J Rehabil Med 2021; 53: jrm00163

REVIEW ARTICLE

REHABILITATION IN PATIENTS WITH LYMPHOMA: AN OVERVIEW OF SYSTEMATIC REVIEWS

Bhasker AMATYA, MD, MPH, DMedSc[1,2,3], Fary KHAN, MBBS, MD, FAFRM (RACP)[1,2,3,4], Thomas E. LEW, MBBS (Hons)[4] and Michael DICKINSON, MBBS (Hons), DMedSci, FRACP, FRCPA[4]

From the [1]Department of Rehabilitation Medicine, Royal Melbourne Hospital, [2]Department of Medicine (Royal Melbourne Hospital), University of Melbourne, [3]Australian Rehabilitation Research Centre, Royal Melbourne Hospital and [4]Department of Clinical Haematology, The Royal Melbourne Hospital and Peter MacCallum Cancer Centre, Parkville, Victoria, Australia

Objective: **To evaluate existing evidence from published systematic reviews for the effectiveness of rehabilitation interventions in patients with lymphoma.**

Data sources: **A comprehensive literature search was conducted using medical/health science databases up to 1 October 2020. Bibliographies of pertinent articles, journals and grey literature were searched.**

Data extraction and synthesis: **Two reviewers independently selected and reviewed potential reviews for methodological quality and graded the quality of evidence for outcomes using validated tools. Any discrepancies were resolved by final group consensus.**

Results: **Twelve systematic reviews ($n = 101$ studies, 87,132 patients with lymphoma) evaluated 3 broad categories of rehabilitation interventions (physical modalities, nutrition and complementary medicine). Most reviews were of moderate-to-low methodological quality. The findings suggest: moderate-quality evidence for exercise programmes for improved fatigue and sleep disturbance; low-quality evidence for exercise therapy alone and qigong/tai chi for improved symptoms and overall quality of life, and an inverse association between sunlight/ultraviolet radiation exposure and incidence of non-Hodgkin's lymphoma; and very low-quality evidence for beneficial effects of yoga for sleep disturbances. Association between physical activity and lymphoma risk is indistinct.**

Conclusion: **Despite a range of rehabilitation modalities used for patients with lymphoma, high-quality evidence for many is sparse. Beneficial effects of exercise programmes were noted for fatigue, psychological symptoms and quality of life. More research with robust study design is required to determine the effective rehabilitation approaches.**

Key words: lymphoma; rehabilitation; systematic review; critical appraisal.

Accepted Feb 16, 2021; Epub ahead of print Mar 12, 2021

J Rehabil Med 2021; 53: jrm00163

Correspondence address: Bhasker Amatya, Department of Rehabilitation Medicine, Royal Melbourne Hospital, Royal Park Campus, 34-54 Poplar Road, Parkville, Victoria 3050, Australia. E-mail: Bhasker.amatya@mh.org.au

LAY ABSTRACT

Lymphoma and its treatment cause significant disability and morbidity, often requiring comprehensive rehabilitation. Currently, a range of rehabilitation interventions are applied in patients with lymphoma. This review systematically evaluated evidence from published systematic reviews of clinical trials to determine the effectiveness of rehabilitation interventions in patients with lymphoma. The findings suggest that there is moderate-quality evidence for exercise programmes in improving fatigue and sleep disturbance. There was low-quality evidence for exercise therapy alone and qigong/tai chi for improved symptoms and overall quality of life, and very low-quality evidence for beneficial effects of yoga for sleep disturbances. The evidence for association of vitamin D or physical activity and lymphoma risk is limited.

Lymphomas are a heterogeneous group of malignant neoplasms of the haematopoietic system, characterized by the aberrant proliferation of mature lymphoid cells or their precursors (1). Traditionally lymphoma is classified broadly into 2 major groups: non-Hodgkin's lymphoma (NHL, 90%) and Hodgkin's lymphoma (HL) (1); however, lymphomas can also be stratified by cell of origin, as in the World Health Organization (WHO) classification (B-cell, T-cell/natural killer-cell (T/NK) and HL), or clinical behaviour (aggressive or indolent) (2, 3). An estimated 590,000 new cases of lymphoma (3.2% of all cancers) were diagnosed worldwide in 2018, the majority being NHLs (509,590 cases, 2.8% of all cancers) (4). NHL is a leading cause of death amongst the haematological malignancies globally, estimated to cause over 248,000 deaths (2.6% of all cancers) in 2018 (4). The incidence of lymphoma is increasing, with total worldwide incidence projected to reach approximately 919,000 by 2040 (5).

The total global economic burden of lymphoma is unknown; however, treatments and supportive care requirements are resource-intensive and associated with significant financial costs for patients/families and healthcare systems. Productivity losses arise from disease and treatment-associated morbidity and premature mortality (6). In 2018, the mean monthly healthcare and utilization costs per patient for diffuse large B-cell lymphoma (DLBCL) and follicular lymphoma (FL) in the USA were approximately US$11,890 and $10,460, respectively (6). In Spain, in 2017 lymp-

doi: 10.2340/16501977-2810

homa represented 45.4% of productivity losses due to haematological malignancies, resulting in €121 million in losses due to premature mortality (7).

Current therapeutic advances and cancer detection/diagnosis have improved survival rates for patients with lymphoma (PwL). The age-standardized 5-year net survival of lymphoid malignancies in adults ranges from 40% to 70% globally in 2010–14, with a 5–10% increase in trend for the period 2000–04 (8). The 5-year survival rate in the US in 2010–16 was estimated to be 72.7% for NHL and 87.4% for HL (9). As the incidence of NHL is strongly associated with increasing age, improved supportive care and availability of reduced intensity chemotherapy regimens (such as prednisone, etoposide, procarbazine, and cyclophosphamide – 'PEP-C'; rituximab, doxorubicin, cyclophosphamide, vincristine, and prednisone – 'R-miniCHOP', rituximab, cyclophosphamide, vincristine, prednisolone – 'R-CVP') are critical to facilitate deliverable therapy to older patients. Despite these factors, certain lymphomas and their treatment are associated with short- and medium-term residual neurological deficits, leading to physical, cognitive, psychosocial and behavioural impairments, limiting activities of daily living (ADL) and participation (10–13). Treatment procedures can be extensive (e.g., radiotherapy, chemotherapy and/or surgery), and associated with a range of side-effects/complications, such as neuropathy, cardiotoxicity, cachexia, fatigue, deconditioning, myopathy, etc. (14–16). Furthermore, in the transitional period, various adjustment issues are reported, such as increased care needs, inability to drive and return to work, financial constraints, relationship stress, and limitation in societal participation (11, 14, 17, 18). Distressing symptoms, such as fatigue, is a major complaint, reported in 60–100% of patients during or after cancer treatment, which persists for several years after treatment (19–21). Therefore, patients require routine surveillance to monitor complications and relapse and integrated longer-term management, including rehabilitation (22–24).

Rehabilitation is an integral part of any cancer management, and there is evidence suggesting the beneficial effect of comprehensive rehabilitation (25–31). Furthermore, a major limitation of delivery of chemotherapy and predictor of inferior outcome is poor performance status (32). As the incidence of older patients treated for lymphoma requiring rehabilitation before or after anti-lymphoma therapy increases, effective evidence-based rehabilitation strategies are expected to play critical and expanding roles in best practice. Currently, a range of rehabilitation interventions are trialled in the management of lymphoma pre-treatment, during adjuvant therapies, and late phases of care, and, for the longer-term, care continuum in the community. The aim is to maximize patient function, promote independence and participation, and improve psychological well-being and quality of life (QoL) (28, 29). Reports suggest that patients with haematological malignancies, including lymphomas, can make functional gains in inpatient rehabilitation settings (31). Maximal exercise capacity seems to decrease before treatment in PwL, especially in patients with advanced disease, and tends to return to close to normal during and/or after treatment (33). Furthermore, comprehensive exercise programmes were found to be effective in reducing disability and symptoms (depression, anxiety, fatigue, pain, etc.), improving functional capacity, muscular strength and QoL (19, 31, 34, 35). One systematic review reported that NHL survivors who met public health exercise guidelines defined by the American College of Sports Medicine (i.e. engaging in >30 min/day of at least moderate physical activity (PA) on ≥5 days/week, or >150 min a week) reported a clinically important better health-related quality of life (HRQoL) than their counterparts who did not meet exercise guidelines (11). Aerobic exercise training interventions were associated with positive effects on cardiorespiratory fitness, fatigue and self-reported physical functioning, and were feasible and safe in PwL (33). Other complementary and alternative therapies, such as mindfulness-based cognitive therapy, meditation, yoga, and tai chi, have shown improvement in cognitive function and QoL (36–38). Another recent systematic review reported that a combination of PA together with mental exercise may be more beneficial to PwL (39). There remains, however, an unmet need in the cancer population, and only a limited number of survivors receive the appropriate rehabilitation intervention that they need (40, 41). Furthermore, despite acknowledging rehabilitation as an integral component of the management of cancer patients, rehabilitation-specific guidelines for many cancer groups are limited, and many general cancer guidelines do not incorporate recommendations for specific rehabilitation interventions (42–44).

As mentioned above, various systematic reviews have evaluated the current evidence regarding the effectiveness and safety of different rehabilitation interventions in PwL. However, these published reviews vary in scope, methodology and quality, with diverse, and occasionally discordant, conclusions. The heterogeneity of the lymphoma rehabilitation literature warrants a comprehensive review, with a focus on the evidence for efficacy and potential harm of various rehabilitative strategies. A systematic review of systematic reviews is a new approach to synthesize current evidence across the same or similar interventions, to

summarize treatment effect in a much broader concept (45). This approach allows comparison of results from multiple reviews, thereby providing a comprehensive evidence-based summary (45, 46). To our knowledge, systematic reviews of rehabilitation strategies for PwL have not been thoroughly and qualitatively appraised to date. Therefore, this review aimed to systematically evaluate existing evidence from published systematic reviews for the effectiveness of rehabilitation strategies for improved function, impairments and participation in PwL. Specific questions addressed include: Are rehabilitation interventions effective in minimizing impairment, activity limitation, participation restriction and treatment-related complications in PwL?, and: What specific types of rehabilitation interventions are effective in PwL, and in which setting?

