The Effects of Kinesiophobia on Outcome following Total Knee Replacement: A Systematic Review

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25 26 27 28 29 30 31 32	Statements regarding this article: Conflict of interest statement: The authors declare that they have no conflict of interest related to this article Funding: There is no funding source Ethical approval: This article does not contain any studies with human participants or animals performed by any of the authors

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Abstract

38 Introduction

Kinesiophobia, the fear of physical movement and activity related to injury vulnerability, has been
linked to sub-optimal outcomes following total knee replacement (TKR). This systematic review has
two aims: to define the relationship between kinesiophobia and functional outcomes, pain and
range of motion following TKR, and to evaluate published treatments for kinesiophobia following
TKR.

4546 Materials and Methods

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48 A primary search of electronic databases, grey literature, and trial registries was performed in March

- 49 2020. English-language studies recruiting adult primary TKR patients, using the Tampa Scale of
- 50 Kinesiophobia (TSK) were included. Outcome measures were grouped into short (<six months),
- 51 medium (six-12 months), and long term (>12 months). Study quality was assessed using the
- 52 Newcastle Ottawa Scale for cohort or case control studies, and the Cochrane Collaboration Risk of
- 53 Bias tool for randomised controlled trials.
- 54

55 Results

56

All thirteen included papers (82 identified) showed adequately low risk of methodological bias. TSK1 (activity avoidance) correlated with WOMAC functional score at 12 months in three studies (r=0.20

- 59 p<0.05, R=0.317 p=0.001, and correlation coefficient 0.197 p=0.005). TSK score significantly
- 60 correlated with mean active range of motion (ROM) at two weeks (65.98 (SD=14.51) vs 47.35
- 61 (SD=14.48) p=0.000), four weeks (88.20 (SD=15.11) vs 57.65 (SD=14.80) p=0.000), and six months
- 62 (105.33 (SD=12.34) vs 85.53 (SD=14.77) p=0.000) post-operation. Three post-operative interventions
- 63 improved TSK score vs control following TKR: a home-based functional exercise programme (TSK -
- 64 14.30 (SD=0.80) vs -2.10 (SD=0.80) p<0.001)), an outpatient Cognitive behavioural therapy (CBT)
- programme (TSK 27.76 (SD=4.56) vs 36.54 (SD=3.58), and video-based psychological treatment (TSK
 24 (SD=5) vs 29 (SD=5) p<0.01).
- 67

68 Conclusions

- 69 70 Kinosianhahis -
- Kinesiophobia negatively affects functional outcomes up until one year post-operatively, while active
 ROM is reduced up to six months post procedure. Post-operative functional and psychological
- 72 interventions can improve kinesiophobia following TKR.
- 73
- 74
- 75 **Keywords:** kinesiophobia; TKR; outcomes; treatments; systematic review
- 7677 Statements regarding this article:
- 78 Conflict of interest: The authors declare that they have no conflict of interest related to this article
- 79 Funding: There is no funding source
- 80 Ethical approval: This article does not contain any studies with human participants or animals
- 81 performed by any of the authors
- 82

83	
84	Introduction
85	
86 87	Total knee replacement (TKR) is performed to alleviate pain and improve function in patients with osteoarthritis (OA) [1]. Outcomes following TKR are influenced by surgical
88	technique, prosthesis design, and patient co-morbidities [2], although the importance of
89	psychological factors are recognised [2-4]. With the number of total knee replacements
90	(TKR) and set to double in the United Kingdom between 2010 and 2035 [5], rehabilitation
91	post-TKR is gaining importance on a population level.
92	Destruction of the life of the state of the foreign of the state of the destruction of the life of the state of
93	Post-operative renabilitation is crucial to improve function and reduce disability following
94 05	TKR [6]. Nearly 20% of patients report moderate to severe pain at one year post-operatively
95	with a detrimental effect on their post-operative recovery [8]. The 'fear avoidance' model
90 97	describes the relationship of behaviour, emotional, and cognitive factors in pain responses
98	Two responses to pain have been described: confrontation of pain. leading to reduction of
99	fear over time and resumption of normal activity; and the avoidance and exacerbation of
100	fear. Based on this, Kori, Miller and Todd developed the term 'kinesiophobia' which
101	describes an excessive, irrational, and debilitating fear of physical movement and activity
102	resulting from a feeling of vulnerability to painful injury or re-injury [9-10].
103	
104	Kinesiophobia has gained greater attention recently. It has been hypothesised that mal-
105	adaptive cognitive behaviours can create a vicious cycle of pain and disability [6].
106	Kinesiophobia can be seen as a normal physiological reaction in the early stages post-
107	surgery, but is associated with the transition from acute to chronic pain and reduced health-
100	lower back pain [16], kinesiophobia has subsequently been associated with poerer
110	functional outcomes in hip arthronlasty. ACL reconstruction and natellofemoral pain [17-
111	19].
112	
113	With mounting evidence that kinesiophobia results in poorer outcomes in a variety of
114	injuries and procedures, treatment strategies have gained attention. These have focussed
115	on both physiological and psychological rehabilitation. Functional exercises have been
116	shown to provide greater efficacy than isometric muscle exercises and range of motion
117	exercises [20], while an outpatient-based Pilates programme has proven successful in lower
118	back pain kinesiophobia [21]. Psychological treatments have focussed on strategies aimed at
119	decreasing fear of movement [18], including imagining the execution of a motor function
120	[22]. Although some strategies have been suggested, there are no specific systematic
121	reviews of these following TKR.
122	To data, no systematic reviews have investigated kinesianhohia following TKP specifically
123 124	With an expanding post-operative patient cohort, the ability to understand the role of
125	kinesiophobia and provide effective treatment to aid rehabilitation is gaining importance
126	The aim of this review is two-fold, to evaluate the existing evidence on the effect of
127	kinesiophobia on outcomes following TKR, and to evaluate published treatments for
128	kinesiophobia following TKR.
129	

