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Patient and public involvement to inform the protocol of a clinical trial comparing total hip arthroplasty with exercise: A qualitative study

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ABSTRACT

Objective: To explore patient, clinician, and decision maker perceptions on a clinical trial evaluating the effectiveness of total hip arthroplasty (THA) compared with exercise to inform the trial protocol.

Design and Methods: This is a qualitative study using a constructivistic paradigm. Participants were enrolled into three key stakeholder groups: patients eligible for THA, clinicians, and decision makers. Focus group interviews were conducted according to group status using open-ended semi-structured interview guides. Interviews were recorded, transcribed verbatim, and thematic analysed.

Results: We conducted 6 focus group interviews comprising 14 patients, 4 clinicians (2 orthopaedic surgeons and 2 physiotherapists), and 4 decision makers. Two main themes emerged. *'Perceptions that may influence the management of hip osteoarthritis'* covered three supporting codes: Treatment without surgery is unlikely to lead to recovery; Clinician authority impacts the management narrative; The 'surgery versus exercise' debate. *'Considerations for a trial protocol in the current Danish healthcare context'* highlighted three supporting codes: Who is considered eligible for surgery; Facilitators and barriers for a clinical trial comparing surgery and exercise; Most important and meaningful outcomes for patients with hip osteoarthritis.

Conclusions: Patients and clinicians had beliefs and perceptions on the management of hip osteoarthritis that may lead to sampling bias during enrolment procedures, treatment crossovers, and reduced generalizability of our clinical trial. Therefore, we included a

parallel observational study investigating the generalizability, developed an enrolment procedure using generic guidance and balanced narrative conveyed by an independent clinician to facilitate communication of clinical equipoise, and adopted change in hip pain and function as the primary outcome to improve methodological rigorousness of our trial protocol.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This qualitative patient and public involvement study was used to inform the protocol of a randomised controlled trial evaluating the effectiveness of total hip arthroplasty compared with exercise.
- Focus group interviews were performed with patients, clinicians, and decision makers to provide multiple perspectives and extend the scope of the findings.
- An independent researcher conducted the data analysis to decrease the possibility of interpretation bias.
- One focus group interview was conducted for each of the groups with clinicians and decision makers due to pragmatic reasons reducing the likelihood of data saturation in these two groups.
- All participants in the patient group were scheduled for total hip arthroplasty and 3 out of 14 had previously undergone this procedure, which may have influenced their perceptions.

Keywords

Hip Osteoarthritis, Total Hip Arthroplasty, Exercise, Patient and Public Involvement, Qualitative Study

INTRODUCTION

Hip osteoarthritis (OA) is a major cause of pain, disability, and decreased quality-of-life[1]. The overall prevalence of hip OA is 11%,[2] and the disorder is the leading reason for undergoing total hip arthroplasty (THA) surgery.[3] The number of THAs performed each year has increased dramatically over the past decade with more than one million procedures annually undertaken worldwide.[3] THA is considered an effective treatment to reduce pain, improve physical function, and increase quality-of-life for severe hip OA.[4 5] However, there is a risk of severe complications and up to 23% of the patients report long-term residual pain after THA surgery.[3 6]

Guidelines recommend exercise and patient education as first-line treatment in the management of hip OA.[7 8] Specifically, progressive resistance training (PRT) appears to provide moderate improvements in patient-reported outcomes and functional performance even in patients with severe hip OA.[9 10] Furthermore, exercise and patient education might postpone the need for surgery and reduce patients' willingness to undergo THA,[11 12] but less than 40% of the patients are recommended or referred to first-line treatment.[13] Despite the large number of THA surgeries performed annually, no clinical trial has investigated the comparative effectiveness of THA and non-surgical treatment in the management of hip OA.[14] This comparison is of importance as non-surgical treatment has been shown to be a viable alternative to surgery for many musculoskeletal disorders.[15]

Several clinician and patient barriers to participation in clinical trials have been identified. Main clinician barriers comprise lack of support staff and inadequate research training and difficulty with the consent procedure, while notable patient barriers include treatment preferences, worry caused by uncertainty, and concerns about

information and consent.[16] Moreover, clinical trials comparing surgical procedures with non-surgical treatment have suffered from low enrolment rates and difficulties in retaining participants to their allocated treatments.[17-21] With limited participation in these sort of clinical trials a risk exists for research inefficiency and possibly biased findings that may drive clinical decision making.[22]

Patient and public involvement (PPI) strategies involve key stakeholders in the design, conduct, and dissemination of research.[23 24] Evidence suggests that PPI strategies have the potential to increase enrolment rates of participants and improve selection of outcome measures.[23 24] However, only few clinical trials within the orthopaedic area have reported use of PPI,[25] although more than 90% of the authors of surgical trials claim some incorporation of PPI.[23] Thus, based on the benefits and paucity of current evidence in this area effective PPI strategies may help optimize clinical trials comparing surgery to non-surgical treatment.

To our knowledge, this is the first qualitative PPI study preceding a clinical trial comparing surgical to non-surgical treatment as previous trials did not report any engagement from patients and other key stakeholders.[17-21] Therefore, we aimed to explore patient, clinician, and decision maker perceptions on a clinical trial evaluating the effectiveness of THA compared with exercise to inform the trial protocol.

METHODS

Study design

We used an explorative qualitative design based on a constructivistic paradigm as data was co-constructed by the researchers and participants.[26] This study was reported in agreement with the Consolidated Criteria for Reporting Qualitative Research (COREQ)

checklist,[27] and preceded the Progressive Resistance Training Versus Total Hip Arthroplasty (PROHIP) trial.[28] The PROHIP trial was approved by The Regional Committees on Health Research Ethics for Southern Denmark (Project-ID: S-20180158) and registered on ClinicalTrials.gov (NCT04070027). This study was approved by The Danish Data Protection Agency (Journal No 18/23994), while no ethical approval was required according to the Danish Act on Research Ethics. Written informed consent was obtained from each participant in accordance with the Helsinki Declaration.

Sampling and participants

Participants were enrolled into three key stakeholder groups: patients, clinicians (orthopaedic surgeons and physiotherapists), and decision makers (**Figure 1**). Key stakeholders were engaged at the level of consultation to obtain input on several research decisions and implement the findings into our trial protocol[29].

Please insert Figure 1 about here

Patients were recruited consecutively by orthopaedic surgeons from the orthopaedic departments at Vejle Hospital and Odense University Hospital. The eligibility criteria was similar to the PROHIP trial to ensure a typical patient response [28]. Briefly, eligible patients were aged ≥50 years, diagnosed with clinical and radiographic hip OA, and considered eligible for THA.

A convenience sample of clinicians not involved in the design of the PROHIP trial with >2 years of clinical experience in treating patients with hip OA from

the orthopaedic and physiotherapy departments at the two hospitals were contacted personally face-to-face or by email and invited to participate in the study.

A purposive sample of decision makers with >2 years of political experience from the spectrum of political parties and relevant non-governmental organisations from the Region of Southern Denmark were approached by email and invited to participate in the study.

Data collection

Data were collected through open-ended, semi-structured focus group interviews allowing the advantage of dynamic group interactions.[30] Each interview included two to five key stakeholders, lasted between 90 to 120 minutes, and was conducted from September 2018 to March 2019 by a female physiotherapist (KST), MSc with 10 years of clinical orthopaedic experience and trained in qualitative methodologies. Prior to each focus group interview, the interviewers' profession was disclosed to the key stakeholders. The interviewer was neither affiliated with the PROHIP trial group nor had previous interaction with key stakeholders. Group specific open-ended semi-structured interview guides (**online Supplementary File 1**) were developed by the first author (TF) to explore topics related to the PROHIP trial.[31] The number of focus group interviews were not predetermined for the patients, whereas one interview was planned for the clinicians and decision makers due to pragmatic reasons. For the patients, the semi-structured interview guide was continuously adjusted after each focus group based on field notes made during the interviews by the first author. Data saturation was considered attained, if no new themes, perspectives, and knowledge developed within two consecutive interviews. All interviews were digitally audio-recorded, transcribed

verbatim, and translated into English by an independent linguist. The transcripts and findings were not returned to the key stakeholders for comments. All data were pseudo-anonymized and stored in digital format on a password-protected hospital server conforming to current data protection standards. The focus group interviews were performed face-to-face in undisturbed conference rooms at Vejle Hospital and Odense University Hospital, according to group status. The interviewer and the first author were present during all focus group interviews.

Key stakeholder characteristics were obtained using a participant-reported questionnaire. Additionally, the patient group completed the Oxford Hip Score (OHS)[32] and Hip disability and Osteoarthritis Outcome Score (HOOS).[33]

Data analysis

An independent qualitative researcher (CM) not affiliated with the PROHIP trial group conducted a thematic analysis to explore and identify patterns of meaning across the data set using an inductive approach with no predetermined themes.[34] This process involved coding and then abstracting connected data to common themes. Initially, line-by-line inductive coding was performed on interviews to define and develop a code list. Then the code list was used to code subsequent interviews deductively. However, according to the constant comparison method, new codes may emerge and will again be applied across all interviews.[35] Related codes were also further organized into code families. As the analysis progressed, coding shifted from descriptive to explanatory, resulting in a number of axial codes. Finally, a thematic network was developed.[36] The analysis was performed using Computer Assisted Qualitative Data Analysis software (CAQDAS, Atlas Ti, Version 8).

Implementation of findings into the trial protocol

After the data analysis was completed, findings were presented to the PROHIP trial group for implementation consideration. We assessed the feasibility of findings for implementation into the trial protocol and categorized these across relevant emerging domains. Disagreements were resolved by discussion until consensus.

Patient and public involvement

Patients or members of the public were not involved in the design, conduct, reporting or dissemination of this qualitative study, but constituted the PPI strategy used in the development of the PROHIP trial.[28]

RESULTS

We conducted 6 focus group interviews with 14 patients, 4 clinicians (2 orthopaedic surgeons and 2 physiotherapists), and 4 decision makers (**online Supplementary File 2**). Participant characteristics are presented in **Table 1**. Two main themes emerged from the thematic framework. *'Perceptions that may influence the management of hip osteoarthritis'* covered three supporting codes: Treatment without surgery is unlikely to lead to recovery; Clinician authority impacts the management narrative; The 'surgery versus exercise' debate. *'Considerations for a trial protocol in the current Danish healthcare context'* highlighted three supporting codes: Who is considered eligible for surgery; Facilitators and barriers for a clinical trial comparing surgery and exercise; Most important and meaningful outcomes for patients with hip osteoarthritis. (**Figure 2**).

Table 1. Characteristics of the Key Stakeholder Groups.*

Characteristic	Patients (N=14)	Clinicians (N=4)	Decision Makers (N=4)
Female sex — no. (%)	8 (57)	1 (25)	2 (50)
Age — yr	68.5 [51.0-80.0]	48.0 [38.00-52.00]	56.5 [23.0-68.0]
Height — m	1.72 [1.62-1.80]	-	-
Weight — kg	73.8 [61.0-100.0]	-	-
Body-mass index — kg/m^2	24.5 [20.2-31.3]	-	-
Duration of hip symptoms‡ — yr	2.3 [0.3-10.0]	-	-
Clinical and radiographic hip osteoarthritis — no. (%)	14 (100)	0 (0)	0 (0)
Previous total hip arthroplasty — no. (%)	3 (21)	0 (0)	0 (0)
OHS§	21.5 [10.0-38.0]	-	-
HOOS subscale scores¶			
Pain	42.5 [20.0-77.5]	-	-
Symptoms	32.5 [15.0-80.0]	-	-
Function in activities of daily living	47.8 [20.6-86.8]	-	-
Hip-related quality of life	31.3 [12.5-68.8]	-	-
Function in sports and recreation	25.0 [0-62.5]	-	-
Clinical profession — no. (%)			
Orthopaedic surgeon	-	2 (50)	-
Physiotherapist	-	2 (50)	-
Clinical experience – yr	-	16.0 [3.0-18.0]	-
Hospital affiliation — no. (%)			
Vejle Hospital	-	2 (50)	-
Odense University Hospital	-	2 (50)	-
Political experience – yr	-	-	5.0 [3.0-5.0]
Political affiliation — no. (%)			
The Liberal Party of Denmark (V)	-	-	1 (25)
The Danish People's Party (O)	-	-	1 (25)
The Social Democratic Party (A)	-	-	1 (25)
The Danish Rheumatism Association	-	-	1 (25)

* Values are median [range] unless otherwise indicated.

‡ Two patients had missing values.

§ The Oxford Hip Score (OHS) ranges from 0 to 48, with higher scores indicating better disease status.

¶ For all five subscales, the Hip disability and Osteoarthritis Outcome Score (HOOS) ranges from 0 to 100, with higher scores indicating better disease status.

Please insert Figure 2 about here

Perceptions that may influence the management of hip osteoarthritis

Treatment without surgery is unlikely to lead to recovery

Patients had high expectations of a complete reduction of hip pain, fast return to desired activities-of-daily-living and functional performance approximating their pre-symptomatic state after THA surgery.