METHODS

Literature search

A comprehensive review of the literature for published systematic reviews/meta-analyses evaluating the efficacy of rehabilitation interventions for PwL was undertaken, using a multipronged approach. A search of health science databases was conducted, including: Cochrane Library, PubMed, EMBASE, and CINAHL (from inception to 1 October 2020). The search strategy included combinations of multiple search terms (both MeSH and keyword text terms) for 3 themes: lymphoma; systematic review; and rehabilitation (Appendix I). A full description of the search strategy (with EMBASE as an example) is given in Appendix II. A manual search of bibliographies of pertinent articles and relevant journals for additional references was conducted. A grey literature search was performed using different internet search engines and websites: such as System for Information on Grey Literature in Europe; New York Academy of Medicine Grey Literature Collection and Google Scholar. Furthermore, websites of various healthcare institutions; and governmental and non-governmental organizations associated with haematological cancers were searched for any potential reviews. It was planned to contact authors and known experts in the field for information; however, this was not necessary, as any further data was not required for the analyses.

All systematic reviews that focused specifically on rehabilitation interventions conducted in any settings (inpatient, ambulatory, home-based or community rehabilitation settings) for the management of PwL were included. Systematic reviews involving other cancer groups/haematological malignancies, where data specifically provided for lymphoma sub-groups, were also included. Exclusion criteria were: reviews solely evaluating diagnostic, pharmacological and/or surgical interventions; those conducted in the paediatric population; non-English publications; narrative reviews; theses; health technology appraisal and reviews listed only in conference proceedings.

Study selection and data extraction

All studies identified through the search process and other sources were exported to an EndNote X9 (Clarivate, London, UK) database for the removal of duplicates. Two authors (BA, FK) independently screened and shortlisted all abstracts and titles of reviews identified by the search strategy for inclusion and appropriateness, based on the pre-specified inclusion/exclusion criteria described above. The study selection process was performed in accordance with Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. Each study was independently evaluated, and the full-text article was obtained for assessment to determine the likelihood of inclusion. Any disagreement regarding the possible inclusion/exclusion of any individual study was resolved by consulting with other authors and by a final consensus. All relevant data were extracted using standard proforma, which included: publication and search date; objectives; characteristics of included studies and study subjects; intervention; findings/patient outcomes in the review; and limitations. Any discrepancies were resolved by discussion with other authors (TL, MD) and by re-reviewing the study.

Assessment of methodological quality of included reviews

Two reviewers (BA, FK) independently assessed the methodological quality of each included review, using the revised "A Measurement Tool to Assess Systematic Reviews" (AMSTAR-2) appraisal tool (Table I) (47). The AMSTAR-2 consists of 16 assessment items, with 7 being critical methodological items (items 2, 4, 7, 9, 11, 13, 15) and the rest outcome variables of items (1, 3, 5–6, and 10–16). Based on predefined criteria, each item was categorized as "Yes" (if the item was answered completely correct and well-documented, "Partial yes" (if the item was answered correctly with limited evidence), and "No" (if the item was not subject to relevant evaluation or improper evaluation) (47). Based on the judgment on the 16 individual appraisal items, overall methodological quality and confidence in the results of each systematic review were rated into 4 levels: "high" (no or 1 non-critical weakness), "moderate"' (more than 1 non-critical weakness), "low" (1 critical flaw with or without non-critical weaknesses), or "critically low" (more than 1 critical flaw with or without non-critical weaknesses) (47). Any disagreements were resolved by consensus among all review authors.

The Grade of Recommendation, Assessment, Development and Evaluation (GRADE) tool (48) was used to assess the quality of evidence for each outcome according to the following features:

- Study limitations (risk of bias): internal validity of the evidence.
- Inconsistency: heterogeneity or variability in the estimates of effect across studies.
- Indirectness: degree of differences between population, intervention, comparator, for the intervention and outcome of interest.
- Imprecision (random error): extent to which confidence in the effect estimate is adequate to support a particular decision.
- Publication bias: degree of selective publication of studies.

The quality of evidence was classified as (48): "high-quality": very confident that the true effect lies close to that of the estimate of the effect; "moderate-quality": moderately confident in the effect estimate, such that the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different; "low-quality": confidence in the effect estimate is limited, and the true effect may be substantially different from the estimate of the effect, and "very low-quality": very little confidence in the effect estimate and the true effect is likely to be substantially different from the estimate of the effect.

Any discrepancies were resolved by a final consensus amongst all reviewers.

Table I. Quality assessment (A Measurement Tool to Assess Systematic Reviews" (AMSTAR-2) appraisal tool; AMSTAR-2) of included systematic reviews

	Study, year											
AMSTAR 2 items*	Brown et al., 2012 (50)	Heywood et al., 2018 (51)	Jochem et al., 2014 (54)	Knips et al., 2019 (49)	Liu et al., 2019 (39)	Mishra et al., 2012 (30)	Vermaete et al., 2013[a] (19)	Vermaete et al., 2013[b] (33)	Park et al., 2019 (52)	Felbel et al., 2014 (38)	Wayne et al., 2018 (53)	Zeng et al., 2019 (37)
1. Research questions/inclusion criteria include PICO components	Yes	Yes	No	Yes	Yes	Yes	No	No	No	Yes	No	No
2. Contains an explicit statement that the review methods were established before the conduct of the review and justify any significant deviations from the protocol	No	Partial	No	Yes	No	Yes	No	No	No	Yes	No	No
3. Explained their selection of the study designs for inclusion	Partial	Yes	Partial	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
4. Used a comprehensive literature search strategy	No	Partial	No	Partial	Partial	Yes	Partial	Partial	Partial	Partial	Partial	Partial
5. Performed study selection in duplicate	Yes	Yes	No	Yes	Yes	Yes	No	No	Yes	Yes	No	No
6. Performed data extraction in duplicate	No	Yes	No	Yes	Yes	Yes	No	No	No	Yes	Yes	N
7. Provided a list of excluded studies and justify the exclusions	No	No	No	Yes	Yes	Yes	No	No	No	Yes	No	No
8. Described the included studies in adequate detail	Partial	Yes	Partial	Yes	Partial	Yes	No	No	Yes	Yes	Partial	Partial
9. Used a satisfactory technique for assessing the RoB in included individual studies	Yes	Yes	Partial	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes
10. Reported on the sources of funding for the studies included	No	No	No	Yes	No	Yes	No	No	No	Yes	No	No
11. If meta-analysis was performed, used appropriate methods for statistical combination of results	Yes	NA	Yes	Yes	Yes	Yes	Yes	NA	Yes	Yes	Yes	Yes
12. If meta-analysis was performed, assessed the potential impact of RoB in individual studies on the results of the meta-analysis or other evidence synthesis	Yes	NA	Partial	Yes	Yes	Yes	Yes	NA	No	Yes	No	No
13. Accounted for RoB in individual studies when interpreting/discussing the results	Yes	No	Partial	Yes	Yes	Yes	Yes	No	Yes	Yes	v	No
14. Provided a satisfactory explanation for, and discussion of, any heterogeneity observed in the results	Yes	No	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	No
15. If quantitative synthesis performed, carried out an adequate investigation of publication bias and discuss its likely impact on the results	No	NA	Yes	Yes	No	Yes	No	No	Yes	No	No	No
16. Reported any potential sources of conflict of interest, including any funding they received	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No
Overall rating[a]	Low	Low	Low	High	Mod	High	Low	Low	Mod	Mod	Mod	Low

*A Measurement Tool to Assess Systematic Reviews 2 (AMSTAR-2) (47). Item criteria: Y = Yes, criteria met, NY = No, criteria not met, P: Partial Yes, NA: Not applicable. [a]*Overall rating*: HIGH: high quality (no or 1 non-critical weakness); Mod: moderate quality (more than 1 non-critical weakness); Low: low quality (1 critical flaw with or without non-critical weaknesses); or Clow: critically low quality (more than 1 critical flaw with or without non-critical weaknesses).
PICO: Population, Intervention, Comparator, Outcomes; RoB: risk of bias.

RESULTS

The search retrieved 901 published systematic reviews. Of these, 29 reviews evaluating rehabilitation interventions currently used in the management of PwL met the abstract inclusion criteria and were selected for closer scrutiny. Full texts of these articles were retrieved, and both reviewers performed the final selection. Two systematic reviews that met the inclusion criteria were identified from the manual search of bibliographies of relevant articles. Overall, a total of 12 reviews were included: 3 published in the Cochrane Library database (30, 38, 49) and 8 published in other academic journals (19, 33, 37, 39, 50–54). A PRISMA flow diagram of the study selection process is shown in Fig. 1. Lists of excluded reviews with reasons for exclusion are tabulated in Appendix III.

There was marked heterogeneity amongst the included reviews in terms of: included primary studies, lymphoma patients, intervention protocols, rehabilitation settings, and outcomes measured. The included reviews were published (or updated) between 2012 and 2019. The majority of reviews (8 reviews) limited the searches to only randomized controlled trial (RCT) or clinical controlled trial (CCT) designs, and 2 reviews (33, 52) included all study design, and another 2 (19, 54) included only cohort and case-control studies. Of the 12 reviews, 6 solely included lymphoma cohorts (19, 33, 38, 39, 52, 54), the rest involved different cancer groups and/or haematological malignancies and provided data on PwL. Overall, these 12 reviews included 23 RCTs and 78 other design (ODs) studies, with a total of 87,132 participants with lymphoma. Ten of the 12 included systematic reviews performed meta-analyses (19, 30, 37–39, 49, 50, 52–54), and the other 2 provided only a qualitative description of findings (33, 51).

