Interactive Multiobjective Optimization for Finding The Most Preferred Exercise Therapy in Knee Osteoarthritis

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Abstract

Background*:* The primary purpose of this study is to develop a decision support approach to support physicians or other healthcare professionals in comparing different exercise therapies and identifying the most preferred one by balancing among cost, ability of improving physical function and reducing pain in patients with knee osteoarthritis.

Methods: Thirty-one exercise therapies were selected from twenty-one randomized controlled trials from a previous meta-analysis. A multiobjective optimization model was designed to characterize the goodness of an exercise therapy based on five conflicting criteria: minimizing cost, maximizing pain reduction and disability improvement, minimizing the number of supervised exercise sessions and the length of the treatment period. Costs were estimated based on personal expenses regarding the information given in the collected randomized controlled trials. A novel interactive multiobjective optimization method was introduced to solve the model, where the physician's preferences were taken into account in finding the most preferred exercise therapy.

Results: An experienced physiotherapist was involved as a decision maker in the interactive solution process testing the proposed decision support approach. He iteratively provided preference information until he was satisfied with the set of therapies shown. After a more in-depth detailed analysis of selected therapies, the decision maker was able to find the most preferred exercise therapy based on the patient's needs and health status.

Conclusions: The proposed interactive multiobjective optimization method is promising in supporting the decision maker in balancing among conflicting criteria to find the most preferred exercise therapy for patients with knee osteoarthritis. Moreover, the proposed method is generic enough to be applied in any field of medical and healthcare settings, where several alternative treatment options exist.

Background

Osteoarthritis (OA) is the most common form of arthritis[1] and a leading source of chronic pain and disability worldwide[2]. Knee OA, in particular, causes a heavy burden to the population as pain and stiffness in this large weight-bearing joint often lead to significant disability requiring surgical interventions. The prevalence of radiographic knee OA varies between 4% and 79% depending on the age category, country of origin and sex distribution of the study population[3]. The high prevalence of knee OA and the predicted aging of population will accentuate the burden of knee OA on health care systems. While there are no good structure modifying drugs to prevent or treat OA, exercise therapy is an important means in the control of OA induced pain and loss of function.

Previous meta-analyses of randomized controlled trials (RCTs) on the effects of exercise therapy in the treatment of patients with knee OA show that exercise therapy improves physical function[4, 5], reduces pain[4, 5], eases depression[6], decreases anxiety[7] and improves the quality of life[4, 5]. In general, since in exercise therapy, adherence is often a problem, supervised therapies are expected to give better results than non-supervised exercise therapies in some diseases. Some studies also confirm the superiority of the supervised exercises on pain reduction and disability improvement for the patients with knee OA[8]. However, supervised training is more expensive than non-supervised training, which represents a conflict between the cost and recovery. More research is needed to understand better which type of exercise therapy is most suitable in terms of improving physical function and reducing pain while keeping cost at an acceptable level.

Multiobjective optimization methods are designed to support a decision maker (DM) in identifying an acceptable balance between conflicting objectives (see, e.g.,[9–12]). The objectives are functions to be minimized or maximized. Support is needed when they are conflicting, since there exists no well-defined best or optimal solution but several compromises, with different tradeoffs. Nonetheless, eventually, only a single solution must be chosen to be implemented. Therefore, the DM with domain expertise plays a vital role in finding the most preferred solution by providing his/her preferences. Interactive methods[13] enable the DM to iteratively provide preference information, modify preferences if needed and learn about the interdependencies among the objectives.

This paper introduces a novel interactive multiobjective optimization method incorporating DM’s preferences. It is inspired by the NIMBUS method[14], which generates a group of compromise solutions (satisfying the preferences as well as possible) to be shown to the DM in each iteration. Here, by a DM, we refer to a physician or some other healthcare professional. By solutions, we mean exercise therapies. In the set of compromise solutions, none of the conflicting objectives characterizing therapies can be improved without impairing at least one of the others. Based on the patient's needs and health status, the DM will choose and prescribe the most preferred exercise therapy from the set of compromises identified by the proposed method.

To the best of our knowledge, this is the first application of multiobjective optimization methods to support decision making and treatment analysis in OA. Multiobjective optimization has been applied in healthcare related problems e.g., in different aspects of medical management and technologies such as emergency management systems[15, 16], scheduling[17], transport and logistics[18], resource and location-allocation[19, 20], patient allocation[21], radiation therapy[22] and brachytherapy[23].

This study proposes a decision support approach utilizing multiobjective optimization to help a DM in identifying the most preferred exercise therapy for patients with knee OA. The goodness is characterized by considering multiple objectives simultaneously. This means that both best cost and best effect are to be sought simultaneously. Thus, disability improvement, pain reduction, number of supervised sessions and length of treatments are considered as objectives besides cost. All these five objectives are conflicting with each other. The focus of this study is to develop methodology to be used as a decision support tool by physicians or other healthcare professionals in comparing different exercise therapies, based on the patient's characteristics, in knee OA.

Methods

As mentioned earlier, the paramount aim of this paper is to support a DM in studying, analyzing and comparing available exercise therapies by considering various (conflicting) objectives simultaneously. Besides a DM, the consideration involves an analyst whose responsibility is generating information, modeling, identifying a suitable solution method and taking care of all mathematical parts. An analyst can be a human, a computer program or their combination[10].

