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Long-term outcomes of exercise-based rehabilitation and immunometabolic parameters in adult hematopoietic stem cell transplantation recipients: an updated systematic review

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - This systematic review was conducted as part of a postgraduate Master of Research (MRes) programme at the University of Winchester. The protocol was developed and finalised prior to data extraction (January 2025) but was not registered externally at that time due to limited awareness of prospective registration requirements within the academic programme. An update has been completed in November 2025 and again in February 15, 2026 in anticipation of this submission. All stages followed PRISMA 2020 guidelines with predefined eligibility criteria and a priori outcome domains. The protocol is available from the corresponding author on request.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202620054

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 February 2026 and was last updated on 17 February 2026.

INTRODUCTION

Review question / Objective In adult recipients of allogeneic or autologous hematopoietic stem cell transplantation (HSCT), does participation in structured exercise-based rehabilitation, compared to usual care or control interventions, improve long-term (three months or more) physical, psychosocial, immunological or metabolic outcomes?

Rationale Previous systematic reviews suggested that exercise can improve short-term outcomes around the transplant period. However, these reviews did not specifically evaluate the sustained effects of exercise interventions in the long-term survivorship phase or examine emerging immunometabolic endpoints that have become increasingly recognised as important for this population. This review addresses these gaps by synthesising RCTs published between 2019 and February 2026 that assess the effects of exercise-based rehabilitation on physical function, fatigue, QoL, immune reconstitution and metabolic outcomes at three months or more post-transplant in adult HSCT recipients. By focusing on this contemporary evidence window, we capture trials incorporating telehealth delivery models accelerated by the COVID-19 pandemic and the first trial to include immunological biomarker endpoints.

Condition being studied Long-term health outcomes following hematopoietic stem cell transplantation (HSCT) for haematological malignancies and other disorders. Specifically: physical deconditioning, cancer-related fatigue, reduced quality of life, impaired immune reconstitution, and metabolic syndrome in adult HSCT survivors.

METHODS

Search strategy Search strategy: Combined HSCT-related terms (hematopoietic stem cell transplantation, bone marrow transplantation, allogeneic, autologous) with exercise intervention terms (exercise, physical activity, rehabilitation, resistance training, aerobic training) and outcome terms (physical function, fatigue, quality of life, immune reconstitution, metabolic). Database-specific adaptations were made for indexing conventions and controlled vocabulary. Filters: human studies, English language, publication dates January 2019 to February 2026. No geographic restriction. Reference lists of relevant systematic reviews and included studies were also screened.

Participant or population Inclusion: Adults aged 17 years or older who have undergone allogeneic or autologous HSCT for any indication, including leukaemia, lymphoma, multiple myeloma and other haematological disorders. Studies conducted during hospitalisation or in the post-transplant period were eligible provided outcomes were assessed at three months or more post-transplantation.
Exclusion: Exclusively paediatric populations (aged under 17 years).

Intervention Structured exercise-based rehabilitation programmes incorporating aerobic, resistance, combined, interval, flexibility, balance or multimodal training. Any setting (inpatient, outpatient, home-based, telehealth) and any intensity. Co-interventions such as dietary counselling, psychosocial support or mindfulness were permitted if exercise was the primary component.

Comparator Usual care, standard rehabilitation, attention control, waitlist or placebo/stretching programmes.

Study designs to be included Randomised controlled trials (RCTs), including cluster-RCTs, published in peer-reviewed English-language journals from 1 January 2019 to 15 February 2026. When multiple publications arose from a single RCT, the primary outcomes paper was prioritised.

Eligibility criteria As described above.

Information sources Databases searched: MEDLINE/PubMed, Embase, Scopus, PEDro (Physiotherapy Evidence Database), Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL).
Search dates: Initial searches conducted Q1 2025; updated and confirmatory re-run 15 February 2026.

