

Follow Up of Women with Early Stage Breast Cancer

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Abstract

Worldwide there are over 6 million women with a personal history of breast cancer. Survivors may experience a range of issues as a consequence of treatment for breast cancer, including physical, emotional and psychological, and practical issues. Additionally, cancer diagnosis and treatments impact on relationships, caregivers and family members. Current follow up care is often inadequate as women may not have the broad range of consequences adequately managed. Together with looming shortages within the health workforce, these issues present major challenges to the delivery of ideal care for survivors. This paper reviews issues that may be encountered by survivors, preferences indicated by survivors and professionals regarding follow up, and considers a broad range of models that have been examined. These models include follow up by general practitioners (primary care physicians), nurse-led and patient-initiated reviews. Follow up need not be face to face, nor routinely scheduled. Comprehensive rehabilitation programs as well as exercise and dietary interventions may result in health benefits for breast cancer survivors.

Introduction

Worldwide, breast cancer is the most common cancer in women. Incidence rates vary dramatically: from around 19 per 100,000 women in Eastern Africa to 90 per 100,000 women in Western Europe.(1) In many nations, the incidence of breast cancer is increasing. Pleasingly, survival rates are also improving (1, 2). There are now 6.3 million women, worldwide, living with a history of breast cancer (3). How to best care for this overwhelming number of survivors and to address their complex long-term needs (with a shortage of oncology professionals in many countries(4)) is an enormous challenge. This review briefly discusses issues that women may experience after completing initial treatment for breast cancer before reviewing a range of models of post-treatment care.

Issues for women after treatment for breast cancer

Breast cancer survivors face many potential medical, psychological and social issues. These are important in their own right, though they may also impact on adherence to treatments, which may compromise oncological outcomes. Management of these issues is a challenge, for individual patients and clinicians and for health systems worldwide. This review does not detail the management of each of these potential effects, though readers are referred to a useful, recent review (5).

Medical issues

Although the large majority of breast cancer survivors do not experience disease recurrence, long term surveillance is required to allow timely identification and management of recurrence should that occur (6). Patients may be cured of their disease through detection of salvageable recurrence (7, 8).

Many breast cancer treatments may have long term physical consequences. Breast surgery may result in neuropathic pain, and alterations in body image. Axillary surgery is associated with lymphoedema of the arm and/or breast, paraesthesias and shoulder dysfunction (9).

Radiotherapy is associated with long term breast and chest wall pain and tenderness, and a

small incidence of more serious side effects such as pneumonitis, cardiac toxicity and radiation-induced sarcoma (10-12).

Chemotherapy frequently results in weight gain and early menopause, is frequently associated with fatigue, can have long term effects on cognitive function and very occasionally is associated with leukaemia (13). Many agents may result in peripheral neuropathy. Cognitive effects of cancer and its treatment have been reported in 30-70% of breast cancer patients at the end of chemotherapy (14). Cognitive deficits are also seen in women with breast cancer who do not receive chemotherapy, suggesting these impacts are multifactorial (14). Some women report that cognitive deficits impact their ability to return to work, daily activities, role function and relationships.

Ovarian failure as a consequence of treatment impacts both fertility and menopausal status. The effects of chemotherapy on ovarian function vary widely and are age, dose and drug dependent. Most premenopausal women develop amenorrhea during chemotherapy with high serum gonadotropin levels, but menstrual function often returns months to several years later. For many patients, the impact on fertility can be profound.

Induction of early menopause via chemotherapy or ovarian ablation is a common consequence of breast cancer therapy. Endocrine therapy often results in or exacerbates pre-existing menopausal symptoms. Sleep disturbance is a common problem experienced by women with breast cancer, and may be related to hot flashes.

Bone health must be considered in breast cancer survivors. Chemotherapy-induced early menopause and treatment with aromatase inhibitors is associated with loss of bone density, which may increase the patient's risk of fracture. A high incidence of secondary causes of low bone density has been identified in breast cancer patients, and these should be sought and addressed (15). Monitoring of bone density should occur in postmenopausal patients taking aromatase inhibitors.