Information of different exercise modalities can be collected from previous meta-analyses of RCTs. This data has to be pre-processed based on clinical objectives that are set by a DM. Based on this information, a relevant multiobjective optimization problem can be formulated. We suggest using an interactive multiobjective optimization method to support the DM in finding the compromise solutions that best reflects the DM's preference information (see, e.g.,[10, 13, 24] and references therein for the basic features of interactive methods). This means that the DM augments the available data with one's domain expertise and iteratively provides one's preference information and sees what kinds of therapies reflect the preferences best and what kinds of trade-offs exist. At the same time, the iterative nature reduces the cognitive load since the DM can concentrate on therapies that satisfy the preferences best. Furthermore, the DM can modify the preferences based on the insight gained and eventually identify the most preferred exercise therapy considering the patient's needs and health status. One should note that we are not providing a global answer or recommendation. The DM involved can analyze the suggested therapies by the proposed approach and prescribe the most appropriate one based on the individual patient characteristics.

Figure 1 describes an overall view of the proposed decision support approach for finding the most preferred exercise therapy in knee OA, where the DM and an analyst participate. Different phases of the proposed approach (i.e., boxes in the figure) are described as follows.

Inclusion Criteria and Data Extraction (Phases 1 and 2)

As a starting point, we consider RCTs selected in the meta-analysis in Goh et al.[5] that evaluated the efficacy of exercise therapies in knee OA, hip OA, and knee and hip OA. The authors[5] made a literature search systematically from *"the dates of inception"* to December 2017. They included papers reporting trials, where a comparison was made between an exercise intervention with a non-exercise one in the knee and hip OA treatment. They also established specific eligibility criteria after the literature search. They included trials if participants; 1) had not undergone knee or hip joint replacement surgery, 2) had only exercise therapy without additional treatment and 3) were assigned to usual care in the control group. The reported outcomes were pain, function, performance and quality of life (QoL).

In Goh et al.[5], 77 RCTs were selected for the meta-analysis based on the literature search and the specific eligibility criteria. We used the same inclusion criteria for the exercise therapy studies as Goh et al.[5], except that we included the studies with the patients of knee OA only and where the data of the WOMAC (Western Ontario and McMaster Universities) scale had been used as an outcome measure for pain and function. Besides, we ruled out the studies where the patients underwent an exercise therapy program before knee replacement surgery. The WOMAC was chosen as it is recommended and most commonly used as a disease-specific outcome instrument in OA patients[25], whereas the KOOS (Knee injury and Osteoarthritis Outcome Score) is intended to be used particularly for knee injuries that can result for a variety of reasons, including OA. Preoperative exercise programs were excluded in turn, because people waiting for knee replacement surgeries often have mobility restrictions due to the pain and disabilities, and we do not know how much physical activity is safe and feasible for people with severe knee OA[26]. Apart from these, for performance outcomes, several testing types and results were listed. This heterogeneity makes a comparison between the outcomes of different therapies challenging in a quantitative way. In addition, QoL outcomes were not measured in a majority of the RCTs (33 papers). Therefore, in this paper, we do not consider outcomes for performance and QoL measurements. Figure 2 summarizes the papers (and therapies) meeting our inclusion criteria mentioned above.

According to the reasoning above, we collected data from the selected papers (see Table 1 in supplementary material A). We listed the therapies, the outcomes for pain and function in the WOMAC scale, the number of supervised sessions and the lengths of the therapies. We also adjusted the ranges of the WOMAC scale into the same range (0-20 for pain, 0-68 for function), if the reported outcomes had different ranges for the WOMAC scale. It should be noted that the values we collected from the papers are average scores since the individualized data is not given in these papers.

Multiobjective Optimization for Knee OA (Phase 3)

As mentioned earlier, the focus of this study is in finding the most preferred exercise therapy for a patient with knee OA. To characterize the goodness of an exercise therapy, we consider five conflicting objectives: minimizing cost, maximizing pain reduction and function improvement, minimizing the number of supervised exercise sessions and the length of the treatment period and we want to optimize all of them simultaneously. As they are conflicting, there does not exist any therapy that can have the best performance in all objectives, but there exist compromises with tradeoffs, as mentioned in the introduction. With the help of multiobjective optimization methods[10], we can support the DM to identify the most preferred exercise therapy among the compromises, and them make the final choice based on the patient's characteristics.

One should note that the objectives considered could also be selected differently if some other aspects characterize the goodness of therapies better. For example, some more objective functions, such as improvement in performance and QoL, can be added. As mentioned, our selection of objectives is explained by the data available. Since no information about combinations of exercise therapies was available, only one therapy can be chosen as the final decision. In what follows, we discuss the objectives in some more detail.

Minimize the Cost of Therapy

We estimate the cost of each exercise therapy based on personal expenses, such as the number of supervised or unsupervised training sessions, length of each session, number of trainees in each group, types of equipment and possible checkpoint calls. Moreover, cost is measured from the time between the baseline and end-point of the outcome measure (later follow-ups are not included). Cost is estimated with the current prices (early 2020) in Finland. However, this can simply be adapted for any time in any other country. Details of cost estimation can be found in the supplementary material D.

