Clin Orthop Relat Res (2022) 480:2075-2088
DOI 10.1097/CORR.0000000000002183

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

Clinical Research

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Many Patients With Persistent Pain 1 Year After TKA Report Improvement by 5 to 7 Years: A Mixed-methods Study

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Received: 22 October 2021 / Accepted: 1 March 2022 / Published online: 21 March 2022

Abstract

Background Approximately 20% of patients report pain 12 months after TKA. No studies have investigated patients' experiences of living with persistent postsurgical pain 5 to 7 years after TKA by combining a qualitative and quantitative methodology.

Question/purpose In a mixed-methods study, we explored patients' experiences of living with persistent pain up to 7 years after primary TKA. We asked: In a subgroup analysis of patients who reported persistent pain 1 year after TKA surgery, how do patients live

The institution of one or more of the authors (VBS) received funding from Lovisenberg Diaconal College University, the Kirsten Rønnings Legacy, Dr. Jan Pahles Legacy, and The Norwegian Nursing Association.
The institution of one or more of the authors (MFL, AA, AL) received funding from the Research Council of Norway (grant #287816 /H10) and the South-Eastern Norway Regional Health Authority (grant #2018060, #2018110, and #2022007).
Each author certifies that there are no funding or commercial associations (consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article related to the author or any immediate family members.
All ICMJE Conflict of Interest Forms for authors and *Clinical Orthopaedics and Related Research®* editors and board members are on file with the publication and can be viewed on request.
Ethical approval for this study was obtained from the Regional Committee for Medical and Health Research Ethics (reference number 2011/1755).
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with persistent pain at the 5- to 7-year postoperative timepoint?

Methods This follow-up study was part of a longitudinal study of pain, symptoms, and health-related quality of life in patients who underwent TKA for osteoarthritis. The present study targeted a subgroup of patients (22% [45 of 202]) identified in the longitudinal study who reported no improvement in pain interference with walking at 12 months after surgery. Inclusion criteria were: all 31 patients in this subgroup who attended their 5-year follow-up at the hospital and lived within a 2-hour drive from the hospital. Eight patients declined or were unable to participate due to illness or death. Hence, the final sample consisted of 23 patients (13 women and 10 men). The participants' mean age at surgery was 66 ± 10 years. There were no differences in sociodemographic baseline data between the 23 included and the 22 excluded participants. A mixed-methods approach was employed, in which the quantitative data were followed up and investigated with qualitative interviews. Instruments used were the Brief Pain Inventory preoperatively, 12 months, and 5 years after surgery, as well as a semistructured interview guide. The individual interviews were conducted at one timepoint 5 to 7 years postsurgery to capture how pain was experienced at that timepoint. The interviews were audiorecorded, transcribed, and analyzed using qualitative content analysis. Meaning units were identified, condensed, and sorted into subthemes that were interpreted and abstracted into themes, guided by the research question. With a small sample, the quantitative analysis focused on descriptive statistics and nonparametric statistics when comparing demographics of included and nonincluded patients. In addition, two multivariate mixed models for repeated measures were employed to estimate within-patient and between-patient variations as well as to assess the effect of time on the pain outcomes.

Results Pain with walking decreased from 12 months to 5 years postoperatively (estimated mean score 7 versus 4, difference of means -3 [95% CI -5 to -2]; $p < 0.001$). Pain with daily activity decreased from 12 months to 5 years postoperatively (estimated mean score 6 versus 3, difference of means -3 [95% CI -4 to -1]; $p < 0.001$). Pain intensity (average pain) decreased from 12 months to 5 years postoperatively (estimated mean score 5 versus 4, difference of means -1 [95% CI -3 to 0]; $p = 0.03$). The results are presented as point estimates rounded up to whole numbers. The qualitative data analysis yielded three themes: persistent limitations after TKA, regained wellness over time, and complexity in physical challenges. Intermittent pain with certain movements resulted in limitations with some activities in everyday life and seemed to persist beyond 5 years. Multiple painful body sites and presence of comorbidities seemed to interfere with regained wellness over time.

Conclusion In this subgroup of patients experiencing postsurgical persistent pain 12 months after primary TKA, persistent postsurgical pain still limited certain activities for the participants, although pain seemed to be less influential in their everyday lives after 5 years to 7 years. Clinicians may use these findings to inform and guide patients with delayed improvements in pain into more realistic expectations for recovery, rehabilitation, and strategies for coping with pain and impaired function. However, it is imperative to rule out other reasons for pain in patients reporting pain 12 months and longer after surgery and to be attentive of possible changes in pain over time.

Level of Evidence Level III, therapeutic study.

Introduction

Most patients report improvement in pain, functional outcomes, and health-related quality of life after TKA [3, 4, 37]. However, approximately 20% of patients experience persistent postsurgical pain 12 months or more after TKA [2, 7, 25]. Persistent postsurgical pain is defined as pain that develops or increases in intensity after a surgical procedure, lasts at least 3 to 6 months, and substantially affects health-related quality of life [32, 36, 43].

Persistent postsurgical pain is best understood through the patient's perspective. Few studies have used a qualitative approach to explore patients' experiences with persistent pain 12 months or more after TKA [16, 19, 31]. These studies focused on accepting pain by adjusting to it, living with stressful pain, high expectations of total recovery, and the importance of rehabilitation for adjusting to the new joint. To our knowledge, no studies have investigated patients' experiences of living with persistent postsurgical pain 5 to 7 years after TKA with a combination of a quantitative and qualitative methodology. Using a mixed-methods approach by combining questionnaires with qualitative interviews may enable a comprehensive and rich understanding of the patients' complex experience of persistent postsurgical pain.

The current study originates from a larger longitudinal study that identified a subgroup of patients who underwent TKA (22% [45 of 202]) and reported no improvement in pain with walking from preoperative levels to 12 months after surgery [25]. Using a mixed-methods approach for the evaluation of this group of patients, we asked the following: In a subgroup analysis of patients who reported persistent pain 1 year after TKA surgery, how do patients live with persistent pain at the 5- to 7-year postoperative timepoint?

