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Chapter 8

Exercise and comorbidity: *the i3-S strategy for developing comorbidity- related adaptations to exercise therapy*

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Abstract

Purpose. Exercise therapy is effective in a wide range of chronic diseases. Comorbid disease necessitates adaptations to exercise therapy. Guidance on how to develop such adaptations is currently not available. We present an innovative strategy for the development of comorbidity-related adaptations to exercise therapy in an index disease.

Methods. We previously developed comorbidity-related adaptations to exercise therapy in osteoarthritis. We now broaden this approach into a general strategy for the development of comorbidity-related adaptations to exercise therapy in an index disease.

Results. The i3-S strategy consists of four steps. The first three steps involve creating an inventory of comorbid disease, an inventory of contraindications and restrictions on exercise therapy, and an inventory of potential adaptations to exercise therapy. In the fourth step, this information is synthesized into guidance on comorbidity-related adaptations to exercise therapy in the index disease. The adaptations concern physiological, behavioural and environmental factors.

Conclusion. In view of the general effectiveness of exercise therapy and the high prevalence of comorbidity in older people, there is a great need for comorbidity-related adaptations to exercise therapy. We recommend to use and evaluate the i3-S strategy in future research.

Introduction

Exercise therapy is effective in a wide range of chronic diseases, with controlled studies showing consistent evidence that exercise therapy results in reduced morbidity, reduced symptoms and better functioning¹⁻³. However, comorbid disease frequently leads to the exclusion of patients from treatment⁴. One example is comorbid diabetes, which leads to patients being excluded due to concerns related to hypoglycaemia. When patients with comorbid disease are referred, therapists often reduce the intensity of exercise to a level that is unlikely to be effective⁵. Because patients are inclined to do likewise, comorbid disease may result in non-adherence to exercise recommendations⁶.

Patients with comorbid disease can exercise, provided that the exercise regimen is adequately adapted to the comorbidity. A patient with osteoarthritis of the knee and comorbid diabetes is allowed to exercise if their blood glucose level is monitored and the exercise is adapted accordingly. Current guidelines provide guidance on exercise therapy in the index disease (e.g., osteoarthritis as index disease, or diabetes as index disease). These guidelines fail to provide proper guidance on adaptations required because of the presence of comorbidity next to the index disease. For example, no adaptations because of diabetes were provided in a guideline on exercise therapy in osteoarthritis⁷. Conversely, no adaptations because of osteoarthritis were provided in a guideline on exercise therapy in diabetes^{8,9}. General advice on exercise describes adaptations to the presence of disease, but does not describe how exercise in an index disease needs to be adapted to comorbidity (e.g.,¹⁰).

We have previously developed comorbidity-related adaptations to exercise therapy in osteoarthritis of the knee^{11,12}. We now broaden this approach into a general strategy for the development of comorbidity-related adaptations to exercise therapy in an index disease. Researchers and clinicians can use this strategy to develop comorbidity-related adaptations of exercise therapy in an index disease. We illustrate the strategy using our experience in developing comorbidity-related adaptations to exercise therapy for osteoarthritis of the knee as an example.

The i3-S strategy

The i3-S strategy consists of four steps – three inventories and a synthesis. The first three steps involve the gathering of relevant information and include creating an inventory of comorbid disease, an inventory of contraindications and restrictions on exercise therapy, and an inventory of potential adaptations to exercise therapy. In the fourth step, this information is synthesised into guidance on the adaptation of exercise therapy to comorbid disease (Figure 1).

Step 1 involves creating an inventory of relevant comorbid diseases: given a specific index disease, which comorbid diseases should be included? Criteria for selecting



comorbid diseases include comorbidity prevalence, comorbidity-related exercise risk and the impact of comorbidity on functioning. For example, we identified 11 diseases as relevant comorbidities in osteoarthritis of the knee: coronary artery disease, heart failure, hypertension, type 2 diabetes, obesity, chronic obstructive pulmonary disease (COPD), depression, chronic pain, low back pain and visual or hearing impairments^{11,13}.

Step 2 involves creating an inventory of comorbidity-related contraindications and restrictions on the application of exercise therapy in the index disease. Contraindications are conditions, which entirely preclude the application of exercise because the patient's safety cannot be guaranteed (e.g., chest pain before or during exercise in a patient with coronary artery disease). Restrictions are conditions, which limit the application of exercise therapy, necessitating adaptations to the therapeutic protocol (e.g., left ventricular ejection fraction of less than 30%). However, restrictions do not entirely preclude the application of exercise.

