Title:

A randomized trial of a telephone-delivered exercise intervention for non-urban dwelling women newly diagnosed with breast cancer: Exercise for Health

Running head:

Exercise for Health intervention: rural women with breast cancer

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A randomized trial of a telephone-delivered exercise intervention for non-urban dwelling women newly diagnosed with breast cancer: Exercise for Health-rural

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Abstract

Background Physical activity is important following breast cancer. Trials of non-face-to-face interventions are needed to assist in reaching women living outside major metropolitan areas.

Purpose To evaluate the feasibility and effectiveness of a telephone-delivered, mixed aerobic and resistance exercise intervention for non-urban Australian women with breast cancer.

Methods A randomized controlled trial comparing an eight-month intervention delivered by Exercise Physiologists (Tel; *n = 73)* to usual care (UC; *n = 70).*

Results 61% recruitment rate and 96% retention at 12 months; 79% of *Tel* group women received at least 75% of calls; odds (OR; 95% CI) of meeting intervention targets favored the *Tel* group for resistance training (OR 3.2; 1.2, 8.9) and aerobic (OR 2.1; 0.8, 5.5) activity.

Conclusions Given limited availability of physical activity programs for non-urban women with breast cancer, results provide strong support for feasibility and modest support for the efficacy of telephone-delivered interventions.

Keywords: breast cancer, physical activity, behavior change intervention, telephone, rural, randomized trial

Background

Breast cancer is the most common invasive cancer among Australian women, and with 5-year survival rates reaching 88% (1), there are increasing numbers of breast cancer survivors needing support to enhance recovery and improve long-term quality of life outcomes (2). Rural women comprise one third of all Australian women with breast cancer, and their geographic location has been shown to negatively influence stage at diagnosis, access to cancer care, type of treatment and related outcomes (3).

A large evidence base supports the ability of physical activity to enhance recovery both during and following breast cancer treatment (4, 5). Recent US cohort study findings suggest that post-diagnosis physical activity may also improve overall and cancer-specific survival (6-9). However, internationally and in Australia, most women with breast cancer engage in insufficient physical activity to reap health benefits (10, 11).

As women live longer following a diagnosis of breast cancer, research needs to address means of supporting them to initiate and maintain physical activity. While many excellent breast cancer rehabilitation programs are offered in tertiary hospital settings, these are accessible only to women living in metropolitan areas (1, 3). Similarly, most physical activity trials in breast cancer have evaluated intensive clinic-based interventions involving face-to-face delivery (12). Thus, the extant evidence as yet provides limited guidance on how best to deliver such programs to women unable or unwilling to attend such programs, including those living outside metropolitan areas.

Several trials have evaluated non-face-to-face intervention delivery methods, during (13-15) and after breast cancer treatment (16-20). All focussed on home-based aerobic

exercise and three included resistance training (13, 16, 17). Interventions were delivered via telephone following an initial face-to-face session (13-15, 18); via print materials (20); or, the combination (16, 17). While outcomes reported across trials varied considerably, the majority observed significant treatment effects for physical activity-related outcomes (i.e., aerobic capacity, physical function, meeting physical activity guidelines; 13, 15- 18) with a minority also reporting improvements in quality of life (17, 20). No studies specifically targeted non-urban women, despite the fact that non-face-to-face intervention delivery is particularly well-suited for this population subgroup.

The telephone-delivered intervention model is particularly advantageous, as it can be adopted by existing telephone cancer support and information services and it provides an efficient, evidence-based referral source for busy clinicians. Our previous research on telephone-delivered lifestyle interventions in other chronic disease populations suggests that the telephone is an intervention delivery mechanism that can promote both initiation (21, 22) and maintenance of health behavior change (23) and that it is cost-effective (24).

The current trial adopted behavior change strategies underpinned by Social Cognitive Theory (SCT)(25), specifically developing knowledge and skills related to the SCT construct of self-efficacy. Participants were encouraged to set small, measurable and achievable physical activity goals to facilitate a sense of confidence and mastery that was built upon as physical activity levels were progressed throughout the intervention.

Exercise for Health-rural (EfH) was a pragmatic trial that evaluated the feasibility and effectiveness of a telephone-delivered exercise intervention, beginning soon after surgery, and targeting women with breast cancer residing in regional and rural Queensland, Australia.

Methods

Study Design

A randomised controlled trial was conducted, evaluating an eight-month mixed (aerobic and resistance training) exercise intervention delivered via telephone by tertiary-qualified Exercise Physiologists, commencing six weeks post-surgery for newly diagnosed breast cancer patients, compared to usual care. Assessments occurred at baseline, 6-months and 12-months post-surgery (see Figure 1 in the Electronic Supplementary Material). Primary outcomes were feasibility indicators (recruitment and retention rates, sample representativeness, intervention implementation and participant satisfaction). Secondary effectiveness outcomes were meeting intervention targets for aerobic and resistance training, quality of life, fatigue, anxiety and upper body function. The trial was reviewed and approved by the Ethics Committee at The University of Queensland and at each of the participating hospitals. Data were collected from April 2007 to April 2009 with analysis from February to October 2010. Trial protocol is available from the corresponding author. EfH-rural was run concurrently with a larger, urban trial that evaluated a telephone-delivered exercise intervention arm and a face-to-face arm, compared to usual care (26).