130	Materials and Methods
131	
132	Search Strategy
133	A primary search of electronic databases (EMBASE, CINAHL, AMED, PubMed, PEDro and
134	PsychINFO) via the Healthcare Databases Advanced Search platform was performed from
135	inception until March 2020. Grey literature and trial registry searches were performed on
136	OpenGrey, ISRCTN Registry, PDQT Open and the International Clinical Trials Registry
137	Platform. The following PRISMA compliant search strategy was used for electronic
138	databases and grey literature: ["kinesiophobia" OR (fear adj2 avoidance) OR (fear adj2
139	move*) AND ("total knee arthroplasty" OR "total knee replacement" OR "TKR" OR "TKA")].
140	In addition to our primary search, reference lists of all suitable articles were screened for
141	additional papers.
142	
143	Inclusion/Exclusion Criteria
144	Inclusion criteria:
145	Studies recruiting patient having undergone primary TKR
146	 Kinesiophobia or fear of movement included as a measured variable or outcome
147	 Kinesiophobia measured using the Tampa Scale of Kinesiophobia (TSK)
148	 Patient cohort age ≥18 years
149	Exclusion criteria:
150	 Non-English language papers
151	
152	All full-tests that met the eligibility criteria were included in the final review. Study
153	identification was independently performed by one reviewer (LH) and verified by another
154	(CD) after reviewing titles and abstracts. The search strategy was run, titles and abstracts
155	were reviewed, and relevant full papers were extracted. A further round of relevancy of the
156	full papers was undertaken by three reviewers (OB, LH, CD).
15/	
158	Data Extraction
139	Two authors (OB, LH) independently extracted all key data from included studies onto a pre-
161	defined data extraction table. This was then verned by another author (CD). All data were
162	assessed for homogeneity and study type. Studies were grouped into those investigating the
162	kingsionhobia after TKP. A data extraction spreadsheet was synthesised to present all key
164	demographic information and results. Where data were not easily extracted or emitted
165	corresponding authors were contacted
166	corresponding authors were contacted.
167	Methodological Appraisal
168	Study quality was assessed using the Newcastle Ottowa Scale (NOS) for cohort or case-
169	control study as appropriate shown in <i>Table 1</i> and <i>Table 2</i> respectively
170	
171	All randomised controlled trials (RCTs) were assessed using the Cochrane Collaboration Risk
172	of Bias (RoB 2.0) tool where five categories (randomisation, blinding, completeness of
173	outcome data, selection of outcomes reported and other sources of bias) were assessed and
174	itemized in Table 3 . Each study was evaluated against the checklist/tool by two reviewers

- 175 (OB, LH) and verified by a third (CD). Any disagreements were resolved through a consensus.
- 176

177 <u>Comparisons</u>

178

179 Comparison 1: The effect of kinesiophobia on outcome following TKR

180

181 Outcome measures were split into short (less than six months), medium (six-12 months) and

182 Long term (greater than 12 months) time periods for grouped analysis. Primary outcome

183 measures consisted of: Functional outcome, measured using various patient-reported

184 outcome measures (PROMS) and clinical tests. The Western Ontario and McMaster

185 Universities Osteoarthritis Index (WOMAC) [23], Oxford Knee Score (OKS) [24], Knee Society

186 Score (KSS) [25], and Knee Injury and Osteoarthritis Outcome Score (KOOS-4) [26] were used

to assess functional outcomes. The secondary outcome measures were pain and range ofmotion (ROM). Pain was stratified using either a Visual Analogue Scale (VAS) or a numerical

- 189 rating scale. Range of motion was calculated actively or passively using a goniometer.
- 190

191 Comparison 2: Treatment of kinesiophobia following TKR

- 192
- 193 Outcome measures were split into short (<six months), medium (six-12 months) and Long

194 term (>12 months) time periods for grouped analysis. Various modalities to improve

- 195 kinesiophobia following TKR will be assessed. Our primary outcome was TSK score at six
- 196 months. The Tampa Scale for Kinesiophobia (TSK) was developed by Miller et al. [27]. TSK is
- 197 a self-completed 17-item questionnaire, designed to assess subjective rating of
- 198 kinesiophobia. Each item is provided with a four-point Likert scale, with the final score
- 199 ranging from 17 to 68, where a greater score indicates a higher degree of kinesiophobia
- 200 [27][28]. Studies investigating the role of kinesiophobia used values between 38 and 40 as
- 201 'cut-points' between high and low TSK scores. There were no secondary outcomes for this
- 202 comparison.

203204 Data Analysis

205 An assessment of study heterogeneity was made by visual assessment of the data extraction

- tables. Data was presented as mean \pm standard deviation (SD) where possible. Where the
- 207 data were heterogeneous, a narrative review of the evidence was presented.
- 208 209

210 211

Results

212 Search Results

213 The search strategy identified 82 papers and were all exported as titles and abstracts.

214 Screening based on abstracts, 35 papers were excluded. 47 full-text papers were retrieved,

and 13 papers were reviewed as shown in a PRISMA flowchart *Figure 1*.