Contraindications and restrictions are derived from the literature on exercise therapy in patients with specific diseases. We created an inventory of contraindications and restrictions for exercise therapy in osteoarthritis of the knee¹¹, related to the 11 comorbid diseases identified in step 1. We began by reviewing the literature on exercise therapy in coronary artery disease to identify contraindications and restrictions related to coronary artery disease, followed by a similar process for type 2 diabetes and the remaining nine comorbid diseases.

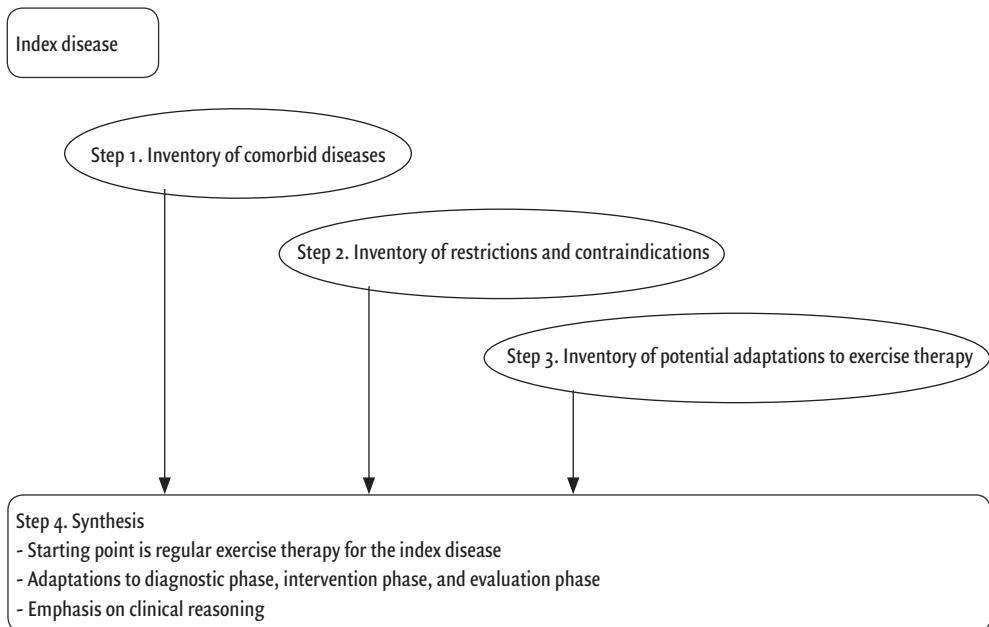


Figure 1. The i3-S strategy for developing comorbidity-related adaptations to exercise therapy.

Step 3 involves creating an inventory of potential adaptations to exercise therapy. These adaptations are derived from guidelines on regular exercise therapy in each comorbid disease (e. g., the guideline on exercise in COPD). In cases where no guideline is available, general guidelines on exercise (e. g., the American College of Sports Medicine guideline¹⁰), general medical guidelines on the treatment of the disease (e. g., guidelines for depression) and expert opinion provide relevant information on adaptations. From these sources of information, principles are derived on how to adapt regular exercise therapy for the index disease to restrictions associated with a specific comorbid disease. The adaptations concern the duration, frequency, intensity and type (content) of exercise therapy. In osteoarthritis of the knee, we created an inventory of potential adaptations related to coronary artery disease (e. g., adapted intensity of individual aerobic exercise), an inventory of potential adaptations related to diabetes (e. g., postponement of exercise when blood glucose is below or above specific cut-off values), and inventories of potential adaptations for all other comorbid diseases¹².

Step 4 involves the synthesis of the information obtained in the previous steps into guidance on the adaptation of exercise therapy to comorbid disease. Guidance on regular exercise therapy in the index disease is the starting point: this guidance is then adapted to the comorbid disease. For example, starting with the guideline on exercise therapy in osteoarthritis of the knee^{14,15}, we specified how the guideline should be adapted to comorbid disease¹².