Patients and Methods

Study Design

This follow-up study used a mixed-methods approach with a combination of quantitative and qualitative phases

described by Ivankova et al. [15]. In the quantitative phase, we identified a subgroup of patients experiencing persistent postsurgical pain 12 months after TKA [25]. Further quantitative data were collected at the 5-year follow-up. In the qualitative phase, new research questions were posed and answered through individual interviews [5] (Fig. 1). The research questions and an interview guide were constructed based on the quantitative results at 12 months [25] as well as previous research [16, 39]. Further quantitative data were collected at the 5-year follow-up. The mixed-methods integration strategies we used were structured questionnaires connected to semistructured interviews. The quantitative and qualitative data sets were analyzed separately, then combined, and the results were finally integrated in a joint display [5, 13, 14, 17].

Participants and Setting

This follow-up study was part of a longitudinal study of pain, symptoms, and health-related quality of life during the first postoperative year in patients who underwent TKA for osteoarthritis in a high-volume joint reconstruction unit [25-27]. The inclusion criteria were age 18 years or older; the ability to read, write, and understand Norwegian; and patients who were scheduled to undergo primary TKA. Patients were excluded if they underwent unicompartmental or revision surgery. The anesthesia, surgery, and postoperative pain management procedures were standardized, and all patients received the hybrid Profix cruciate-retaining prosthesis (Smith & Nephew) without patellar resurfacing [25, 27]. This follow-up study used purposive sampling to recruit patients from the subgroup comprising 22% (45 of 202) of patients identified in the longitudinal study. They were classified as nonimprovers based on their trajectories of self-reported pain interference with walking scores from the Brief Pain Inventory (BPI) at 12 months postoperatively. Of the total study sample (n = 202), the improvers had a mean score on interference with walking of 5.6 ± 2.2 preoperatively and a score of 1.58 ± 14 at 12 months (interference with walking). The nonimprovers (22% [45 of 202]) had a higher mean score on pain interference with walking preoperatively (6.9 ± 2.0) as well as at 12 months (6.9 ± 1.4), as reported by Lindberg et al. [25]. The 31 patients who had the same characteristics as nonimprovers were invited to participate in this follow-up study if they attended their 5-year follow-up at the hospital and lived within a 2-hour drive from the hospital. Eight patients declined or was unable to participate due to illness or death (Fig. 2). The theoretical model of

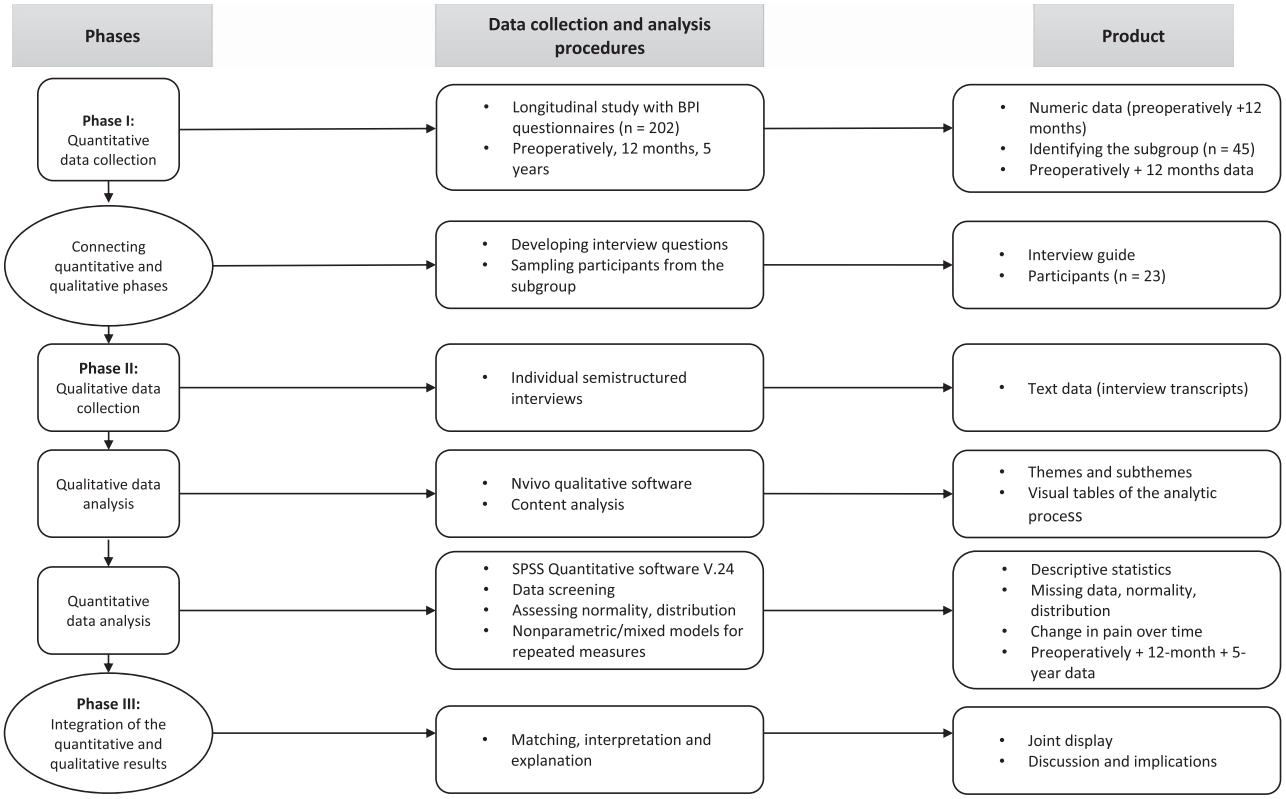


Fig. 1 This visual model shows the mixed-methods, sequential, explanatory design procedures. Adapted from Haynes-Brown and Fetters [14] and Ivankova et al. [15].

information power [30] was employed to evaluate sample size. According to this model, sufficient information power is generated when a study has a narrow study aim, includes participants who have characteristics that are highly specific for the study aim, and has an interview dialogue that enables the participants to share and describe their specific experiences. Thus, a smaller sample is required [30]. Based on preliminary analyses during the data collection and evaluation of information power, we increased the sample size from 15 to 23 participants to acquire a richer data set. Thirteen women and 10 men accepted the invitation to participate (Fig. 2) and were interviewed.

