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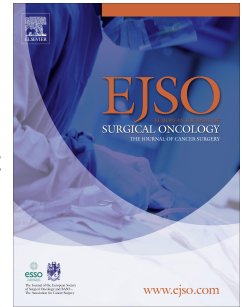
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Physical activity and breast cancer outcome: A brief review of evidence, current practice and future direction

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ABSTRACT

There have been several publications of large scale studies with long-term follow up addressing the role of physical activity in the management of breast cancer. Of the twelve studies specifically addressing the effect of physical activity on breast cancer survival, eight showed a statistically significant 50% risk reduction in breast cancer mortality in women who engaged in moderate intensity physical activity before and after their diagnosis of breast cancer. Four smaller studies demonstrated no benefit. Almost all of these observational studies predominantly involved white, professional women from North America and Europe. The positive effects of physical activity were seen for all stages of cancer, with the greatest benefit in steroid receptor positive breast tumours. These studies relied on self-reported questionnaires for recording the levels of physical activity. Despite including thousands of patients, published studies offer no data related to the optimum type, duration and timing of physical activity. Only a few studies provided objective data on physical activity, cardio-respiratory and general fitness. Thus, potential role of physical activity in the management of breast cancer remains far from established. If the beneficial effect of physical activity as demonstrated in the observational studies can be replicated in robust, well designed and well executed prospective randomised controlled trials, this would provide a tremendous opportunity to enhance adjuvant treatment of breast cancer. By adding physical activity to the spectrum of adjuvant therapies offered to women survival from breast cancer may be enhanced.

BACKGROUND

The early detection and treatment of breast cancer has improved significantly over the past decade and continues to contribute to the enhanced survival of 45,000 women diagnosed with breast cancer each year in the UK. The overall absolute survival benefit of chemotherapy, radiotherapy, endocrine and biological treatments vary from 5% to 12%. Despite this progress, breast cancer remains one of the commonest causes of mortality in women in the UK suggesting that the fight against this disease is far from over calling for more research to improve the outcome of this group of patients. Lifestyle interventions, in particular participation in regular physical activity, may potentially have a significant role in enhancing the prognosis of breast cancer.

This review aims to consider the evidence to date regarding the possible role of physical activity in the management of breast cancer in terms of survival and quality of life. A detailed discussion of the postulated biological mechanisms is beyond the scope of this article and only a brief review will be presented, the current practice and advice about physical activity in the context of breast cancer will be discussed. We will conclude with suggestions for future research in this field.

WHAT IS PHYSICAL ACTIVITY?

Physical activity is defined as any bodily movement produced by skeletal muscles resulting in energy expenditure, which can be measured in kilocalories (as energy expenditure). Physical activity in daily life can be divided into occupational, sports, conditioning, household and others. Exercise is defined as a subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective of improvement or maintenance of physical fitness 1. Aerobic or cardio-pulmonary exercise is defined as any activity that uses large muscle groups for over 20 or more minutes. Anabolic or resistance exercise involves performing sets of repetitive movements against a resistance during which neuromuscular fatigue occurs within 6-12 repetitions 2. The measure of physical activity is Metabolic Equivalent Tasks (MET) (defined as a ratio of the working and the resting metabolic rate) and MET per hour score which is a measure of the intensity of physical activity 3; 150 minutes of moderate intensity physical activity per week could be regarded as (roughly) equivalent to 500 MET-minutes per week (3.3 MET for 150 minutes per week is equal to 500 MET-min per week) 4.

PHYSICAL ACTIVITY AND BREAST CANCER OUTCOME

Physical activity before and after the diagnosis of breast cancer can affect both the survival and quality of life on women treated for breast cancer. 5. The beneficial effects of physical activity on breast cancer survival are shown to be either limited to or more evident in women with a hormone receptor positive tumour, suggesting that physical activity may enhance the prognosis of breast cancer by hormonally mediated mechanisms, justifying further research about physical activity and breast cancer.