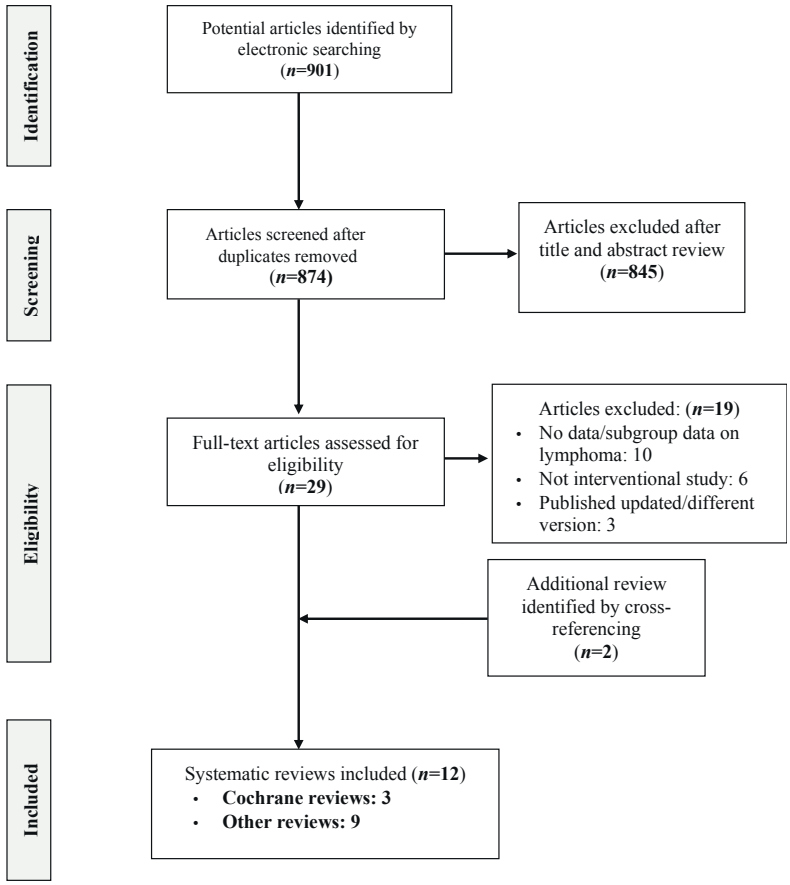

Fig. 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) flow diagram showing a selection of reviews.

Methodological quality of included reviews

The risk of bias of primary studies within included reviews was not re-assessed; instead, overall quality of the included reviews was critically assessed using the AMSTAR-2 tool (Table I). Only 2 reviews (both Cochrane reviews) were judged to be of "high quality" (30, 49), 4 reviews were of "moderate quality"' (38, 39, 52, 53), 4 reviews were of "low quality" (19, 50, 51, 54), and 1 was judged to be of "critically low quality" (33) (see Table I). The majority of reviews (6 reviews) (30, 38, 39, 49–51) used the Patient Intervention Control Outcomes (PICO) description as an organizing framework in the research question and inclusion criteria, the remainder specifically failed to detail comparator groups. Only 3 reviews (all Cochrane reviews) (30, 38, 49) provided an explicit statement on registered information of the protocol before the review, and none reported any significant deviation from the prior protocol. All reviews searched within 24 months of completion of the review; however, a comprehensive literature search was performed only by Mishra et al. (30), whereas others either did not include a grey literature search or contacted the experts in the field. Five reviews did not provide details on study selection and data extraction in duplicate (19, 33, 37, 53, 54). Lists of excluded studies were described in only 4 reviews (30, 38, 39, 49). The majority of reviews adequately described details of the included studies in tables. All reviews, except 2 (19, 33), assessed the scientific quality of the included primary studies using the validated risk of bias (RoB) tools. There was heterogeneity amongst the included reviews in the RoB tools used: 7 reviews used core items of the Cochrane RoB tool, 1 each used the PEDro (50), Newcastle Ottawa Scale (52), and 2 adapted tools used previously by other authors (19, 54). Ten reviews applied appropriate methods for statistical synthesis (meta-analysis) (19, 30, 37–39, 49, 50, 52–54), of which 3 reviews (37, 52, 53) did not assess the potential impact of RoB in individual studies on the results of the synthesis. Eight reviews (30, 38, 39, 49, 50, 52–54) provided satisfactory explanations for any heterogeneity in the results, carried out an adequate investigation of publication bias and discussed its likely impact on the results of the review. The majority of reviews, except 2 (37, 51) provided their funding sources and declared their potential source of conflict of interest; however, surprisingly; the majority (all 9 non-Cochrane reviews) (19, 33, 37, 39, 50–54) did not

address the potential competing interests and source of support of authors of the primary studies.

Evidence synthesis of rehabilitation interventions

The rehabilitation approach to patients with haematological malignancies including PwL included a range of interventions. Of the included systematic reviews evaluating various interventions, most ($n=8$ reviews) addressed different PA, physical fitness status and exercise programmes in isolation or concomitant with other interventions; 3 reviews evaluated different complementary and alternative medicine (CAM) interventions (yoga, tai chi and qigong); and 1 review examined the efficacy of vitamin D. The findings indicate that, although a spectrum of interventions is used in PwL, the evidence for many of these is limited, unclear, or both, because of a paucity of methodologically robust studies. The existing best-evidence synthesis for rehabilitation interventions in PwL is summarized in Table II. The impact of the outcomes of these interventions, based on the type of intervention, is summarized below.

Table II. Characteristics of the included reviews

Author, year	Number of studies and participants Search date Meta-analysis	Interventions	Outcome measures	Main findings	Grade
Physical activities, Exercise					
Brown et al., 2012 (50)	37 RCTs (2 in PwL) 2,929 participants with different Ca types (PwL = 161, with all types of lymphoma) Search date: 18 November 2010 Meta-analysis: Yes	All type of exercise: walking, stationary cycling, weight machines, resistance bands, yoga	Depressive symptoms	Sub-group analyses: no significant difference in depressive symptoms among PwL ($d_+ = -0.3$, 95% CI −0.26 to −0.01, $p = 0.424$) In overall Ca patients: Reduced depression ($d_+ = -0.13$, 95% CI −0.26 to −0.01, $p = <0.001$) Increase in weekly volume of aerobic exercise reduced depressive symptoms in dose-response fashion ($p = 0.03$) Reduced depressive symptoms most when exercise sessions were supervised ($p = 0.01$), and when cancer survivors were aged between 47–62 years ($p = 0.01$)	Low
Heywood et al., 2018 (51)	16 RCTs, 9 non-RCTs (4 RCTs in PwL) 1,188 participants with different Ca types (PwL = 197, with all types of lymphoma) Search date: 1 March 2017 Meta-analysis: No	All type of structured exercise programmes	Physical function (exercise capacity, muscular strength), QoL, fatigue, psychological function, body composition, sleep quality, pain, survival	No subgroup analysis in PwL In overall Ca patients: Significant improvements in ≥1 measure of physical function ($p < 0.05$) Significant improvement in ≥1 fatigue measure (8 studies) ($p < 0.05$) Significant improvement in QoL (in 11 studies) ($p < 0.05$) Improvement in psychological function (5 studies) Some reduction in pain (29%) ($p < 0.05$) (2 studies) Improvement in sleep quality (4 studies) Improved body composition (e.g. reduction in lean body mass) (5 studies)	Low
Jochem et al., 2014 (54)	15 cohort and 8 case control studies (15 studies in PwL) 1,648,601 participants with different Ca types (PwL = 15,173, with all types of lymphoma) Search date: June 2013 Meta-analysis: Yes	PA	Risks of Ca	PA showed statistically non-significant associations with risks of lymphoma or other Ca Comparing high vs low PA levels, RR for NHL: 0.91 (95% CI 0.82–1.00); HL: 0.86 (95% CI 0.58–1.26), leukaemia: 0.97 (95% CI 0.84–1.13), multiple myeloma: 0.86 (95% CI 0.68–1.09); DLBCL: 0.95 (95% CI 0.80–1.14), FL: 1.01 (95% CI 0.83–1.22), all haematological cancers: 0.93 (95% CI 0.88–0.99)	Low
Knips et al., 2019 (49)	18 RCTs (3 RCTs in PwL) 1,892 participants with different Ca types (PwL = 292, with all types of lymphoma Search date: July 2018 Meta-analysis: Yes	Aerobic exercise in addition to strength training	Overall survival, QoL, fatigue, physical performance, anthropometric measurements	No subgroup analysis in PwL In overall Ca patients: Significant improvement in improves fatigue (SMD 0.31; 95% CI 0.13–0.48; 9 trials, 826 patients) Some improvement in depression (SMD 0.19; 95% CI 0.0–0.38; 6 trials, 445 participants) No effect on overall survival (RR = 0.67; $p = 0.112$, 1 study) No improvement in QoL (SMD 0.11; 95% CI −0.03 to 0.24; 8 trials, 1,259 participants), physical functioning (SMD 0.15; 95% CI −0.01 to 0.32; 8 trials, 1329 participants), and anxiety (SMD 0.03; 95% CI −0.30 to 0.36;6 trials, 445 participants)	Moderate-Low
Liu et al., 2019 (39)	6 RCTs 429 participants All types of lymphoma Search date: 8 Jan 2013 Meta-analysis: Yes	All kinds of PA designed to improve physical and mental health (aerobic endurance training, sensorimotor training, strength Training, moderate cycling, walking, running, swimming, yoga, qigong, tai chi chuan, and others)	QoL, fatigue, sleep function, depression	No improvement in QoL ($p = 0.30$, 3 studies) Some improvement in fatigue ($p = 0.06$, 5 studies) No improvement in sleep quality ($p = 0.06$, 4 studies) No improvement in depression ($p = 0.34$, 2 studies) Aerobic exercise has little improvement in fatigue and sleep ($p > 0.05$) Significant improvement in sleep ($p = 0.04$, 3 studies) and depression ($p = 0.004$, 3 studies) after mind-body exercise intervention	Low

