The structure of research questions in randomized-controlled trials in rehabilitation field: a methodological study

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Abstract

Objective: The aim of this study is to assess whether and how PICO format is described to frame research questions in randomized controlled trials (RCTs) looking at effectiveness of rehabilitation interventions.

Design: A methodological study was conducted. RCTs in the rehabilitation field, published between July 1st, 2019 and December 31st, 2019 were included. The framing of the primary research question (RQ) from each trial was evaluated.

Results: Ninety-seven RCTs were included in the analysis. The most frequent framing of the primary RQ was as an "objective" statement (55%) and in 33% of the articles this was stated as an "objective" together with a "hypothesis" description. All PICO elements were present in 55% of RQ, but only 49% have used the statement suggested by Cochrane. The results showed that the most frequent framing of primary RQ was "objective" using all PICO elements, but few articles followed the statement suggested by Cochrane to describe them.

Conclusion: our findings suggest that a specific item about the "*research question*" and the rationale that drove to the proposed design following the form suggested by Cochrane is included in the RCTRACK checklist.

Keywords: rehabilitation, framing research question, PICO format

What is known

- A structured research question could be associated with better methodological quality;

- A structured RQ could guide the development of a research study to evaluates the effectiveness/efficacy of an intervention

What is new

- Currently the primary research question of published RCTs is most often framed as an "objective";

- Currently few published RCTs describe the PICO elements as recommended by Cochrane;

- The findings suggest that a specific item about the "*research question*" and the rationale that drove to the proposed design following the form suggested by Cochrane is included in the RCTRACK checklist

Introduction

Randomized controlled clinical trials (RCTs) are considered the gold standard study design to evaluate the effectiveness/efficacy of interventions in biomedical research[1]. The choice of an appropriate study design is informed by a clear research question (RQ)[2–5]. The RQ represents the starting point for research studies to evaluate the effectiveness/efficacy of interventions because it guides the definition of the population, interventions and outcomes; consequently, this influences the development of the right study design to answer the question of interest.

Clinical epidemiologists have proposed the use of a structured RQ to guide the development of a research study that evaluates the effectiveness/efficacy of interventions[6]. The RQ should contain the following four elements: Population, Intervention, Comparator and Outcomes. These elements are commonly referred to by the acronym PICOs. A well-structured RQ increases the likelihood of finding a solution to the problem, informs selection of the study design, guides analysis decisions and the interpretation of results[2]. The explicit statement of the four PICOs elements prompts the researcher to think about the design to use and to consider the balance between RQ and the feasibility to answer it. Some studies show that a structured research question could be associated with better methodological quality, but more research is needed to confirm this finding[2–5].

In rehabilitation research, a scoping review by Arienti et al.,[7] reported a lack of clarity in the RQs and that RCTs in the rehabilitation field rarely use the PICOs format to define key terms. Several authors have argued that RCTs in rehabilitation frequently use inadequate designs for answering RQs related to rehabilitation and this could depend on how the RQ is formulated. The detailed

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specification of the RQ requires consideration of several key components which can be encapsulated by the 'PICO' element that practicing clinicians, healthcare professionals, researchers, policy makers, and patients deal with[8]. The accuracy of RQ framing is one of the main methodological issues described in rehabilitation research.

In recognition of this problem, Cochrane Rehabilitation highlighted the need to develop a specific checklist to guide the design, conducting, and reporting of trials in the rehabilitation field[9]. During the second Cochrane Rehabilitation Methodological Meeting held in Kobe, Japan, in 2019, the RCT Rehabilitation Checklist (RCTRACK) project was launched to produce a reporting guideline for rehabilitation RCTs. During the kick-off meeting, 8 topics were identified for the RCTRACK Technical Working Groups (TWGs): one of these was the "research question".

Therefore, the aim of this study is to assess whether and how PICO format is described to frame research questions in RCTs about efficacy/effectiveness of rehabilitation interventions and if it is an important element that should be put and described in RCTRACK checklist.

