Screening to identify postoperative pain and cross-sectional associations between factors identified in this process with pain and function, three months after total knee replacement

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Conflicts of interest

The authors have no conflicts of interest to declare relating to the submitted work.

ABSTRACT

Objectives

Describe the screening and recruitment process of a randomised trial and evaluate associations with knee pain and function three months after total knee replacement (TKR).

Methods

To screen for a multi-centre trial, 5036 patients were sent an Oxford Knee Score (OKS) questionnaire 10 weeks post-TKR. Patients who reported pain in their replaced knee (≤14 on OKS pain component), completed a second OKS 12 weeks post-TKR. Those still experiencing pain 12 weeks post-TKR completed a detailed questionnaire 13 weeks post-TKR. These data were used to characterise pain in a cross-sectional analysis. Multivariable regression was performed, identifying factors associated with pain and function at 13 weeks post-TKR.

Results

We received OKS questionnaires from 3058/5063 (60%) TKR patients, 907/3058 (30%) reported pain in their replaced knee 10-weeks post-operatively. By 12-weeks, 179/553 (32%) patients reported improved pain (OKS>14). At 13-weeks, 192/363 (53%) who completed a detailed questionnaire reported neuropathic pain, 94/362 (26%) reported depression symptoms and 95/363 (26%) anxiety symptoms. More severe pain at 13-weeks post-

operatively was associated with poorer general health, poorer physical health, more pain worry and lower satisfaction with surgery outcome. More severe functional limitation was associated with higher levels of depression, more pain worry, lower satisfaction with surgery outcome and higher pain acceptance.

Conclusions

Screening after TKR identified people with pain. We identified several potential targets (physical and mental health outcomes, acceptance of pain and quality of life) for tailored intervention to improve outcomes for patients. Trials of multidisciplinary interventions are now needed.

Key words

Total knee replacement; chronic pain; function; neuropathic pain; post-operative screening

Significance and innovations

- Good uptake to early postoperative screening of pain and function after TKR
- Half of patients with pain at three months after TKR report neuropathic pain symptoms
- A quarter of patients with pain at three months after TKR report depression and/or anxiety
- Multiple factors such as quality of life, physical and mental health outcomes and acceptance of pain are associated with more severe pain and function after TKR, highlighting the need for multidisciplinary interventions

Primary total knee replacement (TKR) is a common operation, with over 100,000 operations performed in the UK's National Health Service (NHS) in 2019 (1, 2). The main indications for TKR are chronic pain and functional limitations, predominately related to osteoarthritis. Although the operation is successful for many, 10-34% of patients experience ongoing pain in the months and years after surgery (3). Despite its prevalence, knowledge about the onset and postoperative trajectory of chronic pain after TKR is not well understood (4). The evidence base for treatment and management is sparse (5, 6), and referrals for assessment and care are inconsistent (7, 8). As yet there is no pre-operative model that can accurately predict who will have chronic pain after surgery (5, 9). People with chronic pain after TKR can feel abandoned by healthcare services and struggle to understand ongoing pain (10).

The improvement trajectory following TKR is variable: however, most pain relief occurs within the first three months postoperatively (11). Persistent pain at three months could be due to slower recovery or an early indication of longer-term chronic pain. Chronic pain is difficult to treat once established (12) and the identification and characterisation of pain early in the recovery trajectory could facilitate the delivery of targeted interventions to support recovery and improve longer-term pain outcomes. Hence, there is potential for early identification of these patients to explore whether intervention is warranted.

Previous studies have described pain after TKR (3, 13-17), but these studies have methodological shortcomings that have contributed to the poor quantification and characterisation of pain after TKR, These include: use of surgeon-administered tools to assess pain, limited assessment of the multidimensional nature of pain, variable definitions of pain resulting in different prevalence estimates, and single centre studies, limiting generalisability (3, 16, 18). A robust method of identifying patients with pain after TKR using the OKS pain component has been developed (19). Using data from a national population-based cohort across England, patients with a postoperative score of ≤14 on the OKS pain component were

identified as having pain likely to negatively impact on health-related quality of life (19). Applying this method for identification of patients with pain in the first three months post-operatively allows the early investigation of pain characteristics. The aim here is to describe our screening procedures to identify people with postoperative pain and to identify associations with pain and function amongst patients with pain in the first three months after primary TKR.