Survival

The studies of effect of physical activity on the survival of breast cancer are summarised in Table 1. The Nurses' Health Study 6, North Carolina study 7, the Women's Healthy Eating and Living Study 8, the Alberta Study 9 and recently the California Teachers study 10 as well as Norwegian counties 11 study; all showed a beneficial effect of pre-diagnosis moderate intensity physical activity leading to approximately 50% reduction in Relative Risk of breast cancer death. While the Women's Collaborative and Longevity Study (CWLS) 12 and the Healthy, Eating, Activity, and Lifestyle Study (HEALS) 13 demonstrated that moderate intensity, post-diagnosis physical activity conferred significant survival advantage of about 50%. However, Life After Cancer Epidemiology study (LACE) 14 and other smaller scale studies, did not confirm the beneficial effect of physical activity on the survival of breast cancer.

The Nurses' Health Study A publication from the Nurses' Health Study (n=2,900) showed an absolute 6% risk reduction in breast cancer mortality at 10 years in patients undertaking moderate intensity exercise for five days a week 6,. An overall risk reduction of 50% was demonstrated in women who undertook regular moderate intensity exercise RR 0.50 (95% CI, 0.34-0.74). Physical activity related risk reduction was observed in all stages of breast cancer and was found to be dose dependent. The beneficial effect of physical activity was most marked in women with steroid receptor positive tumours and patients with stage III disease. The evidence from this seminal study, based on robust prospective data and substantial number of patients, has focussed attention to define the role of physical activity in the management of breast cancer. The evidence provided in this study, relates to middle class, white, professional females only. Despite the vigour of the data collection process employed by the Nurses' Health Study, the figures from observational studies could be subject to bias of various kinds. The exercise was self-reported and this may raise implications for data accuracy.

North Carolina Study After a follow up period of 8 years, a study of 1264 patients found a 22% risk reduction in mortality in obese and overweight women if they were engaged in physical activity one year before the diagnosis (HR, 0.70; 95% CI, 0.49-0.99) 7. Despite large numbers of patients in the study and long follow-up , data on physical activity, which has been collected after the diagnosis of breast cancer making this study prone to recall bias.

The Women's Healthy Eating and Living Study The Women's Healthy Eating and Living Study (WHEL) reported a relative survival advantage of 50% in women

who were engaged in the MET equivalent of walking for 30 minutes six days a week as well as consuming five or more portions of fruit and vegetables 8. This study included 1,490 women diagnosed with breast cancer with a reported 10-year absolute survival benefit of 7%. Unlike the Nurses' Health Study, the beneficial effect on the prognosis of breast cancer was limited to hormone receptor positive tumours. Despite demonstrating that physical activity is associated with the largest absolute survival benefit when compared to all such studies, this is an observational study and the level of evidence is only III. This study supports further research into the role of physical activity and breast cancer in a scientifically robust manner.

The Women's Collaborative and Longevity Study The Women's Collaborative and Longevity Study (CWLS) provides further support that overall mortality from breast cancer among women is decreased if they engage in moderate intensity physical activity after diagnosis 12. This prospective study of post-diagnosis self-reported physical activity levels in 4,482 women showed that women who engaged in greater levels of physical activity compared to sedentary women (define as those expending <2.8 MET-h/wk in physical activity), had a significantly better survival. This is a particularly important study as the positive impact of physical activity was seen after the diagnosis of breast cancer regardless of age, disease stage, and body mass index. A weakness of this study is its observational nature. Nevertheless, the positive benefit of post-diagnosis physical activity cannot be ignored. The information from this study does lend support to investigate the hypothesis that post-diagnosis physical activity may enhance survival from breast cancer.

The Health, Eating, Activity and Lifestyle Study The Health, Eating, Activity, and Lifestyle Study (HEALS) demonstrated that (993 patients) moderate-intensity physical activity after diagnosis of breast cancer might improve prognosis 13. Women who increased their levels of physical activity after diagnosis of breast cancer had a 45% lower risk of death (HR = 0.55; 95% CI, 0.22 to 1.38). While those women who decreased their levels of physical activity after diagnosis had a four-fold greater mortality risk of (HR = 3.95; 95% CI, 1.45 to 10.50). This study provided evidence (Level III) that increasing physical activity after the diagnosis of breast cancer may enhance survival. The most important finding of this study was that decreasing physical activity after the diagnosis of breast cancer can lead to increased mortality. However, the result of this study has to be interpreted with caution. Physical activity after the diagnosis of recurrent breast cancer may decrease because of 2nd line chemotherapy or disease progression. Therefore, reduction in physical activity may be an indirect manifestation of progression of metastatic disease.