Table II. *Cont.*

Author, year	Number of studies and participants Search date Meta-analysis	Interventions	Outcome measures	Main findings	Grade
Mishra et al., 2012 (30)	38 RCTs, 2 CCTs (4 RCTs in PwL) 3,694 participants with different Ca types (PwL=192, with all types of lymphoma) Search date: October 2011 Meta-analysis: yes	All type of exercise: strength training, resistance training, walking, cycling, yoga, qigong, or tai chi	Overall HRQoL or at least one HRQoL domain	No subgroup analysis in PwL In overall Ca patients: Improvement in global HRQoL at 12 weeks (SMD 0.48; 95% CI 0.16–0.81), and at 6 months (SMD 0.46; 95% CI 0.09–0.84), but no difference at between 3 and 6 months (SMD 0.14; 95% CI −0.38 to 0.66) Decreased anxiety at 12-week follow-up (SMD −0.26; 95% CI −0.07 to −0.44) Decrease fatigue at 12-week (SMD −0.82; 95% CI −1.50 to −0.14) and between 12 weeks and 6 months (SMD −0.42; 95% CI −0.02 to −0.83) Decrease pain at 12 weeks (SMD −0.29; 95% CI −0.55 to −0.04)	Moderate-Low
Vermaete et al., 2013[a] (19)	12 studies (7 case–control, 5 cohort studies) 1,278,469 participants (PwL: 11,511, with all types of lymphoma) Search date: 8 Jan 2013 Meta-analysis: Yes	PA: total, occupational, recreational	Influence of PA on lymphoma risk, PA level, duration	No significant influence of PA on risk of lymphoma (pooled OR = 0.90; 95% CI 0.79–1.02; $p = 0.10$) Significant protective influence of PA on risk of lymphoma only in case control studies (pooled OR = 0.81; 95% CI 0.68–0.96; $p = 0.02$), but not in cohort studies (pooled OR = 1.02; 95% CI 0.88–1.19; $p = 0.76$) No significant differences between results for HL and NHL (χ^2=0.16; $p = 0.69$), no significant difference between recreational and occupational activities ($\chi^2 = 1.01$; $p = 0.31$)	Low
Vermaete et al., 2013[b] (33)	13 articles (all design) 2,450 participants (PwL: 2,399 with all types of lymphoma) Search date: July 2012 Meta-analysis: No	PA, physical fitness or exercise training (aerobic exercise)	PA duration, Fatigue, QoL, Cardiovascular fitness (VO2 max), 6MWD, Lung function (FVC, FEV1), depression, anxiety, body weight	21–29% of PwL meet the public health guidelines for PA Maximal exercise capacity was decreased before treatment, especially in patients with advanced disease, and was close to normal during and/or after treatment Lower levels of PA and lower physical fitness associated with more fatigue Aerobic exercise training interventions were feasible and safe and had positive effects on cardiorespiratory fitness, fatigue and self-reported physical functioning	Very low
Vitamin D					
Park et al., 2019 (52)	30 articles (all design) 56,458 participants with NHL Search date: Feb 2018 Meta-analysis: Yes	Sunlight/ultraviolet radiation (UVR) exposure, dietary intake, and serum/plasma 25(OH) D levels	NHL risk	Significant protective effects of overall sunlight/UVR exposure on NHL (RR = 0.80; 95% CI 0.71–0.90) Results consistent with various classifications of sunlight/UVR exposure Non-significant effect of dietary vitamin D intake (RR = 1.03; 95% CI 0.90–1.19) and serum/plasma 25(OH)D levels (RR = 0.97; 95% CI 0.82–1.15) on NHL and the subtypes	Low
Yoga					
Felbel et al., 2014 (38)	1 RCT 20 participants All types of lymphoma Search date: 4 Feb 2014 Meta-analysis: Yes	Yoga	HRQoL, overall survival, adverse events	No improvement in distress (MD −0.30, 95% CI −5.55 to 4.95; $p = 0.91$) No beneficial effect in fatigue (MD 0.00, 95%: −0.94 to 0.94; $p = 1.00$), anxiety (MD 0.30, 95% CI −5.01 to 5.61; $p = 0.91$) or depression (MD −0.70, 95% CI −3.21 to 1.81; $p = 0.58$) Improvement is overall quality of sleep (MD −2.30, 95% CI −3.78 to −0.82; $p = 0.002$) AEs not reported	Very low
Tai chi, qi gong					
Wayne et al., 2018 (53)	15 RCTs (1 RCT in PwL) 1,283 participants with different Ca types (PwL = 96, with NHL) Search date: 30 June 2013 Meta-analysis: Yes	Tai chi and qigong	Fatigue, sleep difficulty, pain, mood, QOL	No subgroup analysis in PwL In overall Ca patients: Significant improvement in fatigue (ES = −0.53, $p < 0.001$), sleep difficulty (ES = −0.49, $p = 0.018$), depression (ES = −0.27, $p = 0.001$), and overall QOL (ES = 0.33, $p = 0.004$) No significant improvement in pain (ES = −0.38, $p = 0.136$)	Low
Zeng et al., 2019 (37)	12 RCTs (2 RCTs in PwL) 915 participants with different Ca types (PwL = 204, with all types of lymphoma) Search date: 30 Sept 2018 Meta-analysis: Yes	Qigong or tai chi	QoL, physical and psychological effects	No subgroup analysis in PwL In overall Ca patients: Significant positive effects on reducing fatigue (SMD 2.05, $p = 0.005$, 95% CI 0.63 to 3.47, 8 studies) Beneficial effect in sleep quality ($p < 0.001$, 3 studies) No effect on anxiety, stress, depressive symptoms, and improved overall QoL ($p > 0.05$)	Low

Ca: cancer; CRP: C-reactive protein; DLBCL: diffuse large B-cell lymphoma; d_+: weighted mean effect size value; ES: effect size; FL: follicular lymphoma; FVC: forced vital capacity; FEV1: forced expiratory volume; HRQoL: health-related quality of life; MD: mean difference; MET: metabolic equivalent task; NHL: non-Hodgkin's lymphoma; PA: physical activity; PwL; patients with lymphoma; QoL: quality of life; RR: relative risk, SMD: standard mean difference, VO2 max: maximum volume of oxygen consumption, 25(OH)D: 25-hydroxyvitamin D, 95% CI: 95% confidence interval; 6MWD: 6-m walking distance.

Physical therapeutic modalities

Exercise programmes. Different exercise programmes, both during and after treatment, are increasingly being recognized as an important component of the rehabilitation modalities of cancer survivors, including PwL. Despite the variation in the evaluated exercise programmes, in terms of the types, intensity, duration, settings (institution, community, or home); the overall findings support the effectiveness of exercise programmes in PwL in improving functional capacity, muscular strength, functional mobility, fatigue, psychological well-being, treatment complications and QoL.

One systematic review ($n=6$ RCTs, 429 participants) evaluated the effects of various exercise programmes (aerobic endurance training, sensorimotor and strength training) on QoL and other health outcomes, for adults with lymphoma (39). The findings indicated that exercise showed a significant positive effect, specifically on fatigue (effect size (z): 1.905, $p=0.05$); however, despite showing some improvement, the magnitude of the effect size did not reach the statistically significant level for QoL, sleep quality and/or depression ($p>0.05$ for all). A subgroup analysis according to different types of exercises showed that aerobic exercise exhibited little improvement in aspects of QoL and fatigue, but mind-body exercise (such as qigong, yoga) showed a beneficial effect in improving sleep ($z=2.07$, $p=0.04$) and depression ($z=2.87$, $p=0.004$) (39). The authors, however, highlighted the need for further investigation due to a small number of included studies with marked heterogeneity.

In an updated Cochrane review (18 RCTs, 1,892 participants), Knips et al. evaluated the efficacy, safety and feasibility of aerobic physical exercise in patients with haematological malignancies, including lymphoma (3 RCTs, 292 participants) (49). The authors did not conduct a subgroup analysis for the PwL. The overall post-intervention findings showed significant improvement in fatigue (standard mean difference (SMD) 0.31; 95% CI 0.13–0.48) and some improvement in depression (SMD 0.19; 95% CI 0.0–0.38). There was no conclusive evidence for favourable effect of aerobic exercises on overall survival (relative risk (RR)=0.67; $p=0.112$), and improvement in QoL (SMD 0.11; 95% CI –0.03–0.24), physical functioning (SMD 0.15; 95% CI –0.01 to 0.32), and anxiety (SMD 0.03; 95% CI –0.30 to 0.36) (49).

Another Cochrane review ($n=38$ RCTs and 2 CCTs, 3,694 participants) analysed the effect of various exercise interventions on HRQoL in adult cancer survivors after treatment, including lymphoma survivors ($n=4$ RCTs, 192 participants) (30). There was marked heterogeneity amongst the included trials in terms of the patient population; mode/type, duration, and intensity of intervention. The authors did not perform any sub-group analysis according to cancer types. The overall results suggest exercise programmes showed a beneficial effect in improving global HRQoL at 12 weeks (SMD 0.48; 95% CI 0.16–0.81) and at 6 months (SMD 0.46; 95% CI 0.09–0.84). Exercise programmes also resulted in improvement in fatigue (SMD –0.82; 95% CI –1.50 to –0.14), anxiety (SMD –0.26; 95% CI –0.07 to –0.44) and pain (SMD –0.29; 95% CI –0.55 to –0.04) at 12 weeks follow-up (30). There was no conclusive evidence suggesting the beneficial effect of an exercise intervention on cognitive and/or physical functioning, general health perspective, role function, or spirituality (30).

In another systematic review ($n=16$ RCTs, 9 non-RCTs, 1,188 participants) Heywood et al. evaluated the efficacy of exercise interventions (aerobic exercise and/or resistance training) in patients with advanced cancers, including lymphoma ($n=4$ RCTs, 197 participants) (51). The authors did not conduct a subgroup analysis based on cancer types. The overall results suggest that exercise interventions were effective in significant improvements in physical function, and fatigue ($p<0.05$ for all). Between- and within-group improvements were reported with exercise for psychological function, sleep quality and body composition (e.g., reduction in lean body mass) (51). There was inconclusive evidence for the advantageous effects of exercise in reducing pain and survival rates. Based on these findings, the authors recommend the inclusion of exercise interventions as an adjunct therapy for patients with advanced cancers, including lymphoma (51).

