

Impact of an Allied Health Prehabilitation Service for Haematologic Patients Receiving High Dose Chemotherapy in A Large Cancer Centre

Jessica Crowe (✉ jess.crowe@petermac.org)

Peter MacCallum Cancer Centre <https://orcid.org/0000-0002-7913-0013>

Jill Francis

The University of Melbourne Melbourne School of Health Sciences

Lara Edbrooke

Peter MacCallum Cancer Centre

Jenelle Loeliger

Peter MacCallum Cancer Centre

Trish Joyce

Peter MacCallum Cancer Centre

Christina Prickett

Peter MacCallum Cancer Centre

Alicia Martin

Peter MacCallum Cancer Centre

Amit Khot

Peter MacCallum Cancer Centre

Linda Denehy

Melbourne School of Health Sciences: The University of Melbourne Melbourne School of Health Sciences

The Centre for Prehabilitation and Peri-operative Care

Peter MacCallum Cancer Centre

Research Article

Keywords: prehabilitation, implementation, allied health, autologous stem cell transplant, high dose chemotherapy.

Posted Date: June 7th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-447123/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at Supportive Care in Cancer on October 5th, 2021. See the published version at <https://doi.org/10.1007/s00520-021-06607-w>.

Abstract

Purpose

To evaluate the impact of routine multidisciplinary allied health prehabilitation care in haematologic cancer patients receiving high-dose chemotherapy with autologous stem cell transplant (AuSCT).

Methods

In a tertiary cancer centre, 12-months of prospectively collected data was retrospectively analysed. Patients were referred to the service for individualised exercise prescription, nutrition intervention and, if indicated through screening, psychological intervention. Impact and operational success were investigated based on the RE-AIM framework: patient uptake of the service and sample representativeness (Reach); Effectiveness in terms of changes in outcomes from initial to pre-transplant assessment; Adoption of the service by key stakeholders; fidelity of the prescribed exercise program (Implementation); and the extent to which the service had become part of routine standard care (Maintenance).

Results

183 patients were referred to the AuSCT service, of whom 133 (73%) were referred into the prehabilitation service, 128 (96%) were eligible and 116 (91%) participated. Significant improvements were demonstrated between initial and pre-transplant assessments particularly six-minute walk distance (n = 45); mean difference (95% CI) 39.9m (18.8 to 61.0, $p < 0.005$). Missing data were an issue for assessment of effectiveness. Fidelity of exercise prescription was moderate with 72% of eligible patients receiving the intended aerobic and resistance exercise interventions.

Conclusion

The prehabilitation service was well adopted by clinicians. Clinically relevant improvements in outcomes were demonstrated. Recommendations, including development of well-integrated discipline-specific assessment intervention and measurement protocols, are highlighted to improve the service. Prehabilitation should be routinely considered to support the care of patients undergoing AuSCT.

Introduction

The adverse effects of cancer and its treatments are well known and include both physical and psychosocial morbidity [1]. The prevalence and diversity of functional impairments among people with cancer have stimulated the development of intervention strategies that aim to identify and reduce these to maintain or recover pre-diagnosis levels of function [2]. High dose chemotherapy followed by

autologous stem cell transplant (AuSCT) is an intensive treatment for people with haematological cancers, aiming to achieve cure or substantially prolong disease control. Treatment and disease related side-effects for these patients include reduced physical function and health-related quality of life (HRQoL); and increased fatigue, infection, oral mucositis, nausea, and diarrhea [3].

Cancer prehabilitation is defined as a process on the care continuum prior to major oncological treatment that involves thorough screening, assessment, and treatment of physical and psychological impairments with targeted interventions [4]. Multidisciplinary prehabilitation interventions include optimisation in the control of chronic medical conditions, respiratory education, individualised exercise prescription, nutritional optimisation, psychological support, and health behavior change strategies [5]. The aim of cancer prehabilitation is to reduce post-treatment complications, enhance functional capacity and empower the patient to withstand the stressors of their treatment [5]. There is growing evidence in the oncological surgical population supporting prehabilitation [6, 7].

Exercise prior to AuSCT is safe and feasible [8, 9]. Preliminary evidence demonstrates mitigation of the decline in aerobic capacity, muscle strength, HRQoL and increased fatigue that is experienced during conditioning, with the potential for improvements in post-transplant outcomes relating to survival, morbidity and resource utilisation [9, 10]. Nutrition therapy is indicated and should be initiated early for patients prior to AuSCT, individualised nutrition interventions, coupled with exercise and psychological interventions are likely to be beneficial for this patient cohort [11].

Despite the treatment side effects and preliminary efficacy findings, few health services in Australia or indeed world-wide have implemented prehabilitation into routine care. One model that guides assessments of the impact of clinical interventions is 'RE-AIM' (reach, effectiveness, adoption, implementation, maintenance). This framework was developed over 20 years ago [12] and is now often used to plan and assess the translation of interventions into practice in clinical settings [13].

At the participating centre, the anaesthetics department established a prehabilitation service approximately 10 years ago. This service involved dedicated anaesthetics, medical and nursing assessment, haematinic and pharmacologic optimisation for high-risk surgical patients. The current study examined the impact, over 12 months, of adding a standardised multidisciplinary allied health prehabilitation clinical service as standard care for haematologic cancer patients receiving intensive chemotherapy prior to AuSCT.

Methods

Setting and Study Design

A retrospective evaluation of a tertiary cancer centre cohort, analysing prospective data collected between March 2019 (allied health service commencement) to March 2020. The model of standard care is detailed in Figure 1.

Program development:

Staff delivering the service were physiotherapists/exercise physiologists (EPs), dietitians and clinical psychologists with an average of 3, 5 and 4 years specialist oncology experience respectively. Further information about program development and staff training is in supplementary file 2.

Procedure

Intervention component reporting follows the Template for Intervention Description and Replication (TIDiER) [14] guidelines as described in supplementary file 3.

Patients, referral and enrolment:

Eligible patients were adults being considered for high dose chemotherapy and AuSCT in the haematology service who were medically and cognitively able to participate in exercise.