In the diagnostic phase, comorbidity-related restrictions and contraindications for exercise therapy should be evaluated, the need for additional medical examination is evaluated, and comorbidity-adapted treatment goals are set, taking into account diagnostic findings related to both the index disease and the comorbid diseases. In the intervention phase, comorbidity-related adaptations to the duration, frequency, intensity and type (content) of exercise therapy are indicated. The exact adaptations depend on the restrictions on exercise therapy identified in the diagnostic phase. In the evaluation phase, treatment goals and the need for changes to the treatment plan are evaluated, with a specific emphasis on comorbidity.

Throughout the entire process, there is an emphasis on applying clinical reasoning (or professional reasoning) when developing exercise therapy that is appropriate for patients with a comorbidity^{16,17}. Patients should be viewed in their entirety, with consideration of integrated body structures, functions and activities as a whole, rather than as separate organs. In the diagnostic phase, clinical reasoning may indicate the need for further medical examination to exclude contraindications. Similarly, clinical reasoning guides the selection of treatment goals, taking into account diagnostic findings related to both the index disease and the comorbid diseases. In the intervention phase, clinical reasoning is necessary when deciding on the specific exercise adaptations (duration, frequency, intensity and type of exercise) required for an individual patient. As comorbidity may impose several, sometimes even contradictory, requirements on exercise, clinical reasoning is essential when dealing with the range of exercise adaptations. An example is comorbid heart failure with osteoarthritis of the knee. While the osteoarthritis guideline



emphasises the need for strength training, due to heart failure a rapid increase in the level of peripheral resistance should be avoided, as this increases the afterload and risk of decompensation.

Physiological, behavioural and environmental adaptations

We initially developed 11 adapted exercise therapy protocols, in which regular evidence-based exercise therapy in osteoarthritis of the knee was tailored to each of the 11 comorbid diseases. However, during a pilot study, we found that these 11 protocols could be condensed to only three: a protocol for physiological exercise adaptations – related to coronary artery disease, heart failure, hypertension, type 2 diabetes, obesity and COPD; a protocol for behavioural exercise adaptations – related to chronic pain, non-specific low back pain and depression; and a protocol for environmental exercise adaptations – related to visual and hearing impairments¹². A few examples include adjusted individual aerobic exercise intensity as a physiological exercise adaptation, a graded activity program as a behavioural exercise adaptation, and a larger font size of exercise instructions as an example of environmental adaptations. Although it is an open question whether categorisation into physiological, behavioural and environmental adaptations is applicable to index diseases other than osteoarthritis and to other comorbid diseases, this categorisation appears to be quite generalisable.

Perspective

In view of the general effectiveness of exercise therapy and the high prevalence of comorbidity in older people, there is a great need for a strategy for developing comorbidity-related adaptations to exercise therapy. We recommend to use and evaluate the i3-S strategy for the development of comorbidity-related adaptations to exercise therapy in an index disease in future research.

In a recent systematic review (see Appendix), we identified two other studies describing the development of comorbidity- adapted exercise, in patients with acute exacerbations of COPD¹⁸ and in older adults living with HIV¹⁹, in addition to our own study on patients with osteoarthritis of the knee¹. All three studies described the development of specific comorbidity-related adaptations to exercise therapy, focusing on a specific index disease. None of these studies provided general guidance on how to develop comorbidity-related adaptations to exercise therapy in an index disease. A general strategy for developing such adaptations (i.e., the i3-S strategy) could facilitate future studies on the development of comorbidity-related adaptations to exercise therapy in an index disease. Remarkably, the other two studies used an approach which is rather similar to our original approach¹² (see Appendix). The similarity of the approach in these three studies suggests the usefulness of the general i3-S strategy. We believe the i3-S strategy will prove to be a useful approach for developing comorbidity-related adaptations to exercise therapy in index diseases.

The i3-S strategy structures the adaptation of regular exercise therapy for the index disease to co-existing comorbidity. In a patient with osteoarthritis of the knee (index disease), exercise is adapted to coexisting cardiac disease. Conversely, after a cardiac

event (index disease), exercise therapy is adapted to coexisting osteoarthritis of the knee. An obvious alternative would be to take a multi-morbidity approach, and to develop guidance on exercise therapy for patients with osteoarthritis and cardiac disease, and possibly other diseases as well. We strongly prefer the comorbidity approach used in the i3-S strategy, because (i) patients tend to present with specific symptoms, associated with a specific index disease, (ii) therapists tend to structure their treatment around the index disease, and (iii) this approach allows to preserve the detailed guidance on exercise for the index disease, and then add comorbidity-related adaptations. We recommend that the i3-S strategy should be used to develop adaptations of exercise therapy to comorbid disease.