216

217 Quality Assessment

218 All 13 papers described their cohorts' characteristics and eligibility criteria and

219 demonstrated adequate reporting of background and objectives. The reporting of

220 methodology was variable. All the cohort studies failed to report how potential sources of

bias would be addressed and how the study size was calculated (*Table 1*). One study by

Filardo et al [29] described potential bias due to using different prostheses in their cohort

but attributed their robust results to the large cohort. Eight studies failed to report

statistical methods used to examine missing data or loss to follow up and how participants

with missing data may have affected the results. Four studies specified the number of

patients at each stage of their study and whether there were any patients lost to follow up.

227 Only two papers specified that the investigators were not involved in the patient

questionnaire completion process. No studies reported on whether the investigator measuring flexion and extension was blinded to other patient factors. Most studies hav

229 measuring flexion and extension was blinded to other patient factors. Most studies have 230 demonstrated adequate reporting of their results and discussions. Two papers did not

- disclose any funding associated with their study.
- 232

233 Using NOS, all cohort studies and Unver et al.'s [30] case-control study were of 'good'

234 quality (*Table 2*). Four RCTs described their randomisation process. The results of the

235 Cochrane Risk of Bias tool is shown in *Table 3*. Degirmenci et al [31], Monticone et al [6] and

236 Cai et al [32] demonstrated low risk of bias, whereas Russo et al [33] failed to describe how

- their data were analysed, and whether if it was in accordance with pre-specified analysis
- 238 plans.239

240 Study Design and Demographics

241

A total of 1,191 patients were identified, ranging from 31 to 200 per study (*Table 4*). Russo

243 et al [33] did not specify the gender split and Body Mass Index (BMI) in their study but

244 stated that the two groups were homogenous in terms of pre-operative age, gender,

245 functional and psychological scores. Degirmenci et al [31] did not specify the mean BMI, but

- stated BMI over 40 in the exclusion criteria. Of 12 studies, 34.9% (380 of 1,089) were men.
- 247 Study follow up duration ranged from no follow up (ie time of discharge) to 36 months.
- 248

249 <u>Clinical Findings</u>

250

251 Thirteen studies were reviewed, four were RCTs eight were cohort studies and one case-

252 controlled study. Three studies assessed the change in TSK over time as their primary

253 outcome, six studies measured function as a primary outcome using validated scores such

- as WOMAC in four studies, KOOS in one study and OKS in one study. Four studies used
- 255 functional assessments such as two- or six-minute walk test (2-MWT/6-MWT), Going Up and
- 256 Down Scale (GUDS) and Timed Up and Go Test (TUGT) as their primary outcome. Other

- outcome measures include pain measured using a Numerical Rating Scale (NRS) or McGill
 Pain Score (MPS) in 13 studies and flexion or change in ROM in seven studies.
- 259
- 260

60 <u>Comparison 1: The role of kinesiophobia in outcomes following TKR</u>

261262 Primary outcomes:

Functional outcomes were assessed by ten studies (Doury-Panchout et al [34], Kocic et al [2], Sullivan et al [35], Sullivan et al [36], Filardo et al [37], Guney-Deniz et al [38], Filardo et al [29], Brown et al [39], Unver et al [30], and Degirmenci et al [31]). The results from these studies are shown in **Table 5**.

267

268 Functional outcomes at less than six months:

- 269 Six minute walk test (6-MWT) distance was measured by Doury-Panchout et al [34] on
- hospital discharge, with TSK cut-point at 40. The less than 40 group had a distance of 309
- 271 (SD 83.6), versus the 40 plus group with 264 (SD 96.5), p=0.048. Guney-Deniz et al [38]
- 272 measured the 2-MWT and TUGT at day two post-surgery, with a TSK cut-point at 39.5. TSK
- 273 <39.5 2-MWT were 36.77 (SD 6.04), versus 39.5 plus at 26.42 (SD 5.07), p<0.01, and TUG for
- TSK <39.5 were 51.91 (range 33.56-59.11) versus 51.99 (range 32.7-58.7) (non-significant).
- 275 Degirmenci et al [31] measured the 2-MWT and TUGT at days two and five post-surgery,
- with mean values of day two and five reported, using a TSK cut-point of 40. TSK <40 2-MWT were 36.15 (SD 4.16) versus 40 plus at 25.76 (SD 4.5), p<0.001. TUGT for <40 were 44.7 (SD
- were 36.15 (SD 4.16) versus 40 plus at 25.76 (SD 4.5), p<0.001. TUGT for <40 were 44.7 (SD
 5.6) versus 48.7 (SD 6.2), p=0.011. Sullivan et al [36] found TSK correlated with function
- (r=0.38) at six weeks post op (p<0.005) with Bonferroni corrected alpha set at 0.005.
- 280 Regression analysis showed that TSK predicts post-surgical WOMAC physical function score
- 281 (beta = 0.24, p=0.06).
- 282
- 283 Functional outcomes six-12 months:
- 284 Kocic et al [2] measured the OKS at six months, with a TSK cut-point at 38. The TSK <38
- 285 group had an OKS of 34.48 (SD 7.93) vs 25.82 (SD 6.90) for the 38 plus group.
- Filardo et al [29] found a correlation between TSK1 and Physical Health SF-12 subscale at six months, p = 0.001, R = -0.334, and a correlation between WOMAC at six months of followup (p = 0.005, R = 0.279). At six months, Unver et al [30] found a correlation between TSK
- 289 and GUDS r=0.468, p<0.001.
- 290
- 291 Functional outcomes at 12 months plus:
- TSK was split into its constituent parts, TSK1 (activity avoidance) and TSK 2 (harm) in three
- studies. Sullivan et al [35], Filardo et al [29], and Filardo et al [37] found a correlation of
- TSK1 to physical function measured by WOMAC score at 12 months (r=0.20 p<0.05, p = 0.001, B = 0.217, and p=0.005 correlation coefficient=0.107 respectively). This was also
- 0.001, R = 0.317, and p=0.005 correlation coefficient=0.197 respectively). This was also
 proven with multivariate analysis by Filardo et al [37] p=0.011, however no correlation was
- found at the final mean three-years follow up by Filardo 2015 [29].
- 298

