



# Physical activity and health-related quality of life of patients with chronic knee pain after total knee replacement: Analysis of the PEP-TALK trial



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## ABSTRACT

**Background:** Chronic pain is a major challenge for some people after total knee replacement (TKR). The changing impact of this complication during the first post-operative year remains unclear. This analysis aimed to examine how physical activity and health-related quality of life (HRQoL) evolved over the first year after TKR for patients with and without post-operative chronic knee pain.

**Methods:** We conducted a secondary analysis of data from a randomised controlled trial (PEP-TALK), which tested the effectiveness of a behaviour change physiotherapy intervention compared with usual rehabilitation after TKR. Mean UCLA Activity Score and EQ-5D-5L for participants with and without chronic knee pain (14 points or lower in the Oxford Knee Score Pain Subscale (OKS-PS) at six months post-TKR) were compared at six and 12 months post-TKR. **Results:** Data from 83 participants were analysed. For those with chronic knee pain, UCLA Activity Score remained unchanged between baseline to six months (mean: 3.8 to 3.8), decreasing at 12 months (3.0). Those without post-operative chronic knee pain reported improved physical activity from baseline to six months (4.0 vs 4.9), plateauing at 12 months (4.9). Participants with chronic knee pain reported lower baseline HRQoL (0.28 vs 0.48). Both groups improved health utility over one year. Of those without chronic pain at six months, 8.5% returned to chronic pain by 12 months.

**Conclusions:** Monitoring clinical outcomes after six months may be indicated for those at risk of chronic pain post-TKR. Further, sufficiently powered analyses are warranted to increase the generalisability of this exploratory analyses' results.

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**Abbreviations:** AMTS, Abbreviated Mental Test Score; BMI, body mass index; CCI, Charlson Comorbidity; HRQoL, Health-related quality of life; NICE, National Institute for Health and Care Excellence; OKS, Oxford Knee Score; OKS-PS, Oxford Knee Score pain subscale; PROMs, patient reported outcome measures; RCT, randomised controlled trial; TKR, Total knee replacement; UCLA, University of California Los Angeles.

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## 1. Introduction

Total knee replacement (TKR) has been widely reported as a successful management approach for people with end-stage knee osteoarthritis [1,2]. Patients are frequently older, have on average four medical co-morbidities and have chronic knee pain pre-operatively. The latter has been reported as a major barrier to physical activity and reduced health-related quality of life (HRQoL). Whilst successful for many patients, approximately 20% of people following primary TKR report on-going chronic pain post-operatively [3]. This has been defined as pain that develops or increases in intensity after TKR and lasts a minimum of three to six months [4,5]. Previous work has identified a cut-off point on the pain subscale of the Oxford Knee Score (OKS-PS) to identify patients with persistent high levels of pain six months after TKR [6]. Through this, patient reported outcome measures (PROMs) have demonstrated the ability to categorise chronic pain for individuals six months post-TKR.

The PEP-TALK randomised controlled trial (RCT) tested the effectiveness of a behaviour change physiotherapy intervention to increase physical activity compared with usual rehabilitation after TKR. In total, 224 participants (117 TKRs; 107 total hip replacements) were recruited from eight UK NHS hospitals. They received either six 30-minute weekly group-based exercise sessions (usual care), or the same six weekly, group-based exercise sessions, each preceded by a 30-minute cognitive behaviour discussion group aimed at challenging barriers to physical inactivity following surgery (experimental)[7]. There was no clinically or statistically significant difference between the control and experimental group in six- or 12-month UCLA Activity Score [8] measuring physical activity, or EQ-5D-5L [9] measuring HRQoL. Whilst originally designed to evaluate the effectiveness of a behaviour change intervention, the trial is unusual in TKR RCTs to provide data on both physical activity and HRQoL over initial 12 months post-TKR. This therefore offers an opportunity to develop new insights in the relationship between these measures.

