Translational Value of Exercise in Routine Care Following Hematopoietic Stem Cell Transplantation: A Retrospective Analysis

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Abstract

Purpose: Exercise is an effective adjuvant therapy to address many of the symptoms experienced by Hematopoietic Stem Cell Transplant (HSCT) recipients. However, there is little translational research examining meaningful clinical effects. A retrospective analysis of a community-embedded exercise program based at a large urban comprehensive cancer hospital was conducted, with the aim of establishing the translational value of exercise in a clinical setting. A secondary aim was to determine the impact of baseline function on exercise response.

Methods: The Living Well Program is an evidence-based program supervised by Accredited Exercise Physiologists, delivered through the Chris O'Brien Lifehouse. HSCT recipients are prescribed individualised, once-weekly 1-hour aerobic, resistance and balance training. Changes in physical function (6-minute walk distance, strength, and balance), fatigue, and quality of life measures from baseline to post-intervention were analysed, and also assessed in relation to session attendance. Participants were then stratified as low- or high-function for each measure of physical function.

Results: Data from 48 participants (male $n=27$, age $=54.3 \pm 11.7$ -years) was included in the analysis. Significant improvements were found for all outcome measures, with improvements exceeding minimal clinically important differences for 6-minute walk distance (6MWD) and 30-second sit-to-stand. Greater session attendance correlated with improvements in 6MWD and strength outcomes. Exercise response was greater among those with lower baseline scores for 6MWD only ($p < 0.001$).

Conclusions: An existing exercise program embedded in cancer care was successful in eliciting improvements that are both significant and clinically relevant. Further investigations into key factors that influence the efficacy of these programs are required.

Introduction

Haematological malignancies are becoming increasingly prevalent in Australia, with the number of Australians diagnosed rising by 38% over the past decade [1]. Hematopoietic Stem Cell Transplantation (HSCT) is a common treatment for haematological malignancies. Although beneficial in improving survival rates, HSCT is associated with complications such as infections, graft-versus-host disease, muscle toxicity, significant functional decline, and cancer-related fatigue [2, 3].

HSCT is accompanied by debilitating and persistent functional limitations and physical deconditioning [3, 4]. Prior to HSCT, individuals with haematological cancers typically present with significantly poorer exercise capacity and muscle strength compared to sex- and age-matched controls [5]. Deconditioning is then exacerbated as a consequence of extended periods of hospitalisation following HSCT. Without targeted intervention, the acute functional decline occurring in the first 6-months post-transplant are often not regained within 5-years [5, 6]. Fatigue is also a considerable concern. Up to 90% of recipients report high levels of fatigue in the acute post-HSCT period [7] and 41% experience severe fatigue during the first

5-years [3]. These factors contribute to a reduced quality of life (QoL) and ability to perform daily tasks in this cohort [8].

As a powerful adjunct therapy, exercise has been shown to address physiological and psychological consequences of HSCT. Evidenced in a 2013 meta-analysis [9], exercise across multiple treatment timings produces significant, moderate effects for cardiorespiratory fitness, lower body strength, and fatigue. Small but significant effects for upper body strength and QoL have also been demonstrated. However, evidence for exercise initiated post-HSCT is mixed. Individual controlled trials confirm the benefit of commencing exercise in the weeks to months following HSCT, with significant improvements seen for cardiorespiratory fitness and muscle strength [8, 10, 11]. It is worth noting that with the exception of QoL, a more recent meta-analysis did not support these findings [12]; however, these conclusions are limited by the small sample size, stringency of inclusion criteria, and the potential for bias associated with the medium methodological quality of studies pooled for analysis. The efficacy of exercise programs for improving grip strength and sit-to-stand (STS) is also mixed across individual RCTs [8, 11, 13], and no known meta-analyses are available. Further research is therefore required to enhance understandings of the benefits of exercise exclusive to post-HSCT settings.

Although individuals are reported to respond positively to exercise post-HSCT, the extent to which baseline function impacts this response has not been well-established in an HSCT cohort. Among other populations, greater responses to exercise are known to be associated with poorer performance at baseline [14–16]. This is likely due to a ceiling effect limiting the degree of improvement possible among those with higher baseline scores. Therefore, less deconditioned individuals likely require a greater volume or intensity of exercise to elicit the same level of benefit [17]. A recent meta-analysis of post-treatment exercise among individuals with cancer explored this relationship [18]. Baseline strength was shown to significantly moderate the response to exercise, whilst improvements in aerobic fitness did not differ according to baseline level. However, the ability to generalise these findings to HSCT-specific contexts is impaired due to the inclusion of multiple cancer and treatment types. Only one known study has explored this concept among HSCT recipients [17], whereby participants with low baseline scores demonstrated a significantly greater response to exercise. These participants did not undergo the same degree of deconditioning as those with high baseline scores, with this functional decline attenuated for three of the five physical outcomes. However, the initiation of exercise and stratification of participants pre-HSCT limits the generalisability of the findings to all HSCT contexts, thereby necessitating similar investigations in exclusively post-HSCT settings.