Psychological issues

The psychological impacts of a breast cancer diagnosis on an individual, her partner and family vary widely. For most patients there will be a period of adjustment, which may require them to reassess life priorities, cope with changes in relationships and expectations of family members and friends and develop personal strategies to live well against a backdrop of uncertainty. After a period of readjustment most women continue to live a healthy life,

however some women will have more complex psychological needs. A proportion of women will experience high levels of fear of cancer recurrence, manifesting as difficulties adjusting to the post-treatment period, intrusive thoughts about the cancer, and high levels of anxiety (16).

Sexuality

Changes in sexual function and intimacy may occur as a consequence of menopausal symptoms, psychological consequences of cancer diagnosis and treatment and altered body image after breast surgery, and may lead to changes in libido and strain on relationships.

Social issues

Breast cancer diagnosis and therapy can also have significant social impacts. There may be direct impacts on work, study and finances, and often there are indirect impacts on others. The patient is often in a situation where others are physically, psychologically and financially dependent on her being able to function normally, and when this is not possible there can be many social consequences. Such consequences can be compounded by the patients' socio-economic background, culture, personal support network and financial situation.

Long-term quality of life in breast cancer survivors

Women may experience persistent consequences of cancer treatments, which can be long-lasting. Although long-term quality of life is similar to the general population, many survivors report ongoing symptoms, including pain, cognitive impairment, restrictions in physical and social functioning, and persisting financial harms (17, 18). Survivors who had systemic treatments (chemotherapy, hormonal therapy) report worse quality of life in the first year (19) and in later follow up (20).

Guidelines for follow up / guidance around post-treatment care

A number of international guidelines provide recommendations regarding follow up care (7). The principal goals of follow up are to enhance the survival and wellbeing of women. There is strong evidence supporting strategies to detect recurrent disease and second primaries (6).

Guidelines emphasise the detection and management of consequences of cancer treatments (7). Follow-up should be tailored to the needs of individual patients. Medical aspects of follow up are dealt with in more detail elsewhere (5-7).

Preferences for follow-up care

Patients and health professionals vary in their preferences for follow up. There is also significant variation internationally, reflecting differences in primary care (21). There is a strong expectation that follow up should be undertaken (22, 23). Despite a broad range of proposed and tested alternative models of care (see below), specialist oncologists deliver most long-term care in most developed countries around the world.

Survivors' preferences

Cancer survivors have identified fear of cancer recurrence as their main concern and they report that their anxiety about recurrence is temporarily diminished by the reassurance they receive at regular follow-up visits. Continuity of care, an unhurried consultation, and the provision of psychosocial support as well as medical reassurance have been reported as important factors for patients (24).

In Australia, the UK, Canada and the United States, survivors indicate a preference to see their surgical, medical and/or radiation oncologist for follow-up care (23, 25-27). Other practitioners, including breast care nurses/nurse practitioners, primary care physicians (PCP) or breast physicians (PCPs with additional qualifications in breast medicine), are viewed as acceptable alternatives by patients in some circumstances (25-28).

Providing survivors and GPs with information, such as a survivorship care plan (SCP, see below), guidelines for follow up, clear communication with specialists and rapid access to specialist care, should this be necessary, improves the confidence of both patients / survivors and GPs (23, 25, 27). The need to educate patients about the limitations of follow-

up care, including the limitations of tests and the inability of follow-up consultations to conclude that cancer is 'cured' has been identified (23).

Health professional preferences

Health professionals have been surveyed to explore their preferences for care. A study of 938 PCPs and 1088 oncologists in the United States found that PCPs favoured a shared care model (sharing long-term care with the oncologist) and that very few feel confident enough in their skills to be the main provider of survivorship care (to patients with bowel or breast cancer) (29). They did, however, express a willingness to take on more responsibility if more information and support was available. In the same survey, the majority of oncologists preferred an oncologist-based model of care rather than delegating or sharing this responsibility. A survey of health professionals in Australia found that although specialist oncologists felt that too much of their time was spent on follow-up care (taking them away from newly diagnosed patients needing their expertise), they too were reluctant to consider discharging patients to primary care or to breast care nurses (30). In the United Kingdom, there is also reluctance from oncologists to increase the role of general practitioners (GPs) in cancer follow-up; GPs, however, believe that they could deliver this care with appropriate support and referral pathways (24).