Main outcome(s) Physical function and performance: peak oxygen uptake (VO_2peak), six-minute walk distance (6MWD), grip strength, sit-to-stand repetitions, gait speed, Short Physical Performance Battery.
Fatigue: assessed by validated instruments including Multidimensional Fatigue Inventory (MFI), Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F), EORTC QLQ-C30 fatigue subscale, PROMIS-Fatigue.
Quality of life: assessed by validated instruments including SF-36, FACT-BMT, EORTC QLQ-C30, Trial Outcome Index, HADS, DASS-21.
All outcomes assessed at three months or more post-transplant or post-intervention.

Additional outcome(s) Immune reconstitution: lymphocyte subsets (T-cell, B-cell, NK-cell counts), inflammatory markers (cytokines, sICAM-1), immunoglobulin levels, vaccination immunogenicity.
Metabolic outcomes: body composition (lean mass, fat mass, phase angle via bioelectrical impedance), lipid profiles, glucose metabolism, metabolic syndrome incidence.
Adverse events: exercise-related injuries, cardiovascular events, infection rates, GVHD incidence, relapse, non-relapse mortality.
Feasibility: session adherence, retention rates, participant satisfaction.

Data management Study selection: Search results were imported into reference management software and duplicates removed. Titles and abstracts were screened against predefined eligibility criteria. Full texts of potentially relevant studies were retrieved and assessed in detail. The PRISMA flow diagram documents each screening step and exclusion rationale.
Data extraction: Data were extracted using standardised forms capturing: study characteristics (authors, year, country, design, sample size), population details (diagnosis, HSCT type, demographics, enrolment timing),

intervention specifics (exercise type, supervision, setting, frequency, intensity, duration), control conditions, and outcome data at the longest available follow-up (mean differences, effect sizes, 95% confidence intervals, p-values).
Limitation: All stages were conducted by a single reviewer (DB) with periodic supervisory consultation (PN). This departs from PRISMA 2020 recommendations for independent duplicate assessment. Predefined eligibility criteria were applied rigorously; however, the absence of formal independent verification may have increased the risk of missed studies or data extraction inconsistencies.

Quality assessment / Risk of bias analysis Included trials were assessed using the Cochrane Risk of Bias 2.0 tool (RoB 2), evaluating five domains: (1) randomisation process, (2) deviations from intended interventions, (3) missing outcome data, (4) measurement of the outcome, and (5) selection of the reported result. Each domain was rated as low risk, some concerns or high risk, with an overall judgement assigned per the RoB 2 algorithm. Assessment was performed by a single reviewer (DB) with supervisory consultation (PN).

Strategy of data synthesis Due to the clinical and methodological heterogeneity across included trials, encompassing differences in exercise modalities (aerobic, resistance, whole-body vibration, multimodal), intervention timing (peri-transplant to long-term survivorship), patient populations (autologous vs. allogeneic, frail vs. non-frail), and outcome instruments (five different fatigue tools, five different QoL instruments), results were synthesised qualitatively using narrative synthesis.
Meta-analysis was deemed inappropriate.
Findings are presented narratively by outcome domain (physical function, fatigue, quality of life, immunometabolic outcomes, safety), highlighting patterns of consistency and discrepancy across studies, statistical significance, and clinical relevance relative to established minimal clinically important differences (MCIDs).
Publication bias was assessed qualitatively through trial registry searches (ClinicalTrials.gov, ISRCTN, ANZCTR); no unpublished large-scale trials were identified.

Subgroup analysis Pre-specified subgroup considerations included: (1) transplant type (allogeneic vs. autologous), (2) intervention timing (peri-transplant vs. long-term survivorship), (3) exercise modality (supervised vs. telehealth/home-based), and (4) baseline functional status. Due to the small number of included trials (n=5), formal subgroup analysis was not possible; however, these factors were examined narratively when interpreting between-study differences.

Sensitivity analysis As above.

Country(ies) involved Residents of United Kingdom; Filipino and Indian nationals.

Keywords hematopoietic stem cell transplantation; bone marrow transplantation; exercise; rehabilitation; physical function; fatigue; quality of life; immune reconstitution; metabolic syndrome; systematic.

Dissemination plans Publication on a journal (provisionally EJHaem).

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