There were no differences in sociodemographic baseline data between the 23 included and the 22 excluded participants. The mean participant age at the time of surgery was 66 ± 10 years (median [range] age 67 years [48 to 84]) (Table 1). In the quantitative dataset, four patients had missing data at 5 years of follow-up; thus, the sample size was 19 for quantitative analyses (Table 2).

Instruments

We collected quantitative data on preoperative and postoperative pain using the BPI questionnaire, which consists of four items that evaluate pain intensity using a numeric rating scale from 0 to 10, where 0 constitutes no pain and 10 the worst possible pain. The BPI also includes seven items that evaluate pain-related interference with walking, daily activity, mood, ability to work, social relations, sleep, and enjoyment of life, using a numeric rating scale from 0 to 10, as well as a body map to indicate pain locations. Scores ranging from 0 to 3 are defined as mild pain, 4 to 6 as moderate pain, and 7 to 10 as severe pain [9, 41]. As

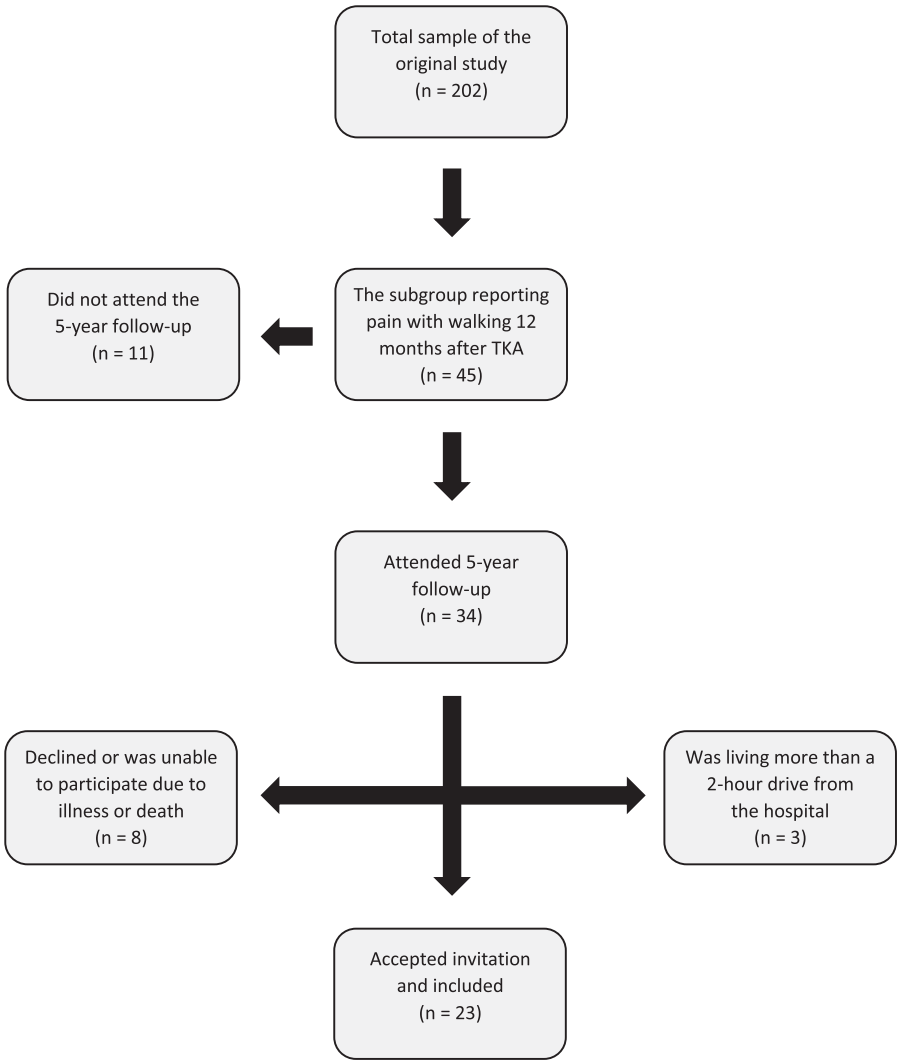


Fig. 2 This flowchart shows the patients who were included in this study.

Table 1. Demographic characteristics of the larger cohort, nonimprovers, and the study sample versus the nonincluded patients

Patient demographics	Total sample of the original study (n = 202)	Nonimprovers identified in the original study (n = 45)	Study sample (n = 23)	Nonincluded (n = 22)	p value for study sample vs. nonincluded
Age at surgery, mean	68 ± 9.2	67 ± 10.9	66 ± 9.8	68 ± 12.1	0.36
Age at surgery, median (range)	69 (41 - 90)	68 (41-87)	67 (48-84)	71 (41-87)	
Women	68% (138)	67% (30)	57% (13)	77% (17)	0.14
Cohabitation status					
Lives with partner or family	60% (122)	67% (30)	57% (13)	68% (15)	0.43
Lives alone	40% (80)	38% (17)	43% (10)	32% (7)	0.06
Education	(n = 199)				
Lower education	49% (97)	49% (22)	35% (8)	64% (14)	
Higher education	51% (102)	51% (23)	65% (15)	36% (8)	
Work	(n = 199)				0.63
Paid work	35% (70)	40% (18)	43% (10)	36% (8)	
Not in paid work	65% (129)	60% (27)	57% (13)	64% (14)	
Chronic illness					0.40
Yes	26% (52)	33% (15)	26% (6)	41% (9)	
Missing	0		13% (3)	5% (1)	

Data presented as mean ± SD, median (range), or % (n).

defined by Salaffi et al. [35], Farrar et al. [10], and Dworkin et al. [8], a minimum clinically important difference is defined as a decrease of 1 point or a reduction of 15% in pain, and a clinically important improvement is defined as an improvement of 2 points or a reduction of 33% in pain. In this analysis, the ratings of pain-related interference with walking, daily activities, and average pain intensity were used. These items were selected based on the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) recommendations for core outcome domains to be considered in clinical trials [42]. In line with this, pain-related interference with daily activity and walking

Table 2. Change in pain intensity and pain interference over time (n = 19)