Breast care nurses/nurse practitioners have consistently expressed enthusiasm for involvement in survivorship care in a supportive environment, and welcome the opportunity to take on much of the traditional role of the oncologist (31).

Barriers to 'ideal' survivorship care

Comprehensive long-term care for breast cancer survivors (care that meets all psychosocial needs, detects recurrence / new disease early and effectively manages long-term symptoms) has many barriers. Specialist oncologists report lack of time, lack of evidence-based guidance, insurance restrictions and lack of knowledge about general preventive care (30, 32, 33). PCPs report lack of time, expertise/confidence in cancer care, fear of litigation and lack of support and referral pathways (23, 32). Barriers reported by survivors include the time and cost required to travel long distances to see an oncologist, lack of confidence in the skills of a PCP or nurse and a survivor perception of requiring high-level specialist care (25, 34).

Models of care following treatment for breast cancer

The pivotal US Institute of Medicine report 'From Cancer Patient to Cancer Survivor, Lost in Transition' suggests that ideal survivorship care should comprise four broad aspects: (1) prevention of recurrent and new cancers, and other late effects from treatments; (2) surveillance for cancer recurrence and second cancers, as well as for medical and psychosocial late effects; (3) interventions to deal with the broad consequences of cancer and cancer treatments (which might be medical, psychological, or practical), and (4) coordination between specialists and primary care providers to ensure all of the survivor's needs are met (35).

Follow up of women with early-stage breast cancer is associated with improved cancer survival, through detection of local recurrence and additional primary cancers (6). However, as noted, post-treatment care should have a much broader focus. Oeffinger and McCabe have described the dominant medically-led, hospital-based model of survivorship care and suggested models of shared care and examples of specialist survivorship clinics (36). England's National Cancer Survivorship Initiative recognises that, with appropriate information and training, and with ready and rapid access to the health care system, many survivors can effectively self-manage (37). Key to effective and efficient survivorship care is a process to match services to survivors' needs and their risk of future issues, including the risk of cancer recurrence as well as the risk of developing late and long-term effects (38). Ganz and colleagues have provided a set of resource-stratified recommendations regarding supportive care for survivors of breast cancer (39).

A number of studies have been undertaken comparing alternative methods of follow up to traditional hospital-based specialist care. It should be remembered that the major focus of follow up care in these studies has been on the second broad aspect of the IOM report, namely surveillance for cancer recurrence and second cancers and to a lesser extent, medical and psychosocial late effects.

Primary care-led versus hospital-led follow up

Two systematic reviews have suggested that disease outcomes, patient quality of life and satisfaction are similar when follow up of cancer survivors is conducted by GPs in the

primary care setting (24, 40). Data is largely drawn from studies examining follow up of women with early stage breast cancer.

Grunfeld and colleagues have conducted a series of studies examining follow up of women with early stage breast cancer. A first randomised controlled trial (RCT) enrolled 296 women, who undertook routine follow up in hospital or in general practice (41). Follow up in general practice appeared safe, with no difference noted in time from presentation with symptoms suggestive of recurrence to confirmation. There was no increase in anxiety or deterioration in quality of life in the general practice group. Patients were more satisfied with care in the community (42). Costs to individual patients and to the health care system were lower in the general practice setting (43).

A second RCT conducted in Canada recruited 968 women who were between 9 and 15 months from diagnosis. Again, women were randomised to follow up in hospital or by their GP (44). The primary outcome was rate of recurrence-related events and the secondary outcome was health-related quality of life. No significant differences were found on either outcome.

Taggart and colleagues emphasise that a number of patients were excluded from the above studies, limiting the ability to generalise from the above findings (6). The same reviewers also note that both studies were underpowered and follow up was too short to determine any possible impact on overall survival.

Shared care models

Using SEER-Medicare linked data, Snyder and colleagues examined preventative care received by breast cancer survivors, and compared this to non-cancer controls (45). They found substantial variation; particularly dependent on whether survivors saw their oncologist, PCP or both, in follow up. They concluded that better coordinated care between oncology specialists and PCPs might improve outcomes for breast cancer survivors.