> '*I find it important to get rid of the pain, but also to get back to being physically active. Those two are equally important to me. I think. Because it used to be such a big part of my life'* (Patient 3, age 60-69 years).

Patients had uncertain and/or sceptical expectations about exercise, but believed that exercise could lead to improvements.

> '*I have not been informed about the possibility of exercising the pain away*' (Patient 5, age 70-79 years).

Patients and decisions makers perceived exercise as a more appropriate treatment for mild to moderate stages of hip OA or as an adjunct to THA in the pre- and/or postoperative phases to improve the outcome of THA.

> '*But if a hip is in a better state, then there is still a possibility to improve the person's condition without surgery. At the early stages of hip deterioration, exercise may seem like the best way forward'* (Decision maker 3, age 60-69).

'*It is important to do exercise both before and after the surgery, to make your muscles as powerful as possible'* (Patient 1, age 60-69 years).

Patients with severe hip pain perceived themselves as highly disabled and considered any treatment without THA surgery unlikely to lead to their recovery.

'Having a defect hip is constraining both physically and mentally. Totally disabling.' (Patient 6, age 60-69 years).

'I don't believe that it is possible to remove the symptoms just by means of exercising. I don't believe that is possible' (Patient 7, age 50-59 years).

Clinician authority impacts the management narrative

Patients expressed a need to be guided verbally through the trial protocol and information by a competent and trustworthy clinician. In this regard, the orthopaedic surgeons were seen as the most authoritative clinician.

'When I consulted the orthopaedic surgeon, the doctor. We were told absolutely everything about it [THA surgery], and he does it very well. There was no doubt in my mind' (Patient 5, age 70-79 years).

Orthopaedic surgeons tended to describe THA as a core treatment, with exercise being considered as a postsurgical adjunct treatment, and thus reinforced the perception of

their status as the most authoritative clinician group by virtue of their control over the THA treatment narrative.

> '*It is quite clearly "the surgery of the century". If the surgery is made on the right patient, it is both a safe and effective surgery. The degree of satisfaction is generally very high, both seen from the patients and the surgeons' perspectives'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).

Patient respondents highlighted that both orthopaedic surgeons and physiotherapist tended to use a management narrative suited to their preferred treatment and at times these narratives were juxtaposed.

> '*The orthopaedic surgeon said: You can get a new hip, but I suggest you try to exercise for a period and then you can return to me when the pain gets too severe. The physiotherapists, they are very eager avoid surgery. At least the ones I have met, they have told me that I can exercise the pain away'* (Patient 2, age 50-59 years).

Clinicians were aware of the potential impact of their authority on patient perceptions of treatment effectiveness. This practice was viewed with concern as the PROHIP trial relies on trial participants perceiving THA and exercise as equal treatments.

> *'It is possible to talk about the different possibilities in a fairly objective way through a standardized text. And then it is important not to laugh… when the patient asks us, what would you choose?'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).

The 'surgery versus exercise' debate

Clinicians were aware of an ongoing discourse, pitching other surgical procedures and exercise against one another. Both the orthopaedic surgeons and physiotherapists agreed that fuelling a debate of choosing one approach over another was not a desirable in the context of the PROHIP trial.

> '*This became quickly exercise against surgery, very much head-to-head and completely out of context of reality. We did not recognize, nor in the media the picture they created with the interpretation that you should rather exercise or carelessly get surgery'* (Clinician [Physiotherapist 2], age 30-39 years).

Rather than pitching the two treatments against one another, an orthopaedic surgeon highlighted that it was important to develop a narrative emphasizing surgery and exercise as fundamentally different, yet complementary.

> '*But the question is whether surgery and exercise can be considered equal. Because surgery is dangerous, exercise is not very dangerous. Surgery is invasive, irreversible. Exercise is something you try out, and if*

it does not work, then you can have surgery' (Clinician [Orthopaedic surgeon 2], age 40-49 years)

Considerations for a trial protocol in the current Danish healthcare context

Who is considered eligible for surgery?

Patients highlighted variations in the nature of hip OA, and perceived that radiographic findings were the primary indication criteria for determining treatment selection.

'*If a person is in pain and has a lot of cartilage left, then this person should be offered exercise and surgery should be postponed.* (Patient 1, age 60-69 years).

Physiotherapists questioned the indication criteria for THA used in the clinical assessment, since they had observed a substantial variation in hip pain and functional performance among patients prior to surgery.

'*At the information meetings, we see people who walk normally, and we then wonder why these people need new hips, because this person does not seem to be in pain, nor to be functionally impaired'* (Clinician [Physiotherapist 1], age 50-59 years).

For orthopaedic surgeons, improvements from exercise was associated with an incorrect diagnosis or considered as secondary to hip OA.

> '*You need to be absolutely certain that the patient suffers from osteoarthritis. I believe that the patients who experience improvements by exercise, they suffer from a problem with the soft tissue. Something they have had in any circumstances or is secondary to the osteoarthritis'*
> (Clinician [Orthopaedic surgeon 1], age 50-59 years).

Facilitators and barriers for a clinical trial comparing surgery and exercise

Based on responses, it seemed that younger patients were less likely to select surgery as first-line management. This appeared to be driven by health beliefs and concerns for the durability of THA. Patients perceived both THA and exercise as treatments to provide pain management without usage of analgesics. However, THA was clearly seen as a means to abolish severe pain, whereas less clarity was observed for exercise as residual hip pain was viewed as both a driver and barrier for continued adherence. Exercise was considered a low-risk treatment, while THA was perceived as a last resort treatment with a risk of serious adverse events. Patients indicated that improvements derived from exercise would encourage to continued adherence, whereas a failure of exercise to provide sufficient improvements in hip pain and activities-of-daily living were a driver for THA. Patients were more likely to undergo THA once presented with radiographic findings visualizing degenerative changes and/or progression of OA. Finally, patients considered establishing and maintaining exercise habits as important, and emphasized the importance of supervision to provide clinical expertise and motivation during exercise sessions. Potential facilitators and barriers for THA surgery and exercise in the PROHIP trial are summarized in **Table 2**.

Table 2. Facilitators and barriers for surgery and exercise in the Progressive Resistance Training Versus Total Hip Arthroplasty (PROHIP) trial.

	Surgery	Illustrative quote(s)	**Exercise**	Illustrative quote(s)
Facilitators	Severe hip pain	*'I am currently in a lot of pain, and I am looking forward to being released from that pain'* (Patient 1, age 60-69 years).	Patient age	*'…people who feel too young to have hip surgery… because they see themselves as being physically active and capable of exercising the pain away'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).
	Low quality-of-life	*'I cannot walk more than 100 meters, even with a cane'* (Patient 6, age 60-69 years).	Pain management without analgesics	*'Those four exercises are very valuable to me… I almost never take pills'* (Patient 2, age 50-59 years).
	Ineffective first-line management	*'I have not been able to reduce my pain by means of exercise or physical activity, I need to have surgery to be able to live a tolerable life'* (Patient 6, age 60-69 years).	Low risk of adverse events	*'It [exercise] will not harm them, and if they see improvements that is great.'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).
	Analgesics dependency	*'I ate so many pills, we agreed that something had to be done'* (Patient 2, age 50-59 years). *'They foresee that they will not be forced to take pills and at the same time, they will get well. Therefore, they choose surgery'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).	Perception of improvement	*'If I was able to feel a signification improvement after the 12-weeks exercise program, then I would be motivated to continue'* (Patient 5, age 70-79 years).
	Diagnostic imaging	*'When I got here the second time and saw the x-rays, I saw how much cartilage had disappeared since last time – in that short period of time - I said to myself that the actual bone may be next in line. I said to myself that there was no point in waiting any longer'* (Patient 2, age 50-59 years).	Habitualised exercise	*'Well, naturally I have spoken to other people about exercise, and I have asked them why they do not exercise, and they have a hard time getting started with it. Then I suggest that we go together, because the social aspect of it is very important, for some people at least'* (Patient 11, age 70-70 years).
	Loss of livelihood	*'I may be rejected from the labour market because of my age, and I am not entitled to pension. So, I cannot afford not having surgery now'* (Patient 6, age 60-69 years).	Supervision	*'It is also beneficial to have the presence of a professional person who can inform us about how the specific exercises help you, …where we are supposed to feel the pain if we do them correctly, which muscle is used and how to recognize this muscle'* (Patient 4, age 70-79 years).
			Context of exercise	*'I would appreciate to be in a place together with a group of people,*

				where one person would instruct the others. And if you meet with a group of people several times, then you feel like being part of a community, and you can talk about the same things… That motives me' (Patient 2, age 50-59 years).
			Tracking and gamification	*'It matters a lot, I think. Just like when you use a pedometer or a health app, I like that. I like to be able to see the result of my efforts… like Endomondo – get notified about having completed something'* (Patient 3, age 60-69 years).
Barriers	Patient age	*'…the uncertainty about whether the hip will last 10, 15, 20 years, and whether I will be able to get a new replacement at that time'* (Patient 2, age 50-59 years). *'I am also concerned about the durability of the total hip arthroplasty, because wearing out an artificial hip would result in a second surgery'* (Clinician [Physiotherapist 1], age 50-59 years).	Too much or too little hip pain	*'I have to say that when you are in pain, it is easy to exercise. But then when you don't feel pain, then you tend to forget to do your exercises one day, and then next day and so on. So, when everything is fine, then I have a hard time getting motivated to do exercises'* (Patient 1, age 60-69 years). *'Some people benefit a lot from exercise, but other people come back to me and explain that exercise only worsened the pain'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).
	Risk of adverse events	*'A small risk of the surgery not being successful. That the pain ends up being much worse than before. I think that we all fear that… It would be so devastating if that should happen to us'* (Patient 2, age 50-59 years). *'Well, if the result is a foot drop, then I will not consider the surgery a success'* (Patient 7, age 50-59 years).	Low motivation	*'What is bad for me is that I always come up with a good excuse for not going… working out at home does not work for me, it is better if I go to a fitness centre with other people around'* (Patient 3, age 60-69 years).
			Continuity interruptions	*'…doing exercises in the fitness centre. But, I have also… Maybe I have taken some breaks, I could have put more efforts into it'* (Patient 3, age 60-69 years).

Most important and meaningful outcomes for patients with hip osteoarthritis

Patients and clinicians indicated change in hip pain and hip function as the most important outcomes to evaluate the treatment effect of surgery or exercise.

> *'My biggest problem is that I feel pain in all the different kinds of movements I do. No matter what kind of movement I do, I feel the pain'* (Patient 12, age 50-59 years).

Patients and clinicians also highlighted quality-of-life, functional performance (gait), patient acceptable symptom state, muscle strength, treatment crossover (i.e. number of THA surgeries in the exercise group), return-to-work, and leg-length discrepancy as other meaningful outcomes to measure in the PROHIP trial.

Methodological implementation strategies for the trial protocol

Based on our data, we identified four domains for methodological implementation strategies to optimize the PROHIP trial protocol, and these were: patient 'buy in', enrolment strategies, patient information materials, and important clinical outcomes. The domains, their thematic association and supporting coding are illustrated in **Table 3**.

Table 3. Methodological implications derived from the listed domains, main themes and supporting codes used to inform the Progressive Resistance Training Versus Total Hip Arthroplasty (PROHIP) trial protocol.

Domain	Main theme	Supporting code	Methodological implications for the PROHIP trial protocol
Patient 'buy in'	Perceptions that may impact the management of hip osteoarthritis	Treatment without surgery is unlikely to lead to recovery	Guided implementation of a parallel observational study investigating the generalizability of the clinical trial, since many patients probably may decline participation in the trial.
		Clinician authority impacts the management narrative	Guided development of retention procedures (i.e. instructions of study personnel to encourage patient completion), statistical analysis plan (i.e. handling of missing data, sensitivity and exploratory analyses, and subgroup and causal mediation analysis), and exercise protocol (i.e. effective supervision and habitualised exercise protocol).
		The 'surgery versus exercise' debate	
	Considerations for a trial protocol in the current Danish healthcare context	Who is considered eligible for surgery?	
		Facilitators and barriers for a clinical trial comparing surgery and exercise	
Enrolment strategies	Perceptions that may impact the management of hip osteoarthritis	Clinician authority impacts the management narrative	Guided development of instruction and training strategy in the enrolment procedures.
		The 'surgery versus exercise' debate	Guided implementation of generic guidance and neutral narrative during enrolment procedures to provide verbal information about the trial.
	Considerations for a trial protocol in the current Danish healthcare context	Who is considered eligible for surgery?	Guided clinician roles in enrolment procedures (i.e. eligibility assessment, provider of trial information to the patients) and selection of an independent clinician group to provide detailed verbal information about the trial to facilitate communication of clinical equipoise.