Methods

Study design and search strategy

A methodological study, described as a study for the assessing research methods and summarizing methodological issues in the conduct, analysis, and reporting of health research[10,11], was conducted by "Research Question" TWG, on RCTs in the rehabilitation field published between July 1st, 2019 and December 31st, 2019 in journals suggested by the European Society

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of Physical Rehabilitation and Medicine (PRM) were included. This study conforms to all PRISMA guidelines and reports the required information accordingly (see **Supplemental Checklist, Supplemental Digital Content 1, http://links.lww.com/PHM/B146**). Specific criteria[12–14] for inclusion of these journals were: 1) belong to the first quartile (Q1) according to the Journal Impact Factor (JIF) from the Web of Science Journal Citation Reports and 2) they were journals dealing with "Rehabilitation" medicine and related disciplines specifically. The eligible journals were: *Annals of Physical and Rehabilitation Medicine (JIF=4.196), Archives of Physical Medicine and Rehabilitation (JIF= 2.697), Clinical Rehabilitation (JIF= 2.738), Disability and Rehabilitation (JIF= 2.054), European Journal of Cancer Care (JIF= 2.421), IEEE Transactions on Neural Systems and Rehabilitation Engineering (JIF= 3.478), Journal of Fluency Disorders (JIF= 2.349), Journal of Head Trauma Rehabilitation (JIF= 2.667), Journal of NeuroEngineering and Rehabilitation (JIF= 3.582), Journal of Neurologic Physical Therapy (JIF= 2.614), Journal of Orthopaedic & Sports Physical Therapy (IF= 3.058), Journal of Physiotherapy (JIF= 5.551), Manual Therapy (JIF= 2.622), Neurorehabilitation and Neural Repair (JIF= 3.757), Physical Therapy (JIF= 3.043), Physiotherapy (JIF= 2.534), PM&R - The journal of injury, function and rehabilitation (JIF= 1.902), Supportive Care in Cancer (JIF= 2.754), the American Journal of Physical Medicine & Rehabilitation (JIF= 1.908), the European Journal of Physical and Rehabilitation Medicine (JIF= 2.101), the International Journal of Rehabilitation Research (JIF= 1.378) and the Journal of Rehabilitation Medicine (JIF= 1.907).* The search for eligible RCTs published in those journals was conducted on PubMed on May 12th, 2020 and performed by an author (SGL) as general search. See **Supplementary Table 1 (Supplemental Digital Content 2, http://links.lww.com/PHM/B147)** for the full search strategy.

Eligibility and screening

We included all RCTs addressing a RQ regarding effectiveness/efficacy of interventions in the field of rehabilitation published in print or ahead of print in the targeted period. Cross-over and non-randomized clinical trials (NRCTs), secondary analysis of RCTs data, preliminary results, pilot studies, protocols, RCTs in which the randomization process was stratified by any factor and articles addressing not-rehabilitation interventions were excluded.

The selection process was performed in duplicate by two independent authors (SGL and MP) during: a) title and abstract and b) full text screening phases. A third author (CA) resolved the discrepancies.

Rating the framing of the research question

We used the methodology proposed by Rios (2010) to analyze how the research question was described[2]. In brief, the framing of the primary RQ of each study was evaluated firstly based on the introduction and secondly from the title and methodology sections. This evaluation was performed regardless of whether the RQ was formulated as a question, objective or hypothesis. Each reviewer identified a paragraph/ or sections where the RQ was discussed and then identified whether the four elements of PICO were present in those sections. We used a "PICO score" with a possible score between 0 and 4, as a measure of the completeness of the description of the primary research question, study objective or research hypothesis. A score of 4 confirmed that all PICO elements were described (Complete PICO). Reports that did not describe these 4 elements (Incomplete PICO) did not qualify as providing a structured RQ. Next, the adequacy of

question formulation was evaluated based on the structure recommended by Cochrane. Cochrane proposes that the statement of a RQ should begin with a precise statement of the primary objective, ideally in a single sentence. The recommended sentence style and order is as follows: *«to assess the effects of [intervention or comparison] for [health problem] in [types of people, disease or problem and setting if specified]»*[15]. This specific order helps to clarify the aim of an RCTs, enhancing a reader's understanding of the goal of a study of the effectiveness/efficacy of an interventions,. For the purpose of this study, this specific statement was defined as the "PICO structure" and scored score of 1 was assigned if it was used, and a score of 0 if it was not used.

