BMJ Open

Life after breast cancer: moving on, sitting down or standing still? A prospective study of Canadian breast cancer survivors

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To cite: Sabiston CM, Wrosch C, Fong AJ, *et al*. Life after breast cancer: moving on, sitting down or standing still? A prospective study of Canadian breast cancer survivors. *BMJ Open* 2018;**8**:e021770. doi:10.1136/bmjopen-2018-021770

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2018-021770).

Received 19 January 2018
Revised 14 June 2018
Accepted 18 June 2018

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ABSTRACT

Introduction Breast cancer (BC) is associated with serious physical and psychological health sequelae that affect quality and quantity of life. Physical activity (PA) and sedentary behaviour can prevent or diminish these sequelae; yet, little is known about how these lifestyle behaviours change after cancer treatment and if these changes affect post-treatment health. The first aim of this study is to describe natural trends in lifestyle behaviours (ie, PA, sedentary behaviour) in women treated for BC. The second aim is to examine the longitudinal associations between lifestyle behaviour changes and (1) physical health (eg, acute symptoms, chronic conditions, body composition, patient-reported fatigue, pain and functioning), (2) psychological health and illness (eg, depression, stress, affect, post-traumatic growth, cancer worry, mood, body image) and (3) biological functioning (eg, cortisol and C-reactive protein). The third aim is to examine modifiable self-regulation (ie, goal adjustment strategies) and motivation constructs (ie, self-determined regulations) that predict trends in lifestyle behaviours.

Method and analysis This is a prospective longitudinal study of 201 women treated for BC. Data (eg, surveys, accelerometers, saliva, blood) are collected every 3 months during the first year after women complete systemic treatment for a first diagnosis of BC, and once every year for 4 years thereafter. Data analyses assess trends and changes in PA and sedentary lifestyle behaviours, examine associations between these trends and changes in health outcomes and identify modifiable predictors of PA and sedentary lifestyle behaviours using multilevel modelling.

Ethics and dissemination Ethical approval was obtained from the University of Toronto (REB# 28180) and has been funded by the Canadian Institutes of Health Research (#186128). Study findings will be disseminated through peer-reviewed publications, academic conferences, local community-based presentations such as the Canadian Cancer Society and similar organisations.

Strengths and limitations of this study

- First study to examine natural changes in lifestyle behaviors and health outcomes in the immediate period following breast cancer (BC) treatment for over six years.
- By using both self-report and objective measures that span facets of physical, biological and psychological health, this study will obtain high-quality data that informs the development and delivery of health-related programmes and policy to improve the quality of life in BC survivors during this critical post-treatment period.
- Limitations include the convenience sample and no control group for comparisons.

INTRODUCTION

Breast cancer (BC) is the leading cancer diagnosis among women, with one in every eight Canadian women diagnosed in their lifetime.[1] With survival rates approaching 88%, over 150 000 women in Canada require long-term surveillance and treatment for the potential side effects and comorbidities of living with BC. Women with a history of BC are at greater risk of comorbidities,[2 3] disability[4 5] and mortality[1] and they are also more vulnerable to experiencing psychological and biological health challenges. After a BC diagnosis and treatment, women report higher levels of depressive symptoms,[6] experience more pain,[7] fatigue[8] and sleep problems,[9] have higher rates of physical and cognitive function decline[5 10] and are more likely to be overweight[11] compared with women in the general population. This underscores the burden that can accompany BC and suggests that initiatives are needed to help minimise health problems associated with the aftermath of a BC diagnosis and treatment.

Increasing physical activity (PA) levels is a non-pharmacological strategy that can help mitigate the adverse effects of BC while improving quality of life during survivorship. PA can effectively protect BC survivors from physical and psychological health

sequelae.[12–20] Accordingly, researchers have assessed PA levels in women with a history of BC and shown that few BC survivors are physically active at recommended levels.[21–24] While informative, most of this evidence is based on cross-sectional, retrospective or short-term intervention studies that limit the conclusions made regarding *natural* trends in PA over time. Understanding these trends is needed to identify potential transition points when women are most vulnerable to decreases in PA and to guide research and practice. In addition, cross-sectional designs limit examination of the longitudinal associations between PA and both psychological and biological health outcomes.