The Alberta Study In the Alberta study, pre-diagnosis physical activity in a cohort of 1,231 women followed up for a minimum of 8.3 years, demonstrated a decreased risk of all cause and breast cancer mortality among women in the highest versus the lowest quartiles of recreational activity (MET-hr/week/year) (HR = 0.54, 95% CI = 0.36-0.79) 9. Both moderate (0.56, 95% CI = 0.38-0.82) and vigorous recreational activity (0.74, 95% CI = 0.56-0.98) decreased the risk of breast cancer death. Moderate intensity recreational activity also decreased the risk of a recurrence, progression or new primary cancer development (0.66, 95% CI = 0.48-0.91). The authors concluded that pre-diagnosis recreational activity conferred a

benefit for survival after breast cancer. Moderate intensity recreational activity was particularly protective 9. This observational study has the longest follow up and provides useful information about the benefit of different forms of physical activity in protecting against breast cancer mortality. This study also correlated the effect of recreational, occupational and household physical activity with breast cancer outcome. This is the only study to demonstrate a protective effect of physical activity against contralateral breast cancer.

The California Teachers Study The California Teachers Study of a cohort of 3,539 women with invasive breast cancer found that high or intermediate levels of long-term pre-diagnosis physical activity was associated with a lower risk of breast cancer death (RR, 0.53; 95% CI, 0.35-0.80; and RR, 0.65; 95% CI, 0.45-0.93, respectively) 10. These associations were confined to overweight women and were consistent across oestrogen receptor status and disease stage. The authors conclude that consistent long-term participation in physical activity before breast cancer diagnosis may lower the risk of breast cancer death 10.

Norwegian Study A population-based survival study of 1,364 breast cancer cases within the Norwegian Counties found that obese post-menopausal women had a 66% reduction in overall mortality if they regularly exercised before diagnosis compared with sedentary women (HR = 0.34, 95% CI 0.16-0.71) 11. This study also found metabolic markers of obesity were associated with increased breast cancer mortality. Authors concluded that these factors may all be important targets for intervention to enhance survival of breast cancer patients¹¹.

However, other studies, with smaller number of patients and shorter duration of follow up, failed to demonstrate a statistically significant effect of physical activity on breast cancer.

Life after Cancer Epidemiology Study The protective effect of physical activity on breast cancer specific mortality however was not confirmed in the 1,970 participants of the Life After Cancer Epidemiology study (LACE), a prospective investigation of behavioural risk factors and health outcomes 14. Nevertheless a statistically significant protective association between physical activity and all-cause mortality was found on multivariable analyses (hazard ratio, 0.66; 95% confidence interval, 0.42-1.03; P for trend = 0.04) 14.

The Italian Study An Italian study of 1,453 women with invasive breast cancer demonstrated no significant relationship with survival after breast cancer and physical activity 15. This study was primarily set up to study the effect of obesity on breast cancer survival and retrospective analyses of data did not find physical activity of any benefit for breast cancer survival.

Australian Study A study of 412 patients demonstrated no beneficial effect of pre-diagnosis recreational physical activity on the mortality of breast cancer 16. This study used estimated levels of Physical activity and perhaps was too small to detect a survival difference.

Canadian Study Breast cancer specific mortality was found to be unaffected by life time physical activity in a cohort of 603 women with breast cancer

after a follow of 10 years 17. This study again has small number of patients and one off estimated physical activity rendering the results difficult to interpret.

In summary, the current available data is supportive of physical activity in improving the survival. However, these data produce results which are variable, inconsistent and not robust enough to enforce a change in current clinical practice. The reasons for these inconsistencies could be retrospective nature of the publications, subjective and self-reported collection of physical activity data, lack of consistency in measuring and reporting physical activity and variability in the grades, stages and treatment of breast cancer.