The allied health service was initiated as part of routine care by the clinical haematology AuSCT team; the planned referral pathway involved the AuSCT nurse consultant referring all eligible patients following acceptance into the AuSCT service by haematologists. Patients were telephone screened by a clinician, for exercise program eligibility using the validated Australian-modified Karnofsky Performance Status (AKPS) [15]. Scores range between 10 and 100 (higher reflecting improved function), based on the patients' ability to perform regular tasks relating to activity, work, and self-care. Patients with an AKPS <50 were ineligible. Patients with bone involvement were eligible if cleared to exercise by their haematologist. Psychology eligibility screening was completed using the patient health questionnaire (PHQ-4), a valid tool for detecting anxiety and depressive disorders [16]. Patients were eligible for clinical psychology if they scored > 2 (mild distress).

Eligible patients were then invited to participate in the service and those accepting were booked for individual assessments with each discipline and clinical psychologist if eligible. Program duration was individualised, depending on the timing of referral in relation to medical treatment interventions.

Exercise Intervention:

An initial, individual assessment (60-minute) at the hospital was conducted. Supplementary file 4 presents safety criteria for starting and ceasing supervised exercise assessments/exercise. Treatment was commenced at initial assessment after baseline measures were completed. An individually tailored exercise program consisting of continuous moderate intensity aerobic and resistance exercise was prescribed. The exercise intervention was based upon initial assessment findings and aimed to progress towards meeting the Exercise and Sports Science Australia [17] recommendations of 150 minutes of moderate-intensity aerobic exercise and two resistance exercise sessions per week. Supplementary file 5 provides further details. Patients completed the program either independently at home, in a local gym, supervised at a community health centre or at the hospital gym. The program location was determined by patient residential location and preference and level of supervision needed. Programs were progressed to

maintain moderate intensity, with weekly/fortnightly telehealth or phone reviews. Program adherence was monitored using patient self-report.

Nutrition intervention:

Initial assessment considered relevant clinical, anthropometric and biochemical markers, dietary intake, and estimation of nutritional requirements. The nutrition intervention consisted of 20-minute individualised sessions (hospital or phone), with the goals of care including maintenance/improvement in nutrition status. Intervention included medical nutrition therapy, information about the benefits of nutrition prehabilitation, prescription of relevant therapeutic diet, educational materials (supplementary file 6) and nutrition prehabilitation goal setting. Between 1-4 follow up appointments were scheduled if indicated at initial assessment, and treatment modifications were based on outcome changes.

Clinical Psychology intervention:

A full psychological initial assessment (60-minute, hospital) with individualised psychological support based on findings. Between 1-7 hospital follow-up appointments were scheduled and interventions included cognitive behavioural approaches to managing worry and pain, maintaining motivation, and activating supports in preparation for AuSCT.

Outcomes:

Evaluation of the impact of the prehabilitation program was measured using the RE-AIM framework (reach, effectiveness, adoption, implementation and maintenance). Table 1 describes the evaluation method for each dimension of the framework. Effectiveness outcomes are described below.

Effectiveness Outcomes as part of the RE-AIM framework measurements:

Patients completed outcome measures at baseline (T0, referral), pre-transplant (T1) and 30 days post-procedure (T2). The 6MWT is a commonly used submaximal test of functional exercise capacity [18] and is valid and reliable in cancer patients [19]. The 6MWT was completed using a 30-meter corridor and standardised encouragement. The Baseline Lite Hydraulic handgrip dynamometer (Fabrication Enterprises Inc.) was used to assess hand-grip strength and data from this device correlates with the Jamar dynamometer [20], which has demonstrated validity and reliability in the oncology population [21]. The validated 30-second sit-to-stand test (30secSTS), performed according to standard protocols, assessed lower limb strength and function [22].

Nutritional status was measured using the valid and reliable Patient-Generated Subjective Global Assessment (PG-SGA) [23] and percentage weight change. HRQoL was measured using the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire Core 30 (EORTC-QLQ-C30)[24]. The International Physical Activity Questionnaire-Short Form (IPAQ-SF) is a reliable and valid [25] self-reported tool that assesses physical activity (PA) level.

Data management and analysis:

A research electronic data capture (REDCap) database was used [26]. Descriptive statistics were reported as counts and percentages, means and standard deviations or medians and interquartile ranges, as appropriate, to summarise variables. The change in objective and patient-reported measures from initial assessment (baseline) to pre-procedure was assessed using paired t-tests or the Wilcoxon signed rank test depending on the data distribution normality (continuous) and Mc Nemar's test (categorical). No analyses involved all three time points. All tests of significance ($p < 0.05$) performed are described and no adjustment was made for the number of outcomes assessed [27].

Results

Findings relating to each of the dimensions of the RE-AIM framework are described in turn below.

Reach

In 2018, 1180 adult (>15yo) patients underwent an AuSCT in Australia, 25% (296) of these were in the state of Victoria [28]. The study hospital performs an average of 140 AuSCT a year, approximately half of all Victorian transplants. Demographic and clinical characteristics of Australian AuSCT recipients included: 55% were ≥ 60 years of age, 61% male* (*this gender percentage includes allograft transplant patients) and were diagnosed with multiple myeloma (57%) or lymphoma (35%) [28]. Patients who took up the allied health prehabilitation service were broadly representative of Australian data with 65% being ≥ 60 years of age, 64% male, and diagnosed with multiple myeloma (64%) or lymphoma (32%).

Figure 2 gives the flow of participants through the study, 73% of patients referred to the AuSCT service were referred onto prehabilitation. Of the 133 patients referred to the service, five were ineligible, and another seven declined.

Baseline characteristics of patients who participated, those who declined the service, and patients who were referred to the AuSCT service but not referred to the allied health prehabilitation service between March 2019 and March 2020 are given in table 2. Patients were 64 years, predominantly had multiple myeloma and one third were rurally located. When comparing demographic (age, sex) and clinical (diagnosis) characteristics at a hospital level, the only significant difference was the age of patients referred compared to those who were not referred (age (years), median (IQR): referred ($n=131$) 63 (56, 69) versus not referred 58 (53, 65), $p=0.011$). There were no significant differences with respect to age, sex, or diagnosis for those who took up referral compared to those who declined referral. Location of patients as metro, rural or remote are given in table 2. There was a higher percentage of rural and remote patients in the non-referred patient cohort (29/50, 58%) compared with the referred patients (47/133, 35%), $p=0.009$.