Patient information materials	Perceptions that may impact the management of hip osteoarthritis	Treatment without surgery is unlikely to lead to recovery	Guided and informed content for the written patient materials and this included information on current evidence of treatment effects for surgery and exercise, trial objective and procedures, randomisation process, content of baseline and follow-up sessions, risks and harms, treatment crossover and withdrawal procedures, clinical implications and funding.
		Clinician authority impacts the management narrative	
		The 'surgery versus exercise' debate	
	Considerations for a trial protocol in the current Danish healthcare context	Facilitators and barriers for a clinical trial comparing surgery and exercise	Guided development of the neutral narrative used in the written patient materials to facilitate communication of clinical equipoise.
Important clinical outcomes	Perceptions that may impact the management of hip osteoarthritis	Treatment without surgery is unlikely to lead to recovery	Guided selection of hip pain and function as primary outcome.
	Considerations for a trial protocol in the current Danish healthcare context	Most important and meaningful outcomes for patients with hip osteoarthritis	Guided selection of hip-related quality-of-life and functional performance (i.e. gait function) as key secondary outcomes
			Guided selection of patient acceptable symptom state and muscle strength as exploratory outcomes.

Patient 'buy in'

We identified sampling bias as a potential external validity threat in the clinical trial. In response, a parallel observational study was conceptualized to investigate the generalizability of the clinical trial, since many patients probably may decline participation in the trial. Additionally, we addressed facilitators and barriers for surgery and exercise among patients that could systematically affect retention rates and lead to treatment crossover in the clinical trial. Consequently, in an effort to optimize retention and reduce treatment crossovers, we developed a more focused retention procedure (i.e.

instructions of study personnel to encourage patient completion) and tailored exercise protocol with a greater focus on effective supervision during exercise sessions and implementation of a habitualised exercise protocol. Furthermore, a nuanced statistical analysis plan was prioritized in regards to handling of missing data, sensitivity and exploratory analyses, subgroup and causal mediation analysis.

Enrolment strategies

We identified preconceived beliefs and perceptions among clinicians as a potential threat to sampling in the trial. In response, we implemented an instruction and training strategy for orthopaedic surgeons and project coordinators in standardized verbal information about the trial to facilitate communication of equipoise during enrolment procedures. Focus was placed on the creation of a neutral narrative to be used when verbal information was provided during enrolment. To encourage clinical equipoise, we provided guidance to clinicians with respect to their roles during the enrolment process and an independent clinician group was involved to provide detailed verbal information about the trial.

Patient information materials

We identified preconceived beliefs and perceptions among patients that needed to be addressed in the written patient materials, which covered current evidence of treatment effects for surgery and exercise, trial objective and procedures, randomization process, content of baseline and follow-up sessions, risks and harms, treatment crossover and withdrawal procedures, clinical implications using a balanced a neutral narrative.

Important clinical outcomes

Patient and clinician responses led to three distinct adaptations to the outcomes in the trial protocol. We adopted hip pain and function as primary outcome and implemented hip-related quality-of-life and functional performance (i.e. gait function) as key secondary outcomes. We also included patient acceptable symptom state and muscle strength as exploratory outcomes.

DISCUSSION

Main findings

This novel qualitative PPI study explored patient, clinician, and decision maker perceptions of a clinical trial evaluating the effectiveness of THA compared with exercise to inform protocol development. Our findings showed that patients with severe pain perceived themselves as highly disabled and considered treatment without THA unlikely. Patients expected a fast recovery with complete reduction of hip pain, restored functional performance, and return to activities-of-daily-living after THA, while more uncertainty and scepticism about the effects of exercise was expressed. All key stakeholders, except the physiotherapists, deemed exercise as most appropriate for mild to moderate stages of hip OA or as an adjunct treatment to THA. We found that clinicians tended to use a management narrative suited to their preferred views on diagnostic eligibility, treatment selection, and relative treatment effectiveness. We also identified several facilitators and barriers for surgery and exercise, which mainly included patient age, pain management without analgesics, risk of adverse events, perception of improvement, diagnostic imaging, supervision, and habitualised exercise. Patients and clinicians indicated change in hip pain and hip function as the most

important outcomes to evaluate the effectiveness of surgery or exercise. Based on these findings, we included a parallel observational study investigating the generalizability, developed an enrolment procedure using generic guidance and balanced narrative conveyed by an independent clinician to facilitate communication of clinical equipoise, and adopted change in hip pain and function as the primary outcome in the PROHIP trial protocol.[28]

Comparison with previous studies and interpretation of findings

In line with our findings, a recent qualitative study also found clear and high expectations for surgery among Swedish patients with knee or hip OA.[37] However, several patients reconsidered their treatment options and changed attitudes towards either accepting or declining surgery after participation in a digital non-surgical program, emphasizing the importance of providing sufficient information about management options to facilitate shared-decision making.[37] Our findings also indicated that patients displayed uncertainties about the potential benefits of exercise. This could be driven by uncertainties and lack of knowledge about the effectiveness of exercise amongst clinicians,[38] and due to less than 40% of the patients are recommended or referred to first-line management.[13] Based on previous qualitative studies,[39 40] recovery expectations among patients in this study were related to the criterion of resolution for surgery and redefinition for exercise, which could indicate that patients accepting participation may differ from those declining participation in our clinical trial in terms of recovery expectations, hip pain, and functional status potentially reducing the generalizability of the PROHIP trial.

Our findings showed that clinicians tended to use a management narrative suited to their preferred treatment. This strategy is in contrast to the information needs desired by patients with hip OA during clinical encounters,[41] and since clinicians have a considerable influence on the attitudes and beliefs of patients this may result in misconceptions and uninformed decisions.[41 42] This suggests that both orthopaedic surgeons and physiotherapists could sway patient opinions about THA surgery and exercise in either direction during enrolment procedures in the PROHIP trial by highlighting the benefits of their preferred treatment option, whilst simultaneously accentuating the limitations of the other treatment possibly leading to sampling bias.

In consistency with previous studies,[43-45] clinicians in this study displayed conflicting views on the indication criteria for THA. More interestingly, patients in this study perceived findings or progression of hip OA on radiographic imaging to be the primary determinant for THA, although there is low agreement between hip pain and radiographic hip OA.[46] This may suggest that the patients still have an outdated 'wear-and-tear' conception of hip OA that contradicts up-to-date insights on pathogenesis, considering OA as a whole-joint disease.[47] This misconception of OA has previously been shown to be facilitated by clinicians' language and explanations,[48] which emphasize the need of neutral and evidence based information during enrolment in the PROHIP trial.

In line with the Osteoarthritis Research Society International recommendations,[49] our findings highlighted change in hip pain and function as the most important outcome. Several patient-reported outcome measures are available to evaluate pain and functional status in patients with hip OA.[49 50] However, the OHS

appears to have the best validated clinometric properties,[50] indicating this as an appropriate primary outcome measure.

Limitations and strengths

Our study has limitations and strengths. A major limitation is that we conducted only one focus group interview for both the clinicians and decision makers reducing the likelihood of data saturation. Thus, we may have missed important perspectives in these key stakeholder groups. However, we considered the patients perceptions as the most important for our clinical trial. Another limitation is that 3 out of 14 patients had previously undergone THA surgery, which may have influenced their perceptions, as previous surgery has been suggested to affect patient expectations.[37] Furthermore, all patients were scheduled for THA surgery prior to their participation in this study, which further could have primed them to be in favour of surgery. In contrary, this may increase generalizability of our findings as previous THA is not used as an exclusion criterion in the PROHIP trial,[28] and all patients will be informed that they are considered eligible for a THA prior to accepting participation. Strengths of our study comprise the variety in the sample of patients interviewed, including females and males of varying ages and different levels of hip pain and disability recruited from both a regional hospital and a university hospital, thereby increasing the generalizability of our findings for this group. Additionally, we interviewed three key stakeholder groups involved in receiving and delivering treatment and making decisions about the management of hip OA to provide multiple perspectives and extend the scope of the findings. Lastly, an independent researcher conducted the data analysis from reading and coding of the transcripts to development of themes before presenting the findings to

the other authors, thus decreasing the possibility of interpretation bias due to clinical interest of conflict.

CONCLUSION

Patients and clinicians had beliefs and perceptions on the management of hip osteoarthritis that could possibly affect enrolment procedures resulting in sampling bias and reduced generalizability of our clinical trial. Moreover, facilitators and barriers for surgery and exercise could influence retention rates and treatment crossovers in the trial. Therefore, we implemented three main strategies to improve methodological rigorousness of our trial protocol. Firstly, we added an observational study investigating the generalizability to address a potential low enrolment rate. Secondly, we developed an enrolment procedure using generic guidance and balanced narrative conveyed by an independent clinician to facilitate communication of clinical equipoise. Thirdly, we adopted change in hip pain and function as the primary outcome. Our findings suggest that future comparative clinical trials evaluating surgical and non-surgical management should explore key stakeholder perceptions of the treatments of interest prior to designing the trial protocol to reduce bias in the studies.

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Traumatology, Odense University Hospital for their involvement in the recruitment of patients.

Authors' contributions

Conception and design: TF, IM, LRM, SO, KGI, and CM designed the study. Analysis and interpretation of the data: TF, KST, and CM. Drafting of the article: TF, KGI and CM. Critical revision of the article for important intellectual content: TF, KST, SO, IM, LRM, KGI, and CM. Final approval of the article: TF, KST, SO, IM, LRM, KGI, and CM. Obtaining of funding: TF and KGI. Collection and assembly of data: TF and KST. Development of interview guides: TF.

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Competing interest

All authors have completed the ICMJE disclosure form available at www.icmje.org/disclosure-of-interest/ and declare that we have no competing interest for the submitted work.

Ethics approval

This study was approved by The Danish Data Protection Agency (Journal No

18/23994), while no ethical approval was required according to the Danish Act on Research Ethics.

Data availability statement

Data are available upon reasonable request. Data comprise digital voice recordings of each focus group interview, verbatim transcriptions in Word files, and participant-reported questionnaire responses in PDF files. These data are stored in a password-protected hospital server only accessible to the researchers. Digital audio recordings and individual participant-reported questionnaire responses contain identifiable data and will not be made available on request to maintain participant anonymity. Transcriptions of each focus group interview and the participant characteristics data-set with de-identified participant data may be made available upon reasonable request.

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FIGURE LEGENDS

Figure 1. Eligibility criteria for each key stakeholder group: Patients, Clinicians and Decision makers.

Figure 2. Main themes and supporting codes identified in focus groups with patients with hip osteoarthritis considered eligible for total hip arthroplasty, clinicians (orthopaedic surgeons and physiotherapists) from orthopaedic and physiotherapy departments, and decision makers from a political party or non-governmental organisation.

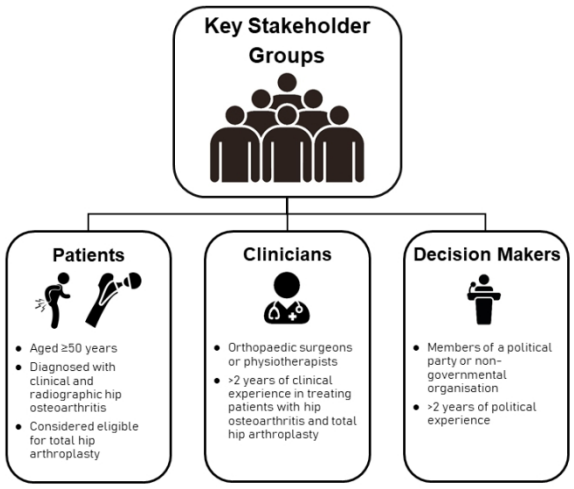

Figure 1. Eligibility criteria for each key stakeholder group: Patients, Clinicians and Decision makers.

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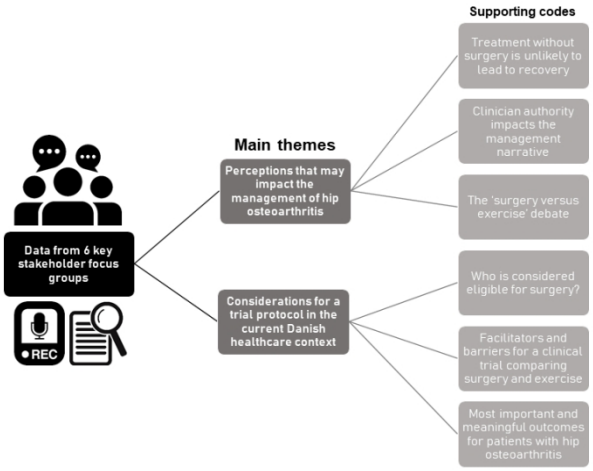

Figure 2. Main themes and supporting codes identified in focus groups with patients with hip osteoarthritis considered eligible for total hip arthroplasty, clinicians (orthopaedic surgeons and physiotherapists) from orthopaedic and physiotherapy departments, and decision makers from a political party or non-governmental organisation.