Similarly, researchers have proposed a new cancer survivorship research agenda examining sedentary behaviour among cancer survivors.[25] Specifically, sedentary behaviour is distinct from PA and is defined as any waking behaviour done while lying, reclining, sitting or standing, with no ambulation irrespective of energy expenditure.[26] Recent cross-sectional data based on direct measures of sedentary behaviour indicate that women spend an average of 66% (ie, ~9 hours) of their day in sedentary pursuits post-treatment for BC. There are also data to suggest that sedentary behaviour is associated with markers of adiposity, comorbidities and psychosocial health in BC survivors.[21 25 27 28] However, sedentary behaviour may have short-term psychological benefits in clinical populations by providing distraction or relaxation time for individuals including women recently treated for BC. More research is needed to describe trends in sedentary behaviour in women with a history of BC and relate these trends to psychological and biological health outcomes.

It is also important to identify modifiable protective factors that are associated with PA and sedentary lifestyle behaviours to inform the development of effective behaviour change interventions. Based on theoretical perspectives of self-regulation,[29–31] goal adjustment capacity might predict lifestyle behaviour in this population. BC survivors are often confronted with physical or psychological obstacles and barriers that may constrain goal-related activities (eg, work, career, sexuality) and interfere with the attainment of an active lifestyle. In such circumstances, the ability to adjust goals that are no longer feasible may provide resources that are necessary to deal with the BC experience and to engage in effective lifestyle changes. There is emerging evidence that the capacity to disengage from goals that are not feasible and to re-engage in new goals can predict PA among BC survivors, and in turn enhance emotional well-being.[28] Findings from other at-risk populations (eg, asthma) also suggest that goal- adjustment capacities can predict levels of depression, diurnal cortisol output, C-reactive protein and physical health problem.[32–34]

Motivation for PA may be another key determinant of PA.[35] Self-determined (also called autonomous) motivation promotes positive psychological and behavioural functioning, while controlled forms of motivation thwart such outcomes.[36] Autonomous motivation regulations have been associated with emotional adaptation, whereas controlled motivation regulations have been linked to poorer psychological well-being.[37] To date, there are no longitudinal studies examining the influence of self-regulation and motivation constructs on lifestyle behaviours in BC survivors.

In addition to understanding the natural PA and sedentary behaviour patterns and identifying modifiable factors that might potentiate or hinder these lifestyle behaviours in the early survivorship period following BC diagnosis and treatment, associations between PA, sedentary behaviour and important psychological and biological health outcomes need to be tested. For example, there is evidence linking PA and sedentary behaviour to psychological health outcomes such as depression, affect, post-traumatic growth stress and body image in cancer survivors.[12 38 39] It is important to assess both positive and negative psychological health outcomes since the absence of one does not infer the presence of the other[40 41] and both are uniquely impacted by lifestyle behaviours.

Psychological distress[42–44] and adaptation[45] are also associated with diurnal cortisol secretion. Both acute and chronic distress activate the hypothalamic-pituitary-adrenal (HPA) to release cortisol into the circulation.[46 47] Exposure to enduring challenges (such as cancer survivorship) can also create a rebound effect and reduces cortisol secretion to below normal levels.[34 48] Thus, different patterns of cortisol dysregulation are possible during the experience of stress and challenge, and different patterns may present over the survivorship period but to date have not been elucidated. It is conceivable that emotional distress is a health risk and emotional adaptation may protect breast cancer survivors' (BCS) health statuses via biological functioning that can be examined by collecting cortisol samples over time.

Inflammatory pathways are important to cancer development and progression, and C-reactive protein (CRP) is an acute-phase reactant inflammation protein that is synthesised in response to cytokines within the tumour environment.[49] While this is a low-grade systemic marker of inflammation, BCS who are in a state of chronic inflammation are at risk for recurrence and metabolic disturbances, and factors associated with reducing CRP are proposed to improve morbidity and mortality outcomes.[50–52] Given that inflammatory pathways develop over time,[53] it is important to collect longitudinal prospective data to capture the antecedents and outcomes of CRP profiles. Similar to their role on stress regulation, lifestyle activities (PA and sedentary behaviours) may regulate CRP through mechanisms diminishing health risk[54] and CRP has decreased following PA among BCS.[55 56] However, the natural changes in CRP and links to PA and sedentary behaviour over time have not been studied.