Effectiveness

Table 3 presents results of objective measures and patient-reported outcomes for patients who completed assessments at baseline, pre-procedure and 30-day post-procedure time points. Baseline data

collection for this evaluation was censored on March 12th 2020. Eighty-nine of the 116 (77%) patients participating in prehabilitation had undergone their AuSCT, and 84 (72%) were >30 days post AuSCT at data analysis. The number of patients who completed outcome measures at T0 and T1 was low; 45/89 (51%) completed the 6MWT at both timepoints (Table 3). For patients who did complete assessments at both T0 and T1 functional exercise capacity, lower limb strength and function, hand grip strength and physical activity levels improved significantly following prehabilitation (Table 3). The 6MWT distance and 30secSTS changes were a mean difference (95% CI) of 39.9m (18.8 to 61.0, $p<0.005$) and median (IQR) of 12.0 stands (10.0-14.0) versus 15.0 stands (13.0-18.0), $p<0.005$, respectively. Significantly more patients reported meeting the physical activity guidelines following prehabilitation (T0 28% versus T1 52%, $p=0.002$). Global HRQoL was not significantly different following prehabilitation (significant improvements in the fatigue symptom scale ($p=0.005$) and dyspnoea single item ($p=0.018$)) (Table 3).

Thirty-day outcome data were not evaluated statistically due to attrition at this timepoint; 17/84 (20%) patients had completed the 6MWT at the three timepoints.

Adoption

As reported in figure 2, 73% ($n=133$) were referred to the allied health prehabilitation service. Of the total numbers referred, 92% ($n=122$) were received from the hematology (including AuSCT) nurse consultants as per the planned referral pathway. The remaining referrals were received from haematology consultants (7.5%, $n=10$) and an allied health professional (0.5%, $n=1$).

Implementation

As discussed in Table 1, exercise prescription was the focus in the implementation domain. Of the 116 patients who received an initial assessment with an exercise clinician; 72% ($n=84$) were prescribed a combined aerobic and resistance home-based exercise program. This represents moderate fidelity of delivery [29]. However, reporting of the exercise parameters for each domain varied between 0-85% (supplementary file 7), making it difficult to analyse 'true' fidelity of delivery. We reviewed 15 records with the lowest fidelity (those where aerobic and/or resistance exercise was prescribed but no parameters were documented in the medical records) and compared medical record documentation to documentation recorded separately using the physiotherapy exercise prescription software, SimpleSet [30]. We found exercise prescription parameters were more consistently reported in SimpleSet compared to the medical records especially in the resistance programs where 62.5% of records had all parameters documented on SimpleSet when not documented in the medical records.

The mean attendance rates for individual disciplines appointments was high ranging from 80 – 92% (supplementary file 8). Eighteen percent ($n=21$) of patients attended supervised group exercise class at the hospital, and on average attended 5.7 group exercise sessions during their prehabilitation period.

Maintenance

The number of patients referred to the prehabilitation service over the 12 months compared to total referrals into the AuSCT team was 73% (monthly breakdown in supplementary file 9), however it can be broken down further into three key time periods:

1. Service initiation including communication and promotion of the service to the relevant stakeholders and referrers (Jan – April 2019) - referral rate 52%.
2. Service maintenance as prehabilitation becomes routine care for AuSCT candidates (May 2019 – Jan 2020) - referral rate 81%.
3. COVID-19 impact (Feb – March 2020) - referral rate 56%.

Considering the disruptive impact of the COVID-19 pandemic on healthcare practice, it may be that the most accurate assessment of Maintenance after the service initiation period was from May 2019 to January 2020 (81%). This reflects a high level of maintenance of multidisciplinary prehabilitation in this setting.

Discussion

In this study the RE-AIM framework [13] was applied to evaluate the impact and operational success of the service. Findings relating to all five dimensions of the framework inform the judgement as to the current impact of this service and avenues for enhancement of future, improved services for this population. In summary, the sample was representative of Australian AuSCT patients, and effectiveness was demonstrated with improvements at follow-up for the 6MWT, 30secSTS, grip strength and several patient-reported outcomes. However, modifications are required to increase outcome measure completion as there was a high level of missing data. Adoption of the service by referrers, at 73%, was moderate to high. Implementation (fidelity of exercise intervention delivery) was moderate; however, this assessment relied on documentation in patients' case notes, which may have been suboptimal; not all components of exercise prescription principles (frequency, intensity, time, type) were routinely documented. The referral trend over time (Maintenance) was high after the initiation period, although interrupted by the onset of COVID-19 restrictions in March 2020. Based on the findings from the RE-AIM analysis, the impact of the prehabilitation intervention in this patient group was high, with reason to infer that impact on the wider population of eligible patients across the nation would be similarly moderate-to-high, if sites were to initiate this service. The framework provided a feasible, comprehensive, and informative approach to evaluating impact.

There is emerging evidence to suggest that multimodal prehabilitation should be initiated as an oncology health service [31]. More than 90% of eligible, referred patients went on to participate in the allied health prehabilitation service, demonstrating excellent uptake. Our results are consistent with those from the United Kingdom where uptake of cancer prehabilitation prior to gastrointestinal and lung surgery was high [31]. This finding could be attributed to an engaged haematology service, this hypothesis is strengthened by the extent of adoption from these referrers. Prior to the COVID-19 pandemic the referral

rate into the service over the previous nine months was > 80% of eligible patients. This excellent adoption contrasts with current evidence regarding oncology clinicians' referral patterns to exercise specialists [32].

The current study, conducted in real-world conditions, reports measurable improvements with allied health prehabilitation in functional exercise capacity, lower limb strength and function, grip strength, physical activity and HRQoL domains (fatigue and dyspnoea). This is consistent with two small studies in allogeneic and AuSCT, where positive trends were found for prehabilitation in physical activity, physical function, HRQoL and fatigue [9, 10] and a significant positive change in lean body weight [10]. Our findings should be interpreted with caution due to the absence of a control group. Furthermore, there is no reported minimal clinically important difference (MCID) for the outcome measures used specific to haematology oncology patients. Our 6MWT difference of 40m is consistent with clinically significant differences in similar populations (22-42m, lung cancer [33]). However, given the small patient numbers and the fact that only one 6MWT was performed at each assessment, interpretation of the results should be interpreted with caution, as there is a known learning effect with the 6MWT [34].

It was difficult to evaluate the nutrition intervention due to missing data. However, it is clinically appropriate for a patient's nutritional status to be maintained or improved whilst receiving prehabilitation nutrition therapy and this was observed in this patient cohort [11].