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Online Supplementary File 1A. Interview guide for the patient group

Topic	Main question	Supplementary probing questions
Treatment for hip osteoarthritis (THA surgery)	What do you think about surgery as treatment for hip osteoarthritis?	1. When and why did you start considering surgery as a treatment option? 2. How was the decision of surgery taken? 3. When do you know when you are ready for surgery? (physically and mentally) 4. How do you think the information was about the surgery, including risks and other treatments? 5. What expectations do you have for the surgery? 6. What do you consider to be the advantages of surgery? 7. What do you consider to be the disadvantages of surgery? 8. What is the main reason/motivation to undergo surgery? (or declining surgery)
Treatment for hip osteoarthritis (exercise)	What do you think about exercise as treatment for hip osteoarthritis?	9. What treatments have you otherwise tried before surgery? (type, systematics and durations) 10. How have your experiences been with exercise? (type, systematic, duration and effect) 11. How have your experiences been with other treatments? (effect) 12. What do you consider to be the advantages of exercise? 13. What do you consider to be the disadvantages of exercise?
Participation in a clinical trial	CASE DESCRIPTION (Detailed information about the PROHIP trial)	14. What do you think about participating in a trial where you are randomly being assigned to surgery (total hip arthroplasty) or exercise (with the option of later surgery if needed)? 15. What do you consider to be of importance to whether you would participate in the trial? 16. What would affect your considerations about participating in the trial?
Patient material and information	How would you prefer to receive information about this trial?	17. When do you think, it is best to present the information about the trial for potential participants? 18. What do you think the patient information should contain?
Exercise protocol	If you were to participate in 12-weeks of exercise, how do think this should be?	19. What do you think about resistance training in machines? 20. What significance do the physical frames have for you? (location, duration, and environment) • How many times a week is it possible for you to exercise? • How long would you spend on one training session? 21. What significance does it have for you, if you have to drive for the training sessions? 22. What significance does it have for you whether a physiotherapist supervises the training sessions? 23. How do you think you can continue to exercise on your own after a 12-week training program?

Outcomes	If we were to measure the effect of your surgery/exercise program – What do you consider is the most important thing to measure upon?	24. What else do you think is important to measure upon? 25. What is your main problem right now (due to hip osteoarthritis)? 26. How would you describe whether a surgery has been successful? 27. How would you describe whether an exercise program has been successful? 28. What do you think about the questionnaires you filled out? (Relevance, number of items, etc.)

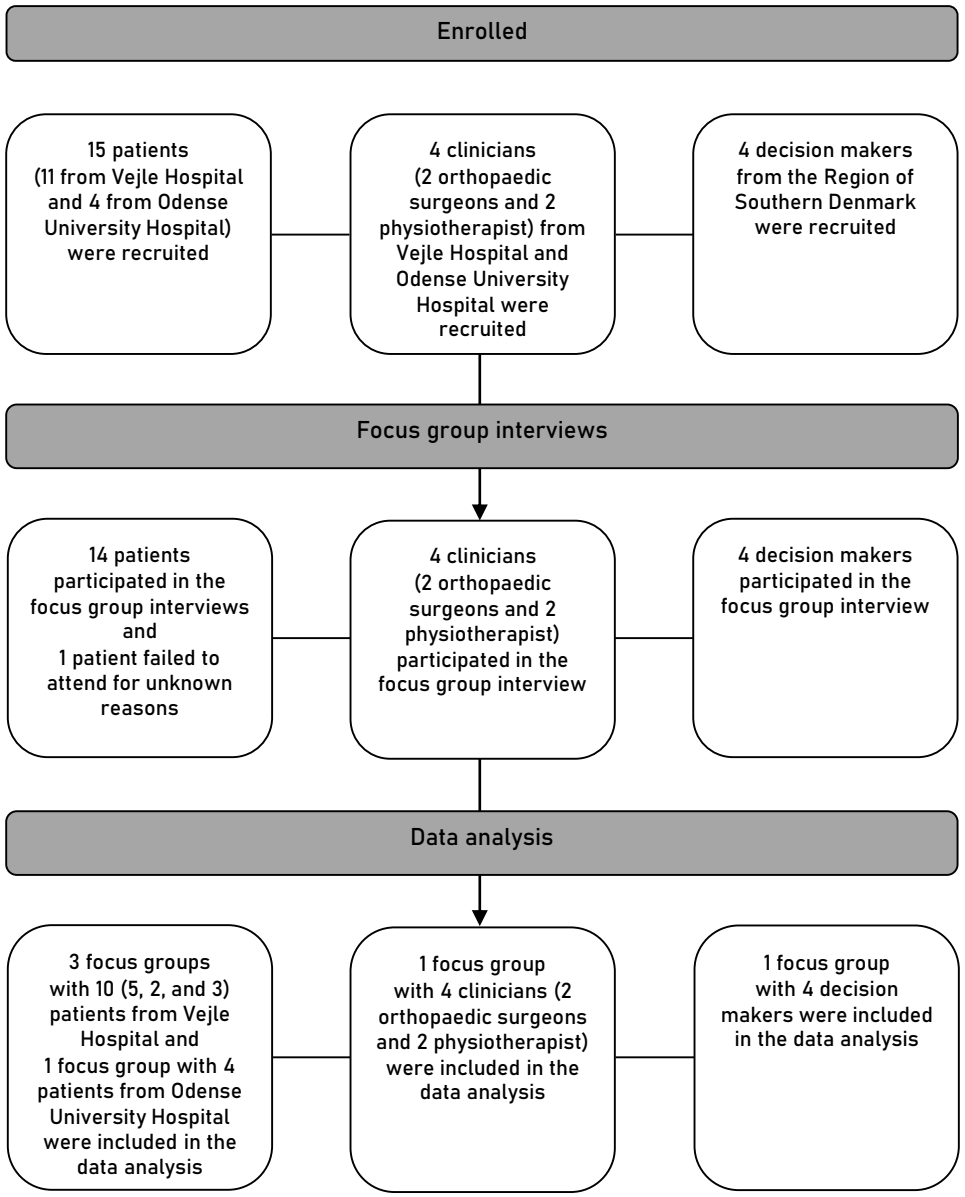
Online Supplementary File 1B. Interview guide for the clinician group

Topic	Main question	Supplementary probing questions
Treatment for hip osteoarthritis (surgery)	What do you think about surgery as treatment for hip osteoarthritis?	1. How do you experience the patients' perception of surgery (THA) as treatment for hip osteoarthritis? 2. What do you experience patients with hip osteoarthritis indicate as main reason/motivation to undergo surgery? 3. What do you consider to be the advantages of surgery? 4. What do you consider to be the disadvantages of surgery? 5. When do you think a patient with hip osteoarthritis is eligible for a THA?
Treatment for hip osteoarthritis (exercise)	What do you think about exercise as treatment for hip osteoarthritis?	6. How do you experience the patients' perception of exercise as treatment for hip osteoarthritis? 7. What do you experience patients with hip osteoarthritis indicate as main reason/motivation in choosing exercise rather than surgery? 8. What do you consider to be the advantages of exercise? 9. What do you consider to be the disadvantages of exercise? 10. When do you think a patient with hip osteoarthritis should try exercise instead of getting a THA? 11. How do you interpret the results of this trial?[20] 12. How have you experienced the debate on surgery (total knee arthroplasty) and exercise? 11. How do you think this debate affects the patients? 12. What do you consider to be the advantages of this debate? 13. What do you consider to be disadvantages of this debate?
Participation in a clinical trial	CASE DESCRIPTION (Detailed information about the PROHIP trial)	14. What is your perception of a trial, in which patients are randomly assigned to surgery (THA) or exercise (with the option of later surgery if needed)? 15. What challenges do you consider there are in recruiting for a trial, in which patients are randomized to THA or resistance training? 16. How do you think it is ensured that clinician (e.g. orthopedic surgeons, physiotherapists, and nurses) do not color the patients' decision to participate? 17. How are orthopedic surgeons and physiotherapists motivated to participate in the trial? 18. How is collaboration between surgeons and physiotherapists in relation to the project created? 19. How would you conduct the screening and recruitment procedure in this trial? 20. What do you consider as of importance for whether patients with hip osteoarthritis will participate in the study?
Patient material and information	How do you think the patient information regarding the trial should be presented for potential participants?	21. When do you think, it is best to present the information about the trial for potential participants?

Exercise protocol	How do you think the exercise intervention should be conducted in the trial?	22. What exercises do you think are relevant to include in the exercise program? 23. How long do you think one training session should last? 24. How do you think we will get the patients to continue to exercise after the 12-week intervention period?
Outcomes	Which outcome do you consider to be the primary to measure in patients with hip osteoarthritis?	25. Which secondary outcomes do you consider to be important to measure in patients with hip osteoarthritis? 26. What do you experience patients with hip osteoarthritis indicate as being the primary problem (symptoms/limitations) that is of importance to the treatment? 27. How would you describe whether surgery (THA) has been successful? 28. How would you describe whether exercise has been successful?

Online Supplementary File 1C. Interview guide for the decision maker group

Topic	Main question	Supplementary probing questions
Treatment for hip osteoarthritis (surgery)	What do you think about surgery as treatment for hip osteoarthritis?	1. How do you experience the patients' perception of surgery (THA) as treatment for hip osteoarthritis? 2. What do you consider to be the advantages of surgery? 3. What do you consider to be the disadvantages of surgery?
Treatment for hip osteoarthritis (exercise)	What do you think about exercise as treatment for hip osteoarthritis?	4. How do you experience the patients' perception of exercise as treatment for hip osteoarthritis? 5. What do you consider to be the advantages of exercise? 6. What do you consider to be the disadvantages of exercise? 7. How do you interpret the results of this trial?[20] 8. How do you think we can avoid this trial to encounter similar diverse attitudes from the "media"/colleagues? 9. How have you experienced the debate on surgery and exercise?
Participation in a clinical trial	CASE DESCRIPTION (Detailed information about the PROHIP trial)	10. What is your perception of a trial, in which patients are randomly assigned to surgery (THA) or exercise (with the option of later surgery if needed)? 11. What challenges do you consider there are in recruiting for a trial, in which patients are randomized to THA or resistance training? 12. In case, the effect of resistance training is lower than surgery (THA), but withholds patients from undergoing surgery because the patients consider the non-surgical treatment as successful - how would you interpret the results? 13. What ethical considerations do you think are in this trial?
Patient material and information	What do you think the patient information should contain?	14. How would you prefer to receive information about this trial? (Content and method) 15. When do you think, it is best to present the information about the trial for potential participants?
Implementation of findings	Which barriers and facilitators, do you think, affect the implementation of the results from the trial into clinical practice?	16. What consequences do you think the trial may have politically in relation to the treatment of patients with hip osteoarthritis? 17. What consequences do you think the trial may have on clinical practice? 18. What challenges do you think there may be in implementing the results from the trial into clinical practice? 19. Which factors do you think will be decisive for a successful implementation of the results from the trial into clinical practice? 20. How do you think that we may optimize the implementation of the results from the trial into clinical practice?



Online Supplementary File 2. Flowchart of key stakeholder participants in the study.

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	7
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	7
Occupation	3	What was their occupation at the time of the study?	7
Gender	4	Was the researcher male or female?	7
Experience and training	5	What experience or training did the researcher have?	7
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	7
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	7
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	7
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	5 + 8
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	6-7 + Figure 1
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	6-7
Sample size	12	How many participants were in the study?	9 + Table 1
Non-participation	13	How many people refused to participate or dropped out? Reasons?	SuppFile 2
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	8
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	8
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	9 + Table 1
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	7 + SuppFile 1
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	7
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	7-8
Field notes	20	Were field notes made during and/or after the inter view or focus group?	7
Duration	21	What was the duration of the inter views or focus group?	7
Data saturation	22	Was data saturation discussed?	7 + 26
Transcripts returned	23	Were transcripts returned to participants for comment and/or	8

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	8
Description of the coding tree	25	Did authors provide a description of the coding tree?	9 + Figure 2
Derivation of themes	26	Were themes identified in advance or derived from the data?	8
Software	27	What software, if applicable, was used to manage the data?	8
Participant checking	28	Did participants provide feedback on the findings?	8
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	11-19+Table2
Data and findings consistent	30	Was there consistency between the data presented and the findings?	9-23 + Table 2
Clarity of major themes	31	Were major themes clearly presented in the findings?	9-24+ Figure2
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	9-26+ Figure2

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

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BMJ Open

Patient and public involvement to inform the protocol of a clinical trial comparing total hip arthroplasty with exercise: An exploratory qualitative case study

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Article Type: Original research article

Patient and public involvement to inform the protocol of a clinical trial comparing total hip arthroplasty with exercise: An exploratory qualitative case study

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ABSTRACT

Objective: To explore patient, clinician, and decision maker perceptions on a clinical trial evaluating the effectiveness of total hip arthroplasty (THA) compared with exercise to inform the trial protocol.

Design and Methods: This is an exploratory qualitative case study using a constructivistic paradigm. Participants were enrolled into three key stakeholder groups: patients eligible for THA, clinicians, and decision makers. Focus group interviews were conducted according to group status using semi-structured interview guides. Interviews were recorded, transcribed verbatim, and thematic analysed.

Findings: We conducted 4 focus group interviews with 14 patients, 1 focus group interview with 4 clinicians (2 orthopaedic surgeons and 2 physiotherapists), and 1 focus group interview with 4 decision makers. Two main themes were generated. *'Treatment expectations and beliefs impact management choices'* covered three supporting codes: Treatment without surgery is unlikely to lead to recovery; Clinician authority impacts the management narrative; The 'surgery versus exercise' debate. '*Factors influencing clinical trial integrity and feasibility'* highlighted three supporting codes: Who is considered eligible for surgery?; Facilitators and barriers for surgery and exercise in a clinical trial context; Improvements in hip pain and hip function are the most important outcomes.

