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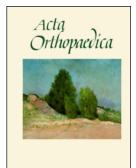
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Preoperative psychosocial risk factors for poor outcomes at 1 and 5 years after total knee replacement

A cohort study of 266 patients

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Background and purpose — Psychosocial factors are important risk factors for poor outcomes in the first year after total knee replacement (TKR), however their impact on long-term outcomes is unclear. We aimed to identify preoperative psychosocial risk factors for poor outcomes at 1 year and 5 years after TKR.

Patients and methods — 266 patients were recruited prior to TKR surgery. Knee pain and function were assessed preoperatively and at 1 and 5 years postoperative using the WOMAC Pain score, WOMAC Function score and American Knee Society Score (AKSS) Knee score. Preoperative depression, anxiety, catastrophizing, pain self-efficacy and social support were assessed. Statistical analyses involved multiple linear regression and mixed effect linear regression.

Results — Higher anxiety was a risk factor for worse pain at 1 year postoperative. No psychosocial factors were associated with any outcomes at 5 years postoperative. Analysis of change over time found that patients with higher pain self-efficacy had lower preoperative pain and experienced less improvement in pain up to 1 year postoperative. Higher pain self-efficacy was associated with less improvement in the AKSS up to 1 year postoperative but more improvement between 1 and 5 years postoperative.

Interpretation — Preoperative anxiety was found to influence pain at 1 year after TKR. However, none of the psychosocial variables were risk factors for a poor outcome at 5 years post-operative, suggesting that the negative effects of anxiety on outcome do not persist in the longer-term.

Total knee replacement (TKR) is an effective operation for many patients, however approximately 20% of patients experience chronic pain and functional limitations following their TKR (Beswick et al. 2012). These poor outcomes have a negative impact on patients' quality of life (Jeffery et al. 2011) and

investigations of the cause of continuing pain incurs significant healthcare costs (Kassam et al. 2012). To improve patient outcomes after TKR, research has evaluated whether there are preoperative risk factors for poor outcomes after TKR (Judge et al. 2012, Lewis et al. 2015, Alattas et al. 2016). If modifiable preoperative risk factors could be identified (e.g. BMI, anxiety, functional ability), this would allow patients to be targeted with individualized care to optimize these factors prior to surgery and potentially improve outcomes. If non-modifiable risk factors were identified (e.g. sex, age, ethnicity), patients could be informed of their increased risk of a poor outcome to make a decision about whether to proceed with surgery.

A variety of patient characteristics that are risk factors for a poor outcome have been identified, including more severe preoperative knee pain and functional limitations, pain elsewhere, medical co-morbidities, lower socioeconomic status, female sex and older age (Judge et al. 2012, Singh and Lewallen 2013, Lewis et al. 2015, Alattas et al. 2016). Psychosocial factors have also been found to be have an important influence on outcomes, explaining approximately 7–14% of the variation in postoperative pain and function (Lopez-Olivo et al. 2011). Psychosocial variables that have been identified in systematic reviews as risk factors for outcome after TKR include catastrophizing, self-efficacy (the conviction that one can successfully execute the behaviour required to produce the outcomes), depression, anxiety and poor coping skills (Vissers et al. 2012, Magklara et al. 2014, Burns et al. 2015, Khatib et al. 2015, Lewis et al. 2015, Alattas et al. 2016). Other psychosocial factors have also been found to influence outcome in cohort studies including social support, locus of control and perceived injustice (Lopez-Olivo et al. 2011, Yakobov et al. 2014).

To date, the majority of research in this field has investigated whether psychosocial factors influence outcome in the first 6–24 months after TKR (Lopez-Olivo et al. 2011, Vissers

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et al. 2012, Magklara et al. 2014, Burns et al. 2015, Khatib et al. 2015, Lewis et al. 2015, Alattas et al. 2016). There is a lack of research evaluating whether risk factors for short-term outcomes remain risk factors for outcome in the longer-term. Our aim was to identify preoperative psychosocial risk factors of poor patient-reported and clinician-assessed outcomes at 1 year and 5 years after TKR.

Patients and methods

Reporting follows recommendations of the STROBE initiative and a STROBE checklist was used.

Study design

The data presented are from an ongoing single-centre cohort study evaluating the 10-year outcomes of the Triathlon knee replacement (Stryker, Limerick, Ireland) (Wylde et al. in press).