Eligibility criteria

Women with a first diagnosis of invasive breast cancer aged 20 to 69 years, treated at one of eight regional, or four large metropolitan, Queensland hospitals and residing within a postal code considered inner regional, outer regional, remote or very remote according to the Australian Standard Geographical Classification (27) were eligible for participation. Women were excluded for: pregnancy or lactation, plans for additional surgery (e.g., breast reconstruction) during the study period, and medical conditions that would prohibit participation in the home-based exercise intervention (e.g., unstable hypertension).

Participant Recruitment

Breast Care Nurses at the participating hospitals were asked to approach all women receiving surgery for breast cancer to ascertain consent for researcher contact. Research assistants called potential participants 3-4 weeks post-surgery to explain the trial, screen for eligibility and obtain informed consent.

Randomization

Following baseline assessment, the project manager randomized women, individually to the intervention (Tel, *n=73)* or usual-care (UC, *n=70)* group via a computer-generated, unblocked, sequence of random numbers.

Telephone-Delivered Exercise Intervention

The intervention, described in detail elsewhere (26), involved 16 calls of 15-30 minutes duration over eight months (once/week for 2 months, once/fortnight for 2 months and once/month for 4 months) delivered by an Exercise Physiologist (EP). The intervention was underpinned by SCT (25), with an emphasis on increasing women's self-efficacy

for exercise, and was implemented according to the Chronic Disease Self-Management Intervention Model adapted from our previous trials (28, 29). Each session assessed exercise progression during the previous period and ascertained any presence or change in treatment-related symptoms. Exercise achievements were acknowledged, barriers resolved, subsequent behaviourally-specific exercise goals agreed upon, continued self-monitoring of exercise was encouraged, and necessary follow-up support identified. The intervention target for all women was to exercise at least four days per week, for at least 45 minutes, including aerobic-based (moderate-to-vigorous intensity) exercise (such as brisk walking) each session, as well as strength-based exercise at least twice per week (4). However, the exercise starting parameters and rate of progression were individualised according to baseline functional capacity, treatment-related side-effects, exercise preferences and previous exercise history, with women gradually building up to these targets. When a woman was not reached for a call, multiple call-back attempts were allowed to encourage maximum participation. EPs had undergraduate degrees in exercise physiology and completed three weeks of study-specific training. EPs met weekly to fortnightly with study investigators for clinical supervision related to intervention delivery.

Study workbook and exercise tracker

An exercise workbook (available on request), developed by the study investigators, was provided to all intervention participants and used during telephone sessions. It contained information on treatment-related side-effects, benefits of being active during treatment, exercise safety, types, frequency and intensity of activity and how to progress exercise. It also depicted several strength and flexibility-based exercises. EPs

explained these exercises and encouraged women to check for correct technique in the mirror. A weekly exercise tracker was provided to promote self-monitoring.

Usual care group

Women in the *UC* group participated in all study assessments but had no intervention contacts. The workbook and exercise tracker were mailed to *UC* participants following study completion.

Data Collection

Breast Care Nurses in each participating hospital recorded the number of women approached. Representativeness was established by comparing data obtained from the Queensland Cancer Registry (QCR) for the EfH sample with the same data for the 1488 breast cancers diagnosed in 2007 among women from non-urban postcodes. Call completion and adverse events were recorded by EPs in case management folders after each call for those in the *Tel* group.

Data were collected by telephone interviews (for physical activity) and postal questionnaires (demographics, treatment, quality of life, fatigue, anxiety and upper body function). Further treatment and pathology data were obtained from the QCR for most extensive surgery, stage, type of cancer, lymph node status, tumor size and tumor grading. Data collections were scheduled at: baseline/5-6 weeks post-surgery (pre-intervention); six months post-surgery (mid-intervention and following the period of more regular contact with the EP for those in the *Tel* group); and, 12 months post-surgery (approximately two months post-intervention) (Figure 1). These timepoints coincide with the endpoints from our recent prospective cohort study (11). On average, the

assessments occurred close to the scheduled times, however there was some variability in the time between assessments, much of which was due to variation in how soon baseline data collection occurred after surgery.

Measures – Patient-Reported Outcomes

Physical activity was assessed by the Active Australia Survey (AAS), which has been reported as reliable and has acceptable validity with the Australian adult population (30); is responsive to change following intervention (31) and has been used with Australian cancer patients (10, 32, 33); and in our previous trials (21, 29). Total minutes of physical activity was calculated from the sum of walking, moderate and 2 × vigorous minutes and truncated at 1,680 minutes per week (30). Strength training was assessed via CHAMPS (Community Healthy Activities Models Programs for Seniors), a reliable, valid and responsive instrument aimed at older adults (34, 35), which has also been used in cancer patients (19, 36). The primary study outcomes were meeting EfH targets for aerobic activity (>4 times/wk and >180 minutes of moderate-to-vigorous activity) and resistance training (>2 sessions/wk).