Conclusions: Based on key stakeholder treatment expectations and beliefs, we implemented three main strategies to improve the methodological rigorousness of our trial protocol. Firstly, we added an observational study investigating the generalizability to address a potential low enrolment rate. Secondly, we developed an enrolment procedure using generic guidance and balanced narrative conveyed by an independent

clinician to facilitate communication of clinical equipoise. Thirdly, we adopted change in hip pain and function as the primary outcome. These findings highlight the value of patient and public involvement in the development of trial protocols to reduce bias in comparative clinical trials evaluating surgical and non-surgical management.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This qualitative patient and public involvement study was used to inform the protocol of a randomised controlled trial evaluating the effectiveness of total hip arthroplasty compared with exercise.
- Focus group interviews were performed with patients, clinicians, and decision makers to provide multiple perspectives and extend the scope of the findings.
- An independent qualitative researcher conducted the data analysis to improve neutrality in the interpretation and development of themes and supporting codes.
- Only one focus group interview was conducted for each of the groups with clinicians and decision makers due to time limitations. This may impact the certainty of achieving data saturation in these two responder groups.
- All participants in the patient group were scheduled for total hip arthroplasty and 3 out of 14 had previously undergone this procedure, which may have influenced their perceptions.

Keywords

Hip Osteoarthritis, Total Hip Arthroplasty, Exercise, Patient and Public Involvement, Qualitative Study

INTRODUCTION

Hip osteoarthritis (OA) is a major cause of pain, disability, and decreased quality-of-life[1]. The overall prevalence of hip OA is 11%,[2] and the disorder is the leading reason for undergoing total hip arthroplasty (THA) surgery.[3] The number of THAs performed each year has increased dramatically over the past decade with more than one million procedures annually undertaken worldwide.[3] THA is considered an effective treatment to reduce pain, improve physical function, and increase quality-of-life for severe hip OA.[4 5] However, there is a risk of severe complications and up to 23% of the patients report long-term residual pain after THA surgery.[3 6]

Guidelines recommend exercise and patient education as first-line treatment in the management of hip OA.[7 8] Specifically, progressive resistance training (PRT) appears to provide moderate improvements in patient-reported outcomes and functional performance even in patients with severe hip OA.[9 10] Furthermore, exercise and patient education might postpone the need for surgery and reduce patients' willingness to undergo THA,[11 12] but less than 40% of the patients are recommended or referred to first-line treatment.[13] Despite the large number of THA surgeries performed annually, no clinical trial has investigated the comparative effectiveness of THA and non-surgical treatment in the management of hip OA.[14] This comparison is of importance as non-surgical treatment has been shown to be a viable alternative to surgery for many musculoskeletal disorders.[15]

Several clinician and patient barriers to participation in clinical trials have been identified. Main clinician barriers comprise lack of support staff and inadequate research training and difficulty with the consent procedure, while notable patient barriers include treatment preferences, worry caused by uncertainty, and concerns about

information and consent.[16] Moreover, clinical trials comparing surgical procedures with non-surgical treatment have suffered from low enrolment rates and difficulties in retaining participants to their allocated treatments.[17-21] With limited participation in these sort of clinical trials, a risk exists for research inefficiency and possibly biased findings that may drive clinical decision making.[22]

Patient and public involvement strategies involve key stakeholders in the design, conduct, and dissemination of research.[23 24] Evidence suggests that patient and public involvement strategies have the potential to increase enrolment rates of participants and improve selection of outcome measures.[23 24] However, only few clinical trials within the orthopaedic area have reported use of patient and public involvement,[25] although more than 90% of the authors of surgical trials claim some incorporation of such strategies .[23] Thus, based on the benefits and paucity of current evidence in this area effective patient and public involvement strategies may help improve clinical trials comparing surgery to non-surgical treatment.

To our knowledge, this is the first qualitative patient and public involvement study preceding a clinical trial comparing surgical to non-surgical treatment as previous trials did not report any engagement from patients and other key stakeholders.[17-21] Therefore, we aimed to explore patient, clinician, and decision maker perceptions on a clinical trial evaluating the effectiveness of THA compared with exercise to inform the trial protocol.

METHODS

Study design

We used an explorative qualitative design based on a constructivistic paradigm as data was co-constructed by the researchers and participants.[26] This approach was used as we aimed to gain a detailed understanding of a multifaceted phenomenon by exploring the experiences, attitudes, and beliefs of the key stakeholder participants. This study was reported in agreement with the Consolidated Criteria for Reporting Qualitative Research (COREQ) checklist,[27] and preceded the Progressive Resistance Training Versus Total Hip Arthroplasty (PROHIP) trial.[28] The PROHIP trial was approved by The Regional Committees on Health Research Ethics for Southern Denmark (Project-ID: S-20180158) and registered on ClinicalTrials.gov (NCT04070027). This study was approved by The Danish Data Protection Agency (Journal No 18/23994), while no ethical approval was required according to the Danish Act on Research Ethics. Written informed consent was obtained from each participant in accordance with the Helsinki Declaration.

Sampling and participants

Participants were enrolled into three key stakeholder groups: patients, clinicians (orthopaedic surgeons and physiotherapists), and decision makers (members of a political party or non-governmental organisation) (**Figure 1**). Key stakeholders were engaged at the level of consultation to obtain input on several research decisions and implement the findings into our trial protocol.[29]

Please insert Figure 1 about here

Patients were recruited consecutively by orthopaedic surgeons from the orthopaedic departments at Vejle Hospital and Odense University Hospital. The eligibility criteria was similar to the PROHIP trial to ensure a typical patient response. The complete list of inclusion and exclusion criteria have been published previously.[28] Briefly, eligible patients were aged ≥50 years, diagnosed with clinical and radiographic hip OA, and considered eligible for THA.

A convenience sample of clinicians not involved in the design of the PROHIP trial with >2 years of clinical experience in treating patients with hip OA from the orthopaedic and physiotherapy departments at the two hospitals were contacted personally face-to-face or by email and invited to participate in the study.

A purposive sample of decision makers with >2 years of political experience from the spectrum of political parties and relevant non-governmental organisations from the Region of Southern Denmark were approached by email and invited to participate in the study.

Data collection

Data were collected through open-ended, semi-structured focus group interviews allowing the advantage of dynamic group interactions.[30] Each interview included two to five key stakeholders, lasted between 90 to 120 minutes, and was conducted from September 2018 to March 2019 by a female physiotherapist (KST), MSc with 10 years of clinical orthopaedic experience and trained in qualitative methodologies. Prior to each focus group interview, the interviewers' profession was disclosed to the key stakeholders. The interviewer was neither affiliated with the PROHIP trial group nor had previous interaction with key stakeholders. Group specific open-ended semi-structured interview

guides (**online Supplementary File 1**) were developed by the first author (TF) to explore topics related to the PROHIP trial.[31] The number of focus group interviews were not predetermined for the patients, whereas one interview was planned for the clinicians and decision makers due to pragmatic reasons. For the patients, the semi-structured interview guide was continuously adjusted after each focus group based on field notes made during the interviews by the first author. Data saturation was considered attained, if no new themes, perspectives, and knowledge developed within two consecutive interviews. All interviews were digitally audio-recorded, transcribed verbatim, and translated into English by an independent linguist. The transcripts and findings were not returned to the key stakeholders for comments and validation because we expected that their reflective answers would develop during the focus group interview. Quotes from the interviews are used to support claims and illustrate the generated themes and supporting codes. All data were pseudo-anonymized and stored in digital format on a password-protected hospital server conforming to current data protection standards. The focus group interviews were performed face-to-face in undisturbed conference rooms at Vejle Hospital and Odense University Hospital, according to group status. The interviewer and the first author were present during all focus group interviews.

Key stakeholder characteristics were obtained using a participant-reported questionnaire. Additionally, the patient group completed the Oxford Hip Score (OHS)[32] and Hip disability and Osteoarthritis Outcome Score (HOOS).[33]

Data analysis

An independent qualitative researcher (CM) not affiliated with the PROHIP trial group conducted a code book thematic analysis using an inductive approach with no

predetermined themes following the six-step framework described by Braun and Clark.[34 35] Initially, this process involved familiarisation with the data by reading and re-reading the transcripts. This was followed by generating initial codes, in which line-by-line inductive coding was performed on interviews to define and develop a code list. This code list was used to code subsequent interviews deductively, but according to the constant comparison method, as new codes developed these were again applied across all focus group interviews.[36]. As the analysis progressed, coding shifted from descriptive to explanatory, resulting in a number of axial codes. Then related axial codes were organised into preliminary main themes. Lastly, main themes and supporting codes were refined and a final thematic network was developed followed by writing of the manuscript.[34 35] The analysis was performed using Computer Assisted Qualitative Data Analysis software (CAQDAS, Atlas Ti, Version 8).

Implementation of findings into the trial protocol

After the data analysis was completed, the generated thematic network comprising main themes and supporting codes were presented to the PROHIP trial group. We assessed these findings and identified methodological implementation considerations and strategies for the trial protocol and categorized these across relevant identified domains. Disagreements were resolved by discussion until consensus.

Patient and public involvement

Patients or members of the public were not involved in the design, conduct, reporting or dissemination of this qualitative study, but constituted the patient and public involvement strategy used in the development of the PROHIP trial.[28]

FINDINGS

We conducted 4 focus group interviews with a total of 14 patients, 1 focus group interview with 4 clinicians (2 orthopaedic surgeons and 2 physiotherapists), and 1 focus group interview with 4 decision makers (**online Supplementary File 2**). Participant characteristics are presented in **Table 1**. Two main themes were generated from the thematic framework. *'Treatment expectations and beliefs impact management choices'* covered three supporting codes: Treatment without surgery is unlikely to lead to recovery; Clinician authority impacts the management narrative; The 'surgery versus exercise' debate. '*Factors influencing clinical trial integrity and feasibility'* highlighted three supporting codes: Who is considered eligible for surgery?; Facilitators and barriers for surgery and exercise in a clinical trial context ; Improvements in hip pain and hip function are the most important outcomes (**Figure 2**).

Table 1. Characteristics of the Key Stakeholder Groups.*

Characteristic	Patients (N=14)	Clinicians (N=4)	Decision Makers (N=4)
Female sex — no. (%)	8 (57)	1 (25)	2 (50)
Age — yr	68.5 [51.0-80.0]	48.0 [38.00-52.00]	56.5 [23.0-68.0]
Clinical and radiographic hip osteoarthritis — no. (%)	14 (100)	0 (0)	0 (0)
Previous total hip arthroplasty — no. (%)	3 (21)	0 (0)	0 (0)
OHS‡	21.5 [10.0-38.0]	-	-
HOOS subscale scores¶			
Pain	42.5 [20.0-77.5]	-	-
Symptoms	32.5 [15.0-80.0]	-	-
Function in activities of daily living	47.8 [20.6-86.8]	-	-
Hip-related quality of life	31.3 [12.5-68.8]	-	-
Function in sports and recreation	25.0 [0-62.5]	-	-
Clinical profession — no. (%)			
Orthopaedic surgeon	-	2 (50)	-
Physiotherapist	-	2 (50)	-
Clinical experience – yr	-	16.0 [3.0-18.0]	-
Hospital affiliation — no. (%)			
Vejle Hospital	-	2 (50)	-
Odense University Hospital	-	2 (50)	-
Political experience – yr	-	-	5.0 [3.0-5.0]
Political or non-governmental affiliation — no. (%)			
The Liberal Party of Denmark (V)	-	-	1 (25)
The Danish People's Party (O)	-	-	1 (25)
The Social Democratic Party (A)	-	-	1 (25)
The Danish Rheumatism Association	-	-	1 (25)

* Values are median [range] unless otherwise indicated.

‡ The Oxford Hip Score (OHS) ranges from 0 to 48, with higher scores indicating better disease status.

¶ For all five subscales, the Hip disability and Osteoarthritis Outcome Score (HOOS) ranges from 0 to 100, with higher scores indicating better disease status.

Please insert Figure 2 about here

Treatment expectations and beliefs impact management choices

Treatment without surgery is unlikely to lead to recovery

Patients had high expectations of a complete reduction of hip pain, fast return to desired activities-of-daily-living and functional performance approximating their pre-symptomatic state after THA surgery.

> '*I find it important to get rid of the pain, but also to get back to being physically active. Those two are equally important to me. I think. Because it used to be such a big part of my life'* (Patient 3, age 60-69 years).

Patients had uncertain and/or sceptical expectations about exercise, but believed that exercise could lead to improvements.

> '*I have not been informed about the possibility of exercising the pain away*' (Patient 5, age 70-79 years).

Patients and decisions makers perceived exercise as a more appropriate treatment for mild to moderate stages of hip OA or as an adjunct to THA in the pre- and/or postoperative phases to improve the outcome of THA.

