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Complete List of Authors:	He, Yu; Shengjing Hospital of China Medical University, Department of Rehabilitation; Second Clinical College China Medical University, Department of Physical Medicine and Rehabilitation Han, Xiaochai; Shengjing Hospital of China Medical University, Department of Rehabilitation Zou, Wenchen; Shengjing Hospital of China Medical University, Department of Rehabilitation Liu, Xuemin; Second Clinical College China Medical University, Department of Physical Medicine and Rehabilitation Sun, Nianyi; Shanghai Fourth People's Hospital, Department of Rehabilitation Zhou, Fenghua; Shengjing Hospital of China Medical University, Department of Rehabilitation; Second Clinical College China Medical University, Department of Physical Medicine and Rehabilitation
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Telerehabilitation programs for cancer patients and survivors: a protocol for a systematic review

Yu He,[1, 2] Xiaochai Han,[1] Wenchen Zou,[1] Xuemin Liu,[2] Nianyi Sun,[2, 3] Fenghua Zhou [1, 2*]

[1]Department of Rehabilitation, Shengjing Hospital of China Medical University, Shenyang 110134, China.

[2]Department of Physical Medicine and Rehabilitation, The Second Clinical College, China Medical University, Shenyang 110122, China.

[3]Department of Rehabilitation, Shanghai Fourth People's Hospital, School of Medicine, Tongji University, Shanghai 200434, China.

* Corresponding author

Key words: telerehabilitation; telehealth; cancer; rehabilitation; systematic review; protocol

ABSTRACT

Introduction The global cancer burden is a major public health problem. Cancer rehabilitation is an essential component of survivorship care to prevent complications, decrease symptoms, improve functioning and quality of life (QOL). In addition to

preexisting challenges, the coronavirus disease 19 (COVID-19) pandemic has greatly impacted cancer rehabilitation programs and their delivery to patients. This comprehensive systematic review will assess the efficacy and safety of telerehabilitation on functional outcomes and QOL in cancer patients and survivors.

Methods and analysis This protocol was developed in line with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P). The following key electronic bibliographic databases will be searched from inception to April 2021: MEDLINE, EMBASE, CINAHL, CENTRAL, and PEDro. We will include randomised controlled trials (RCTs) published in English that examine the effects of telerehabilitaion programs on cancer patients and survivors. The concepts of 'intervention', 'participants' and 'study design' will be combined with the 'AND' operator in our search strategy. Two reviewers will independently complete the study screening, selection, data extraction, and quality rating. The PEDro scale will be used to assess the methodological quality of the included studies. A narrative or quantitative synthesis will be conducted based on the final data. The planned start and end dates for the study were 1 March 2021 and 1 May 2022.

Ethics and dissemination Ethical approval will not be required for this review. The results of this review will be disseminated in a peer-reviewed journal.

Registration details PROSPERO International prospective register of systematic review registration number: CRD42021243467.

Strengths and limitations of this study

- This protocol and the final review will be developed in accordance with the PRISMA and recommendations from the Cochrane handbook.
- Five key databases will be searched: MEDLINE, EMBASE, CINAHL, CENTRAL, and PEDro.
- Two reviewers will independently complete the study screening, selection, data extraction, and quality rating. Possible disagreement will be resolved by discussion or with consultation of a third author.
- The different type, site and stage of cancer and anticancer treatment may lead to a large degree of heterogeneity.

INTRODUCTION

Cancer ranks as the second leading cause of death and an important barrier to increasing life expectancy worldwide.[1, 2] The magnitude of cancer is rapidly growing globally, it is estimated that 19.3 million new cancer cases and almost 10.0 million cancer deaths occurred in 2020.[2] The global cancer burden is predicted to be 22.2 million new cases in 2030 and 28.4 million in 2040.[2, 3]

Cancer diagnosis, progression as well as aggressive treatment often make cancer patients and survivors suffer functional impairments and disabilities, both physically and psychologically, which may lead into a decreased health-related quality of life (QOL).[4] Therefore, cancer rehabilitation, an essential component of survivorship care, is needed to prevent complications, decrease symptoms, improve functioning and QOL, attain independence, and improve prognosis.[5-7] However, several challenges are present

in the movement to expand traditional face to face cancer rehabilitation, especially in developing countries.[7, 8] Rehabilitation programs are often long in duration and resource intensive, while access to cancer rehabilitation services is limited due to lack of specialized providers (most of whom clustered in tertiary care centers), travel burdens, financial burdens, time constraints, physical limitations, psychological and emotional burdens along with other hardships.[7-12] A possible solution to address these challenges is to provide telerehabilitation services. Additionally, the coronavirus disease 2019 (COVID-19) pandemic has broadly disrupted medical care and accelerated the growth of telerehabilitation services for cancer patients and survivors.[9, 13]

As a domain of telehealth, telerehabilitation makes use of a variety of information and communication technologies or commonly referred to as "telehealth" technologies, to deliver rehabilitation services to people over a distance, closing geographic, physical, and motivational gaps.[14, 15] Under this term, the services can include evaluation, assessment, monitoring, prevention, intervention, supervision, education, consultation, and coaching.[14, 15] The information and communication technologies used in telerehabilitation may integrate but are not limited to e-mail programs, text messaging, telephone follow-up, video and audio conferencing, wearable technologies, sensor technologies, mobile health applications, patient portals or platforms, virtual reality programs, therapeutic gaming technologies, and robotics.[14-17] There has been increasing interest in the use of this burgeoning field of telerehabilitation services as technologies continue to evolve.[15] Many examples in the current literature have explored the

acceptability, feasibility, efficacy and cost-effectiveness of telerehabilitation in neurological,[18-20] cardiopulmonary,[21-24] musculoskeletal,[25-27] and postoperative[28, 29] rehabilitation services, showing the promise in this field.