Quality of life was assessed using the Functional Assessment of Cancer Therapy – Breast (FACT-B+4) questionnaire (37). Fatigue was measured using the FACIT (Functional Assessment of Chronic Illness Therapy) - Fatigue Scale (38). These instruments have been widely used in cancer research and have excellent reliability and validity (37-39). Internal consistency was high for both these measures (Cronbach's α = 0.89, 0.94, respectively). State anxiety was measured using the six-item State Trait Anxiety Inventory (STAI-Sf), which has good reliability and validity (40) (Cronbach's α = 0.86). Subjective upper body function was assessed using the Disability of Arm,

Shoulder and Hand (DASH) questionnaire (41), which has been used for breast cancer patients (42-44) (Cronbach's α = 0.95). Confidence to exercise (self-efficacy) was assessed via 6-items on a 5-point Likert scale adapted from a valid and reliable scale (45) and had acceptable internal consistency (Cronbach's α = 0.83).

A study-specific evaluation questionnaire was administered to the *Tel* group. Three items asked about how helpful the program and its resources had been in recovery from breast cancer (1 = "very unhelpful" to 7 = "very helpful"). Two items covered interest in program delivery via face to face and via the internet (1 = "much less interested" to 7 = "much more interested").

Higher scores indicate better (FACT-B+4, fatigue) or worse (anxiety, DASH) health. Minimum differences of interest on our primary effectiveness outcomes, based on published evidence where available and convention where not, were: 10% for physical activity targets, 8 points for quality of life (37), 3 for fatigue (39), half a standard deviation (here, 7.8 points) for anxiety (46) and 10% of the baseline mean (here, 2.2 points) for DASH (42).

Statistical analysis

The sample size (n=143) was based on available resources. It provides 80% power (5% significance, two-tailed) to detect between-groups differences of: 30% in meeting EfH aerobic activity and resistance training targets, 8 points for FACT-B+4, 6 for fatigue, 8 for anxiety and 7 for DASH. Significance was set at $p<0.05$ (two-tailed).

Mixed models were used, with random intercepts for each individual and for each hospital, to accommodate repeated measures without requiring complete case analysis

(47) and to correct for clustering within hospitals. Physical activity data did not conform to any distribution that could be modeled continuously; hence, we examined categorical outcomes with a binomial distribution and logit link. Quality of life, fatigue, anxiety and DASH were examined continuously as change scores (i.e. 6-month value minus baseline value), as change scores approximated a normal distribution, using models that assumed a normal distribution. All models adjust for baseline values of the outcome (to control possible regression to the mean) and, if significant at $p<0.2$, for time between surgery and baseline (weeks), and any other variable that was meaningfully imbalanced (i.e. by ≥10%) between groups at baseline, or any treatment-related variable that was imbalanced between groups over the course of the program.

Analyses were intention-to-treat, however, missing /invalid values were not imputed using baseline carried forward or last-value carried forward methods as the assumption of no change is not realistic over a period of fluctuating recovery from breast cancer. The data appeared to be missing completely at random, as there was no association between observed characteristics and the likelihood of data being missing (data not shown).

Mediational analysis (48) was used to examine whether intervention effects on physical activity and resistance training (minutes and sessions per week) were mediated by changes in confidence to exercise, as measured on a 6-item scale, scored from 1 (lowest) to 5 (highest) (45).

Results

Feasibility

Recruitment rate: Over 14 months of recruitment (March 2007 – April 2008), 383 women were approached for trial participation; 234 were deemed eligible, of whom 143 (61%) consented to participate (Figure 2). Refusal did not vary by hospital and eligible women who refused were of a similar age to participating women (mean (SD): 53.6 (8.7) vs 52.9 (8.9) years, p=0.69).

Retention: Retention was 97% at 6 months and 96% at 12 months, with only 5 *Tel* and 1 *UC* participant withdrawing from the study (p=0.209 for group difference in withdrawal).

Figure 1 About Here

Sample Characteristics and Representativeness: The sample of women, diagnosed between November 2006 and April 2008, was aged 29 to 69 years, with 34.3% being overweight and 25.2% obese (Table 1). Just over half of participants had less than high school education and most were not working at the time of study entry. The majority of the sample received one or more adjuvant therapies (chemotherapy, 64%; radiation, 63%; hormone therapy, 66%) before or (mostly) during the trial. The study sample was slightly younger, but similar in terms of disease characteristics (i.e., tumor size, number of positive nodes, histological type) to non-urban women diagnosed with breast cancer in Queensland in 2007 (see Table 1 in the Electronic Supplementary Material).

Intervention Implementation: *Tel* group participants who remained in the program completed a median of 14/16 calls with their EP (from 5 to 16); 79% completed the majority (>75%) of calls. In total, three adverse events were reported that may be

related to exercise intervention participation (muscle soreness (n=2), musculoskeletal injury (n=1); none were serious and none required discontinuation of participation.

