

Is exercise really safe, feasible, and effective for all people diagnosed with cancer? (Letter)

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TITLE: Is exercise really safe, feasible and effective for all people diagnosed with cancer?

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Over the past 20 years, a consistent and ever-growing evidence base has demonstrated the benefits of physical activity, including through planned, purposeful, regular exercise. Benefits to functional, psychosocial and quality of life outcomes have been identified for physical activity and exercise pre-, during and following treatment for cancer. Over the past 5 years, high quality observational evidence suggests that physical activity post-cancer may also improve survival outcomes. While the mechanisms through which physical activity influences health and survival outcomes remain poorly understood, emerging findings from epigenetic studies, including a recent study published in the Asia Pacific Journal of Clinical Oncology involving colorectal cancer patients, suggest that physical activity may influence gene expression¹.

Together, this evidence base has led to recommendations by oncology associations for *all* people with cancer to be regularly physically active, including participation in at least 150 minutes of mixed mode (aerobic and resistance exercise), moderate intensity exercise each week². Yet, when the evidence is scrutinised, it is clear that recommendations are largely derived from studying cancer types with 5-year survival rates typically equal to, or higher than the 69% 5-year survival rate for all-cancers combined. Cancer types with poorer prognosis are associated with later stage at diagnosis, more invasive/intensive treatment and more severe treatment-related side effects; factors which may influence exercise safety, feasibility and efficacy. As such, it is reasonable to question whether these recommendations are truly appropriate for *all* people with cancer *or* instead are only appropriate (at least, at this point in time) for *certain cancer types*.

We therefore compared the results of two independent, published meta-analyses prospectively registered on PROSPERO, which were conducted to assess the safety, feasibility and effects of exercise following colorectal cancer (CRC)³ and lung cancer (LC)⁴, and recently

presented the findings at the Clinical Oncology Society of Australia 47th Annual Scientific Meeting⁵. These two cancers represent the top five most common cancers diagnosed in Australia. CRC has excellent 5-year survival rate, while LC is associated with a lower survival rate (18%). The meta-analyses evaluated AEs between exercise and usual care (risk difference; RD), and effects of exercise on health outcomes (standardised mean difference; SMD).

The reviews include 19 (n=1293) CRC and 32 LC (n=2109) trials, respectively. Exercise-related AE risk was similar between the cancer types and was low (CRC: RD=0.00, p=0.92; LC: RD=-0.01, p=0.31). Feasibility was also similar between CRC and LC, although favoured CRC slightly (median withdrawal rate for CRC and LC: 12% (0-22%) and 14% (0-50%); adherence rate: 86% (42-91%) and 80% (44-100%), respectively). However, median recruitment rate was lower for CRC than LC (38% versus 59%). Compared with usual care, meaningful benefits of exercise (p<0.05) were observed in both cancers for quality of life (SMD: CRC=0.21; LC=0.31), aerobic fitness (SMD: CRC=0.57; LC=0.54), strength (SMD: CRC=0.39; LC=0.59), depression (SMD: CRC=0.35; LC=0.49) and sleep (SMD: CRC=0.66; LC=0.31; Table 1). The meta-analyses reported significant limitations, including the generally poor reporting of safety outcomes, questionable representativeness of samples studied (e.g., participants tended to be more well) and that the tightly controlled environment under which exercise is typically evaluated may not reflect real-world practice. Nonetheless, the similarity of results among such diverse cancer groups with different treatment pathways, treatment-related side effect profiles and prognoses suggest exercise as a beneficial adjunct to treatment. Future research will determine whether similar findings are derived from studies that evaluate more rare cancer types or subtypes, complex patients such as those with multiple comorbidities, or pragmatic interventions. In the meantime, these findings suggest that although it's relevant to remain cautious and cognisant of the current limitations of exercise oncology research, promotion of physical activity to cancer patients and incorporation of targeted exercise into cancer care will likely lead to improved health outcomes post-cancer, irrespective of prognosis.

Table 1. Overview of meta-analysis results for lung and colorectal cancer trials.

	Lung cancer (n=32 RCTs) ^a	Colorectal cancer (n=19 RCTs) ^b
Quality of life	✓	✓
Fatigue	-	✓
Aerobic fitness	✓	✓
Upper-body strength	✓	✓
Lower-body strength	✓	-

Anxiety	✓	✓
Depression	✓	✓
Sleep	✓	✓
FEV1	✓	?
Dyspnea	-	?
Pain	-	?
Length of hospital stay	-	?
Body fat	-	✓

a: sample size range, 14-235; age of participants, mean 64±3; 3 trials with stage I-II, 7 trials with stages III-IV, 22 trials with stages I-IV; timing of intervention: pre-surgery (n=12), post-surgery (n=20)

b: sample size range, 18-284; age of participants, mean 65±7; only one trial included patients with IV disease; timing of intervention: pre-surgery (n=4), during chemotherapy (n=5), post-treatment (n=10)

✓ : SMD range = 0.21 to 0.66; all p<0.05

- : SMD ≤0.21 and not supported statistically (p>0.05)

?: not sufficiently assessed for inclusion in meta-analysis

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