	Mean	Mean change in BPI at 5 years vs. preoperative (β with 95% CI)[a]	p value (preoperative)	Mean change in BPI 5 years vs. 12 months (β with 95% CI)[a]	p value (12 months)
Pain interference with walking					
Preoperative	7				
12 months	7	0 (0 to 2)	0.27		
5 years	4	-3 (-5 to -1)	0.004	-3 (-5 to -2)	< 0.001
Pain interference with daily activity					
Preoperative	6				
12 months	6	0 (-1 to 1)	> 0.99		
5 years	3	-3 (-4 to -1)	0.002	-3 (-4 to -1)	< 0.001
Average pain					
Preoperative	6				
12 months	5	-1 (-2 to 0)	0.03		
5 years	4	-2 (-4 to -1)	< 0.001	-1 (-3 to 0)	0.03

All models were adjusted for age and sex.
[a]Adjusted unstandardized regression coefficients β.

were used to represent physical functioning, and average pain was used to represent pain intensity. The BPI provides a standardized outcome specifically designed for chronic pain, which facilitates comparability across chronic pain studies [10] and is considered suitable to assess chronic pain after TKA [47]. The validity and reliability of the BPI is also well established [20] in TKA patients [6].

Sociodemographic data included age, sex, cohabitation status (cohabitating versus living alone), education (high school versus college or university degree of 3 to 5 years), employment (working versus not), and chronic illnesses (any versus none).

To facilitate reflection and conversation, we developed a semistructured interview guide with open-ended questions based on previous research on patients with TKA [16, 39] and key topics in the longitudinal study [25] from where the patients were recruited. The guide contained questions concerning the patients' experiences of living with persistent postsurgical pain 5 to 7 years after TKA. The interview guide was pilot tested on three patients, and no changes were needed (Supplementary Digital Content 1; http://links.lww.com/CORR/A766).

Data Collection

Phase I: Quantitative Questionnaire Data

Pain data were collected preoperatively and at 1 year and 5 years after surgery, in 2013, 2014, and in 2018 to 2019 using BPI questionnaires.

Statistical Analysis

We conducted statistical analyses using IBM SPSS version 24. BPI data are presented for each patient to show the clinical pathway in a plot. Given the small sample size of this dataset, we employed descriptive statistics and nonparametric tests to compare the included and nonincluded patients. To assess the effect of time on the pain outcome, we used multiple generalized linear regression models for repeated measures. Each included patient was assessed three times to estimate within-patient and between-patient variations and to assess the effect of time on the pain outcome despite the sample size being limited. To account for statistical dependencies because we mesured the same individuals three times, we fitted linear mixed models for repeated measures for all three main outcomes. We used an unstructured covariance matrix and did not force any parametric structure on the data. The models were further adjusted for age and sex as possible confounders. These coefficients can be interpreted as the estimated mean change from 12 months to baseline and from 12 months to 5 years. All results from the mixed model are reported as the estimated regression coefficient β with 95% confidence intervals. A p value < 0.05 was considered statistically significant.

Phase II: Qualitative Interview Data

We conducted individual semistructured interviews at one timepoint, the 5- to 7-year postoperative juncture, from February 2018 to August 2020. Each interview lasted 45 to 70 minutes and was conducted at the patient's home or in a private room at the hospital, according to the patient's preference. The first five interviews were conducted by a female senior qualitative researcher (AD), with the first author, a female junior researcher (VBS), as an observer in the latter two interviews. In the next three interviews, the researchers switched roles. The last 15 interviews were conducted by the first author (VBS). This facilitated a more similar approach in interviewing, ensuring that all the questions in the interview guide were addressed in each interview. Neither interviewer was part of the clinical team at the orthopaedic unit where the participants underwent TKA. The interviewers posed follow-up questions, asked for examples, or asked the participants to elaborate on issues they raised or alluded to. The participants were given opportunities to mention issues they felt were important and were free to tell their stories. The interviews were audiorecorded and transcribed verbatim by a professional transcriber.

Qualitative Analysis

NVivo software version 12 was used to organize and analyze the qualitative interview data. The interviews were analyzed using a qualitative content analysis [12, 28]. First, the interviews were read several times to understand the entire material through a manifest analysis. Meaning units were identified and condensed using descriptions close to the text. The condensed meaning units were explored for similarities, nuances, and differences. This categorization guided the process, searching for latent content, which is an interpretation of the underlying meaning of the text, sorting the condensed meaning units into subthemes. Guided by the research question, the subthemes were interpreted and abstracted to themes discussed and agreed upon by three of the authors (VBS, SAS, AD) (Table 3).

Trustworthiness

Qualitative data collection and data analysis was affected by the researchers' preconceptions. One author (VBS) was aware that the patients were selected on the basis of having pain 12 months after primary TKA. She had worked as an

Table 3. The content analysis

Meaning unit	Condensed meaning unit	Description close to text	Subtheme	Theme
I don't like stairs and such any longer. No, I don't like it. Going downhill and downstairs, that is the worst. Yes, it's this pressure pain. It feels like it pushes against something (Patient 2).	I don't like stairs—going downstairs and downhill is the worst	Pain when going downstairs and downhill	Pain with certain movements	Persistent limitations
I can't even sit on my knees on top of my mattress in bed. If I am to crawl up to pull the sheet on the bed, it hurts. Pressure pain is what I call it. It's not like it's a tendon or muscular pain, it is just physically painful where that pressure is (Patient 17).	I can't even sit on my knees on top of my mattress in bed. Pressure pain is what I call it, it is just physically painful where the pressure is	Painful to sit on knee	Pain with certain positions	
But do you know what? I am just so happy that I can walk because I had such pains before the surgery. So, I don't have those pains now. And I tell everyone that it is very good. Very happy about it. Trying to focus on what I can do. What I can't … No I am just very happy for this now (Patient 14).	I am so happy that I can walk. I had such pains before the surgery. So, I don't have those pains now	Assessing the outcome Regaining function Less pain	Regaining function Less pain	Regaining wellness
Now I use paracetamol in the evening before I go to bed. Otherwise, I seldom take any pain medications at all. At least not anything stronger than paracetamol. So, that is another life entirely (Patient 17).	I seldom take pain medication. At least not anything stronger than paracetamol. It is another life entirely	Seldom need for use of pain medication; a better life than before	Recovering	
What is keeping me from doing the walks I would like to do, is more my ankle than my knee. I get tired from other things as well, but I really want to try to go for more walks. Not just for the exercise, but because it is good for my mental health being out in nature (Patient 11).	What is keeping me from the walks I would like to do is more my ankle than my knee	Ankle is painful when walking	Other pains more demanding	Complexity in other physical challenges
I guess I always have pain to different degrees. I have rheumatoid arthritis as well. So, it is not clear to me what is what (Patient 22).	I always have pain. I have rheumatoid arthritis as well, so it is not clear to me what is what	Rheumatoid arthritis also causing pain, difficult to differentiate pains	Other physical challenges interfering with the healing process	