Assessment of the quality of reporting in included studies

The included studies were assessed for reporting using the CONSORT Statement for Randomized Trials of Nonpharmacologic Treatments checklist (CONSORT-NPTs checklist) to assess the quality of reporting in nonpharmacologic trials. This is an extension of the CONSORT checklist, developed to improve the reporting of RCTs investigating nonpharmacological treatments[16,17].

The CONSORT-NPT checklist includes 45 items and each of them was scored 1 if it was reported and 0 if it was not clearly stated or definitely not stated. Item 4a) "Eligibility criteria for participants; When applicable, eligibility criteria for centers and for care providers" has been split to address both topics independently. Therefore, an overall quality score (OQS) was defined with possible value between 0 (no adherence) and 45 (complete adherence) points to measure the completeness of the reporting, i.e. adherence with the CONSORT-NPT checklist. A pre-training

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quality of reporting assessment was performed by the reviewers (SGL and MP) to define the evaluation criteria for the reporting quality. After the reporting evaluation, any disagreements were resolved involving a third reviewer (CA).

Data extraction

We used a standardized data abstraction form to extract data from each article. We collected the following article characteristics: first author, year, title, the RQ description and type (question, objective or hypothesis format) firstly described in introduction section and secondly in title and methods section, outcome measures from each trial, rehabilitation interventions and PICO format. Two reviewers blinded to each other's ratings extracted data independently and rated the framing of the RQ, they resolved any disagreement through consensus.

Statistical analysis

We calculated the percentage of trials that clearly stated each PICO element and associated 95% confidence interval (95% CI). We reported descriptive statistics on categorical data as frequencies and percentages. We reported scores (i.e., PICO score and OQS) as median and interquartile range (IQR). Considering, the not normally distribution of the data (Shapiro e Wilk's test), we evaluated if high PICO score was associated with high reporting quality by conducting linear regression analysis with PICO score and OQS as variables using Spearman's correlation coefficient (Spearman's rho r_s). Variables were considered to be statistically significant at alpha = 0.05. We conducted all analyses using STATA V.14.0 (StataCorp LP, College Station, TX, USA).

Results

After removal of duplicates, 227 records were screened; of these, 97 RCTs met the inclusion criteria and were included in the analysis. The characteristics of the included studies are reported in **Supplementary Table 2 (Supplemental Digital Content 3, http://links.lww.com/PHM/B148)**. The reasons for exclusion and the number of articles excluded, at title-abstract and at full text screening stage, are listed in the PRISMA flow diagram (**Figure 1**). Twenty seven percent (n=26) of articles were published in the journal Clinical Rehabilitation, 14% (n=14) in Archives of Physical Medicine & Rehabilitation, 13% (n=13) in the American Journal of Physical Medicine & Rehabilitation and 10% (n=10) in European Journal of Physical and Rehabilitation Medicine (see **Table 1 for details of the search strategy**). The most frequent framing of the primary RQ was as an "objective" statement (55%) and in 33% of the articles this was as "objective" together with a "hypothesis" description. The frequency of each PICO element reported in allincluded articles is provided in **Table 2**. Patients, interventions and outcomes were often adequately described, whilst in 36% of the articles, the comparison interventions were not described. All PICO elements were present in 55% of RQ, but only 49% have used the statement suggested by Cochrane. Of these, 85% had the completeness of PICO (PICO score median of 4 (2-4)).