Indirect evidence that physical activity can affect the prognosis of breast cancer has come from randomised control trials, which have demonstrated that biomarkers of breast cancer are more favourable in patients who undertake regular physical activity. 18-20. The role of biomarkers is discussed later in the paper. In addition, obesity which is generally associated with lower levels of physical activity is found to be associated with poor outcome and advanced stage of breast cancer 21;22.

Quality of Life

Meta-analyses suggest that regular physical activity can improve the quality of life of women with breast cancer. A recent systematic review and meta-analysis of the effect of physical activity interventions in breast cancer patients demonstrated that such interventions can improve physical function and quality of life 23. In addition, a Cochrane Library review concluded that exercise during adjuvant treatment for breast cancer could be regarded as a supportive self-care intervention,

which results in improved physical fitness. The capacity for performing activities of daily life, which may otherwise be impaired due to inactivity during treatment can be improved by physical activity. Two additional randomised controlled trials conducted in the UK, which post-date previous reviews, have also demonstrated significant improvements in quality of life, physical functioning and psychological health in breast cancer patients and survivors 24;25. Specifically, Mutrie *et al* (2007) found that women randomised to receive a community based exercise intervention over 12 weeks had significantly better functional and psychological health, relative to usual care at six months of follow-up. Other randomised controlled trials have shown that physical activity improve quality of life, at least in the short term, immediately after completion of chemotherapy 26.

MECHANISMS BY WHICH PHYSICAL ACTIVITY MAY INFLUENCE THE PROGNOSIS OF BREAST CANCER

The exact mechanism(s) by which physical activity might improve the outcome of breast cancer is not fully understood 27. A full discussion on the merits of various proposed mechanisms is beyond the scope of this article, however postulated biological mechanisms are briefly summarised here. These include improvements in the steroid and sex hormone profile, correction of metabolic hormone imbalance such as insulin resistance, and possible improvement in inflammatory and immunological markers 22;28.

Inhibition of Carcinogenesis at the Cellular Level

In vitro experiments suggest that physical activity promotes the carcinogen detoxification pathway by enhancing activity of enzymes such as cytochrome P 450 and Hepatic glutathione-S-transferase. 29. At the same time, regular physical activity promotes and activates a variety of DNA and protein repair systems by reducing oxidative damage within cells. The studies of carcinogenesis at cellular level suggest that physical activity may prevent tumour progression by altering cell proliferation, differentiation, and apoptosis with a possible role of p53.

Immune Mechanisms

The immune system may reduce the risk of cancer through tumour suppression. Physical activity increased the number and enhances the function of circulating leucocytes.30. Regular moderate intensity physical activity enhances Natural Killer cell function, as well as enhancing the chemotactic, phagocytic and lysozymal activity

of macrophages 31,32 potentially promoting the elimination of abnormal cancer cells. Natural Killer cells also have a direct role in tumour suppression. The research on the immunological aspect of physical activity is limited at present.

Inflammatory markers

The association between chronic inflammation, markers of inflammation and cancer is long established 33. Pro-inflammatory markers such as C Reactive Protein, Interleukin 6, Tumour Necrosis Factor alpha, and decreased levels of anti-inflammatory markers like adiponectin are associated with increased risk of cancer 34. Physical activity has shown to decrease these markers of inflammation 28. It is not understood if physical activity mediates anti-inflammatory activity by its effect on adipocytes and adipocytokines.

Steroid Hormones

Lower serum levels of steroid hormones are thought to be one mechanism by which physical activity can lower the risk of breast cancer 35. Physical activity may alter biosynthesis, bioavailability and metabolism of steroid hormones including Testosterone 35. An increase in physical activity may alter the pathways for oestradiol metabolism, including a decrease in the synthesis of oestrogens from androstenedione. Physical activity may promote the metabolism of endogenous oestradiol via 2-hydroxylation in preference to 16 hydroxylation, thus producing less active oestrogen metabolites decreasing the exposure of body to the proliferative effects of oestrogens 36.