Participant satisfaction

The majority of *Tel* group participants rated the EfH program, workbook, and telephone sessions with the EP as “helpful” to “very helpful” in their breast cancer recovery (90%, 89%, and 92%, respectively). The majority of participants also reported that they would have been at least “interested” in the EfH program if it had been delivered via face-to-face (83%) and over the internet (76%).

Effectiveness

There was no evidence of failure of randomization (i.e. all baseline group differences were p>0.05), however there were some notable group differences (>=10%) in terms of income (<$52,000 per annum), receipt of radiotherapy at baseline, overall receipt of chemotherapy, surgery type and lymph node status.

Physical Activity

Table 2 presents participants’ physical activity at each assessment. Meeting program targets was more common, and doing no activity was less common, for the *Tel* compared with the *UC* group at both follow-up assessments. Only results for resistance training reached statistical significance. Observing the percentages achieving each outcome at each time point, for the *Tel* group, the most improvement occurred by six-months post-surgery; for the *UC* group, improvements only occurred by 12-months post-surgery.

Mediational analysis (see Table 2 in the Electronic Supplementary Material) showed no statistically significant effect of the intervention on physical activity or strength training mediated by confidence to exercise. Confidence to exercise increased significantly more for intervention than control groups at only 6-months post surgery (by 0.3 points). Increases in confidence between baseline and 12-months post surgery were associated with increases in physical activity over the same period: 1.1 sessions per week (significant); and, nearly one hour per week (only significant at $p<0.1$).Other associations were mostly positive in direction, but small and not statistically significant.

Quality of Life, Fatigue, Anxiety, Upper Body Function

Table 3 presents participants' baseline values and adjusted mean changes in outcomes from baseline to follow-up. Improvements in outcomes were all larger in the *Tel* than the *UC* group, however, none of the comparisons were statistically significant and only the 12-month group difference in upper body function was of a meaningful magnitude. Only upper body function improved significantly or meaningfully between baseline and six-months post-surgery. Significant improvements were seen by 12-months post-surgery in all outcomes within the *Tel* group, and in all outcomes except anxiety within the *UC* group. The amount of change was meaningful in quality of life (Tel only), fatigue, and upper body function.

Discussion

Despite recruitment occurring during a very challenging part of the cancer treatment trajectory, results from our trial suggest that a focus on promoting physical activity as part of breast cancer recovery soon after surgery holds strong appeal and is feasible to

deliver via telephone to women living outside urban areas. The trial had high participation and very high 12-month retention rates; participant satisfaction ratings were very high; no serious adverse events were reported; and, the majority of *Tel* group participants completed most of the scheduled calls. Our results are somewhat consistent with previous trials of non-face-to-face exercise interventions *during* adjuvant treatment (13-15) in that retention at six-months is consistently high: 80% (15), 88% (13), and 90% (14). However, consent rates are variable: 15% (14), 33% (15), and 88% (13).

Effectiveness results were more modest. A statistically significant between-groups effect of the program was only seen for resistance training. While not conclusive, examination of within-groups changes suggested a pattern of earlier recovery in terms of physical activity outcomes for women in the *Tel* group. Observing the percentages achieving each outcome at each time point, for the *Tel* group, the most improvement occurred by six-months post-surgery; for the *UC* group, improvements only occurred by 12-months post-surgery. While there were no significant intervention effects mediated by confidence to exercise, results should be interpreted cautiously as the total intervention effects were modest to begin with, the mediational analyses were exploratory (not powered a priori) and may have been affected by non-normality of the data.

All outcomes except anxiety showed some improvement in the *UC* group, which contributed to the lack of difference between groups. The reasons for the *UC* improvements are unclear. Such change would be expected for some outcomes (e.g. quality of life) from the usual recovery trajectories (49). Quality of life improvements between six- and 12-months post-surgery (7.6 points in *Tel,* 5.5 points in *UC)* were

similar to improvements over this period in the Australian Pulling Through Study (PTS) cohort study (49). For physical activity, however, normative data suggests no change over the six- to 12-month post-surgical period (11). Although we did not see biased non-participation, possibly the sample were a more motivated group than the broader population (which we could not assess).

The lack of intervention effects on other patient-reported outcomes (i.e., quality of life, fatigue, anxiety and upper body function) is likely partly attributable to the small and non-significant improvements in aerobic activity. Especially for quality of life, ceiling effects may also have hampered intervention outcomes, as our sample had higher than expected scores at baseline; at 12-months post surgery, both *Tel* and *UC* participants had higher average quality of life compared to published data on non-urban Queensland women with breast cancer (data not shown) (50).

In the trial with outcomes most comparable to ours, Cadmus and colleagues reported no intervention effect on self-reported physical activity or quality of life (FACT-B) (14). For these outcomes, they concluded, as have we, that high baseline levels reduced the ability to demonstrate a treatment effect. Schwartz et al (13) found an effect on preservation of bone mineral density, aerobic capacity and muscle strength, but quality of life was not reported. Segal et al (15) found a treatment effect on their primary outcome of physical function (measured by the SF-36 (51)), but not for overall quality of life (SF-36 and FACT-B), and no effect on aerobic capacity or weight. The authors (15) suggested that the FACT-B may lack sensitivity to change in exercise intervention trials.