orthopaedic nurse, although not with patients who underwent TKA. This author's preconception was that patients who had a TKA generally suffer from more postoperative pain than patients who undergo THA. To enhance reflexivity and transparency, preconceptions were discussed with senior researchers. The interview guide included open-ended questions so the patients could express and elaborate on issues that were important to them, and follow-up questions allowed participants to rule out misinterpretations of their statements. Researcher triangulation (VBS, SAS, AD) was applied [33] to the qualitative analysis's discussions and interpretations. Because the researchers had different clinical and research expertise (orthopaedics, anesthesiology, and palliative care), this facilitated divergent perspectives in the analytic process [33]. The first author (VBS) analyzed the data and the two coauthors (SAS, AD) asked critical questions during the analytic process to explore alternative interpretations. All authors agreed on the final themes.

For enhancing transferability of our results, sample, data collection, and the analytic process were described, and the analytic process was also visualized in tables to provide a decision trail throughout the analysis [11]. In addition, we provided descriptions of the analysis (Table 3) and the results [33] with relevant quotes (Supplementary Digital Content 2; http://links.lww.com/CORR/A767) so that others may consider whether the results are applicable to their context. Mixing methods in this paper also led to a triangulation of findings, which is visualized in the joint display as well as in the discussion of results combining and interpretating the two results.

Phase III: Overall Integration of Quantitative and Qualitative Results About Persistent Postoperative Pain

The results were combined and are presented in a joint display, including a column for interpretation. When combining the datasets, we compared the similarities and differences of the patients' experiences of persistent postsurgical pain in the quantitative and qualitative results. The quantitative dataset was then listed, matched, and checked against the qualitative subthemes and themes for integration of the two datasets. Four researchers (VBS, SAS, MFL, AD) matched, checked, and discussed the integrated datasets. In this study, the qualitative data carries more weight than the quantitative data because the statistical analyses were limited and the interviews were extensive.

Ethical Approval

The study was approved by the Regional Committee for Medical and Health Research Ethics (reference number 2011/1755) and the Data Protection Officer at Lovisenberg Diaconal Hospital. Patients were informed about the study in writing and orally. All participants signed an informed consent form before the quantitative longitudinal study and qualitative individual interviews. Participants had the right to withdraw from the study at any time until the results were published, and their confidentiality and anonymity were safeguarded according to local regulations.

Results

Quantitative Results: Change in Pain Over Time

Clinically important changes in pain levels [9, 10, 35] over time were revealed when comparing 12-month to 5-year findings using multivariate linear mixed models for repeated measures that were adjusted for age and sex (Table 2). For pain interference with walking and daily activity, the estimated mean scores improved by about 3 points each when comparing 12-month and 5-year results. These two pain interference measures did not differ by sex but were associated with age, with older patients reporting less pain interference. For pain intensity the estimated mean scores improved by more than 1 point at 5 years compared with 12 months. The results are presented as point estimates rounded up to whole numbers. The effects of age and sex on pain intensity were not statistically significant (Table 2).

Qualitative Results

Three themes were identified from the qualitative data analysis: (1) persistent limitations after TKA, (2) regaining wellness over time, and (3) complexity in physical challenges.

Persistent Limitations After TKA

Most participants (n = 21) experienced a degree of limitations in everyday life after TKA. Such limitations included pain with certain movements and pain after or with physical activities. Participants highlighted the painful sensations as something occurring with certain activities only. Pain with specific activities was expressed by most participants and was experienced as pain that lasted briefly with certain types of movements, such as walking downhill and downstairs, but not as an ongoing pain. Many participants feared such movements but said that they could not avoid walking downstairs and downhill because they are inevitable movements in everyday life.

Some patients stated that pain occurred with certain knee positions. For example, sitting still with the knee bent caused acute knee pain for some and could only be stopped or decreased by changing the knee's position. This positional pain contributed to limitations in situations when an individual must sit in cramped places or when squatting or kneeling. Not being able to squat or kneel was most often linked with difficulties doing house chores, gardening, and occasionally during religious ceremonies.

Others experienced pain after being physically active or if they "overdid" their physical activities. Participant 18 described pain with physical activity: "It can start hurting on the inside and outside of the knee, but that is more if I go for longer hikes, I can do 1-hour hikes in the mountains, and that is lovely. If I walk for a long time, go for hikes, the knee does not look swollen on the outside, … but it feels like it is swollen on the inside."

For some younger participants, high-impact activities such as running and skiing—both downhill and cross country—were found difficult to resume because of pressure pain and pain with high-impact in the joint (such as, going up-hill "herringbone" and plowing downhills for reducing speed).

Regaining Wellness Over Time

All participants described regaining wellness over time. Regained wellness was expressed as regained function, less pain, needing less pain medication, and with time, feeling better. The participants sometimes had increased knee awareness; however, their overall condition was better than it was before surgery. Many highlighted being able to walk and participate in physical activities with family and friends.

Most participants expressed that they no longer needed any pain medications for their knee. Although some needed acetaminophen periodically, only a few took stronger pain medications but not every day. Furthermore, many emphasized that it took time to heal, at least 2 years, before regaining wellness. When asked, most participants expressed that they did not regret undergoing TKA. They stated that they did not have a choice because of the limitations and pain they had at the time of surgery.