References

1. Naci H, Ioannidis PJ. Comparative effectiveness of exercise and drug interventions on mortality outcomes: metaepidemiological study. *BMJ* 2013; 347:f5577.
2. Taylor NF, Dodd KJ, Shields N, Bruder A. Therapeutic exercise in physiotherapy practice is beneficial: a summary of systematic reviews 2002–2005. *Aust J Physiother* 2007; 53:7–16.
3. Smidt N, de Vet HC, Bouter LM, et al. Effectiveness of exercise therapy: a best-evidence summary of systematic reviews. *Aust J Physiother* 2005; 51:71–85.
4. Boyd CM, Vollenweider D, Puhan MA. Informing evidence-based decision-making for patients with comorbidity: availability of necessary information in clinical trials for chronic diseases. *PLoS One* 2012; 7:e41601.
5. Holden MA, Nicholls EE, Young J, et al. UK-based physical therapists' attitudes and beliefs regarding exercise and knee osteoarthritis: findings from a mixed-methods study. *Arthritis Rheum* 2009; 61:1511–21.
6. Holden MA, Nicholls EE, Young J, et al. Role of exercise for knee pain: what do older adults in the community think? *Arthritis Care Res (Hoboken)* 2012; 64:1554–64.
7. Fernandes L, Hagen KB, Bijlsma JW, et al. EULAR recommendations for the non-pharmacological core management of hip and knee osteoarthritis. *Ann Rheum Dis* 2013; 72:1125–35.
8. American Diabetes Association. Standards of medical care in diabetes – 2012. *Diabetes Care* 2012; 35:S11–63.
9. Colberg SR, Albright AL, Blissmer BJ, et al. Exercise and type 2 diabetes: American College of Sports Medicine and the American Diabetes Association: joint position statement. *Exercise and type 2 diabetes. Med Sci Sports Exerc* 2010; 42:2282–303.
10. Durnstine JL, Moore GE. ACSM's Exercise management for persons with chronic diseases and disabilities. Champaign (IL): Human Kinetics; 2009.
11. de Rooij M, Steultjens M, Avezaat E, et al. Restrictions and contraindications for exercise therapy in patients with hip and knee osteoarthritis and comorbidity. *Phys Ther Rev* 2013; 18:101–11.
12. de Rooij M, van der Leeden M, Avezaat E, et al. Development of comorbidity-adapted exercise protocols for patients with knee osteoarthritis. *Clin Interv Aging* 2014; 9:829–42.
13. Reeuwijk KG, de RM, van Dijk GM, et al. Osteoarthritis of the hip or knee: which coexisting disorders are disabling? *Clin Rheumatol* 2010; 29:739–47.
14. Zhang W, Moskowitz RW, Nuki G, et al. OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage* 2008; 16:137–62.
15. Peter WFH, Jansen MJ, Bloo H, et al. Herziening van de KNGF- richtlijn artrose heup-knie (Revised KNGF Guideline osteoarthritis of the hip or knee). *Nederlands Tijdschrift voor Fysiotherapie* 2010; 120:2–15.
16. Rothstein JM, Echternach JL, Riddle DL. The Hypothesis-Oriented Algorithm for Clinicians II (HOAC II): a guide for patient management. *Phys Ther* 2003; 83:455–70.
17. Dekker J. Osteoarthritis: promoting exercise for OA in ambivalent older adults. *Nat Rev Rheumatol* 2012; 8:442–4.
18. O'Brien KK, Solomon P, Trentham B, et al. Evidence-informed recommendations for rehabilitation with older adults living with HIV: a knowledge synthesis. *BMJ Open* 2014; 4:e004692.
19. Camp P, Reid WD, Yamabayashi C, et al. Safe and effective prescription of exercise in acute exacerbations of chronic obstructive pulmonary disease: rationale and methods for an integrated knowledge translation study. *Can Respir J* 2013; 20:281–4.