Ours is the first study to evaluate an exercise intervention begun soon after breast cancer surgery that targets women living outside of major metropolitan areas (an understudied group). Retention was high, and drop-out did not appear to be systematic; hence, results are likely to be minimally affected by non-response bias. The timing of study assessments allowed comparison with normative data, but did not coincide exactly with the end of intervention (the usual trial endpoint). The use of self-report measures of physical activity, known to be subject to over-reporting (52), is also a limitation.

Future trials would do well to consider use of objective measurement of physical activity, longer-term follow-ups to address the important issue of maintenance, as well as inclusion of cost-effectiveness analysis. As suggested by women in this trial, other non-face-to-face means of intervention delivery (e.g. Internet) should also be investigated.

Conflict of Interest Statement

The authors have no conflict of interest to disclose.

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Figure Legend

Figure 1 - Flow chart of participant recruitment and retention

Table 1. Baseline characteristics of participants in the Exercise for Health Trial (n=143)

	TC (n=73)	UC(n=70)
Age (yrs), *mean (SD)*	51.7 (9.0)	54.1 (8.7)
BMI (kg/m) ^{2}, *mean (SD)*	26.8 (5.4)	27.7 (7.8)
Income		
<$52,000	36 (49.3)	43 (61.4)
$52,000 - $93,599	22 (30.1)	13 (18.6)
$93,600 - $130,000+	7 (9.6)	5 (7.1)
Education n (%) > *Year 12*	35 (47.9)	32 (45.7)
Currently working		
No	49 (67.1)	46 (65.7)
Full-time	11 (15.1)	10 (14.3)
Part-time/casual/other	13 (17.8)	13 (18.6)
Living arrangements		
Alone or with children/relatives/friends	18 (24.7)	17 (24.3)
Couple with no children	33 (45.2)	33 (47.1)
Couple with children	22 (30.1)	20 (28.6)
Treatment and Disease Characteristics [a]		
Chemotherapy (Baseline / Any)		
Yes	27 (37.0) /49 (67.1)	21 (30.0) /37 (52.9)
No	46 (63.0) / 20 (27.4)	49 (70.0) / 29 (41.4)
Radiotherapy (Baseline / Any)		
Yes	4 (5.5) / 42 (57.5)	11 (15.7) / 43 (61.4)
No	69 (94.5) / 26 (35.6)	59 (84.3) / 23 (32.9)
Hormone Therapy (Baseline / Any)		
Yes	11 (15.1) / 47 (64.4)	9 (12.9) / 41 (58.6)
No	62 (84.9) / 23 (31.5)	61 (87.1) / 23 (32.9)
Herceptin (Baseline / Any)		
Yes	2 (2.7) / 12 (16.4)	2 (2.9) / 7 (10.0)
No	71 (97.3) / 55 (75.3)	68 (97.1) / 56 (80.0)
Most extensive surgery		
Lumpectomy	29 (39.7)	37 (52.9)
Mastectomy	39 (53.4)	30 (42.9)
Cancer Stage		
0/I	26 (35.6)	31 (44.3)
II +	38 (52.1)	32 (45.7)
Type of Cancer		
Infiltrating ductal	55 (75.3)	49 (70.0)
Infiltrating lobular	3 (4.1)	9 (12.9)
Mixed ductal/lobular	3 (4.1)	2 (2.9)
Carcinoma In-situ	2 (2.7)	1 (1.4)

Other invasive carcinoma	4 (5.5)	5 (7.1)
Lymph Node Status		
negative	34 (46.6)	42 (60.0)
positive	30 (41.1)	22 (31.4)
none removed	3 (4.1)	1 (1.4)
Tumor Size, *Mean (SD)*	24.6 (20.3)	23.8 (18.8)
Tumor Grading -Overall Histological Grade		
Grade 1	10 (13.7)	7 (10.0)
Grade 2	28 (38.4)	33 (47.1)
Grade 3	26 (35.6)	23 (32.9)

Table presents Mean (SD) or N (%). Figures sum to N<73 (TC)/ 70 (UC) and <100% where data are missing.

[a] In those completing the questionnaires, item non-response regarding chemotherapy, radiotherapy, hormone and herceptin, is assumed to reflect no treatment. Participants classed as “missing” are those who never reported the treatment and did not return at least one follow-up questionnaire.

Table 2. Adjusted odds of physical activity outcomes for telephone counseling (Tel) versus usual care (UC) participants

		% (Unadjusted)		*Tel* vs *UC* Adjusted OR [b] (95% CI)
		Tel **(N=68)** [a]	***UC*** **(N=67)**[a]	
Four or more sessions AND at least 180 min/wk of moderate-to-vigorous physical activity (MVPA)	*Baseline*	22.1	31.3	
	Six months post surgery	41.2	29.9	2.1 (0.8, 5.6)
	Twelve months post surgery	52.2	40.3	2.1 (0.8, 5.5)
Two or more sessions of strength training per week[c]	*Baseline*	5.9	9.0	-
	Six months post surgery	45.6	10.4	8.2 (2.6, 25.3)*
	Twelve months post surgery	40.3	17.9	3.2 (1.2, 8.9)*