Despite the recognised benefits, the majority of Australians with cancer fail to meet recommended exercise guidelines [19], with safety concerns and poor access to facilities commonly precluding participation [20, 21]. Embedding exercise into routine cancer care may be an effective strategy to overcome such barriers, as supported by a recent position statement from the Clinical Oncology Society of Australia (COSA) [19]. However, as exercise is rarely integrated with HSCT-care, it is unknown whether the benefits seen in controlled settings translate into ‘real world’ programs.

The primary aim of this retrospective analysis was to evaluate a community-embedded outpatient exercise program for individuals following HSCT, and to assess the effectiveness of exercise in a translational setting. The secondary aim was to determine the extent to which baseline physical function impacts exercise response.

Methods

Participants

This study was a retrospective analysis of data collected through The Living Well program at Chris O'Brien Lifehouse Comprehensive Cancer Hospital (Sydney, Australia) in the supportive care and integrative oncology outpatient department. Individuals were referred to the program by their haematologist, nurse or general practitioner following HSCT. Inclusion criteria for the program included: aged > 18 years, specialist referral following hematopoietic stem cell transplant, haemoglobin > 6.5dL, platelets > $15 \times 10^9/L$, capable of walking $\geq 100m$, able to give informed consent, and willing and able to comply with program requirements. Exclusion criteria included: Eastern Cooperative Oncology Group (ECOG) performance status ≥ 3 or Karnofsky score < 60, inability to read and understand English, and presence of concurrent illness or symptoms that precluded safe exercise participation. Ethical approval, with waiver of consent, was granted by the Sydney Local Health District (RPAH zone) Human Research Ethics Committee [X17-0147 & LNR/17/RPAH/2179.47/AUG19].

The Living Well Program

The Living Well program is a multi-modal rehabilitation program for HSCT recipients. This analysis includes people (N = 48) who participated in the program between July 2014 and June 2019. Participants were initially fee paying and prescribed a once weekly hospital outpatient-based individualised exercise program comprising progressive aerobic, resistance and balance training, delivered over an 8-week period (maximum 8 sessions). From July 2017 to June 2019, with participation free of charge due to a philanthropic donation, the restriction on maximum number of sessions was removed. One-hour sessions were conducted in a group setting and supervised by an Accredited Exercise Physiologist. Moderate intensity aerobic exercise was monitored by rate of perceived exertion (RPE), and prescribed using treadmill or cycle ergometer (upright, recumbent or arm). Resistance training intensity was prescribed based on 1 repetition maximum (1RM) testing conducted at baseline where appropriate. Participants performed 2 sets of 12 repetitions at a perceived exertion equivalent to an intensity of 60–70% 1RM during weeks 1–3. This was increased 3x10 at 75% 1RM (weeks 4–6) and 4x8 at 80% 1RM (weeks 7 and beyond). Exercises included leg press, seated row, bicep curls, triceps dips/extensions, TRX squats, latissimus dorsi pulldowns, and hip and trunk stability. Progressive balance training was delivered using tandem walking, single-leg ball throwing, and unsteady surface standing. Support sessions were provided at the conclusion of exercise sessions; facilitated by dietitians, psychologists or yoga instructors. Participants also received 4–6 sessions of evidence-based complementary therapies in the form of oncology massage, reflexology or acupuncture according to need and preference. These therapies were

provided by credentialed practitioners of the supportive cancer and integrative oncology outpatient department in which the study was conducted.

Protocol

Outcomes were assessed prior to the intervention (baseline) and following the final exercise session (post-intervention). Measurements of physical function and patient-reported outcomes were obtained.