In recent years, there have been a proliferation of literature reporting telehealth-related oncology research, most of which focusing on feasibility and technical properties of technologies, diagnosis and treatment, user experience, or symptom monitoring.[30] Earlier systematic reviews regarding telehealth interventions in this territory involved the application research on current technology and services provided,[31, 32] acceptability studies,[33] studies focusing on self-management program,[34, 35] studies targeting a certain type of tumor.[36-39] In addition, clinical effectiveness measures were mostly psychosocial, symptomatic or QOL-related.[40-46]

However, in the field of telerehabilitation programs for cancer patients and survivors, there are only a small number of evidences and they are with diverse emphasis. Two studies have systematically reviewed evidence regarding the benefits of psycho-educational interventions using telecommunication technologies for cancer patients,[47, 48] with hopeful findings. A recent review explored and confirmed the usefulness of telehealth approach for occupational therapy practice in cancer survivors,[49] while the results of another two reviews focusing on remotely delivered physical activity were not that positive as expected.[50, 51] Additionally, the COVID-19 pandemic has expedited the transition of cancer rehabilitation programs to a remote-delivery format, which increases the urgency of understanding the efficacy and safety of such a model. Given the current status of the research in this field, this

comprehensive systematic review aims to study the efficacy and safety of telerehabilitation on functional outcomes and QOL in cancer patients and survivors, and we hope that this study will be helpful for future work.

METHODS

Study registration

This protocol has been registered on Prospero (registration number: CRD42021243467) and was developed according to the PRISMA-P.[52] The final systematic review will be conducted in line with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) statement,[53] and the guidance of the Cochrane Handbook for Systematic Reviews of Interventions.[54]

Inclusion criteria for study selection

Studies will be included in final review if they meet the following inclusion criteria:

Types of participants

Adult cancer patients or survivors (≥18 years of age) were considered irrespective of sex, race, site of cancer, type and stage of cancer, and type of anticancer treatment received.

Types of interventions

Participants in the experimental group received telerehabilitation programs. We will include interventions if they met with the following definition of telerehabilitation: "the delivery of rehabilitation services via information and communication technologies".[14, 15] Telehealth interventions for the purposes of patient education or communication, self-administered management without therapist supervision, remote symptoms or

physiological parameters monitoring alone (i.e. telemonitoring), without delivery of cancer rehabilitation, were excluded.

Types of comparator(s)/control

We will include studies that compare telerehabilitation programs with face to face rehabilitation treatments, such as center-based (outpatient) rehabilitation, inpatient rehabilitation or home visits, or a no rehabilitation control.

Types of outcome measures

Primary outcomes

1. Health-related QOL such as Functional Assessment of Cancer Therapy General (FACT-G) and related site-specific cancer module, The European Organization for Research and Treatment of Cancer - Core Quality of Life Questionnaire, version 3.0 (EORTC QLQ-C30) and related site-specific cancer module, Short Form (36) Health Survey (SF-36).

2. Physical function which were measured using 6-min walk, timed up-and-go, cardiopulmonary exercise tests (CPETs), moderate and vigorous physical activity (MVPA), strength, flexibility, endurance, and related validated tests and scales, etc.

Secondary outcomes

Cancer-related symptoms such as pain, fatigue, nausea/vomiting, dyspnoea, sleep disturbances, appetite loss, constipation, and diarrhoea. Anxiety and depression, anthropometrics, biomarker analysis, survivorship, adverse events, and compliance. These outcomes should be measured by validated tests and scales.

Types of studies

Randomised controlled trials (RCTs) reported in English and published as full text will be included. Studies will be excluded if they were quasi-randomized trials and other types of studies such as animal research, uncontrolled trials or case reports, conference proceedings/abstracts, dissertations, reported in books, or with no available data for analysis.

Search methods for the identification of studies

The following key electronic bibliographic databases will be searched from inception to April 2021: MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), and Physiotherapy Evidence Database (PEDro). The RCTs that evaluate the effectiveness of telerehabilitaion programs for cancer patients and survivors by setting comparators/controls mentioned above will be included. The strategy will search for 'telerehabilitation' AND 'neoplasms' AND 'RCTs'. For each of the 'intervention', 'participants' and 'study design' concept, we will combine synonyms and MeSH terms with the 'OR' operator. The proposed search strategy for MEDLINE via Ovid is listed in online supplemental material appendix 1. This strategy will be adapted for use in the other databases. In addition, we will check the reference lists of all the included trials and relevant systematic reviews to identify any potentially eligible studies.

Data collection

Study selection

The retrieved records will be imported into the bibliographic software Endnote (V.X9). Any duplicates will be identified and removed using Endnote. Two review authors (YH

and NS) will independently screen the titles, abstracts and keywords of the remaining articles with predefined criteria. After preliminary screening, we will retrieve the full-text of all potentially eligible articles and two review authors (YH and NS) will independently review them in detail, and the explicit reasons for exclusion of ineligible studies will be recorded. We will resolve any disagreement through discussion or consultation with a third author (FZ). The flow chart of the selection procedure is presented in figure 1.

Data extraction and management

Two review authors (YH and NS) will use a pre-designed data collection Excel form to extract the following data from the included studies independently:

1. General information: article title, journal, publication year, first author, corresponding author, country of study, aim of study, trial registration, study funding source, and possible conflicts of interest.

2. Study characteristics: study design, method of randomization, method of blinding, allocation concealment, completeness of outcome data.

3. Participants: sample size, baseline participant characteristics, site of cancer, type and stage of cancer, type of anticancer treatment, comorbidities.

4. Interventions: type, frequency, intensity and duration for telerehabilitation and comparators.

5. Outcomes: outcome measurements, time points reported, follow-up duration, adverse events.

Methodological quality assessment

Two review authors (YH and NS) will independently assess the methodological quality of each selected study using the Physiotherapy Evidence Database (PEDro) scale.[55] Possible disagreement will be resolved by discussion or with consultation of a third author (FZ). The PEDro scale is considered to be a valid and reliable measure of the methodological quality of RCTs in physiotherapy.[55, 56] This scale consists of 11 criteria, and considering that the 1st item is not utilized to calculate the score, the scale has a possible range of 0 to 10, with higher scores suggesting higher quality. On this scale, the cut-off for high quality of methodology is a score $\geqslant$6 points.[55]

Data analysis and synthesis

The Cochrane Review Manager Version 5 software will be used for meta-analysis. In our study, a meta-analysis concerning the effect of telerehabilitation programs will be conducted if at least two studies used the homogeneous outcome measure or measured similar constructs.