Patient recruitment

Between October 2006 and October 2009, patients listed for a Triathlon knee replacement with a diagnosis of primary osteoarthritis were recruited from preoperative clinics at a regional elective orthopaedic centre. Patients listed for revision surgery or who were unable or unwilling to provide informed consent were excluded.

Outcomes

All outcome measures were collected preoperatively and at 1 and 5 years after surgery. At each time point participants completed questionnaires and were assessed by a physiotherapist. Pain and self-reported function was assessed using the Western Ontario McMasters University Osteoarthritis Index (WOMAC) (Bellamy et al. 1988). This questionnaire assesses the severity of knee pain when performing 5 activities and the degree of difficulty experienced when performing 17 everyday tasks. Separate WOMAC Pain and WOMAC Function scores were calculated, and transformed to range from 0 to 100 (worst to best). Clinician-assessed outcomes were evaluated using the American Knee Society score (AKSS) Knee Score (Insall et al. 1989). This involved a physiotherapist assessing alignment, range of motion, knee stability, and pain. The Knee Score was calculated, ranging from 0–100 (worst to best).

Preoperative psychosocial variables

Depression, anxiety, catastrophizing, pain self-efficacy and social support were assessed preoperatively using validated patient-reported outcome measures. Depression and anxiety were assessed using the Hospital Anxiety and Depression Scale (HADS) (Zigmond and Snaith 1983). The anxiety and depression subscales were calculated separately, with scores for each scale ranging from 0–21 (best to worst). Catastrophizing was evaluated using the catastrophizing scale of the abbreviated version of the Coping Strategies Questionnaire

(Rapp et al. 2000); scores range from 0–30 (best to worst). Self-efficacy was assessed with the Pain Self-efficacy Questionnaire (Nicholas 2007) which assesses confidence to perform general activities despite pain and produces a score from 0–60 (worst to best). Social support was evaluated with the MOS Social Support Survey (Sherbourne and Stewart 1991). This questionnaire assesses positive social interaction, affectionate support, tangible support and emotional/information support with the overall functional social support index score ranging from 0–100 (worst to best).

Confounders

There is some evidence to suggest that older age, female sex, medical co-morbidities and higher BMI may be associated with functional limitations and pain after joint replacement (Alattas et al. 2016, Buirs et al. 2016). Therefore, data on participants' age, sex and number of medical co-morbidities (Sangha et al. 2003) were collected in the preoperative questionnaire. Body mass index (BMI) was extracted from medical records prior to surgery.

Sample size

This study is a cohort study to evaluate long-term outcomes of the Triathlon knee replacement. No formal sample size calculation was performed, and the sample size was pragmatically determined by the number of patients that were recruited over the 3-year period.

Statistics

Separate analyses were carried out for each of the 3 outcomes considered. Changes in outcome measure scores from preoperative to 1 and 5 years postoperatively were tested using Wilcoxon signed-rank tests. Spearman's rank correlations were used initially to assess the association between preoperative variables and outcomes measured at each time point.

Multiple linear regression was used to assess the association between preoperative psychosocial variables and outcome measures at 1 and 5 years, adjusted for the preoperative outcome measure and confounders. Missing data was assumed to be missing at random. The regression analyses, assessing the association between the psychosocial variables and outcomes at different time points, were restricted to those with data on all psychosocial variables, confounders and the outcome of interest preoperatively and at the end time point of interest.

Mixed effect linear regression was used to analyse the association between covariates and repeated outcome measures, including random effects for both intercept and slopes. Change over time was modelled using linear splines with a knot at 1 year. Psychosocial variables were included as fixed effects. Fixed effects were also included to adjust for age, sex, BMI and number of comorbidities as potential confounders. To investigate if any of the psychosocial factors were associated with changes in outcomes after surgery, we tested for interactions between the spline terms and the psychological







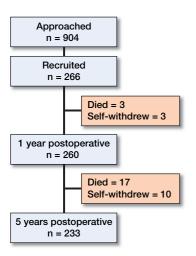


Figure 1. Participant numbers

Table 1. Baseline characteristics (n = 266)

	Median (IQR) or n (%)		Missing data (n)
Depression Anxiety Catastrophizing Pain Self-efficacy Social Support Age Female sex BMI Number of comorbidities Cruciate retaining prosthesis	5 6 8 37 89 70 169 30	(3-8) (3-9) (3-14) (26-46) (70-99) (62-77) (64%) (27-35) (1-3)	16 17 26 27 24 0 0 32
IQR: Interquartile ra	ange		