Previously, pain, function, HRQoL and healthcare resources have been assessed for patients with and without chronic pain using data from prospective cohort studies after TKR [10]. However, there is currently limited understanding of how chronic pain post-TKR affects physical activity and HRQoL in the shorter-term. The aim of this study was therefore to perform an exploratory analysis of the PEP-TALK trial data to examine how physical activity and HRQoL evolve in a defined cohort of patients with post-operative chronic pain over the initial 12 months post-TKR period.

## 2. Materials and methods

### 2.1. Study design

A fuller report of the PEP-TALK trial has been previously presented [7,11].

### 2.2. Participants

For this analysis, we identified PEP-TALK participants who underwent a primary TKR due to degenerative joint pathology (not trauma) with complete Oxford Knee Score (OKS) data at six months post-randomisation. The OKS [12] is a valid and reliable PROM assessing disease-specific knee pain and function. It is scored from 0 to 48, where higher scores indicate better disease-specific outcomes. The OKS-PS consists of seven of the 12 items (1,4,5,6,8,9 and 10) from the OKS specifically measuring levels of pain while working, walking, standing, night pain, limping, and levels of confidence in the knee during the prior four weeks. As noted previously [6], participants with chronic pain have been identified using a cut-point of 14 or lower in the OKS-PS at six months after TKR. Patients scoring above 14 on the OKS-PS at six months were considered not to have chronic pain.

### 2.3. Data collection

For all PEP-TALK participants, we identified baseline data including: gender, age, height and weight, Charlson Comorbidity Index [13] and Abbreviated Mental Test Score [14]. For this analysis, follow-up University of California Los Angeles (UCLA) Activity Score [8] and EQ-5D-5L [9] data were gathered from the trial participants [7,11]. The UCLA Activity Score [8] is a validated and reliable patient reported outcome measure (PROM) of physical activity. It is scored from one to 10, where higher scores indicate greater physical activity. The EQ-5D-5L is a valid and reliable measure of HRQoL [9]. It consists of five Likert-type scale questions with response levels enquiring about problems with mobility, self-care, usual activities, pain and discomfort, depression and anxiety. Responses are converted into a preference-based index based on preferences of the English general population which is anchored at zero, representing death, and one representing perfect health [9]. The EQ-5D-5L index was calculated using the Crosswalk Index Value Calculator based on the mapping method developed by van Hout et al [15].

### 2.4. Statistical methods

Mean UCLA Activity Score and EQ-5D-5L values for participants with chronic pain and non-chronic pain were calculated. One thousand bootstrap samples of equal size to the original dataset were generated (for each time point and chronic pain

group) by randomly sampling from the data with replacement. The percentile method was applied on the one thousand samples to derive 95% confidence intervals (CI).

We investigated the chronic pain trajectory of participants at different time points for both groups. Each participant's chronic pain group status at baseline, six and 12 months was determined by their observed OKS-PS. We tracked their movement in and out of a chronic pain status at each time point and reported the number of participants that remained in chronic pain, recovered from chronic pain, or fluctuated between chronic pain and non-chronic pain over 12 months post-TKR. The number of participants moving in and out of chronic pain groups was represented in an alluvial diagram. All analyses were conducted in R-using specific packages [16–18] for data cleaning and statistical analysis [19].

## 2.5. Patient and public involvement

Patient involvement began at trial protocol development. This continued throughout the trial conduct. A patient-member (non-trial participant) attended trial oversight committee meetings. The same patient-member was a trial coinvestigator. In relation to this secondary analysis, he provided insights to help interpret the findings.

## 3. Results

### 3.1. Participant characteristics

A total of 117 participants received a TKR during the trial. Excluding 34 (29.1%) who did not report their OKS-PS at six months, the final sample comprised of 83 participants; their demographics are shown in Table 1. There was no substantial difference between the characteristics of those included compared to excluded from the final analysis (Supplementary File 1). Twelve participants (14.5%) were classified as having chronic pain at six months post-TKR, 71 participants (85.5%) did not have chronic pain. Whilst broadly comparable over most characteristics, participants in the chronic pain group at six months were younger (63 vs. 68 years) and more frequently male (67.1% vs. 58.3%).