Complexity in Physical Challenges

Most participants felt that their knee was just one among other physical challenges that entailed other painful sites, comorbidities, and chronic diseases such as rheumatoid arthritis or fibromyalgia. Other painful sites or worries complicated the healing process, which disturbed the patient's focus on improvements in the newly operated-on knee. A few linked their pain to complications after TKA. One participant talked about a drain that was difficult to remove, and how they still felt pain at the site from which the drain was removed. A patient with arthrofibrosis expressed that it was painful when bending their knee. Another participant had prosthetic loosening and underwent revision surgery after the 5-year follow-up but experienced less pain at the time of the interview, 7 years after the index surgery.

Overall Integration With Joint Display

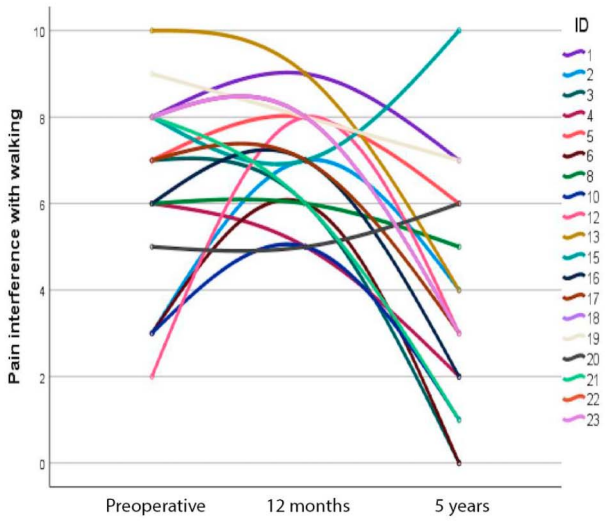
The quantitative and qualitative results showed a decrease in pain across all three BPI items. Most patients still experienced certain limitations after TKA, even if they also regained wellness. One patient scoring high (8 points) for pain intensity at all timepoints did not, in the interview, consider the pain as a problem in everyday life, but they still used stronger pain medication periodically. Another patient who scored higher at the 5-year timepoint was later found to have a prosthetic loosening, which can explain their higher pain intensity score at the 5-year follow-up. Other patients taking stronger medications expressed that they took these for other ailments. Some patients pointed out that that although they had rated knee pain on the BPI, the questionnaire may not have captured that their pain was short-lived or only occurred with certain movements or activities (Fig. 3).

Discussion

TKA is a procedure with well-documented effect on reducing pain, and the number of procedures are increasing in most countries [2, 34]. Even so, approximately 20% of patients still report pain 12 months after surgery [2, 24]. More information on these patients' experiences of living with pain over time may identify actions to improve the care for this subgroup of patients. We are not aware of any studies that have investigated patients' experiences of living with persistent postsurgical pain 5 to 7 years after TKA by combining a qualitative and quantitative methodology. Therefore, we aimed to do that by studying a cohort who reported pain during activity 1 year after surgery. In our sample, most participants experienced improvements from 1 to 5 years after surgery in pain intensity, pain with walking, and pain interference with daily activity. However, some patients still experienced pain with walking downhill and downstairs or pain with certain other movements.

Limitations

This study has several limitations. Patients were eligible for inclusion in this study based on their 12-month BPI score,

Quantitative	Qualitative	Interpretation
	**Patient 1:** "I don't have pains now. It's just when I walk downhill or downstairs, I get this pressure pain inside the knee, you know?" Score at 5 years: **7.** **Patient 2:** "I easily walk for 1 or 2 hours. The longest I have gone is 3 ½ hours. I don't have much pain while walking. Perhaps it is because I enjoy walking so much. But it starts aching when I get home and at night." Score at 5 years: **4.** **Patient 15:** "It is obviously better now. If you look largely at it all, I can walk now. I couldn't walk before" (because of prosthetic loosening). Score at 5 years: **10.** **Patient 19:** "Difficult to walk on the stairs, it hurts, mostly downstairs. I don't walk because I enjoy it, I walk because I must." Score at 5 years: 7. **Patient 20:** "It is when I get up and walk in the morning, I feel it sometimes that I have pains." Score at 5 years: **6**.	Decreasing pain interference with walking from 12 months to 5 years for all but two patients. Several patients were more or less pain free when walking, except short-lived pain in specific situations or with certain movements (such as, walking downhill or downstairs). Some experienced more pain with walking than others. One participant who scored higher than the others at 5 years reported decreasing pain with walking in the interview.
A IDs missing for quantitative data on patients 7, 9, 11, 14		

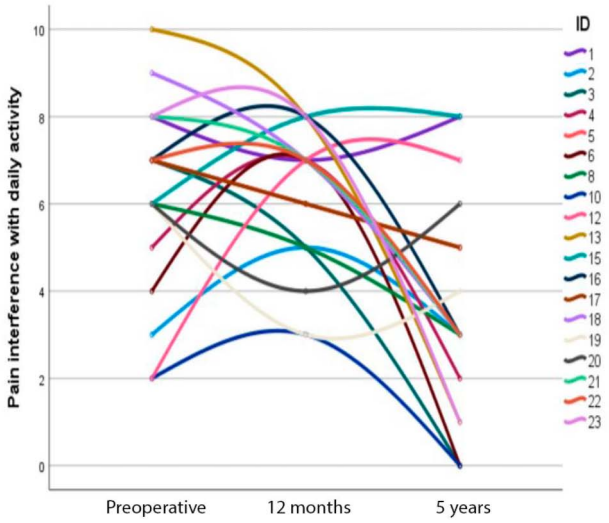
Quantiative	Qualitative	Interpretation
	**Patient 15**: "Recently, I have had nights when I wake up at 2 or 3 o´clock with pain and unrest. I can't find rest and relax. It hurts when I try to find a new position in the bed." Score at 5 years: **8**. **Patient 16**: "There are some things one can't do like before. I feel it when trying to do gardening for example and when cleaning the house. Getting down on the knees and back up again is a whole process in itself." Score at 5 years: **3**. **Patient 17**: "I can't even sit on the knee on top of the bed. It's that pressure pain. It is physically painful where I press down." Score at 5 years: **5**. **Patient 21:** "I feel I can do almost all I could before, except I can't run. If I see the bus, and there are 50 meters or 20 meters to it, I don't have a chance to run for it. I just have to wait. I can´t do it. Not one single meter." Score at 5 years: **3.**	Decreasing pain interference with daily activity from 12 months to 5 years. Most participants still experienced some pain interference with daily activities and thus limitations in everyday life. Examples of limitations: difficulties with running, skiing, house chores/ kneeling, sitting with knee bent. One participant expressed disturbed sleep due to pain.
B IDs missing for quantitative data on patients 7, 9, 11, 14		

Fig. 3 A-C This joint display shows the combination and interpretation of the quantitative and qualitative results: (**A**) pain with walking, (**B**) pain with daily activity, and (**C**) pain intensity.