299 Secondary outcomes:

- 300
- 301 Pain outcomes at less than six months (*Table 6*)
- 302 Guney-Deniz et al [38] had a TSK cut-point of 39.5, and measured pain at day two post-
- 303 surgery using a VAS. TSK <39.5 had a VAS of 2.3 (range 1.2-4.2) versus 3.2 (range 1.4-6.3)

for TSK 39.5, p=0.003. They correlated TSK with pain at day two post-surgery r = 0.80, p 305 <0.001. Degirmenci et al [31] had a TSK cut-point of 40, and measured pain levels Day 5 306 post-op using a VAS. TSK <40 had a VAS of 4.2 (SD 0.8) versus TSK 40 plus at 6.6 (SD 0.9), 307 p<0.001.

308

309Filardo et al [29] correlated TSK1 with day five post-operative pain via numerical rating scale310(p=0.031, R = 0.225).Pain on discharge day for Doury-Panchout et al's [34] TSK <40 cohort</td>311was 8.9 ± 10.5 mm, vs 11.3 ± 12.2 (non-significant). Kocic et al [2] used a numerical rating312scale, with TSK cut-point at 38. Pain at two weeks was 5.03 (SD 1.54) for <38 versus , 6.09</td>313(SD 1.33) for TSK 38 plus, p=0.0123. Pain at four weeks was 3.12 (SD 1.23) for <38 versus</td>3145.00 (SD 1.49) for 38+ (p=0.000). Sullivan et al [36] did not correlate TSK and pain post315operatively using the WOMAC pain score (r=0.31, p<0.005). This remained non-significant</td>

- 316 with regression analysis (beta = 0.07).
- 317
- 318 Pain outcomes six-12 months (*Table 6*)
- 319 Kocic et al [2] correlated TSK and pain via a numerical rating scale at six months with TSK
- 320 cut-point of 38. TSK <38 had pain ratings of 1.81 (SD 1.50), vs 3.24 (SD 1.98), p=0.0035.
- 321 Unver et al [30] found a correlation between pain and TSK at six months (r=0.236, p=0.004).
- 322
- 323 Pain outcomes 12 months plus: (*Table 6*)
- 324 Sullivan et al [35] did not correlate TSK and WOMAC pain scale at 12 months (r=0.23). TSK
- 325 did not correlate significant unique variance to the prediction of follow up pain severity
- 326 (beta = 0.10). Filardo et al [29] correlated TSK1 with 12-month post-operative pain via
 327 numerical rating scale (p=0.018, R= 0.234).
- 328
- 329 ROM outcomes less than six months (*Table 7*)
- 330 Guney-Deniz et al [38] measured active knee flexion on day two post-operative, with TSK
- 331 <39.5 having flexion of 71.67° (SD 8.35°) versus 65.95° (SD 6.73°), p=0.025. TSK was found to 332 correlate with range of motion at two days post-operative (r=-0.47, p<0.001).</p>
- 333 Doury-Panchout et al [34] compared TSK <40 to TSK 40 plus on discharge day, finding
- maximum passive flexion of 114.3° (SD 7.3°) in TSK <40 versus 11.34° (SD 9.4°) in 40 plus
- 335 (non-significant). Maximum active extension in <40 was -6.7° (SD 5.9°) vs -5.9° (SD 6.5°) for
- 336 40 plus (non-significant). Degirmenci et al [31] measured active knee flexion on day five
- post-operatively, with a TSK cut-point of 40. TSK <40 had flexion of 84.1° (SD 6.3°) versus
- 338 TSK 40 plus at 64.9° (SD 8.1°), p<0.001.
- 339
- Kocic et al [2] found those with TSK <38 had active knee flexion of 65.98° (SD 14.51°) at two
 weeks versus 47.35° (SD 14.48°) for 38+, p=0.000. At four weeks <38 active knee flexion was
 88.20° (SD 15.11°) versus 57.65° (SD 14.80°) in 38 plus, p=0.000.
- 343
- 344 ROM outcomes six-12 months (*Table 7*)
- 345 Kocic et al [2] measured active knee flexion at six months, finding TSK <38 at 105.33° (SD
- 346 12.34°) versus 85.53° (SD 14.77°), p=0.000. Kocic et al also found a strong negative
- 347 correlation between TSK score and flexion at all points assessed (p<0.001).
- 348
- 349 Comparison 2: Treatment of kinesiophobia following TKR
- 350

351 Primary outcome: TSK score

- 352 The effect of various interventions to improve kinesiophobia, measured by the TSK scale
- 353 was investigated by five studies: Monticone et al [6], Cai et al [32], Russo et al [33], Brown et
- 354 al [39], and Degirmenci et al [31]. Results for these can be seen in Table 8. Monticone et al
- 355 [6] compared a six-month period of home based functional exercises to standard
- 356 physiotherapy following TKR. Pre-TKR, there was no statistical difference between the two
- groups (TSK experimental group 34.14 (SD 7.54) versus control 34.40 (SD 5.51), p=0.842). 357
- 358 Significant differences existed between groups at six and 12 months post TKR however: six-359
- months experimental group TSK -14.30 (SD 0.80) versus control -2.10 (SD 0.80) (MD -12.2 (-
- 360 14.5 to -9.9)) p<0.001; 12 months experimental group -18.30 (SD 0.80) versus control -2.80
- 361 (SD 0.80) MD -15.4 (-17.7 to -13.2), p < 0.001.
- 362