Maximize Pain Reduction

As mentioned before, we have only average values of WOMAC scores for pain reduction. We do not have individual data for the patients in exercise and control groups in each exercise therapy. Therefore, we consider the differences between the mean of the WOMAC pain scores pre- and post-intervention as the pain reduction. Furthermore, to take into account the control groups and to be able to measure clinically important change or improvement, we consider the expected net change in pain as the pain reduction objective. We define the net change as the difference between the mean change in exercise and control groups.

Maximize Improvement in Physical Function

Similar to pain, we consider the expected net change in WOMAC score for physical function as the disability improvement objective.

Minimize the Number of Supervised Training Sessions

Organizing the supervised training sessions is always challenging. Besides, some patients (e.g., because of disability, additional time and expenses, pollution, travel distances, quarantine limitations causing by an epidemic or pandemic such as COVID-19) or physicians (e.g., due to lack of time and other duties) prefer to have as few (physical) supervised sessions as possible. We consider this as the fourth objective.

Minimize the Length of Treatment

Finally, the fifth objective is minimizing the length of treatment, which often is of concern for both patients and healthcare professionals.

Proposed Multiobjective Optimization Problem

With the objectives discussed so far, we formulate a multiobjective optimization problem to support decision making and analysis of different therapies to find the most preferred one. (Mathematical formulations are given in equation (1) in the supplementary material B):

minimize   cost of therapy

maximize   expected net improvement in pain reduction

maximize   expected net improvement in physical function

minimize   number of supervised training sessions minimize   length of treatment

subject to   one therapy is selected from a list of options.

The Proposed Interactive Method (Phases 4-6)

In this section, we propose a new interactive multiobjective optimization method to be applied to solve the problem formulated. The interaction means that the preferences of the DM are taken iteratively into account in the solution process in finding the most preferred therapy. The proposed interactive method is inspired by the NIMBUS method[14] in which multiple solutions reflecting the preferences as well as possible are generated and shown to the DM in each iteration. However, in NIMBUS, the DM's preferences are expressed by classifying the objective functions into pre-defined classes, which is not the case in this study. Our method differs from NIMBUS in two perspectives; 1) preference type, 2) way of showing solutions to the DM.

As preferences, we use desirable upper and lower bounds for the possible outcomes of our five objectives (also called objective values), since they are meaningful and understandable for the DM. They form a so-called preferred range. Accordingly, we propose a novel interactive method incorporating the preferred ranges in the solution process. Then we generate different compromise solutions reflecting these DM's preferences as well as possible. In this, we introduce two kinds of solutions since it may not be possible to find a solution that meets all the DM's preferences. The first kind of solutions (group I) meets all the desired preferred ranges, while the second kind of solutions (group II) only meets some preferred ranges. Even though solutions in the latter group violate some preferred ranges, the DM gets more insight of the trade-offs in the compromise solutions. In this way, the DM can learn what is achievable and what is not. Different visualizations have been utilized to illustrate solutions in the multiobjective optimization literature[27, 28]. In this paper, we visualize the solutions with parallel coordinate plots which are able to represent several objectives and solutions at once[29].

In different iterations, the DM can update one's preferences based on the increasing understanding of the available therapies and the existing trade-offs between the objectives. The solution process continues until the DM is satisfied and has found the most preferred therapy.

Figure 3 depicts the iterative steps together with some other steps of the interactive method to support decision making in knee OA. The steps are explained below. The technical details of the proposed interactive method are given in the supplementary material C.

Step 1. The best and the worst values of each objective function are identified and shown to the DM to give an overview of what is feasible. Then, the DM provides his/her preference information as a preferred range for each objective.

Step 2. The multiobjective optimization problem is solved and a desired number of compromise therapies reflecting the preferences as well as possible is shown to the DM. In the visualization, the group I solutions are highlighted while the others (group II) are represented in shading, meaning that some sacrificing in some preferred ranges are needed to get the higher values offering by these solutions in some other objectives. Note that if the objective values exceed the DM's desired values, the relevant solutions are still counted as group I solutions.

Step 3 (optional). The DM can compare and analyze the compromise exercise therapies in more detail e.g., checking the exercises from the clinical aspects, if so desires.

Step 4. If the DM wants to continue and provide different preferences, the solution process continues from *Step 2*. Alternatively, if the DM is satisfied with the current compromise exercise therapies, the process continues with *Step 5*.

Step 5. Finally, after analyzing the compromise therapies, the DM prescribes the most preferred and suitable exercise therapy according to the patient's needs and clinical status. This ends the solution process.

Results

In this section, we demonstrate the proposed interactive method in finding the most suitable compromise therapy for the problem formulated. The source code is openly accessible at the GitHub repository[1]. The data used in the solution process is available in Table 1 in the supplementary material A. An experienced physiotherapist was the DM in this solution process. In the beginning, the DM was informed of the terminology used, idea of the interactive solution process and how one can provide preference information, as presented in Figure 3. As our subject, we consider a patient with mild knee OA who has pain in his knees and some physical difficulty in the daily routines. His budget is around 300€. However, he can bear up to 600€ if there is a chance to improve his physical functionality and pain by at least 25% in two/three months. In addition, because of the distance, he prefers to have as few supervised sessions as possible, although he would participate in as many sessions as needed. Moreover, his current health status and clinical background did not show any severe disease or limitations in doing high-performance exercises. Given this information, at each iteration of the solution process, the DM was asked to provide a preferred range for each objective. As mentioned, these preferences were incorporated in solving the multiobjective optimization problem to find multiple compromise therapies that reflect the preferences of the DM set based on the patient's characteristics.