### 3.2. Evolution of UCLA activity Score and HRQoL

Participants with and without post-operative chronic pain had similar UCLA Activity Score prior to surgery but different mean values at six and 12 months (Table 2; Figure 1). On average, the non-chronic pain group improved from a mean of 4.0 at baseline to 4.9 six months post-TKR; this plateaued at 4.9 at 12 months. Participants with chronic pain reported a mean pre-operative UCLA Activity Score of 3.8 which remained at the same after six months (mean: 3.8), and then worsened to 3.0 at 12 months post-TKR.

Overall, participants with and without chronic pain improved their mean health utility (EQ-5D-5L) from baseline to 12-months (Table 2; Figure 2). Those in the non-chronic pain group reported an improvement in utility score from 0.48 to 0.73 at six months, plateauing to 0.72 at 12 months. In contrast, participants in the chronic pain group reported a lower baseline score (0.28) improving at six months (0.44) but worsening at 12 months (0.37).

Reported UCLA Activity scores and EQ-5D indexes at six and 12 months were found to be statistically significant between chronic and non-chronic groups based on the bootstrapped CIs 95% estimation (Table 2).

**Table 1**

Study participants demographics between chronic and non-chronic pain status at six months post-TKR.

Variable	Chronic pain at 6 months (n = 12, 14.5%)			Non-Chronic pain at 6 months (n = 71, 85.5%)			Total (n = 83)			p-value *
	N (%)	Mean	Range	N (%)	Mean	Range	N (%)	Mean	Range	
<b>Age</b>	12	63.9	(52–84)	71	68.9	(50–85)	83	68.1	(50–85)	0.111
<b>Gender</b>										0.765
Female	7 (58.3)			48 (67.6)			55 (66.3)			
Male	5 (41.7)			23 (32.4)			28 (33.7)			
<b>CCI (continuous)</b>	12	2.4	(1–4)	71	2.9	(1–6)	83	2.8	(1–6)	0.162
<b>CCI (dichotomised)</b>										0.882
1–3	9 (75)			58 (81.7)			67 (80.7)			
4+	3 (25)			13 (18.3)			16 (19.3)			
<b>AMTS</b>	12	9.6	(9–10)	71	9.7	(8–10)	83	9.7	(8–10)	0.642
<b>BMI</b>										0.759
Healthy Weight (<25)	1 (8.3)	23.5	(23.5–23.5)	8 (11.3)	23.9	(21.7–25.0)	9 (10.8)	23.8	(21.7–25.0)	
Overweight (25–29.9)	3 (25)	29.3	(28.3–29.8)	25 (35.2)	27.7	(25.2–29.9)	28 (33.7)	27.8	(25.2–29.9)	
Obese (30–34.9)	2 (16.7)	33.4	(32.0–34.8)	17 (23.9)	32.4	(30.3–34.2)	19 (22.9)	32.5	(30.3–34.8)	
Morbidly Obese (>34.9)	6 (50)	39.8	(35.4–46.3)	21 (29.6)	38.6	(35.1–48.9)	27 (32.5)	38.8	(35.1–48.9)	