The outcome indicators involved in this study are mostly continuous data, standardized mean differences (SMD) as well as 95% confidence interval (CI) will be computed.

The chi-squared test and I^2 statistic will be used to assess heterogeneity across studies.[54, 57] If $p>0.1$, and $I^2<50\%$, a fixed-effect model will be adopted for data combination; if $p>0.1$, and $I^2 \geqslant 50\%$, a random-effect model will be adopted for data combination, and obvious heterogeneity is considered between the studies; if $p \leqslant 0.1$, statistical significance is considered in this case, and a subgroup analysis or a narrative description will be performed.[54]

When sufficient data are available, prespecified subgroups will be conducted based on gender; comorbid condition; the type, frequency, intensity and duration of telerehabilitation programs; the site, type and stage of cancer, to explore factors that might be related to the strength of the effect. In addition, if data permitted, sensitivity analyses will be performed to examine the robustness and reliability of the results by omitting specific trials from the overall analysis.

If more than 10 trials are included in a result of a meta-analysis, we will construct a funnel plot to explore the potential publication bias.

The overall quality of each summarised evidence will be evaluated using Grading of Recommendations Assessment, Development and Evaluation (GRADE) system at four levels: high, moderate, low or very low.[58] Two review authors (YH and NS) will independently assess the quality of the evidence using GRADEpro software (https://gradepro.org), and possible discrepancies will be resolved through discussion or consultation with a third author (FZ).

Patient and public involvement

This protocol for a systematic review does not directly involve patients or the general public. The data will be collected from published articles retrieved from the main databases and manual searches.

Ethics and dissemination

Ethical approval will not be required for the performance of this review protocol. The results of the final review will be disseminated in a peer-reviewed journal.

DISCUSSION

The COVID-19 pandemic has prompted calls for accelerated introduction of alternative models of cancer rehabilitation service delivery that include home-based telerehabilitation.[9, 13] This review will systematically and comprehensively assess the efficacy and safety of telerehabilitation programs on functional outcomes and QOL in cancer patients and survivors. This protocol provides with the current status of the research in this field, and we hope that the final review will be helpful to support decision-making related to health policies and rehabilitation programs.

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Contributors YH, NS and FZ contributed to the conception and design of the study. NS registered the protocol in the PROSPERO database. YH drafted the protocol. FZ revised the protocol critically for important intellectual content. XH, WZ and XL designed the search strategy. YH, XH, WZ, XL, NS and FZ participated in the design of data acquisition, analysis and interpretation. All authors have read and approved the final protocol. FZ is the guarantor of this protocol.

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Competing interests: We declare that there is no conflict of interest regarding the publication of this protocol.

Patient consent for publication Not required.

Ethical approval: Ethical approval will not be required for the performance of this protocol for a systematic review.

Data sharing No additional data are available.

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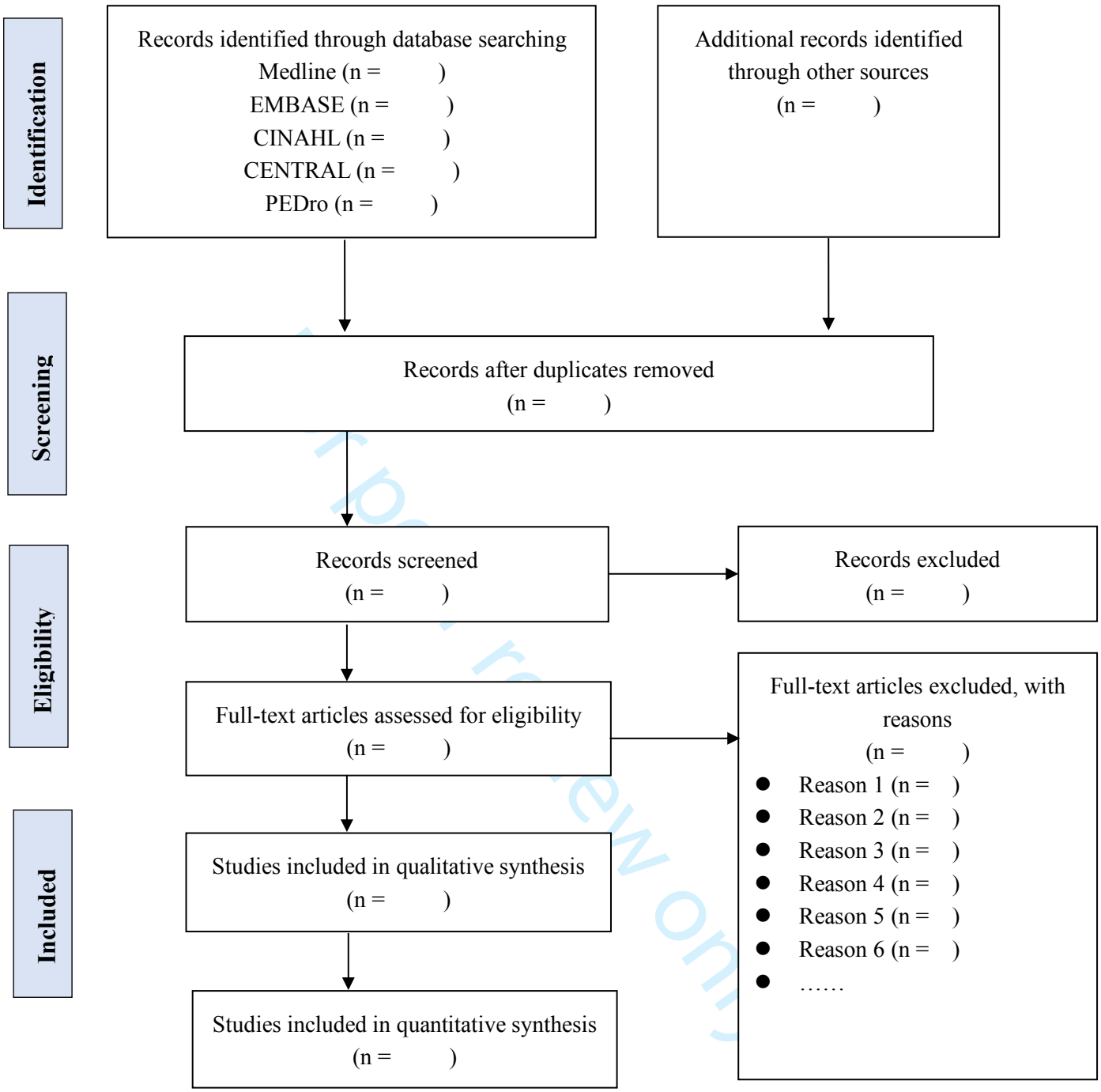
FIGURE LEGENDS