The first research aim of this project is to describe trends in PA and sedentary behaviour in women with a history of BC. The focus is on the early post-treatment period (ie, the first 15 months post-treatment and then

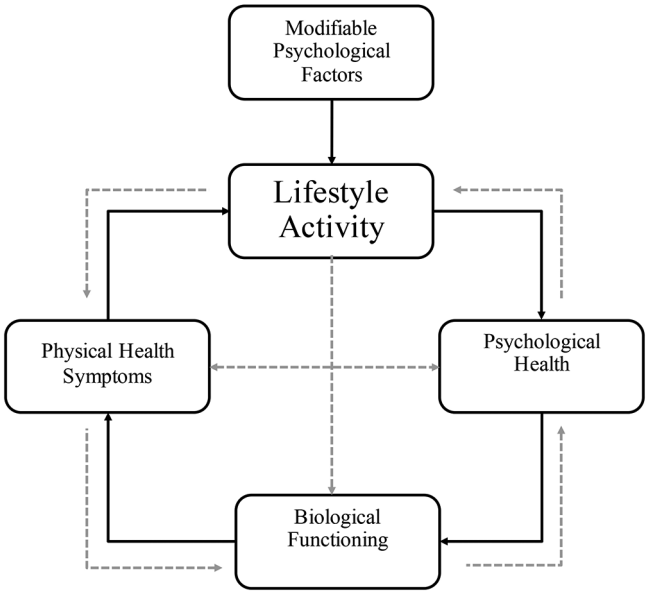

Figure 1 Conceptual model identifying hypothesised associations between lifestyle activity (physical activity and sedentary behaviour), psychological health, biological functioning and physical health symptoms in breast cancer survivors.

four more years) as this stage of cancer survivorship is less understood compared with the diagnosis and treatment periods.[57] The second aim is to examine the longitudinal associations between changes in PA and sedentary behaviour and (1) physical health, (2) psychological health and (3) biological functioning. The third aim is to examine if self-regulation (ie, goal adjustment strategies) and motivation (ie, self-determined regulations) constructs predict trends in PA and sedentary behaviour, to determine if these strategies should be targeted in patient-centred interventions for this population. Examining BCS in the early post-treatment period, identifying and understanding longitudinal changes in PA and sedentary behaviour and describing the relationships between changes in lifestyle behaviour and physical and psychological health will address important gaps in the current BC literature. The conceptual framework guiding this study (see figure 1) represents a theoretical integration of the motivational theory of lifespan development,[58] self-determination theory/organismic integration theory[59 60] and the biobehavioral model of cancer stress.[61] The integration of these theoretical perspectives can improve our understanding of the processes involved in health behaviour change insofar as '…integrated theories are invaluable as they highlight the essential psychological variables and processes that do most of the 'work' when it comes to predicting and explaining behaviour' (Hagger[62] p 190). The constructs and processes embedded in our model can then be targeted in theory-based interventions.[63] Furthermore, previous mixed-methods findings and related research on psychological growth,[64] self-regulation[29] and stress and coping[65] support many of the theoretically integrated associations in this integrative model.

METHODS AND ANALYSIS

Study design

This is a longitudinal study spanning 6 years of survivorship following treatment for a first diagnosis of BC. In the first year (ie, immediately post-treatment), data were collected every 3 months to gain a consistent and persistent assessment of the main variables for five data collections (time 1 through 5; T1–T5). A grant renewal enabled data collection to continue approximately 1 year after and every year for four additional data points (T6–T9). Participants were recruited immediately after their own treatment completion and thus every woman was assessed with different timing within the confines of the study timeline (eg, every 3 months for five data collections and then every year thereafter for four additional data collections). The first participant was recruited in 2010 and the last participant was recruited in 2013. Data collection will be complete in 2018.