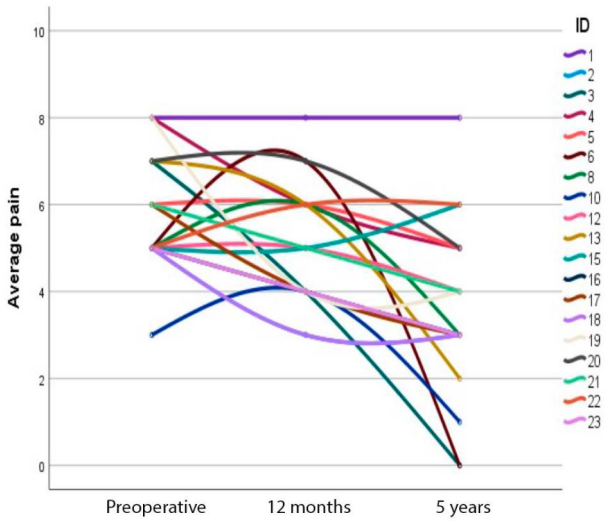
Quantitative	Qualitative	Interpretation
	**Patient 1**: "But it's not painful in that way that I need a pill every day. There are pains inside the joint. But the pain is minimal now, and I can take a pill for it. Sometimes, I take one every day. But now, I haven't taken one in 3 to 4 weeks or something." Score at 5 years: **8**. **Patient 12**: "I don't have those pains in the knee now. I have pain in the other knee. But nothing like before. It truly was a 10 plus, but now it is below 5. But there is a soreness when I feel the knee. Like a tooth ache, I would say." Score at 5 years: **4**. **Patient 17**: "I seldom use pain medication and only paracetamol maybe before I go to sleep, mostly for my fibromyalgia." Score at 5 years: **3**. **Patient 20**: "I don't think it is all that bad when it is like this. The pain only lasts a little while. Other times, it can be a weak dull pain." Score at 5 years: **5**. **Patient 22**: "Sometimes, it's like a sharp pain. Other times, it's more an aching and just very painful, but I also have rheumatism so it's not good to know what is what." Score at 5 years: **6**.	Pain intensity decreased from 12 months to 5 years for all except two patients. Patient 1 reported unchanged scores of 8 over all three timepoints. The score at 5 years were not in accordance to what were expressed in the interviews. Very few needed pain medications for their knee every day and most of those who still needed it, only used milder pain medications. Other physical challenges affected the experience of pain.
C IDs missing for quantitative data on patients 7, 9, 11, 14		

Fig. 3 A-C *Continued*

which is not a disease-specific scoring system. To avoid including patients with pain unrelated to the knee, patients were classified as nonimprovers after TKA based on their scores on pain-related interference with walking. With this approach, we identified a subgroup of patients who underwent TKA (22% [45 of 202]) who reported no improvement in pain interference with walking at the 12-month follow-up [25]. This subgroup is comparable to findings in other studies using knee-specific instruments [2]. Pain-related interference with walking is an outcome that captures both pain and function. The ability to walk without pain is an important outcome for patients who underwent TKA, thus we believe that we have identified patients who are representative of nonimprovers after TKA.

We collected qualitative data through individual interviews conducted by two authors (VBS, AD). To minimize the risk of inconsistency during the data collection [12], the first author (VBS) received training from a senior qualitative researcher (AD) and a semistructured interview guide was used.

We recognize that only half (n = 23) of the subgroup (n = 45) was included in this study. However, there were no differences in sociodemographic baseline data between the included and the excluded participants (Table 1).

We used the validated BPI to measure patients' experience with pain intensity, pain interference with walking, and daily activity. The BPI is a generic pain-specific tool and includes a body map for pain locations that is helpful to distinguish pain elsewhere from knee pain. BPI is recommended to assess chronic pain after TKA [47] and is a reliable and valid instrument for those who undergo TKA [6]. We believe that with our focus on intermediate-term persistent postsurgical pain, the BPI served this study's purpose well.

The cohort of 45 patients with no improvement in pain 1 year after surgery consisted of 67% females, whereas our sample of 23 had 57% females. Thus, we adjusted for sex in the multivariate statistical model. We did not find any differences between the sexes. However, our sample may have been too small to identify such differences as previous studies have identified female sex as associated with persistent postsurgical pain after TKA surgery [18, 40].

When subgroups are investigated, they often constitute a small number of patients, which may result in a lack of statistical power [44]. We acknowledge that our sample size is limited; however, each included patient was assessed at three different timepoints. This makes it possible to estimate variations within each patient and between patients better and also assess the effect of time on the outcome. Our aim was not to compare groups. Instead, we aimed to describe changes over time and therefore argue that the results from the mixed model are useful and informative. In addition, our quantitative results were supported with the findings from the qualitative part of the study.

One participant who reported increased pain beyond 12 months was found to have prosthetic loosening at the 5-year follow-up. Implant loosening is one of several identifiable explanations for pain after TKA. It was not an aim for our study to exclude patients with specific and known explanations for their persistent postsurgical pain. Therefore, we decided to include this patient to achieve more variation in our

material and to include a natural/real-life material of patients who experience pain for various reasons.

The combination of the BPI questionnaire with individual interviews revealed discrepancies between the two datasets, but it also allowed complexities regarding persistent postsurgical pain to be addressed more thoroughly. During the interviews, several patients stated that when completing the questionnaire, they were not able to explain that their pain was short-lived and occurred only with certain movements. The patients were, however, able to highlight this through the individual interviews. Thus, triangulating methods allowed for rigor and greater validity [33].

Discussion of Key Findings

We found that pain with walking, pain with daily activity, and pain intensity all decreased at 5 years compared with preoperatively and 12 months postoperatively.