Table 2. Median scores (interquartile range) for preoperative, 1 year and 5 years postoperative outcome measures

	Median	(IQR)	p-value ^a
WOMAC Pain			
Preoperative	40	(30-55)	
1 year	90	(75-100)	< 0.001
5 years	90	(70-100)	< 0.001
WOMAC Function	า	,	
Preoperative	45	(34-54)	
1 year	81	(65-93)	< 0.001
5 years	84	(60-96)	< 0.001
AKSS Knee score	Э		
Preoperative	40	(31-49)	
1 year	82	(64–90)	< 0.001
5 years	91	(68–95)	<0.001

^a Comparison with preoperative outcome measure using Wilcoxon sign rank test

variables. Mixed effect regression allowed the inclusion of all individuals who had the outcome measured for at least 1 time point. We therefore included individuals with data on all psychosocial variables, confounders and the outcome measure of interest for at least 1 time point for the analyses looking at the association between psychosocial factors and the outcome measures and changes in the outcome after surgery.

Results are presented as effect size estimates (average change in outcome per unit increase in covariate) with 95% confidence intervals (CI) to indicate uncertainty. We have based our conclusions on these estimates with their CIs. We also present p-values for additional information. Statistical analyses were performed using Stata 14 (StataCorp LP, College Station, TX).

Ethics, funding and potential conflicts of interest

The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2000. Ethical approval was obtained from Southmead Local Research Ethics Committee (06/Q2002/80) and all participants provided informed written consent. This study was funded by Stryker UK. The funder had no involvement in the study design, data collection, data analysis, interpretation of data or writing of the manuscript. The authors have no conflicts of interest to declare.

Results

Participant characteristics

904 patients listed for a Triathlon knee replacement were approached about the study and 266 patients consented to participate (29% recruitment rate) (Figure 1, Table 1). Demographics of non-participants were similar to participants (64%)

female; median age of 72 years (interquartile range 64–79)). Median scores for the 3 outcome measures were 40–45 preoperatively, 81–90 at 1 year and 84–91 at 5 years postoperative (Table 2).

Associations between preoperative psychosocial factors and outcomes at 1 and 5 years

Associations between preoperative psychosocial variables and outcome measure scores at each assessment time are presented in Appendix 1, see Supplementary data. All psychosocial variables except social support correlated with preoperative WOMAC Pain, WOMAC function and AKSS Knee score. At 1 year postoperative, all psychosocial variables correlated with WOMAC Function except social support. The only psychosocial variable that correlated with WOMAC Pain at 1 year postoperative was anxiety. No psychosocial variables correlated with AKSS Knee score at 1 year postoperative. At 5 years postoperative, no psychosocial variables correlated with WOMAC Pain, WOMAC Function or AKSS Knee score with the exception of social support which correlated with WOMAC Function.

Associations between preoperative psychosocial factors and outcomes at 1 year and 5 years postoperative were investigated using linear regression models (Table 3). The unadjusted models are presented in Appendix 2 (see Supplementary data) and models only adjusted for preoperative outcome in Appendix 3, see Supplementary data. After adjustment for preoperative scores, higher preoperative anxiety was associated with worse pain at 1 year postoperative. No psychosocial factors were associated with any of the outcome measures at 5 years postoperative (Figure 2).

Associations between preoperative psychosocial factors and change in outcomes over time

