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Tackling the adverse health effects of excess body fat in breast cancer: where does physical activity fit in?

JM Saxton¹* o and C Wilson²

¹School of Sport, Exercise & Rehabilitation Sciences, Faculty of Health Sciences, University of Hull,
Cottingham Road, Hull HU6 7RX, UK

²Department of Oncology and Metabolism, The Medical School, University of Sheffield, Beech Hill Road,
Sheffield S10 2RX, UK

Weight gain is commonly observed during and after breast cancer treatment due to chemotherapy and endocrine therapies, induced menopause, changes in metabolism and food intake and decreased physical activity. Systematic reviews show that women who are overweight or obese at diagnosis, and those who gain weight, have poorer breast cancer survival outcomes than women of a healthy weight, irrespective of menopausal status. Excess body weight after breast cancer also increases the risk of type 2 diabetes mellitus and CVD. The adverse impact of excess body weight on survival outcomes is clearly shown for women with oestrogen receptor-positive (ER+) breast cancer, which accounts for 70 % of all breast cancer cases. Higher body fat is thought to increase the risk of ER+ recurrence because of increased aromatase activity. However, this could be compounded by other risk factors, including abnormal insulin and adipokine metabolism, impaired anti-tumour immunity and chronic low-grade systemic inflammation. Observational evidence linking poorer survival outcomes with excess body fat and low physical activity in women recovering from early-stage curative-intent breast cancer treatment is reviewed, before reflecting on the proposed biological mechanisms. The issues and sensitivities surrounding exercise participation amongst overweight breast cancer patients is also discussed, before providing an overview of the co-design process involved in development of an intervention (support programme) with appropriate content, structure and delivery model to address the weight management challenges faced by overweight ER+ breast cancer patients.

Breast cancer: Weight gain: Diet: Exercise: Co-design

Excess body fat and impact on health outcomes in breast cancer

Published studies show that approximately two-thirds of women have excess body weight (overweight or obesity) at breast cancer diagnosis⁽¹⁻³⁾. Furthermore, significant weight gain is frequently observed during

and after breast cancer management and this has been linked to chemotherapy treatment, being (or becoming) postmenopausal after diagnosis, changes in metabolism and food intake and decreased activity levels^(4–7). Systematic review evidence shows that women who are overweight/obese at breast cancer diagnosis, and those who gain weight, have poorer breast cancer and overall

Abbreviations: ER+, oestrogen receptor-positive; PA, physical activity. *Corresponding author: John Saxton, email john.saxton@hull.ac.uk



survival outcomes than healthy weight women, irrespective of menopausal status^(8–10). Excess body weight also increases the risk of type 2 diabetes mellitus, CVD^(11,12) and CVD mortality in breast cancer survivors⁽¹³⁾ and is linked to the primary occurrence of 12 other cancers⁽¹⁴⁾.

The adverse impact of excess body weight on postdiagnosis survival outcomes is clearly shown for women with oestrogen receptor-positive (ER+) disease^(15,16), which accounts for 70% of all incident cases⁽¹⁷⁾. Higher body fat increases the risk of ER+ recurrence because of increased aromatase activity and circulating levels of oestrogens and androgens (18). This is compounded by other risk factors, including abnormal insulin and adipokine metabolism, impaired anti-tumour immunity and chronic low-grade systemic inflamma $tion^{(6,15)}$. However, the adverse health impact of excess body weight after primary treatment extends beyond poorer survival outcomes, as overweight/obese ER+ breast cancer patients who gain weight after diagnosis (≥5% increase) are also reported to have poorer health-related quality of life and higher levels of cancerrelated fatigue in comparison with women who maintain a stable body weight⁽¹⁹⁾. Although associations between intentional weight loss and survival outcomes in overweight/obese women recovering from primary breast cancer treatment are (as yet) less well established (20), considered together, this evidence provides a strong rationale for the development and evaluation of interventions that can provide the support women need to manage body weight after primary treatment for early-stage ER+ breast cancer⁽²¹⁾.