There are many well-documented challenges around translating research findings into routine practice in health care [35]. For effective and sustained system change in health care, sophisticated implementation strategies must be paired with timely and relevant data collection [35]. A notable challenge during the evaluation of this service was effective and timely patient-level data collection. Only 51% (45/89) of patients completed the 6MWT at baseline and pre-procedure. Indeed, the final time point at 30 days after AuSCT had significant attrition (17/84 (20%) 6MWT completion). This could lead to bias as it is possible that a more engaged cohort of patients returned for their follow-up assessments. This is likely to be due to multiple factors including lack of clinician time, administrative resources, the COVID-19 pandemic restricting hospital appointments, and patient factors of residential distance from the centre, disease status, treatment toxicity and appointment burden. Similar administrative and logistical challenges in patient flow were found in a Canadian study of patients with cancer resulting in only 35% of patients attending their final follow up appointment in the roll-out phase of the study [36]. Considering this, dedicated administrative funding should be built into any budget bid for development of future multidisciplinary prehabilitation programs.

An important consideration when assessing the credibility of an effectiveness study is intervention fidelity [37]. High intervention fidelity helps prevent incorrect or inaccurate interpretation of the results [38]. Despite the importance of this, the quality of intervention fidelity reporting generally remains poor [14]. We used the implementation dimension of the RE-AIM framework to evaluate this and similar to Poltawski et al, 2014 [37] found assessing intervention fidelity difficult. Only 72% of eligible patients received the combined aerobic and resistance exercise intervention. Documentation of exercise parameters was variable (0–85%) and could be due to several factors including time constraints, exercise

templates which did not require all exercise parameters be recorded, and staff priorities. Based on the SimpleSet [30] documentation, we can extrapolate that the documentation of exercise prescription parameters in the medical records may underestimate the 'true' level of fidelity, as apparent low fidelity may be attributable to reporting omissions. With the initiation of electronic medical records (EMR) in August 2020, data is now directly fed from SimpleSet into the EMR. A further limitation of the study was our uni-dimensional assessment of implementation fidelity, evaluating clinicians' delivery of the intervention, without having the tools to review patients' adherence to the prescribed program.

Waterland et al, 2020 [39] found 72% of patients prior to oncological surgery would prefer exercise prehabilitation in a home-based environment. Although initial work has been done to optimise the home-based service, especially in the wake of the COVID-19 pandemic, further scoping needs to occur involving app-based, web-based, or virtual reality methodologies to improve treatment fidelity when exercising at home [40].

Eight suggested program modifications and future service goals are provided in Box 1. The next steps are to evaluate the fidelity of the nutrition and psychology interventions and to examine the hard endpoints for benefit of the program, including morbidity, infections and mortality indicators, length of hospital stay and patient satisfaction. A powered multidisciplinary randomised controlled study would raise the level of evidence relating to interventions in this patient population.

Box 1. Eight top tips for developing a multidisciplinary prehabilitation program

Prior to service implementation:

- o Ensure adequate administrative staffing to allow for timely scheduling of appointments and to minimise patients lost to follow up.
- o Provide all relevant allied health staff with the training and resources required to conduct face to face and telehealth assessments and interventions.
- o In addition to offering supervised exercise classes, consider virtual exercise classes via telehealth to service rural and remote patients.
- o Ensure adequate implementation and communication strategies are utilised for service promotion to key referrers.

For exercise prehabilitation:

- o Where possible revise medical record templates to improve exercise prescription documentation, especially pertaining to FITT principles. Train relevant staff regarding the importance of this.

Following implementation:

- o Review patient prehabilitation outcomes as part of the clinical decision-making process regarding fitness for transplant.
- o Review processes every two months and update clinical training to ensure consistency with prescription and outcome measurement.
- o Conduct an annual formal evaluation of the program with all stakeholders with a view to assessment of impact and continued service improvement

Conclusion

The allied health prehabilitation service was well adopted by patients and clinicians and sustainable within the haematology and allied health services. It demonstrated clinically relevant improvements in outcomes, although gaps in data collection and intervention fidelity need to be addressed. The service continues to evolve based on these findings, on-going patient and clinician feedback, and as the body of research evidence increases. This model and recommendations can be used to inform the development of future multidisciplinary prehabilitation clinics in haematology and other cancer patient populations.

Declarations

Funding

No funding was provided in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript. The authors have no relevant financial or non-financial interests to disclose.

Conflicts of interest/ Competing interests

The authors declare that they have no competing interests or conflicts of interest that are relevant to the content of this article

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Code availability

Not applicable

Authors' contributions

AM developed the successful allied health business case that led to the implementation of the service. AK, TJ, LD, LE, JC, JL, CP and AM contributed to the service development, implementation and evaluation. JC and LE contributed to the data collection and storage. LD, JF, LE, AK and JC contributed to the data analysis, interpretation and the design of the study. JC completed this manuscript as part of her postgraduate research through the University of Melbourne. JC is supervised by LD, JF, LE and AK. All authors contributed to the manuscript writing and had final approval of the manuscript. The CPPOC group represents the multidisciplinary team of clinicians at Peter MacCallum Cancer Centre that either contributed to the development of the prehabilitation service (surgical and haematology cohorts) or who are clinically responsible for the daily operations of the service and patient care. For further details about CPPOC please contact sonia.coleman@petermac.org.

Ethics approval and consent to participate

The study received ethical approval by the Peter MacCallum Cancer Centre human research ethics committee on 6th October 2020, Project ID: QA/67920/PMCC-2020. Patient and implementation data were collected during usual clinical care, so no patient consent was required, and the study conducted in accordance with the Declaration of Helsinki.