Mixed effect linear regression models were used to evaluate







Table 3. Adjusted multiple linear regression for outcomes at 1 and 5 years

		1 year			5 years	
	Effect	[CI]	p-value	Effect	[CI]	p-value
WOMAC Pain		(n = 165)			(n = 138)	
Depression	0.54	[-0.72 to 1.80]	0.4	1.13	[-0.45 to 2.70]	0.1
Anxiety	-1.12	[-2.02 to -0.23]	0.01	-0.93	[-2.02 to 0.15]	0.09
Catastrophizing	-0.18	[-0.60 to 0.25]	0.4	0.04	[-0.50 to 0.57]	0.9
Pain Self-efficacy	0.01	[-0.26 to 0.27]	0.9	0.05	[-0.29 to 0.39]	8.0
Social Support	-0.07	[-0.20 to 0.05]	0.3	-0.01	[-0.17 to 0.15]	0.9
WOMAC Function		(n = 154)			(n = 122)	
Depression	0.06	[-1.20 to 1.31]	0.9	0.83	[-0.78 to 2.44]	0.3
Anxiety	-0.81	[-1.68 to 0.06]	0.07	-0.51	[-1.59 to 0.57]	0.4
Catastrophizing	-0.25	[-0.66 to 0.16]	0.2	-0.31	[-0.88 to 0.25]	0.2
Pain Self-efficacy	0.04	[-0.23 to 0.31]	0.8	0.05	[-0.29 to 0.39]	8.0
Social Support	-0.08	[-0.20 to 0.04]	0.2	0.05	[-0.10 to 0.21]	0.5
AKSS Knee Score		(n = 140)			(n = 130)	
Depression	-0.23	[-1.56 to 1.09]	0.7	0.18	[-1.13 to 1.49]	0.8
Anxiety	-0.16	[-1.14 to 0.83]	0.8	0.76	[-0.17 to 1.68]	0.1
Catastrophizing	-0.10	[-0.57 to 0.38]	0.7	-0.20	[-0.66 to 0.26]	0.4
Pain Self-efficacy	-0.22	[-0.51 to 0.06]	0.1	0.15	[-0.12 to 0.41]	0.3
Social Support	-0.05	[-0.19 to 0.09]	0.5	0.02	[-0.12 to 0.15]	0.8

Adjusted for preoperative measurement of outcome variable, age, sex, BMI and number of comorbidities

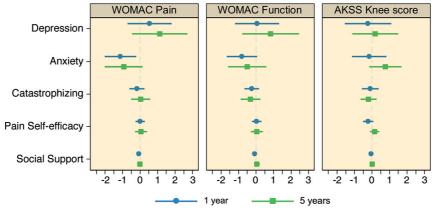


Figure 2. Forest plot of adjusted multiple linear regression results for outcomes at 1 and 5 years. Results shown as effect size estimates with 95% confidence intervals. Adjusted for preoperative outcome measure and confounders.

the association between psychosocial factors and the preoperative outcome measures and their effect on changes in these outcome measures after surgery. Results from univariable and multivariable unadjusted mixed effect linear regression models are presented in Appendix 4, see Supplementary data. Results from multivariable mixed effect linear regression models after adjustment for age, sex, BMI and number of comorbidities are presented in Table 4. Where evidence was found from likelihood ratio tests for the inclusion of effects on change over time these interaction effects have been included. Results from mixed effect linear regression models adjusted for confounders, but not including interaction terms are presented in Appendix 5, see Supplementary data. After adjustment, worse preoperative pain was associated with higher anxiety and

higher social support. Worse preoperative self-reported function was associated with lower pain self-efficacy. There were no associations between any of the preoperative psychosocial factors and the preoperative AKSS Knee score. Higher pain self-efficacy was associated with less improvement in pain up to 1 year postoperative; patients with higher self-efficacy had less preoperative pain and similar pain levels at 1 year postoperative compared to patients with lower self-efficacy (Figure 3). Pain self-efficacy did not influence the change in pain levels between 1 and 5 years postoperative. Higher preoperative pain self-efficacy was associated with less improvement in the AKSS Knee score up to 1 year postoperative but a greater improvement in the AKSS Knee score between 1 year and 5 years postoperative (Figure 4).







Table 4. Adjusted multivariable mixed effects regression models

	Effect	[CI]	o-value			
WOMAC Pain (n = 191), adjusted with interaction						
Depression	-0.21	[-1.03 to 0.61]	0.6			
Anxiety	-0.64	[-1.22 to -0.06]	0.03			
Catastrophizing	-0.10	[-0.38 to 0.18]	0.5			
Social Support	-0.09	[-0.17 to 0.00]	0.04			
Pain Self-efficacy	0.44	[0.25 to 0.63]	< 0.001			
Pain Self-efficacy & change						
in WOMAC Pain up to 1 year	-0.41	[-0.66 to -0.16]	0.001			
Pain Self-efficacy & change						
in WOMAC Pain after 1 year	0.01	[-0.05 to 0.06]	0.8			
WOMAC Function (n = 188), adjus	ted					
Depression	-0.28	[-1.12 to 0.56]	0.5			
Anxiety	-0.43	[-1.03 to 0.17]	0.2			
Catastrophizing	-0.10	[-0.39 to 0.19]	0.5			
Pain Self-efficacy	0.45	[0.27 to 0.62]	< 0.001			
Social Support	-0.05	[-0.14 to 0.04]	0.2			
AKSS Knee Score (n = 188), adjusted with interaction						
Depression	-0.22	[-0.95 to 0.51]	0.6			
Anxiety	-0.01	[-0.53 to 0.52]	0.9			
Catastrophizing	-0.14	[-0.40 to 0.11]	0.3			
Social Support	-0.01	[-0.081 to 0.07]	0.9			
Pain Self-efficacy	0.17	[-0.01 to 0.36]	0.06			
Pain Self-efficacy & change						
in WOMAC Pain up to 1 year	-0.40	[-0.65 to -0.14]	0.002			
Pain Self-efficacy & change						
in WOMAC Pain after 1 year	0.07	[0.01 to 0.13]	0.02			