The CONSORT-NPT Checklist assessment revealed that the articles described 80% (36) of all checklist items, with median OQS of 36 (26-41). Items for which the lowest adherence to the checklist was found were: the adherence of care providers (2%) and participants (35%) to interventions, blinding description (16%) and the description of any attempts to limit the blinding as bias (5%), the period of recruitment and follow-up description (23%), the presentation of both

absolute and relative effect size in binary outcomes (15%) and the description of generalizability of the trial findings according to the intervention, comparators, patients, care providers and centers involved in the trial (44%). The highest adherence to the checklist was observed in the description of title and abstract (91%), background and aim (100%), trial design (93%), participants (100%), interventions (86%), outcomes (100%), sample size (80%), statistical methods (99%) and interpretation of results. Eighty six percent of the RCTs were registered in a trial registration database (see **Supplementary Table 3, Supplemental Digital Content 4, http://links.lww.com/PHM/B149)**. The Spearman's correlation coefficient between the completeness of PICO and the overall reporting quality was r_s=-0.051.

Discussion

This study evaluated whether and how PICO format is described to frame research questions in RCTs addressing effectiveness/efficacy of rehabilitation interventions published in the highest-ranking rehabilitation journals during the second half of the year 2019.

The results showed that the most frequent framing of primary RQ was in a form of a statement about study objective using all PICO elements, but few articles followed the statement suggested by the Cochrane (PICO structure) to describe them. The comparison intervention was the least frequently described element when compared to the other elements (i.e. population, intervention and outcome). The lack of comparison intervention description is quite frequent in rehabilitation context in which establishing the control treatment is difficult because: 1. this type of intervention is rarely a single specific item with a high level of heterogeneity in terms of name used for defined it and of protocol ingredients, leading to a non-linear causal-effect relationships

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[18]. 2. The rehabilitation setting, wherethe control intervention is delivered, usually represents a complex clinical situation that could affect the clinical replicability of interventions[14]. Therefore, our study showed that the overall reporting quality, evaluated with CONSORT-NPT checklist, was satisfactory, with 80% of reporting completeness and the best items described were those more related to PICO elements, but it was not directly related to the completeness of PICO. This could be explained by the characteristics of CONSORT-NPT checklist that is an extension of CONSORT and includes 20 more items regarding more details on the description of the experimental treatment, comparator, care providers expertise, centers, blinding status, adherence to the protocol and the treatment, statistical methods and the generalizability of the trial findings according to the intervention, comparators, patients, care providers and centers involved in the trial[16,17]. These specific items represent the main methodological issues found in rehabilitation research[7]. Most of them are related to the methodological quality rather than reporting quality, in particular to the conduct of the study that include elements such as allocation concealment (selection bias), method of blinding (performance and detection bias), incomplete outcome data (attrition bias), protocol availability (reporting bias) and compliance related biases[19]. All these biases could affect the treatment estimates of RCTs and consequently the effectiveness/efficacy of rehabilitation interventions[20]. Therefore, a structured RQ could be associated with better methodological quality and could facilitate and make the research question more understandable to guide clinicians and researchers in the literature search, in the protocol development and in the conduct of a study[2] in rehabilitation research. The incompleteness and unclearness of RQ have been also found in other fields in biomedical research, such as endocrinology[21], urology[22], venous ulcer disease[3], surgery[23] and anesthesia[5] literature. These studies highlighted a significant association between the completeness of the RQ description and quality of reporting and this

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could involve the overall quality of methodology of the studies[6]. Since the risk of bias assessment, one of methodology quality element, is closely linked to quality of reporting, further research should include the evaluation of both reporting and methodological quality[24]. A structured RQ might be considered as a systematic way to construct the RQ and to conduct a study with the aim to give information for the clinical decision-making[6] in rehabilitation research. These considerations highlight the need to develop a specific checklist for the rehabilitation field, like RCTRACK, which includes a specific item on the framing of RQ to guide the development of future RCT studies.

The limitations were: firstly, the PICO score and OQS are not validated and have not been rigorously tested for validity and reliability. Secondly, the inter-rater agreements were not calculated; however, the reviewers performed a pre-training reporting quality assessment to define the evaluation criteria and the disagreements were always resolved by consensus with the third reviewer.