The solution process was started by showing the best and worst values of each objective to the DM to inform him of the ranges of the available therapies. Then, the DM provided the number of solutions (4 solutions) to be shown at each iteration and the preferred ranges for each objective. First, the DM set the cost between 300 and 600 euros, based on the patient budget. The DM wished to find therapies that improve pain reduction and functionality by 30% and 25%, respectively. For both these objectives, the minimum improvement was set to 15%. According to his previous experiences and the patient's requests, he preferred self-exercises that can be done in a short time. Therefore, the desired values of the fourth and fifth objectives were given near to their minimum observed values (0 and 8, respectively). Upper bounds for these objectives were specified as 15 supervised sessions and 26 weeks.

After the first iteration, only one solution met all the desired ranges (group I) and is highlighted in Figure 4. The DM wanted to see four solutions and, thus three more therapies (from group II) were found and are shown in the figure in shading to make the DM aware of other possible solutions near to his preferred ranges.

It was easy for the DM to compare the solutions since their number was so low. Because all solutions shown are compromise therapies, the DM knew that something had to be sacrificed in order to improve some other objectives. The therapy best matching the preferences (described in Cheung et al.[30]) was not satisfactory for the DM since there were other solutions that had better improvement in pain reduction and function, although they had more supervised training sessions. E.g., therapy from Krasilshchikov et al.[31], as can be seen in Figure 4.

After having seen solutions of the first iteration, the DM was interested in a better functionality improvement than pain reduction. To get such therapies, the DM was willing to sacrifice in the number of supervised sessions and duration of the treatment. Therefore, he provided new preference information for the objectives as shown in Table 1.

Table 1: Preferences in different iterations

		Costs(€)	Pain change (%)	Function change (%)	Supervised sessions	Period (w)
Iteration 1	Preferred	300	+30%	+25%	0	8
	ranges	600	+15%	+15%	15	26
Iteration 2	Preferred	200	+25%	+40%	0	12
	ranges	500	+15%	+15%	30	26

Three group I solutions reflecting the preferences well, described in Krasilshchikov et al.[31], Braghin et al.[32] and Lin et al.[33], were obtained and are highlighted in Figure 5. Since the DM wanted to see four solutions, one more solution[34] (from group II) were found closest to the provided preference information. From these four compromise therapies, the DM selected the therapy described in Krasilshchikov et al.[31] as the most preferred solution. It has the most significant functionality improvement and still improves in pain reduction very well. However, to achieve these improvements, one needs to pay more money and take more supervised sessions than in some other solutions. It was noticed that comparing a subset of solutions (3-5) in an interactive way helped the DM in assessing the objectives simultaneously. He reached the satisfactory solution in only two iterations.

Footnote:

[1] https://github.com/industrial-optimization-group/Interactive-Multiobjective-Optimization-for-Finding-the-Most-Suitable-Exercise-Therapy-in-Knee-Osteo

Discussion

We have demonstrated how multiobjective optimization can help decision making in the choice of applicable exercise therapies. Characteristics of the desirability of therapies were augmented by the domain expertise of a DM. We paid special attention to five objectives in selecting exercise therapies, where cost of individual therapies, WOMAC pain and function, number of supervised exercise sessions and length of treatment period were the conflicting objectives.

In an interactive solution process, where the DM iteratively provided preferences for each objective, two iterations were carried out to find acceptable and preferred exercise therapies. The first iteration reflected slightly higher therapy costs and pain reduction, lower functionality improvement and fewer supervised exercise sessions. It resulted in a Yoga type exercise described in Cheung et al.[30]. While the treatment period stayed at 8 weeks in the therapies found in both iterations, the second iteration reflected slightly lower therapy cost and pain reduction, slightly higher functionality improvement and more supervised exercise sessions. It resulted in therapies described in Krasilshchikov et al.[31], Braghin et al.[32] and Lin et al.[33]. From these, the combined resistance and aerobic exercise program in Krasilshchikov et al.[31] had a superior improvement in pain and function, although it had also the biggest cost. Thus, based on clinical outcomes and patient's characteristics, in our case, the choice was a mixed type exercise experienced in Krasilshchikov et al.[31].

As mentioned earlier, because of the conflicting objectives, instead of a single optimal solution, multiobjective optimization problems have several compromise solutions, in this case, therapies. Therefore, the DM can find promising compromises with the help of a multiobjective optimization method and finally choose the most preferred exercise therapy amongst the compromises found based on his/her analysis and patient characteristics. Naturally, the preferences of the DM are specific to each patient. Thus, the choice depends on different symptoms and needs (e.g., a patient with chronic pain but rather good functionality may need a different treatment from another one who has less pain but needs more improvement in functionality). Based on the particular preferences, in each case, various compromise solutions will be found and shown to the DM, and the final choice will be different accordingly. Therefore, the patient characteristics in question affect the preferences of the DM and the most preferred therapy as the final choice.