Adjusted for age, sex, BMI and number of comorbidities

Discussion

This cohort study evaluated whether psychosocial factors were risk factors for poor outcomes at 1 and 5 years after TKR. At 1 year after surgery, higher preoperative anxiety was a risk factor for worse pain. No psychosocial factors were associated with WOMAC Function or AKSS Knee score at 1 year

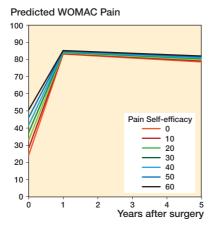


Figure 3. Predicted WOMAC Pain at each time point for varying levels of Pain Self-efficacy from mixed effect linear regression models, adjusted for confounders and with an interaction term for pain self-efficacy. All other covariates were assigned their median values. Higher WOMAC Pain scores indicate lower levels of pain.

after TKR. At 5 years after TKR, no psychosocial factors were found to be associated with any outcomes. Analysis of change in outcomes over time found that patients with higher pain self-efficacy had lower preoperative pain and experienced less improvement in pain up to 1 year postoperative. Higher pain self-efficacy was associated with less improvement in the AKSS Knee score up to 1 year postoperative but more improvement between 1 year and 5 years postoperative.

This study has a number of potential limitations which need to be acknowledged when interpreting the results. The study was designed as a cohort study to evaluate outcomes after the Triathlon knee replacement, and a sample size calculation was not performed; therefore the analysis may have been underpowered. The recruitment rate for the study was only 29%, likely reflecting the high participation burden involved in completing multiple questionnaires over a long follow-up period. However, demographics of participants are similar to those reported in the National Joint Registry of England, Wales and Northern Ireland (National Joint Registry for England 2016) suggesting the sample is representative of patients undergoing TKR. Although a number of psychosocial factors were assessed using validated questionnaires, other factors which could be potential risk factors were not assessed, for example perceived injustice (Yakobov et al. 2014) and locus of control (Lopez-Olivo et al. 2011). Also the focus of this study was on preoperative risk factors, although postoperative psychosocial factors may also have an important influence on outcomes (Magklara et al. 2014). Finally, a limitation of the cohort study design is the impact of sources of potential bias that we did not control for and this should be considered when interpreting the results.

There has been considerable interest in the influence of psychosocial factors on outcome after TKR, as demonstrated by the number of systematic reviews on this topic (Vissers et al.

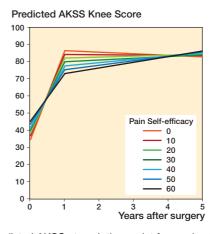


Figure 4. Predicted AKSS at each time point for varying levels of Pain Self-efficacy from mixed effect linear regression models, adjusted for confounders and with an interaction term for pain self-efficacy. All other covariates were assigned their median values. Higher AKSS Knee scores are better.







2012, Magklara et al. 2014, Burns et al. 2015, Khatib et al. 2015, Alattas et al. 2016). The majority of the literature to date has only evaluated the influence of these factors on outcomes in the first year after TKR (Vissers et al. 2012, Magklara et al. 2014, Burns et al. 2015, Khatib et al. 2015, Alattas et al. 2016). Although catastrophizing was not found to be a risk factor for outcome after TKR in this study, it has previously been found to be one of the strongest psychosocial risk factors for a poor outcome after TKR (Vissers et al. 2012, Burns et al. 2015, Lewis et al. 2015). The evidence in relation to anxiety is less clear, with some studies finding it to influence outcome (Alattas et al. 2016) but others not showing this (Lopez-Olivo et al. 2011, Lewis et al. 2015). Depression, social support and pain self-efficacy were not associated with outcome at 1 year after TKR in our study, which is similar to findings of systematic reviews (Vissers et al. 2012, Lewis et al. 2015). Our study suggests that anxiety is important in influencing outcome at 1 year after TKR. Therefore, patients may benefit from a targeted psychological intervention to reduce anxiety prior to surgery. Further research into the clinical and cost-effectiveness of interventions to reduce preoperative anxiety is needed.