363 Cai et al [32] conducted a RCT comparing inpatient physiotherapy plus an outpatient four 364 week Cognitive behavioural therapy (CBT) programme designed to treat kinesiophobia with

- 365 standard inpatient physiotherapy. There was no significant difference between the groups
- 366 at baseline (TSK 46.98 (SD 5.44) versus 47.72 (SD 6.17), p=0.526. At six months post TKR,
- 367 experimental group TSK was 27.76 (SD 4.56) versus 36.54 (SD 3.58) in the control group.
- 368 Analysis revealed a group effect (p<0.001) between CBT and non-CBT groups.
- 369

370 Video treatment to produce positive insight into kinesiophobia was investigated by Russo et

- 371 al [33], pre-operatively and at three months post TKR. Both groups showed a significant
- 372 (p<0.001) difference between baseline and follow-up TSK, and there was a significant 373 difference between video and no video groups at follow up (TSK 24 (SD 5) versus control 29
- 374 (SD 5) p<0.01).
- 375

376 Brown et al [39] investigated the effect of showing patients an intra-operative photograph 377 of their knee's maximal passive flexion as an incentive to improve ROM. Post-operatively, 378 the mean active knee flexion among the photo group was 99° (SD 17.4°) versus 106.1° (SD 379 14.4°) for the control group, p=0.1. Passive flexion in the photo group was 94.1° (SD 18.5°)

versus 100.9° (SD 15.5°), p=0.14. There were no secondary outcomes for this comparison.

380 381

382 Degirmenci et al [31] conducted a randomised controlled trial comparing regional

- 383 anaesthesia and deep sedation with regional anaesthesia and light sedation, measuring
- 384 kinesiophobia with TSK score at days two and five post-operatively. Deep sedation was
- 385 defined as Bispectral Index Score (BIS) of 60-70, while light sedation was defined as BIS up
- 386 to 80. Significant differences between the two groups were shown at both time points: day
- 387 two deep sedation TSK 40.5 (SD 6.1) versus light sedation 46.9 (SD 10.4) (p=0.005); day five
- 388 deep sedation TSK 37.7 (SD 5.7) versus light sedation 46.4 (SD 10.0) (p<0.001).
- 389 390

391	Discussion
392	
393	In this systematic review, we have found that kinesiophobia, measured by TSK score,
394	negatively influences functional outcomes following TKR. This was found to be true at all
395	three time points investigated. Functional outcomes measured included the Two- and Six-
396	Minute Walk Tests (2/6-MWT), the Oxford Knee Score (OKS), the WOMAC functional score,
397	and the Timed Up-and-Go (TUG test). Only the TUG test at day two post operatively,
398	measured by Guney-Deniz et al [38], was not significantly different between high-TSK and
399	low-TSK groups. Multivariate analysis conducted for functional outcomes and TSK score
400	agreed that a correlation existed. When TSK1 (activity avoidance) and TSK2 (harm) were
401	separated, it was TSK1 that correlated with WOMAC score at 12 months, but not at mean
402	three years follow-up.
403	
404	Sullivan et al [35], Sullivan et al [36], Filardo et al [37] and Filardo et al [29] found that
405	kinesiophobia can predict post-surgical function independently of other psychological and
406	physical variables. It was also demonstrated by Filardo et al that the effects of
407	kinesiophobia can be seen for up to one year [37], and although its impact decreases in
408	longer term follow up, higher TSK scores may still present with lower final outcomes [29].
409	
410	Studies differed widely on the correlation between pain and TSK score. While Doury-
411	Panchout et al [34] and Guney-Deniz et al [38] measured pain on day two and discharge
412	date respectively, finding no significant differences between high-TSK and low-TSK groups;
413	Degirmenci et al [31] found pain and TSK score correlated at day five post operatively. Kocic
414	et al [2] found high-TSK and low-TSK groups to be significantly different at two and four
415	weeks, and six months. This could be explained by a longer hospital stay demonstrated in
416	kinesiophobic patients, apart from the fact that Sullivan et al [36], Sullivan et al [35], and
41/	Unver et al [30] all found no correlation between TSK and pain score. Again, Filardo et al
410	[29] Touriu TSKI Significant on day five post operatively but not TSK2. As a result, it is not
419	based on our findings
420	based on our midnigs.
421 422	There were fewer data sets available for range of motion, but a mixed nicture was also
423	provided by our results. Kocic et al [2] demonstrated active knee flexion to be higher in low-
474	TSK groups at two and four weeks, and at six months with a strong negative correlation at
425	all points assessed. Guney-Deniz et al [38] Brown et al [39] and Degirmenci et al [31] also
426	found a correlation between TSK and active knee flexion. However, Doury-Panchout et al
427	[34] found no significant difference between high-TSK and low-TSK groups in max passive
428	flexion and max active extension on discharge day, and Filardo et al [29] found no
429	correlation between TSK1 and TSK2 in active or passive ROM. Measuring outcomes on
430	discharge day could result in significant length of stay related biases, however. Our evidence
431	suggests that there may be a negative relationship between active knee flexion and
432	kinesiophobia, but not all studies are in agreement.
433	
434	In our second comparison, increased levels of anaesthetic sedation were correlated with a
435	reduced TSK score at days two and five post-operatively by Degirmenci et al [31], as well as
436	superior performance in the 2-MWT and TUGT, and reduced pain. Intra-operative use of