Figure 1. Flowchart of the study selection procedure



Appendix 1

Search Strategy Example: MEDLINE (via Ovid) search

Terms specific to Telerehabilitation

#1 exp Telemedicine/

#2 exp Telerehabilitation/

#3 (ehealth or e-health or mhealth or m-health or telehealth or tele-health or mobile health or telemetry or telerehab* or tele-rehab* or remote rehabilitation* or virtual rehabilitation* or telehomecare or tele-homecare or telecoaching or tele-coaching or telecommunication* or tele-communication* or teleconference* or tele-conference* or videoconferenc* or video-conferenc* or teleconsultation* or tele-consultation* or videoconsultation or video-consultation or telecare or tele-care).ab,ti.

#4 (telephone or smartphone or phone or mobile or video or audio or radio or internet or web* or network or on-line or computer* or sensor* or wearable or modem or email or message or media or tablet or handheld device or personal digital assistant or portable data terminal or podcast or application or App or Apps or software or virtual reality* or game*).ab,ti.

#5 exp Rehabilitation/

#6 #1 or #2 or #3 or (#4 and #5)

Terms specific to cancer

#7 exp Neoplasms/

#8 exp Carcinoma/

#9 (cancer* or tumor* or tumour* or neoplas* or malignanc* or onco* or carcinoma*).ab,ti.

#10 #7 or #8 or #9

Terms for identifying randomized controlled trials

#11 randomized controlled trial.pt.

#12 controlled clinical trial.pt.

#13 (random* or placebo or sham or trial or groups). ab,ti.

#14 #11 or #12 or #13

Combination of terms to identify randomized controlled trials of telerahabilitation programs for cancer patients and survivors

#6 and #10 and #14

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review Main Document Page 1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number Main Document Page 2, 6
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author Main Document Page 1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review Main Document Page 12
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments NA
Support:		
Sources	5a	Indicate sources of financial or other support for the review Main Document Page 12
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known Main Document Page 3-5
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) Main Document Page 6-8
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review Main Document Page 6-8
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage Main Document Page 8-9
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated Main Document Page 8
Study records:		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review Main Document Page 9

Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis) Main Document Page 9
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators Main Document Page 9
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications Main Document Page 9
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale Main Document Page 9
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis Main Document Page 10
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised Main Document Page 10-11
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ) Main Document Page 10-11
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) Main Document Page 10-11
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned Main Document Page 10-11
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies) Main Document Page10-11
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE) Main Document Page 11

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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Telerehabilitation programmes for cancer patients and survivors: A protocol for a systematic review

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Telerehabilitation programmes for cancer patients and survivors: A protocol for a systematic review

Yu He,[1, 2] Xiaochai Han,[1] Wenchen Zou,[1] Xuemin Liu,[2] Nianyi Sun,[3, 2] Fenghua Zhou [1, 2*]

[1]Department of Rehabilitation, Shengjing Hospital of China Medical University, Shenyang 110134, China.

[2]Department of Physical Medicine and Rehabilitation, The Second Clinical College, China Medical University, Shenyang 110122, China.

[3]Department of Rehabilitation, Shanghai Fourth People's Hospital, School of Medicine, Tongji University, Shanghai 200434, China.

* Corresponding author

Dr. Fenghua Zhou, Department of Rehabilitation, Shengjing Hospital of China Medical University, No.16 Puhe Street, Shenyang 110134, Liaoning Province, People's Republic of China. All correspondence should be addressed to Dr. Zhou at zhoufenghua77@163.com

ABSTRACT

Introduction: The global cancer burden is a major public health problem. Cancer rehabilitation is an essential component of survivorship care for preventing

complications, decreasing symptoms, and improving functional quality of life (QOL). In addition to preexisting challenges, the coronavirus disease 2019 (COVID-19) pandemic has greatly affected cancer rehabilitation programmes and their delivery to patients. This comprehensive systematic review will assess the efficacy and safety of telerehabilitation on functional outcomes and QOL in cancer patients and survivors.

Methods and analysis: This study was conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols. The following key electronic bibliographic databases will be searched from their inception to April 2021: MEDLINE, Embase, Cumulative Index to Nursing and Allied Health Literature, Cochrane Central Register of Controlled Trials, and Physiotherapy Evidence Database (PEDro). We will include randomised controlled trials (RCTs) published in English that examine the effects of telerehabilitation programmes on cancer patients and survivors. The terms 'telerehabilitation', 'neoplasm', 'RCT', and their analogous terms will be used in our search strategy. Two reviewers will independently complete the study screening, selection, data extraction, and quality rating. The PEDro scale will be used to assess the methodological quality of the included studies. Narrative or quantitative synthesis will be conducted on the basis of the final data. The planned start and end dates for the study are 1 March 2021 and 1 May 2022, respectively.

Ethics and dissemination: Ethical approval will not be required for this review, and the results will be disseminated in peer-reviewed journals.

Registration details: PROSPERO (international prospective register of systematic review) registration number CRD42021243467.