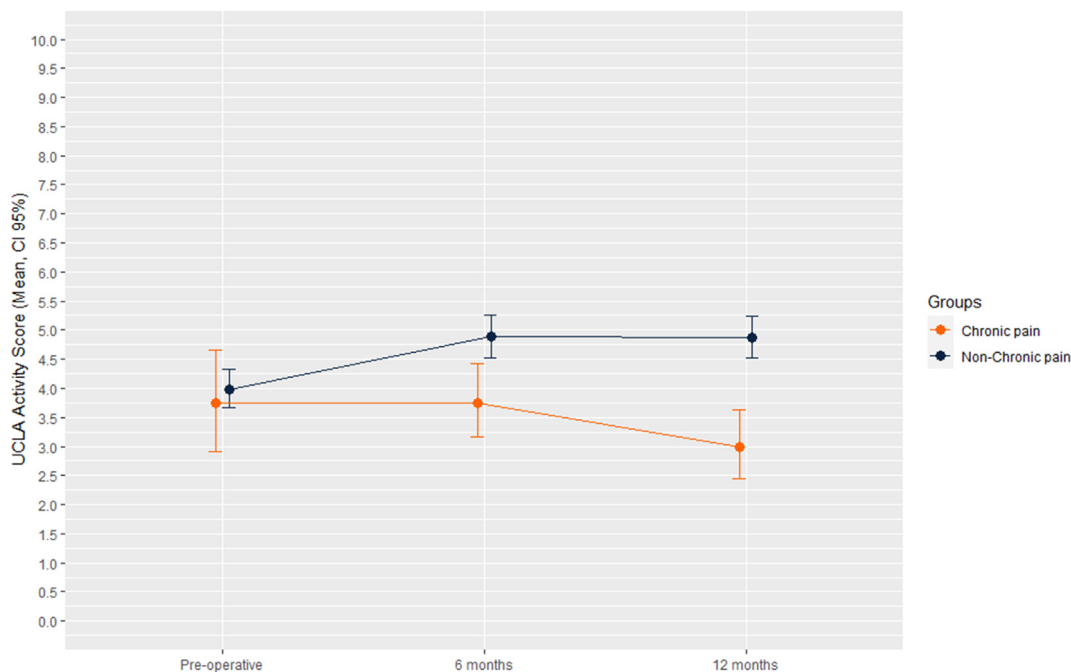
\* Systematic differences in continuous and categorical variables between the chronic pain and non-chronic pain groups were tested with a t-test and  $\chi^2$  test, respectively – the p-values are not meant for formal statistical comparison.

AMTS: Abbreviated Mental Test Score; BMI: body mass index; CCI: Charlson Comorbidity Index.

**Table 2**  
UCLA Activity score and EQ-5D-5L outcomes comparing the chronic and non-chronic pain groups.

Variable	Chronic pain (n = 12)			Non-Chronic pain (n = 71)			Total (n = 83)		
	N	Mean	95% CI	N	Mean	95% CI	N	Mean	95% CI
<b>UCLA Activity score</b>									
Baseline	12	3.75	(2.919–4.667)	71	3.99	(3.662–4.324)	83	3.95	(3.528–4.06)
6 months	12	3.75	(3.167–4.417)	71	4.89	(4.521–5.254)	83	4.72	(4.561–5.183)
12 months	11	3.00	(2.455–3.636)	70	4.87	(4.514–5.242)	81	4.62	(4.351–5.01)
<b>EQ-5D-5L Score</b>									
Baseline	12	0.28	(0.14–0.432)	71	0.48	(0.428–0.534)	83	0.45	(0.383–0.472)
6 months	12	0.44	(0.32–0.541)	69	0.73	(0.678–0.768)	81	0.68	(0.639–0.724)
12 months	11	0.37	(0.203–0.51)	70	0.72	(0.662–0.769)	81	0.67	(0.617–0.715)

UCLA Activity score: ranges from 1 to 10 where higher scores indicate greater physical activity performance. EQ-5D-5L: Health-related quality of life index estimated based on responses to EuroQol 5-level questionnaire, where 0 represents being dead and 1 perfect health.



**Figure 1.** Trajectory of UCLA Activity Scale by chronic pain status.

### 3.3. Transition between chronic pain status

At 12 months after surgery, the number of participants with a chronic pain status was 15/117 (12.8%), those in non-chronic pain were 73/117 (62.4%), and 29/117 (24.8%) did not report their OKS hence were categorised as missing. [Figure 3](#) and [Supplementary File 2](#) illustrate the transition in and out of chronic pain over the 12 months post-TKR based on corresponding OKS-PS scores. The change in OKS -PS over time from baseline to 6 months to 12 months, comparing the chronic pain and non-chronic pain groups, is presented a [Supplementary File 3](#). This indicated a gradual increase in pain score from baseline through the time horizon for those with chronic pain, whereas pain scores plateau at six months for those in the non-chronic pain group.