[a] n with data on covariates and outcomes at one or more follow-ups. N=68 *Tel,* N=67 *UC* for 6-month estimates N=67 *Tel,* N=67 *UC* for 12-month estimates

*p<0.05

[b] Mixed models (binomial distribution, logit link) include random intercepts for person and hospital. Odds ratios are adjusted for baseline values of the outcome (all models) and: time between surgery and baseline (weeks), age, baseline radiotherapy (yes/ no or unknown), any prior chemotherapy (yes/ no or unknown), surgery (mastectomy/ lumpectomy) [Physical Activity Targets]; time between surgery and baseline, age, baseline radiotherapy, surgery (mastectomy/ lumpectomy) [Strength Targets].

Table 3. Baseline values and adjusted [a] mean change from baseline in continuous outcomes at 6- and 12-months post surgery among telephone counselling (Tel) and usual care (UC) participants

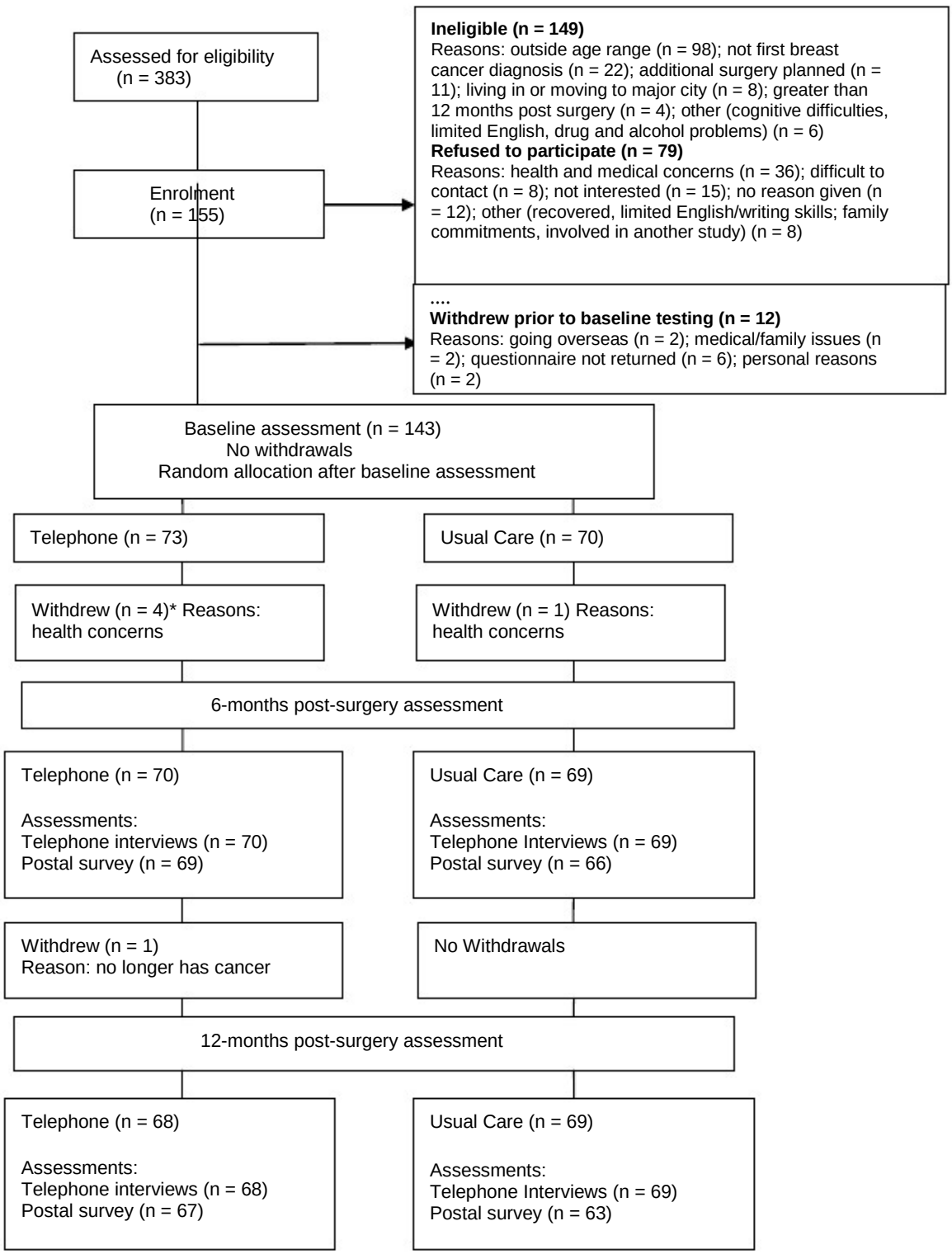
		Tel (n=73) Mean (SD, SE)	n	*UC* (n=70) Mean (SD, SE)	n	*Tel-UC* Mean difference (95%CI)	p
Quality of life (FACTB +4) [b] *(0 to 160)*	Baseline: *mean (SD)*	118.5 (18.0)	68	121.0 (19.4)	64	-	
	6-months: *mean change (SE)*	3.1 (1.7)	68	1.6 (1.8)	63	1.5 (-3.6, 6.6)	0.549
	12-months: *mean change (SE)*	10.7 (1.7)***	66	7.0 (1.8)***	60	3.7 (-1.5, 8.9)	0.156
Fatigue (FACIT) [b] *(0 to52)*	Baseline: *mean (SD)*	36.8 (10.7)	68	35.2 (12.1)	63	-	
	6-months: *mean change (SE)*	1.2 (1.1)	68	-0.8 (1.2)	63	2.0 (-1.4, 5.3)	0.233
	12-months: *mean change (SE)*	5.6 (1.1)***	66	3.7 (1.2)**	59	1.9 (-1.5, 5.3)	0.259
Anxiety (STAI) [b] *(20 to 80)*	Baseline: *median (25th, 75th)*	40.0 (33.3, 51.7)	68	36.7 (26.7, 46.7)	62	-	
	6-months: *mean change (SE)*	-3.1 (1.7)	66	-2.8 (1.7)	62	-0.3 (-5.2, 4.6)	0.891
	12-months: *mean change (SE)*	-7.2 (1.7)***	64	-2.1 (1.8)	55	-5.1 (-10.1, +0.0)	0.050
Function (DASH) [b] *(0 to 100)*	Baseline: *median (25 , 75)* th th	21.7 (7.5, 31.7)	69	18.3 (17.5, 29.6)	64	-	
	6-months: *mean change (SE)*	8.7 (1.2)***	69	-8.5 (1.2)***	64	-0.21 (-3.7, 3.3)	0.902
	12-months: *mean change (SE)*	-11.7 (1.2)***	67	-8.9 (1.2)***	60	-2.9 (-6.4, 0.7)	0.107