Strengths and limitations of this study

- This protocol and the final review will be developed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis and recommendations from the *Cochrane Handbook for Systematic Reviews of Interventions*.
- Five key databases will be searched: MEDLINE, Embase, Cumulative Index to Nursing and Allied Health Literature, Cochrane Central Register of Controlled Trials, and Physiotherapy Evidence Database.
- Two reviewers will independently complete the study screening, selection, data extraction, and quality rating. Possible disagreements will be resolved via discussions or consultations with a third author.
- Different types, sites, and stages of cancer and anticancer treatments may lead to a large degree of heterogeneity.

INTRODUCTION

Cancer ranks as the second-leading cause of death and is an important barrier to increasing life expectancy worldwide.[1, 2] The magnitude of cancer is rapidly growing globally, and there were an estimated 19.3 million new cancer cases and 10.0 million cancer deaths worldwide in 2020.[2] The global cancer burden is predicted to be 22.2 and 28.4 million new cases in 2030 and 2040, respectively.[2, 3]

Cancer diagnosis, progression, and aggressive treatment often cause functional

impairment and disability in both cancer patients and survivors. Physical or psychological injury may lead to decreased health-related quality of life (QOL) in this population.[4] Cancer rehabilitation, which is an essential component of survivorship care, is needed to prevent complications, decrease symptoms, improve functioning and QOL, attain independence, and improve prognosis.[5-7] However, several challenges hinder the expansion of traditional face-to-face cancer rehabilitation, particularly in developing countries.[7, 8] Rehabilitation programmes are often long in duration and resource intensive, and access to cancer rehabilitation services is limited because of the lack of specialised providers (most of whom are clustered in tertiary care centres), as well as travel burden, financial burden, time constraints, physical limitations, psychological and emotional burden, and other hardships.[7-12] A possible solution to address these challenges is to provide telerehabilitation services.

As a domain of telehealth, telerehabilitation uses of a variety of information and communication technologies (ICTs) to deliver rehabilitation services to people over long distances, thus closing geographic, physical, and motivational gaps.[13, 14] Telerehabilitation services can include evaluation, assessment, monitoring, prevention, intervention, supervision, education, consultation, and coaching.[13, 14] The ICT used in telerehabilitation may integrate but are not limited to email programmes, text messaging, telephone follow-up, video and audio conferencing, wearable technologies, sensor technologies, mobile health applications, patient portals or platforms, virtual reality programmes, therapeutic gaming technologies, and robotics.[13-16] There has been increasing interest in the use of this burgeoning field of telerehabilitation services as

technologies continue to evolve.[14] Many examples in the current literature have explored the acceptability, feasibility, efficacy, and cost-effectiveness of telerehabilitation in neurological,[17-19] cardiopulmonary,[20-23] musculoskeletal,[24-26] and postoperative[27, 28] rehabilitation services, thus showing that this field is promising.

In recent years, there have been a proliferation of studies on telehealth-related oncology, most of which focus on the feasibility and technical properties of technologies, diagnosis and treatment approaches, user experience, or symptom monitoring.[29] Earlier systematic reviews regarding telehealth interventions in this territory involved application research on current technology and services,[30, 31] acceptability studies,[32] studies on self-management programmes,[33, 34] and studies on certain types of tumours.[35-38] In addition, clinical effectiveness measures were mostly psychosocial, symptomatic, or QOL related.[39-45]

However, only a small amount of evidence exists on the effectiveness of telerehabilitation programmes for cancer patients and survivors, and most pieces of evidence have diverse emphasis. Two studies systematically reviewed evidence on the benefits of psychoeducational interventions that use telecommunication technologies for cancer patients[46, 47] and showed promising findings. A recent review explored and confirmed the usefulness of the telehealth approach for occupational therapy practice in cancer survivors,[48] but two other studies on remotely delivered physical activity showed results that were not as positive.[49, 50] Additionally, the coronavirus disease 2019 (COVID-19) pandemic has broadly disrupted medical care and expedited the transition of cancer rehabilitation programmes to a remote-delivery format,[51] thus increasing the

urgency of understanding the efficacy and safety of such a model. Given the current status of research in this field, this comprehensive systematic review aims to study the efficacy and safety of telerehabilitation on functional outcomes and QOL in cancer patients and survivors to inform future models of care for cancer rehabilitation.

METHODS

Study registration

The planned start and end dates for the study are 1 March 2021 and 1 May 2022, respectively. This protocol has been registered on PROSPERO (registration number: CRD42021243467) and was developed according to the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) Protocols.[52] The final systematic review will be conducted in line with the PRISMA statement[53] and the guidance of the *Cochrane Handbook for Systematic Reviews of Interventions*.[54]

Inclusion criteria for study selection

Studies will be included in the final review if they meet the inclusion criteria defined by PICO elements (P = participant, I = intervention, C = comparison, and O = outcomes) [55] and the types of studies. Table 1 shows a summary of the inclusion criteria.

Types of participants

Adult cancer patients or survivors (≥18 years of age) will be considered irrespective of sex, race, site of cancer, type and stage of cancer, and type of anticancer treatment received. Cancer survivors refer to those who have been diagnosed with cancer, have successfully completed curative treatments, or have transitioned to maintenance or prophylactic therapy.[56, 57]

Types of interventions

Participants in the experimental group will receive telerehabilitation programmes. In the context of this study, telerehabilitation is considered as any rehabilitation programme delivered by health care professionals (physical, occupational, or speech therapists; exercise trainers; neuropsychologists; etc.) via ICT to cancer patients and survivors. Telerehabilitation can be delivered to a satellite healthcare centre or directly into the patient's home and can be performed in a group or individually. Telerehabilitation programmes that use 'store and forward'/asynchronous or real-time/synchronous interaction will be included. Telehealth interventions for the purposes of patient education or communication, self-administered management without the supervision of healthcare professionals, remote symptoms, or monitoring of physiological parameters alone (i.e., telemonitoring) will be excluded.