Metabolic and lipid profile

Metabolic syndrome and its various components such as altered lipid profile, insulin resistance and hypertension have all been associated with increased incidence and poor prognosis of breast cancer 37. The constellation of factors referred to as the metabolic syndrome leads to extra-glandular oestrogen production, reduced levels of Sex Hormone-Binding Globulin resulting in increased bioavailability of free oestradiol and insulin biosynthesis. Both free oestrogen and insulin have been shown to be mitogenic for neoplastic breast epithelial cells 38;39. A study of obese postmenopausal women engaged in moderate and progressive physical activity demonstrated improved insulin sensitivity and enhanced oxidative capacity within muscle in conjunction with favourable alterations in lipid profile 40. Obesity, lack of physical activity and abnormal lipid profile are associated with increased risk of recurrence of breast cancer and moderate intensity physical activity can improve many of these risk factors hence favourably affecting the outcome of breast cancer as shown in a study of 932 European middle aged women 41. Obesity, type 2 diabetes and metabolic syndrome are all shown to be associated with increased plasma leptin and decreased plasma adiponectin levels 39. In vitro studies suggest leptin stimulates, and adiponectin inhibits, tumour cell proliferation and the microvessel angiogenesis. 39. The relationship between physical activity and breast cancer prognosis may be mediated, in part, through changes in insulin levels and/or changes in body fat or fat deposition 42. A randomised controlled trial of 82 sedentary, overweight breast cancer patients showed that there was a trend towards decreased fasting insulin concentrations and improvement in insulin resistance in the physically active group at 16 week follow up 43.

Growth factors

There is consistent epidemiological evidence that IGF-1 promotes development of cancer either directly by acting on cells causing cell growth via mTOR activation with Akt and Ras/MAPK signalling pathway 44 or indirectly by its effect on other cancer related molecules such as p53 44. Animal experiments suggest that hyperinsulinaemia promotes hepatic synthesis of IGF-1 and decreases the synthesis of IGFBP-1 thus promoting bioavailability of IGF-1 45. Thus, Insulin and IGF-1 have mitogenic properties, promoting cell proliferation and decreasing apoptosis and physical activity may protect against cancer development and recurrence by enhancing insulin sensitivity.

Reactive oxidative species

Accumulation of Reactive Oxygen Species (ROS) as a by-product of normal energy metabolism has been associated with the pathogenesis of cancer 46. ROS can act as both an initiator and promoter of breast cancer by damaging DNA, proteins and other large cellular molecules and also by acting as a cell-signalling molecule. Experiments using mouse models suggest that long-term exercise may reduce oxidative damage, as measured by decreased formation of nuclear 8-hydroxydeoxyguanine in certain body tissues 47. However, there has been general lack of success in establishing a therapeutic or preventative role of anti-oxidant in cancer management thus far; suggesting that further research is needed.

LEVELS OF PHYSICAL ACTIVITY IN BREAST CANCER PATIENTS

Despite the positive effect that physical activity may have on breast cancer survival, the data suggests that patients' physical activity levels reduce significantly after a diagnosis of breast cancer. On average, physical activity is decreased by 11% with an estimated 2-hour loss of house hold and sport related physical activity per week 48. A study from the USA reported that only 32% of breast cancer survivors participated in the recommended levels of physical activity defined as 150 min per week of moderate to vigorous-intensity sports/recreational physical activity 49. A study of 2885 breast cancer survivors registered in the American Cancer Society's SCS-II cohort also demonstrated that only 37% of women met the recommended Physical activity guidelines 50. Less than 22% of cancer survivors were found to be undertaking optimum levels of physical activity in a study of self-reported physical activity in 114,355 Canadian cancer patients 51. Together these data suggest that a drop in physical activity after diagnosis of breast cancer is a global problem that needs to be addressed.

PHYSICAL ACTIVITY ADVICE CURRENTLY GIVEN TO BREAST CANCER PATIENTS IN THE UK

The report by the Chief Medical Officer recommended a total of at least 30 minutes a day of at least moderate intensity physical activity on five or more days of the week for general health. The Chief Medical Officer has reported that physical activity is associated with a reduced risk of breast cancer among postmenopausal women 52. The National Institute for Health and Clinical Excellence has

recommended that primary care health providers should take every opportunity to promote exercise with their patients 53. The British Association of Surgical Oncology guidelines do not make any recommendation regarding life style choices in the management of breast cancer. Furthermore, a very recent study of specialist breast consultant surgeons and oncologists revealed that only 43% gave patients advice regarding physical activity and in <50% did the advice correspond to DOH guidelines 54.