Outcome measures

Physical function The distance achieved in the six-minute walk test (6MWD) was used as an indicator of functional exercise capacity and cardiorespiratory fitness [22]. Upper and lower body strength was assessed using 1 repetition maximum (1RM) testing for seated row and leg press, respectively. The 30-second sit-to-stand test (30s-STT) was used to assess lower limb functional strength and endurance [23]. Participants were instructed to perform as many repetitions as possible in 30-seconds without the use of the upper limbs. Grip strength was assessed using a hand-held dynamometer (SAEHAN-SH5001 (Glanford Electronics Ltd, Scunthorpe, United Kingdom) or Deyard EH101 (Deyard tech)). The same device was used at baseline and post-intervention for each participant. for consistency. The best of three attempts was recorded for both the left and right hands, with the average of the two used for analysis. This measurement is widely considered an indicator of health status and predictor of future mortality and disability [24]. Static balance was assessed through time (in seconds) participants were able to maintain balance on one leg.

Patient-reported outcomes The Brief Fatigue Inventory (BFI) is a simple and rapid means of evaluating daily fatigue, validated for use among individuals with cancer [25]. A global fatigue score was obtained by averaging the 9-items of the BFI, whereby a higher score indicates more significant fatigue. QoL was assessed through the self-reported Functional Assessment of Cancer Therapy – Bone Marrow Transplantation (FACT-BMT) questionnaire, which was developed and validated for use with HSCT recipients [26]. Higher scores indicate greater QoL.

Statistical Analysis

Data are expressed as means $\pm$ standard deviation (s.d) and significance set at $p \leq 0.05$, unless otherwise stated. Descriptive statistics were used for participant demographics. Percentage change from baseline to post-intervention was calculated for all outcomes. Following tests for normality, the overall effect of the program was assessed using paired sample t-tests or its non-parametric equivalent (Wilcoxon signed-rank test) to detect differences between baseline and post-intervention values. The relationship between changes in outcome measures and the number of exercise sessions attended was determined using Person's correlation or its non-parametric equivalent (Spearman Rank order correlation). Correlations are classified as weak ($r = 0.1$), moderate ($r = 0.4$) and strong ($r \geq 0.7$) [27].

Participants were stratified into low- and high-function groups for each physical function measure according to baseline scores. It was not possible to differentiate participants according to predicted

norms as utilised in similar research [17, 28] as the majority fell below age- and gender-matched normative values for 6MWD, leg press, grip strength, 30s-STS and balance [29–31]. A median split was instead used to distinguish groups, with < median scores categorised as low-function and ≥median scores as high-function [32]. Repeated measures ANOVAs (time & group x time) – or Mann Whitney U tests for non-parametric data – were conducted for each outcome to examine differences in exercise response between groups.

Due to the small sample size for each outcome, Hedge’s g (g) was used to indicate the magnitude of effect. Small, medium and large effect sizes are defined as 0.2, 0.5 and 0.8 respectively [33]. IBM SPSS Statistics for Macintosh Version 26 (IBM Corp., Armonk, N.Y., USA) was used for data analysis.

Results

Forty-eight participants (male 56%, aged 54.3 ± 11.7 years) were included from an original sample of 82 (Table 1). Myeloma was the most common cancer type of those included (56.3%), and the majority of participants (58.3%) had autologous transplants. These participants were included due to the presence of complete baseline and post-intervention data for at least one outcome measure. Data from 34 participants was excluded, with reasons for missing data including bone disease, technical faults with equipment, acute injuries or pain at time of assessment, and difficulties with scheduling. Participants were on average 76 ± 45 days post-transplant at baseline.

Table 1: Participant characteristics at baseline

	Included Participants (N=48)		Excluded Participants (N=34)	
Age (years; mean $\pm$ s.d)	54.3 $\pm$ 11.7		52.7 $\pm$ 14.0	
Time since transplant (days; mean $\pm$ s.d)	76.0 $\pm$ 45.0		126.0 $\pm$ 177.0	
	Number	Percentage (%)	Number	Percentage (%)
Male	27	56.2	14	41.2
Female	21	43.8	20	58.8
Cancer Type				
Myeloma	27	56.3	9	26.5
Leukemia	11	22.9	5	24.7
Hodgkin Lymphoma	0	0	1	26.5
Non-Hodgkin Lymphoma	4	8.3	9	2.9
Other	5	10.4	5	14.7
Unknown	1	2.1	5	14.7
Transplant Type				
Autologous	28	58.3	14	41.2
Allogeneic	17	35.4	9	26.5
Unknown	3	6.3	11	32.4
Participation Before / After Philanthropic Donation				
Before	39	81.3	6	17.6
After	9	18.7	28	82.4

Table 2 presents the overall effect of the program on outcome measures. Significant improvements were demonstrated for all functional measures ($p \leq 0.05$), with moderate effects seen for 6MWD and 30s-STs ($g \geq 0.5$). Significant effects were also observed for physical activity, fatigue and overall QoL, in addition to social wellbeing, functional wellbeing and bone marrow transplant subscales ($p \leq 0.05$).