- 437 anaesthesia may therefore influence the early post-operative fear avoidance behaviour.
- 438 Whether this continues to affect kinesiophobia more long-term is uncertain.
- 439
- Our second comparison indicated that three of the four post-operative interventions to
 treat kinesiophobia had a positive impact. Home based functional exercises, an outpatient
 CBT programme, and video treatment could be used separately or in combination
 depending on the individual patient's needs to improve quality of care for kinesiophobic
 patients. Brown et al [39] proved that showing a patient a photograph of their maximal
 passive knee flexion in theatre did not improve their active or passive ROM. Kinesiophobia is
 defined as an irrational fear, so it makes sense that trying to cure it based on appealing to
- 447 rational thought processes may not yield the intended results.
- 448
- The three successful interventions focussed on physiotherapy or psychotherapy, and acombination between the these two may yield the most successful result.
- 451
- 452 Using the TSK score has enabled an excellent means of stratifying kinesiophobia, and most
- 453 of our papers used it to separate patients into high and low-TSK groups. All included studies
- had a threshold within two points of each other, but the decision to choose cut-off points by
- individual studies was not completely explained. This raises the possibility that these
- decisions may have affected outcomes. Filardo et al [29] split the TSK score into its
- 457 component parts, activity avoidance and harm, enabling further analysis. This highlighted
- that TSK1 correlates better with pain and function, although this could not be compared tothe cohorts of other studies.
- 460
- 461 This systematic review presented with a number of limitations. For example heterogeneity 462 amongst studies in terms of outcome, whether reporting statistical significance between 463 two groups or an overall correlation following regression analysis, restricted our ability to 464 perform statistical comparisons. The statistical reporting of data also varied widely between 465 studies, with some using standard deviation and others quoting ranges. The discrepancy 466 between studies' TSK thresholds also acted to prevent direct comparison between studies 467 or meta-analysis, and is a metric that must be established for future research. 468
- 469 **Conclusion**
- 470

The role of kinesiophobia in outcomes post-TKR is inherently complicated, but our results indicate that functional outcomes are negatively influenced by its presence at time frames up to one year. Pain is correlated with kinesiophobia at six months. Active range of motion is negatively affected by kinesiophobia, but cannot be treated by simply showing patients that it is possible to achieve good ROM in theatre. Kinesiophobia can be improved through post-operative functional and psychological interventions such as long term physiotherapy, CBT, and video-based psychological therapy.

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484	Tables and Figures
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504	Table 1: Newcastle-Ottowa Quality Assessment form for Cohort Studies
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	Doury- Panchout et al., 2015	Kocic et al.,2015	Sullivan et al., 2011	Sullivan et al., 2009	Filardo et al., 2016	Güney- Deniz et al., 2017	Filardo et al., 2015	Brown et al., 2015
Selection								
(max 4)								
1	*	\star	*	\star	*	\star	\star	\star
2	*	\star				\star		\star
3	*	\star	*	\star	*	\star	\star	\star
4	*	*	*	*	*	*	*	*
Comparability (max 2)								
1 Outcome (max 3)	**	**	**	**	**	**	**	**
1	*	*	*	*	*	*	*	*
2		*	*	*	*		*	*
3	*	*	*	*	*	*	*	*
Total	8	9	8	8	8	8	8	9
Quality	Good	Good	Good	Good	Good	Good	Good	Good

⁵⁰⁶

Table 1. Selection Q2 (selection of non-exposed cohort). As all participants in these studies were subject to a
TKR, the exposure for the purposes of this review will be defined as a patient scoring highly on the TSK.
Selection Q4, the 'outcome of interest' is usually present at start of study (eg pain, range of movement) but
the primary outcome measures are changes in the outcome, therefore we have assumed the 'outcome of

511 interest' is not present at the start.

512

514	Table 2: Newcastle Ottowa Score for case-controlled studies

al., 2014 Selection (max 4) 1 ★ 2 ★ 3 4 ★ Comparability
Selection (max 4) 1 ★ 2 ★ 3 4 ★ Comparability
(max 4) 1 ★ 2 ★ 3 4 ★ Comparability
1 ★ 2 ★ 3 4 ★ Comparability
2 ★ 3 4 ★ Comparability
3 4 ★ Comparability
4 ★ Comparability
Comparability
(max 2)
1 \star
Exposure
(max 3)
1
2 🖈
3 🛧
Total 6
Quality Good

Table 3: RoB 2.0 tool

	Monticone et al., 2013	Cai et al., 2017	Russo et al., 2017	Degirmenci et al. 2020
Randomisation	L	L	L	L
Deviation from intended intervention	L	L	L	L
Missing outcome data	L	L	L	L
Measurement of outcome	L	L	L	L
Selection of reporting	L	L	SC	L
Overall	L	L	SC	L

Table 3. L = Low risk of bias, SC = some concerns, H = high risk of bias Attempts were made to contact authors for their study protocol to accurately assess their 'selection of reporting'. One author responded and stated

525 their protocol was not written in English and would be difficult to retrieve.