One systematic review ($n=37$ RCTs, 2,929 participants) evaluated the efficacy of exercise in reducing depressive symptoms in cancer survivors, including lymphoma ($n=2$ RCTs, 161 participants) (50). Exercise modalities evaluated included: walking, stationary cycling, weight machines, resistance bands and yoga, with a mean duration of 13.2±11.7 weeks and 3.0±2.5 sessions per week. The findings in all cancer survivors demonstrated that exercise interventions provided a small significant reduction in depressive symptoms (weighted mean effect size value (d_+) –0.13, 95% CI –0.26 to –0.01, $p<0.001$) (50). An increase in the weekly volume of aerobic exercise was found to reduce depressive symptoms in a dose-response fashion ($p=0.03$), and most when exercise sessions were supervised ($p=0.01$) in cancer survivors between ages 47 and 62 years ($p=0.01$). Subgroup analyses in PwL showed no significant reduction in depressive symptoms ($d_+=-0.30$, 95% CI –0.89 to 0.29, $p=0.424$) (50). The authors recommend treating clinicians should discuss the safety and feasibility of exercise to optimize depressive symptom management in all patients with advanced cancers (50).

Physical activity and fitness. There is consensus amongst treating clinicians that cancer survivors should be regularly engaged in PA. PA is considered an effective

intervention for improving QoL and overall well-being in patients with cancers, including PwL (33).

In a systematic review, Vermaete et al. evaluated PA and physical fitness in PwL ($n=13$ all design studies, 2,450 participants, PWL 2,399) before, during and after treatment. The authors reported that only 21–29% of lymphoma survivors met the public health guidelines for PA, as defined by the American College of Sports Medicine (i.e., engaging in >30 min/day of at least moderate PA on ≥5 days/week, or >150 min a week) (33). The maximal exercise capacity was decreased before treatment, especially in PwL with advanced disease, but was close to normal during and/or after treatment. Lower levels of PA and lower physical fitness were associated with more fatigue. Aerobic exercise training interventions were feasible and safe, with positive effects on cardiorespiratory fitness, fatigue and self-reported physical functioning (33).

One meta-analysis ($n=15$ cohort and 8 case-control studies, 1,648,601 participants; including 15,173 PwL in 15 studies) evaluated the relationship of PA with subtype-specific haematological cancers. No associations were identified between PA and risks of lymphoma (HL or NHL), multiple myeloma, or leukaemia (54). Comparison of high vs low levels of PA revealed statistically non-significant associations with risk of NHL (RR 0.91, 95% CI 0.82–1.00), HL (RR 0.86, 95% CI 0.58–1.26), leukaemia (RR 0.97, 95% CI 0.84–1.13), or multiple myeloma (RR 0.86, 95% CI 0.68–1.09). Similar results were found for subtypes of NHL; i.e., for DLBCL (RR 0.95, 95% CI 0.80–1.14) and for follicular lymphoma (RR 1.01, 95% CI 0.83–1.22) (54). The authors indicated that these findings may not represent a true lack of associations given the variation in high vs low physical activity definitions, the quality of PA assessments, and the variability in haematological cancer classification schemes in primary studies.

In another meta-analysis ($n=7$ case-control, 5 cohort studies, 1,278,469 participants, PwL 11,511) evaluated the association between PA and risk of lymphoma (19). The authors reported no significant effect of PA on the risk of developing lymphoma (pooled odds ratio (OR)=0.90; 95% CI 0.79–1.02; $p=0.10$). In a subgroup analysis the authors found some significant protective influence of PA on the risk of lymphoma in case control studies (pooled OR=0.81; 95% CI 0.68–0.96; $p=0.02$), but not in cohort studies (pooled OR=1.02; 95% CI 0.88–1.19; $p=0.76$) (19). There were no significant differences for HL and NHL subgroups ($\chi^2=0.16$; $p=0.69$), and no significant difference between recreational and occupational activities ($\chi^2=1.01$; $p=0.31$) (19).

The descriptive nature of the primary studies from which these analyses are derived precludes definitive conclusions regarding the relationship between PA and lymphoma risk, due to the possibility of unknown confounders. Nevertheless, based on these large cohorts, no clear association between PA and lymphoma risk was identified.

Nutritional intervention (vitamin D)

Healthy nutrition, weight management, and maintenance of a healthy lifestyle are important for vitality, functioning, and QoL for cancer patients, including PwL.

In a meta-analysis ($n=30$ articles, 56,458 participants) Park et al. investigated the effect of various measures of vitamin D status (sunlight/ultraviolet radiation (UVR) exposure, dietary intake, and serum/plasma 25(OH) D levels) in NHL and its subtypes (52). The authors identified a significantly lower relative risk of NHL among subjects with high sunlight/UVR exposure compared with subjects with lower exposure (RR=0.80; 95% CI 0.71–0.90). There were significant inverse associations between overall sunlight/UVR exposure and DLBCL (RR=0.72, 95% CI 0.54–0.97), FL (RR=0.81, 95% CI 0.73–0.90), and marginal zone lymphoma (MZL) (RR=0.70, 95% CI 0.57–0.87), but not for chronic lymphocytic leukaemia and small lymphocytic lymphoma (CLL/SLL) (RR=0.87, 95% CI 0.68–1.11), B-cell NHL (RR=0.84, 95% CI 0.68–1.05), and T-cell NHL (RR=0.70, 95% CI 0.48–1.01) (52). These associations were non-significant when the analyses were restricted to prospective studies only. Dietary vitamin D (>200 IU/day) (RR=1.03; 95% CI 0.90–1.19) and serum/plasma 25-(OH) D levels (RR=0.97; 95% CI 0.82–1.15) were not associated with NHL incidence and its subtypes (52). All included studies were cohort or case-control studies, and a direct causal/protective relationship cannot be concluded, as unmeasured confounding variables may have resulted in the observed associations.

Complementary and alternative medicines

Many PwL uses CAM approaches as an adjunct to other mainstream therapies; however, few are reported as being effective in enhancing clinical outcomes (55).

Yoga. In a Cochrane review ($n=1$ RCT with 20 PwL) Felbel et al. assessed the effects of yoga practice in addition to standard cancer treatment (38). The authors found no evidence that yoga improves distress (mean difference (MD) –0.30, 95% CI –5.55 to 4.95; $p=0.91$), fatigue (MD 0.00, 95% CI –0.94 to 0.94; $p=1.00$), anxiety (MD 0.30, 95% CI –5.01 to 5.61; $p=0.91$) or depression (MD –0.70, 95% CI –3.21 to 1.81; $p=0.58$) in PwL (38). There was very low-quality evidence that yoga improves the overall quality of sleep (MD –2.30,

95% CI –3.78 to –0.82; $p=0.002$) (38). The influence of yoga on HRQoL and overall survival rate was not reported.

Tai chi and qigong. In an updated systematic review ($n=12$ RCTs, 915 participants) Zeng et al. examined the effectiveness of qigong/tai chi on cancer survivors including lymphoma ($n=2$ RCTs, 204 PwL). The authors did not perform a subgroup analysis for PwL (37). The overall results suggest significant positive effects of qigong/tai chi on reducing fatigue (SMD 2.05, $p=0.005$, 95% CI 0.63–3.47) and sleep quality ($p<0.001$). No beneficial effect was observed for improvement on anxiety, stress, depressive symptoms, and overall QoL ($p>0.05$ for all) (37).

Wayne et al. in another systematic review ($n=15$ RCTs, 1,283 participants; 1 RCT with 96 NHL patients) reported similar advantageous treatment effects of tai chi/qigong (53). The findings suggest significant improvement in fatigue (effect size (ES) = −0.53, $p<0.001$), sleep difficulty (ES = −0.49, $p=0.018$), depression (ES = −0.27, $p=0.001$), and overall QoL (ES = 0.33, $p=0.004$), but not in pain (ES = −0.38, $p=0.136$) (53). The authors concluded that tai chi/qigong show promising results in addressing cancer-related symptoms and QoL in cancer survivors; however, more methodologically robust trials with longer follow-up periods and appropriate comparison groups are needed for definitive symptom-specific recommendations (53).

DISCUSSION

This review systematically analysed the evidence from published systematic reviews to date, for the effectiveness of various rehabilitation interventions on patient outcomes in PwL. The findings indicate that, although a wide range of rehabilitation approaches are commonly recommended and trialled in this population, there is still a lack of high-quality evidence for the effectiveness of many of these modalities. Furthermore, there is a paucity of studies evaluating other rehabilitation strategies that have an evidence base for patients with other oncological conditions, such as multi-disciplinary rehabilitation programmes, self-care and educational programmes, psychological programmes, etc. The overall findings of this review suggest, *moderate-quality evidence* for exercise programmes for improved fatigue, sleep disturbances, *low-quality evidence* for exercise therapy for improved pain, psychological wellbeing (depressive symptoms, anxiety) and overall QoL; and qigong/tai chi for improved fatigue, sleep disturbances, psychological symptoms (depression, anxiety) and overall QoL and an inverse association between sunlight/UVR exposure on lymphoma incidence based on descriptive studies. There was *very-low quality evidence* for yoga for improved sleep disturbances. The evidence suggesting associations of PA with risks of lymphoma is still uncertain.

Rehabilitation programmes have become an integral part of the management of people with various oncological conditions, including haematological malignancies (38, 54). The scope of contemporary oncological rehabilitation has shifted from physical therapeutic modalities alone, to more comprehensive management, including: secondary prevention for symptom and complication management; risk factor education; psychological support; and function and participation (56). Despite established guidelines, and standardized protocols for acute management of PwL (and other haematological malignancies) (57–59), specific guidelines on structured rehabilitation programmes are yet to be published. Furthermore, in PwL, due to diverse clinical presentations, varying levels of patient disability (and impairments), unpredictable prognosis and changing patient needs, a wide spectrum of individualized rehabilitation approaches may be required at different stages of the condition spectrum.

