## BJC

British Journal of Cancer (2014) 110, 829–830 | doi: 10.1038/bjc.2014.12

## Promoting exercise after a cancer diagnosis: easier said than done

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There is a clear need to better understand the risks associated with the development and progression of cancer in order to design effective primary and secondary prevention strategies. However, it is important to remember that we have solid evidence supporting the putative relationship between certain common behaviours or conditions with risk, and therefore, specific interventions that modify these behaviours/conditions could be helpful. Certainly tobacco control represents a partial victory in the area of behavioural modification to lower the risk of many pathological conditions, including several types of cancer, and vaccines and medications can also prevent cancer but these rely on a traditional medical treatment-based approach. A closely related area focuses on other (non-tobacco) modifiable risk factors for the prevention of recurrence in curatively treated malignancies. In that regard, emerging evidence indicates that regular aerobic (endurance) exercise is associated with significant reductions in recurrence and cancer-specific mortality in patients with early breast, prostate, and colorectal cancers (Betof et al, 2013). If real, this suggests that there are a far greater number of factors that can influence tumour progression than just the genomic abnormalities, the major focus of current oncology research efforts. This means that research must also extend to the 'soil' (as opposed to the 'seed') in terms of metastasis and disease progression. That one intervention could potentially benefit so many different solid tumours suggests an overall pathophysiological effect on the host and multiple organ systems with nearly universal interactions despite the evidence that many cancers have diverse causation and molecular biology. Although scientifically challenging, the hypothesised mechanistic properties of aerobic exercise to inhibit recurrence appear biologically plausible (National Cancer Institute, 2013). As such, given the cost-effectiveness of this strategy, research to elucidate the effects, mechanism, and optimal biologically effective dose in conjunction with research on how to effectively promote, deliver, and maintain exercise would be a prudent investment.

Related to exercise, obesity is a growing public health problem in most Western countries and, increasingly, throughout the world including middle- and low-income nations. The factors behind this unprecedented change in public health are myriad and include easier access to high-calorie, inexpensive food, possibly, changes in the nutritional content/composition of our diets, and increasingly sedentary lifestyles. Regardless of the cause, it is now clear that obesity and overweight are associated with increased risks of several of the most prevalent cancers, including breast (hormone receptor positive and triple negative), colon, high-grade prostate, and some non-Hodgkin's lymphomas among others. Recently, the NIH estimated that overweight and obesity would replace tobacco as the leading modifiable risk factor for cancer in Americans (Rock *et al*, 2012).

While our group and many others seek a deeper understanding of why this relationship exists, on a practical level the solution would seem to be simple: eat less and exercise more. This would move our patients into a more favourable energy balance state and should lower a multitude of health risks. However, as any clinician can report, this is far easier said than done and the experience with weight loss interventions of all types can be broadly summarised as showing some limited successes and a lot of frustration. It is, however, important to note that even modest weight loss, despite, in some circumstances, leaving a patient well above the threshold for obesity, can nonetheless yield physiological and presumed (and demonstrated in some cases) cancer-specific benefits.

The question remains: what can we do to effectively manage weight in our patients? Given the growing ease with which we now can become obese and the challenges associated with maintenance of a healthier weight and energy balance, what effective and evidence-based interventions for exercise behaviour (and possibly weight loss) can we endorse for our patients?

A recent issue of the *British Journal of Cancer* contains a Cochrane analysis of randomised trials of behaviour change strategies designed to promote exercise behaviour in cancer patients defined as sedentary (i.e., conducting  $\leq 30$  mins of self-reported aerobic exercise three times per week) (Bourke *et al*, 2014). A total of 14 RCTs met the eligibility criteria involving a total of 648 patients, mostly early breast cancer survivors. In terms of exercise behaviour change, the authors operationalised 'success' in which the



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behavioural intervention was able to achieve at least 75% adherence to the study-defined goal or 75% of the current national exercise guidelines (Blair *et al*, 2004).

Findings indicated that no studies reported that  $\geq$ 75% of participants assigned to a behavioural intervention were able to achieve the current national guidelines. However, contrary to this finding, seven trials found that exercise tolerance, an objective measure of exercise exposure, significantly increased in patients randomised to a behavioural intervention compared with usual care. The change in exercise behaviour as a continuous variable (e.g., delta change in total minutes of exercise behaviour) was not reported. It was concluded that there is currently a lack of convincing evidence that behavioural interventions can promote exercise behaviour in accordance with the current national guideline recommendations for cancer patients. Although achieving such threshold guidelines is an obvious and important goal for all individuals, not just cancer patients, it is important to remember that a dose-response relationship exists. Of particular importance, large clinically meaningful reductions in disease risk are achieved when moving from the least active (or low fitness) group to a moderately active (fit) group. In other words, only small changes in exercise behaviour may be required in sedentary individuals to produce meaningful reductions in disease recurrence or risk of other chronic diseases (Blair et al, 2004). To this end, other RCTs (not included in the review by Bourke et al, 2014) have found that behavioural interventions incorporating telephone-based, printbased, or oncologist-based approaches can promote significant favourable changes in exercise behaviour levels in the magnitude of  $\sim$  30–60 mins per week in non-sedentary cancer patients (Vallance et al, 2007; Hawkes et al, 2013). In support of this notion, the improvements in measures of exercise tolerance (fitness) reported by Bourke et al may also be clinically important, given work by our group showing that exercise tolerance is a strong independent predictor of all-cause mortality in patients with non-small cell lung cancer and metastatic breast cancer (Jones et al, 2010, 2012a,b).

Nevertheless, the review by Bourke et al serves as an important reminder of the significant research gaps and challenges to promoting exercise or other health behaviour changes in cancer patients. First, Bourke et al identified only 14 RCTs that examined the effectiveness of behavioural strategies to promote exercise in an 'at-risk' population (i.e., sedentary individuals). Second, as noted by the authors, there was considerable heterogeneity and lack of standardised measures between studies, making cross-study comparisons challenging. Third, as in studies examining the effects of structured exercise training interventions in cancer patients, the vast majority of work in exercise promotion has been conducted in early breast cancer patients. Clearly, there is a need for work beyond breast cancer. Fifth, an important long-term goal will be to determine the long-term clinical importance of the observed changes in exercise behaviour. For example, how does a change in a certain number of minutes of exercise per week correlate with change in harder outcomes such as cardiovascular risk profile or even recurrence risk?

We face a quiet crisis. Inactivity, overweight, obesity, and its resulting physiological effects represent an unprecedented public health challenge driving a range of morbidities including diabetes, hypertension, vascular disease, arthritis, and many others including cancer. Slowing or reversing this problem is going to be a major challenge and one that will require close collaboration with several professional groups covering all of human health, not just cancer, concerted public education, realignment of financial incentives in the food industry driven by public and tax policies, and, as highlighted by this Cochrane Review, consistent adherence to the highest standards of scientific methodology while we test interventions. Finally, it is clear that one size does not fit all—there is an urgent need to examine the efficacy of intervention approaches that can be tailored to the individual patient needs, are scalable, and can be delivered in a cost-effective manner so that we test and support interventions like diet and exercise where they will be the most efficacious.

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