While the proportion of participants categorised as having chronic pain at the three different time points was similar. The transition in and out of chronic pain varied between those who were in chronic pain or not at the six months mark. For example, of those who were in chronic pain at six months, 33.3% (4/12) were not in chronic pain at 12 months post-TKR. The majority of those who recovered from chronic pain at six months remained in this group at 12 months (58/71, 81.7%). In contrast, 8.5% (6/71) transitioned from the non-chronic to the chronic pain group at 12 months. For 11/34 (32.4%) participants who had missing OKS-PS at six months, the OKS-PS score was below the cut-point after 12 months, so categorised as not having chronic pain.

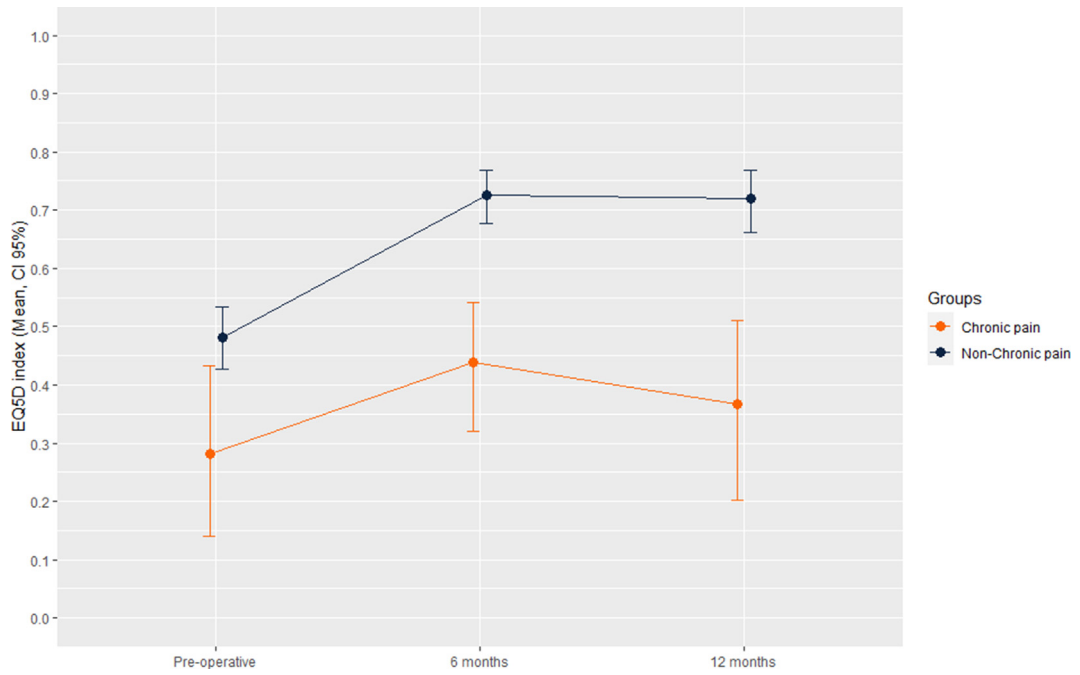
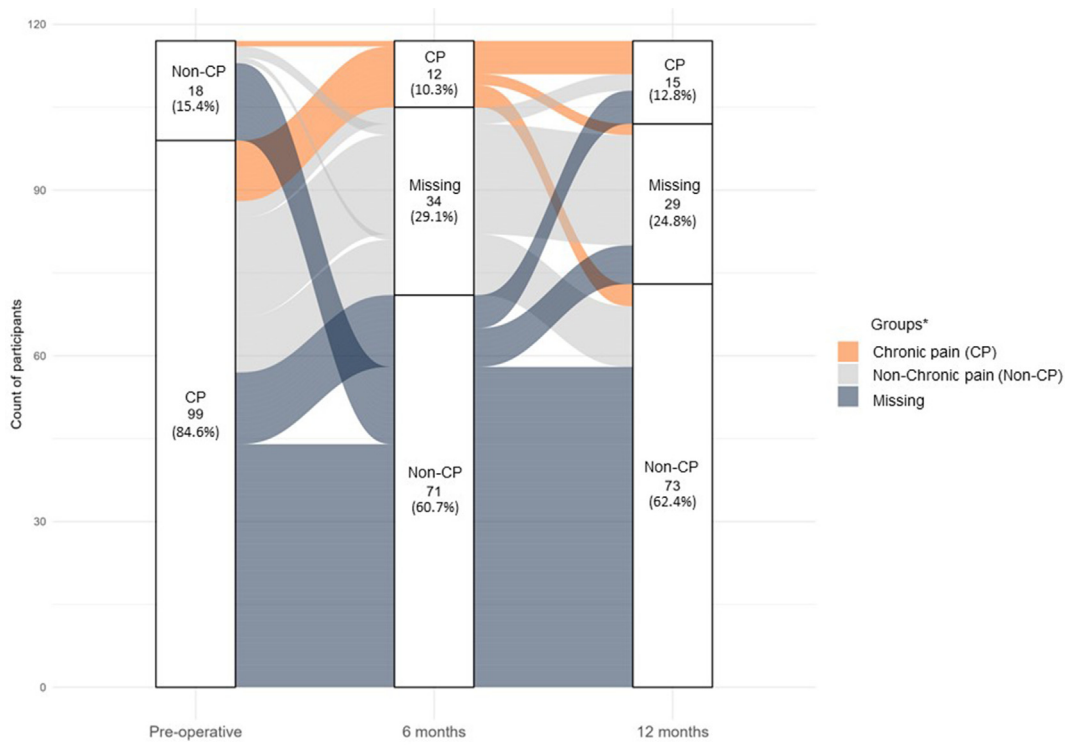