PATIENTS AND METHODS

Design

The data analysed in this article are from the Support and Treatment After joint Replacement (STAR) trial, a multicentre randomised trial evaluating the effectiveness of a care pathway for patients with chronic pain at three months after TKR (20). Screening data included in these analyses were collected before randomisation and are analysed as observational data. Study methods relevant to these analyses are described and reported following STROBE guidance (Supplementary Table 1).

Patient and public involvement (PPI)

This research was conducted in collaboration with the 'Patient Experience Partnership in Research (PEP-R) STAR group, a specialised group comprising five patients with experience of chronic pain after TKR. Through regular group meetings, patient representatives contributed to project design and management.

Participants

Between September 2016 and May 2019, eligible patients were recruited into the STAR trial from eight NHS orthopaedic centres in Bristol, Cardiff, Exeter, Mansfield, Oswestry,

Wrightington, Leicester and Birmingham. Inclusion criteria included adults who received a primary TKR for osteoarthritis and reported pain in their replaced knee 12 weeks post-operatively. Exclusion criteria included lack of capacity to provide informed consent, previous study participation for the contralateral knee, or participation in another project that interfered with STAR. STAR complied with the Declaration of Helsinki and was approved by the South West – Central Bristol Research Ethics Committee (16/SW/0154) and the Health Research Authority. All participants provided written, informed consent, in two stages: first for the screening study only, comprising OKS measurements at 10 and 12 weeks after TKR and, second for the main STAR trial, comprising a detailed baseline questionnaire at 13 weeks after TKR. Identification of patients with pain after TKR began at 10 weeks post-operatively to ensure timely identification of those with pain that persisted at three months post-operatively. We report our findings of screening procedures and the cross-sectional analysis of associations with pain and function at 13 weeks after TKR surgery.

Initial postal screening to identify patients with pain 10 weeks after TKR

Patients who received a primary TKR for osteoarthritis eight weeks previously were sent a study information leaflet, consent form and short initial screening questionnaire, including the OKS (21) and sociodemographic questions. Non-responders received a single reminder. The OKS is a joint-specific measure of pain and function consisting of 12 items with 5 ordinal response options for each (21). There is evidence of validity and reliability, with the OKS being reported as the best performing site-specific patient reported outcome measure in a psychometric review of 32 measures used in hip and knee replacement surgery (22). It has an overall score ranging from 0-48 (worst to best). Two subscales can be calculated: a 5-item OKS function component (raw score of 0-20) and a 7-item OKS pain component (raw score of 0-28). Patients with a score of 0-14 on the raw OKS pain component were considered as having pain that was likely to negatively impact on health-related quality of life (19). It is

recommended that the component scores are standardised to a 0-100 scale (worst to best) for analysis (23).

Second telephone screening to confirm ongoing pain 12 weeks after TKR

All responding patients reporting an OKS pain score ≤14 at 10 weeks were contacted by telephone at 12 weeks and invited to complete a second screening questionnaire repeating the OKS to confirm their pain status. Those still reporting clinically meaningful pain (defined as an OKS pain score ≤14) at 12 weeks were eligible for invitation to enter the trial.

Detailed study questionnaire at 13 weeks after TKR for patients with pain

Participants who gave their consent to the trial completed a third OKS as part of a more detailed study questionnaire prior to randomisation. If questionnaires were not returned within one week, the participant was offered support on the telephone with a researcher.

The outcomes assessed in the questionnaire administered at 13 weeks post-operatively reflected the eight domains of the core outcome set for chronic pain after TKR (24). Pain severity and pain interference were assessed using the Brief Pain Inventory (BPI) (subscale scores from 0-10; best to worst) (25). Knee pain and function were measured using the OKS. Pain with neuropathic features was assessed using two questionnaires. First, the PainDetect (26), which can be analysed as a continuous score (-1 to 38, with a higher score indicating greater likelihood of neuropathic pain) or categorised into nociceptive pain (-1 to 12), possible neuropathic pain component (13-18) or probable neuropathic pain component (19-38). Secondly, the Dolour Neuropathic scale (DN-4) (27), with scores ranging from 0-7 (best to worst) and a score of ≥3 indicating neuropathic pain characteristics. Single questions evaluated the frequency of pain in the past 24 hours and four weeks and how this compared to pre-operative pain. General health was measured using the SF-12 (28), comprising a Physical Component Score (PCS) and a Mental Component Score (MCS) (0-100; worst to