Types of comparator(s)/control

We will include studies that compare telerehabilitation programmes with face-to-face rehabilitation treatments, such as centre-based (outpatient) rehabilitation, inpatient rehabilitation, home visits, or no rehabilitation control.

Types of outcome measures

Primary outcomes

1. Health-related QOL was assessed using validated measures. Examples include the Functional Assessment of Cancer Therapy General and related site-specific cancer module, The European Organization for Research and Treatment of Cancer Core Quality of Life Questionnaire version 3.0, and related site-specific cancer module,

Short Form (36) Health Survey, Patient-Reported Outcomes Measurement Information System (PROMIS) 29, and PROMIS Cancer Function 3D Profile.

2. Physical function was assessed using the validated measures, e.g., the timed up-and-go test and six-minute walk test for testing physical performance; the cardiopulmonary exercise test and moderate-to-vigorous physical activity test for testing functional capacity; and impairment measures for testing range of motion, muscle strength, and flexibility.

Secondary outcomes

Cancer-related symptoms (pain, fatigue, nausea/vomiting, dyspnoea, sleep disturbances, appetite loss, constipation, and diarrhoea), anthropometrics, psychometric properties, biomarker analysis, survivorship, adverse events, patient satisfaction, and compliance. These outcomes should be assessed using validated tests and scales.

Types of studies

Randomised controlled trials (RCTs) reported in English and published as full text will be included. Studies will be excluded if they are quasirandomised trials, animal research, uncontrolled trials, case reports, conference proceedings, abstracts, dissertations, or reports in books or have no available data for analysis.

Search methods for the identification of studies

The following key electronic bibliographic databases will be searched from inception to April 2021: MEDLINE, Embase, Cumulative Index to Nursing and Allied Health Literature, Cochrane Central Register of Controlled Trials, and the Physiotherapy Evidence Database (PEDro). RCTs that evaluate the effectiveness of telerehabilitation

programmes for cancer patients and survivors by setting the comparators/controls mentioned above will be included. The strategy will search for 'telerehabilitation' AND 'neoplasms' AND 'RCTs'. For the 'intervention', 'participants', and 'study design' concept, we will combine synonyms and MeSH terms with the 'OR' operator. Online Supplemental Material Appendix 1 shows the proposed search strategy for MEDLINE via Ovid. This strategy will be adapted for use with other databases. In addition, we will check the reference lists of all included trials and relevant systematic reviews to identify potentially eligible studies.

Data collection

Study selection

The retrieved records will be imported into the bibliographic software EndNote X9. Any duplicates will be identified and removed using EndNote. Two review authors (YH and NS) will independently screen the titles, abstracts, and keywords of the remaining articles by using predefined criteria. After preliminary screening, we will retrieve the full text of all potentially eligible articles, and two review authors (YH and NS) will independently review them in detail. The explicit reasons for the exclusion of ineligible studies will be recorded. Any disagreement will be resolved via discussions or consultations with a third author (FZ). Figure 1 shows a flowchart of the selection procedure.

Data extraction and management

Two review authors (YH and NS) will use a predesigned data collection Excel form to independently extract the following data from the included studies:

1. General information: article title, journal, publication year, first author, corresponding author, country of study, aim of study, trial registration, study funding source, and possible conflicts of interest

2. Study characteristics: study design, randomisation method, blinding method, allocation concealment, and completeness of outcome data

3. Participants: sample size, baseline participant characteristics, cancer site, type and stage of cancer, type of anticancer treatment, and comorbidities

4. Interventions: type, frequency, intensity and duration for telerehabilitation, and comparators

5. Outcomes: outcome measurements, time points reported, follow-up duration, and adverse events

Methodological quality assessment

Two review authors (YH and NS) will independently assess the methodological quality of each selected study by using the PEDro scale.[58] Possible disagreements will be resolved via discussions or consultations with a third author (FZ). The PEDro scale is considered a valid and reliable measure of the methodological quality of RCTs in physiotherapy and has moderate interrater reliability. [58, 59] This scale consists of 11 criteria. Considering that the 1st item is not utilised in calculating the score, the scale has a possible range of 0–10, with higher scores indicating a higher quality. On this scale, the cutoff for high-quality methodology is ≥6 points.[58]

Data analysis and synthesis

Cochrane Review Manager version 5 will be used for the meta-analysis. In our study,

a meta-analysis concerning the effect of telerehabilitation programmes will be conducted if at least two studies used homogeneous outcome measures or measured similar constructs.

The summary results are computed in different ways according to the data type. For continuous data, standardised mean differences as and 95% confidence intervals (CI) will be computed. For dichotomous data, odds ratios and 95% CIs will be computed.

The chi-squared test and I^2 statistic will be used to assess heterogeneity across studies.[54, 60] If $p > 0.1$ and $I^2 < 50\%$, a fixed-effect model will be adopted for data combination. If $p > 0.1$ and $I^2 \geq 50\%$, a random-effect model will be adopted for data combination, and obvious heterogeneity will be considered between the studies. If $p \leq 0.1$, statistical significance will be considered, and a subgroup analysis or a narrative description will be performed.[54] The narrative description will synthetise findings from multiple studies and primarily adopt text and words to summarise and explain the findings from the included studies.[54, 61]

When sufficient data are available, prespecified subgroups will be established on the basis of gender; comorbid condition; type, frequency, intensity, and duration of telerehabilitation programmes; and site, type, and stage of cancer to explore the factors that might be related to the strength of the effect. If the data permit, sensitivity analyses will be performed to examine the robustness and reliability of the results by omitting specific trials from the overall analysis.

If more than 10 trials are included in the meta-analysis, we will construct a funnel

plot to explore the potential publication bias.

The overall quality of each summarised evidence will be evaluated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system at four levels: high, moderate, low, or very low.[62] Two review authors (YH and NS) will independently assess the quality of the evidence by using GRADEpro software (https://gradepro.org), and possible discrepancies will be resolved via discussions or consultations with a third author (FZ).

Patient and public involvement

This systematic review protocol does not directly involve the patients or general public. Data will be collected from published articles retrieved from the main databases and manually searched.