Few studies have evaluated whether preoperative psychosocial factors are associated with longer-term outcomes after TKR, and those that have report different findings. Similar to our study, a cohort study found that anxiety was associated with outcome at 1 year but not 5 years after TKR, although they also found that depression was a risk factors for a lower AKKS at 5 years postoperative (Brander et al. 2007). Another study found that a clinical diagnosis of anxiety or depression prior to surgery was associated with an increased risk of moderate-severe pain at 5 years postoperative (Singh and Lewallen 2013). Similarly, preoperative mental health, assessed using the SF-12 Mental Health Component, has been found to be associated with pain and function at 5 and 10 years after TKR (Jiang et al. 2017). The varying findings between these studies is likely due to heterogeneity in the tools and methods used to assess the psychosocial variables and outcomes, which has been identified as an issue in previous systematic reviews (Magklara et al. 2014, Burns et al. 2015). Our study adds to the literature as it is the first study to include a comprehensive assessment of a number of psychosocial variables to evaluate if they are associated with patient-reported and clinician-assessed outcomes at 1 year and 5 years after TKR. Our findings suggest that although some psychosocial factors are associated with outcomes at 1 year, they are not risk factors for outcome at 5 years after TKR.

Analysis of changes in outcome scores over time revealed some interesting results. Although preoperative pain self-efficacy was not associated with outcome at 1 year or 5 years after TKR, it influenced recovery trajectories. Patients with higher pain self-efficacy had less pain preoperatively. However, this did not confer an advantage in outcomes at 1 year postoperative as these patients experienced less improvement in the first year postoperative. This may be partly due to a ceiling effect

of the WOMAC Pain score limiting the amount of improvement in pain that patients can report. Preoperative pain self-efficacy also influenced changes over time in the AKSS Knee Score. Higher self-efficacy was associated with less improvement in AKSS Knee score up to 1 year postoperative but more improvement between 1 year and 5 years postoperative. Reasons for this are unclear, but given the poor psychometric properties of the AKSS (Lingard et al. 2001, Lopez-Olivo et al. 2011), these findings should be interpreted with caution.

The prevalence of poor outcomes is lower after total hip replacement (THR) compared with TKR (Beswick et al. 2012), however it is important to also consider the influence of preoperative psychological factors on outcomes in patients undergoing THR. Preoperative use of antidepressants and mental health have been found to be associated with outcomes at 6 months to 5 years after THR (Quintana et al. 2009, Judge et al. 2013, Greene et al. 2016). A recent systematic review has highlighted the need for more research evaluating the association between preoperative psychological factors and long-term functional outcomes after THR (Buirs et al. 2016).

Findings from this study also have important methodological implications for future research. Preoperative psychosocial factors were found to have different influences on pain and self-reported function at 1 year after TKR. This is in agreement with previous literature which has found that risk factors for pain and functional limitations up to 1 year postoperative are different (Lopez-Olivo et al. 2011, Judge et al. 2012), highlighting the importance of analysing pain and function separately. This can be achieved with minimal burden to participants, as separate pain and function scores can be calculated from widely used questionnaire, such as the WOMAC and Oxford Knee Score.

In summary, we found that preoperative anxiety influences pain at 1 year after TKR, highlighting that some patients may benefit from targeted psychological interventions to reduce this risk factor and improve outcomes. However, none of the psychosocial variables assessed were associated with outcomes at 5 years postoperative, suggesting that the negative effects of anxiety on outcome does not persist in the longer-term.

Supplementary data

Appendices 1–5 are available in the online version of this article, http://dx.doi.org/ 10.1080/17453674.2017.1334180

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VW and AWB designed the study. VW was involved in data collection. LTL performed the statistical analysis and all authors were involved in the interpretation of data. VW drafted the article and AWB, MRW and LTL revised the article.

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