To the best of our knowledge, this is the first time when multiobjective optimization has been used to support decision making in selecting exercise therapies for patients with knee OA. Therefore, we cannot compare our results with previous studies using multiobjective optimization or similar optimization methods in this patient group. The results of this study are not either comparable with the traditional meta-analyses in the treatment of knee OA patients, as they have been conducted on several clinical trials in an effort to obtain higher statistical power with stronger evidence on the possible effectiveness for the outcomes than from any individual study.

Multiobjective optimization, in turn, offers one or more individual study solutions based on the objectives which have been given for the desired therapy objectives. Ideally, the individual studies obtained as a result of the multiobjective optimization solution process should be in line with the recommendations and guidelines for the management of knee OA. For example, the Yoga exercise[30] found in the first iteration is in agreement with the current treatment guidelines that land-based exercise and mind-body exercise such as Tai Chi and Yoga are effective and safe for all patients with knee OA[35]. Similarly, the other suggested study by Krasilshchikov et al.[31] found in the second iteration is also in harmony with the results of recent meta-analysis showing that aerobic exercise in combination with strengthening exercises are efficient in pain reduction and function improvement[36]. It should be noted that the studies by Cheung et al. [30] and Krasilshchikov et al. [31] had small sample sizes.

Strengths and Limitations

The strength of the approach proposed is the ability to make better decisions by considering conflicting objectives simultaneously. On one hand, the fact that we used trial-specific mean results can be considered as a strength for generalizability. On the other hand, it is a limitation because of two reasons; there may be clinical heterogeneity between the trials, such as different mean OA stages, influencing trial outcomes, and we may not take into account all clinically relevant individual data.

Conclusions And Future Directions

A new approach for determining the most preferred exercise therapy for knee OA was proposed. As a part of it, a novel interactive multiobjective optimization method was introduced. Even though the focus was in the field of rehabilitation medicine, the proposed approach can be utilized in any field of medical and healthcare services, where several alternative treatment options for certain conditions and data about them exist. Our intention is not to provide any global answer or recommendation but a decision support tool. Any physician can analyze the suggested therapies by the proposed approach by incorporating one's preferences (reflecting patient's needs and health status) and prescribe the most appropriate one to the patient in question. We demonstrated and tested the proposed approach to show its benefits and usability on prescribing exercise therapies applied in the treatment of knee OA patients.

Using interactive multiobjective optimization methods in its current form requires an analyst in addition of a domain expert to pre-process the data and formulate the optimization problem. A further step in the development could be creating a user-friendly interface, which does not necessitate the presence of an analyst. Moreover, if we had individual data of each participant in the considered RCTs, the optimization process could be done in a more personalized way. This would improve the accuracy of the model and save the time of the DM in the final analysis. To summarize, designing a user-friendly interface, considering more objectives (like performance and QoL), and individualizing the recommendations are our future research directions.

Abbreviations

OA

Osteoarthritis, RCTs:Randomized controlled trials, DM:Decision maker, QoL:quality of life, WOMAC:Western Ontario and McMaster Universities, KOOS:Knee injury and Osteoarthritis Outcome Score.

Declarations

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Author Contributions

All authors were involved in writing the manuscript, planning, conception and design of the study, analysis and final approval of the manuscript version to be submitted. KM, BA and BS participated in the problem formulation and designing the proposed interactive method. BA and BS participated in data extraction and data analysis, visualizations and running the interactive solution processes. JM and UK participated in cost estimations, clinical discussions and the interpretation of the results. JM played the role of the DM in the experimental study.

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Availability of data and materials

The data used in this study is openly available in the supplementary materials. The source code is openly accessible at the GitHub repository: https://github.com/industrial-optimization-group/Interactive-Multiobjective-Optimization-for-Finding-the-Most-Suitable-Exercise-Therapy-in-Knee-Osteo.