Table 4. Demographic data (SD reported in brackets)

							,						
Paper	Doury-	Kocic	Montic	Sullivan	Sullivan	Cai et	Filardo	Russo	Güney-	Filardo	Brown	Unver	Degir
	Panchout	et al.	one et	et al.	et al.	al.	et al.	et al.	Deniz	et al.	et al.	et al.	menci
	et al.		al.						et al.				et al.
Ν	89	78	110	120	75	100	200	102	46	101	79	36	60
Age	72.6 (8.9)	68.5	67.5	67.0	68.6	65.7	65.7	69.1	63.8	65.6	64.3	65.2	67.7
		(6.6)	(6.6)	(8.1)	(9.8)	(7.7)	(9.1)	(13.0)	(5.2)	(8.0)	(9.1)	(6.5)	(6.7)
BMI	29.6 (5.1)	30.9	28.2	30.8	29.9	26.6	28.2		22.7	28.5	32.1	28.4	<40 in
		(5.6)	(4.3)	(5.2)	(5.3)	(3.9)	(4.1)		(5.5)	(4.3)	(6.6)	(3.2)	all
Gender split (M:F)	37:52	19:59	40:70	47:73	29:46	38:62	66:134		15:31	31:70	39:40	0:36	19:41
Follow up (month s)	0.3	6	12	12	1.4	6	12	3	0 Assesse d on dischar ge day	Mean 38 (24-50)	6	6	0 (asses sed day 2 and 5 post op)

532 Table 5: Comparison one - TSK and functional outcome results, split into time frames

Author	Doury-Panchout	Kocic	Sullivan	Sullivan	Filardo	Guney-Deniz	Filardo	Brown	Unver
Year	2015	2015 2015 2011 2008 2016 2017					2015	2015	2014
Groups	TSK score high and low (cut- off = 40)	TSK score high and low (cut-off =38)	correlation with TSK presented	correlation with TSK presented	TSK split into subsets TSK 1 (activity avoidance) and TSK 2 (harm) and correlation measured	17 point Turkish version of TSK Cut-off 39.5 between high and low	TSK split into subsets TSK 1 (activity avoidance) and TSK 2 (harm) and correlation measured	correlation with TSK presented	patients with TKR and control group
subgroups	TSK <40 TSK >=40 P value	TSK <38 TSK >=38 P value			TSK 1 (activity (harm) avoidance)	low TSK (<39.5) (gp 2) mean TSK 46.01 +/- 10.25 7.13	TSK 1 (activity avoidance), TSK 2 (pain = body damage)		of TKR group, none
Functional outcomes <6 months	6MWT 6MWT distance 309 +/- 83.6 (p=0.048). (discharge day) (discharge day)			Post operation, TSK correlated with function (r=0.38, p<0.005). Regression analysis on TSK predicting physical function: beta = 0.24 p = 0.06		TUG 51.91 (33.56- 59.11), 2MWT 36.77 +/- 6.04 NS, 2MWT 26.42 +/- 5.07 (p<0.01)		distance walked (ft) correlation with TSK. Beta -0.46, SE 2.04, p=0.83	
Functional outcomes 6-12 months		oxford oxford knee knee score (6 score (6 months)months)p=0.0003 34.48 25.82 +/- 7.93 +/- 6.90 (SD) (SD)					TSK correlated with WOMAC score p=0.005, r=0.279 (6 months). Also Physical Health SF-12 subscale at 6 months p = -0.031, R = -0.334		TSK correlation to going up and down scale (GUDS) r=0.468, p<0.001. (at 6 months)
Functional outcomes >12 months			TSK correlated with WOMAC function scale (r=0.22, p<0.01). TSK did not correlate significant unique variance to the prediction of follow up physical function (beta = 0.06)		TSK 1 no correlated with 12- month WOMAC SC2 and score (p=0.005, p=0.197) score.		TSK1 correlated with WOMAC score at 12 months (p=0.001, r=0.317). patients' perceived function at 12m (p=0.025, R=-0.223). TSK1 correlated with SF-12 at 12m (p<0.001, R=-0.320. Physical Health SF-12 subscale at 12 months p = 0.005, R = -0.277		

TSK = Tampa scale of Kinesiophobia, 6MWT = 6-minute walk time, WOMAC score = Western
 Ontario and McMaster Universities Osteoarthritis Index,

Publication author	Do	oury-Panch	nout		Kocic		Sullivan	Sullivan	Filare	do	Guney-Deniz		Filardo	Brown	Unver
Publication year		2015			2015		2011	2008	201	2016 2017		2015	2015	2014	
Groups	TSK score high and low (cut- off = 40)		l low (cut-	TSK s	core high (cut-off =	and low 38)	correlation with TSK presented	correlation with TSK presented	TSK split into subsets TSK 1 (activity avoidance) and TSK 2 (harm) and correlation measured		17 point Turkish version of TSK. Cut-off 39.5 between high and low		TSK split into subsets TSK 1 (activity avoidance) and TSK 2 (harm) and correlation measured	correlation with TSK presented	patients with TKR and control group
timepoints measured	discharge day			2 w	eeks, 4 w month	eeks, 6 s	12 months	6 weeks	12 month TKF	ns post ?	day 2 post-o	р	5 days, and 1, 6, 12 months. Final follow up at average 3.2 years	post op day 1- 4, as well as outpatient follow up week 2,6,12,26	pre-op, discharge date, 2 weeks, 4 weeks, 6 months (most results reported at 6 months)
subgroups	TSK <40	TSK >=40		TSK <38	TSK >=38				TSK 1 (activity avoidance)	TSK 2 (harm)	low TSK high (<39.5) (gp 2) mean TSK (gp 1) mean TSK TSK 46.01 29.01 +/- 7.13		TSK 1 (activity avoidance), TSK 2 (pain = body damage)		of TKR group, none
Pain <6 months	pain intensity (mm) 8.9 +/- 10.5	pain intensity (mm) 11.3 +/- 12.2	non- significant	NRS 2 weeks 5.03 +/-, 1.54, 4 weeks 3.12 +/- 1.23	NRS 2 weeks 6.09 +/- 1.33, 4 weeks 5.00+/- 1.49	2 weeks p=0.0123, 4 weeks p=0.000					VAS/10 VAS/10 = 2.3 = 3.2 (1.2- (1.4- 4.2) 6.3) p (day 2 (day 2 post post op) op)	=0.003	TSK1 correlated with post op pain (NRS) 5 days p=0.031, R = 0.225)		
Pain 6-12 months				NRS 6 months 1.81 +/- 1.50	NRS 6 months 3.24 +/- 1.98	p=0.0035									pain correlation to TSK reported r=0.236, p=0.004)
Pain >12 months													TSK1 correlated with post op pain (NRS) 12 months (p=p=0.018, R= 0.234)		