Physical activity after breast cancer treatment

Published meta-analyses show that a physically active lifestyle after early-stage breast cancer treatment is associated with improved survival outcomes and reduced risk of developing type 2 diabetes mellitus^(12,22-24). Furthermore, evidence suggests that these survival benefits can be gained from achievable levels of physical activity (PA) or structured exercise (i.e. consistent with current public health recommendations of ≥150 min/week of moderate-intensity aerobic activity)(23,25), and with indications of a stronger mortality reduction for overweight and obese women⁽²²⁾. The first large-scale cohort study to investigate this reported a 50 % improvement in breast cancer-specific mortality in women with ER+ tumours achieving the equivalent of a brisk 30 min walk on 6 d of the week v. their most inactive counterparts, a finding that was consistent for overweight/obese women⁽²⁶⁾. A physically active lifestyle after primary ER+ breast cancer treatment is also associated with improved quality of life and physical functioning^(19,27), and studies suggest that regular PA is an effective strategy for reducing fatigue and ameliorating the debilitating effects of other treatment sideeffects, including pain, shortness of breath,

depression, insomnia and lymphoedema after breast cancer treatment (28-33).

PA also has an important role in weight loss and longterm weight loss maintenance^(34,35). Several intervention studies show that PA/structured exercise in combination with tailored dietary advice results in clinically important weight loss (range 5-14%) in overweight breast cancer patients/survivors and postmenopausal women (36-46) and induces greater weight loss than exercise or diet alone^(45,46). The same studies have shown that weight loss of >5 % is accompanied by tangible improvements in biological risk markers of breast cancer recurrence and cardiometabolic disease (i.e. fasting insulin and circulating levels of inflammatory markers, leptin, oestrogens, testosterone and Sex hormone binding globulin (SHBG))^(37,39,41,45,47–49). Furthermore, regular purposeful PA can help to maintain or increase skeletal muscle mass during dietary-induced fat loss(45,50,51) which increases total daily energy expenditure because of the direct association between skeletal muscle mass and BMR^(52,53), thereby enhancing the fat-reducing effects of hypoenergetic diets in ER+ breast cancer patients⁽⁵⁴⁾. Women treated for ER+ tumours receiving Tamoxifen seem to be particularly susceptible to adverse body composition changes (i.e. increases in overall body fat and truncal fat), independent of changes in body weight⁽⁵⁵⁾. Thus, an improved knowledge of body composition changes accompanying weight loss interventions (i.e. changes in body fat compartmentalisation and lean body mass) is important for gaining further insight into the mechanisms underpinning changes in biological risk markers of cancer recurrence and cardiometabolic disease in this population.

Intervention studies

Intervention studies have reported a range of health benefits following interventions to increase PA and improve dietary behaviours after primary treatment for earlystage breast cancer, including sustained PA behaviour change and improvements in body composition, quality of life and risk markers associated with cancer recurrence and cardiometabolic disease^(37,38,41–43,56). While these studies have demonstrated the feasibility and efficacy of lifestyle interventions for breast cancer survivors, an important challenge is to design practically implementable methods of developing the skills and confidence women need for longer-term health behaviour change, while also overcoming the challenges of embedding such provision within the National Health Service. Offering a route to supported lifestyle behaviour change would address an important unmet need for women and their treating clinicians at this opportune 'teachable moment'.

Support for health behaviour change as part of the National Health Service care pathway

Support for health behaviour change after primary treatment for breast cancer is limited to that provided by



prominent UK cancer charities. For example, Breast Cancer Now offers an on-line course and book/printed materials ('Moving Forward') to help women adjust to life after breast cancer treatment. This takes place over half a day for 3 or 4 weeks and aims to provide information, support and professional guidance on how to cope with and adjust to life after breast cancer treatment (57). Macmillan Cancer Support offers the Recovery Package after completion of primary treatment comprising a Holistic Needs Assessment, treatment and cancer care reviews with a healthcare professional and an education/support event such as a Health and Wellbeing Clinic⁽⁵⁸⁾. There remains a gap however, in longerterm provision of tailored (bespoke) lifestyle support, specifically designed to address the barriers to effective weight loss that many women experience after primary treatment for breast cancer. This means that offering a route to accessible and adoptable weight management support would address an important unmet need for women and their treating clinicians at what is frequently an opportune 'teachable moment' for patients⁽⁵⁹⁾.

Understanding the barriers to weight management

It is important to understand factors which can act as barriers to healthy lifestyle behaviours and sustainable weight loss after breast cancer treatment. Qualitative studies have identified a range of emotional needs, concerns and anxieties related to breast cancer and its treatments that interventions for supporting health behaviour change must address, including cancer-related physical symptoms (e.g. upper extremity motion restriction, lymphoedema, fatigue, etc.), low confidence and self-esteem, family and work schedules, body image concerns and fear of recurrence (60–66). In addition, women commonly experience deficits in lifestyle education, citing a lack of accurate information and support from health professionals, particularly regarding the management of treatment-induced physical limitations⁽⁶⁰⁾. Providing a supportive environment to help women address these barriers seems also to be important for helping to build the skills and confidence needed for sustainable lifestyle behaviour change.