best). Health-related quality of life was assessed by the EQ-5D-5L (29) (-0.594 to 1 where 1 indicates 'perfect health' and 0 indicates 'dead') and capability by the ICECAP-A (30) (-0.001 to 1, worst to best). Depression and anxiety were assessed using the Hospital Anxiety and Depression Scale (HADS) (31), with subscale scores (HADS-A; HADS-D) ranging from 0-21 (best to worst) and categorised into unlikely symptoms of depression/anxiety (0-7), possible depression/anxiety (8-10) and probable depression/anxiety (11-21). Worry about pain was assessed with the Pain Catastrophizing Scale (PCS; scored 0-52; best to worse) (32) which consists of three subscales labelled rumination (scored 0-16), magnification (0-12) and helplessness (0-24). The Possible Solutions to Pain Questionnaire (PaSol) (33) was also completed and the four subscales analysed: solving pain (scored 0-24; worst to best), meaningfulness of life despite pain (0-30), acceptance of the insolubility of pain (0-18), and belief in solutions (0-12). Patient satisfaction with the outcome of surgery was measured by the Self-Administered Patient Satisfaction Scale (34), a 4-item arthroplasty-specific score (25-100; worst to best). Painful body regions were indicated on a body diagram, and widespread pain was defined as pain in at least two sections of each two contralateral limbs and in the axial skeleton (35). Sociodemographic questions included age, gender, marital and living status, ethnicity, and education level.

STATISTICAL ANALYSIS

Screening questionnaire

As well as response rates, distributions of screening OKS scores were assessed at each phase using histograms and summary statistics such as means (SD). Regression analyses were performed on the OKS pain and function subscores as the outcome variables to explore the associations with age and gender. Results are presented using regression coefficients, 95%

confidence intervals and p-values. The relationship between the OKS subscales were assessed using scatter plots, replicated stratified by age group (<60; 60-70; 71-80; >80) and gender.

Study questionnaire analyses

Summary statistics for sociodemographic data and patient-reported outcomes were presented using means (SD)/medians (IQR)/counts (%). Distributions of the OKS scales were presented as histograms to assess normality. Correlation coefficients between pain outcomes were evaluated. Linear regression was used to evaluate the factors independently associated with the OKS pain and function scores. Staged regression was then used to select variables systematically for the linear regression model ((36) is an example of this approach). Associations were explored between OKS pain and the following groups of factors: sociodemographic variables; general health; mental health measures. Each group of variables was first explored separately in multivariable regression models, with (iterative) exclusion of variables without strong associations with OKS pain when adjusted for other variables in the model. The process was then extended to consider all groups together, resulting in a 'final' regression model containing only variables that were strongly associated with OKS pain, adjusted for other variables. This process was repeated for OKS function exploring associations with sociodemographic variables and mental health outcomes. In all analyses, the standardised OKS pain and function scores (0-100) were used (23).

Data completeness is reported in the Tables and Figures. For the OKS component scores, the mean of other items on the subscale was used to impute a missing item if only one item was missing. If more than one item was missing, a score was not calculated (37). The approach to missing data for other validated questionnaires followed guidance recommended by the questionnaire developers; further details are in the STAR trial statistical analysis plan (38).

Sample size

The sample size for the STAR trial was based on detecting a minimal clinically important difference between trial arms in the BPI subscales at 12 months after randomisation (20). We did not undertake a separate power calculation for the analyses presented here as our intention was to investigate characteristics of the study population collected prior to randomisation; rather the levels of achieved precision are indicated through the relevant confidence intervals.

RESULTS

Recruitment, screening and participant flow

An overview of participant flow through the study is provided in Figure 1. Screening questionnaires to identify patients with pain after TKR were posted to 5,036 patients who had a TKR at one of eight orthopaedic centres. Completed screening questionnaires were returned by 3,058 patients (61%) at a mean (SD) of 10 (2) weeks post-operatively. Of these, 907 (30%) patients reported pain in their replaced knee at 10 weeks, of whom 553 (61%) completed a second telephone OKS to confirm pain status at 12 weeks (SD = 2 weeks). The mean (SD) age of the 553 patients who completed a telephone questionnaire was 67.7 (8.6) years with 56% being female. Those who did not complete a telephone questionnaire at 12 weeks (n=354) were slightly older, with a mean (SD) age of 69.4 (10.4) years and 62% were female. Patients who completed the 12 week telephone-administered OKS had a slightly higher mean OKS (18.2; SD = 5.4) than those who did not complete a telephone OKS (17.2; SD = 5.7) indicating less pain and better function in responders compared with non-responders at 12 weeks. 363/553 (66%) patients completed a detailed questionnaire at 13 weeks (SD 2 weeks).