IS IT POSSIBLE TO ALTER PHYSICAL ACTIVITY BEHAVIOUR OF BREAST CANCER PATIENTS

Cancer diagnosis signals a “teachable moment”, with patients often demonstrating an enhanced motivation to change lifestyle behaviours; especially within the first year after diagnosis, making patients more receptive to behavioural changes. 55;56. There is strong evidence to suggest that it is possible to increase physical activity levels in women undergoing treatment for breast cancer 57-60. Different types of exercise interventions including supervised one-to-one sessions; community based group exercise classes and home based exercise all have shown to be effective in increasing physical activity in breast cancer patients. Home based exercise interventions were found to be more cost effective and to have a better adherence rate 57.58. A number of studies have also demonstrated that home based exercise interventions can be performed reliably in patients diagnosed with breast cancer (Table 2) 59;61.

FUTURE DIRECTIONS

The challenge to improve the outcome of breast cancer is far from over for today's scientific community. Lifestyle based interventions are potentially attractive options as adjuvant treatment for breast cancer. The current evidence demonstrates that the beneficial effect of physical activity on breast cancer is too strong to overlook but is not sufficiently robust to bring about a change in clinical practice. Further research is required to understand the biological mechanisms linking physical activity with breast cancer. Questions regarding the optimum type of physical activity, in terms of patient's characteristics, needs to be addressed. It remains to be established whether the beneficial effect of physical activity on breast cancer is dependent or independent of weight loss. High quality randomised controlled trials are urgently required to evaluate the role of physical activity in breast cancer outcome. A randomised controlled trial of physical activity and breast cancer prognosis is not without its challenges but the evidence reviewed here would suggest that the embarking of such a trial is worthwhile. Other health benefits of physical activity such as decreased risk of osteoporotic fractures, cardiovascular events etc would make such a trial advisable 62. There is a need for long-term randomised controlled trials comparing biomarker changes associated with physical activity to understand the underlying bio-mechanisms between physical activity weight loss and risk of breast cancer recurrence. Only data from a well-planned and well-executed Randomised Control Trial would convince health care professionals involved in cancer care to promote physical activity as an intervention. Policy makers could then be lobbied based on robust evidence from RCT, to provide the necessary resources and facilities needed to promote physical activity in women as a means to reduce the incidence and death from breast cancer.

CONCLUSION

In conclusion, the data from observational studies has shown that participation in physical activity is associated with improved survival whilst randomised controlled trials have demonstrated a more favourable profile of breast cancer biomarkers in patients who undertake regular physical activity. Evidence from randomised controlled trials also supports the hypothesis that regular physical activity can enhance the quality of life and other health care outcomes of women treated for breast cancer. Despite clear recommendations from the Department of Health, few women with breast cancer undertake regular physical activity and less than 50% of specialist breast consultants provide patients with advice on physical activity. This is a reflection of the paucity of evidence due to the lack of appropriate trials. The question whether physical activity imparts any survival advantage to women with breast cancer is in need of further data in the form of an RCT addressing the issues of optimum amount, timing, duration of physical activity and type and stage of breast cancer.

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Table 1a. . Current evidence of beneficial effect of physical activity on breast cancer specific survival

Met hour per week	Walking Hour per week	Study	Nurses' Health Study	North Carolina Study	Women Healthy Eating & Living Study	Collaborative Women Longevity Study	Healthy Eating And Living Study	Alberta Study	California Teacher's Study	Norwegian Counties
		Year	2005	2006	2007	2008	2008	2009	2009	2009
		No. of patients	2987	1264	1409	4482	993	1231	3539	1362
		Type of study	Observational	Observational	Observational	Observational	Observational	Observational	Observational	Observational
<3	<1		1	1	1	1	1	1		
3-8.9	1-2.9		0.80			0.59				
9-14.9	3-4.9		0.50	0.78	0.56	0.52	0.69	0.56	0.53	0.34
15-23.4	5-7.9		0.56							
>24	>8		0.60			0.44		0.74		