Grunfeld and colleagues conducted a retrospective review through the Ontario Cancer Registry of over 11 000 women with early stage breast cancer (46). Most women saw both their oncologist and PCP in follow up. There was substantial variation from guideline recommendations, with both overuse and underuse of tests and visits.

Several studies suggest that sharing the care of cancer survivors results in better cancer-specific care, but also, better general health care, including preventative care (47, 48). Further trials of formalised shared care arrangements are clearly warranted.

Nurse-led follow up

A systematic review has compared nurse-led versus conventional physician-led follow up of people with cancer (49). The review suggests that, for particular patient groups, nurse-led follow up is an acceptable option. Studies have examined telephone-based or in-person review, scheduled or on demand.

Beaver and colleagues conducted an RCT, comparing hospital follow up with telephone follow up, undertaken by specialist nurses (50). The study was designed as a randomised equivalence study and enrolled 374 women considered to be at low to moderate risk of recurrence. It reported equivalent results with respect to patient anxiety, time to detection of recurrence and the number of clinical investigations. Patients in the telephone group reported higher satisfaction. Patients perceived telephone follow up to be convenient, and they appreciated a structured approach to reviews (51).

Koinberg et al randomised 264 women with stage I or II breast cancer to nurse-led follow up, on demand, or to routine medical review (52). Follow up was for 5 years. They reported no significant differences in anxiety, depression, recurrence rates or survival.

Sheppard and colleagues also conducted a RCT assessing point of need access to a nurse specialist versus regular hospital-based medical reviews (53). There appeared no difference in the two groups with respect to detection of recurrence, psychological morbidity or impact on quality of life.

Kimman and colleagues undertook a 2 x 2 RCT, enrolling 320 women with breast cancer, comparing hospital-based review with nurse-led telephone follow up, with or without an educational group program (54). The primary outcome was health-related quality of life. Secondary outcomes assessed role and emotional functioning and feelings of control and anxiety. No significant differences in quality of life were found between hospital and nurse-led follow up, nor regarding the addition of the education intervention. In the hospital / nurse-led comparison, no differences were found regarding secondary outcomes, or regarding satisfaction (55).

Patient-initiated follow up

Brown and colleagues have reported an RCT in which 61 women with stage I breast cancer either received usual hospital follow up or were provided with education and advised how to contact a breast care nurse, as required (56). There were no major differences in quality of

life and psychological morbidity between the groups. The authors suggest that patient initiated follow up is a potential option for this group of women, with potential cost savings.

Chapman audited a patient-led follow up program, which combined patient information, an education session, mammography and access to a breast cancer clinic as required (57). Patients appear to be satisfied with this approach, without significantly impacting the workload of GPs.

Supported self-management

Increasingly, cancer is considered to be a chronic disease. Following the end of treatment, survivors frequently need to be able to manage their own health (for example, managing symptoms, dealing with long term consequences and undertaking health promotional strategies). A common impediment is lack confidence, though self-efficacy can be enhanced (58).

England has highlighted the importance of a shift to self-management (37). However, survivors (and health professionals) need to be supported, to develop effective self-management skills. Many survivors may not require ongoing formal engagement with health providers, particularly as time increases since the end of treatment.

Chronic disease self-management programs involving people with heart disease, stroke, arthritis and chronic lung conditions can reduce patient distress, improve self-efficacy and reduce outpatient and emergency attendances (59). These programs can also be implemented broadly (60).

Other models of care

Gulliford et al describe preliminary data from a RCT in which women received either conventional hospital follow up or review only at the time of mammogram (61). Although the authors did not report data regarding recurrence or quality of life, they found high acceptability for reduced frequency of visits, without any obvious increase in contact with the person's GP or with a telephone hotline.

Although not assessed in a RCT, there are several reports of other models of care (6). Montgomery has reported a prospective cohort study in which women participated in an automated telephone-based review, replacing a face to face clinic visit (62). The system was easy to use and appeared acceptable to women.

Taken together, there appears good evidence to support a variety of models of post-treatment care for women with breast cancer. Further research might focus on broader goals of survivorship care, including dealing with side effects from treatment, identifying and managing the broad consequences of treatment for breast cancer, and strategies to remain well.