> '*But if a hip is in a better state, then there is still a possibility to improve the person's condition without surgery. At the early stages of hip deterioration, exercise may seem like the best way forward'* (Decision maker 3, age 60-69).

> *'It is important to do exercise both before and after the surgery, to make your muscles as powerful as possible'* (Patient 1, age 60-69 years).

Patients with severe hip pain perceived themselves as highly disabled and considered any treatment without THA surgery unlikely to lead to their recovery.

> *'Having a defect hip is constraining both physically and mentally. Totally disabling.'* (Patient 6, age 60-69 years).

> *'I don't believe that it is possible to remove the symptoms just by means of exercising. I don't believe that is possible'* (Patient 7, age 50-59 years).

Clinician authority impacts the management narrative

Patients expressed a need to be guided verbally through the trial protocol and information by a competent and trustworthy clinician. In this regard, the orthopaedic surgeons were seen as the most authoritative clinician.

> *'When I consulted the orthopaedic surgeon, the doctor. We were told absolutely everything about it [THA surgery], and he does it very well. There was no doubt in my mind'* (Patient 5, age 70-79 years).

Orthopaedic surgeons tended to describe THA as a core treatment, with exercise being considered as a postsurgical adjunct treatment, and thus reinforced the perception of their

status as the most authoritative clinician group by virtue of their control over the THA treatment narrative.

> '*It is quite clearly "the surgery of the century". If the surgery is made on the right patient, it is both a safe and effective surgery. The degree of satisfaction is generally very high, both seen from the patients and the surgeons' perspectives'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).

Patient respondents highlighted that both orthopaedic surgeons and physiotherapists tended to use a management narrative suited to their preferred treatment and at times these narratives were juxtaposed.

> '*The orthopaedic surgeon said: You can get a new hip, but I suggest you try to exercise for a period and then you can return to me when the pain gets too severe. The physiotherapists, they are very eager avoid surgery. At least the ones I have met, they have told me that I can exercise the pain away'* (Patient 2, age 50-59 years).

Clinicians were aware of the potential impact of their authority on patient perceptions of treatment effectiveness. This practice was viewed with concern as the PROHIP trial relies on trial participants perceiving THA and exercise as equal treatments.

> *'It is possible to talk about the different possibilities in a fairly objective way through a standardized text. And then it is important not to laugh… when the patient asks us, what would you choose?'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).

The 'surgery versus exercise' debate

Clinicians were aware of an ongoing discourse, pitching other surgical procedures and exercise against one another. Both the orthopaedic surgeons and physiotherapists agreed that fuelling a debate of choosing one approach over another was not a desirable in the context of the PROHIP trial.

> '*This became quickly exercise against surgery, very much head-to-head and completely out of context of reality. We did not recognize, nor in the media the picture they created with the interpretation that you should rather exercise or carelessly get surgery'* (Clinician [Physiotherapist 2], age 30-39 years).

Rather than pitching the two treatments against one another, an orthopaedic surgeon highlighted that it was important to develop a narrative emphasizing surgery and exercise as fundamentally different, yet complementary.

> '*But the question is whether surgery and exercise can be considered equal. Because surgery is dangerous, exercise is not very dangerous. Surgery is invasive, irreversible. Exercise is something you try out, and if it does not*

work, then you can have surgery' (Clinician [Orthopaedic surgeon 2], age 40-49 years)

Factors influencing clinical trial integrity and feasibility

Who is considered eligible for surgery?

Patients highlighted variations in the nature of hip OA, and perceived that radiographic findings were the primary indication criteria for determining treatment selection.

'*If a person is in pain and has a lot of cartilage left, then this person should be offered exercise and surgery should be postponed.* (Patient 1, age 60-69 years).

Physiotherapists questioned the indication criteria for THA used in the clinical assessment, since they had observed a substantial variation in hip pain and functional performance among patients prior to surgery.

'*At the information meetings, we see people who walk normally, and we then wonder why these people need new hips, because this person does not seem to be in pain, nor to be functionally impaired'* (Clinician [Physiotherapist 1], age 50-59 years).

For orthopaedic surgeons, improvements from exercise was associated with an incorrect diagnosis or considered as secondary to hip OA.

> '*You need to be absolutely certain that the patient suffers from osteoarthritis. I believe that the patients who experience improvements by exercise, they suffer from a problem with the soft tissue. Something they have had in any circumstances or is secondary to the osteoarthritis'* (Clinician [Orthopaedic surgeon 1], age 50-59 years).

Facilitators and barriers for surgery and exercise in a clinical trial context

Based on responses, it seemed that younger patients were less likely to select surgery as first-line management. This appeared to be driven by health beliefs and concerns for the durability of THA. Patients perceived both THA and exercise as treatments to provide pain management without usage of analgesics. However, THA was clearly seen as a means to abolish severe pain, whereas less clarity was observed for exercise as residual hip pain was viewed as both a driver and barrier for continued adherence. Exercise was considered a low-risk treatment, while THA was perceived as a last resort treatment with a risk of serious adverse events. Patients indicated that improvements derived from exercise would encourage to continued adherence, whereas a failure of exercise to provide sufficient improvements in hip pain and activities-of-daily living were a driver for THA. Patients were more likely to undergo THA once presented with radiographic findings visualizing degenerative changes and/or progression of OA. Finally, patients considered establishing and maintaining exercise habits as important, and emphasized the importance of supervision to provide clinical expertise and motivation during exercise sessions. Potential facilitators and barriers for THA surgery and exercise in the PROHIP trial are summarized in **Table 2**.

Table 2. Facilitators and barriers for surgery and exercise in the Progressive Resistance Training Versus Total Hip Arthroplasty (PROHIP) trial.

	Surgery	Illustrative quote(s)	**Exercise**	Illustrative quote(s)
Facilitators	Severe hip pain	*'I am currently in a lot of pain, and I am looking forward to being released from that pain'* (Patient 1, age 60-69 years).	Patient age	*'…people who feel too young to have hip surgery… because they see themselves as being physically active and capable of exercising the pain away'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).
	Low quality-of-life	*'I cannot walk more than 100 meters, even with a cane'* (Patient 6, age 60-69 years).	Pain management without analgesics	*'Those four exercises are very valuable to me… I almost never take pills'* (Patient 2, age 50-59 years).
	Ineffective first-line management	*'I have not been able to reduce my pain by means of exercise or physical activity, I need to have surgery to be able to live a tolerable life'* (Patient 6, age 60-69 years).	Low risk of adverse events	*'It [exercise] will not harm them, and if they see improvements that is great.'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).
	Analgesics dependency	*'I ate so many pills, we agreed that something had to be done'* (Patient 2, age 50-59 years). *'They foresee that they will not be forced to take pills and at the same time, they will get well. Therefore, they choose surgery'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).	Perception of improvement	*'If I was able to feel a signification improvement after the 12-weeks exercise program, then I would be motivated to continue'* (Patient 5, age 70-79 years).
	Diagnostic imaging	*'When I got here the second time and saw the x-rays, I saw how much cartilage had disappeared since last time – in that short period of time - I said to myself that the actual bone may be next in line. I said to myself that there was no point in waiting any longer'* (Patient 2, age 50-59 years).	Habitualised exercise	*'Well, naturally I have spoken to other people about exercise, and I have asked them why they do not exercise, and they have a hard time getting started with it. Then I suggest that we go together, because the social aspect of it is very important, for some people at least'* (Patient 11, age 70-70 years).
	Loss of livelihood	*'I may be rejected from the labour market because of my age, and I am not entitled to pension. So, I cannot afford not having surgery now'* (Patient 6, age 60-69 years).	Supervision	*'It is also beneficial to have the presence of a professional person who can inform us about how the specific exercises help you, …where we are supposed to feel the pain if we do them correctly, which muscle is used and how to recognize this muscle'* (Patient 4, age 70-79 years).
			Context of exercise	*'I would appreciate to be in a place together with a group of people,*

				where one person would instruct the others. And if you meet with a group of people several times, then you feel like being part of a community, and you can talk about the same things… That motives me' (Patient 2, age 50-59 years).
			Tracking and gamification	*'It matters a lot, I think. Just like when you use a pedometer or a health app, I like that. I like to be able to see the result of my efforts… like Endomondo – get notified about having completed something'* (Patient 3, age 60-69 years).
Barriers	Patient age	*'…the uncertainty about whether the hip will last 10, 15, 20 years, and whether I will be able to get a new replacement at that time'* (Patient 2, age 50-59 years). *'I am also concerned about the durability of the total hip arthroplasty, because wearing out an artificial hip would result in a second surgery'* (Clinician [Physiotherapist 1], age 50-59 years).	Too much or too little hip pain	*'I have to say that when you are in pain, it is easy to exercise. But then when you don't feel pain, then you tend to forget to do your exercises one day, and then next day and so on. So, when everything is fine, then I have a hard time getting motivated to do exercises'* (Patient 1, age 60-69 years). *'Some people benefit a lot from exercise, but other people come back to me and explain that exercise only worsened the pain'* (Clinician [Orthopaedic surgeon 2], age 40-49 years).
	Risk of adverse events	*'A small risk of the surgery not being successful. That the pain ends up being much worse than before. I think that we all fear that… It would be so devastating if that should happen to us'* (Patient 2, age 50-59 years). *'Well, if the result is a foot drop, then I will not consider the surgery a success'* (Patient 7, age 50-59 years).	Low motivation	*'What is bad for me is that I always come up with a good excuse for not going… working out at home does not work for me, it is better if I go to a fitness centre with other people around'* (Patient 3, age 60-69 years).
			Continuity interruptions	*'…doing exercises in the fitness centre. But, I have also… Maybe I have taken some breaks, I could have put more efforts into it'* (Patient 3, age 60-69 years).

Improvements in hip pain and hip function are the most important outcomes

Patients and clinicians indicated change in hip pain and hip function as the most important outcomes to evaluate the treatment effect of surgery or exercise.

> *'My biggest problem is that I feel pain in all the different kinds of movements I do. No matter what kind of movement I do, I feel the pain'* (Patient 12, age 50-59 years).

Patients and clinicians also highlighted quality-of-life, functional performance (gait), patient acceptable symptom state, muscle strength, treatment crossover (i.e. number of THA surgeries in the exercise group), return-to-work, and leg-length discrepancy as other meaningful outcomes to assess in the PROHIP trial.

Methodological implementation strategies for the trial protocol

Based on our data, we identified four domains for methodological implementation strategies to optimize the PROHIP trial protocol, and these were: patient 'buy in', enrolment strategies, patient information materials, and important clinical outcomes. The domains, their thematic association and supporting coding are illustrated in **Table 3**.

Table 3. Methodological implications derived from the listed domains, main themes and supporting codes used to inform the Progressive Resistance Training Versus Total Hip Arthroplasty (PROHIP) trial protocol.

Domain	Main theme	Supporting code	Methodological implications for the PROHIP trial protocol
Patient 'buy in'	Treatment expectations and beliefs impact management choices	Treatment without surgery is unlikely to lead to recovery Clinician authority impacts the management narrative The 'surgery versus exercise' debate	Guided implementation of a parallel observational study investigating the generalizability of the clinical trial, since many patients probably may decline participation in the trial. Guided development of retention procedures (i.e. instructions of study personnel to encourage patient completion), statistical analysis plan (i.e. handling of missing data, sensitivity and exploratory analyses, and subgroup and causal mediation analysis), and exercise protocol (i.e. effective supervision and habitualised exercise protocol).
	Factors influencing clinical trial integrity and feasibility	Who is considered eligible for surgery? Facilitators and barriers for surgery and exercise in a clinical trial context	
Enrolment strategies	Treatment expectations and beliefs impact management choices	Clinician authority impacts the management narrative The 'surgery versus exercise' debate	Guided development of instruction and training strategy in the enrolment procedures. Guided implementation of generic guidance and neutral narrative during enrolment procedures to provide verbal information about the trial. Guided clinician roles in enrolment procedures (i.e. eligibility assessment, provider of trial information to the patients) and selection of an independent clinician group to provide detailed verbal information about the trial to facilitate communication of clinical equipoise.
	Factors influencing clinical trial integrity and feasibility	Who is considered eligible for surgery?	

Patient information materials	Treatment expectations and beliefs impact management choices Factors influencing clinical trial integrity and feasibility	Treatment without surgery is unlikely to lead to recovery Clinician authority impacts the management narrative The 'surgery versus exercise' debate Facilitators and barriers for surgery and exercise in a clinical trial context	Guided and informed content for the written patient materials and this included information on current evidence of treatment effects for surgery and exercise, trial objective and procedures, randomisation process, content of baseline and follow-up sessions, risks and harms, treatment crossover and withdrawal procedures, clinical implications and funding. Guided development of the neutral narrative used in the written patient materials to facilitate communication of clinical equipoise.
Important clinical outcomes	Treatment expectations and beliefs impact management choices Factors influencing clinical trial integrity and feasibility	Treatment without surgery is unlikely to lead to recovery Improvements in hip pain and hip function are the most important outcomes	Guided selection of hip pain and function as primary outcome. Guided selection of hip-related quality-of-life and functional performance (i.e. gait function) as key secondary outcomes Guided selection of patient acceptable symptom state and muscle strength as exploratory outcomes.

