al. Relationships between profiles of physical activity and major mobility disability in the life study. J Am Geriatr Soc 2020;68:1478–83.
55 Fielding RA, Guralnik JM, King AC, et al. Dose of physical activity, physical functioning and disability risk in mobility-limited older adults: results from the life study randomized trial. PLoS One 2017;12:e0182155.
56 Ku P-W, Hamer M, Liao Y, et al. Device-measured Light-intensity physical activity and mortality: a meta-analysis. Scand J Med Sci Sports 2020;30:13–24.
57 Barnett A, van den Hoek D, Barnett D, et al. Measuring moderate-intensity walking in older adults using the ActiGraph accelerometer. BMC Geriatr 2016;16:211.
58 Venook AP, Niedzwiedzi D, Lenz H-J, et al. Effect of First-Line Chemotherapy Combined With Cetuximab or Bevacizumab on Overall Survival in Patients With KRAS Wild-Type Advanced or Metastatic Colorectal Cancer. JAMA 2017;317:2392–401.
59 Conroy T, Desseigne F, Ychou M, et al. Folfirinox versus gemcitabine for metastatic pancreatic cancer. N Engl J Med 2011;364:1817–25.
60 Janjigian YY, Shitara K, Moehler M, et al. First-Line nivolumab plus chemotherapy versus chemotherapy alone for advanced gastric, gastro-oesophageal junction, and oesophageal adenocarcinoma (CheckMate 649): a randomised, open-label, phase 3 trial. Lancet 2021;398:27–40.
61 Langbaum T, Smith TJ. Time to study Metastatic-Cancer survivorship. N Engl J Med 2019;380:1300–2.
62 Guidarelli C, Lippin C, Stoyles S, et al. Remote administration of physical performance tests among persons with and without a cancer history: establishing reliability and agreement with in-person assessment. J Geriatr Oncol 2022. doi:10.1016/j.jgo.2022.02.002. [Epub ahead of print: 14 Feb 2022].
63 Pekmezci D, Fontaine K, Rogers LJ, et al. Adapting multiple behavior interventions that effectivity improve (AMPLIFY) cancer Survivor health: program project protocols for remote lifestyle intervention and assessment in 3 inter-related randomized controlled trials among survivors of obesity-related cancers. BMC Cancer 2022;22:471.