Consent for publication

Not Applicable

References

1. Soerjomataram I, Lortet-Tieulent J, Parkin DM, Ferlay J, Mathers C, Forman D, et al. Global burden of cancer in 2008: a systematic analysis of disability-adjusted life-years in 12 world regions. *Lancet*. 2012;380(9856):1840-50.
2. Carli F, Zavorsky GS. Optimizing functional exercise capacity in the elderly surgical population. *Curr Opin Clin Nutr Metab Care*. 2005;8(1):23-32.
3. Chakraborty R, Hamilton BK, Hashmi SK, Kumar SK, Majhail NS. Health-Related Quality of Life after Autologous Stem Cell Transplantation for Multiple Myeloma. *Biol Blood Marrow Transplant*. 2018;24(8):1546-53.
4. Silver JK, Baima J. Cancer prehabilitation: an opportunity to decrease treatment-related morbidity, increase cancer treatment options, and improve physical and psychological health outcomes. *Am J Phys Med Rehabil*. 2013;92(8):715-27.
5. Macmillan Cancer Support. Prehabilitation for people with cancer 2017.
6. Gillis C, Li C, Lee L, Awasthi R, Augustin B, Gamsa A, et al. Prehabilitation versus rehabilitation: a randomized control trial in patients undergoing colorectal resection for cancer. *Anesthesiology*. 2014;121(5):937-47.
7. West MA, Loughney L, Lythgoe D, Barben CP, Sripadam R, Kemp GJ, et al. Effect of prehabilitation on objectively measured physical fitness after neoadjuvant treatment in preoperative rectal cancer patients: a blinded interventional pilot study. *Br J Anaesth*. 2015;114(2):244-51.
8. Wood WA, Phillips B, Smith-Ryan AE, Wilson D, Deal AM, Bailey C, et al. Personalized home-based interval exercise training may improve cardiorespiratory fitness in cancer patients preparing to undergo hematopoietic cell transplantation. *Bone Marrow Transplantation*. 2016;51(7):967-72.
9. van Haren I, Staal JB, Potting CM, Atsma F, Hoogeboom TJ, Blijlevens NMA, et al. Physical exercise prior to hematopoietic stem cell transplantation: A feasibility study. *Physiother Theory Pract*. 2018;34(10):747-56.
10. Coleman EA, Coon S, Hall-Barrow J, Richards K, Gaylor D, Stewart B. Feasibility of exercise during treatment for multiple myeloma. *Cancer Nursing* 2003 Oct-Nov;26(5):410-419. 2003.
11. Arends J, Bachmann P, Baracos V, Barthelemy N, Bertz H, Bozzetti F, et al. ESPEN guidelines on nutrition in cancer patients. *Clin Nutr*. 2017;36(1):11-48.
12. Glasgow RE, Vogt TM, Boles SM. Evaluating the public health impact of health promotion interventions: the RE-AIM framework. *Am J Public Health*. 1999;89(9):1322-7.
13. Glasgow RE, Harden SM, Gaglio B, Rabin B, Smith ML, Porter GC, et al. RE-AIM Planning and Evaluation Framework: Adapting to New Science and Practice With a 20-Year Review. *Front Public Health*. 2019;7:64.
14. Hoffmann TC, Glasziou PP, Boutron I, Milne R, Perera R, Moher D, et al. Better reporting of interventions: template for intervention description and replication (TIDieR) checklist and guide. *BMJ*. 2014;348:g1687.
15. Abernethy AP, Shelby-James T, Fazekas BS, Woods D, Currow DC. The Australia-modified Karnofsky Performance Status (AKPS) scale: a revised scale for contemporary palliative care clinical practice

- [ISRCTN81117481]. *BMC Palliat Care*. 2005;4:7.
16. Kroenke K, Spitzer RL, Williams JB, Lowe B. An ultra-brief screening scale for anxiety and depression: the PHQ-4. *Psychosomatics*. 2009;50(6):613-21.
 17. Hayes SC, Newton RU, Spence RR, Galvao DA. The Exercise and Sports Science Australia position statement: Exercise medicine in cancer management. *J Sci Med Sport*. 2019;22(11):1175-99.
 18. Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, et al. An official European Respiratory Society/American Thoracic Society technical standard: field walking tests in chronic respiratory disease. *Eur Respir J*. 2014;44(6):1428-46.
 19. Schmidt K, Vogt L, Thiel C, Jager E, Banzer W. Validity of the six-minute walk test in cancer patients. *Int J Sports Med*. 2013;34(7):631-6.
 20. Mathiowetz V, Kashman N, Volland G, Weber K, Dowe M, Rogers S. Grip and pinch strength: normative data for adults. *Arch Phys Med Rehabil*. 1985;66(2):69-74.
 21. Trutschnigg B, Kilgour RD, Reinglas J, Rosenthal L, Hornby L, Morais JA, et al. Precision and reliability of strength (Jamar vs. Biodex handgrip) and body composition (dual-energy X-ray absorptiometry vs. bioimpedance analysis) measurements in advanced cancer patients. *Appl Physiol Nutr Metab*. 2008;33(6):1232-9.
 22. Jones CJ, Rikli RE, Beam WC. A 30-s chair-stand test as a measure of lower body strength in community-residing older adults. *Res Q Exerc Sport*. 1999;70(2):113-9.
 23. Bauer J, Capra S, Ferguson M. Use of the scored Patient-Generated Subjective Global Assessment (PG-SGA) as a nutrition assessment tool in patients with cancer. *Eur J Clin Nutr*. 2002;56(8):779-85.
 24. Aaronson NK, Ahmedzai S, Bergman B, Bullinger M, Cull A, Duez NJ, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85(5):365-76.
 25. Craig CL, Marshall AL, Sjostrom M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. *Med Sci Sports Exerc*. 2003;35(8):1381-95.
 26. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42(2):377-81.
 27. Perneger TV. What's wrong with Bonferroni adjustments. *BMJ*. 1998;316(7139):1236-8.
 28. ABMTRR. Australasian Bone Marrow Transplant Recipient Registry: Annual Data Summary 2018. Darlinghurst, NSW, Australia: Australasian Bone Marrow Transplant Recipient Registry; 2019.
 29. Borrelli B. The assessment, monitoring, and enhancement of treatment fidelity in public health clinical trials. *J Public Health Dent*. 2011;71 Suppl 1:S52-63.
 30. SimpleSet. SimpleSet 2009 [Available from: <https://simpleset.net>].
 31. Moore J, Merchant Z, Rowlinson K, McEwan K, Evison M, Faulkner G, et al. Implementing a system-wide cancer prehabilitation programme: The journey of Greater Manchester's 'Prehab4cancer'. *Eur J Surg Oncol*. 2020.