Sociodemographic characteristics of responders and non-responders to the screening questionnaire at 10 weeks are provided in Table 1(A). Mean age was comparable (70 years), although females were slightly less likely to respond than males (55% vs. 62%). The OKS overall and component scores are in Table 1(A) and Supplementary Figures 1 and 2. Overall, 907/3,058 patients (30%) reported clinically meaningful pain in their replaced knee at 10 weeks (OKS pain component ≤14).

Scatter plots of the OKS component scores demonstrated a linear relationship between pain and function, with similar patterns when stratified by gender and age (Supplementary Figures 3-5). Younger age and female gender were associated with worse knee pain severity and functional limitations at 10 weeks (Table 2).

Of the 533/907 patients to complete the OKS by telephone, 179 (32%) reported an improvement in their pain (>14 OKS) but 374 (68%) remained in pain. Summary statistics of age, gender and week 10 OKS scores for those who did and did not respond at week 12 are presented in Table 1(B). Responders were slightly younger than non-responders at 12 weeks with a lower proportion of females responding (Table 1(B)). Responders at 12 weeks had slightly higher 10 week OKS scores compared with those who did not respond at 12 weeks.

Characterisation of people reporting pain at 13 weeks post-TKR

Sociodemographic characteristics and patient-reported outcomes for the 363/374 (97%) participants who completed a detailed questionnaire at 13 weeks are in Table 3. These participants had a mean age of 67 years (SD 9) and 60% were female. Neuropathic pain characteristics were common, with half (53%) of participants having a PainDETECT score that indicated likely neuropathic pain (score > 19) and three-quarters (74%) of patients having neuropathic pain characteristics according to the DN-4 (a score of ≥3). 47% of patients had both likely neuropathic pain according to PainDetect and neuropathic pain

according to the DN-4. Poor mental health was also common, with patients having HADS scores indicative of either probable depression (26%) or anxiety (26%); of these 60/362 (17%) reported symptoms of both depression and anxiety. Over the previous four weeks, 96% of patients had experienced pain frequently, defined as pain being present 'often', 'most of the time' or 'all the time'. Almost half (44%) reported their pain as 'a bit worse' or 'much worse' than their pre-operative pain. Despite still being in pain at 12 weeks, most (74%) were satisfied with their overall outcome from TKR and 55% were satisfied with their pain relief, although satisfaction rates with ability to do activities of daily living and leisure activities were lower (39% and 38%, respectively).

Regression analysis

Results of the linear regression model with the OKS pain component as the outcome are displayed in Table 4. In this cross-sectional analysis, having more severe knee pain at 13 weeks was associated with lower general health measured by the EQ 5D 5L utility score, lower physical health measured by the SF-12, higher pain worry (PCS), lower satisfaction with the outcome of surgery.

From the linear regression model with the OKS function component as the outcome (Table 5), in patients with pain at 13 weeks postoperatively, more severe functional limitation was associated with higher levels of depression, higher pain catastrophizing, lower satisfaction with the outcome of surgery and higher levels of acceptance of the insolubility of pain.

DISCUSSION

This study examined characteristics of people reporting pain 10 to 13 weeks after TKR. We used the validated OKS pain component threshold to identify patients with pain in the first three months after TKR. Using this standardised pain definition, 30% of patients reported

pain in their replaced knee 10 weeks after surgery. Of the 553 patients who completed a second OKS by telephone (12 weeks after TKR), 30% reported an improvement in their OKS pain score from the 10 week measurement. However, for the majority (70%), the pain was still present at three months. Applying the OKS pain threshold allowed an in-depth evaluation of the characteristics of patients with pain at three months after TKR. We found that over half of patients reported pain with neuropathic characteristics and a quarter of patients reported probable depression or anxiety, with 17% reporting both depression and anxiety. Despite still having problems with pain, three-quarters of these patients were satisfied with their TKR outcome. Patients with more severe knee pain at three months were likely to have poorer general health, poorer physical health, higher pain worry (measured as pain catastrophizing) and lower satisfaction with the outcome of surgery. Patients with greater functional limitations were more likely to have higher levels of depression, higher pain worry, lower satisfaction with the outcome of surgery, and higher levels of acceptance of the pain's insolubility.