Declaration of conflicting interests

None to disclose.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

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Figures

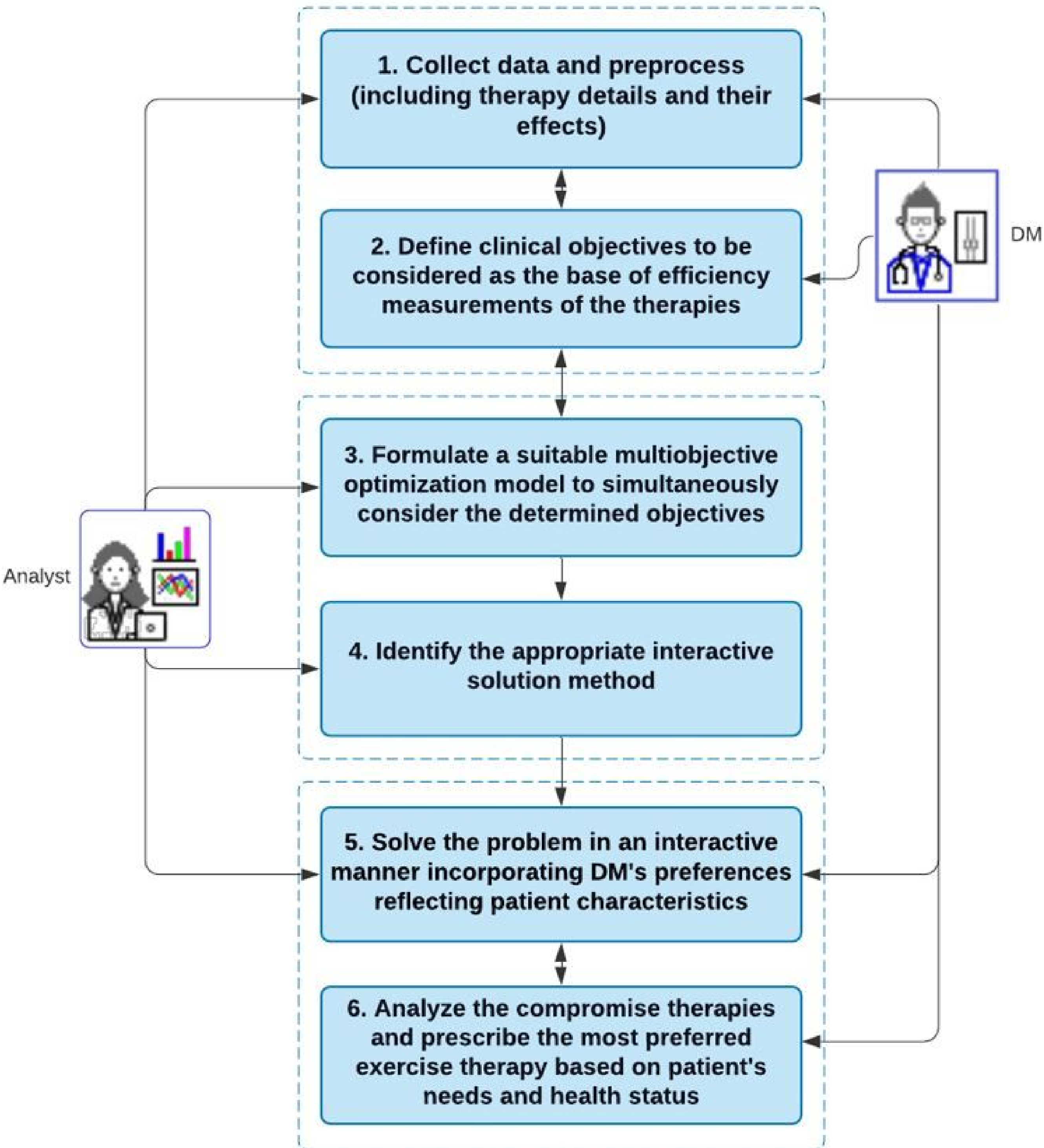

Figure 1

The proposed approach for decision support in knee OA