544 Table 6: Comparison one - TSK and pain results, split into time frames

545 TSK = Tampa scale of Kinesiophobia, NRS = numerical rating scale, VAS = visual analogue 546 scale

Publication author	Doury-Panchout		out	Kocic		Sullivan	Sullivan	Filardo		Guney-Deniz			Filardo	Brown	Unver	
Publication year			2015		2011	2008	2016		2017			2015	2015	2014		
Groups	TSK score high and low (cut-off = 40) discharge day			TSK score high and low (cut-off =38) 2 weeks, 4 weeks, 6 months		correlation with TSK presented	correlation with TSK presented 6 weeks	TSK split into subsets TSK 1 (activity avoidance) and TSK 2 (harm) and correlation measured 12 months post TKR		17 point Turkish version of TSK. Cut-off 39.5 between high and low			TSK split into subsets TSK 1 (activity avoidance) and TSK 2 (harm) and correlation measured	correlation with TSK presented post op day 1- 4, as well as outpatient follow up week 2,6,12,26	patients with TKR and control group pre-op, discharge date, 2 weeks, 6 months (most results reported at 6 months)	
timepoints measured						12 months				day 2 post-op		5 days, and 1, 6, 12 months. Final follow up at average 3.2 years				
subgroups	TSK <40	TSK >=40		TSK <38	TSK >=38				TSK 1 (activity avoidance)	TSK 2) ^(harm)	low TSK (<39.5) mean TSK 46.01 +/- 10.25	high TSK (>39.5) mean TSK 29.01 +/- 7.13		TSK 1 (activity avoidance), TSK 2 (pain = body damage)		of TKR group, none
ROM <6 months	max passive flexion degrees 114.3 +/- 7.3. max active extension -6.7 +/- 5.9 (discharge day)	max passive flexion degrees 113.4 +/- 9.4. Max active extension -5.9 +/- 6.5 e(discharge day)	non- significant	active knee flexion: 2 weeks 65.98 +/- 14.51, 4 weeks 88.20 +/- 15.11	active knee flexion 2 weeks 47.35+/- 14.48, 4 weeks 57.65 +/- 14.80	p=0.000 2 weeks, p=0.000 4 weeks					active knee flexion ROM. 71.67 +/- 8.35	active knee flexion 65.95 +/- 6.73	p=0.025	no correlation between TSK1 or TSK2 and active or passive ROM	TSK correlation with active and passive knee flexion. Negative correlation 1 point increase in TSK associated with 0.47degree decrease in active knee flexion (B=- 0.47, SE 0.18, p<0.01) and 0.66 degree decrease in passive knee flexion (B=- 0.66, SE 0.18, p<0.01)	
ROM 6-12 months				active knee flexion 6 months 105.33 +/- 12.34	active knee flexion 6 months 85.53 +/- 14.77	p=0.000										
ROM >12 months																

547 Table 7: Comparison one – TSK and range of motion results, split into time frames

548 TSK = Tampa scale of Kinesiophobia

564Table 8: Comparison two results

Author	1	Monticone et al			Cai et al		Russo et al			
Year		2013			2017		2017			
Description	RCT compar exercises f physiother	ing home based or six months to apy (used Italia version of TSK)	d functional o standard n 13-point	RCT compariı C	ng CBT program BT programme	nme with no	comparison of video treatment with group without video treatment			
Groups	home based functional exercises	control	statistical significance	СВТ	non-CBT	statistical significance	video to produce positive insight	no video	statistical significance	
Timepoints measured	at dischar months programme	ge from rehab u after (t1 - when stopped), and post Dx (t2)	init (t0), 6 n rehab 12 months	day 1 or 2 po	ost-TKR, 4 week	s, 6 months	pre operatively, and 3 months after surgery			
baseline	31.14 +/- 7.54 (at discharge)	34.40 +/- 5.51 (at discharge)	p=0.842	46.98 +/- 5.44	47,72 +/- 6.17	p=0.526	36 +/- 8	38 +/- 6	p<0.01	
Less than 3 months				38.90 +/- 5.07 (4 weeks)	44.18 +/- 5.83 (4 weeks)					
3-11 months	baseline - 14.30 +/- 0.80 (6 months)	baseline -2.10 +/- 0.80 (6 months)	MD -12.2 (- 14.9 to - 9.9), p<0.001	27.76 +/- 4.56 (6 months)	36.54 +/- 3.58 (6 months)	F=33.867, p<0.001	24 +/- 5	29 +/- 5	p<0.01	
12 months plus	baseline - 18.30 +/- 0.80 (12 months)	baseline -2.80 +/- 0.80 (12 months)	MD -15.4 (- 17.7 to - 13.2) p<0.001							

565 RCT = Randomised controlled trial, TSK = Tampa scale of Kinesiophobia, MD = mean

566 difference, CBT = cognitive behavioural therapy



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