Patient 'buy in'

We identified sampling bias as a potential external validity threat in the clinical trial. In response, a parallel observational study was conceptualized to investigate the generalizability of the clinical trial, since many patients probably may decline participation in the trial. Additionally, we addressed facilitators and barriers for surgery and exercise among patients that could systematically affect retention rates and lead to treatment crossover in the clinical trial. Consequently, in an effort to optimize retention and reduce treatment crossovers, we developed a more focused retention procedure (i.e.

instructions of study personnel to encourage patient completion) and tailored exercise protocol with a greater focus on effective supervision during exercise sessions and implementation of a habitualised exercise protocol. Furthermore, a nuanced statistical analysis plan was prioritized in regards to handling of missing data, sensitivity and exploratory analyses, subgroup and causal mediation analysis.

Enrolment strategies

We identified preconceived beliefs and perceptions among clinicians as a potential threat to sampling in the trial. In response, we implemented an instruction and training strategy for orthopaedic surgeons and project coordinators in standardized verbal information about the trial to facilitate communication of equipoise during enrolment procedures. Focus was placed on the creation of a neutral narrative to be used when verbal information was provided during enrolment. To encourage clinical equipoise, we provided guidance to clinicians with respect to their roles during the enrolment process and an independent clinician group was involved to provide detailed verbal information about the trial.

Patient information materials

We identified preconceived beliefs and perceptions among patients that needed to be addressed in the written patient materials, which covered current evidence of treatment effects for surgery and exercise, trial objective and procedures, randomization process, content of baseline and follow-up sessions, risks and harms, treatment crossover and withdrawal procedures, clinical implications using a balanced a neutral narrative.

Important clinical outcomes

Patient and clinician responses led to three distinct adaptations to the outcomes in the trial protocol. We adopted hip pain and function as primary outcome and implemented hip-related quality-of-life and functional performance (i.e. gait function) as key secondary outcomes. We also included patient acceptable symptom state and muscle strength as exploratory outcomes.

DISCUSSION

Main findings

This novel qualitative patient and public involvement study explored patient, clinician, and decision maker perceptions of a clinical trial evaluating the effectiveness of THA compared with exercise to inform protocol development. Our findings showed that patients with severe pain perceived themselves as highly disabled and considered treatment without THA unlikely. Patients expected a fast recovery with complete reduction of hip pain, restored functional performance, and return to activities-of-daily-living after THA, while more uncertainty and scepticism about the effects of exercise was expressed. All key stakeholders, except the physiotherapists, deemed exercise as most appropriate for mild to moderate stages of hip OA or as an adjunct treatment to THA. We found that clinicians tended to use a management narrative suited to their preferred views on diagnostic eligibility, treatment selection, and relative treatment effectiveness. We also identified several facilitators and barriers for surgery and exercise, which mainly included patient age, pain management without analgesics, risk of adverse events, perception of improvement, diagnostic imaging, supervision, and habitualised exercise. Patients and clinicians indicated change in hip pain and hip function as the most important outcomes

to evaluate the effectiveness of surgery or exercise. Based on these findings, we included a parallel observational study investigating the generalizability, developed an enrolment procedure using generic guidance and balanced narrative conveyed by an independent clinician to facilitate communication of clinical equipoise, and adopted change in hip pain and function as the primary outcome in the PROHIP trial protocol.[28]

Comparison with previous studies and interpretation of findings

In line with our findings, a recent qualitative study also found clear and high expectations for surgery among Swedish patients with knee or hip OA.[37] However, several patients reconsidered their treatment options and changed attitudes towards either accepting or declining surgery after participation in a digital non-surgical program, emphasizing the importance of providing sufficient information about management options to facilitate shared-decision making.[37] Our findings also indicated that patients displayed uncertainties about the potential benefits of exercise. This could be driven by uncertainties and lack of knowledge about the effectiveness of exercise amongst clinicians,[38] and due to less than 40% of the patients are recommended or referred to first-line management.[13] Based on previous qualitative studies,[39 40] recovery expectations among patients in this study were related to the criterion of resolution for surgery and redefinition for exercise, which could indicate that patients accepting participation may differ from those declining participation in our clinical trial in terms of recovery expectations, hip pain, and functional status potentially reducing the generalizability of the PROHIP trial.

Our findings showed that clinicians tended to use a management narrative suited to their preferred treatment. This strategy is in contrast to the information needs

desired by patients with hip OA during clinical encounters,[41] and since clinicians have a considerable influence on the attitudes and beliefs of patients this may result in misconceptions and uninformed decisions.[41 42] This suggests that both orthopaedic surgeons and physiotherapists could sway patient opinions about THA surgery and exercise in either direction during enrolment procedures in the PROHIP trial by highlighting the benefits of their preferred treatment option, whilst simultaneously accentuating the limitations of the other treatment possibly leading to sampling bias.

In consistency with previous studies,[43-45] clinicians in this study displayed conflicting views on the indication criteria for THA. More interestingly, patients in this study perceived findings or progression of hip OA on radiographic imaging to be the primary determinant for THA, although there is low agreement between hip pain and radiographic hip OA.[46] This may suggest that the patients still have an outdated 'wear-and-tear' conception of hip OA that contradicts up-to-date insights on pathogenesis, considering OA as a whole-joint disease.[47] This misconception of OA has previously been shown to be facilitated by clinicians' language and explanations,[48] which emphasize the need of neutral and evidence based information during enrolment in the PROHIP trial.

In line with the Osteoarthritis Research Society International recommendations,[49] our findings highlighted change in hip pain and function as the most important outcome. Several patient-reported outcome measures are available to evaluate pain and functional status in patients with hip OA.[49 50] However, the OHS appears to have the best validated clinometric properties,[50] indicating this as an appropriate primary outcome measure.

Limitations and strengths

Our study has limitations and strengths. A major limitation is that we conducted only one focus group interview for each of the groups with clinicians and decision makers due to time limitations. This may impact the certainty of achieving data saturation, and thus we may have missed important perspectives in these key stakeholder groups. Another limitation is that 3 out of 14 patients had previously undergone THA surgery, which may have influenced their perceptions, as previous surgery has been suggested to affect patient expectations.[37] Furthermore, all patients were scheduled for THA surgery prior to their participation in this study, which further could have primed them to be in favour of surgery. Strengths of our study comprise the variety in the sample of patients interviewed, including females and males of varying ages and different levels of hip pain and disability recruited from both a regional hospital and a university hospital. Additionally, we interviewed three key stakeholder groups involved in receiving and delivering treatment and making decisions about the management of hip OA to provide multiple perspectives and extend the scope of the findings. Lastly, an independent researcher conducted the data analysis to improve neutrality in the interpretation and development of themes and supporting codes due to clinical interests of conflict amongst the rest of the authors.

CONCLUSION

Key stakeholders had treatment expectations and beliefs that could possibly affect enrolment procedures resulting in sampling bias and reduced generalizability of our clinical trial. Moreover, facilitators and barriers for surgery and exercise could influence retention rates and treatment crossovers in the trial. Therefore, we implemented three main strategies to improve methodological rigorousness of our trial protocol. Firstly, we

added an observational study investigating the generalizability to address a potential low enrolment rate. Secondly, we developed an enrolment procedure using generic guidance and balanced narrative conveyed by an independent clinician to facilitate communication of clinical equipoise. Thirdly, we adopted change in hip pain and function as the primary outcome. These findings highlight the value of patient and public involvement in the development of trial protocols to reduce bias in comparative clinical trials evaluating surgical and non-surgical management.

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Authors' contributions

Conception and design: TF, IM, LRM, SO, KGI, and CM designed the study. Analysis and interpretation of the data: TF, KST, and CM. Drafting of the article: TF, KGI and CM. Critical revision of the article for important intellectual content: TF, KST, SO, IM, LRM, KGI, and CM. Final approval of the article: TF, KST, SO, IM, LRM, KGI, and CM. Obtaining of funding: TF and KGI. Collection and assembly of data: TF and KST. Development of interview guides: TF.

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Competing interest

No competing interest.

Ethical Approval

This study was approved by The Danish Data Protection Agency (Journal No 18/23994), while no ethical approval was required according to the Danish Act on Research Ethics.

Data availability statement

Data are available upon reasonable request. Data comprise digital voice recordings of each focus group interview, verbatim transcriptions in Word files, and participant-reported questionnaire responses in PDF files. These data are stored in a password-protected hospital server only accessible to the researchers. Digital audio recordings and individual participant-reported questionnaire responses contain identifiable data and will not be made available on request to maintain participant anonymity. Transcriptions of each focus group interview and the participant characteristics data-set with de-identified participant data may be made available upon reasonable request.

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FIGURE LEGENDS

Figure 1. Eligibility criteria for each key stakeholder group: Patients, Clinicians and Decision makers.

Figure 2. Main themes and supporting codes identified in focus groups with patients with hip osteoarthritis considered eligible for total hip arthroplasty, clinicians (orthopaedic surgeons and physiotherapists) from orthopaedic and physiotherapy departments, and decision makers from a political party or non-governmental organisation.

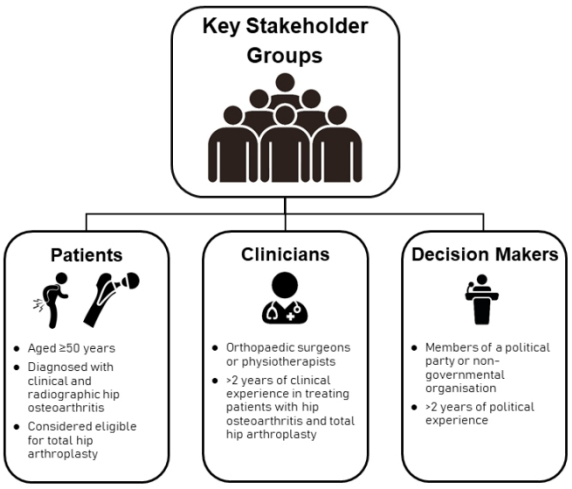

Figure 1. Eligibility criteria for each key stakeholder group: Patients, Clinicians and Decision makers.

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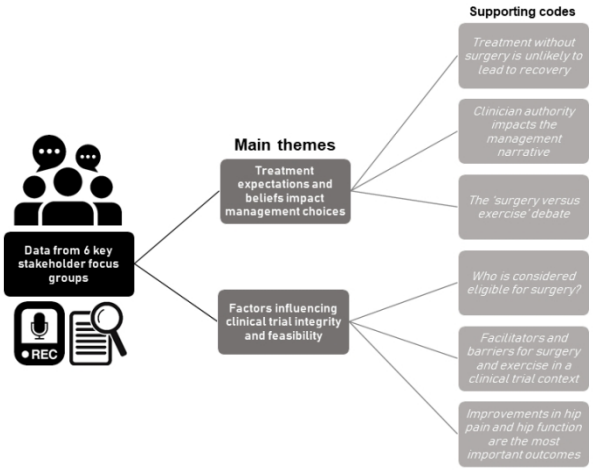


Figure 2. Main themes and supporting codes identified in focus groups with patients with hip osteoarthritis considered eligible for total hip arthroplasty, clinicians (orthopaedic surgeons and physiotherapists) from orthopaedic and physiotherapy departments, and decision makers from a political party or non-governmental organisation.

338x190mm (96 x 96 DPI)

Online Supplementary File 1A. Interview guide for the patient group

Topic	Main question	Supplementary probing questions
Treatment for hip osteoarthritis (THA surgery)	What do you think about surgery as treatment for hip osteoarthritis?	1. When and why did you start considering surgery as a treatment option? 2. How was the decision of surgery taken? 3. When do you know when you are ready for surgery? (physically and mentally) 4. How do you think the information was about the surgery, including risks and other treatments? 5. What expectations do you have for the surgery? 6. What do you consider to be the advantages of surgery? 7. What do you consider to be the disadvantages of surgery? 8. What is the main reason/motivation to undergo surgery? (or declining surgery)
Treatment for hip osteoarthritis (exercise)	What do you think about exercise as treatment for hip osteoarthritis?	9. What treatments have you otherwise tried before surgery? (type, systematics and durations) 10. How have your experiences been with exercise? (type, systematic, duration and effect) 11. How have your experiences been with other treatments? (effect) 12. What do you consider to be the advantages of exercise? 13. What do you consider to be the disadvantages of exercise?
Participation in a clinical trial	CASE DESCRIPTION (Detailed information about the PROHIP trial)	14. What do you think about participating in a trial where you are randomly being assigned to surgery (total hip arthroplasty) or exercise (with the option of later surgery if needed)? 15. What do you consider to be of importance to whether you would participate in the trial? 16. What would affect your considerations about participating in the trial?
Patient material and information	How would you prefer to receive information about this trial?	17. When do you think, it is best to present the information about the trial for potential participants? 18. What do you think the patient information should contain?
Exercise protocol	If you were to participate in 12-weeks of exercise, how do think this should be?	19. What do you think about resistance training in machines? 20. What significance do the physical frames have for you? (location, duration, and environment) • How many times a week is it possible for you to exercise? • How long would you spend on one training session? 21. What significance does it have for you, if you have to drive for the training sessions? 22. What significance does it have for you whether a physiotherapist supervises the training sessions? 23. How do you think you can continue to exercise on your own after a 12-week training program?