Group-based lifestyle interventions

Studies show that group-based interventions, incorporating evidence-based behaviour change strategies and providing an opportunity for peer-support and a forum for addressing the anxieties and challenges women face after primary breast cancer treatment, can serve as a strong platform for building the skills and confidence needed to increase engagement in regular PA and healthy dietary behaviours. Successful group-based weight-loss interventions have used a variety of delivery formats, including face-to-face (closed-group) workshops for 8–15 women and individual or group-based telephone support, alongside remote-support methods such as

emails, text-messaging and printed mail-outs^(37,38,41-43,56). The use of self-regulatory behaviour change techniques (e.g. goal setting, self-monitoring), inclusion of an educational component, setting of graded tasks and establishing a structure for frequent contact and social support is consistent with best-evidence strategies for promoting changes in dietary and PA behaviours in the general population⁽⁶⁷⁾ and in people living with and beyond cancer⁽⁶⁸⁾.

Co-design of an accessible and adoptable weight management intervention

Drawing on this empirical evidence and guided by the MRC Framework for Developing and Evaluating Complex Interventions⁽⁶⁹⁾ and the Person-Based Approach to Intervention Development⁽⁷⁰⁾, we set out to co-design an accessible and adoptable weight loss intervention (support programme) that prioritises the issues and concerns faced by overweight women recovering from ER+ breast cancer treatment. The initial phase of this research involved qualitative focus groups with breast cancer patients and healthcare professionals. The results of this qualitative phase were then used to develop two-stage co-design workshops to understand the support structures required to produce and maintain positive health behaviour change in this population, e.g. which elements would be essential to a weight loss programme and which elements would need to have a flexible component.

Intervention delivery model

The intervention comprises a 12-month programme of group-based Support & Skills Workshops, involving educational and practical PA components, delivered by trained instructors and registered dieticians. The design of the group-based intervention enables it to be delivered via video conferencing technologies (e.g. Zoom, Teams, etc.). Having the option to deliver the intervention remotely offers safety advantages in the post-Covid-19 era and removes the need to travel to a facility. Furthermore, having the flexibility of virtual delivery brings other advantages such as improved scalability and cost-efficiency. Workshops are complemented by telephone/email support and participants have access to support from their peers and an instructor via a bespoke web-platform. High-quality intervention materials help women to achieve meaningful PA and dietary behaviour change. The intervention is designed to be more intensive during the first 6 months, followed by a 6-month period of maintenance support.

Feasibility testing

A randomised controlled feasibility study recruited 21 breast cancer patients from two hospital Trusts in the North of England and the intervention was piloted



over 6 months. Women were randomised into two groups (intervention or standard care control) and because of Covid-19 restrictions, the intervention was delivered remotely using video-conferencing. The group-based Support & Skills Workshops involved peer-to-peer virtual interactions between small groups of patients and the instructor. In addition, real-time instructor-led exercise classes were delivered virtually as part of the sessions. The pilot study has yielded positive preliminary results, in terms of weight loss and patient-reported outcomes, and we aim to progress this developmental work into a definitive multi-centre trial.

Summary

In the UK there are over 55 000 new breast cancer cases per year and approximately two-thirds of women are obese or overweight at diagnosis. Obesity, weight gain and low levels of PA after diagnosis are associated with worse survival in women being treated for early-stage disease. The importance of healthy lifestyle behaviours for helping to prevent the adverse effects of weight gain after a breast cancer diagnosis is now widely acknowledged. Exercise in combination with dietary advice has been shown to evoke favourable body composition changes in breast cancer patients (37,38,41-43,56). However, there remains a gap in longer-term provision of tailored (bespoke) lifestyle support which is specifically designed to address the barriers to effective weight loss that many women experience after primary treatment for breast cancer. We used a co-design approach to enable the development of an intervention (support programme) with appropriate content, structure and delivery model to address the weight management challenges faced by overweight ER+ breast cancer patients. Offering a route to supported lifestyle behaviour change addresses an important unmet need for women and their treating clinicians at an opportune 'teachable moment'.

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Conflict of Interest

None.

Authorship

The authors had sole responsibility for all aspects of preparation of this paper.

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