Table 2: Change in physical function and patient-reported outcomes from baseline to post-intervention

Outcome Measure	N	Baseline Mean $\pm$ s.d	Post-intervention Mean $\pm$ s.d	Change Mean $\pm$ s.d	% change Mean	Effect Size Hedges G	p-value
Physical function							
6MWD (m)	32	418.8 $\pm$ 98.4	497.6 $\pm$ 82.0	78.8 $\pm$ 48.2	18.8	0.79	<0.001*
Seated Row 1RM (kg)	18	33.2 $\pm$ 15.0	40.6 $\pm$ 18.0	7.4 $\pm$ 9.7	22.2	0.46	<0.001*
Leg Press 1RM (kg)	21	59.3 $\pm$ 37.4	73.2 $\pm$ 37.9	13.9 $\pm$ 11.5	23.5	0.37	<0.001*
30s-STs (reps)	20	12.0 $\pm$ 3.4	14.9 $\pm$ 5.0	3.0 $\pm$ 2.9	24.7	0.54	<0.001*
Grip Strength (kg) [§]	24	28.7 $\pm$ 12.5	30.6 $\pm$ 11.5	1.9 $\pm$ 4.0	6.6	0.14	0.03*
Balance (secs)	25	34.3 $\pm$ 22.0	42.8 $\pm$ 18.7	8.5 $\pm$ 10.9	24.8	0.38	<0.001*
Patient-reported outcomes							
BFI	28	4.6 $\pm$ 1.9	3.4 $\pm$ 2.2	-1.2 $\pm$ 2.5	-25.7	0.22	<0.001*
FACT-BMT							
Total Score [§]	15	97.5 $\pm$ 16.4	105.5 $\pm$ 16.2	8.1 $\pm$ 10.6	8.3	0.47	0.01*
Wellbeing domains							
Physical	21	19.0 $\pm$ 6.2	21.3 $\pm$ 4.9	2.3 $\pm$ 7.1	12.1	0.30	0.12
Social	22	21.7 $\pm$ 5.6	23.1 $\pm$ 4.6	1.4 $\pm$ 1.5	6.3	0.19	0.02*
Emotional	15	19.6 $\pm$ 2.7	19.5 $\pm$ 2.5	-0.1 $\pm$ 2.3	-0.4	0.02	0.86
Functional [§]	16	17.1 $\pm$ 4.9	19.7 $\pm$ 5.2	2.5 $\pm$ 4.6	14.8	0.41	0.04*
BMT [§]	16	22.2 $\pm$ 4.4	24.0 $\pm$ 4.4	1.8 $\pm$ 3.1	8.1	0.31	0.04*

* significant at $p < 0.05$; #negative change denotes improvement; §analysis using paired samples t-test; 6MWD: six-minute walk distance; 1RM: 1-repetition maximum; 30s-STs: 30-second sit-to-stand; BFI: Brief Fatigue Inventory; FACT-BMT: Functional Assessment of Cancer Therapy – Bone Marrow Transplant

A moderate, positive correlation was observed between the number of exercise sessions attended and change in leg press 1RM ($r = 0.41$), whilst weak correlations were observed for 6MWD ($r = 0.17$), grip strength ($r = 0.32$) and seated row 1RM ($r = 0.37$). No other relationships with session attendance were identified.

The extent to which baseline function impacted exercise response was less consistent (Table 3). A statistically significant difference in exercise response between groups was only observed for 6MWD ($p < 0.01$). Despite this, percentage change from baseline to post-intervention favoured the low-function. Greater effect sizes were also observed within this group for most measures, with large effects seen for 6MWD, seated row 1RM, leg press 1RM, and balance ($g > 0.80$). For 6MWD, improvements in both low- (+ 107.9m) and high-function (+ 49.6m) groups exceeded the minimal clinically important difference (MCID) value of 14-30.5m [34]. Improvements in 30s-STS for both groups (+ 2.5-reps; +3.4-reps) were also within the MCID of 2–3 repetitions [35, 36].