Outcomes	If we were to measure the effect of your surgery/exercise program – What do you consider is the most important thing to measure upon?	24. What else do you think is important to measure upon? 25. What is your main problem right now (due to hip osteoarthritis)? 26. How would you describe whether a surgery has been successful? 27. How would you describe whether an exercise program has been successful? 28. What do you think about the questionnaires you filled out? (Relevance, number of items, etc.)

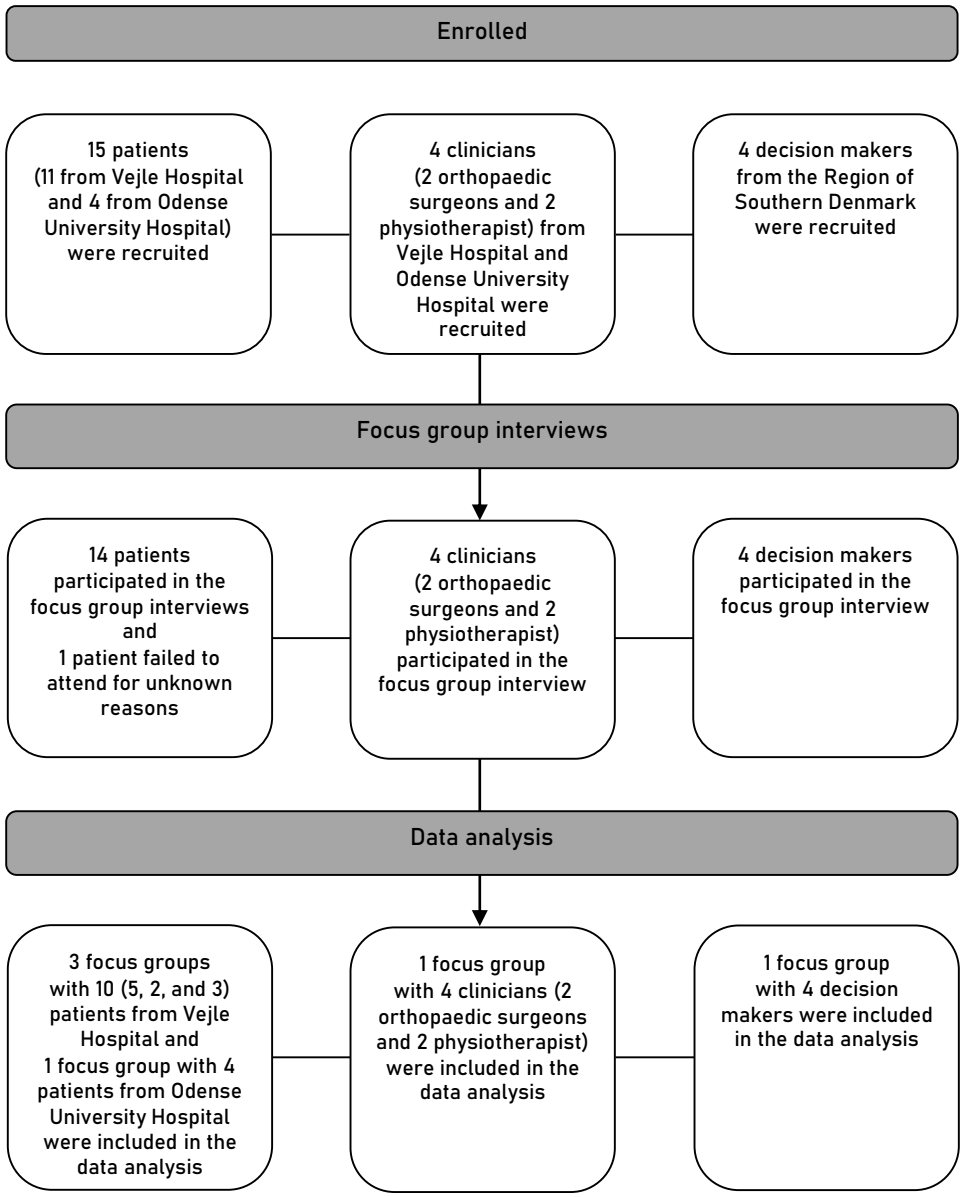
Online Supplementary File 1B. Interview guide for the clinician group

Topic	Main question	Supplementary probing questions
Treatment for hip osteoarthritis (surgery)	What do you think about surgery as treatment for hip osteoarthritis?	1. How do you experience the patients' perception of surgery (THA) as treatment for hip osteoarthritis? 2. What do you experience patients with hip osteoarthritis indicate as main reason/motivation to undergo surgery? 3. What do you consider to be the advantages of surgery? 4. What do you consider to be the disadvantages of surgery? 5. When do you think a patient with hip osteoarthritis is eligible for a THA?
Treatment for hip osteoarthritis (exercise)	What do you think about exercise as treatment for hip osteoarthritis?	6. How do you experience the patients' perception of exercise as treatment for hip osteoarthritis? 7. What do you experience patients with hip osteoarthritis indicate as main reason/motivation in choosing exercise rather than surgery? 8. What do you consider to be the advantages of exercise? 9. What do you consider to be the disadvantages of exercise? 10. When do you think a patient with hip osteoarthritis should try exercise instead of getting a THA? 11. How do you interpret the results of this trial?[20] 12. How have you experienced the debate on surgery (total knee arthroplasty) and exercise? 11. How do you think this debate affects the patients? 12. What do you consider to be the advantages of this debate? 13. What do you consider to be disadvantages of this debate?
Participation in a clinical trial	CASE DESCRIPTION (Detailed information about the PROHIP trial)	14. What is your perception of a trial, in which patients are randomly assigned to surgery (THA) or exercise (with the option of later surgery if needed)? 15. What challenges do you consider there are in recruiting for a trial, in which patients are randomized to THA or resistance training? 16. How do you think it is ensured that clinician (e.g. orthopedic surgeons, physiotherapists, and nurses) do not color the patients' decision to participate? 17. How are orthopedic surgeons and physiotherapists motivated to participate in the trial? 18. How is collaboration between surgeons and physiotherapists in relation to the project created? 19. How would you conduct the screening and recruitment procedure in this trial? 20. What do you consider as of importance for whether patients with hip osteoarthritis will participate in the study?
Patient material and information	How do you think the patient information regarding the trial should be presented for potential participants?	21. When do you think, it is best to present the information about the trial for potential participants?

Exercise protocol	How do you think the exercise intervention should be conducted in the trial?	22. What exercises do you think are relevant to include in the exercise program? 23. How long do you think one training session should last? 24. How do you think we will get the patients to continue to exercise after the 12-week intervention period?
Outcomes	Which outcome do you consider to be the primary to measure in patients with hip osteoarthritis?	25. Which secondary outcomes do you consider to be important to measure in patients with hip osteoarthritis? 26. What do you experience patients with hip osteoarthritis indicate as being the primary problem (symptoms/limitations) that is of importance to the treatment? 27. How would you describe whether surgery (THA) has been successful? 28. How would you describe whether exercise has been successful?

Online Supplementary File 1C. Interview guide for the decision maker group

Topic	Main question	Supplementary probing questions
Treatment for hip osteoarthritis (surgery)	What do you think about surgery as treatment for hip osteoarthritis?	1. How do you experience the patients' perception of surgery (THA) as treatment for hip osteoarthritis? 2. What do you consider to be the advantages of surgery? 3. What do you consider to be the disadvantages of surgery?
Treatment for hip osteoarthritis (exercise)	What do you think about exercise as treatment for hip osteoarthritis?	4. How do you experience the patients' perception of exercise as treatment for hip osteoarthritis? 5. What do you consider to be the advantages of exercise? 6. What do you consider to be the disadvantages of exercise? 7. How do you interpret the results of this trial?[20] 8. How do you think we can avoid this trial to encounter similar diverse attitudes from the "media"/colleagues? 9. How have you experienced the debate on surgery and exercise?
Participation in a clinical trial	CASE DESCRIPTION (Detailed information about the PROHIP trial)	10. What is your perception of a trial, in which patients are randomly assigned to surgery (THA) or exercise (with the option of later surgery if needed)? 11. What challenges do you consider there are in recruiting for a trial, in which patients are randomized to THA or resistance training? 12. In case, the effect of resistance training is lower than surgery (THA), but withholds patients from undergoing surgery because the patients consider the non-surgical treatment as successful - how would you interpret the results? 13. What ethical considerations do you think are in this trial?
Patient material and information	What do you think the patient information should contain?	14. How would you prefer to receive information about this trial? (Content and method) 15. When do you think, it is best to present the information about the trial for potential participants?
Implementation of findings	Which barriers and facilitators, do you think, affect the implementation of the results from the trial into clinical practice?	16. What consequences do you think the trial may have politically in relation to the treatment of patients with hip osteoarthritis? 17. What consequences do you think the trial may have on clinical practice? 18. What challenges do you think there may be in implementing the results from the trial into clinical practice? 19. Which factors do you think will be decisive for a successful implementation of the results from the trial into clinical practice? 20. How do you think that we may optimize the implementation of the results from the trial into clinical practice?



Online Supplementary File 2. Flowchart of key stakeholder participants in the study.

COREQ (COnsolidated criteria for REporting Qualitative research) Checklist

A checklist of items that should be included in reports of qualitative research. You must report the page number in your manuscript where you consider each of the items listed in this checklist. If you have not included this information, either revise your manuscript accordingly before submitting or note N/A.

Topic	Item No.	Guide Questions/Description	Reported on Page No.
Domain 1: Research team and reflexivity			
Personal characteristics			
Interviewer/facilitator	1	Which author/s conducted the interview or focus group?	7
Credentials	2	What were the researcher's credentials? E.g. PhD, MD	7
Occupation	3	What was their occupation at the time of the study?	7
Gender	4	Was the researcher male or female?	7
Experience and training	5	What experience or training did the researcher have?	7
Relationship with participants			
Relationship established	6	Was a relationship established prior to study commencement?	7
Participant knowledge of the interviewer	7	What did the participants know about the researcher? e.g. personal goals, reasons for doing the research	7
Interviewer characteristics	8	What characteristics were reported about the inter viewer/facilitator? e.g. Bias, assumptions, reasons and interests in the research topic	7
Domain 2: Study design			
Theoretical framework			
Methodological orientation and Theory	9	What methodological orientation was stated to underpin the study? e.g. grounded theory, discourse analysis, ethnography, phenomenology, content analysis	5 + 8-9
Participant selection			
Sampling	10	How were participants selected? e.g. purposive, convenience, consecutive, snowball	6-7 + Figure 1
Method of approach	11	How were participants approached? e.g. face-to-face, telephone, mail, email	6-7
Sample size	12	How many participants were in the study?	10 + Table 1
Non-participation	13	How many people refused to participate or dropped out? Reasons?	SuppFile 2
Setting			
Setting of data collection	14	Where was the data collected? e.g. home, clinic, workplace	8
Presence of non-participants	15	Was anyone else present besides the participants and researchers?	8
Description of sample	16	What are the important characteristics of the sample? e.g. demographic data, date	10 + Table 1
Data collection			
Interview guide	17	Were questions, prompts, guides provided by the authors? Was it pilot tested?	7 + SuppFile 1
Repeat interviews	18	Were repeat inter views carried out? If yes, how many?	8
Audio/visual recording	19	Did the research use audio or visual recording to collect the data?	8
Field notes	20	Were field notes made during and/or after the inter view or focus group?	8
Duration	21	What was the duration of the inter views or focus group?	7
Data saturation	22	Was data saturation discussed?	8 + 27
Transcripts returned	23	Were transcripts returned to participants for comment and/or	8

Topic	Item No.	Guide Questions/Description	Reported on Page No.
		correction?	
Domain 3: analysis and findings			
Data analysis			
Number of data coders	24	How many data coders coded the data?	8
Description of the coding tree	25	Did authors provide a description of the coding tree?	10 + Figure 2
Derivation of themes	26	Were themes identified in advance or derived from the data?	8-9
Software	27	What software, if applicable, was used to manage the data?	9
Participant checking	28	Did participants provide feedback on the findings?	8
Reporting			
Quotations presented	29	Were participant quotations presented to illustrate the themes/findings? Was each quotation identified? e.g. participant number	12-20+Table2
Data and findings consistent	30	Was there consistency between the data presented and the findings?	10-24+Table2
Clarity of major themes	31	Were major themes clearly presented in the findings?	10-24+Figure2
Clarity of minor themes	32	Is there a description of diverse cases or discussion of minor themes?	10-26+Figure2

Developed from: Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *International Journal for Quality in Health Care*. 2007. Volume 19, Number 6: pp. 349 – 357

Once you have completed this checklist, please save a copy and upload it as part of your submission. DO NOT include this checklist as part of the main manuscript document. It must be uploaded as a separate file.