Table presents mean (SD) at baseline, and adjusted mean change from baseline (SE) at 6-months and 12-months post surgery

* p<0.05 ** p<0.01 *** p<0.001

[a] Mixed models included random intercepts for person and hospital. 6-month and 12-month data are adjusted for baseline values (all models) and: surgery (mastectomy/lumpectomy), lymph node status (postive/ negative or unkown) [FACTB+4]; surgery type, lymph node status [Fatigue]; baseline radiotherapy, income (<$52, 000 p.a. / 52, 000+ p.a. / missing) [Anxiety]; time between surgery and baseline (weeks), age, baseline radiotherapy (yes/ no or unkown), previous chemotherapy (yes/ no or unkown) [DASH].

[b] Higher scores indicate: higher quality of life (FACTB+4), less fatigue (FACIT), more anxiety (STAI) and poorer upper body function (DASH).



* 3 withdrew prior to both 6-month assessments; 1 withdrew after the 6-month telephone interview but before the 6-month postal questionnaire

CONSORT 2010 checklist of information to include when reporting a randomised trial *

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	Title page
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	2-4
	2b	Specific objectives or hypotheses	3-4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	NA
Participants	4a	Eligibility criteria for participants	5
	4b	Settings and locations where the data were collected	5,7
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	5-7
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed Any changes to trial outcomes after the trial commenced, with reasons	8-10
Sample size	6b	How sample size was determined When applicable, explanation of any interim analyses and stopping guidelines	NA
	7a		9
	7b		NA
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	5
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	NA
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	5
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	NA

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	NA
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9-10
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	9-10
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	29
		For each group, losses and exclusions after randomisation, together with reasons	
Recruitment	13b	Dates defining the periods of recruitment and follow-up	29
	14a	Why the trial ended or was stopped	4
	14b	A table showing baseline demographic and clinical characteristics for each group	4
Baseline data	15		24-25, Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	26-27, Table 2 and 3
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	26-27, Table 2 and 3
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	26, Table 2 % (unadjusted) and OR (adjusted) 26-27, OR Table 2, means Table 3 are adjusted
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	11-12
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	13-16
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	13-16
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	13-16
Other information			
Registration	23	Registration number and name of trial registry	Disclaimer section on

Protocol	24	Where the full trial protocol can be accessed, if available	title pages 6
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Disclaimer section on title pages