Survivorship care plans

The second recommendation from the IOM report was that all cancer patients completing primary treatment, be provided with a comprehensive treatment summary and follow-up care plan, together referred to as survivorship care plan (SCP). The treatment summary provides both disease and treatment information, such as the date of diagnosis, tumour characteristics and details regarding all cancer treatments. The SCP provides guidance regarding possible late and long-term effects, surveillance and follow-up requirements, recommended health behaviours, referrals and resources.

The purpose of the SCP is to promote care coordination, communication between providers, care transition, PCP knowledge regarding survivorship care in particular late and long term effects, and survivor education (63). The SCP is a personalised document, developed by the coordinating oncology clinician, and delivered to the patient and PCP.

Since the IOM recommendations in 2006, many organisations and policy makers have endorsed the provision of SCPs to cancer patients. Nissen et al note these organisations include the American Society of Clinical Oncology, American Cancer Society, Lance Armstrong Foundation and the Commission on Cancer of the American College of Surgeons who require provision of a SCP to patients as part of hospital accreditation (64).

Despite the strong face validity of SCPs, peak body endorsement, and patient preference for these documents there has not been widespread implementation. Implementation is influenced by limited evidence of impact, cost effectiveness, and barriers to implementation.

Salz et al reported on the literature regarding SCPs, including studies of stakeholder's perspectives of SCPs (65). Breast cancer survivors reported wanting more information about diagnosis, treatment, information on physical symptoms (fatigue, weight gain, and hot flushes), late effects (including lymphedema, skin pigment changes and sexual side effects), and signs that might indicate a cancer recurrence (66). Survivors highly value being alerted to and informed about potential psychological issues and consequences. One study of

breast cancer survivors suggested that the SCP should contain information about financial and legal issues (67). Survivors report the SCP would promote self-management by helping monitor for late effects, adopt healthy behaviours and undergo appropriate follow-up and surveillance (66).

Few studies have evaluated the impact of SCP implementation. The only RCT assessing the impact of SCPs recruited women with early-stage breast cancer who were being discharged to primary care following primary cancer treatment (68). It found no significant differences in patient reported cancer-related distress, quality of life, satisfaction with care, or care coordination. This study has been criticised in terms of appropriate dose and timing of the intervention and the measures used (69). Further evaluation of the cost effectiveness of the SCP intervention suggests it was not a cost effective use of health care resources (70).

Nissen et al investigated whether mailing a treatment summary to patients increased patient accuracy in reporting details of their diagnosis and treatment. The study demonstrated an improvement in cancer survivors' knowledge of details about their diagnosis and treatment. Breast cancer survivors showed significant improvements on nearly every variable.(64)

A number of studies have assessed concordance of oncologists and institutions with the IOM SCP recommendations (63, 65, 71). Forsythe et al found that approximately 20% of a US representative sample of medical oncologists reported always or almost always providing SCPs; approximately 13% of PCPs reported always or almost always receiving them (63). A similar study of the National Cancer Institute designated cancer centres reported that approximately 41% (21 of 53 institutions) reported using SCPs for breast cancer patients (65). Barriers to implementing SCPs need to be addressed including requirements for resources, clarity regarding who is responsible for generating and communicating the SCP, auto-population of electronic templates, need for clinician training, timing of delivery, and institutional commitment (63, 65, 71, 72). Strategies for overcoming these issues and a focus on processes and model of care will be important to deliver quality follow-up care (73).

Rehabilitation

The key issues of rehabilitation in breast cancer patients as identified in a Cochrane review reported by Khan and colleagues are improving or restoring physical and psychosocial abilities (74). As discussed above, many patients have to deal with short and long-term side effects and psychological distress related to the disease and its treatment, which have a

substantial impact on their quality of life. Complications include post-surgical pain, decreased range of shoulder movement, lymphoedema, cognitive complaints, fatigue, mood disorders and fear of cancer recurrence (74).

Physical activity related interventions

In a recent meta-analysis of RCTs, physical activity was associated with positive effects on physiology, body composition, physical functions, psychological outcomes and quality of life in breast cancer survivors (75).