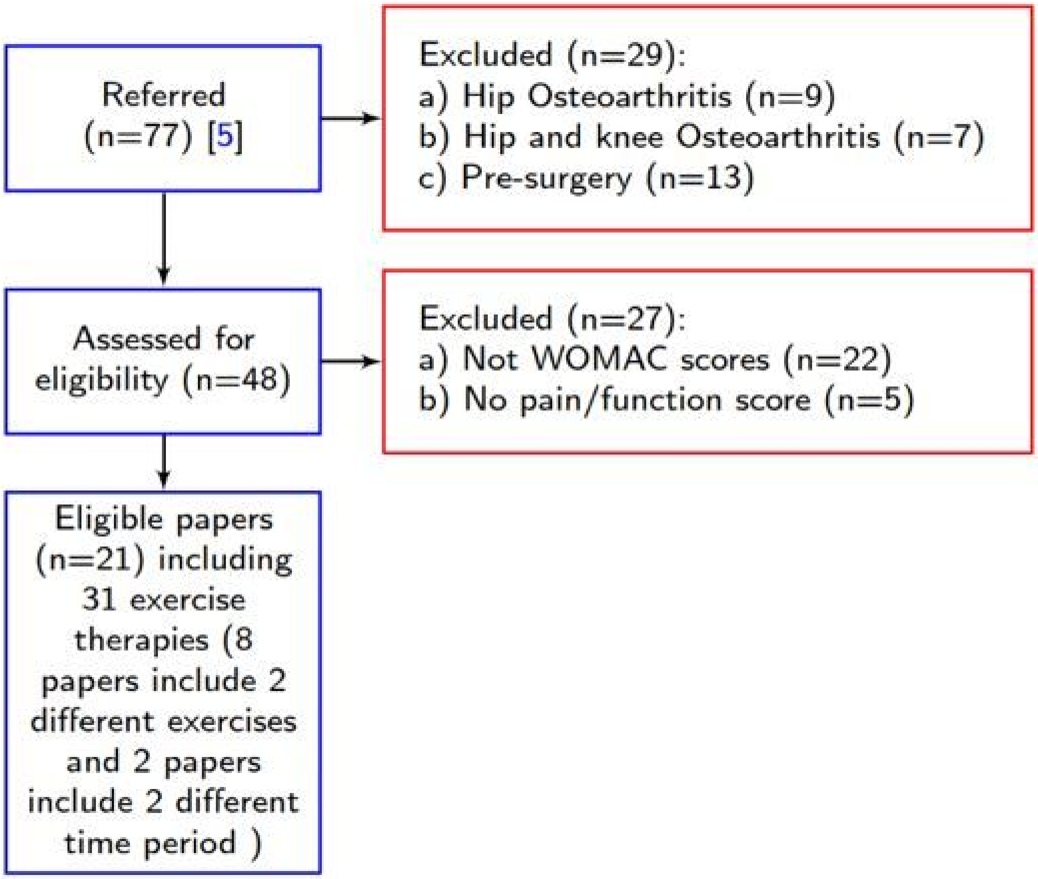

Figure 2

Selection of papers for data collection

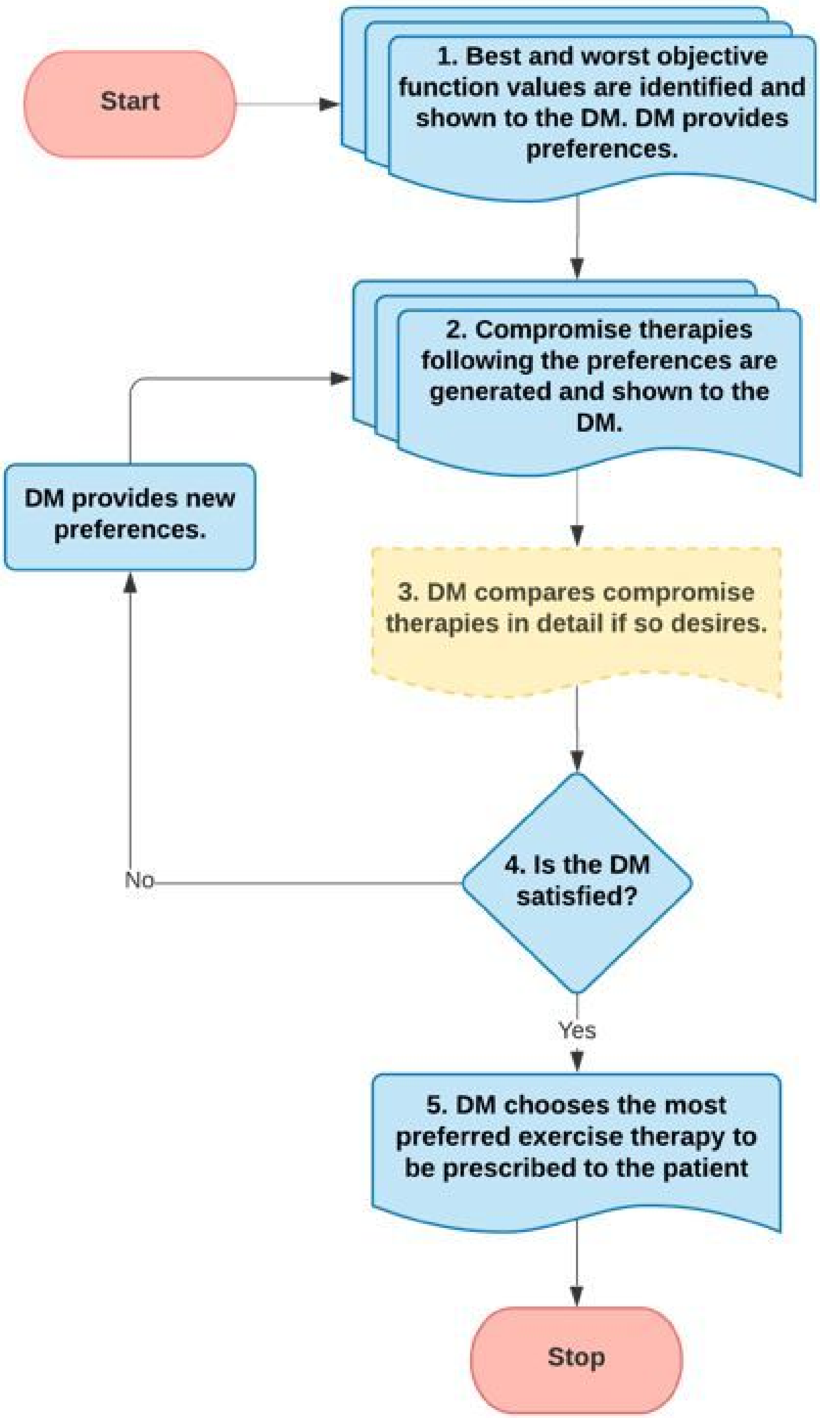

Figure 3

An overview of the interactive method

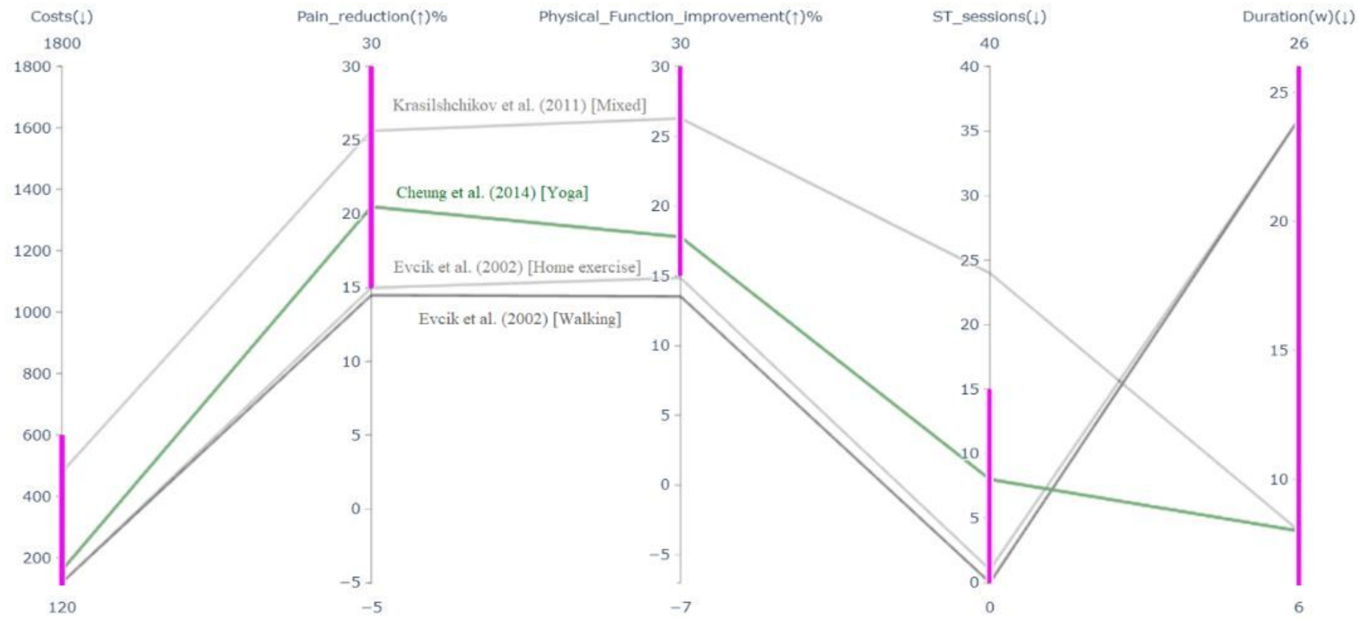

Figure 4

Therapies reflecting the given preference information in the 1st iteration