Previously, the lack of a robust approach to screening has been a barrier to the implementation of new services to improve care for patients with pain after TKR (7). Our study demonstrated that early screening using the OKS definition of chronic pain as a standardised approach to identify patients with pain is achievable. In our large multicentre trial, one third met our definition of pain at 10 weeks; this is not unexpected as TKR has a long recovery period and individual patients' recovery trajectories vary (11). A third of patients with pain at 10 weeks had improved by 12 weeks, demonstrating that patients can experience rapid recovery during this early post-operative period. However, 70% of responding patients with pain at 10 weeks still had pain at 12 weeks, and for some, this pain is likely to persist in the longer-term. Early screening to identify patients with pain at three

months could facilitate targeted care delivery to prevent the transition of acute pain to chronic pain, for example through transitional pain clinics (39).

The prevalence of neuropathic pain after TKR and other types of surgery differs in the literature, likely due to variation in definition and measurement (40). This warrants further research and suggests a potential role for routine screening and treatment of neuropathic pain after TKR. A systematic review has identified inadequate response to pharmacotherapy for neuropathic pain, that relates to modest efficacy, high placebo rates and poor phenotyping (41). Further work could examine the development of targeted interventions including non-pharmacological treatments. For example, the National Institute for Health and Care Excellence (NICE) currently recommends trials comparing the effectiveness of combination therapy versus monotherapy for neuropathic pain (42). Another potential target for intervention is depression and anxiety, reported by a quarter of participants. Given the known association between mental health and chronic pain (43), concurrent treatment of both conditions may improve outcomes for patients. An interesting finding was, despite ongoing pain, satisfaction with treatment was high. This may have been in part influenced by the relatively early timepoint of assessment post-surgery and an acceptance that initial postoperative pain is part of the recovery trajectory. Satisfaction is a complex construct that can be influenced by a wide array of interrelated factors (44). The degree of dissatisfaction experienced by patients with chronic pain after TKR has been associated with various factors including instability in the coronal plane, stiffness and negative social support (17). Further research would help to further understand the factors that influence patients' satisfaction with their outcome.

Our analysis also identified factors that were associated with more severe pain and functional limitations at three months. These associations are consistent with previous studies of pain conditions (44-46) and present potential areas for intervention to improve patient outcomes.

Any such intervention should be multidisciplinary to address the varied nature of factors associated with pain. The association of more severe functional limitations with higher levels of pain acceptance of the insolubility of pain over and above general measures of mental health is highly unusual and deserve further attention. It might be artifactual (floor effect), as 27% of the sample recorded 'not applicable' to the item 'I can accept that there is no solution for my pain'. Many patients found the idea of accepting the lack of a solution as simply not relevant to their early post-operative phase. The association could be explained by some patients entertaining the idea of accepting the insolubility of pain because of severity of symptoms. Speculatively, it could also demonstrate a fatalistic coping strategy in which one expects pain after surgery. This coping style could be negative, acting as a barrier to engaging with treatment seeking for pain, or could be positive, acting as a means to disengage from unachievable goals (47).

There are several factors limiting the interpretation of the results from this study. First, the response rate of 61% to the initial postal screening questionnaire at 10 weeks, although comparable to other surveys of orthopaedic populations (17, 48), may have introduced a responder bias (49). Of note, females were slightly less likely to respond to the screening questionnaire and female gender was associated with more severe pain at 10 weeks; this may underestimate pain prevalence. Second, our screening of patients with pain after TKR began at 10 weeks post-operatively, sooner than the internationally accepted three month definition of chronic post-surgical pain (50). This approach was necessary to ensure the timely identification of patients with post-operative pain at three months. Treatment of pain becomes more difficult once pain is established and becomes chronic. Our study demonstrates that identification of patients with pain early in the recovery trajectory is feasible to undertake (12). Third, the data are cross-sectional so the direction of effects cannot be determined. Fourth, our study sample is limited to those with pain three months after TKR, which limits

the generalisability of our results. When interpreting the baseline factors associated with pain and function, we cannot know if these associations are unique to those with pain three months after TKR. This is further limited by the lack of preoperative data on our patient cohort; this was not feasible although would allow further examination of those at higher risk of post-TKR pain. Finally, the measurement tools limit interpretation; although the PainDetect and DN4 are widely used self-report screening tools for pain with neuropathic characteristics, a detailed clinical examination is recommended to confirm diagnosis (51).