Hayes et al propose a rehabilitation model, which integrates surveillance, prevention education, and management of treatment-associated morbidity with exercise prescription as a key component (76). The authors report evidence showing that exercise may be an important adjunct to breast cancer treatment, and one that is complementary to current standards of care. As with any other form of treatment, the efficacy of exercise is dependent on appropriate prescription regarding type, dosing, and timing that should be specific to each woman. Integrating exercise prescription into the care of women with breast cancer has the potential to realize short- and longer-term cost savings benefits at the individual and public health level.

Kuijpers et al found in a systematic review that web-based, interactive interventions appear to have a beneficial effect on patient empowerment and/or physical activity in people with various chronic conditions (77). Since cancer is increasingly considered as a chronic disease with either on-going or intermittent impact on health status and quality of life, the authors concluded that findings from their review are likely to constitute a basis for the development of an interactive, web-based intervention to specifically empower cancer survivors (77).

A pilot RCT assessing a water-based exercise program showed that an 8 week intervention was feasible for breast cancer survivors with arm lymphedema and that shoulder range of motion could be improved years after cancer treatment had been completed (78).

In a small RCT, Khan and colleagues assessed the effectiveness of a multidisciplinary ambulatory rehabilitation program for women following definitive treatment for breast cancer (79). Whilst the program did not affect patients' activity levels, it did appear to benefit participation.

Dietary interventions

Two large RCTs suggest that dietary interventions may have important impacts for women with early stage breast cancer. The Women's Intervention Nutrition Study (WINS) focused on reducing fat intake to 15% of energy (80). The Women's Healthy Eating and Living (WHEL) study sought to increase fruit and vegetable intake, increase dietary fibre and achieve 20% energy from fat (81). Pierce has compared the two studies (82). WINS suggested a small reduction in the summary 'any breast cancer event,' whereas the WHEL study found no between-group differences with respect to breast cancer events or overall survival. Secondary analysis of the WHEL study suggests that women who did not report hot flashes may gain benefit from this intervention (83). In this group the dietary intervention seemed to reduce distal recurrences.

Psychological interventions

Fear of cancer recurrence is very frequently identified by cancer survivors. This can be persistent and can interfere with adjustment and wellbeing (84). Short term psychotherapeutic interventions such as cognitive-behavioural group therapy or a supportive-experiential group therapy may both reduce fear of cancer recurrence(85), However cognitive-behavioural group therapy may be more cost-effective in a population with high anxiety (86).

The effect of behaviourally based cognitive training interventions for cancer survivors has been examined. Cherrier et al found the intervention to be effective for improving attention abilities and overall quality of life related to cognition (87). Von Ah and colleagues evaluated the acceptability and preliminary efficacy of training in memory or speed of processing in breast cancer survivors (88). Both interventions were associated with improvements in perceived cognitive functioning, symptom distress, and quality of life. Kesler et al conducted a RCT to investigate the feasibility and preliminary effectiveness of a novel, online executive functions training program in long-term survivors of breast cancer (89). The intervention led to significant improvements in cognitive flexibility, verbal fluency and processing speed.

The cultivation of mindfulness is an increasingly popular approach to support people with cancer. Mindfulness-based stress reduction (MBSR) intervention proved to improve mood, breast- and endocrine-related quality of life in women with stage 0 to III breast cancer (90). These results persisted at the three month time-point. An RCT in a Danish based population of women with stage I-III breast cancer showed strong evidence for the positive effect of MBSR on depression and anxiety after 12 months follow-up (91). These findings were

supported in a recent meta-analysis investigating the evidence of the MBSR in improving stress, depression and anxiety in breast cancer patients (92). The authors found a moderate to large positive effect size on the mental health of breast cancer patients. Further studies examining preventive and rehabilitative interventions are needed.

Conclusions

The growing number of survivors of breast cancer, together with the broad range of potential issues and limited healthcare workforce, present significant challenges to ideal care of survivors. A variety of models of post-treatment care have been tested. Although they have not necessarily focussed on the full breadth of ideal survivorship care, they suggest a range of safe and effective alternatives to standard medical review.

Compliance with Ethics Guidelines

Conflict of Interest

Meagan Brennan, Michael Jefford, G. Bruce Mann, Linda Nolte, and Lahiru Russell have nothing to disclose.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

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