Figure 2. Trajectory of EQ-5D-5L by chronic pain status.



\*Colour based on status at 6 months

Figure 3. Alluvial diagram illustrating the counts of participants in chronic pain status over 12 months post-TKR.

#### 4. Discussion

This exploratory analysis of a RCT has reported that during the first 12 months post-TKR, people with post-operative chronic knee pain at six months experience a different trajectory in physical activity and HRQoL recovery compared to those without post-operative chronic pain. Following their TKR, an important proportion of individuals can still be classified as having chronic knee pain and this is consistent to previous literature [10,20–23]. This suggests monitoring for the need of rehabilitation interventions between six and 12 months may be advocated to improve outcomes.

Characterisation of patients in post-operative chronic knee pain using the OKS-PS scale showed an association with poorer UCLA Activity and EQ-5D-5L scores in the short-term, whereas patients not in chronic pain had better average scores. Whilst this may appear self-explanatory, it highlights the importance of managing chronic pain post-operatively. The UK National Institute for Health and Care Excellence (NICE) recommends that physiotherapy rehabilitation for most patients post-TKR should be self-directed [24]. However NICE acknowledge that for some patients, formal, directed rehabilitation may be indicated [25]. The use of the OKS-PS as a screening tool at both six and 12 months may facilitate the identification of this population who are at risk of poor outcome without formal rehabilitation. Given that this study indicates patients may fluctuate in and out of chronic pain in the initial 12 months after surgery, monitoring to this time-point may be indicated.