Conclusion

The lack of well-designed and reported clinical trials reduces confidence in RCT results. Asking a clearly defined RQ is the first step in conducting a well-designed study. Consequently, the key implication of this study is that trialists in the rehabilitation field should pay attention to the proper framing of the research question using a structured approach, such as the PICO format. This should comprise a precise statement of the primary objective, ideally in a single sentence as suggested by Cochrane. This clearly defined RQ should inform how the study is designed, conducted and reported. Consequently, our "Research Question" TWG have now recommended

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that the RCTRACK checklist includes the following specific item about the "*research question*":

"definition of the research question and rationale of the chosen design to answer to the research

question described according to the PICO format".

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References

1. Sackett DL, Wennberg JE. Choosing the best research design for each question. *BMJ*. 1997;315(7123):1636. doi:10.1136/bmj.315.7123.1636

2. Rios LP, Ye C, Thabane L. Association between framing of the research question using the PICOT format and reporting quality of randomized controlled trials. *BMC Med Res Methodol*. 2010;10:11. doi:10.1186/1471-2288-10-11

3. Abbade LPF, Wang M, Sriganesh K, Mbuagbaw L, Thabane L. Framing of research question using the PICOT format in randomised controlled trials of venous ulcer disease: a protocol for a systematic survey of the literature. *BMJ Open*. 2016;6(11):e013175. doi:10.1136/bmjopen-2016-013175

4. Clouse RE. Proposing a good research question: a simple formula for success. *Gastrointest Endosc*. 2005;61(2):279-280. doi:10.1016/s0016-5107(04)02579-9

5. Thabane L, Thomas T, Ye C, Paul J. Posing the research question: not so simple. *Can J Anaesth J Can Anesth*. 2009;56(1):71-79. doi:10.1007/s12630-008-9007-4

6. Brian Haynes R. Forming research questions. *J Clin Epidemiol*. 2006;59(9):881-886. doi:10.1016/j.jclinepi.2006.06.006

7. Arienti C, Armijo-Olivo S, Minozzi S, Lazzarini SG, Patrini M, Negrini S. Methodological issues in rehabilitation research: a scoping review. *BMJ Evid-Based Med*. 2019;24(Suppl 1):A35-A35. doi:10.1136/bmjebm-2019-EBMLive.68

8. Wade D. Rehabilitation - a new approach. Part three: the implications of the theories. *Clin Rehabil*. 2016;30(1):3-10. doi:10.1177/0269215515601176

9. Negrini S, Armijo-Olivo S, Patrini M, et al. The Randomized Controlled Trials Rehabilitation Checklist: Methodology of Development of a Reporting Guideline Specific

to Rehabilitation. *Am J Phys Med Rehabil*. 2020;99(3):210-215. doi:10.1097/PHM.0000000000001370

10. Puljak L, Makaric ZL, Buljan I, Pieper D. What is a meta-epidemiological study? Analysis of published literature indicated heterogeneous study designs and definitions. *J Comp Eff Res*. 2020;9(7):497-508. doi:10.2217/cer-2019-0201

11. Lawson DO, Leenus A, Mbuagbaw L. Mapping the nomenclature, methodology, and reporting of studies that review methods: a pilot methodological review. *Pilot Feasibility Stud*. 2020;6:13. doi:10.1186/s40814-019-0544-0

12. Franchignoni F, Stucki G, Muñoz Lasa S, et al. Publishing in physical and rehabilitation medicine: a European point of view. *J Rehabil Med*. 2008;40(6):492-494; author reply 494. doi:10.2340/16501977-0211

13. Franchignoni F, Ozçakar L, Michail X, Vanderstraeten G, Christodoulou N, Frischknecht R. Publishing in Physical and rehabilitation medicine. An update on the European point of view. *Eur J Phys Rehabil Med*. 2013;49(5):711-714.