Table 3: Comparison of change in physical function in low- and high- function groups from baseline to post-intervention

Variable	N	Baseline Mean $\pm$ s.d	Post- intervention Mean $\pm$ s.d	Change Mean $\pm$ s.d	% change Mean	Effect Size Hedge's G	p-value
6MWD (m)							<0.001*
Low-function	16	342.5 $\pm$ 63.3	450.4 $\pm$ 67.2	107.9 $\pm$ 42.9	31.5	1.67	
High-function	16	495.1 $\pm$ 60.0	544.7 $\pm$ 68.2	49.6 $\pm$ 33.8	10.0	0.81	
Seated Row 1RM (kg)							0.44
Low-function	9	20.8 $\pm$ 5.4	27.5 $\pm$ 6.5	6.7 $\pm$ 2.6	32.2	1.21	
High-function	9	45.6 $\pm$ 10.4	53.6 $\pm$ 16.3	8.1 $\pm$ 13.1	17.8	0.59	
Leg Press 1RM (kg)							0.88
Low-function	10	31.0 $\pm$ 11.5	41.3 $\pm$ 13.1	10.3 $\pm$ 8.1	33.2	0.84	
High-function	11	85.0 $\pm$ 33.8	102.3 $\pm$ 27.8	17.3 $\pm$ 12.6	20.4	0.56	
30s-STs (reps)							0.88
Low-function	10	9.5 $\pm$ 1.8	12.0 $\pm$ 2.4	2.5 $\pm$ 2.2	26.3	0.76	
High-function	10	14.4 $\pm$ 2.7	17.8 $\pm$ 5.3	3.4 $\pm$ 3.4	23.6	0.85	
Grip Strength (kg) [§]							0.03* (Time)
Low-function	12	18.1 $\pm$ 4.2	21.3 $\pm$ 5.3	3.2 $\pm$ 2.1	17.4	0.60	0.13 (Group x Time)
High-function	12	39.3 $\pm$ 8.0	39.9 $\pm$ 7.5	0.7 $\pm$ 5.1	1.7	0.07	
Balance (secs)							0.11
Low-function	12	14.4 $\pm$ 10.0	25.6 $\pm$ 11.0	11.3 $\pm$ 12.7	78.2	1.05	
High-function	13	52.7 $\pm$ 10.4	58.7 $\pm$ 4.7	6.0 $\pm$ 8.8	11.3	0.55	

* significant at $p < 0.05$; § analysis using repeated measures ANOVA; 6MWD: six-minute walk distance; 1RM: 1-repetition maximum; 30s-STs: 30-second sit-to-stand;

Discussion

This study demonstrated the overall effectiveness of an exercise program embedded in cancer care and evaluated the extent to which baseline function impacted the response to exercise following HSCT. The success of the program in improving all measures of physical function is important given the nature of the program provision. These improvements are not surprising as they are in line with much of the

literature of controlled trials, confirming the benefits of exercise for 6MWD and cardiorespiratory fitness in HSCT recipients [8–11, 17]. Recent evidence suggests nearly half of HSCT recipients exhibit moderate to severe impairments in exercise capacity at one-year post-HSCT [28], thus demonstrating the important role for translation of exercise provision into care in this period. It is of note that meaningful relationships were observed between session attendance and improvements in 6MWD and maximal strength (leg press 1RM, seated row 1RM), suggesting session adherence was an important moderator of improvements in these outcomes. Balance also improved in response to the intervention, consistent with evidence from a systematic review among cancer survivors with balance impairments [37]. Furthermore, whilst the efficacy of interventions is commonly quantified using statistical measures, the use of minimal clinically important difference (MCID) values has been proposed as a key evaluator of translational research [38]. Despite differences in responsiveness to exercise according to baseline function, improvements in 6MWD and 30s-STs were both statistically and clinically significant for the two groups, with average improvements exceeding MCIDs for these measures [34–36]. Overall, the program was efficacious for the cohort in addressing the marked treatment related reductions in exercise capacity, strength and balance, which subsequently negatively affect QoL and interfere with daily function [5, 8].

Cancer-related fatigue has a complex aetiology involving inflammation, disease, treatment, demographic and psychological features [39]. Although the mechanisms by which exercise ameliorates fatigue are not well understood, the significant reduction in fatigue seen in the current study supports available literature among HSCT recipients. Whilst promising, post-intervention fatigue levels remained elevated, nearing moderate [25]. However, this is not unexpected as increased levels of fatigue commonly persist in the years following HSCT [3]. It is also noted that the recommended approach to post-treatment cancer-related fatigue is multimodal [42], and as such, the inclusion of evidence-informed complementary therapies may have contributed to the perceived improvement in fatigue.