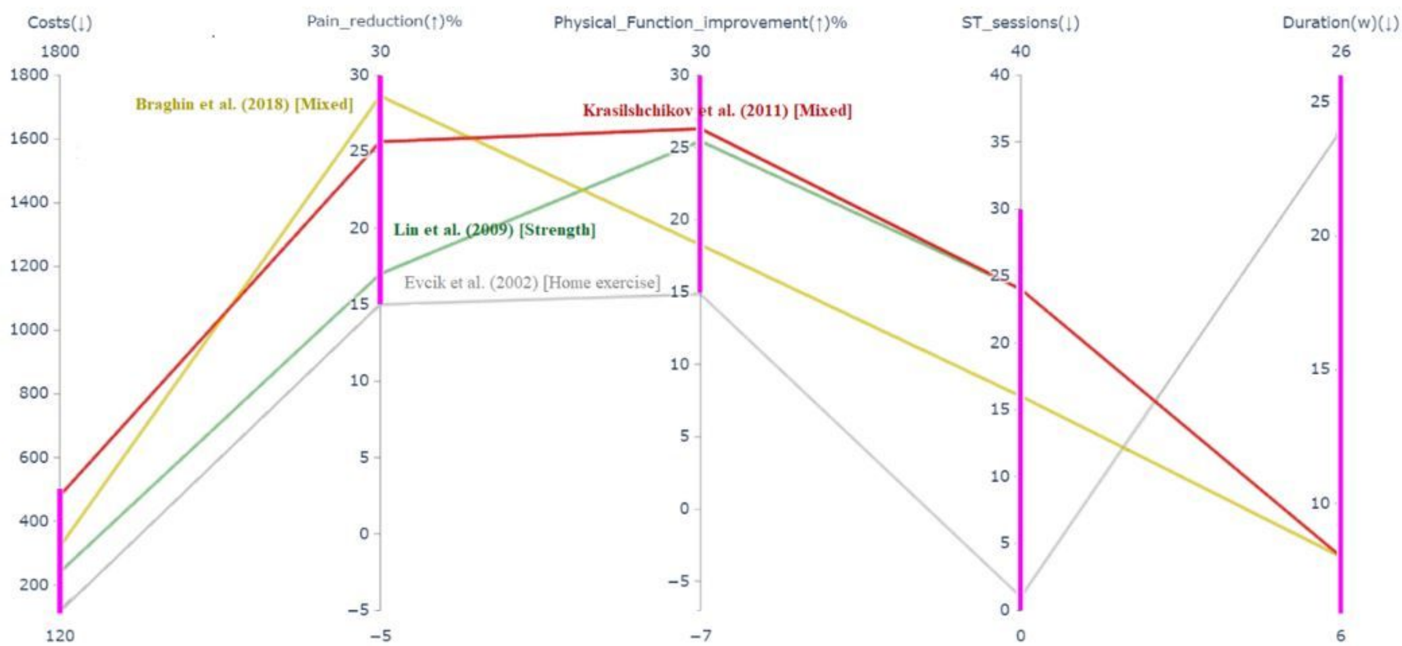

Figure 5

Therapies reflecting the given preference information in the 2nd iteration

Supplementary Files

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- supplement1.pdf
- supplement2.xlsx
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