14. Negrini S, Arienti C, Pollet J, et al. Clinical replicability of rehabilitation interventions in randomized controlled trials reported in main journals is inadequate. *J Clin Epidemiol*. 2019;114:108-117. doi:10.1016/j.jclinepi.2019.06.008

15. Thomas J, Kneale D, McKenzie JE, Brennan SE, Bhaumik S. Chapter 2: Determining the scope of the review and the questions it will address. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA (editors). Cochrane Handbook for Systematic Reviews of Interventions version 6.0 (updated July 2019). Cochrane, 2019. Available from www.training.cochrane.org/handbook.

16. Boutron I, Moher D, Altman DG, Schulz KF, Ravaud P, CONSORT Group. Extending the CONSORT statement to randomized trials of nonpharmacologic treatment: explanation and elaboration. *Ann Intern Med*. 2008;148(4):295-309. doi:10.7326/0003-4819-148-4-200802190-00008

17. Boutron I, Altman DG, Moher D, Schulz KF, Ravaud P, CONSORT NPT Group. CONSORT Statement for Randomized Trials of Nonpharmacologic Treatments: A 2017 Update and a CONSORT Extension for Nonpharmacologic Trial Abstracts. *Ann Intern Med*. 2017;167(1):40-47. doi:10.7326/M17-0046

18. Wade DT, Smeets RJEM, Verbunt JA. Research in rehabilitation medicine: methodological challenges. *J Clin Epidemiol*. 2010;63(7):699-704. doi:10.1016/j.jclinepi.2009.07.010

19. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343:d5928. doi:10.1136/bmj.d5928

20. Armijo-Olivo S, Macedo LG, Gadotti IC, Fuentes J, Stanton T, Magee DJ. Scales to assess the quality of randomized controlled trials: a systematic review. *Phys Ther*. 2008;88(2):156-175. doi:10.2522/ptj.20070147

21. Rios LP, Odueyungbo A, Moitri MO, Rahman MO, Thabane L. Quality of reporting of randomized controlled trials in general endocrinology literature. *J Clin Endocrinol Metab*. 2008;93(10):3810-3816. doi:10.1210/jc.2008-0817

22. Scales CD, Norris RD, Keitz SA, et al. A critical assessment of the quality of reporting of randomized, controlled trials in the urology literature. *J Urol*. 2007;177(3):1090-1094; discussion 1094-1095. doi:10.1016/j.juro.2006.10.027

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23. Balasubramanian SP, Wiener M, Alshameeri Z, Tiruvoipati R, Elbourne D, Reed MW. Standards of reporting of randomized controlled trials in general surgery: can we do better? *Ann Surg*. 2006;244(5):663-667. doi:10.1097/01.sla.0000217640.11224.05