32. Schmitz KH, Campbell AM, Stuiver MM, Pinto BM, Schwartz AL, Morris GS, et al. Exercise is medicine in oncology: Engaging clinicians to help patients move through cancer. *CA Cancer J Clin.* 2019;69(6):468-84.
33. Granger CL, Holland AE, Gordon IR, Denehy L. Minimal important difference of the 6-minute walk distance in lung cancer. *Chron Respir Dis.* 2015;12(2):146-54.
34. Gibbons WJ, Fruchter N, Sloan S, Levy RD. Reference values for a multiple repetition 6-minute walk test in healthy adults older than 20 years. *J Cardiopulm Rehabil.* 2001;21(2):87-93.
35. Bauer MS, Damschroder L, Hagedorn H, Smith J, Kilbourne AM. An introduction to implementation science for the non-specialist. *BMC Psychol.* 2015;3:32.
36. Santa Mina D, Au D, Auger LE, Alibhai SMH, Matthew AG, Sabiston CM, et al. Development, implementation, and effects of a cancer center's exercise-oncology program. *Cancer.* 2019;125(19):3437-47.
37. Poltawski L, Norris M, Dean S. Intervention fidelity: developing an experience-based model for rehabilitation research. *J Rehabil Med.* 2014;46(7):609-15.
38. Taylor KL, Weston M, Batterham AM. Evaluating intervention fidelity: an example from a high-intensity interval training study. *PLoS ONE.* 2015;10(4):e0125166.
39. Waterland JL, Ismail H, Amin B, Granger CL, Denehy L, Riedel B. Patient acceptance of prehabilitation for major surgery: an exploratory survey. *Support Care Cancer.* 2020.
40. Steffens D, Delbaere K, Young J, Solomon M, Denehy L. Evidence on technology-driven preoperative exercise interventions: are we there yet? *Br J Anaesth.* 2020.
41. Department of Primary Industries and Energy and Department of Human Services and Health. Rural, remote and metropolitan areas classification (RRMA). Canberra: Commonwealth of Australia,1994.
42. The Department of Health. Rural, Remote and Metropolitan Areas Classification (RRMA) 2008 [Available from: <https://www1.health.gov.au/internet/publications/publishing.nsf/Content/work-res-ruraud-toc~work-res-ruraud-lis~work-res-ruraud-lis-e>.

Tables

Table 1. Evaluation methods based on the RE-AIM framework [13]

Dimension	Explanation
Reach	Includes the proportion of eligible patients who participate in the program being evaluated, and their representativeness relative to a wider group of eligible patients. We compared the number and characteristics of the patients who were referred to the AuSCT team but did not go onto referral to allied health prehabilitation services, with those who participated in the service and those who declined the service. This included patient location, categorised into metropolitan, regional and remote [41]. These characteristics were then compared to data of AuSCT patients Australia wide.
Effectiveness *	Objective and patient-reported outcomes from initial assessment to pre-transplant assessment and 30-days after transplant were recorded. Tests were standardised and treating clinicians received verbal and written education on each outcome individually prior to service commencement. Further details regarding outcomes are provided in text.
Adoption	The number of referrals received were expressed as a percentage of the overall number of eligible patients at the hospital.
Implementation	<p>Despite the well reported importance of intervention fidelity to allow accurate interpretation of results, the quality of intervention fidelity reporting remains poor, especially in exercise interventions [14]. With this in mind, assessment of <i>implementation</i> (fidelity) involved a retrospective audit of the 116 patients who participated in the exercise prehabilitation program to review how many patients received the exercise intervention as described in the protocol.</p> <p>We accessed the patients' medical records to review the initial assessment with an exercise professional; record of modality of exercise prescribed as well as the exercise parameters that were documented, based upon the frequency, intensity, time and type (FITT) exercise principles, was assessed. If there was a documented reason why the intended program was not initially prescribed the next documented exercise appointment was used to evaluate fidelity. Based on consensus in the literature we regarded 'high fidelity' as 80 to 100% of patients being prescribed an aerobic and resistance individualized home exercise program, with 51-79% representing moderate fidelity of delivery and $\leq 50\%$ deemed low fidelity of delivery [29].</p> <p>For further measures of fidelity we recorded the mean number of sessions attended for each discipline compared to the number of scheduled sessions (attendance rate) for each discipline, and the percentage of people attending supervised exercise class compared to home based exercise including the mean number of supervised classes attended.</p>
Maintenance	We assessed the extent to which referral to the allied health services within the prehabilitation service had become routine care. This involved a descriptive analysis of the trend in referrals over time compared to the number of eligible patients. Patients referred to the AuSCT team from January 2019 onwards were eligible for referral into the prehabilitation service if they were scheduled to receive their transplant at least 3 weeks post service commencement.

Table 2. Baseline Characteristics of Patients

	Referred patients		Non-referred patients
	Patients accepting referral	Patients declining referral	
n	121	7	50
Age at referral, years median (IQR)	64.0 (56.0-69.0)	62.0 (54.0 – 64.0)	58.0 (52.8 - 65.3)
Sex n (%) male	64 (52.9%)	5 (71.4%)	32 (64%)
Cancer diagnosis n (%)	Multiple myeloma 78 (64.5%) Lymphoma 39 (32.2%) *Other 4 (3.3%)	Multiple myeloma 3 (42.9%) Lymphoma 4 (57.1%)	Multiple myeloma 25 (50.0%) Lymphoma 24 (48.0%) *Other 1 (2.0%)
Received neoadjuvant treatment during prehabilitation, n (%) 'yes'	86/115 (74.8%)		
Location n(%)#	Metro: 79 (65.3%) Rural: 41 (33.9%) Remote: 1 (1.0%)	Metro: 4 (57.1%) Rural: 3 (42.9%) Remote: 0 (0.0%)	Metro: 21 (42.0%) Rural: 27 (54.0%) Remote: 2 (4.0%)

*Other: Referred patients; extramedullary plasmacytoma, Waldenstrom's macroglobulinaemia, multiple plasmacytomas, refractory testicular germ cell tumour. Not referred patients; germ cell tumour. # Metropolitan, Rural and Remote classified as per the Australian Rural, Remote and Metropolitan Area (RRMA) Classification [41] and classify areas into seven categories from "Capital city" through to "Other remote area". This is based on population density as well as straight-line distance from urban centres of various sizes [42]. Further information is presented in supplementary file 2.