Ethics and dissemination

Ethical approval will not be required for this review protocol. The results of the final review will be disseminated in peer-reviewed journals.

DISCUSSION

The COVID-19 pandemic has prompted calls for the accelerated introduction of alternative models of cancer rehabilitation service delivery, including home-based telerehabilitation.[9, 51] In the realm of cancer rehabilitation, this new care model has great potential to facilitate access to services; allow the continuity of rehabilitation; improve care equity; and counteract geographic, demographic, and socioeconomic barriers. However, this is likely to reveal new disparities between healthcare professionals and patients. For example, the reliance on technology is central to the delivery of

telerehabilitation, and creative ways to overcome this obstacle maybe needed.[9] In addition, the manner in which to conduct an adapted virtual physical examination also needs particular attention.[9, 63]

The final review will systematically and comprehensively assess the efficacy and safety of telerehabilitation programmes on functional outcomes and QOL in patients with cancer and survivors. This protocol provides the current status of research in this field, and we hope that the final review will be helpful in supporting decision-making processes related to health policies and rehabilitation programmes.

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Contributors YH, NS and FZ contributed to the conception and design of the study. NS registered the protocol in the PROSPERO database. YH drafted the protocol. FZ revised the protocol critically for important intellectual content. XH, WZ and XL designed the search strategy. YH, XH, WZ, XL, NS and FZ participated in the design of data acquisition, analysis and interpretation. All authors have read and approved the final protocol. FZ is the guarantor of this protocol.

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Competing interests: We declare that there is no conflict of interest regarding the publication of this protocol.

Patient consent for publication Not required.

Ethical approval: Ethical approval will not be required for the performance of this

protocol for a systematic review.

Data sharing No additional data are available.

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FIGURE LEGENDS

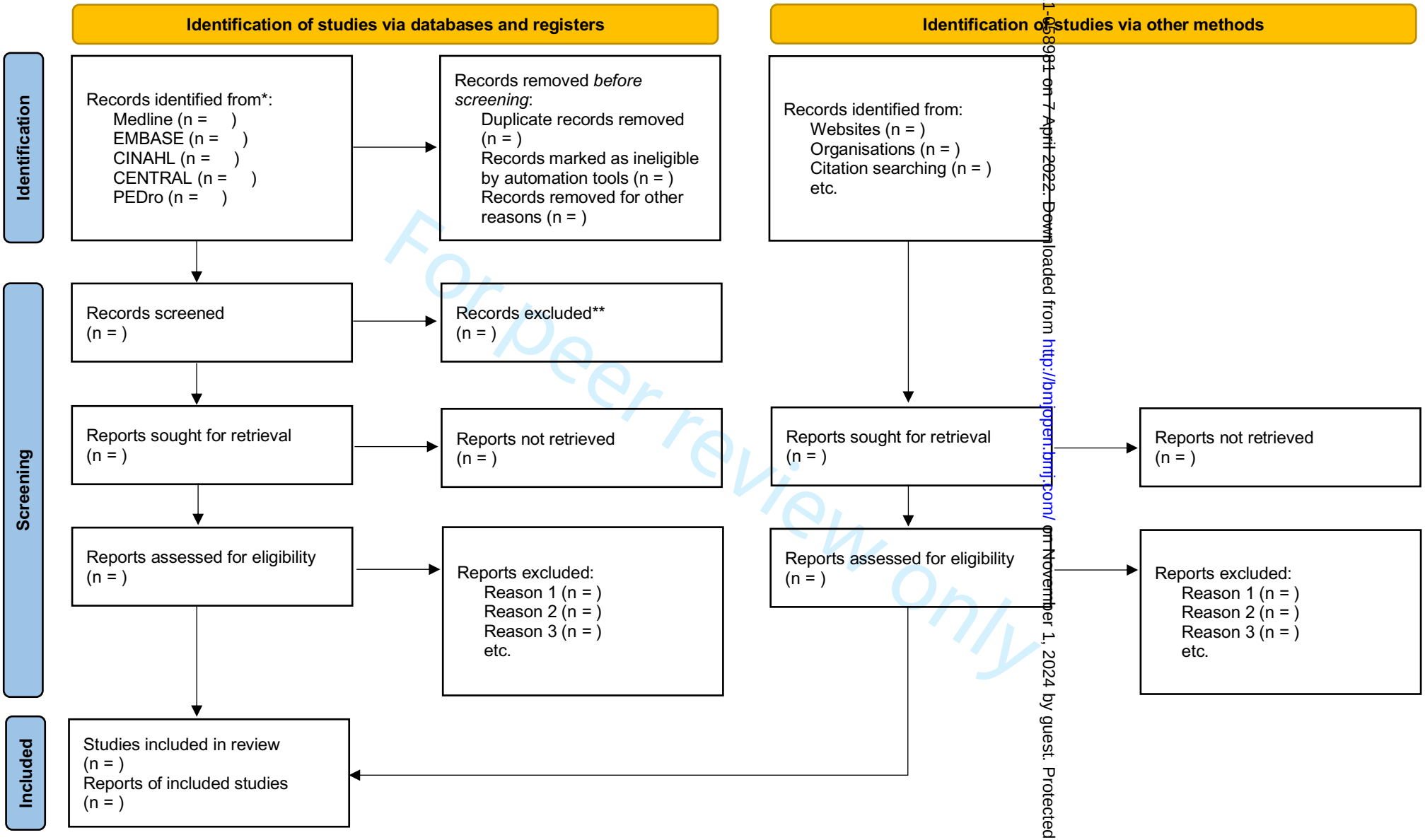
Figure 1. Flowchart of the study selection procedure

TABLE LEGENDS

Table 1. Eligibility criteria

Table 1. Eligibility criteria

PICOS	
Participant	Adult cancer patients or survivors.
Intervention	Telerehabilitation (e.g. remotely guided on-line or virtual reality motor training, occupational exercises at home utilizing sensor technologies.)
Comparison	Face to face rehabilitation, usual care.
Outcome	Primary outcomes: Health-related QOL, physical function Secondary outcomes: Cancer-related symptoms, anthropometrics, psychometric properties, biomarker analysis, survivorship, adverse events, patient satisfaction, and compliance, etc.
Study design	RCT reported in English.