From the interviews, we identified three consistent themes: regained wellness over time, persistent limitations after TKA, and complexity of physical challenges.

Regained Wellness Over Time

Our qualitative findings support the quantitative findings of improved pain scores over time. Our participants expressed in the interviews that they experienced a gradual improvement in pain from about 2 years to 5 years after surgery. Wylde et al. [48] reported that approximately one-third of their patients with TKA had clinically meaningful improvement in pain between 12 months and 2 years postoperatively. Another study that also reported pain improvement over time had a mean follow-up period of 9.1 years but could not be certain of when exactly the improvements occurred [38]. In contrast, a study from the Swedish Knee Arthroplasty registry [1] reported that patients who were poor responders continued to be dissatisfied up to 13 years postoperatively. In these studies, residual pain was a dominant factor for dissatisfaction. As mentioned by Wylde et al. [48], variability in findings for mid-term and long-term pain trajectories may be due to all the different patient-reported outcome measures, endpoints, and follow-up timepoints.

Pain Interference With Walking and With Daily Activity

Although our participants reported improvements in pain and became more physically active and able to walk longer distances without pain, walking downhill or downstairs still posed problems including pain for many. Unmet expectations regarding the ability to walk downstairs 6 months and 12 months postoperatively have been described by Conner-Spady et al. [4]. Although pain with daily activities decreased in our sample, it remained a limitation in many participants' everyday lives, which is consistent with the result of a prior study by Larsen et al. [22]. There was some discrepancy in the data obtained from the BPI questionnaire and interviews. Several participants noted that the quantitative measures did not allow for reporting pain that only occurred with certain movements. The decrease in pain was clinically important for our participants with at least a 2-point decrease in their pain score [10, 35]. The qualitative data identified specific limitations and a more nuanced picture of pain interference in everyday life. Such limitations included pain when kneeling, difficulties with house chores, gardening, running, and sitting with the knee bent. In accordance with our findings, Williams et al. [45] reported that kneeling is difficult, without directly identifying pain as a cause.

A study by Witjes et al. [46] found that younger patients could return to high-impact sports after TKA. In contrast, the younger participants in our study stated that high-impact sports, such as running, cross-country skiing, or downhill skiing, were difficult to resume, owing to knee pain. Younger participants may have higher expectations for resuming physical activities and sports [46], which is noteworthy, given that the demand for primary TKA in younger patients is expected to increase in the future [21]. Older participants in our sample may have had lower expectations of return to physical activities due to high age and comorbidities. When living with persistent postsurgical pain over time, these patients may have learned to better accommodate their new state either by changing their mental perspective or by reducing their physical activity. The latter is shown by Larsen et al. [22], who found that physical activity seemed to decrease in patients with persistent pain for more than 6 months postoperatively. Several of our participants were able to walk and hike for 1 or 2 hours before experiencing pain, which they could not preoperatively or for the first months after surgery. Most of our participants rated their pain with walking in the mild-to-moderate [41] range at the 5-year follow-up, and the better results for our patients may be due to differences in follow-up length [22] or reflect culturally different expectations for physical activity after TKA. Being physically active and going for long walks and hikes is an important part of Norwegian social identity.

Comorbidity as a Confounding Factor for Regaining Wellness?

Most patients in our sample had comorbidities and multiple painful body sites, which is known to be associated with higher levels of pain 12 months after TKA [25]. Variation and nuances among our participants may, to some extent, be explained by their medical histories before and after surgery. Several participants reported having pain in other body sites than the knee, which had contributed to physical

inactivity. Some of these conditions were successfully treated, while others still had painful conditions that influenced everyday life 5 to 7 years postoperatively. Thus, comorbidity and more painful sites may have interfered with the recovery process after the TKA surgery for these patients.

Posttraumatic arthritis is known to predict worse outcomes after TKA [29]. One participant in our study had secondary osteoarthritis caused by severe knee trauma. In the interview, this patient said they still had pain, but they experienced a decrease in pain after the 12-month follow-up. These participant quantitative data at the 5-year follow-up were missing.

Two patients had pain trajectories that differed from the rest (Fig. 3) and illustrate the complexity of the topic and results. These two are addressed in the limitations of the study.

Implications for Further Research

In line with a recent study [38], our study indicates improvement beyond 12 months after TKA. We suggest including patient-reported outcome measures at 5 years in national arthroplasty registers, which could facilitate larger studies to increase our understanding of the dynamics of persistent pain in patients who undergo TKA. Patients in our study expressed that comorbidities and painful body sites elsewhere interfered with regained wellness over time and prolonged the recovery period. Interestingly, studies with other designs [23] found that these factors were associated with higher levels of pain at 12 months. Comorbidities and a history of more painful sites as possible risk factors warrant more research and would be an interesting topic for further longitudinal studies. In this study, we conducted individual interviews at one timepoint with each patient. However, conducting interviews at several timepoints could be interesting for further research for comparing qualitative results in pain trajectories over time, enabling patient participation in discussions on changes, and also reduces a possible recall bias in the participants. This study did not explore coping mechanisms. However, some of the patients in this study may have learned to better accommodate their new state either by changing their mental perspective or by adapting to their limitations. Coping mechanisms can be viewed as modifiable risk factors. Understanding coping mechanisms may be helpful when advising other patients with persistent postsurgical pain and when developing and testing interventions to facilitate more helpful coping mechanisms in these patients.

Conclusion

In this subgroup of patients experiencing persistent postsurgical pain 12 months after surgery, most participants experienced a decrease in pain between 1 year and 5 to 7 years after surgery. The mixed-methods approach revealed more layered and complex experience for the participants. Although persistent postsurgical pain still caused certain limitations for the participants, pain seemed to be less influential in their everyday lives 5 years to 7 years after primary TKA. Clinicians may use these findings to inform and guide patients with delayed improvements in pain into more realistic expectations for recovery, rehabilitation, and strategies for coping with pain, comorbidity, and function. It is, however, imperative to rule out other reasons for pain in patients reporting pain 12 months and longer after surgery and be attentive of possible changes in pain character over time.

Acknowledgments We thank all the patients in this study for participating and sharing their experiences.

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