There has been limited data exploring physical activity trajectories following TKR. Previous analyses of nationally representative cohorts indicate that between pre-operative and 12-month follow-up, people following TKR do not experience a discernible difference in physical activity engagement [26]. Whilst pain frequently improved, this did not necessarily translate to increased physical activity levels. This analysis builds on previous literature suggesting that whilst this may be the case for individuals who have post-operative chronic pain, for those without, physical activity may improve between baseline and six to 12 months post-TKR. The difference therefore between the analyses could be attributed to the separation of pain status post-TKR. The driver of such pain differences has been suggested to be the difference in aetiology of pain between chronic and non-chronic pain post-TKR. Previous authors have reported that there is a difference in the proportions of nociceptive and neuropathic pain within the TKR population, with worsening pain commonly seen between six and 12 months in people with chronic pain as a result of neuropathic aetiology [27,28]). This highlights the importance of pain status when considering not only physical activity but also interpreting functional gains differently for those with or without chronic pain following joint replacement.

Over eight percent of the cohort in this analysis who did not have chronic knee pain at six months, reported chronic pain at 12 months. This change in pain status may be viewed as unexpected. Previous literature has suggested a plateauing of PROM outcomes from six to 12 months [28]. Recovery phases and physiotherapy would be expected to plateau at six months [29]. Equally joint replacement failure is unusual at this early phase of recovery [30]. Nonetheless, given the importance which pain has on overall HRQoL, as illustrated by these data, the ability to identify those at risk of poor outcome or changing pain status in the early post-operative months (i.e. three months) may offer clinicians the ability to target rehabilitation treatment at this later post-operative phase. Further evaluation on prognostic models of later post-operative pain status change, with a sufficiently powered cohort, may therefore be warranted to reconsider if routine monitoring of outcomes should continue longer than six months.

All participants reported greater post-operative health utility scores compared to pre-operatively. Our findings are consistent with those of previous studies showing health utility gains in those with and without chronic pain at six months, but comparatively worse outcomes for those in chronic pain [10]. Interestingly the chronic pain cohort still reported some improvement, albeit not as much compared to the non-pain cohort, from baseline to six months. This may suggest that, even if pain did not improve, other dimensions of quality of life such as mobility, self-care, usual activities, or anxiety/depression might have, yet it is also possible that it represents an atypical finding from the small sample this analysis comprised of. One novel finding from this study is that by determining the transition of patients in and out the chronic pain status, we demonstrated that nine percent of patients fluctuate back into chronic pain at 12 months after initial relief at six months. Although there may be several explanations for such fluctuation, such as individual characteristics or prior pain severity,[10] this result indicates that patients should be counselled on the potential change in pain status during the initial 12-month recovery phase. This change in pain status may also reflect changing health utilisation demands longer than the initial recovery period post-operatively [10]. Such findings may therefore have wider implications on modelling the costs of TKR and associated rehabilitation from the operative intervention to a longer time-horizon.

Patients in this cohort were participants in the PEP-TALK trial [7,11]. This tested a behaviour change physiotherapy intervention compared to usual rehabilitation after TKR. The trial reported no clinically or statistically significant difference between the experimental and control group [7]. It was therefore appropriate to analyse the impact the chronic pain status irrespective of intervention group allocation. This is an efficient use of trial data. However, we acknowledge that given this secondary analysis was not the primary intention of the trial, the findings reported are exploratory and indicative. Further reflection on whether these findings are repeatable with a larger, sufficiently powered cohort, would be valuable.

Early identification of people with chronic pain following TKR is important as timely interventions may improve outcome. Previous literature has provided evidence to support treatments including radiofrequency (RF) treatment of the genicular nerves [31] and analgesic regimes [32]. More recently, the STAR trial group published their RCT comparing a Support and Treatment After Replacement (STAR) care pathway plus usual care versus usual care alone for people with pain three months

post-TKR [33]. The STAR pathway was shown to be clinically and cost-effective for this population. With the offer of an effective treatment pathway, identification of individuals with chronic pain post-TKR is further supported.