Appendix 1

Search Strategy Example: MEDLINE (via Ovid) search

Terms specific to Telerehabilitation

#1 exp Telemedicine/

#2 exp Telerehabilitation/

#3 (ehealth or e-health or mhealth or m-health or telehealth or tele-health or mobile health or telemetry or telerehab* or tele-rehab* or remote rehabilitation* or virtual rehabilitation* or telehomecare or tele-homecare or telecoaching or tele-coaching or telecommunication* or tele-communication* or teleconference* or tele-conference* or videoconferenc* or video-conferenc* or teleconsultation* or tele-consultation* or videoconsultation or video-consultation or telecare or tele-care).ab,ti.

#4 (telephone or smartphone or phone or mobile or video or audio or radio or internet or web* or network or on-line or computer* or sensor* or wearable or modem or email or message or media or tablet or handheld device or personal digital assistant or portable data terminal or podcast or application or App or Apps or software or virtual reality* or game*).ab,ti.

#5 exp Rehabilitation/

#6 #1 or #2 or #3 or (#4 and #5)

Terms specific to cancer

#7 exp Neoplasms/

#8 exp Carcinoma/

#9 (cancer* or tumor* or tumour* or neoplas* or malignanc* or onco* or carcinoma*).ab,ti.

#10 #7 or #8 or #9

Terms for identifying randomized controlled trials

#11 randomized controlled trial.pt.

#12 controlled clinical trial.pt.

#13 (random* or placebo or sham or trial or groups). ab,ti.

#14 #11 or #12 or #13

Combination of terms to identify randomized controlled trials of telerahabilitation programs for cancer patients and survivors

#6 and #10 and #14

PRISMA-P (Preferred Reporting Items for Systematic review and Meta-Analysis Protocols) 2015 checklist: recommended items to address in a systematic review protocol*

Section and topic	Item No	Checklist item
ADMINISTRATIVE INFORMATION		
Title:		
Identification	1a	Identify the report as a protocol of a systematic review Main Document Page 1
Update	1b	If the protocol is for an update of a previous systematic review, identify as such
Registration	2	If registered, provide the name of the registry (such as PROSPERO) and registration number Main Document Page 2, 6
Authors:		
Contact	3a	Provide name, institutional affiliation, e-mail address of all protocol authors; provide physical mailing address of corresponding author Main Document Page 1
Contributions	3b	Describe contributions of protocol authors and identify the guarantor of the review Main Document Page 13
Amendments	4	If the protocol represents an amendment of a previously completed or published protocol, identify as such and list changes; otherwise, state plan for documenting important protocol amendments NA
Support:		
Sources	5a	Indicate sources of financial or other support for the review Main Document Page 13
Sponsor	5b	Provide name for the review funder and/or sponsor
Role of sponsor or funder	5c	Describe roles of funder(s), sponsor(s), and/or institution(s), if any, in developing the protocol
INTRODUCTION		
Rationale	6	Describe the rationale for the review in the context of what is already known Main Document Page 3-6
Objectives	7	Provide an explicit statement of the question(s) the review will address with reference to participants, interventions, comparators, and outcomes (PICO) Main Document Page 6-8
METHODS		
Eligibility criteria	8	Specify the study characteristics (such as PICO, study design, setting, time frame) and report characteristics (such as years considered, language, publication status) to be used as criteria for eligibility for the review Main Document Page 6-8
Information sources	9	Describe all intended information sources (such as electronic databases, contact with study authors, trial registers or other grey literature sources) with planned dates of coverage Main Document Page 8-9
Search strategy	10	Present draft of search strategy to be used for at least one electronic database, including planned limits, such that it could be repeated Main Document Page 8-9
Study records:		
Data management	11a	Describe the mechanism(s) that will be used to manage records and data throughout the review Main Document Page 9-10

Selection process	11b	State the process that will be used for selecting studies (such as two independent reviewers) through each phase of the review (that is, screening, eligibility and inclusion in meta-analysis) Main Document Page 9-10
Data collection process	11c	Describe planned method of extracting data from reports (such as piloting forms, done independently, in duplicate), any processes for obtaining and confirming data from investigators Main Document Page 9-10
Data items	12	List and define all variables for which data will be sought (such as PICO items, funding sources), any pre-planned data assumptions and simplifications Main Document Page 9-10
Outcomes and prioritization	13	List and define all outcomes for which data will be sought, including prioritization of main and additional outcomes, with rationale Main Document Page 9-10
Risk of bias in individual studies	14	Describe anticipated methods for assessing risk of bias of individual studies, including whether this will be done at the outcome or study level, or both; state how this information will be used in data synthesis Main Document Page 10
Data synthesis	15a	Describe criteria under which study data will be quantitatively synthesised Main Document Page 10-12
	15b	If data are appropriate for quantitative synthesis, describe planned summary measures, methods of handling data and methods of combining data from studies, including any planned exploration of consistency (such as I^2, Kendall's τ) Main Document Page 10-12
	15c	Describe any proposed additional analyses (such as sensitivity or subgroup analyses, meta-regression) Main Document Page 10-12
	15d	If quantitative synthesis is not appropriate, describe the type of summary planned Main Document Page 10-12
Meta-bias(es)	16	Specify any planned assessment of meta-bias(es) (such as publication bias across studies, selective reporting within studies) Main Document Page10-12
Confidence in cumulative evidence	17	Describe how the strength of the body of evidence will be assessed (such as GRADE) Main Document Page 12

*** It is strongly recommended that this checklist be read in conjunction with the PRISMA-P Explanation and Elaboration (cite when available) for important clarification on the items. Amendments to a review protocol should be tracked and dated. The copyright for PRISMA-P (including checklist) is held by the PRISMA-P Group and is distributed under a Creative Commons Attribution Licence 4.0.**

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