- There is no standardised reporting mechanism for exercise, therefore some approximation has been carried out to allow relative comparison

Table 1b. Current evidence of no beneficial effect of physical activity on breast cancer specific survival

	Study	Life After Cancer Epidemiology Study	Italian Study	Canadian Study	Australian Study
	Year	2009	2008	2004	1995
	No. of patients	1970	1453	603	412
	Type of study	Observational	Observational	Observational	Observational
Overall Mortality		(Hazard ratio, 0.66; 95% confidence interval, 0.42-1.03; P for trend = 0.04).	NS	NS	NS
Breast cancer specific mortality		(P for trend = 0.26)	NS	NS	NS

Table 2. Summary of Home Based Physical Activity Interventions for Breast Cancer Patients

Study	Patients	Intervention Groups	Details of Intervention	Outcome
Segal <i>et al.</i> (2001)	n=123 Stage I & II Receiving adjuvant treatment Intervention = 26 weeks	Usual care (C)		↑ short form physical functioning in SDE vs C. Largest effect in SDE (p=0.01)
		Self directed exercise (SDE)	Personal counselling with exercise specialist Home exercise prescription Fitness evaluation at 13 weeks Telephone contact every 2 weeks	
		Supervised exercise	Personal counselling with exercise specialist	
Pinto <i>et al.</i> (2005)	n=86 Stage 0 – II Completed adjuvant treatment Intervention = 24 weeks	Contact control group (C)	Asked not to change physical activity Telephone contact weekly Mailed cancer survivorship leaflet weekly for 12 weeks	↑ in physical activity reported by PA vs C (p<0.001) ↑ in energy expenditure by PA vs C PA outperformed C in field tests
		Home based intervention (PA)	Personal counselling & exercise advice Pedometer Telephone contact weekly 12 weeks then monthly for 3 months Mailed cancer survivorship leaflet weekly for 12 weeks Feedback letters on weeks 2, 4, 8 & 12	
Basen-Engquist	n=60	Standard care (C)	Written information (x2) mailed to patients	↑ in performance 6

<i>et al.</i> (2006)	breast cancer Intervention = 24 weeks	Life style intervention (LSI)	90 minute group meeting each week for 16 weeks and every other week for an additional 8 weeks Written information provided	min walk test LSI vs. C (p=0.005) No difference seen in number minutes or number times spent ≥ 30 min moderate activity
Denmark- Wahnefried <i>et al.</i> (2007)	n=543 Early breast or prostate cancer Within 9 months of diagnosis post adjuvant treatment Intervention = 43 weeks	Attention control (C)	Introductory letter & work book Brochures followed by update card x6 ever 7-9 weeks Thank you letter & study incentive	↑ in life style behaviour for both groups
		FRESH start intervention (FST)	Introductory letter & work book (exercise & healthy diet) Tailored newsletters (exercise & healthy diet) followed by update card x6 ever 7-9 weeks Thank you letter & summary tailored newsletter	Greater ↑ seen in FST vs C p<0.0001
Matthews <i>et al.</i> (2007)	n=36 Post-menopausal, stage I-III Completed	Usual care (C)		↑ in reported walking exercise HBI vs C (p=0.01)
		Home based intervention (HBI)	Personal counselling visit aimed at increasing walking Telephone counselling weeks 1, 2, 4, 7 & 10	↑ in activity

	adjuvant treatment in last 12 months Intervention = 12 weeks			recorded by ActiGraph HBI vs C ($p < 0.01$)
Vallance <i>et al.</i> (2007)	n=377 Stage I-IIIa Complete adjuvant chemotherapy & radiotherapy Intervention = 12 weeks	Public health(PH)	Standard recommendation	↑ self reported physical activity in all groups (30, 70, 89 & 87 min for PH, PM, PED & COM respectively) ↑ self reported brisk walking reported for PM, PED & COM vs PH. No significant difference was observed between the groups
		Printed material (PM)	Standard recommendation	
		Step pedometer (PED)	Standard recommendation	
		Printed material & step pedometer (COM)	Standard recommendation Booklet – Exercise for health: An exercise guide for breast cancer survivors Pedometer	