24. Armijo-Olivo S, Stiles CR, Hagen NA, Biondo PD, Cummings GG. Assessment of study quality for systematic reviews: a comparison of the Cochrane Collaboration Risk of Bias Tool and the Effective Public Health Practice Project Quality Assessment Tool: methodological research. *J Eval Clin Pract*. 2012;18(1):12-18. doi:10.1111/j.1365-2753.2010.01516.x
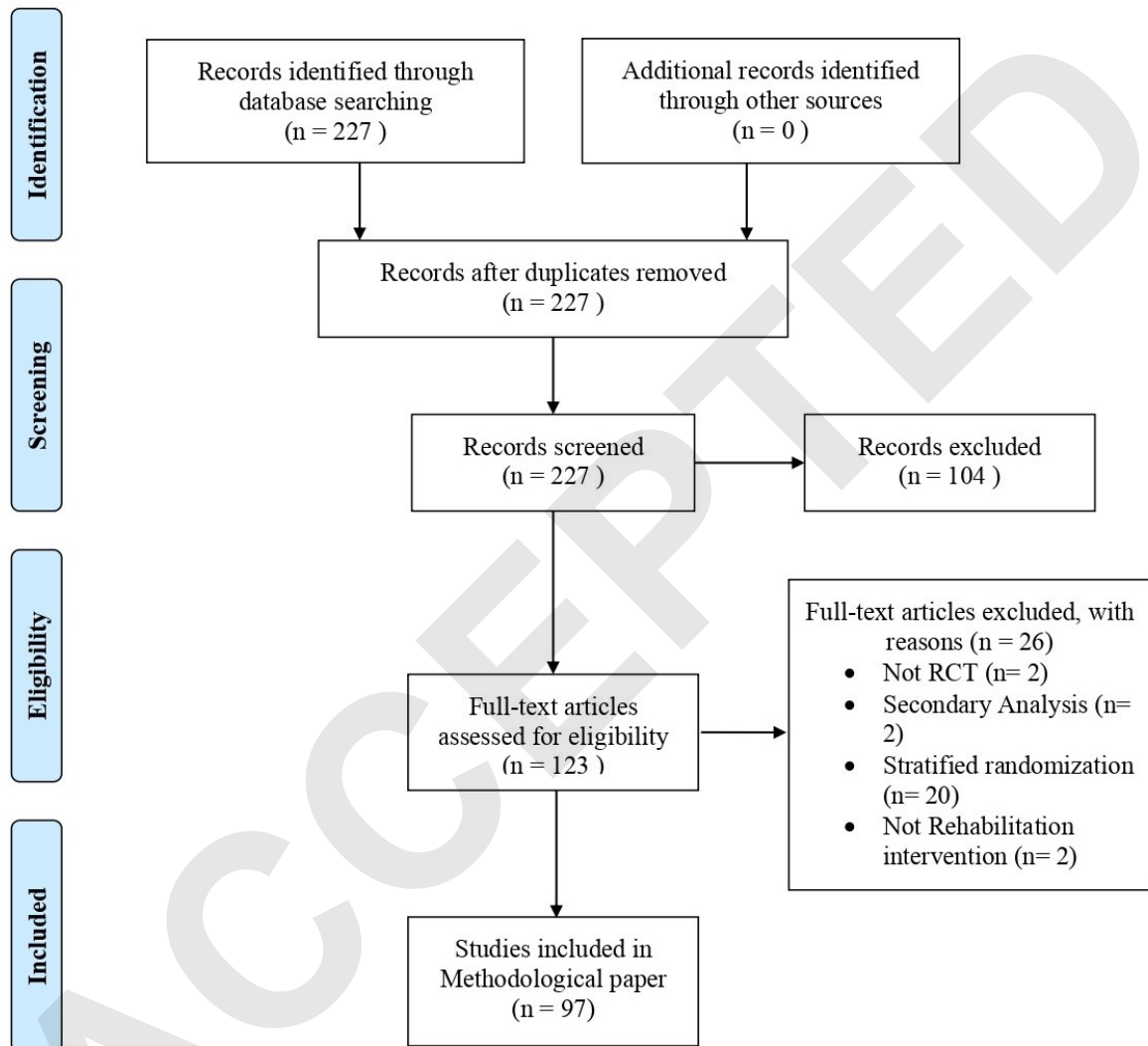
Figure Legends

Fig 1. PRISMA flow diagram

Figure 1

Abbreviations: RCT, randomized controlled trial.

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Table 1. Distribution of included studies among Journals

Journals	All articles (97)	
	n	**%**
Clinical Rehabilitation	26	27%
Archives of Physical Medicine & Rehabilitation	14	14%
American Journal of Physical Medicine & Rehabilitation	13	13%
European Journal of Physical and Rehabilitation Medicine	10	10%
Disability and Rehabilitation	6	6%
Journal of Rehabilitation Medicine	6	6%
Supportive Care in Cancer	6	6%
Neurorehabilitation and Neural Repair	4	4%
Annals of Physical and Rehabilitation Medicine	2	2%
European Journal of Cancer Care	2	2%
International Journal of Rehabilitation Research	2	2%
Journal of Physiotherapy	2	2%
Physiotherapy	2	2%
IEEE Transactions on Neural Systems and Rehabilitation Engineering	1	1%
Physical Therapy	1	1%

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Table 2. Frequency of each PICO element

Research Question	All articles (97)	
	n	**%**
P	95	98%
I	97	100%
C	62	64%
O	81	84%
Complete PICO	53	55%
Structured PICO (Cochrane suggestion)	48	49%