This review identifies different interventions employed for PwL; however, despite reported high prevalence of psychological impact in this population, there is limited relevant research. There is existing evidence indicating the effectiveness of psychological therapies (such as educational, cognitive-behavioural, or coping skills approaches) in facilitating physical and emotional function, immune function, and enhanced survival in other cancer populations (60–62). The review did not identify any studies evaluating the efficacy of rehabilitation interventions on survival length or relapse incidence in PwL. Furthermore, some lymphoma localizations and non-neoplastic complications, such as polyradiculoneuropathy and POEMS syndrome (polyneuropathy, organomegaly, endocrinopathy/oedema, monoclonal-protein and skin change), necessitate the involvement of a multidisciplinary rehabilitation team; however, these are yet to be evaluated. There is also a lack of reviews assessing vocational interventions for enhancing employment and/or education specifically targeting PwL.

This review found many of the evaluated interventions were too broadly described; specifically exercise interventions, without sufficient detail (optimal settings, type, intensity, and duration of therapy, and cost-effectiveness, etc.) to enable replication of the interventions. Furthermore, the structured and conceptual theory constructing these interventions was not adequately defined. The process surrounding the development of common outcome goals, which are achievable through the participation of the patient and the treating professional involved in the patient care

(warranted in rehabilitation settings), was, surprisingly, not mentioned in any included reviews. The WHO International Classification of Functioning, Disability and Health (ICF) framework provides elements of a theory about rehabilitation and provides a taxonomic system of human functioning (63); however, none of the included reviews cited this widely used model. This ICF model can be used as a common framework to help prioritize personalized goals for PwL, to set rehabilitation criteria.

There was heterogeneity amongst the included reviews, even in those evaluating similar outcomes. The methodological quality of the included systematic reviews varied, with only 2 and 4 out of 12 rated as of "high" and "moderate" methodological quality, respectively (AMSTAR-2 score). Most of the reviews included a broad range of cancer populations and only a few focused specifically on lymphoma cohorts. This has reflected with marked heterogeneity of cancer types, clinical presentation, and goals for treatment in the primary trials within the included reviews. The participant characteristics were heterogeneous amongst the studies regarding characteristics of lymphoma (type, lesion location and area, time since lymphoma, other comorbidities, age, etc.), which may have resulted in variability in findings. The included reviews consistently remarked on the poor quality of the primary studies with relatively small numbers of patients. There was also marked heterogeneity in the primary trials regarding the description of control arms, assessment time-points and outcome measures used. Likewise, evidence for the use of rehabilitation approaches targeting different cancer-related outcomes in the included reviews was diverse. This is mainly due to the variation of interventions provided (duration, intensity, settings, timing, etc.), outcome measurement tools, control intervention protocols and length of follow-up. Furthermore, outcome measures used, and assessment time-points also differed. Therefore, pooling data for quantitative analyses were not possible, and a best-evidence synthesis was described using qualitative analyses. The overall evidence for some of the studies was downgraded from actual evidence reported by authors, due to imprecision and inconsistency of findings, use of different outcome measures and inclusion of non-RCTs with poor methodology quality, precluding meta-analysis. Therefore, the quality of evidence and the external validity of the findings should be interpreted with caution. The confounding effects of adjunct rehabilitation therapies coupled with acute treatment need further exploration.

Evidence for the benefits of rehabilitation programmes is well established in various cancer groups (28, 29, 56, 64). Specifically, physical activities are the most commonly trialled and shown to attenuate a range of conditions and/or treatment-related physical and psychological impairments (65). A cancer control framework examining the short-term and long-term effects of PA defines 2 distinctive periods: the rehabilitation period, which immediately follows primary treatment, and the disease prevention/health promotion period, which describes longer-term survival (66). These published reports recommend that the rehabilitation period is highly important and variable (67) and that PA (and other types of rehabilitation programmes) are relevant throughout this period, including the longer-term survival period (66, 67). The benefits of any rehabilitation programme will vary according to the type of cancer and treatment, the cancer stage, and the mode, intensity, and duration of the exercise programme; and the patients' compliance (65, 67). Consistent with the findings of the current review, Spence et al. reported beneficial effects of exercise programmes in cancer patients in improving physical functioning, strength, PA levels, QoL, fatigue, immune function, haemoglobin concentrations, potential markers of recurrence, and body composition (65). The majority of studies included in this review were predominantly conducted in the breast cancer population, and none of the studies included PwL (65).

Close communication between the patient, the rehabilitation team and the treating haematologist is essential, since the goals of care for patients with haematological malignancies can change precipitously with the emergence of relapsed disease, disabling complications (e.g. critical sepsis) or patient frailty precluding further effective therapy. Consensus agreements between treating team and patient regarding the goals of rehabilitation are critical to its appropriate application and success, irrespective of modality. Patients with limited treatment options or persistent frailty despite rehabilitative attempts should be offered palliative care in combination with or, where appropriate, replacing restorative and curative approaches.

To our knowledge, this is the first review to systematically appraise published systematic reviews to evaluate the effectiveness of rehabilitation interventions for various cancer-related outcomes in PwL. This approach not only provides a comprehensive evidence-based summary of the effects of different interventions on various outcomes, but also provides reassurance as to whether the conclusions of individual reviews are consistent (45, 46). The aim was to provide an overview of available evidence for the rehabilitation interventions used in the lymphoma population, to assist and guide treating clinicians in choosing an appropriate treatment approach. Furthermore, it elaborates on the existing gaps in research and limitations in the included systematic reviews for future research and clinical implications.

Study limitations

It is not possible to rule out limitations in methodology and completeness of retrieved literature. Regardless of the comprehensive search employed, this review encompassed published literature written in English in specific health science databases, which may have introduced a selection and reference bias. However, an extensive comprehensive search using broad search terms in most prominent databases was usedand websites of prominent stroke-related organizations were explored to identify the relevant studies. Widely used validated tools to assess methodology (AMSTAR-2) and quality of evidence (GRADE) of included studies were used, despite the limitations of these global tools. The accuracy of the assessor's assessments cannot be guaranteed; however, the selection of studies and quality assessments were independently done by 2 authors, and further group consensus was reached. Due to significant heterogeneity among the included reviews, with high variability in treatment protocols and the participants, the effect of the intervention was only categorized quantitatively. These issues limit the generalizability of the findings. Evaluation of safety related to evaluated rehabilitation interventions was not possible, as reports of adverse events in the included reviews were incomplete or missing. Associated costs and/or economic benefits of interventions were not reported in any review. Some included reviews specifically investigated the association of dietary (vitamin D intake, UV exposure) and physical activities, and risk of lymphoma. However, these interventions were not part of comprehensive rehabilitation programmes within the studies; these reviews were included as there is evidence to suggest that oncological rehabilitation should include risk factor education as a part of a comprehensive programme. Furthermore, the findings are important from the rehabilitation perspective and for the development of structured rehabilitation programmes. The effect of these interventions on patients' disease trajectory requires investigation in future studies. Many included reviews were not up to date, as the last search dates were older than 3 years; hence many recent studies may have been missed. The findings of this review should therefore be interpreted with caution.

Conclusion

The management of patients following lymphoma is complex and challenging. Rehabilitation techniques can benefit PwL throughout the disease-continuum. However, there is still a lack of high-quality evidence for many rehabilitation interventions in lymphoma survivors. Positive effects of exercise programmes were noted for various outcomes (fatigue, psychological symptoms) and overall QoL. Some benefit of qigong/tai chi was found for improved symptoms and overall QoL, and yoga for sleep disturbances. There is a need for studies with robust methodology in larger cohorts, to evaluate the roles of various rehabilitation programmes and longer-term effects. Future studies should consider patient characteristics, outcome measures, timing, mode and intensity of rehabilitation interventions.

ACKNOWLEDGEMENTS

This review was supported by the internal resources of the Rehabilitation Department, Royal Melbourne Hospital, Royal Park Campus, Melbourne, Australia.

The authors have no conflicts of interest to declare.

REFERENCES

1. Mugnaini EN, Ghosh N. Lymphoma. Prim Care 2016; 43: 661–675.
2. Jaffe ES, Barr PM, Smith SM. Understanding the new WHO Classification of lymphoid malignancies: why it's important and how it will affect practice. Am Soc Clin Oncol Educ Book 2017; 37: 535–546.
3. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 2016; 127: 2375–2390.
4. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin 2018; 68: 394–424.
5. International Agency for Research on Cancer. Global Cancer Observatory (GCO),. 2020 [cited 2020 16 Sep]. Available from: https://gco.iarc.fr/.
6. Morrison VA, Bell JA, Hamilton L, Ogbonnaya A, Shih HC, Hennenfent K, et al. Economic burden of patients with diffuse large B-cell and follicular lymphoma treated in the USA. Future Oncol 2018; 14: 2627–2642.
7. Darba J, Marsa A. Burden of Hodgkin and non-Hodgkin lymphoma in Spain over a 10-year period: productivity losses due to premature mortality. Expert Rev Pharmacoecon Outcomes Res 2020: 1–5.
8. Allemani C, Matsuda T, Di Carlo V, Harewood R, Matz M, Niksic M, et al. Global surveillance of trends in cancer survival 2000-14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. Lancet 2018; 391: 1023–1075.
9. National Institute of Health. National Cancer Institute. Cancer stat fact sheets. [cited 2020 28 Sep]. Available from: www.seer.cancer.gov/statfacts/html.
10. Oerlemans S, Issa DE, van den Broek EC, Nijziel MR, Coebergh JW, Mols F, et al. Impact of therapy and disease-related symptoms on health-related quality of life in patients with follicular lymphoma: results of the population-based PHAROS-registry. Eur J Haematol 2014; 93: 229–238.
11. Oerlemans S, Mols F, Nijziel MR, Lybeert M, van de Poll-Franse LV. The impact of treatment, socio-demographic and clinical characteristics on health-related quality of life among Hodgkin's and non-Hodgkin's lymphoma survivors: a systematic review. Ann Hematol 2011; 90: 993–1004.
12. Oerlemans S, Mols F, Nijziel MR, Zijlstra WP, Coebergh JW, van de Poll-Franse LV. The course of anxiety and depression for patients with Hodgkin's lymphoma or diffuse large