The efficacy of the program on QoL varied between subscales, with no improvements evidenced in emotional wellbeing and non-significant improvements observed in physical wellbeing. Evidence for improvements in specific subsets of QoL among HSCT recipients is mixed [4, 13, 43], however the significant improvement in overall QoL is consistent with meta-analyses [9, 12]. With QoL negatively impacted by physiological and psychological consequences of HSCT, the significant improvement in overall QoL and across 3-subscales within the present study, albeit small, is promising.

One variable of interest in evaluating the feasibility of programs embedded in cancer care is the financial burden placed on patients. The relationship between financial support or investment and program attendance is vital in the implementation of exercise in cancer care, especially given the prolonged treatments and financial toxicity associated with haematological malignancies. Correlations between session attendance and magnitude improvement were observed for 4 measures. However few conclusions can be drawn due to the restrictions on session attendance placed upon the majority of participants included in this analysis who attended the program prior to the philanthropic donation. Programs of longer duration or without restrictions on number of permissible sessions should be studied to improve understandings of associations between session attendance and magnitude of improvement.

The impact of baseline function on exercise response was inconsistent. The inverse relationship between 6MWD at baseline and responsiveness to exercise is consistent with prior research in an HSCT setting [17]. However, whilst the ability to draw accurate comparisons with similar research is limited due to timing of exercise around HSCT and measurements used to assess outcomes, the absence of statistically significant differences between groups for remaining outcomes contrasts such research [17]. This disparity may be due to differences in extent of deconditioning at baseline. Participants in the current study were more deconditioned than expected based upon existing literature [8, 10, 11], which influenced the method used to stratify participants. Whilst low- and high-function was used to describe the groups, the overwhelming majority would be classified as low-function based on norms [29–31]. Hence, it is likely a ceiling effect was not present within this sample, thus contributing to the absence of significant differences between groups for most outcomes.

Although the absolute change in physical and functional measures was similar between groups for all outcomes except 6MWD, improvements in proportion to baseline values (percentage change) were consistently higher among the low-function group by virtue of their poorer scores at baseline. Larger effect sizes were also observed within this group for most outcomes. Therefore, despite failing to reach statistical significance for five of the six outcomes, differences in exercise response according to baseline function were present. Understanding such differences is vital in informing realistic goal setting and prescription. Future research should investigate the effect of varying exercise volume and intensity according to baseline function, with suggestions a greater exercise prescription may be necessary for those with higher baseline scores to elicit comparable benefits [17].

Furthermore, this was a multimodal exercise-based program that also included access to evidence-informed complementary medicine interventions and lifestyle education. Although not included in this analysis, future research would benefit from further examination of the impact of patient uptake of these complementary therapies due to understandings of the benefits of an integrative approach to cancer care [42].

Various limitations must be considered in interpreting these findings. Large amounts of data were unaccounted for, which reduced the sample size available for analysis. Although not unexpected given the nature of the retrospective data acquisition, future research would benefit from more defined data collection procedures. The pre-post design also presents a potential for the results to exaggerate a true effect, and without a controlled comparison, the extent to which improvements within the present study are attributable to the prescribed exercise remains open to investigation. As the ethics of conducting an RCT by means of depriving a control group of a recognised standard of care remain the subject of much debate, future research should instead focus on achieving an optimal program design by identifying characteristics of this population that interact with exercise training variables. Whilst evidence specific to HSCT is still in its infancy, greater levels of physical activity are associated with lower mortality risk across other cancer types [44]. As such, future translational research should investigate the potential impact of the program on improved self-efficacy and increased physical activity beyond supervised sessions as measured through validated assessment tools. Despite these limitations, the significant

improvements were obtained from a 'real world' clinical setting. This suggests the improvements observed in specifically designed clinical trials can be translated into practice, thus signifying the efficacy of an existing program embedded in cancer care.

Conclusion

The Living Well Program was successful in improving physical function, fatigue and QoL post-HSCT. Exercise response differed according to baseline function for measures of physical function, however only reached significance in 6MWD. This study supports the clinically meaningful efficacy of a real-world program embedded in cancer care and confirms that implementation of tailored exercise programs will likely benefit HSCT recipients in their recovery.

Declarations

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Code availability: Not applicable.

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Consent to participate: Consent to the program was provided by each participant.

Consent for publication: Waiver of consent provided for de-identified data granted by ethics.

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