In conclusion, large-scale early screening after TKR identified ongoing pain in a relatively high proportion of people, who may benefit from tailored intervention to prevent chronicity. Our study found a high prevalence of pain with neuropathic characteristics and identified several potential intervention targets to improve outcomes for patients with pain at three months post-TKR. Research is needed to build on our findings and evaluate multidisciplinary and targeted interventions to improve outcomes for people with pain after TKR.

Authors' contributions

VW, TJP, NH, JB, CE, and RGH were responsible for study conception and planning. WB contributed to acquisition of data. All authors contributed to management of study conduct. ES and TJP performed the data analyses. VW and ES drafted the manuscript and all authors revised it critically for important intellectual content. All authors gave final approval of the version to be published.

Availability of data and material

The datasets generated during the current study will be available in the University of Bristol Research Data Repository (https://data.bris.ac.uk/data/). Data will be available following publication of the trial results. Access to the data will be restricted to ensure that data is only made available to bona fide researchers for ethically approved research projects, on the understanding that confidentiality will be maintained and after a Data Access Agreement has been signed by an institutional signatory.

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Tables and Figures

Table 1: Characteristics of responders and non-responders to screening questionnaire at 10 and 12 weeks post-TKR

(A) Screening questionnaire at 10 weeks post-TKR	**Responders**	**Non-responders**
N (%)	3058 (61%)	1977 (39%)
Mean age (SD), years	69.7 (8.8)	69.9 (9.8)
% females	54.5%	62.2%
Mean (SD) OKS total score (0-48; worst to best)	29.3 (9.6)	-
Mean (SD) OKS pain component (0-100; worst to best)	62.3 (21.2)	-
Mean (SD) OKS function component (0-100; worst to best)	59.4 (20.8)	-
(B) Telephone-administered screening questionnaire at 12 weeks post-TKR; Eligible at 10 weeks N=907	**Responders at 12 weeks**	**Non-responders at 12 weeks**
N (%)	553 (61%)	354 (39%)
Mean (SD) age	67.7 (8.6)	69.4 (10.4)
% females	56.2%	62.0%
Mean (SD) OKS total score at 10 weeks post-op	18.2 (5.4)	17.2 (5.7)
Mean (SD) OKS pain component at 10 weeks post-op	36.6 (11.3)	35.6 (12.2)
Mean (SD) OKS function component at 10 weeks post-op	40.0 (14.4)	36.2 (15.0)

Table 2: Univariable associations between age, gender, pain and function at 10 weeks after TKR

		OKS pain component		OKS function component	
	N	**Coefficient (95% CI)**	**p-value**	**Coefficient (95% CI)**	**p-value**
Age	2,915	0.29 (0.20, 0.37)	<0.001	0.09 (0.009, 0.18)	0.030
Gender (ref = male)	3,042	-3.09 (-4.60, -1.58)	<0.001	-7.18 (-8.64, -5.71)	<0.001

Table 3: Characteristics of 363 participants with pain at 3months after TKR

Characteristic	**Complete data; N**	
Age	363	
mean (SD)		67.2 (8.7)
median (IQR), range		67 (61, 73) 40-88
Sex, N (%)	363	
Female		217 (60)
Male		146 (40)
Marital status, N (%)	356	
Single		25 (7)
Married/Partner		251 (71)
Divorced /Separated		35 (10)
Widowed		45 (13)
Living arrangement, N (%)	356	
Live alone		78 (22)
With spouse/partner		253 (71)
With someone else		22 (6)
Other		3 (1)
Ethnicity, N (%)	356	
White		335 (94)
Asian		13 (4)
Black		5 (1)
Mixed		1 (<1)
Other		2 (<1)