Table 3. Clinical effectiveness outcomes

Outcome measure	n	Baseline	n	Pre-procedure	Mean difference (95% CI)	p-value	30-days post-procedure
Objective							
6MWT mean (SD) meters	87	496.2 (88.1)	52	534.2 (71.4)	39.9 (18.8 to 61.0)	<0.005* (45 pairs)	507.3 (75.3) (n=29)
ISWT mean (SD) meters	20	588.0 (179.6)	7	527.1 (67.3)	-37.1 (-116.3 to 42.0)	0.295 (7 pairs)	514.0 (85.0) (n=5)
30 second sit-to-stand (number of stands)	103	13.0 (10.5-16.0)	59	15.0 (13.0-18.0)		<0.005* (54 pairs)	14.0 (11.0-18.0) (n=33)
Grip strength (kg)	102	32.0 (26.0-42.0)	59	32.0 (26.0-42.5)		0.007* (54 pairs)	36.0 (25.0-41.0) (n=36)
#PG-SGA continuous score	66	2.0 (1.0-4.0)	57	3.0 (2.0-4.0)		0.195 (34 pairs)	7.5 (5.5-9.5) (n=8)
PG-SGA categorical n (%)	67	A 60 (89.6) B 7 (10.4)	57	A 53 (93.0) B 4 (7.0)		1.000 (35 pairs)	A 6 (66.7) B 3 (33.3)
Weight (kg) mean (SD)	92	77.6 (15.8)	74	78.7 (18.2)	0.4 (-0.5 to 1.4)	0.372 (58 pairs)	78.4 (19.8) (n=37)
Weight change(%)	61	0.0 (-1.4-2.2)					
Patient-Reported							
#IPAQ (n=40 pairs baseline to pre-procedure, n=30 at 30 days post-procedure)							

MET mins/week	97	297.0 (99.0-700.0)	42	667.5 (358.0-1386.0)	<0.005* (40 pairs)	396.0 (231.0-767.3) (n= 30)
Meeting physical activity guidelines n (%) 'yes'	97	2736.7 (27.8)	42	22 (52.4)	0.002* (40 pairs)	11 (36.7)

#EORTC (n=43 pairs baseline to pre-procedure, n=34 at 30 days post-procedure)						
Global QOL	103	66.7 (50.0-75.0)	47	66.7 (54.2-83.3)	0.286	62.5 (50.0-75.0)
Physical function	104	86.7 (73.3-93.3)	47	86.7 (66.7-100.0)	0.454	80.0 (60.0-93.3)
Role function	104	66.7 (41.7-100.0)	47	83.3 (50.0-100.0)	0.215	66.7 (33.3-66.7)
Emotional function	103	83.3 (66.7-100.0)	47	91.7 (70.8-100.0)	0.334	91.7 (75.0-100.0)
Cognitive function	103	83.3 (66.7-100.0)	47	83.3 (66.7-100.0)	0.233	83.3 (66.7-100.0)
Social function	103	66.7 (50.0-83.3)	47	66.7 (50.0-83.3)	0.878	66.7 (50.0-83.3)
Fatigue	104	33.3 (22.2-55.6)	47	33.3 (22.2-50.0)	0.005*	44.4 (33.3-66.7)
Nausea/vomiting	104	0.0 (0.0-16.7)	47	0.0 (0.0-16.7)	0.139	0.0 (0.0-33.3)
Pain	104	16.7 (0.0-33.3)	47	0.0 (0.0-16.7)	0.120	0.0 (0.0-33.3)
Dyspnoea	104	0.0 (0.0-33.3)	47	0.0 (0.0-33.3)	0.018*	0.0 (0.0-33.3)
Insomnia	104	33.3 (0.0-33.3)	47	0.0 (0.0-33.3)	0.570	33.3 (0.0-33.3)
Appetite loss	104	0.0 (0.0-33.3)	47	0.0 (0.0-33.3)	0.549	0.0 (0.0-33.3)
Constipation	104	0.0 (0.0-33.3)	47	0.0 (0.0-33.3)	0.185	0.0 (0.0-0.0)
Diarrhoea	102	0.0 (0.0-33.3)	47	0.0 (0.0-33.3)	0.793	0.0 (0.0-33.3)
Financial problems	103	0.0 (0.0-33.3)	47	0.0 (0.0-33.3)	0.857	0.0 (0.0-33.3)

Footnote: Values are median (IQR) unless otherwise stated. *=statistically significant result

The PG-SGA includes four patient-generated historical components (weight history, food intake, symptoms and activities and function), as well as the components completed by a trained professional: diagnosis, age, metabolic stress, and physical exam. The tool is scored as a global assessment (A = well nourished, B = moderately malnourished or suspected malnutrition, C = severely malnourished), and a total numerical score (ranging from 0-36, with higher scores indicating poorer nutrition).

The IPAQ-SF self-report requires the patient to recall their physical activity levels during the preceding week. Responses are categorised as high/moderate (meeting PA guidelines) or low (not meeting PA guidelines) and as a continuous energy expenditure score (metabolic equivalent of task (MET) minutes per week). Higher scores indicate higher PA.

In the EORTC-QLQ-C30, higher scores on functional domains and the global health status/quality of life scale represent better status, whereas lower scores on symptom domains and single items represent fewer symptoms.