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

Figure

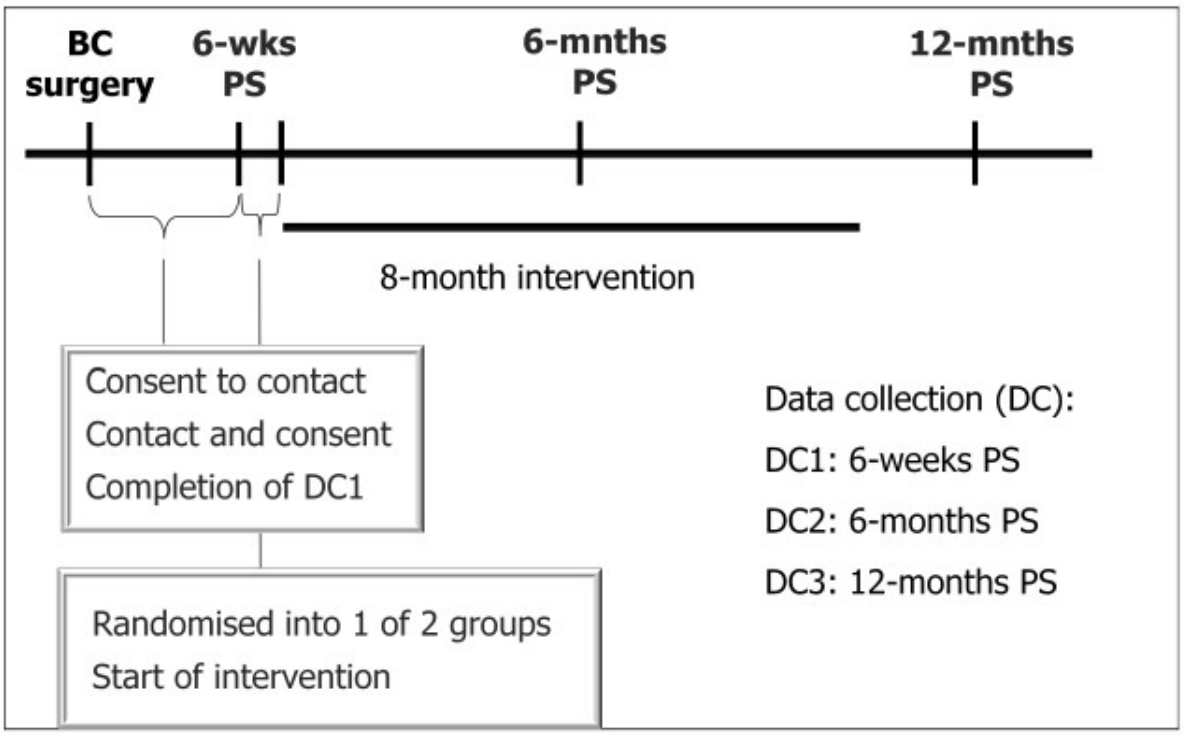


Figure 1- Study design/timeline

BC = breast cancer; PS = post-surgery

Table 1: Baseline demographic and disease characteristics of Exercise for Health study participants (n=143) diagnosed between 2006 and 2008 compared with Queensland Cancer Registry data for breast cancers diagnosed among non-urban women in 2007 (n=1488)

	Study Participants	Cancer Registry
Age at diagnosis (years)	53 (46, 60)	59 (50,68)
Breast cancer size (mm) [a]	15 (10, 30)	16 (10, 27)
Number of nodes examined [a]	10 (5, 15)	8 (2, 14)
Positive nodes (%)[a]	44 (33.1)	479 (34.7)
Histological type [a]		
Infiltrating ductal	100 (75.8)	1072 (72.0)
Infiltrating lobular	9 (7.1)	153 (10.3)
Other	23 (17.1)	263 (17.7)

Table presents median (25 , 75 percentile) or N (%)

Source: Queensland Cancer Registry Data Collection, extracted 24-01-11.

[a] Study data are weighted to the age distribution of non-urban Queensland breast cancer cases

[b] % excludes women of 'unknown' node status / histological type.

Table 2. Mediation [a] of intervention changes in physical activity outcomes at 6- and 12- months by concurrent changes in confidence to exercise[a]

	6- month changes (n=70 *Tel;* n=69 *UC)*			12-month changes (n=68 *Tel;* n=69 *UC)*		
	β (SE)β (95% CI)			β (SE)β (95% CI)		
	abab			*abab*		
Physical Activity						
Minutes / week	0.3(0.1)*	7.5(18.5)	2.5 (-6.9, 18.5)	0.1(0.1)	57.9 (30.7)^	3.0(-11.6, 25.5)
Sessions / week	0.3(0.1)*	-0.2 (0.4)	0.1 (-0.5, 0.3)	0.1 (0.5)	1.1 (0.5)*	0.1 (-0.2, 0.5)
Strength training						
Minutes / week	0.3(0.1)*	10.9 (8.1)	3.7 (-0.4, 16.7)	0.1 (0.1)	8.9 (5.6)	0.5 (-1.6, 4.9)
Sessions / week	0.3 (0.1)*	0.3(0.3)	0.1 (-0.0, 0.4)	0.1 (0.1)	0.4 (0.3)	+0.0 (-0.1, 0.2)

[a] Mediated effect (ab) with bootstrapped 95% confidence intervals (n=5000 iterations). Models adjust for baseline values of the relevant physical activity measures. The *a* pathway is the group difference (Tel – *UC)* in changes in confidence to exercise (adjusted for baseline values); the *b* pathway is the association between changes in confidence and changes in physical activity outcomes (adjusted for group and baseline values).

[b] Confidence to exercise (1-6) (48). Mean (SD) at baseline, 6-months and 12-months were: 3.7(1.0), 4.3(0.6), 4.4 (0.6) [Tel] and 3.6(0.9), 3.8(0.7), 4.0(0.8) [UC] for those with complete data (n=68 *Tel;* n=69 *UC).*

*p<0.05 ^p<0.1