Education level, N (%)	318	
School left <16 years		22 (7)
School left 16 years		194 (61)
College		63 (20)
University		15 (5)
Other postgraduate		24 (8)
BPI Scores	363	
BPI Severity, mean (SD)		5.2 (1.7)
BPI Interference, mean (SD)		6.28 (1.92)
OKS scores	363	
OKS Total, mean (SD)		18.23 (5.83)
OKS- Pain*, mean (SD)		36.75 (12.70)
OKS-Function, mean (SD)		39.70 (14.28)
Pain Catastrophizing Scale	360	
PCS: total, median (IQR)		18 (9.25, 30.5)
PCS: Rumination, median (IQR)		8 (4, 12)
PCS: Magnification, median (IQR)		2 (1, 5)
PCS: Helplessness, median (IQR)		8 (4, 14)
Pain Solution (PaSol)		
PaSol: Solving Pain, median (IQR)	362	18 (14, 22)
PaSol: Meaningful life, median (IQR)	362	22 (18, 26)
PaSol: Acceptance of the insolubility of pain, median (IQR)	358	8 (5, 11)
PaSol: Belief in solution, median (IQR)	359	9 (6, 12)
Patient Satisfaction, mean (SD)	360	62.88 (18.99)
ICECAP-A, median (IQR)	362	0.78 (0.55, 0.89)
SF-12		
Physical Score, mean (SD)	363	33.44 (6.51)
Mental Score, mean (SD)	363	42.19 (11.12)
EQ-5D-5L, median (IQR)	358	0.53 (0.30, 0.62)
DN-4	359	3.79 (1.71)
Score, mean (SD)		
Neuropathic pain characteristics according to DN-4?		
Yes; N(%)		267 (74)
No; N(%)		92 (26)
PainDETECT	363	18.19 (6.77)
Score, mean (SD)		
Neuropathic pain characteristics according to PainDETECT?		
Unlikely; N (%)		76 (21)
Ambiguous; N (%)		96 (26)
Likely; N (%)		191 (53)
HADS: Anxiety	363	
Normal; N (%)		197 (54)

Borderline anxiety; N (%)		71 (20)
Clinical anxiety; N (%)		95 (26)
HADS: Depression	362	
Normal; N (%)		177 (49)
Borderline depression; N (%)		91 (25)
Clinical depression; N (%)		94 (26)
Pain frequency in past 24 hours	361	
Rarely; N (%)		1 (<1)
Sometimes; N (%)		40 (11)
Often; N (%)		98 (27)
Most of the time; N (%)		164 (45)
All of the time; N (%)		58 (16)
Pain frequency in past 4 weeks	362	
Rarely; N (%)		0 (0)
Sometimes; N (%)		14 (4)
Often; N (%)		102 (28)
Most of the time; N (%)		156 (43)
All of the time; N (%)		90 (25)
Satisfaction with…		
…Overall results of TKR	359	
Very dissatisfied; N (%)		21 (6)
Somewhat dissatisfied; N (%)		72 (20)
Somewhat satisfied; N (%)		154 (43)
Very satisfied; N (%)		112 (31)
…Improving pain	359	
Very dissatisfied; N (%)		47 (13)
Somewhat dissatisfied; N (%)		117 (33)
Somewhat satisfied; N (%)		139 (39)
Very satisfied; N (%)		56 (16)
…Improving ability to do housework or gardening	358	
Very dissatisfied; N (%)		65 (18)
Somewhat dissatisfied; N (%)		152 (42)
Somewhat satisfied; N (%)		111 (31)
Very satisfied; N (%)		30 (8)
…Improving ability to do leisure activities	359	
Very dissatisfied; N (%)		86 (24)
Somewhat dissatisfied; N (%)		140 (39)
Somewhat satisfied; N (%)		106 (30)
Very satisfied; N (%)		27 (8)
Comparison of pain to pre-operative pain	362	
Much Better; N (%)		79 (22)
A bit better; N (%)		70 (19)
The same; N (%)		54 (15)
A bit worse; N (%)		77 (21)

Much worse; N (%)		82 (23)
Presence of chronic widespread pain (Manchester definition)	363	
Yes; N (%)		16 (4)
No; N (%)		347 (96)

Table 4: Final model from the linear regression for associations with pain at 3 months after TKR (n=352)

Variable	Coefficient (95% CI)	p-value
EQ-5D-5L	19.9 (14.1, 25.8)	<0.001
ShortForm-12 (physical)	0.25 (0.09, 0.42)	0.003
Pain Catastrophising Scale	-0.27 (-0.36, -0.17)	<0.001
Satisfaction scale	0.11 (0.05, 0.16)	<0.001

Table 5: Final model from the linear regression for associations with function at 3 months after TKR (n=353)

Variable	Coefficient (95% CI)	p-value
HADS depression	-1.18 (-1.55, -0.80)	<0.001
PaSol (acceptance of pain)	-0.52 (-0.78, -0.25)	<0.001
Pain Catastrophising Scale	-0.24 (-0.36, -0.12)	<0.001
Satisfaction scale	0.09 (0.01, 0.16)	0.019

FIGURE LEGENDS

Figure 1: Participant flow