Study population

Participants (N=201) were recruited through advertisements and referrals from oncologists in medical clinics and hospitals in Montreal, Canada. Potential recruits were asked to contact the research team by telephone to obtain details about the study. They were screened for eligibility using the following inclusion criteria: (1) at least 18 years of age; (2) 0–20 weeks post-primary treatment (ie, surgery, chemotherapy, radiation therapy) for stages I–III breast cancer; (3) first cancer diagnosis; (4) able to provide written informed consent, read and speak in English or French and (5) reported no health problems that prevented them from engaging in PA. All participants provided written informed consent before data collection.

A total of 177 women (88% of 201 women recruited) completed all five data collections in the early study period. Following a new consent process, 144 women (72% of the original sample) agreed to participate in the yearly follow-up data collections. Based on 250 simulation models using the initial data collected five times over the first 15 months, with α=0.05, power was estimated at 79.4%–95.9% to detect statistically significant associations with sample sizes ranging from n=115 to 144 in this follow-up data collection period. Cohen's d effect sizes ranged from 0.2 to 1.1 between various measures of PA, sedentary behaviour and health outcomes.

Patient and public involvement

The research study idea emanated from discussions with BCS who identified salient barriers to PA and perceptions of the benefits of participation in PA. These conversations informed the research design and fostered five BCS patient advocates being involved in the study as part of the research team from conception, focus and importance of various target variables, measurement and overall design. These patient advocates were also involved in the grant conceptualisation and writing and guided recruitment through collaboration with their oncologists. They

have also helped to oversee layperson dissemination of the results in study newsletters and for any invited talks and workshops. In fact, all of these advocates have also planned and organised community events focused on physical activity and breast cancer.

Measures

Data are being collected using a combination of reliable and valid self-report and objective measures, most of which were previously translated and used by French and English-speaking participants. As appropriate, additional instruments were translated using established protocols, and tested the psychometric properties of the original and translated scales. Data collection was done in person in the lab at T1 and then has been completed by mail for T2 through T9. At T1, all instructions were presented to the women, details on data collection procedures were clearly presented and tested, and weight and height were taken. Following T1, women were instructed to wear the accelerometer for the week once they received the data collection materials, collect saliva samples on two non-consecutive days during that week, complete mood and physical health symptom checklists on these days, to collect blood via finger prick and to complete the self-report questionnaire before mailing all materials back to the lab using courier services.

Lifestyle activity

At all time points, *self-report PA* is assessed using the Leisure-Time Exercise Questionnaire[66] and the Short Questionnaire to Assess Health-enhancing Physical Activity[67]. A lifetime PA measure[68] is also completed once at T6. *Self-report sedentary behaviour* is assessed using questions on sitting time and screen time[69] for T1 through T9. *Objective PA and sedentary behaviour* are assessed at T1 through T5, and T7 and T9 using GT3X accelerometers (Actigraph, Pensacola, Florida, USA). Participants wear the accelerometer on their hip during waking hours for a 7-day period, except for periods of bathing/showering or other water activities.

Psychological health

At all time points, *negative psychological health* is measured using the Positive and Negative Affect Schedule (PANAS; negative affect subscale[41 70]), the Perceived Stress Scale[71] the 10-item version of the Centre for Epidemiological Studies Depression[72] and the Assessment of Cancer Concerns scale.[73] *Positive psychological health is* assessed using the PANAS (positive affect subscale[41]) and the Post-traumatic Growth Inventory (PTGI[74]). Consistent with other work,[75–78] the PTGI was modified by changing the word 'crisis' to 'cancer'. The Profile of Mood States[79] is used to assess acute levels of adaptation and distress on two non-consecutive days during each data collection. Body image, a key aspect related to women's psychological health, is assessed using the Social Physique Anxiety Scale[80] at T1–T5 and the Weight-related Guilt and Shame Scale[81] at T3–T9.