Appendix

Systematic review on strategies for the development of comorbidity-related adaptations to exercise therapy in an index disease

Aim

To identify and describe strategies for the development of comorbidity-related adaptations to exercise therapy in an index disease.

Methods

A protocol was developed with reference to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines²⁰.

Literature search

The literature was systematically searched from 1985 up to 3 May 2015, using the PubMed database, and using the following search strategy:

("exercise" [MeSH Terms] OR "exercise" [All Fields] OR "exercise therapy" [MeSH Terms] OR "exercise therapy" [All Fields] OR "physical therapy modalities" [MeSH Terms] OR "physical therapy" [All Fields] OR "physiotherapy" [All Fields] AND ("comorbidity" [MeSH Terms] OR "comorbidity" [All Fields] OR comorbidities [All Fields] OR comorbid [All Fields] OR multimorbidity [All Fields] OR multimorbidities [All Fields] OR multimorbid [All Fields] OR coexisting [All Fields]) AND ("1985/01/01" [PDAT]: "2015/12/31" [PDAT]) AND "humans" [MeSH Terms] AND English [lang]). The reference lists of all retrieved studies were also searched, as well as the authors' personal data base.

Inclusion criteria

Inclusion criteria for the present study were the following: (1) The study concerns exercise therapy in one or more specific index diseases; (2) the study describes a strategy or systematic approach towards the development of adaptations of exercise therapy in the index disease(s) to the presence of comorbidity; (3) the study was reported in the format of a full-text article; and (4) the study was published in English.

Data extraction

Data were extracted on the index disease, and on the strategy for the development of comorbidity-related adaptations to exercise therapy in the index disease, by means of a qualitative summary.

Data synthesis

A qualitative summary of the results.

Results

The search yielded 4342 unique references, which were screened on title and abstract. This resulted in 18 full text articles that were evaluated on eligibility. Three studies were included in the present systematic review (15 studies were rejected because they did not meet the selection criteria). The papers included in the present review described the development of comorbidity-adapted exercise in patients with acute exacerbations of chronic obstructive pulmonary disease²¹, in older adults living with HIV²², and in patients with osteoarthritis of the knee (our own study²³).

Camp et al.^{21,24} developed recommendations on exercise in acute exacerbations of chronic obstructive pulmonary disease (COPD). The authors conducted (i) systematic reviews on exercise in COPD, and 11 comorbid conditions (being older, heart failure, ischaemic heart disease, peripheral arterial disease, hypertension, obesity, osteoarthritis, osteoporosis, diabetes type 2, HIV and depression). The next step was (ii) a Delphi process which generated more detailed parameters for both exercise safety and effectiveness, and a corresponding clinical decision tool and patient guide. Further steps consist of (iii) a critical appraisal of the tool and guide by a focus group of health professionals, and (iv) a dissemination and implementation plan.

O'Brien et al.²² conducted a knowledge synthesis combining two streams of evidence: (A) HIV-specific evidence addressing rehabilitation and ageing, and (B) evidence on the effectiveness of non-pharmacological rehabilitation interventions for comorbidities commonly experienced by older adults ageing with HIV. The recommendations were derived from literature, identified through systematic literature searches. The obtained evidence was synthesised, using a three-phase iterative process. This process involved (i) classification, assessing methodological quality, synthesis of the evidence and drafting the preliminary recommendations; (ii) interprofessional team review, grading the evidence, and revision of recommendations incorporating values and preferences; and (iii) external endorsement and final refinement.

Stream A resulted in overarching recommendations (e.g. “Rehabilitation professionals should be prepared to provide care to older adults with HIV who present with complex comorbidities (. . .)”, (Supplement 2, p. 6). Stream B resulted in specific recommendations on rehabilitation, including recommendations on exercise in older adults with HIV, and eight categories of comorbidity, i.e. bone and joint disorders, cancer, stroke, cardiovascular disease, mental health challenges, cognitive impairments, Parkinson’s disease, COPD and diabetes (e.g. “Exercise-based cardiac rehabilitation should be recommended for older adults with HIV who have undergone a myocardial infarction (MI) (otherwise known as a heart attack) (or at risk of an MI) given evidence suggests exercise-based cardiac rehabilitation is effective in reducing cardiac deaths. The ideal frequency, intensity, time and type of exercise to maximize benefits are unclear”. (O’Brien et al.²², Supplement 2, p. 43).