B cell lymphoma: a longitudinal study of the PROFILES registry. J Cancer Surviv 2014; 8: 555–564.
13. Oerlemans S, Nijziel MR, van de Poll-Franse LV. Age-related differences in quality of life among patients with diffuse large B-cell lymphoma. Cancer 2015; 121: 2857–2858.
14. Oerlemans S, Issa DE, van den Broek EC, Nijziel MR, Coebergh JW, Huijgens PC, et al. Health-related quality of life and persistent symptoms in relation to (R-)CHOP14, (R-)CHOP21, and other therapies among patients with diffuse large B-cell lymphoma: results of the population-based PHAROS-registry. Ann Hematol 2014; 93: 1705–1715.
15. Fu JB, Lee J, Smith DW, Shin K, Guo Y, Bruera E. Frequency and reasons for return to the primary acute care service among patients with lymphoma undergoing inpatient rehabilitation. PM R 2014; 6: 629–634.
16. Oerlemans S, Mols F, Issa DE, Pruijt JH, Peters WG, Lybeert M, et al. A high level of fatigue among long-term survivors of non-Hodgkin's lymphoma: results from the longitudinal population-based PROFILES registry in the south of the Netherlands. Haematologica 2013; 98: 479–486.
17. Arts LPJ, Oerlemans S, Tick L, Koster A, Roerdink HTJ, van de Poll-Franse LV. More frequent use of health care services among distressed compared with nondistressed survivors of lymphoma and chronic lymphocytic leukemia: results from the population-based PROFILES registry. Cancer 2018; 124: 3016–3024.
18. Arboe B, Olsen MH, Goerloev JS, Duun-Henriksen AK, Johansen C, Dalton SO, et al. Return to work for patients with diffuse large B-cell lymphoma and transformed indolent lymphoma undergoing autologous stem cell transplantation. Clin Epidemiol 2017; 9: 321–329.
19. Vermaete NV, Wolter P, Verhoef GE, Kollen BJ, Kwakkel G, Schepers L, et al. Physical activity and risk of lymphoma: a meta-analysis. Cancer Epidemiol Biomarkers Prev 2013; 22: 1173–1184.
20. Ahlberg K, Ekman T, Gaston-Johansson F, Mock V. Assessment and management of cancer-related fatigue in adults. Lancet 2003; 362: 640–650.
21. Hjermstad MJ, Fossa SD, Oldervoll L, Holte H, Jacobsen AB, Loge JH. Fatigue in long-term Hodgkin's disease survivors: a follow-up study. J Clin Oncol 2005; 23: 6587–6595.
22. Hathiramani S, Pettengell R, Moir H, Younis A. Lymphoma survivors' experience of participation in a home-based intervention post-chemotherapy. Qual Life Res 2019; 28: 2951–2955.
23. Parker PA, Banerjee SC, Matasar MJ, Bylund CL, Rogers M, Franco K, et al. Efficacy of a survivorship-focused consultation versus a time-controlled rehabilitation consultation in patients with lymphoma: a cluster randomized controlled trial. Cancer 2018; 124: 4567–4576.
24. Rothe D, Cox-Kennett N, Buijs DM, Venner CP, Paterson DI, Gyenes GT, et al. Cardiac rehabilitation in patients with lymphoma undergoing autologous hematopoietic stem cell transplantation: a cardio-oncology pilot project. Can J Cardiol 2018; 34: S263–S269.
25. Dimeo F, Schwartz S, Fietz T, Wanjura T, Boning D, Thiel E. Effects of endurance training on the physical performance of patients with hematological malignancies during chemotherapy. Support Care Cancer 2003; 11: 623–628.
26. Dimeo FC. Effects of exercise on cancer-related fatigue. Cancer 2001; 92: 1689–1693.
27. Guo Y, Fu JB, Guo H, Camp J, Shin KY, Tu SM, et al. Postacute care in cancer rehabilitation. Phys Med Rehabil Clin N Am 2017; 28: 19–34.
28. Khan F, Amatya B, Ng L, Demetrios M, Zhang NY, Turner-Stokes L. Multidisciplinary rehabilitation for follow-up of women treated for breast cancer. Cochrane Database Syst Rev 2012; 12: CD009553.
29. Khan F, Amatya B, Ng L, Drummond K, Olver J. Multidisciplinary rehabilitation after primary brain tumour treatment. Cochrane Database Syst Rev 2013; 1: CD009509.
30. Mishra SI, Scherer RW, Geigle PM, Berlanstein DR, Topaloglu O, Gotay CC, et al. Exercise interventions on health-related quality of life for cancer survivors. Cochrane Database Syst Rev 2012: CD007566.
31. Mishra SI, Scherer RW, Snyder C, Geigle PM, Berlanstein DR, Topaloglu O. Exercise interventions on health-related quality of life for people with cancer during active treatment. Cochrane Database Syst Rev 2012: CD008465.
32. Lin TL, Kuo MC, Shih LY, Dunn P, Wang PN, Wu JH, et al. The impact of age, Charlson comorbidity index, and performance status on treatment of elderly patients with diffuse large B cell lymphoma. Ann Hematol 2012; 91: 1383–1391.
33. Vermaete N, Wolter P, Verhoef G, Gosselink R. Physical activity, physical fitness and the effect of exercise training interventions in lymphoma patients: a systematic review. Ann Hematol 2013; 92: 1007–1021.
34. Brown JC, Huedo-Medina TB, Pescatello LS, Pescatello SM, Ferrer RA, Johnson BT. Efficacy of exercise interventions in modulating cancer-related fatigue among adult cancer survivors: a meta-analysis. Cancer Epidemiol Biomarkers Prev 2011; 20: 123–133.
35. Ferrer RA, Huedo-Medina TB, Johnson BT, Ryan S, Pescatello LS. Exercise interventions for cancer survivors: a meta-analysis of quality of life outcomes. Ann Behav Med 2011; 41: 32–47.
36. Salhofer I, Will A, Monsef I, Skoetz N. Meditation for adults with haematological malignancies. Cochrane Database Syst Rev 2016; CD011157.
37. Zeng Y, Xie X, Cheng ASK. Qigong or tai chi in cancer care: an updated systematic review and meta-analysis. Curr Oncol Rep 2019; 21: 48.
38. Felbel S, Meerpohl JJ, Monsef I, Engert A, Skoetz N. Yoga in addition to standard care for patients with haematological malignancies. Cochrane Database Syst Rev 2014: CD010146.
39. Liu L, He X, Feng L. Exercise on quality of life and cancer-related fatigue for lymphoma survivors: a systematic review and meta-analysis. Support Care Cancer 2019; 27: 4069–4082.
40. Holm LV, Hansen DG, Johansen C, Vedsted P, Larsen PV, Kragstrup J, et al. Participation in cancer rehabilitation and unmet needs: a population-based cohort study. Support Care Cancer 2012; 20: 2913–2924.
41. Veloso AG, Sperling C, Holm LV, Nicolaisen A, Rottmann N, Thayssen S, et al. Unmet needs in cancer rehabilitation during the early cancer trajectory – a nationwide patient survey. Acta Oncol 2013; 52: 372–381.
42. Kim WJ, Novotna K, Amatya B, Khan F. Clinical practice guidelines for the management of brain tumours: a rehabilitation perspective. J Rehabil Med 2019; 51: 89–96.
43. Harris SR, Schmitz KH, Campbell KL, McNeely ML. Clinical practice guidelines for breast cancer rehabilitation: syntheses of guideline recommendations and qualitative appraisals. Cancer 2012; 118: 2312–2324.
44. Reames BN, Krell RW, Ponto SN, Wong SL. Critical evaluation of oncology clinical practice guidelines. J Clin Oncol 2013; 31: 2563–2568.
45. Smith V, Devane D, Begley CM, Clarke M. Methodology in conducting a systematic review of systematic reviews of healthcare interventions. BMC Med Res Methodol 2011; 11: 15.
46. Amatya B, Khan F, Galea M. Rehabilitation for people with multiple sclerosis: an overview of Cochrane Reviews. Cochrane Database Syst Rev 2019; CD012732.
47. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ 2017; 358: j4008.
48. Balshem H, Helfand M, Schunemann HJ, Oxman AD, Kunz R, Brozek J, et al. GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol 2011; 64: 401–406.
49. Knips L, Bergenthal N, Streckmann F, Monsef I, Elter T, Skoetz N. Aerobic physical exercise for adult patients with