Biological functioning

Participants provide five saliva (*cortisol*) samples as they engage in their normal daily activities on two non-consecutive days in a typical week across all (T1–T9) data collections. On each of the days, the participants collect five saliva samples (using salivettes) at specific times of day: awakening, 30 min after awakening, 1400, 1600 and before bedtime. Participants are asked not to eat or brush their teeth immediately prior to saliva collection, nor to participate in physical activity in the 30 min preceding saliva collection. The actual time of day for each saliva collection is also recorded. The saliva samples are stored in participants' home refrigerators until they are returned to the lab within 7 days and then frozen at −80°F until the completion of the study. Cortisol assays are performed at the University of Trier, Germany, in duplicate, using a time-resolved fluorescence immunoassay with a cortisol–biotin conjugate as a tracer.[46] The main measure of cortisol secretion will be the area under the curve (AUC), which will be calculated for each day (in log nmol/Lxh) using the trapezoidal method, based on hours after awakening (see Pruessner *et al*[82]). Peak, slope and other relevant measures of cortisol secretion can also be used.

To measure CRP, participants also provide capillary whole blood collected using a single-use lancet and dropped on Whatman protein saver card (VWR International, Quebec, Canada) which has a sample collection area of five 1.3 cm circles holding 75–80 µL of blood. Drops of blood are allowed to dry and the card is returned to the lab in a biosafety bag and stored at −80°F before being analysed in the Laboratory for Human Biology Research at Northwestern University using a high-sensitive enzyme immunoassay protocol.[83] There is evidence of reliability and validity for these procedures.[83] Duplicates are used for determining the coefficient of variation for both cortisol and CRP.

Physical health

At all time points, self-report *acute physical symptoms* are collected using a patient screening tool[84] where participants are instructed to record information regarding a variety of symptoms suggestive of underlying diseases.[85] Acute symptoms are assessed on the same 2 days that saliva samples are collected, and when ambulatory lifestyle behaviours are tracked using accelerometers. The Pittsburgh Sleep Quality Index[86] and Brief Fatigue Inventory[87] are completed at the end of the week along with the additional self-report measures.

Measures of *weight* to nearest kilogram (kg), *height* (in m) and *waist circumference* (cm) were taken by a trained research assistant during the first laboratory visit to allow body composition scores to be calculated. For all subsequent data collections, participants were asked to self-report their weight using a weight scale and waist circumference using a measuring tape (provided at baseline). Body mass index is calculated as weight (kg) divided by height in m^2. Waist-to-height ratio is calculated as waist circumference divided by height.

Modifiable self-regulation and motivation factors

Goal disengagement and goal reengagement capacities are assessed using the Goal Adjustment Scale[29]. *Motivation* is assessed as autonomous and controlled behavioural regulations (amotivation, extrinsic, introjected, identified and intrinsic regulations) using the Behavioural Regulation in Exercise Questionnaire-2[88].

Potential covariates and confounders

Personal and cancer-specific characteristics include: age, race, level of education, household income, marital status, parental status and number of children, menopausal status, type of treatments, dates and location of treatments, date of diagnosis, date of last systemic treatment, smoking history, alcohol consumption, self-report weekly diet, weight perceptions and weight management actions, social support, health engagement strategies and activity-related passion. Self-esteem, optimism, impulsivity and grit are also assessed. A comprehensive history of medical conditions, diagnoses and medications is collected. At all time points, changes in current health, financial and life events and living conditions are assessed in an open-ended question.

Planned data analyses

Data will be analysed using multilevel modelling (MLM) with restricted maximum likelihood estimation. For aim 1 (ie, trends over time), we will test a series of unconditional models to obtain information on the proportion of variance explained by within-subject (ie, change across time) and between-subject (ie, stable individual differences) effects on lifestyle behaviour, putative predictors of lifestyle behaviour (ie, self-regulation, motivation) and health outcomes (ie, psychological, physical, biological). These models will incorporate linear, quadratic and cubic effects of time. For aim 2, we will examine the associations between putative predictors and baseline levels (ie, intercept-as-outcome model) and changes in lifestyle behaviour (ie, slope-as-outcome model) using separate MLM models by adding the putative predictors to the model as between-person factors. Interaction terms between self-regulation and motivation constructs will be included in the models to test for moderator effects. For aim 3, we will examine the associations of lifestyle behaviour on psychological health, biological functioning and physical health outcomes using multilevel structural equation modelling including different PA intensities (light, moderate, vigorous, combined total) and sedentary behaviour. In this model, the effects of time will be allowed to vary across individuals (ie, random effects). Finally, consistent with the conceptual model, PA and sedentary behaviour lifestyle activity will be tested as outcome-dependent variables (with emotional well-being, biological functioning and physical health symptoms as predictors) using similar analyses over time. Measured confounders and covariates will be included in the models, as necessary. The main analyses will be completed using SPSS (V.24, IBM) and HLM (V.7, Scientific Software International) software.