de Rooij et al.^{23,25} developed comorbidity-adapted protocols for exercise therapy in osteoarthritis (OA) of the knee in five steps. (i) Comorbidities were selected that are



common, and have impact on pain or daily functioning. The following comorbidities were selected: cardiac diseases; hypertension; type 2 diabetes; obesity; COPD; low back pain; chronic pain; depression; and visual or hearing impairments. (ii) An inventory was made of restrictions and contraindications for exercise therapy in patients with OA of the knee and comorbidity, based on a systematic search of the literature. (iii) Guidelines on exercise therapy in each comorbidity were consulted, to derive potential adaptations to exercise therapy. These potential adaptations were incorporated into the guideline on exercise therapy for OA of the knee. (iv) Preliminary versions of the protocols were extensively discussed with clinical experts, and (v) the protocols were field-tested in a pilot study in patients with knee OA and the target comorbidities; feedback from therapists and patients was obtained, leading to further refinement of the protocols. One of these protocols is currently being evaluated in a randomised clinical trial.

Discussion

From these studies, the following characteristics of strategies for the development of comorbidity-related adaptations to exercise therapy in an index disease can be derived. (i) Specifying comorbidities of the index disease (step 1 in the i3-S strategy). All three studies explicitly stated which comorbidities were being studied²¹⁻²³. (ii) An inventory of comorbidity-related restrictions and contraindications for exercise therapy in patients with the index disease (step 2). This is a unique characteristic of the approach of de Rooij et al.^{23,25}, which was not apparent in the other two studies. This step makes the important distinction between absolute contraindications (no exercise therapy allowed) and restrictions (adaptations to exercise therapy required). Furthermore, this step delineates exactly which restrictions need to be taken into account. It sets the agenda for step 3. (iii) Generating potential recommendations from the literature (step 3). All three studies²¹⁻²³ derived these recommendations from the literature and guidelines on interventions for specific comorbidities. Despite differences in the specific approach used, all three studies took basically the same approach: potential adaptations to exercise therapy in the index disease were derived from evidence on exercise therapy in the comorbid diseases (at that stage treated as index disease). For example: adaptations because of comorbid diabetes were derived from literature on exercise therapy in diabetes (as index disease). (iv) Developing specific recommendations on comorbidity-related adaptations to exercise therapy in an index disease (step 4). Expert knowledge and advice was obtained to develop specific recommendations. The studies used various approaches to elicit expert knowledge and advice (i.e. Delphi process, critical appraisal, interprofessional team review, external endorsement, extensive discussions with clinical experts and field-testing)²¹⁻²³. All three studies emphasised the importance of obtaining expert knowledge and advice for the synthesis of the evidence and the development of specific recommendations.

None of these studies provided general guidance on how to develop comorbidity-related adaptations to exercise therapy in an index disease. All three studies described a specific approach towards developing comorbidity-related adaptations to exercise therapy, focusing on a specific index disease. A general strategy for developing such adaptations could facilitate future studies on the development of comorbidity-related adaptations to exercise therapy in an index disease.

References

20. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Int J Surg* 2010; 8:336–41.
21. Camp P, Reid WD, Yamabayashi C, et al. Safe and effective prescription of exercise in acute exacerbations of chronic obstructive pulmonary disease: rationale and methods for an integrated knowledge translation study. *Can Respir J* 2013; 20:281–4.
22. O'Brien KK, Solomon P, Trentham B, et al. Evidence-informed recommendations for rehabilitation with older adults living with HIV: a knowledge synthesis. *BMJ Open* 2014; 4:e004692.
23. de Rooij M, van der Leeden M, Avezaat E, et al. Development of comorbidity-adapted exercise protocols for patients with knee osteoarthritis. *Clin Interv Aging* 2014; 9:829–42.
24. Reid WD, Yamabayashi C, Goodridge D, et al. Exercise prescription for hospitalized people with chronic obstructive pulmonary disease and comorbidities: a synthesis of systematic reviews. *Int J Chron Obstruct Pulmon Dis* 2012; 7:297–320.
25. de Rooij M, Steultjens M, Avezaat E, et al. Restrictions and contraindications for exercise therapy in patients with hip and knee osteoarthritis and comorbidity. *Phys Ther Rev* 2013; 18:101–11.