haematological malignancies. Cochrane Database Syst Rev 2019; CD009075.
50. Brown JC, Huedo-Medina TB, Pescatello LS, Ryan SM, Pescatello SM, Moker E, et al. The efficacy of exercise in reducing depressive symptoms among cancer survivors: a meta-analysis. PLoS One 2012; 7: e30955.
51. Heywood R, McCarthy AL, Skinner TL. Efficacy of exercise interventions in patients with advanced cancer: a systematic review. Arch Phys Med Rehabil 2018; 99: 2595–2620.
52. Park HY, Hong YC, Lee K, Koh J. Vitamin D status and risk of non-Hodgkin lymphoma: an updated meta-analysis. PLoS One 2019; 14: e0216284.
53. Wayne PM, Lee MS, Novakowski J, Osypiuk K, Ligibel J, Carlson LE, et al. Tai Chi and Qigong for cancer-related symptoms and quality of life: a systematic review and meta-analysis. J Cancer Surviv 2018; 12: 256–267.
54. Jochem C, Leitzmann MF, Keimling M, Schmid D, Behrens G. Physical activity in relation to risk of hematologic cancers: a systematic review and meta-analysis. Cancer Epidemiol Biomarkers Prev 2014; 23: 833–846.
55. Buffart LM, van Uffelen JG, Riphagen, II, Brug J, van Mechelen W, Brown WJ, et al. Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials. BMC Cancer 2012; 12: 559.
56. Amatya B, Khan F, Galea MP. Optimizing post-acute care in breast cancer survivors: a rehabilitation perspective. J Multidiscip Healthc 2017; 10: 347–357.
57. Hoppe RT, Advani RH, Ai WZ, Ambinder RF, Armand P, Bello CM, et al. Hodgkin lymphoma, version 2.2020, NCCN clinical practice guidelines in oncology. J Natl Compr Canc Netw 2020; 18: 755–781.
58. Yamaguchi M, Suzuki R. JSH practical guidelines for hematological malignancies, 2018: 7. Peripheral T-cell lymphoma (PTCL). Int J Hematol 2019; 109: 137–140.
59. Wierda WG, Byrd JC, Abramson JS, Bilgrami SF, Bociek G, Brander D, et al. NCCN Guidelines insights: chronic lymphocytic leukemia/small lymphocytic lymphoma, version 2.2019. J Natl Compr Canc Netw 2019; 17: 12–20.
60. Baliousis M, Rennoldson M, Snowden JA. Psychological interventions for distress in adults undergoing haematopoietic stem cell transplantation: a systematic review with meta-analysis. Psychooncol 2016; 25: 400–411.
61. Newell SA, Sanson-Fisher RW, Savolainen NJ. Systematic review of psychological therapies for cancer patients: overview and recommendations for future research. J Natl Cancer Inst 2002; 94: 558–584.
62. Ye M, Du K, Zhou J, Zhou Q, Shou M, Hu B, et al. A meta-analysis of the efficacy of cognitive behavior therapy on quality of life and psychological health of breast cancer survivors and patients. Psychooncol 2018; 27: 1695–1703.
63. World Health Organization. International Classification of Functioning, Disability, and Health (ICF). Geneva: WHO; 2001.
64. Rick O, Langer T. Oncological rehabilitation and cancer survivorship. Oncol Res Treat 2017; 40: 744.
65. Spence RR, Heesch KC, Brown WJ. Exercise and cancer rehabilitation: a systematic review. Cancer Treat Rev 2010; 36: 185–194.
66. Courneya KS, Friedenreich CM. Framework PEACE: an organizational model for examining physical exercise across the cancer experience. Ann Behav Med 2001; 23: 263–272.
67. Courneya KS, Friedenreich CM. Physical activity and cancer control. Semin Oncol Nurs 2007; 23: 242–252.

Appendix I. Search terms used

Theme 1. Lymphoma

lymphoma, lymph node tumour/malignancy/neoplasms, Hodgkin's lymphoma, classic HL, Reed Sternberg disease, Hodgkin's/non-Hodgkin's disease, non-Hodgkin's lymphoma, diffuse large B-cell lymphoma, T-cell lymphoblastic lymphoma, B-cell lymphoblastic lymphoma, anaplastic large cell lymphoma, Burkitt's lymphoma, germino-blastoma, reticulo-lymphosarcoma, lymphogranuloma, malignant lymphogranuloma, malignant lymphogranulomatosis, malignant granuloma, malignant granulomatosis, nodular paragranuloma, follicular lymphosarcoma, giant follicular lymphosarcoma, giant follicular blastoma, giant follicular lymphoblastoma, Brill-Symmers disease, lymphoproliferative disease/disorder, immunoproliferative disease/disorders

Theme 2. Systematic reviews

systematic review, systematic study, meta analysis, meta-analytical, meta-synthesis, integrative review, data synthesis, evidence-based review, comprehensive review, quantitative review, structured review

Theme 3. Rehabilitation

rehabilitation, ambulatory care, physical therapy modalities, physiotherapy, exercise therapy, cognitive therapy, psychotherapy, behavior/behaviour therapy, social work, counselling, occupational therapy, dietetics/nutrition, orthotics/brace/orthoses, acupuncture, patient care team, multidisciplinary/ integrated team, cold treatment/cooling, assistive technology device, hydro/pool therapy, electromagnetic therapy, nerve stimulation, vibration therapy, social participation/ support, vocational rehabilitation

Appendix II. EMBASE Search strategy (01 October 2020)

1. systematic* review*.tw.
2. meta-analysis as topic/
3. (meta-analytic* or meta-analysis or metanalysis or metaanalysis or meta analysis or meta-synthesis or metasynthesis or meta synthesis or meta-regression or metaregression or meta regression).tw.
4. (synthes* adj3 literature).tw.
5. (synthes* adj3 evidence).tw.
6. (integrative review or data synthesis).tw.
7. (research synthesis or narrative synthesis).tw.
8. (systematic study or systematic studies).tw.
9. (systematic comparison* or systematic overview*).tw.
10. ((evidence based or comprehensive or critical or quantitative or structured) adj review).tw.
11. (realist adj (review or synthesis)).tw.
12. exp Lymphoma/
13. *LYMPHOMA/
14. (lymphom* or linfom*).af.
15. exp HEMATOLOGIC NEOPLASMS/
16. (lympho* adj2 (neoplasm* or malign* or tumor* or tumour* or sarcom*)).af.
17. (lympha* adj2 (neoplasm* or malign* or tumor* or tumour* or sarcom*)).af.
18. (hemato* adj (malign* or neoplas*)).ab,ti.
19. (haemato* adj (malign* or neoplas*)).ab,ti.
20. exp nonhodgkin lymphoma/
21. (non-Hodgkin* or non Hodgkin* or nonHodgkin* or no Hodgkin* or nhl).ti,ab.
22. (lymph* adj2 sarcom*).af.
23. lymphosarcom*.af.
24. (reticulum adj2 sarcom*).af.
25. (lymphom* adj2 (cleaved* or noncleaved* or grad* or mixed-cell* or pleomorphic*)).af.21.
26. (lymphom* adj2 (cleaved* or noncleaved* or grad* or mixed-cell* or pleomorphic* or diffus*)).af.
27. (bcell* or b-cell*).af.
28. Hodgkin's lymphoma.ab,ti.
29. Hodgkin*.ab,ti.
30. Hodgkin's*.ab,ti.
31. Reed Sternberg.ti,ab.
32. Burkitt*.ab,ti.
33. germinoblastoma*.af.
34. reticulolymphosarcoma*.af.
35. (lympho* adj2 (granulom* or granulomat* or paragranulom*)).af.
36. (follicular adj2 (lymphosarcom* or blastom* or lumphoblast*)).af.
37. Brill-Symmers Disease.af.
38. (immunoproliferat* adj2 dis*).af.
39. exp rehabilitation/
40. exp ambulatory care/
41. exp physiotherapy/
42. exp home care/
43. exp hospital patient/
44. outpatient.ti,ab.
45. behav* ther*.ti,ab.
46. cognit* ther*.ti,ab.
47. social work*.ti,ab.
48. diet*.mp. or nutrit*.ti,ab. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]
49. counsel*.ti,ab.
50. (multidisciplinary or multi-disciplinary or integrated or interdisciplinary or inter-disciplinary).mp.
51. (rehabilitat* or physiotherap* or physical therap* or speech or occupation* or social work*).mp.
52. (cognitive therap* or behavio?r therap* or counsel?ing or nutrition* or diet* or food).mp.
53. (outpatient* or inpatient* or hospital* or home).mp.
54. or/39–53
55. or/1–11
56. or/12–38
57. (animal/ or nonhuman/) not human/
58. 55 not 57
59. 54 and 56
60. 58 and 59
61. limit 60 to (English language) and ((adult<18 to 64 years> or aged<65+ years>))

Appendix III. List of excluded systematic reviews

Author, year	Systematic review title	Reason for exclusion
Arden-Close et al., 2009	HRQoL in survivors of lymphoma: a systematic review and methodological critique	Not interventional study
Bergenthal et al., 2014	Aerobic physical exercise for adult patients with haematological malignancies	Published updated version; Knips et al. 2019
Beynon et al., 2018	What are the supportive and palliative care needs of patients with cutaneous T-cell lymphoma and their caregivers? A systematic review of the evidence	Not interventional study
Buffart et al., 2012	Physical and psychosocial benefits of yoga in cancer patients and survivors, a systematic review and meta-analysis of randomized controlled trials	Analysis performed specifically in breast cancer patients.
Caorale et al., 2013	Non-Hodgkin's lymphoma: unexpected cause of shoulder pain. A systematic review of the literature	Not interventional study
Daniels et al., 2013	Persisting fatigue in Hodgkin's lymphoma survivors: a systematic review	Not interventional study
de Boer et al., 2015	Interventions to enhance return-to-work for cancer patients	No data on PwL
Hunter et al., 2017	Systematic review of occupational therapy and adult cancer rehabilitation: part 1: impact of PA and symptom management interventions	No subgroup data on PwL
Hunter et al., 2017	Systematic review of occupational therapy and adult cancer rehabilitation: part 2: impact of multidisciplinary rehabilitation and psychosocial, sexuality, and return-to-work intervention	No subgroup data on PwL
Lin et al., 2018	Systematic literature review of HRQoL among aggressive non-Hodgkin's lymphoma survivors	Not interventional study, evaluated HRQoL only
Lamore et al., 2019	Return to work interventions for cancer survivors: a systematic review and a methodological critique	No data on PwL
Mishra et al., 2012	Exercise interventions on HRQoL for people with cancer during active treatment	Duplication of similar article published by the authors
Mewes et al., 2012	Effectiveness of multidimensional cancer survivor rehabilitation and cost-effectiveness of cancer rehabilitation in general: a systematic review	No subgroup data on PwL
Oerlemans et al., 2011	The impact of treatment, socio-demographic and clinical characteristics on HRQoL among Hodgkin's and non-Hodgkin's lymphoma survivors: a systematic review	Not interventional study, evaluated HRQoL only
Salakari et al., 2015	Effects of rehabilitation among patients with advances cancer: a systematic review	No subgroup data analysis on PwL
Salhofer et al., 2016	Meditation for adults with haematological malignancies	No data on PwL
Steins et al., 2012	Cardiopulmonary exercise testing in cancer rehabilitation: a systematic review.	No subgroup data on PwL
Zeng et al., 2014	Health benefits of qigong or tai chi for cancer patients: a systematic review and meta-analyses	Published updated version; Zeng et al. 2019

HRQoL: health-related quality of life, PA: physical activity, PwL: patients with lymphoma