ETHICS AND DISSEMINATION

This longitudinal study of BC survivors has been approved from the University of Toronto Research Ethics Board (REB# 28180) and has been funded by the Canadian Institutes of Health Research (#186128). Study findings will be disseminated through peer-reviewed publications, academic conferences and local community-based presentations to stakeholders and end users.

DISCUSSION

While the study does not include a control group and is not an experimental design, it addresses key gaps in the current literature. Consistent with the purpose and research questions, a strength of the study is the longitudinal data collection that enables a description of the *natural* trends of lifestyle behaviour over time and the links to physical and psychological health in women treated for BC. These data will identify potential transition points when BC survivors are most vulnerable to decreases in PA and increases in sedentary behaviour, as well as the contributions of PA and sedentary behaviour to health outcomes. These data will help shape research questions and intervention by providing critical information on theoretically relevant and modifiable predictors of long-term natural trends in lifestyle activity, which in turn will inform continued cancer care practices that promotes positive lifestyle changes. Lifestyle changes during survivorship may help prevent recurrence and reduce the risk of long-term physical and psychological health problems. Modifiable predictors of lifestyle behaviours have been identified in prominent psychosocial and motivational theories, but rarely tested in clinical populations. This study will demonstrate whether self-regulation (ie, goal adjustment capacities) and motivation (ie, behavioural regulations) are key predictors of lifestyle behaviour that could be targeted in future interventions and practice.

Further, the *Life After Breast Cancer* study evaluates the benefits of light PA. To date, most studies have focused on moderate-to-vigorous PA even though this intensity is not practical for some BC survivors, as reflected in the low participation rates (ie, 60%–88% of BC survivors are not active enough to gain health benefits[21–24]). Given that the overarching public health goal is to promote PA at levels that help achieve and maintain health, it is important to compare the benefits of different PA intensities in regard to physical and psychological health outcomes. Establishing positive associations between light PA and health outcomes would complement mounting evidence that trials are needed to test the benefits of light PA in this population. This could ultimately lead to revision in PA recommendations. Using the data collected in T1–T5, we have already demonstrated the value of light intensity PA on reducing depression symptoms over time.[89]

Additionally, the proposed analytical techniques will help overcome some of the limitations in the extant literature. Most studies of BC survivors use group-level analytical approaches that may mask important individual differences

in trends that could be useful in informing patient-centred healthcare. Considering that treatments are unique to each patient and have different effects (ie, women treated for the same cancer can have divergent experiences) person-centred approaches are necessary. The Canadian Partnership Against Cancer 2017–2022 strategic framework suggests a key priority is to 'ensure that person-centred care is the standard of practice'.[90] Therefore, use of MLM to examine both intraindividual and interindividual associations and trends is appropriate from both a statistical and a healthcare standpoint because it will inform patient-centred care. Using the T1–T5 data, we have already demonstrated the theoretical and practical value of intraindividual and interindividual associations between PA and cortisol secretion[91] and PA and CRP.[92]

Taken together, this study tracks BC survivors during the post-treatment period when they may be most vulnerable to physical and psychological side effects. The results will identify the optimal timing for interventions to promote PA and they will contribute to shaping policy targeting quality of life in the ever-increasing population of BC survivors.

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Acknowledgements We would like to acknowledge the five patient advocates (BCS) who continue to make this project worthwhile, and all participants for your dedication to this work.

Contributors CMS, CW, JB, PG, JO'L and SM helped to identify and design the project and procured funding. CMS and AJF are leading study coordination and managing the project. CMS, AJF and JB drafted the manuscript and all authors read, edited and approved the final manuscript.

Funding This work was supported by the Canadian Institutes of Health Research (#186128).

Competing interests None declared.

Patient consent Not required.

Ethics approval Ethical approval was obtained from the University of Toronto Research Ethics Board (REB# 28180).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Any de-identified data described in this protocol paper will be shared as requested.

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