Figures

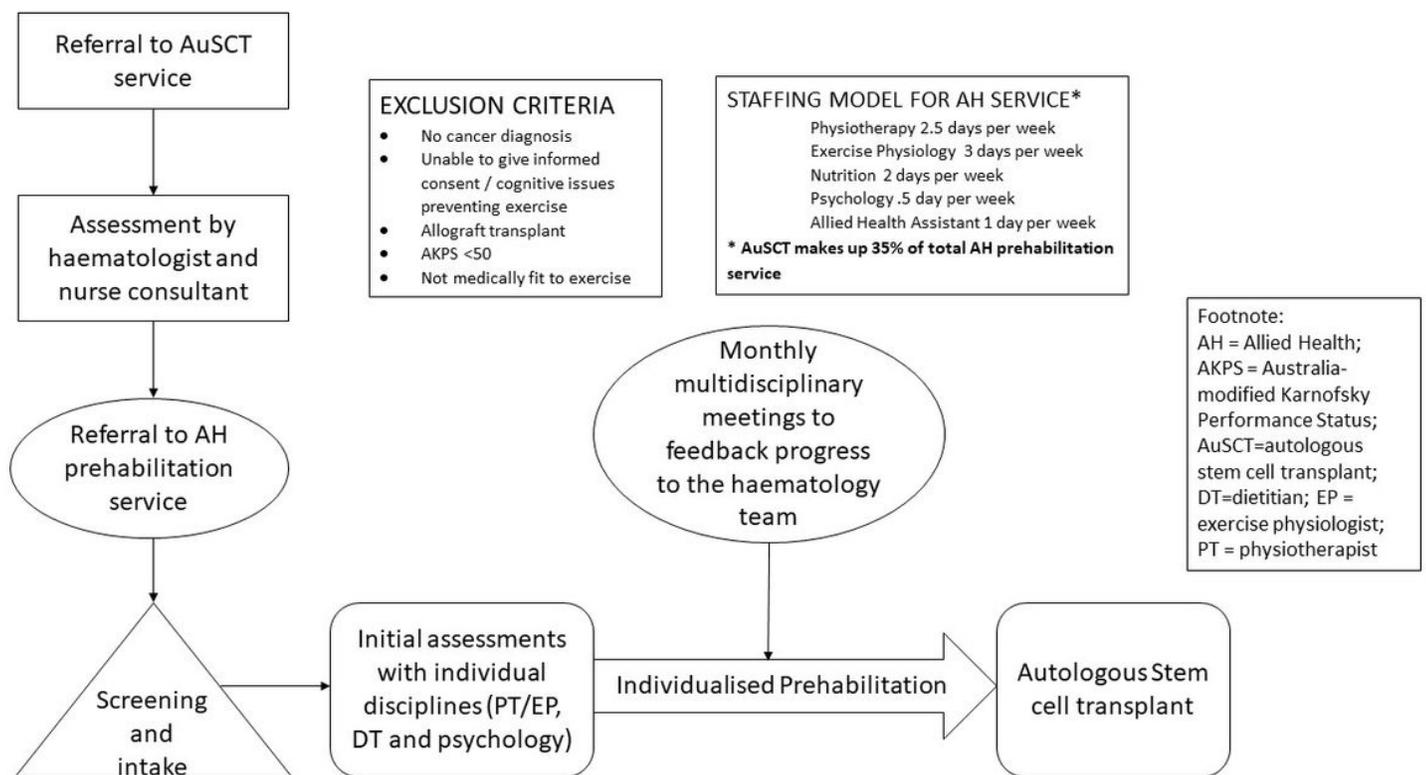


Figure 1

Allied health prehabilitation model of care for AuSCT patients.

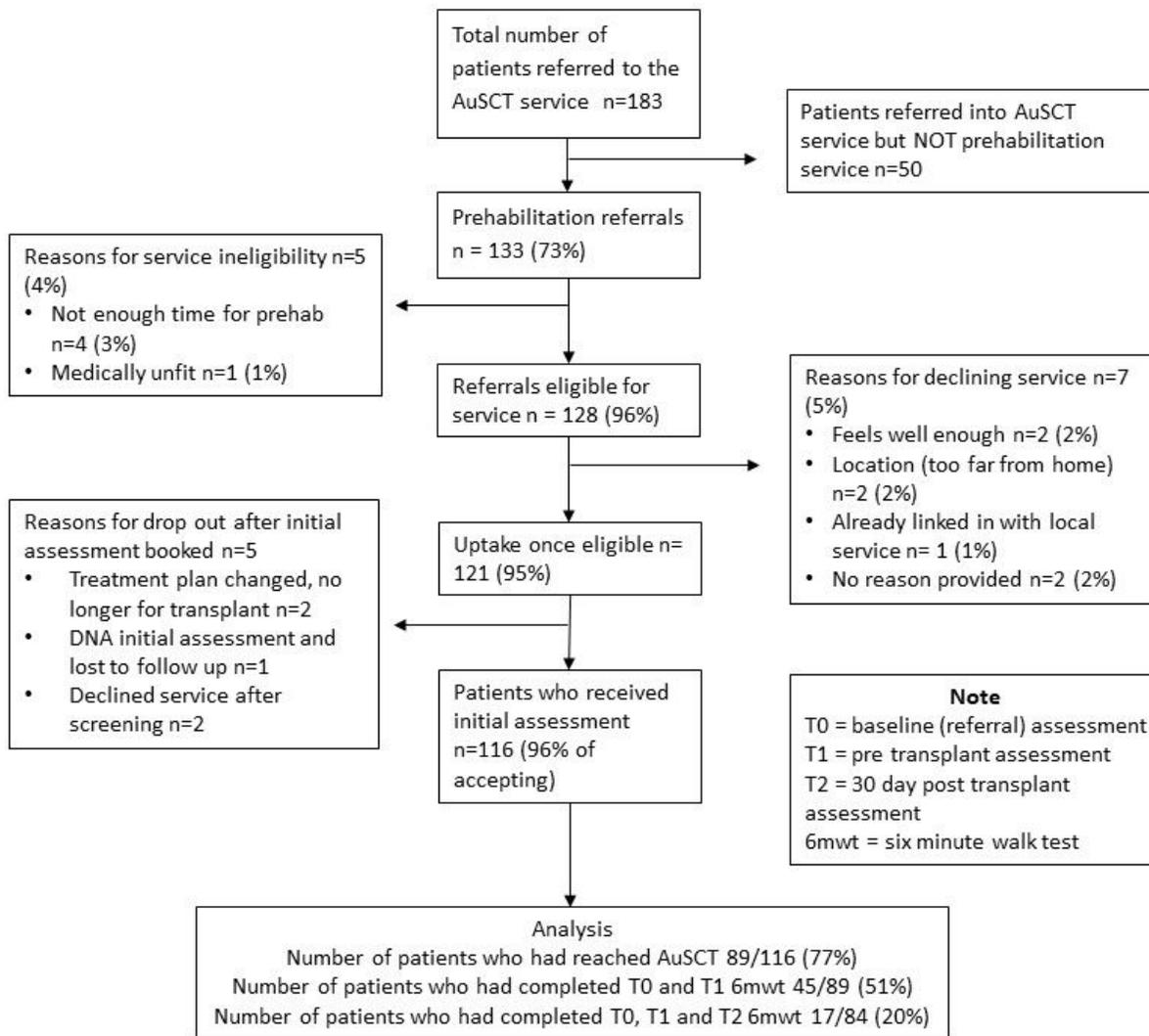


Figure 2

Referral, uptake and receipt of intervention to assess Reach

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [Supplementaryfile1.docx](#)
- [Supplementaryfile2.docx](#)
- [supplemntaryfile3.docx](#)
- [Supplementaryfile4.docx](#)
- [Supplementaryfile5.docx](#)
- [Supplementaryfile6.doc](#)
- [Supplementaryfile7.pptx](#)

- [Supplementaryfile8.docx](#)
- [Supplementaryfile9.pptx](#)