This analysis presented with three key limitations. Firstly, the identification of chronic knee pain was made using a single threshold rather than more complex assessment of pain dimensions. Defining chronic pain using a dichotomised value may explain changes in pain status over time and simplify the complex and diverse dimensions of the pain experience. However, a previous study [6] have effectively used this cut-off point to capture differences between groups with different health outcomes. Also, we identified 14.5% of participants with chronic pain, which is consistent with previous literature which applied different methods to categorise a chronic pain population [10,20–23]. Twenty-nine percent of the potential cohort were excluded due to missing OKS-PS data at six months. Frequently, multiple imputation methods are employed to mitigate the effect of missing data. However, because the definition and transition in and out of chronic pain groups is complex, as described above, imputation methods were not applied. Through this missing data, only 12 participants constitutes the chronic pain group in this analysis. Given the heterogeneity in the post-TKR chronic pain population on pain, disability and demographic characteristics, the generalisability of this cohort to the wider population may be questioned. Whilst this analysis was exploratory and hypothesis generating, the cohort was insufficiently powered to definitively answer the research question and caution should be used when interpreting these findings. Further analyses with a sufficiently powered, generalisable cohort would be a valuable addition to the evidence, to further explore the relationship between early outcomes of physical activity and HRQoL following TKR.

## 5. Conclusions

People with post-TKR chronic knee pain are less physically active and report lower HRQoL compared to those without chronic pain. Whilst both groups reported health benefits, the trajectory of these differed during the initial 12 post-operative months. Those without chronic knee pain at six months post-TKR remain at risk of reverting back to chronic pain up to 12 months post-TKR. Monitoring for outcomes longer than six months and intervening to promote recovery to mitigate the risk of chronic knee pain, are recommended to improve outcome.

## 6. Declarations

Ethics approval and consent to participate: This study involves human participants and was approved by NHS NRES South Central Oxford B (18/SC/0423) Ethics Committee. Participants gave informed consent to participate in the study before taking part. All experiments were performed in accordance with Good Clinical Practice and the Declaration of Helsinki. This study involves human participants and was approved by NHS NRES South Central Oxford B (18/SC/0423). Participants gave informed consent to participate in the study before taking part.

Trial Registration Number ISRCTN29770908, 23/10/2018.

Consent for publication: Informed consent was obtained from all individual participants included in the study.

Consent for publication: not applicable.

Availability of data and materials: Data are available upon reasonable request. Access to the de-identified dataset for purposes of research other than this study, would be at the discretion of the Chief Investigator, Professor Toby Smith and OCTRU. Requests for the de-identified dataset generated during the current study should be made to the Chief Investigator, Professor Toby Smith (email: [toby.o.smith@warwick.ac.uk](mailto:toby.o.smith@warwick.ac.uk)) or OCTRU ([octrtrialshub@ndorms.ox.ac.uk](mailto:octrtrialshub@ndorms.ox.ac.uk)). Professor Toby Smith and OCTRU will consider requests once the main results from the study have been published up until 31 December 2026.

Authors' contributions: GF, TOS, BF, SD, SL, AO, CH SP, RPV researched the topic and devised the study. GF, TOS, SP, AO, BF, SD, CH, SL, RPV provided the first draft of the manuscript. GF, RPV, AO, SD provided statistical analysis and oversight. GF, TOS, SP, BF, AO, SD, CH, AG, SL, RPV contributed equally to manuscript preparation. TS acts a guarantor.

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## CRedit authorship contribution statement

**Gianluca Fabiano:** . **Toby O Smith:** . **Scott Parsons:** Investigation, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Alexander Ooms:** Conceptualization, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Susan Dutton:** Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. **Beth Fordham:** Formal analysis, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Caroline Hing:** Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Sarah Lamb:**

Conceptualization, Funding acquisition, Investigation, Methodology, Supervision, Writing – original draft, Writing – review & editing. **Rafael Pinedo-Villanueva**: Conceptualization, Formal analysis, Investigation, Methodology, Project administration, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.knee.2023.11.012>.

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